# IMPROVING CARE FOR GOUT IN THE SOUTHEAST ENHANCING GOUT MINORITY PATIENTS CARE AND PARTICIPATION IN GOUT CLINICAL RESEARCH (GOUT ED)

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VERSION 3;- JANUARY 17TH,2024

Summary of Changes from Previous Version:

| Affected Section(s) | Summary of Revisions Made | Rationale |
|---|---|---|
| B.2.2 | | |
| B.5.4 | | |
| B.5.1, B.9.1.3 & D,D.2, D.3 | Patient enrollment up to 48 hours within presentation to ED, including text messaging as a method of contact, and updated study site information to include MGH, MetroHealth, and University of Iowa. | To enroll patients that were missed in the ED when research staff is not available to enroll. Text messaging will be used to contact patients that could not be reached via phone call. |
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# Gout ED Protocol Version 10

## A. Significance

We propose to develop and test a health systems intervention aimed at improving identification of gout in the emergency department (ED) setting and improving evidence based treatment, health–related quality of life, and gout patients' experience with medical care. Our intervention also has the potential to reduce ED recidivism and enhance patient outcomes through the reduction of recurrent gout flares and future ED visits. In conjunction with the implementation science component, we will also enhance participation in research projects including the NIAMS-funded P50 INvestigationS In Gout, Hyperuricemia, and comorbidiTies (INSIGHT) Center of Research Translation (CORT) and leverage collaborative experience in the Southeast to enhance minority participation in ongoing and future gout clinical research. In keeping with the theme and leveraging the resources of our INSIGHT CORT, the UAB Minority Health and Health Disparities Research Center (MHDRC) (U54; National Institute of Minority Health and Health Disparities Center of Excellence) will work collaboratively to address and improve the quality of gout care for minority patients, particularly African-Americans, and enhance gout research participation for patients who receive medical care through the ED.

### A.1 Public Health Impact of Gout and Gout in Emergency Departments

Gout affects over 9 million Americans, [1-3] is the most common form of inflammatory arthritis in men, and is associated with poor quality of life.[4-6] The frequency of gout is increasing worldwide, with prevalence rates estimated to be as high as 7% in older men.[2, 7, 8] Gout leads to work absenteeism, loss of productivity, increased healthcare utilization, and premature death.[9-13] In addition, gout and hyperuricemia are strongly associated with comorbid conditions such as chronic kidney disease, hypertension, cardiovascular disease and metabolic syndrome; conditions endemic in the Southeast.[14] The US National ED Sample (NEDS) reports over 200,000 visits annually with gout as the primary diagnosis, accounting for 0.2% of ED visits and over $280 million in annual billable charges.[15] In addition, NEDS data demonstrate a marked increase in the number of ED visits in the US for gout, from 168K to 214K between 2006 and 2014, respectively, with more than 1.7 million people being seen in an ED for acute gout.[16] Gout patients are preferentially prescribed opioids in over 50% of ED encounters, potentially attributable to ED physicians de-prioritizing gout management for patients with more severe conditions.[17] Of note, Alabama and Tennessee are both in the top 10 states for opioid use.[18] The UAB EDs see a combined average of 1150 patients/year with gout. Older age, male sex, lower income, and being an African American were associated with increased ED gout visits and greater gout-related expenses.[19-21] With an aging population that is living longer with more serious chronic comorbid conditions, the societal burden posed by gout is growing exponentially and will substantially burgeon over the coming decades.[22, 23] Based on this epidemiology, the ED is a natural place to improve gout care. Most patients seen in an ED will be discharged home; many with inadequate follow-up. At the time of initial gout symptoms, patients have accumulated significant deposits of urate leading most to life-long intermittent if not chronic symptoms without treatment; gout is also quite frequently accompanied or preceded by other chronic diseases. [24-29] For those with comorbid chronic conditions, continuity of care is the cornerstone for improving patient outcomes and reducing healthcare-related costs.[30-32] Because gout is a chronic condition which develops in the presence of hyperuricemia, achieving low serum urate concentrations long-term is essential for improving outcomes with gout.[1, 33-36] However, an optimal strategy for gout care relies on a complete understanding of gout prevention, good continuity of care, patient empowerment to actively participate in their medical care, and adherence to treatments, which cannot be optimally achieved in the ED setting.

### A.2 Clinical informatics to Improve Healthcare

Over the last 20 years clinical decision support tools have been implemented through electronic medical record (EMR) systems as a means to improve care delivery and outcomes for a variety of conditions in busy clinical settings. [37-41] In this project, we will develop electronic alerts that operate in both Cerner (North Kansas City, MO) and Epic (Verona, WI) platforms, two of the most commonly used EMRs in the U.S. We will build EMR phenotypes that will trigger best practice alerts (BPAs) based on clinical and demographic data available in real time, and we will test the diagnostic accuracy of these phenotypes to identify ED patients with acute gout flares. When an acute gout flare alert is triggered, clinicians can then activate an evidence-based order set and an ED research assistant can be alerted to further evaluate each patient for possible participation in our interventional study and the Gout CORT Registry and Biorepository.

### A.3 Scientific Premise

The premise for this project is the known disparities in gout care, a higher prevalence of gout in the Southeast due to disproportionate endemic obesity and comorbidity burden, lack of gout knowledge/educational resources, and a perceived lack of access/adherence to primary and specialty gout care, which leads to

excessive care delivery in the ED. From prior work in osteoporosis management we have found that stories can influence readiness to behavior change and can act as very likely mediator of follow-up visits for care. [42, 43] Moreover, UAB has proven expertise both in using the ED as a setting for biomedical research and for conducting innovative research to enhance minority patient recruitment into clinical trials.[44-53] The premise for aim 3 of this study is that minority recruitment is low in most studies throughout the US and, under a collaborative NCATS grant aimed at overcoming some of these barriers, we have developed culturally tailored methods we will disseminate in this proposal. Importantly, the current CORT projects that focus on gout mechanisms, genetics, and precision medicine for improving gout outcomes will be enhanced by this proposal are dependent on sufficient phenotypic, genotypic and other patient data as well as having a diversity of participants to markedly improve their generalizability.

### A.4 **Storytelling as Method to Improve Chronic Disease Care**

Narrative communication, also known as "storytelling," is a basic mode of human interaction. Messages that include storytelling are viewed as more personal, realistic, believable, and memorable compared to didactic forms of communication.[54] Storytelling builds on the construct of homophily, whereby persons relate best to stories where they can relate to the narrator and can most easily be "transported" into the story being told. Video-based educational materials employing storytelling by patients, such as those proposed in our study, are engaging and influential in promoting behavioral interventions.[55, 56] Storytelling promotes patient engagement when the patient identifies with the storyteller and can lead to a patient's recognition of the need to treat the condition, improve health outcomes and more effectively confront a patient's barriers to medication adherence, as shown by a meaningful improvement in blood pressure, shown in a recent clinical trial in mostly African American men with hypertension.[55, 56] For example, storytelling promoted social support, decreased participants' sense of isolation, relieved stress, boosted self-confidence and motivated behavior change in African Americans with diabetes.[57] Storytelling in African Americans was better liked, enhanced recall, reduced counter-arguing, increased medical discussions with family members, and was perceived as more novel than an informational video.[56, 58] The potential success of our proposed project, combined with other published data, will represent a major step toward demonstrating the effectiveness of storytelling to improve adherence to care in chronic diseases and will address research priority areas, i.e., health care disparities and health care delivery.[59-63] For example, we developed a behavioral intervention using multimodal video-based narrative communication that increased the readiness for behavior change in women at high risk for future factures.[42, 43] Our team is actively using storytelling to improve medication adherence and outcomes among African Americans with gout in a project supported by a VA Merit Review Grant and led by our collaborator Jasvinder Singh, MD, MPH. We will adapt these already developed stories to make them relevant to this proposal, focused not only on initiation and adherence to gout medications, but to diet, exercise, weight loss and importantly, the need to have adherence on follow-up visits. Due to the intermittently symptomatic nature of gout, patients often don't understand the risk of long-term disease, severity and susceptibility to disease complications, and, therefore, may not balance the barriers and benefits to these important health behaviors.[64] Storytelling will be adapted from our many experiences and used in this project to overcome barriers to gout flare management and clinical research participation.

### A.5 **Minority Participation in Clinical Research and Use of the STRIDE/ REDCap Informed Consent Module to Improve Minority Participation in Clinical Research**

Despite healthcare disparities in gout and other leading chronic disease causes of morbidity and disability, racial and ethnic minorities are under-represented in important research studies that have potential to reduce these disparities. Currently, African American and Latinos represent fewer than 10% of patients enrolled in clinical trials, according to the National Institute on Minority Health and Health Disparities.[45-50] Minority participants often face particular barriers to enrollment in clinical research including skepticism based on distrust and negative connotations, miscommunication, and confusing procedures.[46, 65] Participant barriers include lack of trust stemming from historical abuses, as well as limited research literacy, defined as "the capacity to obtain, process and understand basic information needed to make informed decisions about research participation", each of which may work independently or in concert to preclude research participation.[15, 16]

Recent revisions to the Common Rule highlight the importance of transparency and simplification of informed consent documentation and description of research projects.[66] In an effort to address these issues and improve the engagement of minority population in clinical research, UAB, in collaboration with VUMC and the University of Massachusetts Medical School, have been working together through the National Center for Advancing

Translational Sciences (NCATS)-funded STRIDE initiative to define methods aimed at improving minority enrollment in clinical trials. A key to addressing this issue is personalization and tailoring of consent materials to meet the needs of diverse prospective participants including under-represented minority groups. The STRIDE intervention consists of integrated components, all supporting the information exchange during the informed consent process: i) REDCap software electronic consent (eConsent) platform, as a way to provide a customized enrollment experience in a literacy and culturally-sensitive manner, and ii) storytelling, as a way to enhance understanding and relevance of the informed consent and research studies in general. These components were carefully designed and piloted through an iterative collaborative process with community stakeholders and investigators, and they will all be available to the project proposed.

### A.6 Use of Patient Navigators to Improve Minority Health Care and Participation in Clinical Research

To help address barriers to optimal minority health care and participation in clinical research, Mona Fouad MD, Director, UAB Minority Health and Health Disparities Research Center (MHDRC) and Senior Associate Dean, Diversity and Inclusion, and her team have catalyzed the development of implementation strategies for the inclusion of underrepresented populations in clinical research. As part of this effort, we will leverage this team's successful strategies including the use of patient navigators (a trained, lay individual of similar age, cultural background, and region, who provides personal guidance to patients) in clinical research and health care, using the Community Health Advisors Model Strategy.[67] Work at UAB has shown that lay navigator assistance in oncology results in striking increases in patient referrals, a doubling in enrollment and significant increases in patient retention.[45-48] This model is based on the notion that individuals who are trusted and respected by community members are "natural helpers" and have interest in improving the health status of individuals in their communities. These advisors engage "hard to reach" populations, reduce barriers to health access and encourage healthy behaviors. Through the efforts of the MHDRC UAB U54 and Center for Clinical and Translational Sciences (CCTS) Partner Network, we have successfully implemented and disseminated patient navigation strategies to advance recruitment and retention of minorities in health care programs as well as clinical and translational research initiatives.[67-71] As part of the proposed project, patient navigators will provide continuity of care during transition from the UAB ED and facilitate access to post-gout flare healthcare services needed for preventing recurrent flares.

While there have been numerous ED-based referral focused initiatives implemented in the last 20 years to help redirect patients seeking care in the ED to more appropriate care that provides for continuing disease management in the areas of mental health/substance abuse, palliative care, cancer, and osteoporosis, to our knowledge, our study is the first proposing such an intervention for gout.[72-76] Other innovations are the multi-modal methods we will test to improve care using a point of care EMR alert, culturally tailored educational material including stories delivered on a tablet computer in the ED, lay-navigators, and tailored material to promote minority participation in research.

## B. Approach

### B.1 Overview of Study Design

The study will be conducted within 4 geographically diverse medical centers and will harness the existing collaborative efforts of multi-disciplinary investigative teams with expertise in gout clinical investigation, health services research, emergency medicine, minority health, and clinical informatics. We bring together expertise from two Southeast Clinical and Translational Science Awards (CTSAs) and expert consultation from colleagues at another CTSA (UMass), already collaborating with us on improving minority recruitment in clinical trials. We will first identify gout patients in EDs using complementary innovative clinical informatics methods. We will create simple, "light-touch," generalizable strategies in an integrated gout education program with previously proven successful components in other diseases, aimed to streamline evidence-based care for gout flares in the EDs and will test its effectiveness on adherence to follow-up care, satisfaction, health-related quality of life and appropriate therapeutic utilization. Our overarching goal is to improve patient experience with gout medical care, appropriate continuity in follow-up, health related quality of life, lower health service utilization, decrease opioid use, and enhance other standard gout outcomes (use of urate lowering therapy, weight reduction, and flare frequency) in our regional medically underserved population enriched for minority patients. Concurrently, we will improve the generalizability of findings resulting from our ongoing CORT projects by supporting engagement and enrollment of these patients into our Gout Registry and Biorepository though a novel culturally-sensitive informed eConsent process adapted from our existing collaborations.

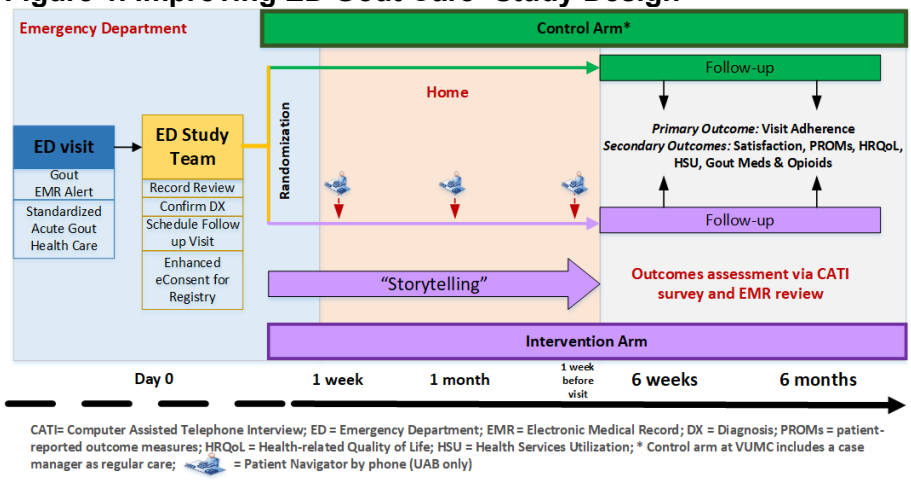
As part of our ongoing CORT we have developed methods of patient identification and recruitment for

participation in the CORT Gout Registry and Biorepository. These efforts have focused on UAB EMR searches utilizing i2b2 interface to identify gout patients not currently receiving medical care in UAB Rheumatology clinics (i.e. diagnosed through ED, primary care clinics) and have systematically approached them to offer participation in our Gout Registry and Biorepository. We oversampled for African American populations through screening phone calls and medical record review. A recent pilot of this recruitment workflow identified 3,032 African Americans patients seen in UAB clinics with an ICD 9/10 gout diagnosis between September 2017 and August 2018. We generated a random sample of 400 patients for initial contact. From this randomly selected sample of African Americans with gout who had been seen at least once at UAB, 15% expressed interest in a research visit and slightly over a 1/3 of those patients (6% overall) successfully enrolled in the CORT Gout Registry and Biorepository. Our strategy has had a 96% success rate in identifying patients from administrative data who later satisfied the 2015 American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) gout classification criteria that utilizes a easy to use scoring system (≥8 points indicates gout).[77, 78] These patients joined an existing, well-characterized Gout Registry and Biorepository bringing our total number of patients enrolled to 257 with samples collected from 154. These samples are being used in current CORT projects to investigate the metabolomics and genetics associated with gout, as well as to optimize lab methodologies (e.g. oxidative stress testing). This experience helped refine our recruitment strategies and through the incorporation of STRIDE to enhance participation, which we will deploy in this revision project, we are confident that we will be able to successfully engage minority patients with gout.

**Aims 1 and 2**

We propose an integrated and coordinated pathway from the ED to gout continuity of care through primary care and specialty providers. We will leverage innovative recruitment and retention strategies that utilize lay patient navigators at our UAB site, a strategy that was successfully pioneered at UAB by our MHDRC team led by Dr. Fouad for medical care and research in other disciplines including oncology.[48, 69-71] Patients classified as having gout based on the 2015 ACR/EULAR criteria[77, 78] who meet the inclusion/exclusion criteria (noted below) will be randomized 2:1 stratified by race/ethnicity, to the intervention or control arm of this demonstration study. **Figure 1** provides an overview of the study design.

**Figure 1. Improving ED Gout Care- Study Design**




CATI= Computer Assisted Telephone Interview; ED = Emergency Department; EMR = Electronic Medical Record; DX = Diagnosis; PROMs = patient-reported outcome measures; HRQoL = Health-related Quality of Life; HSU = Health Services Utilization; * Control arm at VUMC includes a case manager as regular care; = Patient Navigator by phone (UAB only)

## B.2 Patient Population

### *B.2.1 Key inclusion criteria*

- Meets Gaffo criteria for current gout flare or ED physician diagnosis of acute gout flare
- Adult > 18 years of age,
- Able to communicate and understand English language (a future objective, with additional resources, will include Spanish translation of all study materials).
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### *B.2.2 Key exclusion criteria:*

- joint complaint related to significant trauma or recent surgery (< 1 month)
- life expectancy of < 6 months,
- current critical illness leading to admission to high acuity medical care unit (ICU, stepdown unit) or requiring surgical intervention (general anesthesia); confirmed septic arthritis or joint infectious arthritis.

## B.3 Gout Alert Development and Validation (Aim 1)

Prior to the start of the study, clinical staff working in the UAB ED will participate in sessions where they will be trained and coached to appropriately use the novel gout alert for acute gout (flare) identification. Training will occur during monthly face-to-face meetings and via electronic communication (email, list-serves, social media and study website, short training videos). Since busy ED physicians and staff may fail to recall the details of the study or its purpose in real time, we will build electronic reminders (gout alerts) to notify staff to potential eligibility of patients during the ED visit. We will also generate monthly reports that document the number of patients with potential acute gout flares and compare to the number of patients approached by the on-call research coordinator located in each ED. De-identified reports will be shared with practicing clinicians to provide feedback on performance. UAB deploy over 200 different types of alerts, including drug interaction alerts from the Cerner and Epic systems, including both standard alerts and custom alerts that may be overridden by the clinician users. For this study, we will implement a custom alert than can be overridden at the point of care for the Epic and Cerner systems to identify emergency patients who may be having a gout flare. Administrative billing codes (ICD 10), medications (e.g. urate lowering therapy (ULT) such as allopurinol) and healthcare resource utilization of participants will be captured using structured data in conjunction with keywords in unstructured fields. Using this approach, we will identify patients with an existing gout diagnosis and those newly diagnosed during the index ED visit with gout when the alert is activated.

*B.3.1 NLP Algorithm*

The NLP algorithm to create the gout alert in the EMR will be structured and refined with serial pilot testing and chart validation (see B.3.2) initially in the Cerner environment at UAB. We will annotate a set of ED triage chief complaint notes and problem lists for the presence of gout flares and implement a simple algorithm for gout flare ED alerts. The keywords will be used to identify gout patients in the ED possibly experiencing a flare. Patients with a potential acute gout flare will be identified using structured data elements (e.g. prior ICD code for gout) and keywords such as: “gout,” “podagra,” “monoarthritis,” “toe pain” from all data fields in the EMR. These terms shown in Table 1 will be developed as part of the alert development and NLP algorithm. The alert algorithm will be developed iteratively using a gout enriched data cohort until acceptable performance is achieved. Keywords will be normalized using NLP to identify gout patients in the ED possibly experiencing a flare. The algorithm will work on simple Boolean logic and regular expressions and will identify a gout flare based on the presence of a gout keyword to the left of any of the PMH-GAZETEER words OR if there is both a location from the LOCATION-GAZETEER and the gout keyword in the past medical history.

Table 1. Example Description Terms and Gazeteer

| ***GOUT-GAZETEER*** **Case Insensitive** | ***LOCATION-GAZETEER*** **Case Insensitive** | | ***LOCATION-GAZETEER*** **Case Sensitive** | ***PMH-GAZETEER*** **Case Insensitive** |
|---|---|---|---|---|
| *Gout* | toe | knee | LLE | pmh |
| Pain | ankle | wrist | RLE | hx |
| Tender | foot | feet | LUE | pmxh |
| Swelling | thumb | finger | RUE | pmx |
| Swollen | arm | elbow | UE | |
| Stiff | shoulder | hip | LE | |

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The alert algorithm will be developed iteratively in the Cerner environment until acceptable performance achieved. Once acceptable performance is achieved the keywords used and any rules will be provided to other sites as they are identified and approved by the UAB IRB for deployment in the their EHR environments.

*B.3.2 Alert Chart Validation*

An alert development dataset will be created by identifying patients at UAB with an ED visit starting in January 2020 and working back until sample size is met. A random sample of 100 charts with an ICD10 code for gout and 50 charts with no ICD10 code for gout (but for whom the alert was triggered) will be identified and reviewed by two trained abstractionists. Data abstraction will look to confirm: 1) a prior history of gout and 2) a gout flare during the time of the ED visit diagnosis; or 3) other potential diagnosis. The review will include past clinic notes for documentation of a diagnosis and clinical features of gout (based on 2015 ACR/EULAR classification criteria for gout), medication lists for drugs used for treatment of gout, review of laboratory and

other diagnostic tests (serum urate and joint fluid urate results), imaging studies consistent with gout diagnosis and management (joint radiographs, ultrasound and CT/MRI) and detailed review of the ED visit to confirm acute gout flare at that time. The abstraction form will be piloted before implementation, and necessary changes will be made. Following abstraction of chart data elements and compilation of the 150 patient dataset by the physician trained research coordinators, two expert rheumatologists will complete a diagnosis confirmation review. In the event there is discordance a third rheumatology clinician will serve as an adjudicator.

### B.4 **Video Intervention Development**

In order to develop the video intervention, a group of patients who are currently successfully managing their gout will be interviewed and asked to tell their stories about the importance of gout care. The overall goal of the gout interviews is to improve patient gout knowledge and encourage actions that will prevent flares, destigmatize gout, and enhance readiness to adopt available long-term treatments including medications, diet, and exercise. Interviews will be conducted to cover a variety of race/ethnicities that might be seen in the ED with gout. Videos will be compiled from these patient interviews as anecdotes taken from these gout patients and presented to people in the ED who are being seen for a potential gout flare. These videos will seek to motivate participants to seek further gout care from their primary physician and the importance of taking ULT medications post-ED discharge.

Gout patients will be identified through UAB rheumatology/gout clinics and previous UAB led gout clinical trials, and invited to participate based on their previous successes in controlling their gout (lowering of uric acid, resolution of tophi, or reduction in frequency of gout flares). Willing participants will be sent the interview questions ahead of time to familiarize themselves with the interview prompts, and to allow for time so they think about their responses. Upon arrival, the participants will be given an overview of the filming process, incorporating a detailed walkthrough of the entire filming protocol including review of the question prompts. This will be done so the interviewees may get comfortable with interview format and filming procedures. The interviews will be conducted by a research staff member in a conversation-style format allowing the interviewer to expand and deviate from the interview guide to expand further on any topics expressed by the interviewee. Participants will be asked to repeat the question before answering each question, and will be allowed to rephrase or repeat any information presented if unclear. Upon completion, all participants will be debriefed and thanked for their participation.

#### *B.4.1 Identification of Video Themes and Content*

After completion of video recordings all videos will be reviewed by project investigators/staff and edited for relevant themes/content based on a group process completed by study rheumatologists. This group of rheumatologists will be asked to refine the overall message through a group process exercise. Each participant will be asked to generate a list of 5-10 messages that they think will motivate patients to 1) follow up for their gout once discharged from the ED and 2) take medications for gout. Once these lists are generated they will be compiled and sent out to each participating rheumatologist to be ranked from most to least important. This will be followed by a conference call to discuss why they voted in a particular way, and lastly, a second round of voting to determine the most useful ideas that will be communicated to the ED patients. We will then use the messages that are identified by these expert rheumatologists as the most important to relay to their gout patients as a roadmap to compiling the storytelling videos, and to identify any missing themes from or anecdotes in our videos that need further elaboration by patients.

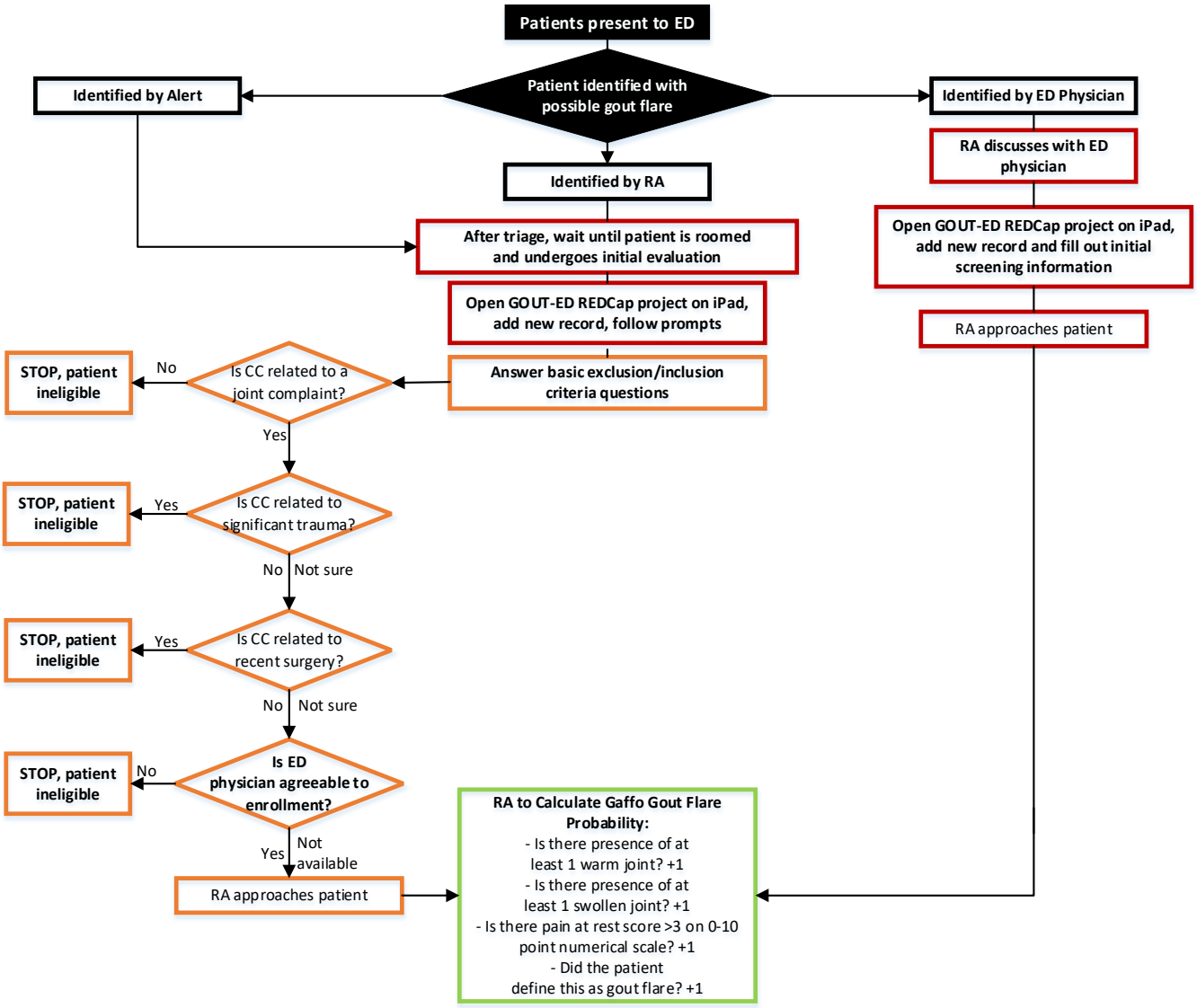
### B.5 **Pilot Study Procedures (Aim 2)**

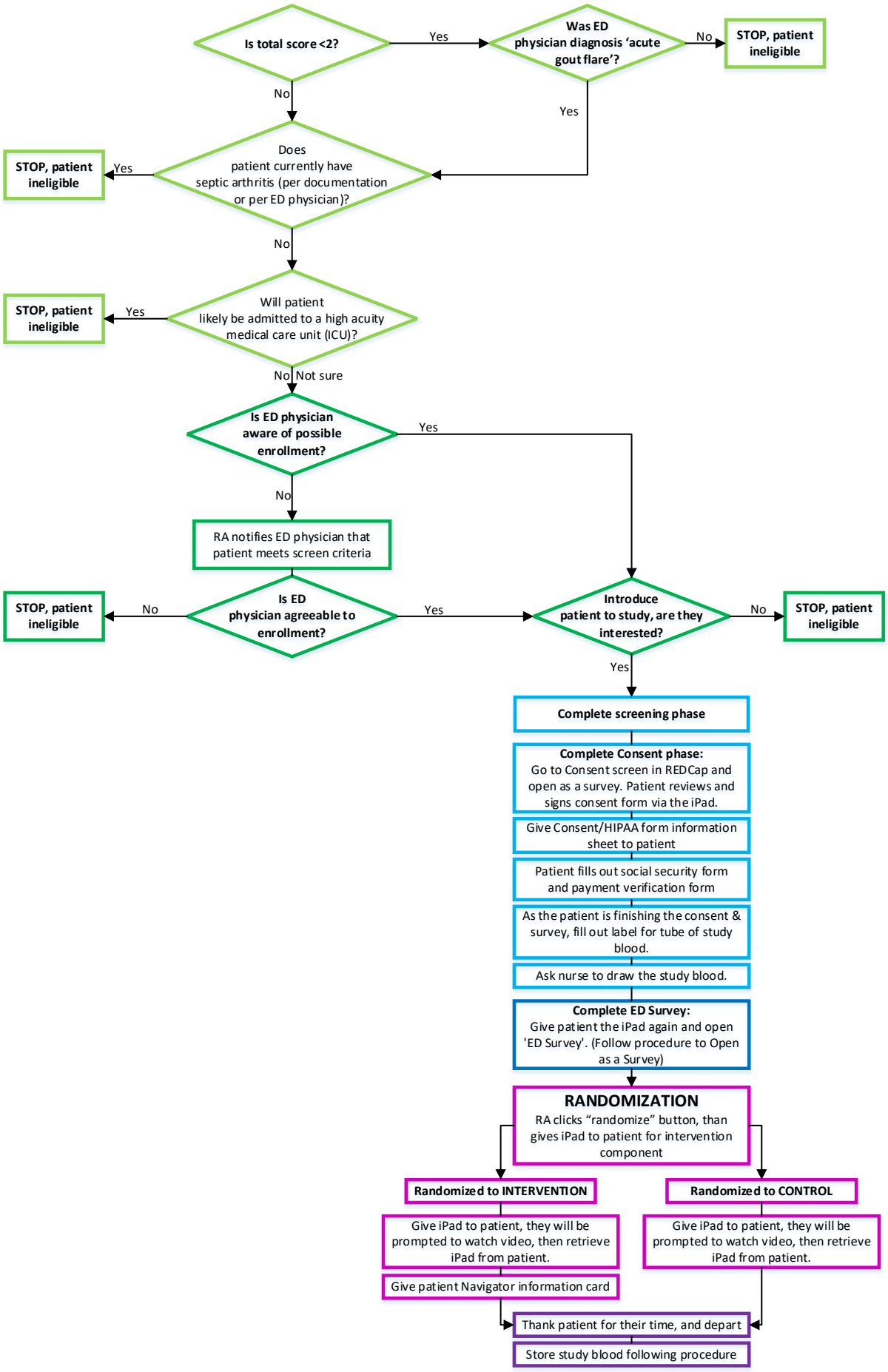
#### *B.5.1 Initial Gout Evaluation During Index ED visit and Confirming Eligibility*

Following the gout alert activation in the ED, research assistants housed in the UAB ED will interview patients in person to further determine possible eligibility, and if potentially eligible, to consider randomization. Randomization, if approved by the ED physician, will be conducted by the research assistant in the ED using a random number generated programmed on the tablet computer that will serve as the primary interface for the study. If the patient was not enrolled in the study at the index ED visit and the treating physician's diagnosis was acute gout flare; the patient may return to the ED for enrollment in the study no later than 48 hours after presentation to the ED. For the purposes of this study, this is considered part of the index ED visit if the patient

is enrolled within 48 hours of initial presentation to ED. This will also include patients admitted to observation status or in-patient status (excluding ICU and surgical admissions, see exclusion criteria above).

Workflow:




Is total score <2?
Yes
Was ED physician diagnosis 'acute gout flare'?
No
STOP, patient ineligible
No
Yes
Does patient currently have septic arthritis (per documentation or per ED physician)?
Yes
STOP, patient ineligible
No
Will patient likely be admitted to a high acuity medical care unit (ICU)?
Yes
STOP, patient ineligible
No
Not sure
Is ED physician aware of possible enrollment?
Yes
No
RA notifies ED physician that patient meets screen criteria
Is ED physician agreeable to enrollment?
No
STOP, patient ineligible
Yes
Introduce patient to study, are they interested?
No
STOP, patient ineligible
Yes
Complete screening phase
Complete Consent phase:
Go to Consent screen in REDCap and open as a survey. Patient reviews and signs consent form via the iPad.
Give Consent/HIPAA form information sheet to patient
Patient fills out social security form and payment verification form
As the patient is finishing the consent & survey, fill out label for tube of study blood.
Ask nurse to draw the study blood.
Complete ED Survey:
Give patient the iPad again and open 'ED Survey'. (Follow procedure to Open as a Survey)
RANDOMIZATION
RA clicks "randomize" button, than gives iPad to patient for intervention component
Randomized to INTERVENTION
Give iPad to patient, they will be prompted to watch video, then retrieve iPad from patient.
Give patient Navigator information card
Randomized to CONTROL
Give iPad to patient, they will be prompted to watch video, then retrieve iPad from patient.
Thank patient for their time, and depart
Store study blood following procedure

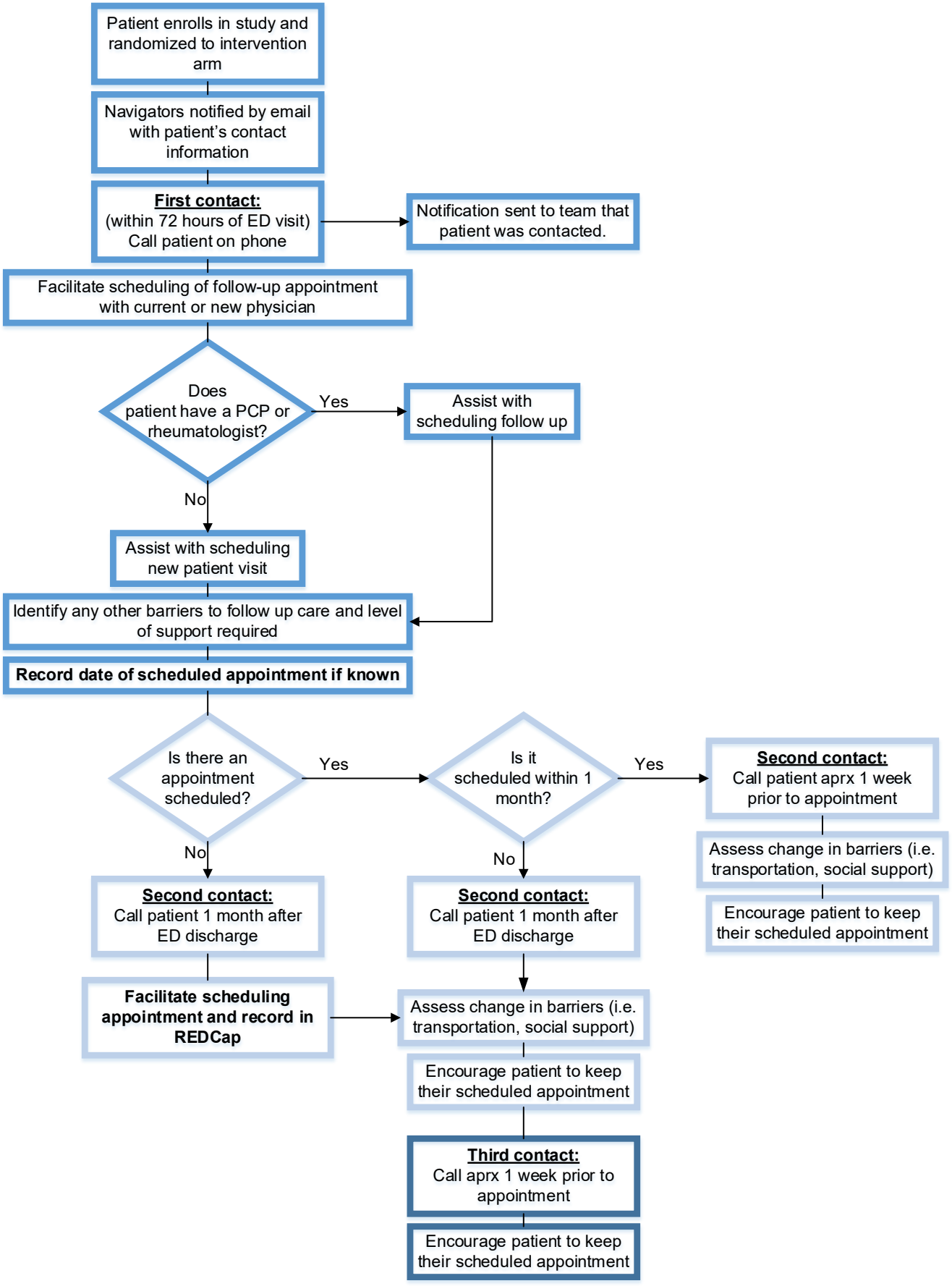
*B.5.2 Intervention Arm -ED Encounter*

During the index ED visit, patients will be offered video-based patient education employing storytelling aimed at promoting evidence-based gout management. These stories will be shown on a tablet computer used in the ED and also available to patients on the web. This health literacy-appropriate and culturally-sensitive educational “storytelling” intervention will aim to improve patient- knowledge of gout, readiness to adopt available treatments, understanding of potential therapeutic complications of therapies and lifestyle approaches to preventing future flares (e.g. weight loss, increased exercise, improved nutrition, and decreased alcohol use).[55, 56] The educational materials will include stories about the appropriate need to start and continue on urate lowering therapy (ULT), which is generally recommended by groups such as the ACR when gout flares occur more than 2 times per year; for flares occurring in the setting of gout comorbidities such as significant chronic kidney disease (grade 2 or greater) or urolithiasis; or if there is evidence of gouty tophi on examination or by imaging studies.[80] Stories will emphasize the key importance of seeking appropriate follow-up care for gout management; the primary outcome of this study. This intervention component will be provided on a tablet computer delivered by ED research assistants to the patient and/or their family, if present. Content of the videos will be adapted to include information on the link between flares and uncontrolled hyperuricemia and used to promote shared decision-making,[53, 81] self-efficacy for gout management,[55, 56] and to improve adherence to ULT, and reduce reliance on opioid analgesics.[42, 43]

The ED team will provide care referral to relevant medical services that might benefit their gout under their existing health plan, such as primary care services (if they do not already have a primary care physician) or to the Cahaba Medical Group (UAB Site) for those under insured or without insurance.

A lay patient navigator working with and trained by the UAB MHRC and the gout research team will contact patients seen in the UAB ED via phone within 72 hours following the ED visit. During this initial phone conversation the navigators will: 1) conduct a baseline assessment to identify barriers to attending an outpatient visit for gout care (e.g. transportation) and to adhering to gout treatment recommendations (medications, diet, exercise) and, 2) determine the level of support and assistance (e.g. transportation support) needed by patient. The patient navigator will help facilitate the follow-up visit with a primary care/gout specialist, identify any barriers (e.g. lack of trust in primary care physician or/and healthcare system),[82] and provide institutional/community resources that can be mobilized for the patient. The navigator will conduct two additional follow-up calls at approximately one month and at one week (anticipated) prior to the visit to confirm the appointment time, the level of support needed (as needs may have changed), and encourage him/her to keep their appointment. In the unlikely event that the appointment with the PCP/gout specialist is sooner than one month, this one-month pre-appointment call will be eliminated and the navigator will have only two calls with the patient **(Figure 2)**. Navigators will be trained using didactic materials, including case simulations and role-play, that will be prepared as part of this study. Participants at all sites will be provided a card with a group picture of the patient navigator team that will contact them.

**Figure 2. Study Workflow – Patient Navigation**




*B.5.3 Usual Care Arm -ED Encounter.*

Similar to the intervention arm patients randomized to the control arm at both institutions will be provided with a follow usual care referral to relevant medical services that might benefit their gout under their existing health plan, such as primary care services (if they do not already have a primary care physician) or to the Cahaba Medical Group at the UAB Site. Timing for this planned follow-up will be consistent with typical wait times to see a specialist or general practitioner for their gout. In most US metropolitan areas, given the limited national supply of rheumatologists, the average wait time is 9 to 10 weeks to see a new patient.[83] To address the issue of an "attention control," all persons randomized to the control arm will receive existing educational e-material on the tablet computer on routine preventive health measures including vaccinations and age-appropriate preventive care measures unrelated to gout or the study outcomes. These materials will also be emailed to them.

*B.5.4 Gout CORT Registry and Biorepository Sample Collection (Aim 3)*

Blood specimens and synovial fluid (if drawn) will be collected for the Gout CORT Registry and Biorepository at the time of the enrollment visit in the ED. Blood specimens and synovial fluid (if collected as part of ED visit) will be collected by ED study coordinators/RAs in PAXGene RNA/DNA tubes and stored in -80º freezer until transport to the UAB Division of Clinical Immunology and Rheumatology for processing and long-term storage (see Shipping Manual). All samples will be labeled with a patient identification (PID) number and date of visit. Documentation of specimens will be stored in the lab computer database, secured and password protected, and distributed to only to authorized personnel. Banked specimens will be available for future research in gout, hyperuricemia, and gout-comorbid conditions (e.g. hypertension, diabetes) and will include samples for genomic DNA, RNA expression, and epigenetic analysis.

## B.6 **Informed Consent (IC)**

Our e-Consent platform includes components designed through the STRIDE project to enhance the informed consent process in a health literacy and culturally sensitive manner, utilizing a simplistic layout with essential features of the consent process described at launch, socio-demographically diverse avatars (selected by patients) that walk through elements of the consent process, definitions for complex terms, and videos to demonstrate procedures. Storytellers share their experiences in research in a way that touches upon key elements, e.g. why research is important, societal gains from research participation and what to expect throughout study participation. The process of IC will be carried out by one of the study investigators in conjunction with the ED study coordinator/research assistants (RA) involved in the screening visit after the participant appears to meet the inclusion criteria above. ED RAs will invite patients in both study arms to enroll in the Gout Registry and Biorepository and will utilize enhanced informed consent material. During the initial ED visit, the RA will provide the study participant the electronic consent tool and launch the REDCap application. In keeping with the guidelines established by the revision of the Common Rule (Federal Register Volume 82, No. 12), the informed consent form (ICF) will begin with and include a summary with key information on the "5 factors" about the study that will be provided to facilitate the subjects' understanding of the proposed research and also ensure that they understand how their data and bio-specimens may be used. This includes a statement that 1) the project is research and participation is voluntary; 2) a summary of the research that will outline duration, purpose, and responsibilities of all parties involved; 3) potential risk or discomforts with participating; 4) potential benefits; and 5) alternatives to participation. In addition, the consent will outline the collection and the use of any private information and how specimens collected for laboratory analysis will be used. Patients will provide electronic informed consent before any study procedures are performed. In addition, we will utilize enhanced consent materials developed for STRIDE to enhance minority participation. To enhance participation in our gout registry we will modify the STRIDE REDCap-based e-Consent platform specifically for the GOUT registry and deploy culturally-sensitive stories with actual patients who have previously participated in registry-based research, which will describe the experience of participating in clinical registries.

Participants will be given as much time as they need to read and ask questions about the ICF. The individual or patient's legally authorized representative will be informed that he/she is not obligated to participate in the study and that it is strictly voluntary and that he/she may withdraw from the study at any time and that withdrawal of consent will not affect his/her subsequent medical treatment or relationship with the treating physician. The IC process will ensure that there is no penalty for not participating in a clinical trial and that treatment will not be compromised if individuals do not participate, or if they cease participation at any time.

By signing the electronic consent form, the participant authorizes the use of their personal health information (PHI), that they understand the study and its benefits and risks, and agree to all other aspects of the study outlined in the form. It allows the participant the opportunity to decide whether they want to participate in a study. During this process, individuals will be informed of all aspects of the study so that they can make an informed decision. Participants will then confirm their willingness to participate in the research study by signing the ICF. A signed version of the consent form will be kept by the study staff in REDCap database and emailed to the participant following consent.

The ICF contains the following:

- Disclosure of relevant information to prospective participants about the research
- The participant's comprehension of the information
- The participant's voluntary agreement to participate in a research study without coercion or undue influence
- Complete disclosure of any appropriate alternative procedures and their risks and benefits
- Disclosure of the extent of confidentiality that will be maintained
- Statement of compensation and/or medical treatment available if injury occurs
- Name, address, and telephone number of the PIs

If there is a change in any of the study procedures that may affect the participant, the ICF will be revised and approved by the Institutional Review Board (IRB). Any participants enrolled in the study prior to a change in procedures will sign the amended consent form. Signed consent forms will be kept as part of the study record for at least 7 years after completion of the study. Participants can withdraw their consent at any time by informing the study coordinator.

### B.7 **Data Management and Entry**

Patients and study coordinators will enter baseline demographic, gout history, patient reported outcomes (PROs) directly into electronic case report forms into a 21CFR and HIPAA compliant REDCap (Nashville, Tennessee) system. We will host REDCap on one of several access-controlled, encrypted servers housed at UAB. Subsequent PROs and other outcome data will be captured by phone in the same REDCap database by the study teams. Baseline laboratory data and medication data will be obtained from our respective EMRs and will be reviewed during the phone calls and by the research assistant during the ED visit.

### B.8 **Study Outcomes**

Study outcomes (**Table 2**) will be collected from patients at 6 weeks and 3 months following the initial ED visit with questionnaires deployed using computer assisted telephone interviews (CATI) programmed in REDCap. Validated items about gout flares and gout medications have been used in the past by our team.[84]

*B.8.1 Primary outcomes Aim 1 and 2.*

**Table 2. Specific Aim 2 Outcomes and Covariates**

| Primary Outcome | Time Point ED | WK 6 | Mo 3 |
|---|---|---|---|
| *Outpatient primary care or specialist visits targeted for gout** | | X | X |
| Secondary Outcomes / Covariates | | | |
| *Social Determinants of Health* | | | |
| Environmental and social factors | X | | |
| *Gout medical care* | | | |
| Number of gout flares (Gaffo criteria)[79, 84] | X | X | X |
| Rates of urate lowering therapy (ULT)** | X | X | X |
| ULT adherence | | X | X |
| Opioid prescriptions* | X | X | X |
| Weight reduction | | X | X |
| *Healthcare resource utilization* (visit number) | | | |
| ED visits (indicative of recidivism)* | | X | X |
| Hospitalizations* | | X | X |
| *Health-related quality of life* | | | |
| European Quality of Life (EQ-5D)[86-88] | X | X | X |
| *Shared decision making*: CollaboRATE scale [90] | | X | X |

* gout follow-up within 3-months of ED visit. ** Assessed through chart or system review

The primary outcome of aim 1 will be the ability of the alert to successfully identify gout patients. For aim 2, it will be the proportion of patients that have a follow-up visit addressing gout in the 3-month period after the ED visit. Many gout patients are not adherent with their follow-up visits due to a lack of awareness of the consequences of untreated gout, poor care access, and/or inadequate assistance to obtain a follow up visit. Even rapidly-scheduled outpatient visits (next business day) following an ED encounter are only attended by 73% of those seen in a recent study and rates of post-ED follow-up for many chronic disease are closer to 50%.[91, 92] Moreover, most patients, ~80%, leave the ED with knowledge deficits that impact adherence and outcomes.[93, 94] Having a usual source of primary care and establishing continuity of care after an ED visit is critical to optimal disease outcomes in all chronic diseases including gout.[30-32] This data will be captured both by self-report on surveys (this will be the primary study outcome) and by review of EMR data within our respective healthcare systems. While self-report will be impacted by recall and possible social desirability bias, this should be non-differential (bias towards the null).[95] EMR data will be more accurate for some outcomes but will miss any gout care delivered outside our urban Southeastern medical centers and their satellite facilities.

B.8.1.1 ***Secondary outcomes - Aim 2***

1) *Gout medical care*- Self-reported flare rates will be captured using the Gaffo gout flare criteria (developed and validated at UAB) and adapted to self-report.[79, 84] Uptake of evidence-based gout care will include self-reported prescribing rates of ULT and opioid analgesics. We also will determine medication adherence based on participant self-report. Since obesity is a major factor associated with gout and weight reduction will be addressed in the stories (as well as how to avoid foods high in purines), we will examine changes in self-reported weight between study entry and follow-up.

2) *Healthcare resource utilization*- outcomes will include repeat ED visits (ED recidivism) and re-hospitalization rates. Outpatient visits to primary care and/or rheumatologists will be measured as the primary outcomes.

3) *Health-related Quality of Life (HRQL), Shared Decision Making and Perception* – HRQL will be recorded using the European Quality of Life (EQ-5D) scale[86-88]. We will use the CollaboRATE scale, a brief patient survey focused on shared decision making, to measure perception of shared decision making from a patient perspective.[90]

B.8.1.2 ***Key Covariates Aim 2.*** To better describe the population we are studying and to adjust for any potential imbalances that might not be addressed by randomization, we will collect key social determinants of health as covariates at baseline and for dynamic measures, again at month 3. These will include:health literacy,[103] economic factors, transportation, discrimination and other key demographics such as educational level, community social economic status, and personal measure of socioeconomic status will be assessed using measures from the Behavioral Risk Factor Surveillance System.[108] We will also capture the time of "stories" watched as a measure of dose-response of the intervention.

## B.9 Study procedures and Assessments

B.9.1.1 ***Screening, Enrollment, and Randomization (see Step-By-Step Guide in Appendix)***

Following the gout alert activation in the ED, research assistants housed in the UAB ED will interview patients in person to further determine possible eligibility, and if potentially eligible, to consider randomization. Patients classified as having acute gout based on the Gaffo criteria who meet the inclusion/exclusion criteria will be

randomized 2:1 stratified by race/ethnicity, to the intervention (storytelling +/- patient navigation) or control arm (usual care). All intervention arm patients in the UAB ED also will be assigned lay navigators to provide personalized support for care transitions and access to post-gout flare medical services needed for preventing recurrent flares.

The following procedures will be completed during the index ED visit:

- Review inclusion/exclusion criteria for registry participation
- Informed Consent
- Review of current/past gout status and medication chart review
- Pain Assessment
- Laboratory
  - Serum uric acid (from chart review)
  - Sample banking
- Survey assessments
  - HRQL
  - SDOH

Laboratory draw will be done in conjunction with ED care blood draw when possible. At the conclusion of visit, participants randomized to navigator arm will be provided navigators picture, contact information, and informed that they will receive a call w/in 72 hours.

### B.9.1.2 *Patient Navigator Contact*

72 hours post ED visit

During this initial phone conversation the navigators will: 1) conduct a baseline assessment to identify barriers to attending an outpatient visit for gout care (e.g. transportation) and to adhering to gout treatment recommendations (medications, diet, exercise) and, 2) determine the level of support and assistance (e.g. transportation support) needed by patient. The patient navigator will help facilitate the follow-up visit with a primary care/gout specialist, identify any barriers (e.g. lack of trust in primary care physician or/and healthcare system), and provide institutional/community resources that can be mobilized for the patient.

4 weeks post ED visit and 24-48 hours prior to appointment (anticipated)

The navigator will conduct two additional follow-up calls at approximately one month (4 weeks) and in the week (anticipated) prior to their visit to confirm the appointment time, the level of support needed (as needs may have changed), and encourage him/her to keep their appointment. In the unlikely event that the appointment with the PCP/gout specialist is sooner than one month, this one-month pre-appointment call will be eliminated and the navigator will have only two calls with the patient.

### B.9.1.3 *6 Week Follow-up Assessment*

At 6 weeks following ED visit, participants will be contacted by the Coordinating Center (CC) to to assess project outcomes via a telephone survey. The following information will be collected, and data collected via the surveys and EMR. Following completion of the follow-up surveys the study coordinator will inform and debrief the patient that they participated in a study evaluating methods to improve continuity of gout care. The debrief will be conducted after the 1st survey. If RA the coordinator is unable to reach participant on the phone, the survey questions used to collect the primary outcomes will be sent via email or text messaging using Mosio, which is an HIPAA-compliant application.

- Survey assessments
  - Patient satisfaction
  - HRQL
  - PROs
- Updated medical history and review of concomitant medications
- Assessment of Adverse Events (AEs) (as meeting NIH definition of Phase III study AEs will be collected)

### B.9.1.4 *3 Month Follow-up Assessment*

At 3 months (anticipated) post ED visit participants will be contacted to complete a second follow-up survey and end of study (EOS) via telephone to assess secondary outcomes (e.g. adherence to orders, medication RX, and labs (if ordered)).

- Survey assessments
  - Patient satisfaction
  - HRQL
  - PROs
- Updated medical history and review of concomitant medications
- Assessment of Adverse Events (AEs) (as meeting NIH definition of Phase III study AEs will be collected)

B.9.1.5 ***Table 1 Visit Schedule***

| Visit description / Study procedures | Screening and Ernollment (ED) | **V1 (phone)** | **V2 (phone)** | V3 | V4 EOS |
|---|---|---|---|---|---|
| | Day 0 | **72 Hours** | **4 WK** | 6 WK° | 3 MO |
| Review of Inclusion/exclusion criteria following alert notification | **X** | | | | |
| Informed consent for INSIGHT Registry | **X** | | | | |
| Medical history | **X** | | | | |
| Laboratory | | | | | |
| SUA | **X** | | | | |
| Sample banking | **X** | | | | |
| Randomization | **X** | | | | |
| Patient Navigator Contact[#] | | **X** | **X**[$] | **X**[$] | |
| Updated medical history and concomitant medications | | **X** | **X** | **X** | **X** |
| Outcome ascertainment | **X** | | | **X** | **X** |
| Study debriefing | | | | **X** | |
| Assess AEs | | | **X** | **X** | **X** |

°Primary outcome assessment will occur at any point upto 6 weeks post ED visit dependent on routine care visit; # For individuals randomized to navigation arm; [$]Navigator will contact participant in the week prior to scheduled follow-up visit

B.9.1.6 ***Blinding and Unblinding***

Participants will blinded to study assignment at enrollment, and following primary outcome ascertainment will be debriefed regarding the study and its purpose/goals.

B.10 **Statistical Analysis Plan**

*B.10.1 Primary Outcome Analysis - Aim 1.*

All analyses will adhere to the principles of rigor, reproducibility and transparency.[109, 110] To determine the effectiveness of our alert system, we will examine the diagnostic properties (sensitivity/specificity) of the EMR alerts against a gold standard of NLP/ML detection (section C.4.2)

*B.10.2 Primary Outcome Analysis- Aim 2.*

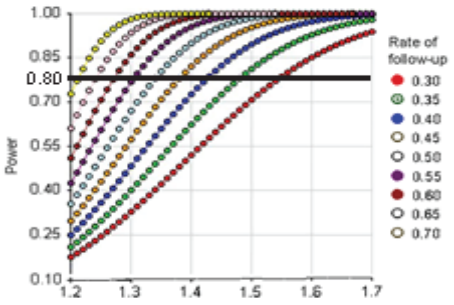
Descriptive statistics, including measures of central tendency (means for continuous, proportions for categorical) and dispersion (variance, interquartile range) will summarize the distribution of baseline characteristics of randomized patients seen in both EDs. Descriptive statistics will be summarized by treatment arm as well as enrollment site. These statistics will inform the successfulness of randomization in creating comparable groups and ascertain our success in recruiting the populations we seek to target (particularly under-represented minorities). We also will compare the descriptive characteristics between those participants who do and don't respond to follow-up surveys to detect and report any evidence of a selective non-response bias. The primary analysis approach for testing treatment effect will be a multivariable logistic regression

model. We have chosen multivariable logistic regression over Cochran-Mantel-Haenszel approaches to allow for effect estimation of multiple covariates (race, gender, age) upon the primary outcome and to allow tests of interactions. Logistic regression models, including interaction terms, will be developed for 6 week outcomes and 3 month outcomes. We will examine the significance of the effects of the intervention as the outcome of persons receiving at least one outpatient gout follow-up visit at 3 months. We will analyze rates on an intent-to-treat basis for the primary analysis. We will conduct all analyses using SAS 9.4 (Cary, NC)

*B.10.3 Secondary Outcome Analyses- Aim 2.*

Patient reported outcomes (PROs) and other process of care measures are of key interest in this study. We will examine secondary outcomes using either two-sample t-tests or multiple linear regression models. Distributional assumptions for residuals (normality, homogeneity of variance) will be examined using normal probability plots and residual plots. We will conduct a set of stratified analyses (contrasts) to examine how the between-site differences in approaches affect outcomes. First, comparing across control arms at the four sites we can estimate the impact of the intervention. Second, comparing across intervention arms at the foursites, we can estimate the difference attributable to case manager versus navigators when all individuals receive story telling. We will also examine sex as a biological variable as well as effects of age and race/ethnicity (heterogeneity of treatment effect). We will conduct sensitivity analyses using multiple imputations to account for missing data. While we provide an example sample size for one such measure, the evaluation of these endpoints will be hypothesis-generating only.

Figure 4. Power for Study Aim 2




B.11 **Sample Size Considerations for Aim 2**

The funding announcement we are responding to seeks to improve care and reduce healthcare disparities for chronic disease in the Southeast. Thus, our approach to this study is to maximize the number of patients we can evaluate and improve gout care outcomes. We based our sample size considerations on experience from prior ED interventions, a pilot study conducted at UAB (section C.3.5) aimed at recruiting minority patients for our CORT Registry and Biorepository, based on a prior diagnosis of gout in the UAB EMR, and experience recruiting clinic patients. Annually in the ED, UAB see approximately 720 and 450, gout patients (with primary or secondary diagnoses), respectively. We anticipate identifying approximately 60% of these patients using the alert in real-time (n = 702). We also estimate that 80% of the ED physicians will respond to the ED alert and activate the gout order set and referral to the study coordinator (this rate may be improved with approaches discussed in section C.4.4) (n =560). Based on the results of our UAB pilot study (that contacted patients without a known recent flare/acute gout), we anticipate that 50% of these patients will remain eligible (based on medical record review and questionnaire). Thus, we conservatively estimate randomizing a combined total of approximately 280 gout patients annually between UAB . Despite plans to offer compensation for survey completion, we anticipate a 30% rate of survey non-response for the primary outcome at 3 months (n = 196, in the per protocol analysis), which we believe will be slightly disproportionate between those receiving the intervention vs. control arm. Based on a sample size of 200 patients and assuming 2:1 randomization in favor of story-telling, the study will have 80% power to detect relative risks of 1.68 or below using a two-tailed Type I error rate of 0.05, assuming the proportion in the control arm scheduling an outpatient primary care or specialist visits targeted for gout within 3 months is above 30% (**Figure 4**). We picked these rates of visit follow-up visits to represent the range of rates of ED follow-up within 3 months for other conditions such asthma, stroke, and diabetes. [111-115]

## C. <u>Adverse Events</u>

As this study meets the NIH definition of a clinical trial, and as outlined in our data safety monitor plan we will collect information including diagnosis errors and participant anxiety from answering questions about their health status. All AEs will be captured on the appropriate electronic case report form.

An **Adverse Event (AE)** is defined as any untoward medical occurrence in a participant who received study intervention regardless of its relationship to the study intervention. This determination will be made by the study

principal investigator. Preexisting conditions will not be considered adverse events; however, worsening of a preexisting condition may be considered an AE. AEs will be assessed as to their relationship to the research, severity, and duration. They will be documented appropriately, regardless of the relationship, with start dates occurring any time after informed consent until 7 days after the last day of study participation. AEs will be reported in aggregate to the Safety Officer (SO), Institutional Review Board (IRB) and NIAMS (through the Executive Secretary) as part of the routine safety report.

A **Serious Adverse Events (SAE)** is any AE that results in death, is life-threatening, results in or prolongs hospitalization, or causes a permanent, persistent or significant disability. SAEs will be reported to the SO, IRB, and NIAMS (Executive Secretary) within 48 hours of the investigator becoming aware of the event. All SAEs will be followed until satisfactory resolution or until the site investigator deems the event to be chronic or the participant is stable.

An **Unanticipated Problem (UP)** includes any incident, experience, or outcome that is unexpected and possibly related to participation in the research. UPs will be reported to the SO, IRB and NIAMS (Executive Secretary) within 48 hours of the investigator becoming aware of the event.

A **protocol deviation** is defined as any substantial divergence from the IRB-approved study protocol. Any protocol deviation impacting patient safety will be reported to the SO, IRB and NIAMS (Executive Secretary) within 48 hours of the investigator becoming aware of the event; all other deviations will be reported as a part of the routine safety report.

For additional details see Data Safety Monitoring Plan.

## D. Study Sites

Investigational study sites are the University of Alabama at Birmingham and Vanderbilty University Medical center, two large academic medical centers. The study site staff will ensure participants are consented and randomized in accordance with established good clinical research practices. Additionally, site investigators and their staff will be required to have prerequisite human subjects training, and will answer study related questions, as needed.

- University of Alabama at Birmingham (UAB), Birmingham, AL, United States
- Massachusetts General Hospital (MGH), Boston, MA, United States
- MetroHealth Meidcal Center, Cleaveland, OH, United States
- University of Iowa, Iowa City, IA, United States

Approximately n= 168 participants will be enrolled at the UAB site and n = 112 from MGH, MetroHealth, and University of Iowa study sites.

### D.1 Participant Recruitment and Consent

The site study staff will:

- Provide participants with adequate information concerning the study procedures, and scope
- Provide adequate opportunity for the participant to consider all available options
- Respond to the participant's questions and concerns
- Ensure that each participant understands all information provided
- Obtain the participant's written voluntary consent to participate
- Sign the consent form as witnesses
- Provide participants with a copy of the consent form

### D.2 Participant Retention/Discontinuation

Participants will have the option to withdraw from the study at any time. Study staff will make at least 3 attempts to contact participants for study intervention visits (ie, Patient Navigation at UAB, MGH, MetroHealth,

and University of Iowa) and outcomes assessment surveys at 6 weeks and 3 months. In order to minimize the chances of losing touch with patients, study staff are collecting email addresses and secondary contact names and phone numbers at the original emergency department visit.

If study staff are not able to reach participants after at least 3 phone attempts, they will attempt to reach the secondary contact listed and/or send an email or text message to the participant. Text messages will be sent through the Mosio application, which is an HIPAA-compliant application.If these methods are not successful in contacting participant, then participant will be considered lost to follow up.

### D.3 **Site Monitoring**

Since this is a four site study, sites will be monitored by the PIs at each respective site according to established monitoring standard operating procedures (SOPs). Study site PIs will oversee the study to assure satisfactory data recording, adherence to the study protocol, Good Clinical Practice (GCP), and study medication accounting. UAB will monitor recruitment utilizing automated reports generated from the study database. UAB investigators and staff MGH, MetroHealth, and University of Iowawill have meetings monthly to monitor site recruitment and to determine any intervention for poor recruitment. The staff listed in the study roster will be responsible for all aspects of the trial. The study will be conducted in compliance with the protocol, International Council for Harmonization/Good Clinical Practice requirements (ICH/GCP), and applicable state, local and federal regulatory requirements.This includes but is not limited to the following:

- Development of the study protocol
- Development of the manual of procedures and its maintenance
- Participant randomization
- Development and implementation of the data flow and data tracking
- Development of procedures for data entry, error identification, and error correction
- AE monitoring and reporting
- Quality control procedures
- Submitting for IRB review and approval
- Creating reports - enrollment, AEs, participant status (e.g., withdrawals)
- Preparing and sending required reports to the Safety Officer and the IRB
- Submitting all required reports to the study appointed Safety Officer.
- Distribution of all changes, updates and policies of above mentioned reports and documents to the study appointed Safety Officer.
- Maintaining the study binder (regulatory and clinical documents)
- Preparation of all study materials- data tables, recruitment materials, official reports
- Identifying, recruiting, screening, and enrolling participants
- Obtaining IC from each participant
- Protecting participants' rights
- Collecting study data and following participants through study completion
- Compliance and accountability of administration of study intervention
- Communicating questions, concerns, and/or observations to the PIs

All of the above activities will be carried out by the study’s project coordinators, project managers, and research assistants on a weekly basis (or more frequently as needed) and monitored by the principal and co-investigators.

In the event a problem is identified by either study site PI or staff, a teleconference/webinar will be scheduled to review the issue. These teleconferences/webinars will include discussions of overall recruitment status and identified barriers to recruitment experienced by the site with the study team. Detailed recruitment issues and suggestions will be discussed, as well as identified barriers.

The study will be conducted under the auspices of the IRBs at UAB. The respective site investigators will ensure that an appropriately constituted IRB that complies with the requirements of the current International Conference on Harmonization (ICH)-GCP version or applicable regulations will be responsible for the initial and continuing review and approval of the clinical study. Prior to initiation of the study, the investigator will forward copies of the protocol, ICF, Investigator's Brochure, Investigator's curriculum vitae (if applicable), study advertisements (if applicable), and all other subject-related documents to be used for the study to the IRB for its review and approval. Before initiating a study, the site PI will have written and dated full approval from the responsible IRB for the protocol. The investigators will also promptly report to the IRB all changes in the study, all unanticipated problems involving risks to human subjects or others, and any protocol deviations, to eliminate immediate hazards to subjects.

## E. Institutional Review Board (IRB)

The study site PI and/or staff will not make any changes in the study or study conduct without IRB approval, except where necessary to eliminate apparent immediate hazards to the subjects. For minor changes to a previously approved protocol during the period covered by the original approval, it may be possible for the study site PI to obtain an expedited review by the IRB as allowed. As part of the IRB requirements for continuing review of approved studies, the Investigators will be responsible for submitting periodic progress reports to the IRB (based on the Committee's requirements), at intervals appropriate to the degree of subject risk involved but no less than once per year. The study site PI should provide a final report to the IRB following study completion. To the maximal extent possible, these functions will be assisted by study personnel at the Coordinating Center (CC), the University of Alabama at Birmingham.

## F. Administrative Procedures

### F.1 Protocol Amendments

Any change that affects the conduct of the study or significantly alters the protocol will be made in the form of an amendment. Any change or addition to this protocol requires a written protocol amendment that must be approved by the CC before implementation. Amendments significantly affecting the safety of participants, the scope of the investigation, or the scientific quality of the study require additional approval by the IRB. Examples of amendments requiring such approval are:

- A significant change in the study design (e.g. addition of a new immunosuppressive)
- An increase in the number of study visits and procedures to which participants are exposed

### F.2 Compliance with law, audit, and debarment

Study site PIs will conduct the study in an efficient and diligent manner and in conformance with this protocol; generally accepted standards of GCP; and all applicable federal, state, and local laws, rules and regulations relating to the conduct of the clinical study. The study site PIs also agree to allow the IRB/Independent Ethics Committee, and regulatory agencies to inspect and review trial-related documents and procedures, and provide for direct access to all study-related source data and documents. The study site PIs will not seek reimbursement from patients, their insurance providers, or from government programs for procedures included as part of the study.

The study site PIs will prepare and maintain complete and accurate study documentation in compliance with GCP standards and applicable federal, state, and local laws, rules and regulations.

Study documentation will be promptly and fully disclosed by the study site PI upon request for inspection, copying, review, and audit at reasonable times by any regulatory agencies. The study site PI agrees to promptly take any reasonable steps that are requested by designated representatives as a result of an audit to cure deficiencies in the study documentation and CRFs.

Persons debarred from conducting or working on clinical studies by any court or regulatory agency will NOT be allowed to conduct or work on this studies.

### F.3 Compliance with Financial Disclosure Requirements

The study site PIs will provide accurate financial information to allow submission of complete and accurate certification and disclosure statements as required by US FDA regulations (21 CFR Part 54). This requirement also extends to sub-Investigators.

### F.4 Publication of results

It is mandatory that the first publication will be based on data from both centers that has been analyzed as stipulated in the protocol. Participating PIs agree not to present data gathered from one center before the full publication, unless formally agreed to by all other PIs.

### F.5 Changes in study personnel

If there is a change of any personnel listed on IRB personnel form, a new form reflecting the change will be completed and forwarded to the IRB along with the new staff member's signed curriculum vitae, medical license (if relevant), and signed financial disclosure statement.

## G. Appendices

### G.1 Video Questions

Q1: What would be the compelling message(s) that videos should make to motivate patients to go to a clinic appointment for gout?

- Gout is a chronic disease that requires ongoing treatment
- Untreated gout affects quality of life
- Visits to the ED can be prevented
- Primary care physicians and specialists can prescribe effective medications for gout
- The sooner the gout is treated the easier it would be to prevent gout flares and complications
- Medications for flares can be prescribed by physicians outside the ED

Q2: What would be the compelling message(s) that videos should make to motivate patients to take gout medications?

- Effective medications for gout exist
- Medications prevent gout flares
- Goal of treatment is SUA < 6 mg/dL
- Limiting certain foods/beverages is helpful, but by itself it is not effective
- Medication regimens are relatively simple
- Most people start taking 2 medications, but in about 6 months only one medication will be needed
- Tophi will dissolve with medications

### G.2 Abbreviations

| | |
|---|---|
| ACR | American College of Rheumatology |
| AE | Adverse Event |
| BPA | Best Practice Alert |
| CATI | Computer Assisted Telephone Interview |
| CC | Coordinating Center |
| CCTS | Center for Clinical and Translational Sciences |

| | |
|---|---|
| CFT | Code of Federal Regulations |
| CORT | Center of Research Translation |
| CT | Computerized Tomography |
| CTSA | Clinical and Translational Science Award |
| DNA | Deoxyribonucleic Acid |
| ED | Emergency Department |
| EMR | Electronic Medical Record |
| EOS | End Of Study |
| EQ-5D | European Quality of Life Scale |
| EULAR | European League Against Rheumatism |
| GCP | Good Clinical Practice |
| HRQL | Health Related Quality of Life |
| HIPAA | Health Insurance Portability and Accountability Act |
| IC | Informed Consent |
| ICD | International Classification of Diseases |
| ICF | Informed Consent Form |
| ICH | International Council for Harmonization |
| ICU | Intensive Care Unit |
| IPQ | Illness Perception Questionnaire |
| IRB | Institutional Review Board |
| INSIGHT | INvestigationS In Gout, Hyperuricemia, and comorbidiTies |
| MGH | Massachusetts General Hospital |
| MHDRC | Minority Health and Health Disparities Research Center |
| ML | Machine Learning |
| MRI | Magnetic Resonance Imaging |
| NCATS | National Center for Advancing Translational Sciences |
| NEDS | National ED Sample |
| NIAMS | National Institute of Arthritis and Musculoskeletal and Skin Diseases |
| NIH | National Institutes of Health |
| NLP | Natural Language Processing |
| PCP | Primary Care Provider/Physician |
| PHI | Protected Health Information |
| PHQ | Patient Health Questionnaire |
| PI | Principal Investigator |
| PID | Patient Identification |

| | |
|---|---|
| PRO | Patient Reported Outcome |
| RA | Research Assistant |
| REDCap | Research Electronic Data Capture |
| RNA | Ribonucleic Acid |
| SAE | Serious Adverse Event |
| SDOH | Social Determinants Of Health |
| SO | Safety Officer |
| SOP | Standard Operating Procedure |
| STRIDE | Strengthening Translational Research in Diverse Enrollment |
| SUA | Serum Uric Acid |
| UAB | University of Alabama at Birmingham |
| ULT | Urate Lowering Therapy |
| UP | Unanticipated Problem |
| | |

## H. References


1. Dalbeth N, Merriman TR, Stamp LK. Gout. Lancet. 2016;388(10055):2039-52
2. Saag KG, Choi H. Epidemiology, risk factors, and lifestyle modifications for gout. Arthritis Res Ther. 2006;8 Suppl 1:S2
3. Chen-Xu M, Yokose C, Rai SK, Pillinger MH, Choi HK. Contemporary Prevalence of Gout and Hyperuricemia in the United States and Decadal Trends: The National Health and Nutrition Examination Survey 2007-2016. Arthritis Rheumatol. 2019
4. Singh JA, Strand V. Gout is associated with more comorbidities, poorer health-related quality of life and higher healthcare utilisation in US veterans. Ann Rheum Dis. 2008;67(9):1310-6
5. Sattui SE, Singh JA, Gaffo AL. Comorbidities in patients with crystal diseases and hyperuricemia. Rheum Dis Clin North Am. 2014;40(2):251-78.Pmc4159668
6. Zhu Y, Pandya BJ, Choi HK. Prevalence of gout and hyperuricemia in the US general population: the National Health and Nutrition Examination Survey 2007-2008. Arthritis Rheum. 2011;63(10):3136-41
7. Mikuls TR, Farrar JT, Bilker WB, Fernandes S, Schumacher HR, Jr., Saag KG. Gout epidemiology: results from the UK General Practice Research Database, 1990-1999. Ann Rheum Dis. 2005;64(2):267-72.PMCID: PMC1755343
8. Roddy E, Doherty M. Gout. Epidemiology of gout. Arthritis Research & Therapy. 2010;12(6):223-
9. Bickel C, Rupprecht HJ, Blankenberg S, Rippin G, Hafner G, Daunhauer A, et al. Serum uric acid as an independent predictor of mortality in patients with angiographically proven coronary artery disease. Am J Cardiol. 2002;89(1):12-7
10. Brook RA, Kleinman NL, Patel PA, Melkonian AK, Brizee TJ, Smeeding JE, et al. The economic burden of gout on an employed population. Curr Med Res Opin. 2006;22(7):1381-9
11. Kleinman NL, Brook RA, Patel PA, Melkonian AK, Brizee TJ, Smeeding JE, et al. The impact of gout on work absence and productivity. Value Health. 2007;10(4):231-37
12. Wu EQ, Patel PA, Mody RR, Yu AP, Cahill KE, Tang J, et al. Frequency, risk, and cost of gout-related episodes among the elderly: does serum uric acid level matter? J Rheumatol. 2009;36(5):1032-40
13. Wu EQ, Patel PA, Yu AP, Mody RR, Cahill KE, Tang J, et al. Disease-related and all-cause health care costs of elderly patients with gout. J Manag Care Pharm. 2008;14(2):164-75
14. Doherty M. New insights into the epidemiology of gout. Rheumatology (Oxford). 2009;48 Suppl 2:ii2-ii8
15. Singh JA, Yu S. Time Trends, Predictors, and Outcome of Emergency Department Use for Gout: A Nationwide US Study. J Rheumatol. 2016;43(8):1581-8.PMC4970881
16. Mithal A, Singh G. OP0185 Emergency department visits for gout: a dramatic increase in the past decade. Annals of the Rheumatic Diseases. 2018;77(Suppl 2):141-2

17. Schlesinger N, Radvanski DC, Young TC, McCoy JV, Eisenstein R, Moore DF. Diagnosis and Treatment of Acute Gout at a University Hospital Emergency Department. Open Rheumatol J. 2015;9:21-6.PMC4475690
18. Rolheiser LA, Cordes J, Subramanian SV. Opioid Prescribing Rates by Congressional Districts, United States, 2016. American Journal of Public Health. 2018;108(9):1214-9
19. Jackson R, Shiozawa A, Buysman EK, Altan A, Korrer S, Choi H. Flare frequency, healthcare resource utilisation and costs among patients with gout in a managed care setting: a retrospective medical claims-based analysis. BMJ Open. 2015;5(6):e007214.PMC4480013
20. Singh JA, Bharat A, Khanna D, Aquino-Beaton C, Persselin JE, Duffy E, et al. Health care utilization in patients with gout: a prospective multicenter cohort study. BMC Musculoskelet Disord. 2017;18(1):233.PMC5452408
21. Yadao AM, Saseen JJ, Nair KV, Agashivala N, Allen RR, Ghushchyan V. Comparison of patient characteristics and gout-related health-care resource utilization and costs in patients with frequent versus infrequent gouty arthritis attacks. Rheumatology. 2012;51(11):2004-12
22. Elfishawi MM, Zleik N, Kvrgic Z, Michet CJ, Jr., Crowson CS, Matteson EL, et al. The Rising Incidence of Gout and the Increasing Burden of Comorbidities: A Population-based Study over 20 Years. J Rheumatol. 2018;45(4):574-9.PMC5880714
23. Aromdee E, Mitchet C, Crowson C, O'Fallon M, Gabriel S. Epidemiology of gout: is the incidence rising? J Rheumatol. 2002;29:2403-6
24. Dalbeth N, House ME, Aati O, Tan P, Franklin C, Horne A, et al. Urate crystal deposition in asymptomatic hyperuricaemia and symptomatic gout: a dual energy CT study. Ann Rheum Dis. 2015;74(5):908-11
25. Towiwat P, Doyle AJ, Gamble GD, Tan P, Aati O, Horne A, et al. Urate crystal deposition and bone erosion in gout: 'inside-out' or 'outside-in'? A dual-energy computed tomography study. Arthritis Res Ther. 2016;18(1):208.Pmc5024428
26. Abraham A, Katzberg HD, Lovblom LE, Perkins BA, Bril V. Uric Acid Levels Correlate with Sensory Nerve Function in Healthy Subjects. Can J Neurol Sci. 2019:1-5
27. Ozalp Kizilay D, Sen S, Ersoy B. Associations Between Serum Uric Acid Levels and Cardiometabolic Risk, Renal Injury in Obese and Overweight Children. J Clin Res Pediatr Endocrinol. 2019
28. Bardin T, Richette P. Impact of comorbidities on gout and hyperuricaemia: an update on prevalence and treatment options. BMC Med. 2017;15(1):123.Pmc5494879
29. Latourte A, Bardin T, Richette P. Uric acid and cognitive decline: a double-edge sword? Curr Opin Rheumatol. 2018;30(2):183-7
30. Bodenheimer T, Wagner EH, Grumbach K. Improving Primary Care for Patients With Chronic Illness: The Chronic Care Model, Part 2. JAMA. 2002;288(15):1909-14
31. Hussey PS, Schneider EC, Rudin RS, Fox DS, Lai J, Pollack CE. Continuity and the Costs of Care for Chronic Disease. JAMA Internal Medicine. 2014;174(5):742-8
32. Wolinsky FD, Bentler SE, Liu L, Geweke JF, Cook EA, Obrizan M, et al. Continuity of Care with a Primary Care Physician and Mortality in Older Adults. The Journals of Gerontology: Series A. 2010;65A(4):421-8
33. Becker MA, Schumacher HR, MacDonald PA, Lloyd E, Lademacher C. Clinical efficacy and safety of successful longterm urate lowering with febuxostat or allopurinol in subjects with gout. The Journal of Rheumatology. 2009;36(6):1273-82
34. Dalbeth N, Bardin T, Doherty M, Lioté F, Richette P, Saag KG, et al. Discordant American College of Physicians and international rheumatology guidelines for gout management: consensus statement of the Gout, Hyperuricemia and Crystal-Associated Disease Network (G-CAN). Nature Reviews. Rheumatology. 2017;13(9):561-8
35. Kiltz U, Smolen J, Bardin T, Cohen Solal A, Dalbeth N, Doherty M, et al. Treat-to-target (T2T) recommendations for gout. Annals of the Rheumatic Diseases. 2017;76(4):632-8
36. Richette P, Doherty M, Pascual E, Barskova V, Becce F, Castañeda-Sanabria J, et al. 2016 updated EULAR evidence-based recommendations for the management of gout. Annals of the Rheumatic Diseases. 2017;76(1):29-42
37. Alsolamy S, Al Salamah M, Al Thagafi M, Al-Dorzi HM, Marini AM, Aljerian N, et al. Diagnostic accuracy of a screening electronic alert tool for severe sepsis and septic shock in the emergency department. BMC Med Inform Decis Mak. 2014;14:105.PMC4261595

38. Kucher N, Koo S, Quiroz R, Cooper JM, Paterno MD, Soukonnikov B, et al. Electronic Alerts to Prevent Venous Thromboembolism among Hospitalized Patients. New England Journal of Medicine. 2005;352(10):969-77
39. Kipnis P, Turk BJ, Wulf DA, LaGuardia JC, Liu V, Churpek MM, et al. Development and validation of an electronic medical record-based alert score for detection of inpatient deterioration outside the ICU. J Biomed Inform. 2016;64:10-9.PMC5510648
40. Escobar GJ, LaGuardia JC, Turk BJ, Ragins A, Kipnis P, Draper D. Early detection of impending physiologic deterioration among patients who are not in intensive care: development of predictive models using data from an automated electronic medical record. J Hosp Med. 2012;7(5):388-95
41. Churpek MM, Yuen TC, Park SY, Gibbons R, Edelson DP. Using electronic health record data to develop and validate a prediction model for adverse outcomes in the wards*. Crit Care Med. 2014;42(4):841-8.PMC3959228
42. Danila MI, Outman RC, Rahn EJ, Mudano AS, Redden DT, Li P, et al. Evaluation of a Multimodal, Direct-to-Patient Educational Intervention Targeting Barriers to Osteoporosis Care: A Randomized Clinical Trial. J Bone Miner Res. 2018;33(5):763-72.Pmc6016546
43. Danila MI, Outman RC, Rahn EJ, Mudano AS, Thomas TF, Redden DT, et al. A multi-modal intervention for Activating Patients at Risk for Osteoporosis (APROPOS): Rationale, design, and uptake of online study intervention material. Contemp Clin Trials Commun. 2016;4:14-24.PMC4955389
44. Nguyen SQ, Mwakalindile E, Booth JS, Hogan V, Morgan J, Prickett CT, et al. Automated electronic medical record sepsis detection in the emergency department. PeerJ. 2014;2:e343-e
45. Hawk ET, Habermann EB, Ford JG, Wenzel JA, Brahmer JR, Chen MS, Jr., et al. Five National Cancer Institute-designated cancer centers' data collection on racial/ethnic minority participation in therapeutic trials: a current view and opportunities for improvement. Cancer. 2014;120 Suppl 7:1113-21.PMC4322861
46. Durant RW, Wenzel JA, Scarinci IC, Paterniti DA, Fouad MN, Hurd TC, et al. Perspectives on barriers and facilitators to minority recruitment for clinical trials among cancer center leaders, investigators, research staff, and referring clinicians: enhancing minority participation in clinical trials (EMPaCT). Cancer. 2014;120 Suppl 7:1097-105.PMC4395557
47. Vickers SM, Fouad MN. An overview of EMPaCT and fundamental issues affecting minority participation in cancer clinical trials: enhancing minority participation in clinical trials (EMPaCT): laying the groundwork for improving minority clinical trial accrual. Cancer. 2014;120 Suppl 7:1087-90.PMC4133979
48. Fouad MN, Acemgil A, Bae S, Forero A, Lisovicz N, Martin MY, et al. Patient Navigation As a Model to Increase Participation of African Americans in Cancer Clinical Trials. J Oncol Pract. 2016;12(6):556-63.PMC4957258
49. Perez-Stable EJ 2016;Pages. Accessed at Resource Centers for Minority Aging Research Annual Meeting, NIA at https://www.nimhd.nih.gov/docs/NIMHD_vision_agenda.pdf on April 12, 2018 2018.
50. Department of Health and Human Services NIoH. Monitoring Adherence to the NIH Policy on the Inclusion of Women and Minorities as Subjects in Clinical Research. 2012.
51. (PCORI) P-CORI 2018;Pages. Accessed at PCORI at https://www.pcori.org/research-results/2017/implementing-shared-decision-making-intervention-chest-pain-er on 3/6/2019 2019.
52. Hess EP, Homme JL, Kharbanda AB, Tzimenatos L, Louie JP, Cohen DM, et al. Effect of the Head Computed Tomography Choice Decision Aid in Parents of Children With Minor Head Trauma: A Cluster Randomized Trial. JAMA Netw Open. 2018;1(5):e182430.PMC6324506
53. Hess EP, Hollander JE, Schaffer JT, Kline JA, Torres CA, Diercks DB, et al. Shared decision making in patients with low risk chest pain: prospective randomized pragmatic trial. Bmj. 2016;355:i6165.PMC5152707 www.icmje.org/coi_disclosure.pdf and declare: JEH has research funding from Alere, Trinity, Siemens, and Roche and has consulted for Janssen. DBD has research funding from Siemens and Roche and has consulted for Janssen. All other authors have no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.
54. Hinyard LJ, Kreuter MW. Using narrative communication as a tool for health behavior change: a conceptual, theoretical, and empirical overview. Health Educ Behav. 2007;34(5):777-92
55. Houston TK, Allison JJ, Sussman M, Horn W, Holt CL, Trobaugh J, et al. Culturally appropriate storytelling to improve blood pressure: a randomized trial. Ann Intern Med. 2011;154(2):77-84

56. Houston TK, Fix GM, Shimada SL, Long JA, Gordon HS, Pope C, et al. African American Veterans Storytelling: A Multisite Randomized Trial to Improve Hypertension. Med Care. 2017;55 Suppl 9 Suppl 2:S50-s8
57. Goddu AP, Raffel KE, Peek ME. A story of change: The influence of narrative on African-Americans with diabetes. Patient Educ Couns. 2015;98(8):1017-24.4492448
58. Kreuter MW, Holmes K, Alcaraz K, Kalesan B, Rath S, Richert M, et al. Comparing narrative and informational videos to increase mammography in low-income African American women. Patient Educ Couns. 2010;81 Suppl:S6-14.3146295
59. Fredericksen RJ, Gibbons L, Brown S, Edwards TC, Yang FM, Fitzsimmons E, et al. Medication understanding among patients living with multiple chronic conditions: Implications for patient-reported measures of adherence. Res Social Adm Pharm. 2018;14(6):540-4.PMC5738290
60. Mugavero M, Ostermann J, Whetten K, Leserman J, Swartz M, Stangl D, et al. Barriers to antiretroviral adherence: the importance of depression, abuse, and other traumatic events. AIDS Patient Care STDS. 2006;20(6):418-28
61. Mugavero MJ. Improving engagement in HIV care: what can we do? Top HIV Med. 2008;16(5):156-61
62. Mugavero MJ, Davila JA, Nevin CR, Giordano TP. From access to engagement: measuring retention in outpatient HIV clinical care. AIDS Patient Care STDS. 2010;24(10):607-13.PMC2965698
63. Pence BW, Ostermann J, Kumar V, Whetten K, Thielman N, Mugavero MJ. The influence of psychosocial characteristics and race/ethnicity on the use, duration, and success of antiretroviral therapy. J Acquir Immune Defic Syndr. 2008;47(2):194-201
64. Spencer K, Carr A, Doherty M. Patient and provider barriers to effective management of gout in general practice: a qualitative study. Annals of the Rheumatic Diseases. 2012;71(9):1490-5
65. Hamel LM, Penner LA, Albrecht TL, Heath E, Gwede CK, Eggly S. Barriers to Clinical Trial Enrollment in Racial and Ethnic Minority Patients With Cancer. Cancer control : journal of the Moffitt Cancer Center. 2016;23(4):327-37
66. Menikoff J, Kaneshiro J, Pritchard I. The Common Rule, Updated. N Engl J Med. 2017;376(7):613-5
67. Fouad MN, Johnson RE, Nagy MC, Person SD, Partridge EE. Adherence and retention in clinical trials: a community-based approach. Cancer. 2014;120 Suppl 7:1106-12.PMC4416644
68. Chaudhry FA, Ismail SZ, Davis ET. A new system of computer-assisted navigation leading to reduction in operating time in uncemented total hip replacement in a matched population. Eur J Orthop Surg Traumatol. 2018;28(4):645-8
69. Fouad M, Wynn T, Martin M, Partridge E. Patient navigation pilot project: results from the Community Health Advisors in Action Program (CHAAP). Ethn Dis. 2010;20(2):155-61
70. Pisu M, Rocque GB, Jackson BE, Kenzik KM, Sharma P, Williams CP, et al. Lay navigation across the cancer continuum for older cancer survivors: Equally beneficial for Black and White survivors? J Geriatr Oncol. 2018
71. Rocque GB, Pisu M, Jackson BE, Kvale EA, Demark-Wahnefried W, Martin MY, et al. Resource Use and Medicare Costs During Lay Navigation for Geriatric Patients With Cancer. JAMA Oncol. 2017;3(6):817-25.PMC5540048
72. Curtis JR, Silverman SL. Commentary: The Five Ws of a Fracture Liaison Service: Why, Who, What, Where, and How? In Osteoporosis, We Reap What We Sow. Current Osteoporosis Reports. 2013;11(4):365-8
73. Ganda K, Puech M, Chen JS, Speerin R, Bleasel J, Center JR, et al. Models of care for the secondary prevention of osteoporotic fractures: a systematic review and meta-analysis. Osteoporosis International. 2013;24(2):393-406
74. Koh MYH, Lee JF, Montalban S, Foo CL, Hum AYM. ED-PALS: A Comprehensive Palliative Care Service for Oncology Patients in the Emergency Department. Am J Hosp Palliat Care. 2019:1049909119825847
75. Hill NTM, Shand F, Torok M, Halliday L, Reavley NJ. Development of best practice guidelines for suicide-related crisis response and aftercare in the emergency department or other acute settings: a Delphi expert consensus study. BMC Psychiatry. 2019;19(1):6.PMC6323675
76. Trethewey SP, Deepak S, Saad S, Hughes E, Tadros G. Evaluation of the Psychiatric Decisions Unit (PDU): effect on emergency department presentations and psychiatric inpatient admissions. Postgrad Med J. 2019

77. Neogi T, Jansen TL, Dalbeth N, Fransen J, Schumacher HR, Berendsen D, et al. 2015 Gout classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Ann Rheum Dis. 2015;74(10):1789-98.PMC4602275
78. Neogi T, Jansen TL, Dalbeth N, Fransen J, Schumacher HR, Berendsen D, et al. 2015 Gout Classification Criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis Rheumatol. 2015;67(10):2557-68.PMC4566153
79. Gaffo AL, Schumacher HR, Saag KG, Taylor WJ, Dinnella J, Outman R, et al. Developing a provisional definition of flare in patients with established gout. Arthritis Rheum. 2012;64(5):1508-17
80. Khanna D, Fitzgerald JD, Khanna PP, Bae S, Singh MK, Neogi T, et al. 2012 American College of Rheumatology guidelines for management of gout. Part 1: systematic nonpharmacologic and pharmacologic therapeutic approaches to hyperuricemia. Arthritis Care Res. 2012;64(10):1431-46
81. Probst MA, Noseworthy PA, Brito JP, Hess EP**.** Shared Decision-Making as the Future of Emergency Cardiology. Can J Cardiol. 2018;34(2):117-24.Pmc5800967
82. Capp R, Kelley L, Ellis P, Carmona J, Lofton A, Cobbs-Lomax D, et al. Reasons for Frequent Emergency Department Use by Medicaid Enrollees: A Qualitative Study. Academic Emergency Medicine. 2016;23(4):476-81
83. Newman ED, Harrington TM, Olenginski TP, Perruquet JL, McKinley K**.** "The rheumatologist can see you now": Successful implementation of an advanced access model in a rheumatology practice. Arthritis Rheum. 2004;51(2):253-7
84. Gaffo AL, Dalbeth N, Saag KG, Singh JA, Rahn EJ, Mudano AS, et al. Brief Report: Validation of a Definition of Flare in Patients With Established Gout. Arthritis Rheumatol. 2018;70(3):462-7
85. Dalbeth N, Petrie KJ, House M, Chong J, Leung W, Chegudi R, et al. Illness perceptions in patients with gout and the relationship with progression of musculoskeletal disability. Arthritis Care Res (Hoboken). 2011;63(11):1605-12
86. Hurst NP, Kind P, Ruta D, Hunter M, Stubbings A**.** Measuring health-related quality of life in rheumatoid arthritis: validity, responsiveness and reliability of EuroQol (EQ-5D). Br J Rheumatol. 1997;36(5):551-9
87. Johnson JA, Coons SJ**.** Comparison of the EQ-5D and SF-12 in an adult US sample. Qual Life Res. 1998;7(2):155-66
88. Johnson JA, Coons SJ, Ergo A, Szava-Kovats G**.** Valuation of EuroQOL (EQ-5D) health states in an adult US sample. Pharmacoeconomics. 1998;13(4):421-33
89. Kroenke K, Spitzer RL, Williams JB**.** The PHQ-9: validity of a brief depression severity measure. Journal of general internal medicine. 2001;16(9):606-13
90. Forcino RC, Barr PJ, O'Malley AJ, Arend R, Castaldo MG, Ozanne EM, et al. Using CollaboRATE, a brief patient-reported measure of shared decision making: Results from three clinical settings in the United States. Health Expect. 2018;21(1):82-9.PMC5750739
91. Carmel A, Steel P, Tanouye R, Novikov A, Clark S, Sinha S, et al. Rapid Primary Care Follow-up from the ED to Reduce Avoidable Hospital Admissions. The western journal of emergency medicine. 2017;18(5):870-7
92. Elliott K, W. Klein J, Basu A, Sabbatini AK**.** Transitional care clinics for follow-up and primary care linkage for patients discharged from the ED. The American Journal of Emergency Medicine. 2016;34(7):1230-5
93. Engel KG, Buckley BA, Forth VE, McCarthy DM, Ellison EP, Schmidt MJ, et al. Patient understanding of emergency department discharge instructions: where are knowledge deficits greatest? Acad Emerg Med. 2012;19(9):E1035-44
94. Engel KG, Heisler M, Smith DM, Robinson CH, Forman JH, Ubel PA**.** Patient comprehension of emergency department care and instructions: are patients aware of when they do not understand? Ann Emerg Med. 2009;53(4):454-61.e15
95. Perinelli E, Gremigni P**.** Use of Social Desirability Scales in Clinical Psychology: A Systematic Review. Journal of Clinical Psychology. 2016;72(6):534-51
96. Marshall GNaRDH**.** The Patient Satisfaction Questionnaire Short Form (PSQ-18). Santa Monica, Calif: RAND Corporation; 1994:P-7865.
97. Thayaparan AJ, Mahdi E**.** The Patient Satisfaction Questionnaire Short Form (PSQ-18) as an adaptable, reliable, and validated tool for use in various settings. Medical education online. 2013;18:21747-

98. La-Crette J, Jenkins W, Fernandes G, Valdes AM, Doherty M, Abhishek A. First validation of the gout activity score against gout impact scale in a primary care based gout cohort. Joint Bone Spine. 2018;85(3):323-5
99. Chandratre P, Mallen C, Richardson J, Muller S, Hider S, Rome K, et al. Health-related quality of life in gout in primary care: Baseline findings from a cohort study. Semin Arthritis Rheum. 2018;48(1):61-9.PMC6089841
100. Chinchilla SP, Doherty M, Abhishek A. Gout Activity Score has predictive validity and is sensitive to change: results from the Nottingham Gout Treatment Trial (Phase II). Rheumatology (Oxford). 2019
101. Khanna PP, Shiozawa A, Walker V, Bancroft T, Essoi B, Akhras KS, et al. Health-related quality of life and treatment satisfaction in patients with gout: results from a cross-sectional study in a managed care setting. Patient Prefer Adherence. 2015;9:971-81.PMC4501348
102. Wallace B, Khanna D, Aquino-Beaton C, Singh JA, Duffy E, Elashoff D, et al. Performance of Gout Impact Scale in a longitudinal observational study of patients with gout. Rheumatology (Oxford). 2016;55(6):982-90.PMC5854089
103. Chew LD, Griffin JM, Partin MR, Noorbaloochi S, Grill JP, Snyder A, et al. Validation of screening questions for limited health literacy in a large VA outpatient population. J Gen Intern Med. 2008;23(5):561-6.PMC2324160
104. Fagerlin A, Zikmund-Fisher BJ, Ubel PA. Helping patients decide: ten steps to better risk communication. J Natl Cancer Inst. 2011;103(19):1436-43.PMC3218625
105. Fagerlin A, Zikmund-Fisher BJ, Ubel PA, Jankovic A, Derry HA, Smith DM. Measuring numeracy without a math test: development of the Subjective Numeracy Scale. Med Decis Making. 2007;27(5):672-80
106. Zikmund-Fisher BJ, Exe NL, Witteman HO. Numeracy and literacy independently predict patients' ability to identify out-of-range test results. J Med Internet Res. 2014;16(8):e187.PMC4137189
107. Weinstein ND. The precaution adoption process. Health Psychol. 1988;7(4):355-86
108. (CDC) CfDCaP 2018;Pages. Accessed at Department of Health and Human Services, Centers for Disease Control and Prevention at https://www.cdc.gov/brfss/questionnaires/index.htm on 03/22/2019 2019.
109. NIH 2016;Pages. Accessed at NIH at https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-011.html on 03.16/2019 2019.
110. Daugherty A, Hegele RA, Mackman N, Rader DJ, Schmidt AM, Weber C. Complying With the National Institutes of Health Guidelines and Principles for Rigor and Reproducibility: Refutations. Arterioscler Thromb Vasc Biol. 2016;36(7):1303-4
111. Zorc JJ, Scarfone RJ, Li Y, Hong T, Harmelin M, Grunstein L, et al. Scheduled follow-up after a pediatric emergency department visit for asthma: a randomized trial. Pediatrics. 2003;111(3):495-502
112. Buletko A, Khawaja Z. Timing of Follow-up After Acute Ischemic Stroke And Readmissions (P5.154). Neurology. 2015;84(14 Supplement):P5.154
113. Zorc JJ, Chew A, Allen JL, Shaw K. Beliefs and barriers to follow-up after an emergency department asthma visit: a randomized trial. Pediatrics. 2009;124(4):1135-42
114. Messina FC, McDaniel MA, Trammel AC, Ervin DR, Kozak MA, Weaver CS. Improving specialty care follow-up after an ED visit using a unique referral system. Am J Emerg Med. 2013;31(10):1495-500
115. Wheeler K, Crawford R, McAdams D, Benel S, Dunbar VG, Caudle JM, et al. Inpatient to Outpatient Transfer of Care in Urban Patients With Diabetes: Patterns and Determinants of Immediate Postdischarge Follow-up. Archives of Internal Medicine. 2004;164(4):447-53
116. Health NIo. Common Terminology Criteria for Adverse Events (CTCAE). In: DHHS, ed. 4.03 ed; 2010:196.