RESEACH STUDY PROTOCOL

PROTOCOL TITLE:
DEVELOPING A GOUT ACTION PLAN IN PRIMARY CARE SETTING IN SINGAPORE

PROTOCOL NUMBER:

VERSION NUMBER: 2

VERSION DATE: 24 MAR 2025

PRINCIPAL INVESTIGATOR:
Liew Siew Lee, Family Physician, SingHealth Polyclinic

PROTOCOL SIGNATURE PAGE

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Declaration of Investigator

I confirm that I have read the above-mentioned protocol and its attachments. I agree to conduct the described study in compliance with all stipulations of the protocol, regulations and ICH E6 Guideline for Good Clinical Practice (GCP).

LIEW SIEW LEE

Name of Principal Investigator:

Signature of Principal Investigator:

Date:

PASIR RIS POLYCLINIC

Name of Study Site:

Note:

- This page should be signed with wet-ink signature or digital signature. Do not paste digital image of a wet-ink signature.

- Signed copies of this signature page should be stored in the study file and in the respective study site's investigator file.

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1. BACKGROUND AND RATIONALE

Gout is a common inflammatory arthritis often seen in primary care. Worldwide prevalence ranges from under 1% to 6.8%.[1] The prevalence of gout has risen over the past three decades, accompanied by an increase in morbidity. [2] In Singapore, prevalence of gout is 4.1% amongst the Singapore Chinese population.[3] Gout is associated with significant morbidity and mortality due to coronary heart disease and kidney disease[3], and has substantial burden and impact in quality of life, with higher healthcare utilization and high unemployment rate observed in middle aged men with gout. [4]

Patients with poorly controlled gout suffer from frequent gout flares, with acute onset of joint pain and swelling, affecting health-related quality of life.[5] A meta-synthesis showed that gout flares impact on patients' lives, including physical, psychological, social and family life. [6] In a primary care institution in Singapore, 28.2% of patients with gout had poorly controlled disease.[7] In a rheumatology clinic in Singapore, 33% of patients with gout visited emergency department at least once for gout flare, while 19.5% had at least one hospitalization for gout.[4]

Acute gout flares can be mitigated by pharmacotherapy. Timely administration of acute medications is important to alleviate the pain leading to early resolution of symptoms. American College of Rheumatology (ACR) Guideline 2020[8] and European League Against Rheumatism (EULAR) 2016 [9] recommend colchicine, non-steroidal anti-inflammatory drugs (NSAIDs) or corticosteroid for treatment of acute gout flare. In primary care clinics in Singapore, colchicine was often prescribed for an acute gout flare.[7] However, colchicine has gastrointestinal side effects such as vomiting and diarrhoea[10], and some patients are not aware of its side effects and exceeded prescribed dose. [10] NSAIDs might improve the pain if given within 24 hours. [11] However, NSAIDs are associated with gastrointestinal, renal and cardiovascular adverse effects, thus they may not be the suitable pharmacotherapy for those with renal, gastrointestinal or cardiovascular comorbidities. [12] NSAIDs also cause hypersensitivity reactions with estimated prevalence of hypersensitivity to NSAIDs to be 0.5 to 1.9% of the general population. [13] For patients who are unable to tolerate NSAIDs or colchicine, or have chronic renal disease, systemic corticosteroid such as oral prednisolone might be a good alternative as it provides similar improvement in pain relief. [11 14]

Aside to pharmacotherapy, dietary control is important to prevent gout flares. ACG guideline 2020 [8] includes conditional recommendations to reduce alcohol intake, adopt a low-purine diet, and prioritize weight loss. A meta-analysis showed that red meat, seafood, alcohol, fructose or sweetened soft drinks increase risk of gout and hyperuricaemia, while consumption of soy foods, dairy products and vegetables reduce risk of gout. [15] However, there is lack of awareness in dietary triggers especially in those with active gout. [16] A recent study in Australia found that patients with gout lack knowledge about the risk and protective factors of gout. [17] Patients resisted dietary changes due to the restrictive nature of the diet, lack of resources for information, and perceived it as unrealistic and unmanageable. [18]

Gout control remains suboptimal despite established guideline. Urate lowering therapy (ULT) remains the key in gout management and its initiation is recommended for patients with recurrent gout flares with treat-to-target strategy. [8] However, in primary care institution in Singapore, it was found that half of the patients with poorly controlled gout were not prescribed urate lowering therapy.[7] In patients with gout, the overall adherence rate to ULT is as low as 47%.[19] Patients with gout demonstrate poor adherence to urate lowering therapy as they have limited knowledge of gout and its treatment, their attitude and perception towards taking long term medications. Some patients avoid ULT due to fear of side effects or flares during initiation, leading to nonadherence. [20] Self-management is important in the management of chronic diseases. [21] Interventions of self-management have been shown to improve self-efficacy, health behavior, subsequently improving health status and quality of life

and reducing healthcare utilization. [22] Self-efficacy refers to an individual's belief in their capacity to execute behaviours necessary to produce specific performance attainments, and it is correlated with self-care. Raising self-efficacy is important to change behavior in self-care. [23]

An action plan is a patient-held guide to support self-management with educational value. In chronic diseases such as asthma, the action plan provides information on how to manage the disease on a day-to-day basis and has proven to encourage self-management, improve health outcomes and quality of life, and reduce unscheduled visits to physicians. [24] [25] Likewise, gout is a chronic condition with acute gout flares intermittently, that will benefit from self-management. In a study in Malaysia, patients were capable in self-management of gout but to variable extent, some practice diet control, some use painkillers during acute gout attacks, some use traditional medicine rather than taking allopurinol, some use exercise or stress-reducing activities, and the type of self-management might be influenced by cultural and social factors. [26]

To our knowledge, there is no well recognised gout action plan. A gout action plan has not been subjected to prior development in terms of content, design and acceptability. We hope that by developing a gout action plan, it will give information to patients about the disease to raise knowledge on gout, to reduce frequency of exacerbation via dietary control and lifestyle measures, to provide information on pain relief medications and the risks of taking painkiller, and urate lowering therapy for those with recurrent gout flares, and safety-netting advice on when to seek help. The study thus aims to develop a prototype of gout action plan by incorporating patients' and primary care physicians' perspectives, hoping to improve quality of life and healthcare utilization among patients with gout.

2. HYPOTHESIS AND OBJECTIVES

Aims

Primary aims

1. Explore primary care professionals' (PCPs) perspectives and challenges in management of gout and assess whether novel gout action plan addresses the challenges.
2. Explore patients' understanding of gout, experiences and challenges of managing gout and medications, and assess whether they are willing to use novel gout action plan.

Secondary aims:

1. Assess the feasibility and acceptability of gout action plan in a pilot open label randomized controlled trial (RCT).
2. Assess preliminary effectiveness of gout action plan in reducing frequency of gout exacerbation, improving gout control and quality of life.

Hypothesis

1. A prototype gout action plan can be developed to aid in management of gout.
2. In primary care professionals who manage patients with gout, there are variable views and perspectives towards gout action plan.
3. Patients have variable understanding and challenges of managing gout and different opinions in using gout action plan.
4. Gout action plan is an effective tool in reducing gout flares, improving gout control and quality of life.

3. EXPECTED RISKS AND BENEFITS

Expected risks

1. Data privacy

As this study involved audio-recording of the interview for transcribing of information and collection of basic demographic information using data collection form, there is a potential risk of data breach affecting participant's confidentiality.

2. Emotional risk
Emotional risk from an adverse emotional response to a sensitive topic breached during the interview process. The interviewer will explain to participants that they may refuse to answer any of the questions if they feel uncomfortable to answer the questions, may take a break at any time during the interview or choose to discontinue the study at any time.

3. Discomfort during blood taking
Patient might experience pain and minimal bleeding during the blood taking.

Benefits
Patients might benefit from the gout action plan and learn to self-manage gout in their daily life.

4. STUDY POPULATION

4.1. List the number and nature of subjects to be enrolled.

The study will be conducted at Pasir Ris Polyclinic, one of the Singhealth Polyclinics. For first part of the study, due to its qualitative nature, we aim to recruit approximately 10-15 patients with gout and 10-15 healthcare professionals until data saturation is reached. For second part of the study on open label randomized controlled trial, we aim to recruit 72 participants.

Adult patients aged 21 and above with the clinical diagnosis of gout who are being followed up at Pasir Ris Polyclinic will be randomly recruited into the study. Healthcare professionals who involve in the care of gout will also be recruited into the first part of the study. Children or minorities will be excluded from the study.

4.2. Criteria for Recruitment and Recruitment Process

Recruitment of patients:
Eligible patients will be identified through either screening from electronic medical records (EMR) using SingHealth Outpatient Appointment System (OAS) and Sunrise Clinical Manager (SCM) or referred by attending physicians to the study team. National Electronic Health Record (NEHR) will not be assessed for research purpose. The study team will obtain prior knowledge of a potential participant's medical appointment from the SingHealth OAS and SCM so that the physician can be reminded about the arrival of potential participant.
If potential patient participants show interest in the study, they will be directed to the study team. The study team will verify the eligibility, and after an initial explanation of the study, participant will be provided a copy of participant information sheet and consent forms to bring home and to think about their participation before the signing of the consent form on the day of interview or focus group discussion. Adequate time will be given to read the documents and questions, emphasizing the voluntary nature of participation and its independence from routine clinical care. Written informed consent will be obtained in-person at the study site, in a quiet and separate room or space, ensuring privacy. The study team member taking the consent will not be the treating physician of the patient. The participant will sign hard copies of the consent form, and the copies will be kept by participant and study team.
Recruitment of healthcare professionals:
Primary care healthcare professionals in Pasir Ris Polyclinic, and other clinics will be invited to participate in the in-depth interview. The study team will conduct a briefing about the study in clinic meeting and invite potential participants to take part. Potential participants who are not present at the clinic meeting will also be contacted by

study team in-person. The study team will ensure that there is no dependent or hierarchical relationship between the team and the potential HCP participants.

4.3. Inclusion Criteria

Inclusion Criteria

Inclusion Criteria (for patients):

- Adults who are 21 years old and above
- Clinical diagnosis of gout as per ACE-EULAR 2015 criteria
- Had at least an episode of gout exacerbation within the last 1 year
- Able to speak and read English
- Singapore citizens or permanent residents
- Able to provide informed consent

Inclusion Criteria (for healthcare professionals):

- Currently still in clinical practice
- Manage gout in their clinical practice

4.4. Exclusion Criteria

Exclusion Criteria

Exclusion Criteria (for patients)

- Mental disorders
- Cognitive impairment
- Hearing and/ or speech impairments
- Pregnant
- Known terminal illness
- Unable to provide informed consent

Exclusion Criteria (for healthcare professionals):

- Not involved in gout management in the practice
- No longer in clinical practice

5. STUDY DESIGN AND PROCEDURES/METHODOLOGY

The study will employ a sequential mixed-method design, which comprises of:

1. Qualitative research to develop and refine prototype of gout action plan by gathering perspectives from both patients and healthcare providers.
2. An open label pilot RCT to assess feasibility and acceptability of gout action plan, and preliminary outcome on effectiveness of gout action plan in reducing gout flares, improvement in uric acid and quality of life.

Part 1- Qualitative phase: Creation of a prototype gout action plan

Using written asthma action plan as a guide, a prototype gout action plan will be drafted based on the latest evidence. The gout action plan outlines how to manage gout, identifying triggers, recognizing when symptoms worsen, appropriate medication usage, and when to seek medical attention. It is categorized into zone system, which consists of green zone (well controlled), yellow zone (mild symptoms), red zone (severe symptoms).

Qualitative phase: In-depth interviews and focus group discussions will be conducted with primary care healthcare professionals (physicians, nurse, pharmacist, and dietician) who are involved in patient care, as well as patients with gout. The interviews and discussions will explore on their understanding of gout and its management, experiences of managing gout, perceptions of self-management, and opinions on the prototype of gout action plan. This will provide insights into iterative refinement of the gout action plan. Prototype will thus be refined down the multiple interactions of interview or discussions till data saturation is reached. For

healthcare professionals, maximum variation sampling will be employed based on their age and years of clinical experience. For patient, maximum variation sampling will be employed based on their age, ethnicity and socioeconomic status. The session will be audio-recorded.

Part 1A

In-depth interviews with patients and focus group discussions with patients will be conducted with patients with gout. The interviews and discussions will explore their understanding of disease and treatment, experience of patient-physician consult, perceptions of self-management, and opinions on prototype gout action plan. Interview guide is developed based on theoretical domain framework.

Basic patient demographics and data on their gout duration, comorbidities and medications will be collected using the attached data collection form.

Research questions to be explored with patients with gout:
1. To understand patients' knowledge, skills, and behaviours related to gout management.
2. To identify factors that influence adherence to treatment and lifestyle modifications.
3. To explore emotional, social, and environmental factors impacting gout management.
4. What is their experience of physician consultation for gout management?
5. What are their barriers and facilitators to gout self-management?
6. What is their opinion on the prototype gout action plan? Is it easily understandable? Is it informative enough? What are the barriers of using gout action plan? When will they use the gout action plan?

Topic guide is as attached in attachment section.
Subjects: primary care patients with gout exacerbation within 1 year
Sampling method: Convenience sampling. Maximum variation sampling will be employed based on their age, ethnicity and socioeconomic status.
Outcome: identification of themes, needs and information that will help in the creation of prototype gout action plan.
Expected participant participation time: 60 minutes

Part 1B

In-depth interviews with patients and focus group discussions with primary care providers, nurses, pharmacist, dietician. The interviews and discussion will explore their understanding of gout and experiences of managing gout, their views on self-management of gout, and views on gout action plan.

Research questions to be explored:
1. What is their understanding of gout and its management?
2. What are their experiences of treating gout patients? Do they know about treatment goals and urate-lowering therapy?
3. What is their perception about self-management?
4. What are their opinions on the prototype of gout action plan? What are the barriers and enablers of action plan? Do they think need any training or resources to support use of gout action plan?

Topic guide is as attached in attachment section.

Subjects: primary care healthcare professionals (physicians, nurses, pharmacist, dietician) who manage patients with gout
Sampling method: Convenience sampling and purposive sampling. Maximum variation sampling will be employed based on their age and years of clinical experience.

Outcome: identification of themes, needs and information that will help in the creation of prototype gout action plan.

Expected participant participation time: 60 minutes

The interviews and discussions will provide insights into iterative refinement of the gout action plan. Prototype will thus be refined down the multiple interactions of interview or discussions till data saturation is reached.

The session will be audio-recorded using audio recorder. After each interview, the interviewer will transfer the audio-recording to a password-protected corporate laptop and erase it from the audio-recorder. The audio recording will be transcribed verbatim using the research department's transcribing software or transcription platforms (such as transcribe.gov.sg or Note Buddy) or engagement of transcriptionist. All participant identifiers will be removed from the transcript to ensure confidentiality. All transcripts will be checked by interviewer for accuracy. De-identified data will be used for analysis. Analysis of data will be performed using a thematic approach. All the audio files and transcriptions of the recordings will have password encryption and stored in the same password-protected corporate laptop in workplace. Only study members will have access to the password. The electronic data will be kept for 6 years post completion of the study.

Participants who consented will be informed on the date and time of the in-depth interviews or focus group discussions. Participants who come for the in-depth interviews and focus group discussions will sign the written consent form before participation. After written consent is obtained, participants will be asked to fill up the data collection form which contains their basic demographics information and health status information. Participants will be de-identified. Participants will be briefed on the purpose of the study, their roles and rights. They will be informed that the interview or discussion will be audio recorded. Field notes will be taken to record non-verbal cues. Interviewer will use topic guide for the interview or discussion.

At the end of the interview or discussion, participant will be given token of appreciation.

Part 2: Open label pilot RCT

Quantitative phase – two-arm pilot randomized controlled trial (RCT)

- Arm 1: usual care + gout action plan for 24 weeks
- Arm 2: usual care

Randomization

Patients will be randomly assigned in a 1:1 ratio to either control or intervention arm in an open-label fashion, using computer-generated random numbers for randomization of subjects. The randomized sequence will be written and kept in an opaque sealed envelope and labelled with a serial number. When patients consent to participate in the study, the team will open the opaque sealed envelope and allocated them to the study arms accordingly. It is impossible to blind the patients and research team members to the patient allocation in view of the nature of the intervention.

Upon recruitment and after patient consented, basic patient demographics and data on their gout duration, comorbidities and medications will be collected using the attached data collection form. They will be asked to recall and self-report frequency of gout flares for the past 6 months prior to recruitment. They will also need to fill up an EQ-5D-5L questionnaire on health-related quality of life which takes approximately 5 minutes to fill it up. They will also be sent for laboratory for blood test to test for uric acid level. Blood will be taken from arm using a syringe and needle, during recruitment and at a 6-month visit, for participants in both intervention and control groups. About 3ml of blood will be taken each time. In total, there will be about 6ml taken over a period of 6 months. The Institutional Review Board waiver under Section 37(3) of the Human Biomedical Research Act

2015 ("HBRA") for the removal of human biological materials is not required. This is because we will collect samples from adults with mental capacity to personally give consent for this research study.

For those patients who are assigned into the intervention arm, they will be sent to care manager to explain on the gout action plan and its details.

Study participants will be followed up for 24 weeks after enrolment. At 24 weeks, they will be asked on their frequency on gout flares after the recruitment and to fill up the EQ-5D-5L questionnaire together. They will also be sent to laboratory for blood test on uric acid level. The follow up survey will be conducted by phone call or questionnaire at a convenient time for them or during the clinic visit.

Participant withdrawal

Participants may choose to withdraw from the study at any time without providing an explanation and this will not result in any punitive consequences.

Potential difficulties and limitations and alternative approaches to achieve the aim

1) Recruitment

- In the event of difficulty recruiting adequate number of patients, proposed measures will include
    1. Email reminders and message reminders to staffs in clinic to look for patients with gout
    2. Obtaining prior knowledge of a potential participant's medical appointment so that the physician of that day can be reminded about the potential participant's arrival.
- In the event of difficulty recruiting adequate number of physicians
    1. Making use of primary care message groups and networks to reach out to potential HCPs participants
    2. Speaking to family medicine department heads or private general practice group heads to help disseminate the need for participants

2) Difficulties during interviews

- As patient participants are recruited on the day of their visit to the clinic, not all will be free for face-to-face interview on the same day. Similarly, not all HCPs will be free for face-to-face interview on the same day as recruitment. Some participants may prefer to have interview done on a different day.

Alternative approach: the research team may offer the option of a face-to-face interview to the participants depending on his or her availability.

3) Lost to follow up

- In open label RCT for 24 weeks, patients might not return for follow up during the subsequent visit. Proposed measures will include message reminders to patients on their follow up visit.

6. SAFETY MEASUREMENTS

6.1. Definitions

Serious adverse event (SAE) in relation to human biomedical research, means any untoward medical occurrence as a result of any human biomedical research which:

- results in or contributes to death
- is life-threatening
- requires in-patient hospitalisation or prolongation of existing hospitalisation
- results in or contributes to persistent or significant disability/incapacity or
- results in or contributes to a congenital anomaly/birth defect

- results in such other events as may be prescribed

Adverse event (AE) in relation to human biomedical research means any untoward medical occurrence as a result of any human biomedical research which is NOT serious. Adverse event can be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease possibly/ probably/ definitely associated with the participant in the human biomedical research.

6.2. Collecting, Recording and Reporting of Serious Adverse Events (SAEs) to CIRB

The reporting requirements will be in accordance to the reporting requirements published on CIRB website at the time when the event took place.

Only related SAEs (definitely/ probably/ possibly) will be reported to CIRB. Related means there is a reasonable possibility that the event may have been caused by participation in the research.

The investigator is responsible for informing CIRB after first knowledge that the case qualifies for reporting. Follow-up information will be actively sought and submitted as it becomes available.

Related AEs will not be reported to CIRB. However, the investigator is responsible to keep record of such AEs cases at the Study Site File.

6.3. Safety Monitoring Plan

After each interview, the interviewer will transfer the audio-recording to a password-protected corporate laptop and erase it from the audio-recorder. The soft copy research data will be stored in institution issued PC and hard copy will be kept under lock and key for 6 years before they are deleted. They will always be password protected, and data will not be transferred using thumb drive of other unsecured means.

6.4. Complaint Handling

All complaints will be reviewed by the study team and escalate to clinic director/ supervisor of Research department.

7. DATA ANALYSIS

7.1. Data Quality Assurance

Study data will be checked and validated by data management executive in Department of Research to ensure that the data obtained from this research is accurate, complete and reliable.

7.2. Data Entry and Storage

Information from the hard copy (data collection forms, questionnaires and consent forms) will be transcribed to a Microsoft Excel document with password protection. The hard copy documents will be kept in a research folder, stored under lock and key in the polyclinic research room at Pasir Ris polyclinic. The folder will not be taken out of the clinic.

After each interview, the interviewer will transfer the audio-recording to a password-protected corporate laptop and erase it from the audio-recorder. The audio recording will be transcribed verbatim using the research department's transcribing software or transcription platforms (such as transcribe.gov.sg or Note Buddy) or engagement of transcriptionist. All participant identifiers will be removed from the transcript to ensure confidentiality. All transcripts will be checked by interviewer for accuracy. De-identified data will be used for analysis. All the audio files and transcriptions of the recordings will have password encryption and stored in the same password-protected corporate laptop in workplace. Only study members will have access to the password.

Information from the data collection form will be transcribed to excel document (with password encryption) in a password-protected corporate laptop in workplace. There will be no USB or removal device used for data storage. The physical consent forms and the electronic data will be kept for 6 years post completion of study. The physical consent forms will be stored in a secure physical archive and the electronic data in an electronic archive. Only the principal investigator and co-investigators will have access to the archives.

8. SAMPLE SIZE AND STATISTICAL METHODS

8.1. Determination of Sample Size

For qualitative part, sample size calculation is not applicable. Prototype of gout action plan will be refined until saturation is reached. Hennink [27] showed that 9-17 interviews or 4-8 focus group discussion reached saturation for studies with relatively homogenous study populations and narrowly defined objectives. Therefore, for this study, we aim to recruit 10-15 participants from each group.

For pilot RCT, based on sample size rule of thumb for pilot study, Browne [28] cites to 'use at least 30 subjects or greater to estimate a parameter', whereas Whitehead [29] suggests that pilot trial sample size to be 25 per treatment arm for small effect size of 0.2 for a main trial designed with 90% power and two-sided 5% significance. With a 6-months follow up visit, assuming a potential 30% attrition rate, the final sample size after buffering for drop out will be 36 per arm (n=72). The sampling method will be convenience sampling.

8.2. Statistical and Analytical Plans

Qualitative and quantitative data will be analyzed separately.

Qualitative data:

Audio recordings of the interviews will be transcribed using the research department's transcribing software or transcription platforms (such as transcribe.gov.sg or Note Buddy) or engagement of transcriptionist. All personal identifiable information will be removed. The transcripts will be sent to the study team through secured email and reviewed for accuracy and completeness prior to data analysis. In the event of significant errors being found, they will be sent back to transcribers or transcribing platforms or transcribing software for amendments. The transcripts will be analyzed to understand the views of healthcare providers and patients on gout action plan. Thematic analysis will be performed by at least 2 study team members after familiarizing with the data. Using grounded theory approach, codes and the respective data extracts will be categorized into broader themes and subthemes to form a coding framework which will be refined iteratively as data from the first 2-3 participants are analyzed. Identification of themes, needs and information will help in creation of prototype of gout action plan. In the event of discrepancies in the coding framework among the study team members, this will be resolved through consensus and if necessary, by engaging another study team member to analyze the data to reach an eventual coding framework.

Computer-assisted qualitative data analysis software Nvivo will be used to help with management and analysis of data.

Quantitative data:

Descriptive statistics will be generated for the baseline characteristics of the study participants, and frequencies and percentages will be presented for categorical variables while mean and standard deviation will be presented for continuous variables.

To assess effectiveness of gout action plan, the continuous outcome between the two groups will be compared using independent t-test. When outcomes are categorized into binary outcomes, Chi-square test will be performed. The baseline outcomes will also be assessed with demographic using either Chi-square test or Fisher's Exact test for categorical variables, and independent t-test or ANOVA for continuous variables to ensure both groups are comparable. Multivariate linear regression model will be performed with each outcome below and the following covariates to determine effectiveness of the intervention: intervention (gout action plan), baseline outcome and any demographic factors with a p-value of less than 0.1 in the bivariate analysis. All

analyses will be performed using SPSS software version 29.0. A p-value of less than 0.05 is considered to be statistically significant.

9. DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

The study team will permit study-related monitoring, audits and/or IRB review and regulatory inspection(s), providing direct access to source data/document.

10. QUALITY CONTROL AND QUALITY ASSURANCE

The study team will perform data and safety monitoring to ensure adherence with the protocol. The study team will be responsible for the evaluation of data quality and monthly review of the collected data.

11. ETHICAL CONSIDERATIONS

This study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with the Good Clinical Practice and the applicable regulatory requirements.

This final Study Protocol, including the final version of the Participant Information and Consent Form, must be approved in writing by the Centralised Institutional Review Board (CIRB), prior to enrolment of any patient into the study.

The principal investigator is responsible for informing the CIRB of any amendments to the protocol or other study-related documents, as per local requirement.

11.1. Informed Consent

After an initial verbal explanation, potential participants will be given patient information sheet and consent forms to bring home and to think about their participation before the signing of the consent form on the day of the interview or focus group discussion. The initial place for verbal consent will be in the consultation room in the clinic, where privacy of patients and quiet environment is assured. The written consent will be taken in a quiet room on the day of the interview or focus group discussion to ensure privacy. Adequate time will be given to the participants to think through their decision and clarify accordingly. The person taking the consent of a patient will not be the treating physician or the treating healthcare worker of the patient. The person taking the consent of a physician will not be the direct superior of the physician.

11.2. Confidentiality of Data and Patient Records

The study will collect 2 types of research data in both hard and soft copy.
Information from the hard copy (data collection forms, questionnaires and consent forms) will be transcribed to a Microsoft Excel document with password protection. The hard copy documents will be kept in a research folder, stored under lock and key in the polyclinic research room at Pasir Ris polyclinic. The folder will not be taken out of the clinic.
After each interview, the interviewer will transfer the audio-recording to a password-protected corporate laptop and erase it from the audio-recorder. The audio recording will be transcribed verbatim using the research department's transcribing software or transcription platforms (such as transcribe.gov.sg or Note Buddy) or engagement of transcriptionist. All participant identifiers will be removed from the transcript to ensure confidentiality. All transcripts will be checked by interviewer for accuracy. De-identified data will be used for analysis. All the audio files and transcriptions of the recordings will have password encryption and stored in the same password-protected corporate laptop in workplace. Only study members will have access to the password. Information from the data collection form will be transcribed to excel document (with password encryption) in a password-protected corporate laptop in workplace. There will be no USB or removal device used for data storage. The physical consent forms and the electronic data will be kept for 6 years post completion of study. The physical consent forms will be stored in a secure physical archive and the electronic data in an electronic archive. Only the principal investigator and co-investigators will have access to the archives.

12. PUBLICATIONS

The investigators adhere to the ICMJE guidelines for authorship, acknowledgements and review procedures for scientific publications.

The primary author will be the person who drafts the manuscript for publication, and the corresponding author will be the individual who takes primary responsibility for communication with the journal during manuscript submission, peer review, and publication process, and ensures that all the journal's administrative requirements, such as providing details of authorship, ethics committee approval, and gathering conflict of interest forms and statements, are properly completed, although these duties may be delegated to one or more co-authors.

13. RETENTION OF STUDY DOCUMENTS

Records for all participants, including CRFs, all source documentation (containing evidence to study eligibility, history and physical findings, laboratory data, results of consultations, etc.) as well as IRB records and other regulatory documentation will be retained by the PI in a secure storage area in the clinic with lock and key access. The records should be accessible for inspection and copying by authorized authorities. Research data will be stored in institution issues PC or drive for 6 years before they are deleted when the study is completed.

14. FUNDING AND INSURANCE

SingHealth Polyclinics Research Seed Fund is applied and pending approval. PI will look for other sources of fund if the SHP Seed Fund is not approved.

List of Attachments

Appendix 1 – References

1 Dehlin M, Jacobsson L, Roddy E. Global epidemiology of gout: prevalence, incidence, treatment patterns and risk factors. *Nature Reviews Rheumatology 2020 16:7* 2020; **16**: 380–390.

2 He Q, Mok TN, Sin TH, Yin J, Li S, Yin Y *et al.* Global, Regional, and National Prevalence of Gout From 1990 to 2019: Age-Period-Cohort Analysis With Future Burden Prediction. *JMIR Public Health Surveill* 2023; **9**. doi:10.2196/45943.

3 Teng GG, Ang LW, Saag KG, Yu MC, Yuan JM, Koh WP. Mortality due to coronary heart disease and kidney disease among middle-aged and elderly men and women with gout in the Singapore Chinese Health Study. *Ann Rheum Dis* 2012; **71**: 924.

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