ASIA PACIFIC LEAGUE OF ASSOCIATIONS FOR RHEUMATOLOGY (APLAR) LONGITUDINAL PROSPECTIVE COHORT STUDY: CLINICAL SCENARIO STAGE ASSOCIATION WITH GOUT

APLAR Scientific Committee Head and Members

Abstract

Purpose – The purpose of this registry is to perform a longitudinal prospective cohort study on gout and to create a baseline description of gout patients in various countries in the Asia-Pacific region. It will analyze the different clinical characteristics of patients with gout, their respective Clinical Scenario Stages. It will include the associated health risks, links and treatments involved with gout across all its clinical stages.

Methodology – This longitudinal prospective cohort study will create a gout cohort that will gather baseline clinical characteristics from gout patients and follow them over one year. Patients' characteristics, risk factors, disease course, and management will be gathered by a rheumatologist or rheumatologist-guided research associate using an online questionnaire accessed from the APLAR website. Data will be grouped and analyzed according to the different Clinical Scenario Stages. Descriptive statistics will analyze demographic and clinical profiles. Frequency/percentages will be used to present categorical data; and, Spearman's Rank Correlation will determine relationships.

Output – The study will determine the baseline clinical characteristics of patients with gout, the time to develop gouty arthritis, the relative risk and attributable risk of Clinical Scenario Stages to develop acute gouty flares and treatment response.

Introduction

Gout is one of the most common inflammatory arthritides affecting man today. It is characterized as a crystal-deposition disease of the joints resulting from chronic elevation of serum urate, presenting as recurrent attacks of acute inflammatory arthritis. Elevated serum urate levels eventually result in monosodium urate deposition in soft tissue and organs. Gout is also noted as the most prevalent inflammatory arthritis in the Asia-Pacific region (Table 1).[1] In 2021, the Asia-Pacific League of Associations for Rheumatology published guidelines for gout management, taking into account the different data and experiences available in the different representative countries.

To properly approach gout in the Asia-Pacific setting, physicians need local gout data to learn more about patients' clinical characteristics, response to medical management, and treatment outcomes. This study uses the different phases of gout as identified by the American College of Rheumatology ("ACR"). The ACR Core Expert Panel created the nine fundamental Clinical Case Scenario/Stage (CCS) during the formation of the 2012 ACR Guidelines for Management of Gout. The CCS reflect the broad differences in the severity of gout and its clinical manifestations. Each clinical scenario exhibits differences in the frequency of symptoms in a year and the presence or extent of chronic findings such as tophi or synovitis.

Table 1. Prevalent Cases, Incident Cases, YLD for Gout in 2017, According to Global Burden of Disease Region*

	Prevalence (95% UI)			Incidence (95% UI)			YLD (95% UI)		
	Count	Age-standardized rate	Percentage change in age-standardized rates between 1990-2017	Count	Age-standardized rate	Percentage change in age-standardized rates between 1990-2017	Count	Age-standardized rate	Percentage change in age-standardized rates between 1990-2017
High-income Asia Pacific	2,593,043 (2,293,599, 2,918,958)	734.6 (652.3, 830.7)	10.6 (8.9, 12.3)	391,556 (341,950, 451,234)	117.1 (103.4, 133.6)	6.3 (4.6, 8)	80,727 (54,585, 111,296)	23.3 (15.5, 32.2)	10.5 (6.8, 14.3)
Australasia	535, 419 (477,579, 600,300)	1,206.4 (1,080.3, 1,350.1)	19.1 (13.9, 24.6)	70,262 (61,605, 80,523)	166.4 (146.6, 189.3)	11.1 (6.1, 16.3)	16,386 (11,174, 22,385)	37.3 (25.2, 51)	18.9 (9.7, 28.8)
Central Asia	352,626 (310,802, 399,205)	446.7 (395.5, 502.8)	9.9 (7.8, 12.4)	70,352 (61,658, 80,263)	86.4 (76.2, 98.7)	8.2 (5.9, 10.7)	11,032 (7,435, 15,197)	13.8 (9.4, 18.9)	10 (4.2, 16.2)
South Asia	6,491,977 (5,736,346, 7,319,184)	458.5 (405.77, 515.5)	2.6 (1.4, 3.7)	1,312,865 91,153,284, 1,497,965)	90.4 (79.6, 102.9)	1.7 (0.5,3)	201,650 (135,764, 276,521)	14.1 (9.6, 19.3)	3.1 (0.2, 6.1)
Southeast Asia	2,827,170 (2,495,901, 3,183,085)	449.3 (397.7, 504.2)	7.9 (6.2, 9.6)	565,700 (495,511, 643,941)	88.5 (77.9, 100.6)	6.5 (4.9, 8.2)	89,153 (59,596, 123,546)	14 (9.5, 19.3)	8.3 (4.4, 12.7)
East Asia	8,779,696 (7,719,051, 9,915,127)	429.4 (379.5, 482.2)	7 (5.6, 8.2)	1,730,978 (1,511,884, 1,984,235	84.9 (74.9, 96.2)	6.2 (4.8, 7.4)	89,153 (59,596, 123,546)	14 (9.5, 19.3)	8.3 (4.4, 12.7)

*YLD = years lived with disability; GBD = Global Burden of Disease study; 95% UI = 95% uncertainty interval

The nine different CCS can be viewed as a spectrum of gout with CCS 1 being the mildest and CCS 9 – the most severe (Figure 1). The CCS is used in the study to examine the full range of gout that patients may experience. From data derived from this and future studies, individualized therapy may be based on each CCS or CCS grouping.

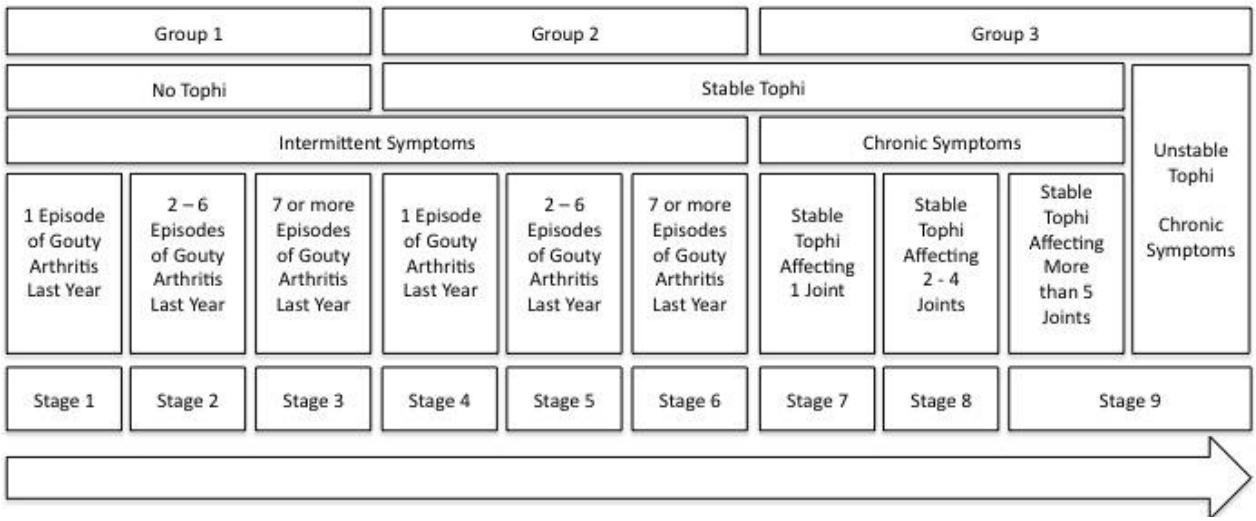

Figure 1. Clinical Case Scenario/Stage

There are 3 distinct groups of CCS: Group 1) no tophi on physical examination but with intermittent symptoms of gout (CCS 1 – 3); Group 2) at least 1 tophi on physical examination with intermittent symptoms of acute gouty arthritis (CCS 4 – 6); and, Group

3) at least 1 tophi on physical examination with chronic joint symptoms due to synovitis attributable to gout, or patients with unstable tophi (CCS 7 – 9).

CCS staging can be done at any time by doctors and would entail proper history taking and physical examination for gout tophi. It is therefore an underutilized tool that can guide doctors in treating gouty arthritis. The analysis of gout by CCS would provide a specific method of identifying risks and treatment appropriate for each CCS or grouping.

This is a longitudinal prospective cohort study on newly diagnosed gout patients seen by the different participating countries. It will collect information on patients' demographic and clinical profile as well as incidence and prevalence of gouty arthritis flares and response to treatment. This study will assess the different CSS, their risk and time to develop gout flares and will determine the effective gout treatment per stage. Following newly diagnosed gout patients, divided into the different CSS, will allow researchers to analyze the development of the disease and relate them to possible associated diseases, risk for gout flares and response to gout treatment.

Related Literature

Gout is primarily a disease of males but may also affect females especially in the postmenopausal age group. Patients are at a higher risk for gout when they have comorbidities such as chronic kidney disease, diabetes and the metabolic syndrome. If left untreated, gout may progress to joint destruction, uric acid deposition in other tissues referred to as tophi, genitourinary stone formation, and kidney failure.

A patient is diagnosed with gout if they achieve sufficient points in the 2015 American College of Rheumatology-European League Against Rheumatism (ACR-EULAR) Gout Classification Criteria.[2] Gout is considered when the patient presents with at least one episode of peripheral joint or bursa swelling, pain or tenderness. Criteria supportive of a gout diagnosis includes the typical pattern of joint involvement (metatarsophalangeal joint involvement), joint characteristics (erythema, exquisite tenderness, loss of function secondary to pain), time course of episodes (complete resolution between symptomatic episodes) and clinical evidence of tophi on physical examination. Laboratory would show elevated serum uric acid and synovial fluid monosodium crystals. Imaging with ultrasound, computed tomography or X-ray is also contributory to a diagnosis of gout when they present with double contour sign, urate deposition and rat-bite erosions respectively (see Appendix A).

Comorbidities associated with gout include obesity, hypertriglyceridemia and glucose intolerance, hypertension and hypothyroidism. Renal insufficiency is more frequently associated with gout; and, certain medications for hypertension, tuberculosis and cancer have been known to exacerbate hyperuricemia and gout. Management of gout should include a thorough evaluation for these conditions and concomitant treatment if indicated.

According to the 2012 ACR Guidelines for Management of Gout,[3,4] the treatment of gout involves patient education on diet, weight loss, lifestyle changes, assessment of co-morbidities and their treatment, and analysis of medications with discontinuation of unnecessary prescriptions. Starting urate lowering medication is indicated in patients with established diagnosis of gout and one of the following: tophi seen physical exam or

imaging, frequent attacks of gout (more than or equal to 2), chronic kidney disease (stage 2 or worse) and a past history of urolithiasis. Anti-inflammatory gout attack prophylaxis may be given concomitantly and includes colchicine, non-steroidal anti-inflammatory drugs (NSAIDs) and/or steroids (see Appendix F).

Health care expenditure in gout patients is expensive. In the United States in 2009, an estimated annual cost of $27 million was due to gout attacks alone.[5] A review conducted using 2005 – 2011 medical data in the United States demonstrated that the national gout-associated expenditure accounted for 24% ($7.7 billion) of all medical expenditures among US adults with gout; and, health care expenditure was more than 2.5 times more increased in patients with gout compared to the entire adult population.[6] These values are expected to grow due to the increasing prevalence of gout.

Objective

General Objective

- To describe patients with gout in the Asia-Pacific using different Clinical Scenario Stages.

Specific Objective

- To define the demographic profile and clinical characteristics including metabolic parameters and cardio-metabolic complications of gout patients in the Asia-Pacific.
- To determine the similarities and differences in diagnostic modalities across Asia-Pacific.
- To determine time from the age of first presentation of gout symptoms to development of current Clinical Scenario Stage.
- To determine the association between uric acid level and Clinical Scenario Stage.
- To determine the risk to develop gout flares among the different Clinical Scenario Stages.
- To determine the responsive treatment for the different Clinical Scenario Stages in gout.
- To determine the responsiveness on urate lowering by treating metabolic comorbidities.
- To determine the choice of first and second line urate lowering therapy across Asia-Pacific

Rationale

Gout patients in Asia Pacific regions have not been comprehensively described. CCS Staging is a relatively fast and free method of determining the current status of a patient diagnosed with gout. The study will help doctors determine the time to develop a CCS from the first presentation of symptoms, and the risk for flare based on CCS Stage. This data will allow doctors to advise patients on the proper treatment for gout as well as push for early management.

Scope and Limitations

The study is limited to patients seen, diagnosed and treated by Rheumatologists in the participating Asia-Pacific countries. It will include newly diagnosed and established gout patients who have a follow-up check-up during the allotted time period of the study.

Methodology

Study Design and Setting – this is a longitudinal prospective, cohort study to be conducted in participating APLAR countries. It will begin on August 1, 2022 and will be conducted for at least 2 years with an initial report after 3 months for streamlining and corroboration of methodology among countries. A biannual review of accumulated data will be published to assess for early trends or for protocol improvements to be incorporated into the study.

The research group will be headed by the APLAR Gout Steering Committee composed of members of the APLAR Gout SIG. Their role is to:

- assess and approve, or reject plans and changes to methodology
- select or approve APLAR Gout Country Managers, APLAR Gout Center Managers and APLAR Gout Researchers to conduct the study at hospitals and clinics
- monitor study process via monthly committee meeting
- resolve conflicts between parties or changes to methodology
- provide expert input on concerns and issues related to study design
- develop policies and study procedures (ie. Possible Common Situations)
- monitor study quality and data integrity and adjust accordingly
- supervise and approve all data analyses which utilize data from the APLAR registry and their subsequent publications and/or sharing

APLAR Gout Country Managers are the overall country study head. They are Rheumatologists selected or approved by the APLAR Gout Steering Committee and report at least once a month their country's progress. APLAR Gout Country Managers may be members of the APLAR Gout Steering Committee. Rheumatologists in APLAR member countries not yet included in the study may apply to the APLAR Gout Steering Committee to become an APLAR Gout Country Manager. Their role is to:

- suggest plans or changes to methodology if needed as per their countries needs
- select and oversee APLAR Gout Researchers conducting the study at hospitals or clinics
- report study process/data at least monthly
- carry out resolutions or changes to methodology
- monitor study quality and adjust accordingly

APLAR Gout Center Managers are in-charge of conducting the study in a Hospital or Clinic. They are Rheumatologists selected by the APLAR Gout Country Manager and they may recruit APLAR Gout Researchers to assist in running the study in their respective center. They report at least once a month their center's progress. APLAR Gout Center Managers may be an APLAR Gout Country Manager. Their role is to:

- suggest plans or changes to methodology if needed as per their center's needs
- select and oversee APLAR Gout Researchers conducting the study at hospitals or clinics
- report study process/data at least monthly
- carry out resolutions or changes to methodology
- monitor study quality and adjust accordingly

APLAR Gout Researchers are Rheumatologists or research associates closely guided by Rheumatologists. They are selected by or may be the APLAR Gout Center Manager. Their role is to:

- conduct the study efficiently, consistently and in a timely manner
- enter data into the online APLAR data collection tool
- report study process/data at least monthly
- carry out resolutions or changes to methodology
- monitor study quality and adjust accordingly

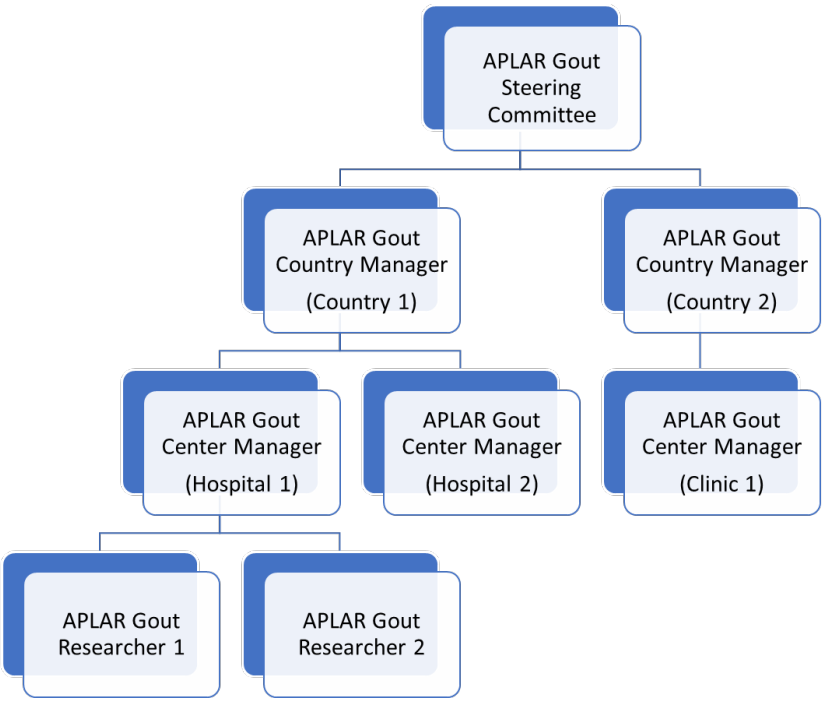

Figure 2. The APLAR Gout Study Committee Framework

Selection Criteria:

Inclusion Criteria –

Adult patients, aged 18 or older

Physician-diagnosed gout (newly diagnosed or established cases)

Patient must be managed and followed by APLAR Gout Center Managers or Researchers

Exclusion Criteria –

Patients initially diagnosed with gout but the gout diagnosis is later changed to another form of arthritis (e.g., patient initially diagnosed with gout but later changed to calcium pyrophosphate (CPP) arthritis following CPP crystal identification).

Methodology Flowchart:

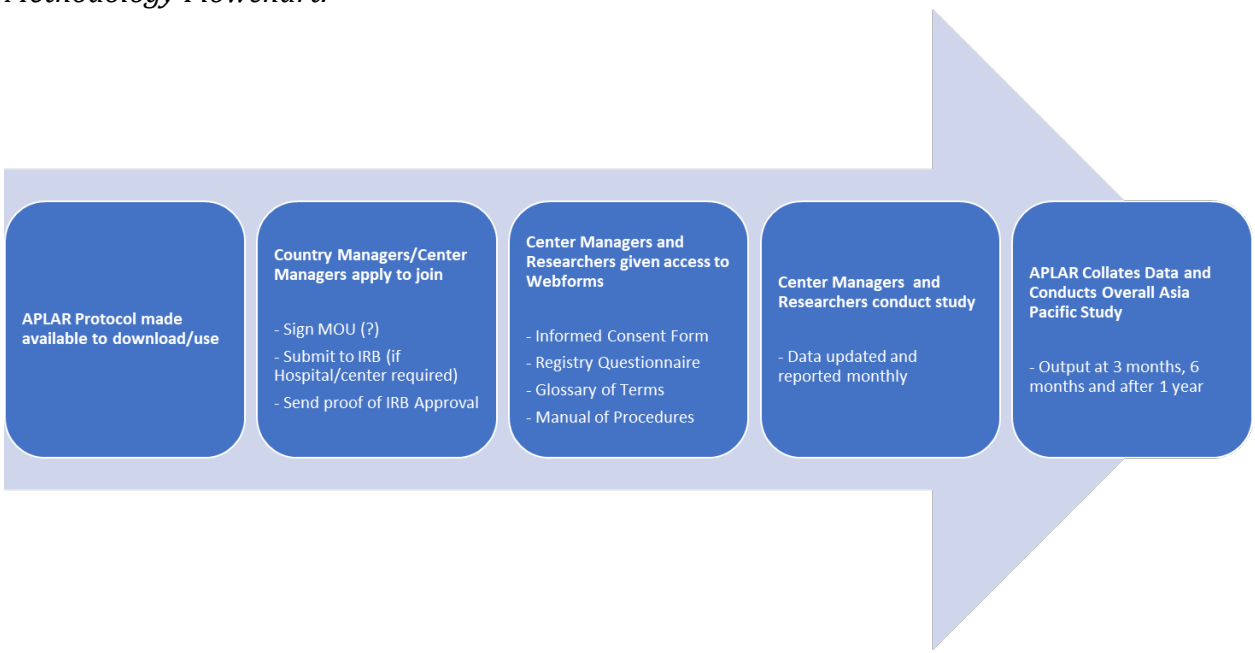

Figure 3. Methodology

Study Proper and Data Collection:
A zoom meeting will be held where APLAR Gout Researchers are trained on the nomenclature of study terms, methodology flowchart and informed consent and survey form answering.

The study will include all patients diagnosed with gout in hospitals or clinics included in the study. Patients will be invited to join. Taking part is purely voluntary and patients may opt not to be included in the study.

Doctors will explain the gout study and get informed consent from their patients (Appendix G and H). Once consent is given, patients will be assigned a special code to protect their confidentiality (Country number - center number - year recruited - Patient Number: XX-XX-XX-XXX). The unique clinic number and patient number will be used to identify patients and will be kept confidential. Patients' initials and birthday will only be written on the consent form and will serve as identifiers to prevent doubling of data. Doctors will then complete the survey form per patient. Each patient's survey form data will be stored inside a designated folder inside the rheumatologist's clinic for storage and safekeeping. Data will be uploaded online via the APLAR Gout Registry website portal.

Informed Consent (Appendix G and H):
Participants shall only be included in the study once the consent is given and the consent form filled up and signed. The purpose, procedure and confidentiality shall be explained in detail by the investigators of the study either in English or their native language. Consent forms should be available in both English and their native language. The doctors will answer any concerns and questions of the participants and shall ensure that they completely understand the content of the consent forms before signing. If the patient cannot sign the consent form, a relative or duly appointed guardian may sign for the patient after they have undergone an informed consent process. No questions will be asked if a patient decides to withdraw anytime during the study. If they decide to

withdraw, consent will be sought and an additional consent form signed, if the gathered data prior to withdrawal can be included in the data analysis.

Patients' Survey Forms (Appendix I, J, K and L):
The patients' survey form is composed of 4 parts: Part I – Patient Characteristics Form (Appendix I), Part II – Clinical Scenario Staging Form (Appendix J), Part III – First Consult Form Appendix K) and Part IV – Follow-up Consult Form (Appendix L).

Parts I to III of the survey form will be completed on joining the Gout Cohort Study during the first consultation; and, Part IV will be accomplished on follow-up. A new Part IV survey form will be completed and recorded on every subsequent visit.

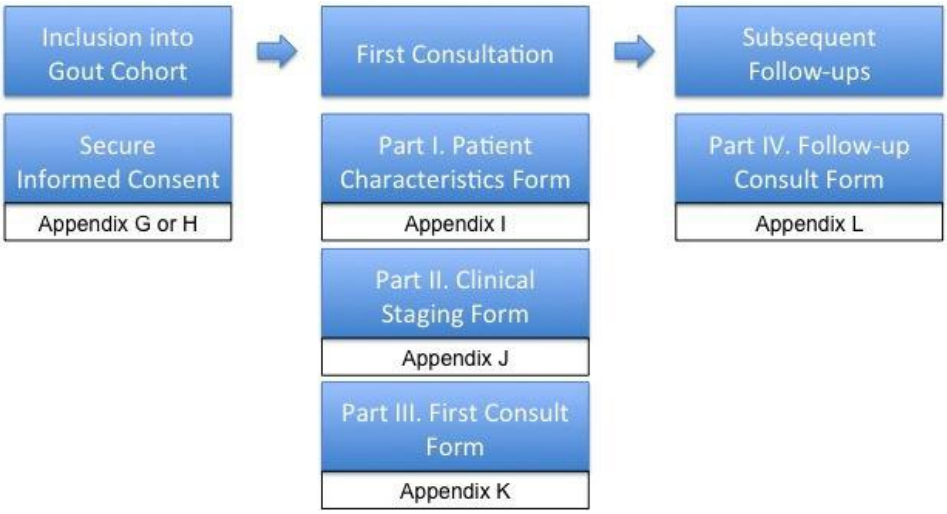

Figure 4. Data Collection.

Part I. Patient Characteristics Form (Appendix I):
Part I of the survey will assess the patient's baseline characteristics. It will collect data from the patient by the interviewing doctor filling up the survey form. Data would include comorbidities, family history of disease and gout data on age of diagnosis, initial manifestations, previous check-ups, and medications and procedures.

Part II. Clinical Scenario Staging Form (Appendix J):
The doctor will complete the Part II Clinical Scenario Staging Form after conducting a physical examination and questioning of the number of gout symptoms experienced during the past year. This is to determine the Clinical Scenario Stage of the patient.

The 9 fundamental Clinical Case Scenarios were created by the ACR Core Expert Panel during the formation of the 2012 ACR Guidelines for Management of Gout (Figure 4). The clinical case scenarios reflect the broad differences in the severity of gout and its clinical manifestations. Each clinical scenario exhibited differences in the frequency of acute gout symptoms in a year and the presence or extent of chronic findings such as tophi or synovitis. There are 3 distinct groups of clinical scenarios: 1) no tophi on physical examination but with intermittent symptoms of gout (Appendix B – A, case 1 – 3); 2) at least 1 tophi on physical examination with intermittent symptoms of acute gouty arthritis (Appendix B – A, case 4 – 6); and, 3) at least 1 tophi on physical examination with chronic joint symptoms due to synovitis attributable to gout (Appendix B – B, case 7 – 9).

Intermittent symptoms are defined as gout symptoms of pain and inflammation that occurs at irregular intervals. It is not continuous or steady and can also be described as sporadic, isolated or patchy.

Chronic joint symptoms due to synovitis attributable to gout are described as persistent and long standing, lasting 6 or more weeks. They are unabating and with long-lasting pain and inflammation even if treated with anti-inflammatory agents. Chronic symptoms are unstable if one or more tophi present with drainage, aggressive mass or connective tissue destructive effects, high risk of infection, very rapid growth or with severe, tophaceous joint inflammation.

The Clinical Scenario Flowchart (Figure 4) will assist in determining a patient's Clinical Scenario Stage. The doctor will follow the flowchart with the corresponding answers derived from the patient interview and physical examination.

The first step is to assess whether a patient has any tophi on physical examination. If the patient has no tophi, the frequency of symptoms experienced during the past year will determine their Clinical Scenario Stage.

Stage 1 – patients with no tophi with 1 episode of gouty arthritis symptoms in the past year.

Stage 2 – patients with no tophi with 2 – 6 episodes of gouty arthritis symptoms in the past year.

Stage 3 – patients with no tophi with 7 or more episodes of gouty arthritis symptoms in the past year.

If the patient has tophi, the next step is to determine if the patient experiences chronic or intermittent gouty symptoms. Patient with intermittent symptoms are assessed on the frequency of symptoms experienced during the past year.

Stage 4 – patients with tophi with intermittent gouty arthritis symptoms experienced in 1 episode in the past year.

Stage 5 – patients with tophi with intermittent gouty arthritis symptoms experienced with 2 – 6 episodes in the past year.

Stage 6 – patients with tophi with intermittent gouty arthritis symptoms experienced with 7 or more episodes in the past year.

If the patient has tophi with chronic symptoms of gouty arthritis, the tophi are examined to assess their stability. Unstable tophi exhibit drainage, destructive effects/deformities, high risk of infection/oozing/bleeding tophi, rapid growth or severe inflammation. Patients with stable tophi are examined to determine the number of joint involvement.

Stage 7 – patients with stable tophi with chronic gouty arthritis symptoms affecting only 1 joint.

Stage 8 – patients with stable tophi with chronic gouty arthritis symptoms affecting 2 to 4 joints.

Stage 9 – patients with stable tophi with chronic gouty arthritis symptoms affecting 5 or more joints.

Patients with unstable tophi are immediately graded with the highest Stage 9.

Stage 9 – patients with unstable tophi with chronic gouty arthritis symptoms.

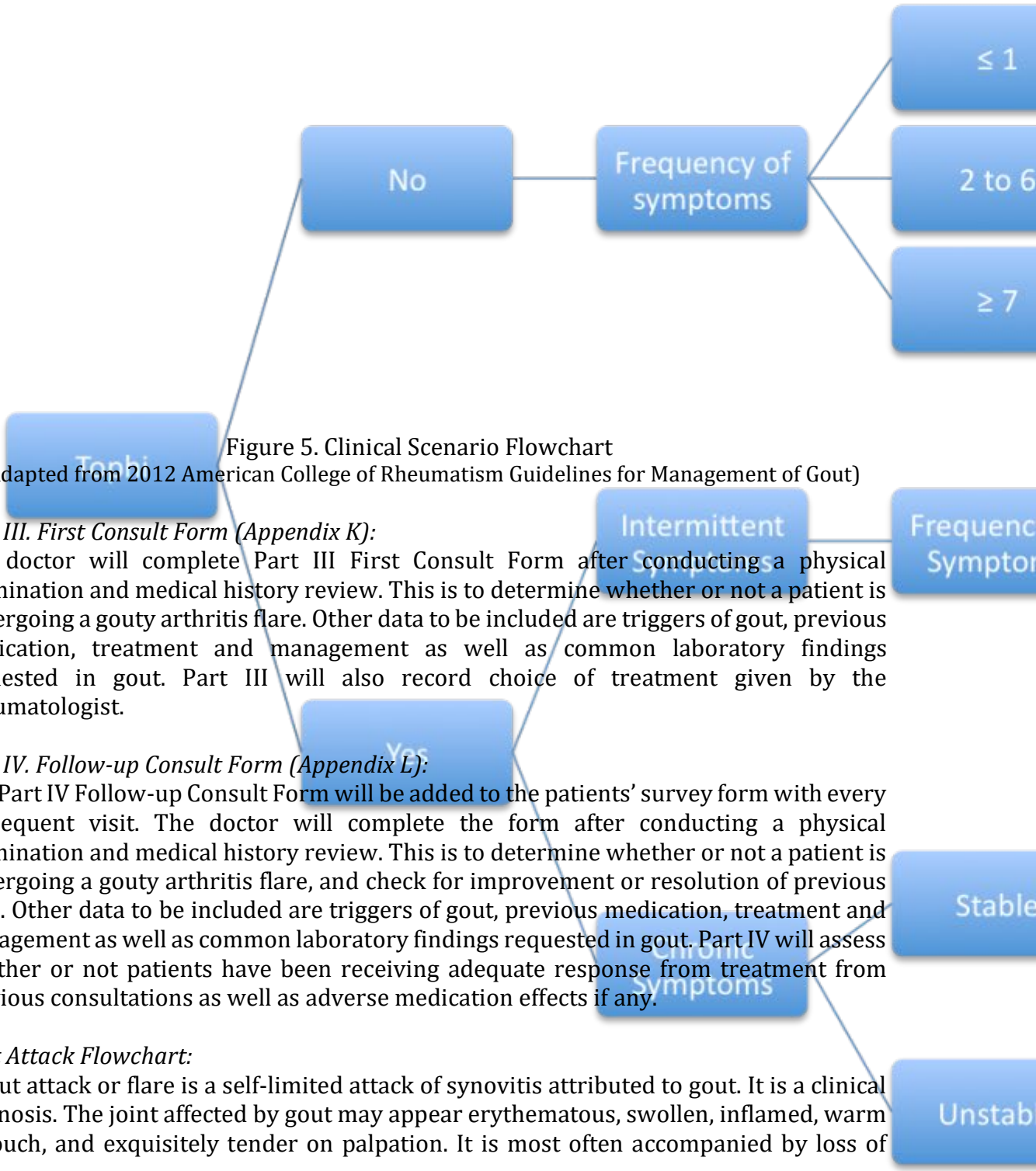

Figure 5. Clinical Scenario Flowchart
(Adapted from 2012 American College of Rheumatism Guidelines for Management of Gout)

Part III. First Consult Form (Appendix K):
The doctor will complete Part III First Consult Form after conducting a physical examination and medical history review. This is to determine whether or not a patient is undergoing a gouty arthritis flare. Other data to be included are triggers of gout, previous medication, treatment and management as well as common laboratory findings requested in gout. Part III will also record choice of treatment given by the Rheumatologist.

Part IV. Follow-up Consult Form (Appendix L):
The Part IV Follow-up Consult Form will be added to the patients' survey form with every subsequent visit. The doctor will complete the form after conducting a physical examination and medical history review. This is to determine whether or not a patient is undergoing a gouty arthritis flare, and check for improvement or resolution of previous flare. Other data to be included are triggers of gout, previous medication, treatment and management as well as common laboratory findings requested in gout. Part IV will assess whether or not patients have been receiving adequate response from treatment from previous consultations as well as adverse medication effects if any.

Gout Attack Flowchart:
A gout attack or flare is a self-limited attack of synovitis attributed to gout. It is a clinical diagnosis. The joint affected by gout may appear erythematous, swollen, inflamed, warm to touch, and exquisitely tender on palpation. It is most often accompanied by loss of

function of the joint or decreased range of motion due to pain. Patients will be evaluated for gout flare on each consult.

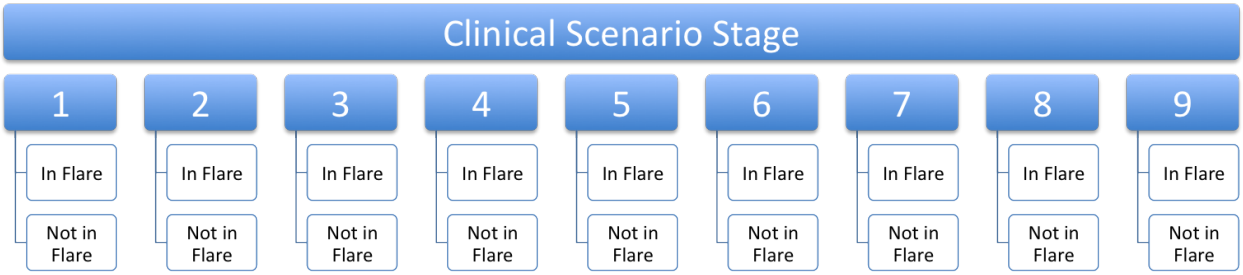

Figure 6. Acute Gout Attack Flowchart

Gout Attack Scoring (Appendix K and L):
Patients in gout flare will be assessed on the severity of the gout attack. It will include the following: 1) intensity of the attack graded from 1 – 10 based on visual analog scale (mild, moderate, or severe), 2) duration of gout attack since onset (Early – less than 12 hours after onset, Well-established – 12 to 36 hours after onset, or Late – more than 36 hours after onset), and 3) extent or number of joints involved in the attack (one or a few small joints, 1 or 2 large joints, or Polyarticular – 4 or more joints) (Figure 6).

Severity of Gout Attack Intensity of Attack Based on Visual Analog Scale (0-10)	
Mild	Less than or equal to 4
Moderate	5 to 6
Severe	More than or more than 7

Duration of Gout Attack Since Onset	
Early	Less than 12 hours after attack onset
Well-established	12 to 36 hours after onset
Late	More than 36 hours after onset

Extent of Gouty Arthritis Attack
One or a few small joints
1 or 2 large* joints *defined as: ankle, knee, wrist, elbow, hip, shoulder
Polyarticular -4 or more joints, with arthritis involving more than 1 region** **Region defined as: forefoot (MTP, toes), midfoot (tarsal), ankle/hindfoot, knee, hip, fingers, wrist, elbow, shoulder, other -Attack involving 3 separate large joints is considered as a form of polyarticular gout

Figure 7. Gout Attack Scoring

Gout Flare Resolution:
Gout flare resolution is defined as the complete disappearance of pain, erythema, swelling and tenderness as well as return of joint function. Complete resolution is improvement with pain scale 0/10 from previously elevated levels. In treating gout flare, the target pain scale after medication is a decrease of pain by at least half from the pain score at the height of the gout flare. Pain scale decreased but by less than half shows a lack of improvement. It may represent a possible need for additional treatment or prolonged management.

Data Collection and Analysis:
Gout cohort data will be compiled and checked every week by the principal investigator to assess for errors. Data will be analyzed after every month.

Gout cohort output will assess the demographic profile of patients, census of the different clinical scenarios of gout, treatment being given, and baseline laboratory. The baseline characteristics of patients by gender and by clinical scenario will also be analyzed. Gout cohort data will be considered as joint property of the Hospital or Center and APLAR. Data will be stored for a minimum period of 5 years as reference.

Statistical Analysis:
Descriptive statistics such as mean and standard deviation will present the data on demographic and clinical profile of the recruited subjects. Frequency and percentages will be used to present categorical data. Spearman's Rank correlation will determine relationships of some variables. A p-value <0.05 will be considered significant.

Outcome Measures
Means, standard deviations, proportions, relative risk ratio, and attributable risk ratio will be used to describe and summarize the data. Data will be analyzed based on gender, clinical scenario, and concomitant gout flare.

Table 2: Sample Raw Baseline Patient Characteristic Data

	1	2	3	4	5	6	7
Patient Code							
Race							
Age (years)							
Male							
Female							
Height							
Weight							
BMI							
Comorbidities:							
Personal Social History:							
Family History:							
Age of first symptoms							
Age at first consult							
Age at diagnosis							
Initial Joint Involvement							
Diagnosed by:							
Previous Procedure (Age):							
Medication previously taken for gout:							
Other Medication taken:							
Gout Medication given by:							

Table 3: Raw Baseline Clinical Scenario Staging

	1	2	3	4	5	6	7
Patient Code							
Number of tophi							
Tophi exhibits drainage, destructive effects/deformity, high risk of infection, rapid growth or severe inflammation (0 - No, 1 - Yes)							
Frequency of symptoms per year							
Clinical Scenario Stage							

Table 4. Demographic and Clinical Characteristics (n =)

	Median (Range); Mean ± SD
Age, years	
Age at symptom onset, years	
Age at first check-up, years	
Age at diagnosis, years	
BMI (kg/m^2)	
Weight (kg)	
Height (cm)	
	Number, Frequency (%)
Sex	
Male	
Female	
Comorbidities	
Hypertension	
Chronic kidney disease	
Diabetes mellitus	
Coronary heart disease	
Dyslipidemia	
Nephrolithiasis	
Stroke	
Metabolic syndrome	
Menopause	
Blood dyscrasia	
Cancer	
Hypothyroidism	
Tuberculosis	
Medication	
Anti-hypertensive	
Lipid lowering drug	
Anti-diabetic	
Diuretic	
Anti-tuberculosis	
Family history	
Hypertension	
Diabetes mellitus	
Gout	
Coronary heart disease	
Dyslipidemia	
Cancer	
Chronic kidney disease	
Blood dyscrasia	
Personal and social history	
Smoker	
Alcohol beverage drinker	

Table 5. Age at First Symptoms and Clinical Case Scenario Distribution

Age at first symptoms	Total	CCS1	CCS2	CCS3	CCS4	CCS5	CCS6	CCS8	CCS9	A (1-3)	B (4-6)	C (7-9)
15-19												
20-24												
25-29												
30-34												
35-39												
40-44												
45-49												
50-54												
55-59												
60-64												
65-69												
70-74												
>75												
Total												

Table 6. Time Periods by Clinical Scenario (1-9)/Disease Groups (A, B, C)

	A (N =)			B (N =)			C (N =)		
	CS1	CS2	CS3	CS4	CS5	CS6	CS7	CS8	CS9
	(n=)	(n=)	(n=)	(n=)	(n=)	(n=)	(n=)	(n=)	(n=)
Diagnosed on First Consult									
Total =									
Consulted on First Symptoms									
Total =									
Diagnosed on First Symptoms									
Total =									

Table 7. Disease Duration to Diagnosis among CCS (1-9) / Disease Groups (A-C)

Disease Duration to Diagnosis	CS1	CS2	CS3	CS4	CS5	CS6	CS8	CS9	A (CSS1-3)	B (CSS4 - 6)	C (CSS7-9)
	(n =)	(n =)	(n =)	(n =)	(n =)	(n =)	(n =)	(n =)	(n =)	(n =)	(n =)
	Frequency (%)										
Early (≤2 years)											
Established (>2 years)											

Table 8. Gout History (n =)

	Number, Frequency (%)
Diagnosis by	
Rheumatologist	
Internal medicine	
General practitioner	
Surgeon/orthopedics	
Family medicine	
Non-medical practitioner	
Other allied health practitioner	
Unrecalled	
Previous procedures	
Arthrocentesis	
Intra-articular (IA) steroid injection	
Arthrocentesis + IA steroid injection	
Debridement, debulking, or excision	
Medications previously taken	
NSAID	
Unrecalled	
Diclofenac	
Celecoxib	
Mefenamic	
Etoricoxib	
Diclofenac + Celecoxib	
Diclofenac + Etoricoxib	
Celecoxib + Etoricoxib	
Celecoxib + Diclofenac + Mefenamic	
Urate lowering agent	
Allopurinol	
Febuxostat	
Allopurinol + Febuxostat	
Colchicine	
Steroid	
Tramadol	
Herbal/Alternative medication	
Paracetamol	
Unrecalled	
Prescriptionist	
Rheumatologist	
Internal medicine	
General practitioner	
Family medicine	
Surgeon/orthopedic	
Unrecalled	
Non-medical practitioner	

Table 9. Identified Gout Flare Triggers (n=)

	Number, Frequency (%)
Number of Identified Triggers	
0	
1	
2	
3	
4	
Flare Triggers	
Food	
Alcohol beverages	
Hospitalization	
Infection	
Blood loss/transfusion	
Allopurinol	
Febuxostat	
Dialysis	
Anti- tuberculosis drugs	
Diarrhea	
Psoriasis	
Surgical procedure	
Unknown	

Table 10. Overall Initial Joint Involvement

Joint Location	Number, Frequency (%)
Ankle	
First metatarsophalangeal	
Knee	
Midfoot	
Toe	
Elbow	
Wrist	
Metacarpophalangeal	
Finger	
Shoulder	
Spine	

Table 11. Joint Involvement on Presentation

Monoarthritis (1 joint) [n = number, frequency]
Ankle
First metatarsophalangeal
Knee
Midfoot
Others:*
Oligoarthritis (2-3 joints) [n = number, frequency
Ankle
First metatarsophalangeal
Knee
Toe
Midfoot
Others:**
Polyarthritis (4 or more) [n = number, frequency]
First metatarsophalangeal
Ankle
Elbow
Toe
Knee
Midfoot
Wrist
Metacarpophalangeal

*Finger, toe, elbow, wrist, metacarpophalangeal
**Wrist, elbow, metacarpophalangeal, shoulder

Table 12. Patient Distribution by Clinical Case Scenario and Group (n=)

Group	CCS	Tophi	Symptom interval		CCS Frequency (%)	Group Frequency (%)
A	1	None	Intermittent	1 attack in the past year		
	2			2-6 attacks in the past yea		
	3			≥7 attacks in the past year		
B	4	Stable	Intermittent	1 attack in the past year		
	5			2-6 attacks in the past yea		
	6			≥7 attacks in the past year		
C	7	Stable	Chronic*	Stable tophi in 1 joint		
	8			Stable tophi in 2-4 joints		
	9			Stable tophi in ≥5 joints		
		Unstable**				

*Persistent symptoms lasting 6 or more weeks

**Could be one or more of the following: drainage, destructive effects/deformity, high risk for infection, rapid growth, severe inflammation.

Table 13. Tophi Characteristics

Group	CCS	Tophi	Symptom Interval	Tophi Frequency (n=)		Tophi Chronicity (n=)		Tophi Stability (n =)	
A	1 2 3	None	Intermittent	No Tophi		----	----	----	----
B	4 5 6	Stable	Intermittent	Tophi		Intermittent		Stable	
C	7 8 9	Stable	Chronic*			Chronic* + Unstable**			
		Unstable**	Chronic*					Unstable **	

*Persistent symptoms lasting 6 or more weeks

**Could be one or more of the following: drainage, destructive effects/deformity, high risk for infection, rapid growth, severe inflammation.

Table 14. Prevalence of Tophi Formation and Disease Duration

Disease duration (years)	No. of patients	Cases with tophi		Cases with unstable* tophi	
		No.	Percent	No.	Percent
5 or less					
6 to 10					
11 to 20					
21 or more					
Total					

*Could be one or more of the following: drainage, destructive effects/deformity, high risk for infection, rapid growth, severe inflammation.

Table 15. Comparison by Tophi

	Current Age				Age at First Symptoms				Time First Symptoms to Current CCS			
	Median	Mode	Range	Mean + SD	Median	Mode	Range	Mean + SD	Median	Mode	Range	Mean + SD
Gout Patients (n = total)												
No Tophi (n =)												
Tophi (n =)												
Intermittent (n =)												
Chronic* + Unstable** (n =)												
Stable (n =)												
Unstable** (n =)												

*Persistent symptoms lasting 6 or more weeks

**Could be one or more of the following: drainage, destructive effects/deformity, high risk for infection, rapid growth, severe inflammation.

SD - Standard Deviation

Table 15. Comparison by Tophi (Continued)

	Initial Joint Involvement Number			Comorbidty				
	1 Joint	2 - 3 Joints	≥4 Joints	HPN	CKD	DM	CHD	Stroke
Gout Patients (n = total)								
No Tophi (n =)								
Tophi (n =)								
Intermittent (n =)								
Chronic* + Unstable** (n =)								
Stable (n =)								
Unstable** (n =)								

*Persistent symptoms lasting 6 or more weeks

**Could be one or more of the following: drainage, destructive effects/deformity, high risk for infection, rapid growth, severe inflammation.

HPN – Hypertension, CKD – Chronic Kidney Disease, DM – Diabetes Mellitus, CHD – Coronary Heart Disease

Table 16. First Consultation Findings (n =)

	Frequency (%); Median (Range)
Days from previous flare	
Flare resolution	
Spontaneous	
Medicated	
Days for flare resolution	
Spontaneous	
Medicated	
Diagnostic modality	
Clinical	
Crystal	
Ultrasound	
X-ray	
Unreported	
Medicines taken prior to consult	
Colchicine	
Oral NSAIDs	
Allopurinol	
Febuxostat	
Steroid	
Paracetamol	
Tramadol	
Herbal	
Tramadol + Paracetamol	
Topical NSAIDs	
Prescriptionist	
Rheumatologist	
Internal Medicine	
Non-medical practitioner	
General practitioner	
Surgeon/Orthopedist	
Family medical doctor	
Obstetrician-gynecologist	
Unrecalled	
Compliance to medication	
Laboratory	
Hemoglobin (g/L) [n=]	
Hematocrit [n=]	
WBC (K/uL) [n=]	
Platelets (K/uL) [n=]	
ALT (IU/L) [n=]	
AST (IU/L) [n=]	
FBS (mmol/L) [n=]	
HBA1c [n=]	

Table 17. Non-Medical Practitioner Medication (n =)

	Number, Frequency (%)
Unrecalled NSAIDs	
Unrecalled NSAIDs + Steroid	
Steroid + Colchicine	
Colchicine + Paracetamol	
Herbal	

Table 18. Overall Medical Course (n =)

	Number, Frequency (%)		
Management	**Outpatient** (n =)	**Admitted** (n =)	**Total**
Treatment during consult/referral			
Colchicine			
Allopurinol			
Febuxostat			
Oral NSAIDs			
Oral steroids			
Tramadol + Paracetamol			
Paracetamol			
Tramadol			
Losartan			
Arthrocentesis			
Intravenous steroids			
Intra-articular steroids			
Topical NSAIDs			
Fenofibrate			
Others			
Education			

NSAID, nonsteroidal anti-inflammatory drug.

Table 19. Gouty Flare on First Consult (n =)

Involved joints	**Number, Frequency (%)**
1 or few small	
1−2 large*	
Polyarticular**	
Pain (Visual Analog Scale 1 - 10)	
Mild <5	
Moderate 5−6	
Severe >6	
Not Reported	
Duration of pain (hours)	
Early <12	
Well Established 12−36	
Late >36	

*Large – ankle, knee, wrist, elbow, hip, shoulder

**4 or more joints, with arthritis involving more than 1 region [forefoot (MTP, toes), midfoot (tarsal), ankle/hindfoot, knee, hip, fingers, wrist, elbow, shoulder, other]. Attack involving 3 separate large joints is considered as a form of polyarticular gout.

Table 20. Medical Course of Patients with Gout Flare (n =)

	Number, Frequency (%)		
Management	**Outpatient** (n =)	**Admitted** (n =)	**Total**
Treatment during consult/referral			
Colchicine			
Allopurinol			
Febuxostat			
Oral NSAIDs			
Oral steroids			
Tramadol + Paracetamol			
Paracetamol			
Tramadol			
Losartan			
Arthrocentesis			
Intravenous steroids			
Intra-articular steroids			
Topical NSAIDs			
Fenofibrate			
Others			
Education			

NSAID, nonsteroidal anti-inflammatory drug.

Table 21. Medical Course of Patients without Gout Flare (n =)

	Number, Frequency (%)		
Management	**Outpatient** (n =)	**Admitted** (n =)	**Total**
Treatment during consult/referral			
Colchicine			
Allopurinol			
Febuxostat			
Oral NSAIDs			
Oral steroids			
Tramadol + Paracetamol			
Paracetamol			
Tramadol			
Losartan			
Arthrocentesis			
Intravenous steroids			
Intra-articular steroids			
Topical NSAIDs			
Fenofibrate			
Others			
Education			

NSAID, nonsteroidal anti-inflammatory drug.

Table 22. First follow-up (n =)

	Frequency (%); Median (Range)
Seen outpatient	
Days from last flare	
Flare on first consult (n =)	
No flare on first consult (n =)	
Days from previous consult	
Flare on first consult (n =)	
No flare on first consult (n =)	
Resolution	
Medicated	
Spontaneous	
Currently in gout attack	
1−2 large joints [n =]	

Table 23. Distribution of Factors for Gout Attacks across Clinical Case Scenario

	1 (n =)	2 (n =)	3 (n =)	4 (n =)	5 (n =)	6 (n =)	7 (n =)	8 (n =)	9 (n =)
	Number, Frequency (%)								
Age at symptom onset, years									
<40									
≥40									
Male									
Hypertension									
BMI									
Underweight									
Normal									
Overweight									
Obese									
Metabolic Syndrome									
Uric acid level (mg/dL)									
Nephrolithiasis									

Table 23. Age at First Symptoms and Sex Distribution

Age	2022		Previous Studies	
Group	Males	Females	Males	Females
15-19				
20-24				
25-29				
30-39				
40-49				
50-59				
60-69				
70-79				
80-89				
Total				

GANTT Chart

APLAR Gout Registry 2022	July-Sept 2022	Sept 2022-Sept 2023	Oct-Nov 2023
Protocol approval			
IRB approval per country			
Data gathering synthesis/month			
Statistical analysis synthesis/month			
Recommendations/Editing of Final Manuscript			

Ethical Considerations

This study will be conducted in accordance with the ethical principles based on the Declaration of Helsinki. The research protocol shall be submitted to the Institutional Review Board of the institution for approval prior to implementation.

In accordance with the data privacy laws of each participating country will be adhered to. Patients' names will not be disclosed outside the research group. Names will only be available to the patient's doctor.

Possible Common Situations:

The following is a list of foreseen circumstances that may hinder the researcher during the study. Listed are the guidelines on how to manage these instances.

Unknown cause of arthritis

When a patient consults for arthritis and is worked up, he/she will only be included in the study when the final diagnosis is gout. If the presenting signs and symptoms are characteristically gout, the patient may be included in the study provided that further work up and symptoms point to gouty arthritis. In the First Consult Form, the "Diagnosis by Clinical" is checked.

Patient determined to be with another cause for arthritis/Misdiagnosed case of gout

If the patient is included in the gout study but is eventually worked up and diagnosed to have a different illness (ex. Rheumatoid arthritis), the patient will be informed of their correct diagnosis and will be advised that he/she will be removed from the study data. The patient will be treated appropriately for the proper diagnosis.

Patient lost to follow-up

"Lost to follow up" is defined as the patient not following up for a scheduled appointment for more than 12 weeks. Any patient lost to follow-up will still be included in the study using data accumulated until they were lost to follow up.

Patient develops multiple gout flares in 1 in-patient admission/referral

For every recurrent gout flare in a prolonged hospitalization situation, it will be analyzed as a new consult for a new gouty flare. All data to be filled up in the Part IV Follow-up Form.

Patient decides to leave from study

If a patient decides to leave from the gout study, no questions will be asked as to why they are leaving and no future data will be collected and recorded. Data collected up to their refusal will only be used in the study if consent has been given and additional consent form signed (Appendix G and H).

Glossary of Terms

Disease elements (14)

MSU crystals - The pathogenic crystals in gout (chemical formula: $C_5H_4N_4NaO_3$)

Urate/serum urate - The circulating form of the final enzymatic product generated by xanthine oxidase in purine metabolism in humans (chemical formula: $C_5H_3N_4O_3^-$)

Hyperuricemia - Elevated blood urate concentration over the saturation threshold (6.8mg/dL)

Gout flare - A clinically evident episode of acute inflammation induced by monosodium urate crystals

Intercritical gout - The asymptomatic period after or between gout flares, despite the persistence of MSU crystals

Chronic gouty arthritis - Persistent joint inflammation induced by MSU crystals

Tophus - An ordered structure of MSU crystals and the associated host tissue response

Subcutaneous tophus - A tophus that is detectable by physical examination

Imaging evidence of monosodium urate crystal deposition - Findings that are highly suggestive of monosodium urate crystals on an imaging test (XRAY, UTZ)

Gouty bone erosion - Evidence of a cortical break in bone suggestive of gout (overhanging edge with sclerotic margin)

Podagra - A gout flare at the 1st metatarsophalangeal joint

Disease states

Gout - A disease caused by MSU crystal deposition with any of the following clinical presentations (current or prior): gout flare, chronic gouty arthritis, or subcutaneous tophus. Gout diagnosis in this study is made by a physician (APLAR Gout Researchers)

Tophaceous gout - Gout with at least one subcutaneous and/or radiographic tophus

Erosive gout - Gout with at least one gouty bone erosion

First gout flare - The first episode of gout flare

Recurrent gout flares - More than one gout flare

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APPENDIX A: ACR-EULAR Gout Classification Criteria

ACR-EULAR GOUT CLASSIFICATION CRITERIA[#]

Entry Criterion (Only apply criteria below to those meeting this entry criterion)		At least one episode of swelling, pain, or tenderness in a peripheral joint or bursa	■Y ■N
Sufficient Criterion (If met, can classify as gout without applying criteria below)		Presence of MSU crystals in a symptomatic joint or bursa (i.e., in synovial fluid) or tophus	■Y ■N
Criteria (to be used if Sufficient Criterion not met): *Score ≥8 required for classification as gout*		**Categories**	**Score**
CLINICAL	**Pattern of joint/bursa involvement during symptomatic* episode(s) ever**	Joint(s) or bursa(e) other than ankle, midfoot or 1st MTP (or their involvement only as part of a polyarticular presentation)	0
		Ankle OR midfoot (as part of monoarticular or oligoarticular episode without MTP1 involvement)	1
		MTP1 (as part of monoarticular or oligoarticular episode)	2
	Characteristics of symptomatic episode(s) ever: i) Erythema overlying affected joint (patient-reported or physician-observed) ii) can't bear touch or pressure to affected joint **iii)** great difficulty with walking or inability to use affected joint	No characteristics	0
		One characteristic	1
		Two characteristics	2
		Three characteristics	3
	Time-course of episode(s) ever: Presence (ever) of ≥2, irrespective of anti-inflammatory treatment: i) Time to maximal pain <24 hours ii) Resolution of symptoms in ≤14 days **iii)** Complete resolution (to baseline level) between symptomatic episodes	No typical episodes	0
		One typical episode	1
		Recurrent typical episodes	2
	Clinical evidence of tophus: Draining or chalk-like subcutaneous nodule under transparent skin, often with overlying vascularity, located in typical locations: joints, ears, olecranon bursae, finger pads, tendons (e.g., Achilles).	Absent	0
		Present	4
LAB	**Serum urate:** Measured by uricase method. Ideally should be scored at a time when the patient was not taking urate-lowering treatment and patient was beyond 4 weeks of the start of an episode (i.e., during intercritical period); *if* practicable, retest under those conditions. The highest value irrespective of timing should be scored.	<4mg/dL [<0.24mM] †	**-4**
		4-<6mg/dL [0.24-<0.36mM]	0
		6-<8mg/dL [0.36-<0.48mM]	2
		8-<10mg/dL [0.48-<0.60mM]	3
		≥10mg/dL [≥0.60mM]	4
	Synovial fluid analysis of a symptomatic (ever) joint or bursa:** Should be assessed by a trained observer.	Not done	0
		MSU negative	**-2**
IMAGING‡	**Imaging evidence of urate deposition in symptomatic (ever) joint or bursa:** Ultrasound evidence of double-contour sign¶ *or* DECT demonstrating urate deposition§.	Absent OR Not done	0
		Present (either modality)	4
	Imaging evidence of gout-related joint damage: Conventional radiography of the hands and/or feet demonstrate at least one erosion.‡‡	Absent OR Not done	0
		Present	4
		TOTAL SCORE	
		CLASSIFY AS GOUT? ■Y	
		(If met sufficient criterion or total score ≥8) ■N	

* Symptomatic episodes are periods of symptoms that include any of swelling, pain, or tenderness in a peripheral joint or bursa.
† If serum urate <4mg/dL (0.24mmol/L), **take away 4 points**; if serum urate ≥4-<6mg/dL (≥0.24mmol/L - <0.36mmol/L), score this item as 0
If polarizing microscopy of synovial fluid from a symptomatic (ever) joint or bursa by a trained examiner fails to show MSU crystals, **take away 2 points. If synovial fluid was not assessed (not done), score this item as 0.
‡ If imaging not available, score these items 0.
¶ Hyperechoic irregular enhancement over the surface of the hyaline cartilage that is independent of the insonation angle of the ultrasound beam (note: false positive DCS (artifact) may appear at the cartilage surface that should disappear with a change in the insonation angle of the probe).[31,32]
§Presence of colour-coded urate at articular or peri-articular sites. Images should be acquired using a dual energy computed tomography scanner, with data acquired at 80 and 140 kV and analysed using gout-specific software with a two material decomposition algorithm which colour-codes urate.[33] A positive scan is defined as the presence of colour-coded urate at articular or peri-articular sites. Nailbed, submillimeter, skin, motion, beam hardening and vascular artefacts should not be interpreted as evidence of DECT urate deposition.[34]
‡‡Erosion is defined as a cortical break with sclerotic margin and overhanging edge; excluding DIP joints and gull wing appearance.

[#]Neogi, et al. *Arthritis & Rheumatology*. 2015;67(10):2557-2568.
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APPENDIX B: Gout Case Scenarios

GOUT CASE SCENARIOS

Symptoms	Tophus or Tophi detected on Physical Exam	Frequency	CASE SCENARIO NUMBER
Intermittent symptoms	NO	Infrequent Symptoms (≤ 1 attack/yr)	*1*
	NO	Frequent Symptoms (2-6 attacks/yr)	*2*
	NO	Very Frequent Symptoms (> 7 attacks/yr)	*3*
Intermittent symptoms	YES	Infrequent Symptoms (≤ 1 attack/yr)	*4*
	YES	Frequent Symptoms (2-6 attacks/yr)	*5*
	YES	Very Frequent Symptoms (> 7 attacks/yr)	*6*

A

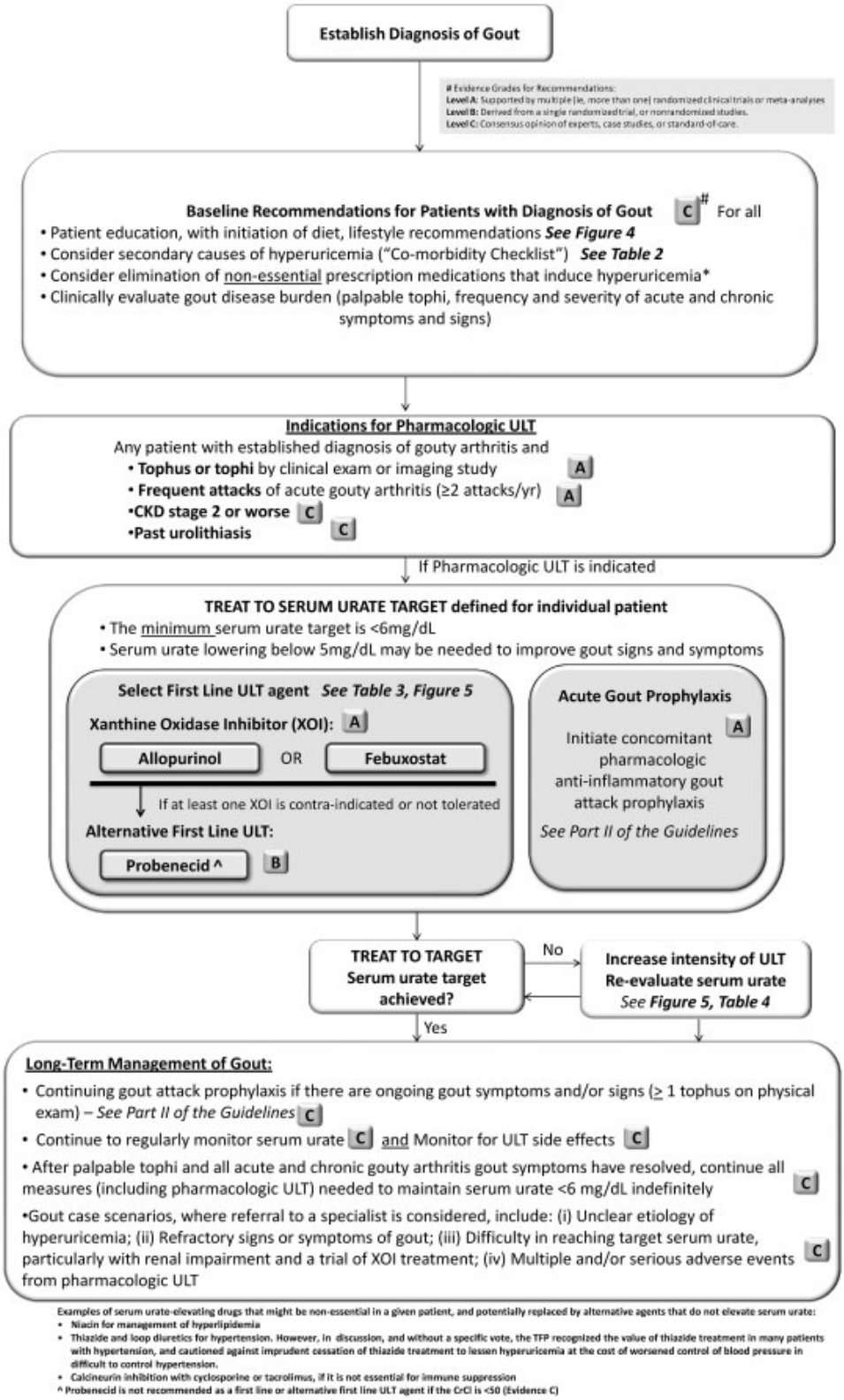
Case scenarios for Chronic Tophaceous Gouty Arthropathy

Disease Severity	Characteristics	CASE SCENARIO NUMBER
Mild	•Simple chronic tophaceous gouty arthropathy •Affecting 1 joint •Stable disease	*7*
Moderate	•Simple chronic tophaceous gouty arthropathy •Affecting 2-4 joints •Stable disease	*8*
Severe	•Chronic tophaceous gouty arthropathy of >4 joints OR • ≥1 unstable, complicated, severe articular tophus or tophi	*9*

B

Fundamental case scenarios evaluated by the task force panel (TFP). The TFP evaluated a broad spectrum of severity of gout, with presenting clinical information comparable to that encountered in practice. Scenarios were formulated iteratively by the core expert panel, as described in the text, and were not intended to serve as disease classification criteria. All case scenarios assumed that the diagnosis of gout was correct, and that there was some evidence of gout disease activity. Three distinct "treatment groups" for these recommendations, each with 3 case scenarios designed to succinctly represent clinically-based decision making and totaling 9 in all, are shown. The treatment group with intermittent attacks of acute gout but no tophi detected on physical examination was subdivided based on increasing yearly frequency of episodes of acute gouty arthritis of at least moderate to severe pain intensity (case scenarios 1–3; A). Gout associated with clinically apparent high body urate burden was evaluated in case scenarios where there were _1 tophi on physical examination, and either A, intermittently symptomatic acute gouty arthritis (case scenarios 4–6), or B, chronic joint symptoms due to synovitis attributable to gout or articular tophus or tophi in case scenarios 7–9 (the domain termed chronic tophaceous gouty arthropathy [CTGA]). Severity of case scenarios in the CTGA domain was distinguished by extent and characteristics of the tophi and chronic arthropathy, with variable inflammatory and deforming features detected on physical examination.

APPENDIX C: Baseline Recommendations and Overall Strategic Plan



Baseline recommendations and overall strategic plan for patients with gout. This algorithm summarizes overall treatment strategies and flow of management decisions for gout. Certain elements, including nonpharmacologic and pharmacologic measures, the approach to refractory disease, and treatment and antiinflammatory prophylaxis of acute gout attacks, are developed further in Tables 2–4 and Figures 4 and 5, and in part 2 of the guidelines, as referenced in the figure. Evidence grades (A–C, as indicated) are summarized for each task force panel (TFP) recommendation, and the text discusses in detail each aspect of clinical decision making. ULT _ urate-lowering therapy; CKD _chronic kidney disease; CrCl _ creatinine clearance.

APPENDIX D: Case Scenario-Specific Escalation of Pharmacologic Urate Lowering Therapy

CASE SCENARIOS 1-9

PHARMACOLOGIC ULT ESCALATION: MEASURE	← No tophi on exam →			← ≥ 1 Tophus on exam →					
	← Intermittent Symptoms →			← CTGA →					
	1	2	3	4	5	6	7	8	9
SINGLE AGENT XOI titrated to maximum appropriate dose (Alternative if XOI contra-indicated or not tolerated : Probenecid)	±§	+	+	+	+	+	+	+	+
Serum urate target not achieved, continuing disease activity									
Add **URICOSURIC* to XOI** with both agents titrated to maximum appropriate dose	±§	+	+	+	+	+	+	+	+
Serum urate target not achieved, continuing disease activity									
PEGLOTICASE	–	–	+	–	±¶	+	+	+	+

Case Scenarios 1-3: Progressively mild, moderate, and severe frequency of intermittent acute gout symptoms (without tophi on physical exam) are evaluated for case scenarios numbered 1, 2, and 3, respectively.
Case Scenarios 4-6: Progressively mild, moderate, and severe frequency of intermittent acute gout symptoms (with one or more tophi detected on physical exam) are evaluated for case scenarios numbered 4, 5, and 6, respectively.
Case Scenarios 7-9: Progressive severity of Chronic Tophaceous Gouty Arthropathy (CTGA), as anatomically mild, moderate, and severe chronic tophaceous arthritis, are evaluated in case scenarios numbered 7, 8, and 9, respectively.

§ Finding of a tophus or tophi on imaging study, or CKD Stage 2-5, or ESRD, are appropriate indications for first line pharmacologic ULT in Scenario 1.

¶ Failure of combination XOI and uricosuric therapy at maximum appropriate doses is an acceptable indication for consideration of Pegloticase therapy in Scenario 5.

***Uricosuric ULT choices in combination with XOI inhibitor therapy can include probenecid, or off-label use of losartan or fenofibrate.**

Case scenario–specific escalation of pharmacologic urate-lowering therapy (ULT) in gout, including approach to refractory disease. The figure, which accompanies Table 4, shows task force panel (TFP) recommendations for patients with continuing gout disease activity and focuses on escalating pharmacologic ULT measures, particularly for refractory disease. Each of the fundamental case scenarios is considered. Case scenario numbering of 1–9 refers to those gout clinical scenarios specifically detailed in Figures 1A and B above. The chronic tophaceous gouty arthropathy (CTGA) case scenarios numbered 7–9 are additionally shown in photographs in Figure 2. These recommendations specifically assume that for each case scenario: 1) the serum urate target needed to achieve improved gout signs and symptoms has not yet been achieved, 2) appropriate nonpharmacologic ULT measures have been applied, and 3) appropriate treatment and antiinflammatory prophylaxis are employed for attacks of acute gouty arthritis. Evidence grades for individual TFP votes to recommend that are shown here are summarized in the text. In the figure, the decision-making symbol _ indicates therapeutic appropriateness, with _ indicative of either a therapeutically inappropriate measure or one with uncertain risk:benefit ratio. The decision-making symbol _ indicates that the TFP recommended this therapeutic measure as appropriate only in specific conditions in a clinical scenario, marked by the symbol § or ¶ that refers to particular circumstances described below the figure. CKD _ chronic kidney disease; ESRD _ end-stage renal disease; XOI _ xanthine oxidase inhibitor.

APPENDIX E: Case Scenario for Gout Attack

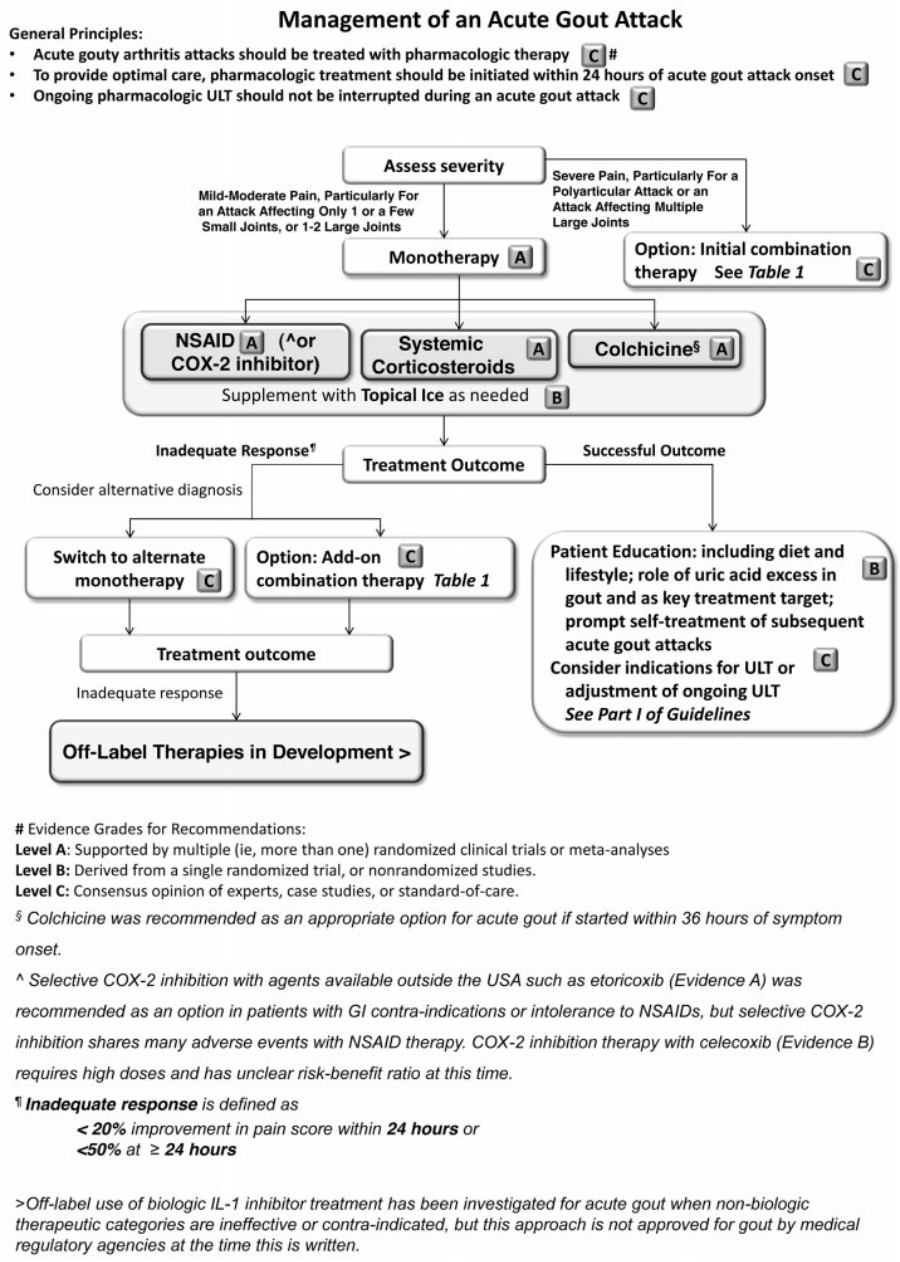
Severity of Acute Gouty Arthritis Attack Intensity of attack based on self-reported pain (0-10 visual analog scale)	
Mild	≤ 4
Moderate	5-6
Severe	≥ 7

Duration of the gouty arthritis attack since onset	
Early	< 12 Hours after attack onset
Well-Established	12 to 36 Hours after attack onset
Late	> 36 Hours after attack onset

Extent of acute gouty arthritis attack Based on number of active joints
One or a few small joints
1 or 2 large* joints ** defined as: ankle, knee, wrist, elbow, hip, shoulder*
Polyarticular • 4 or more joints, with arthritis involving more than 1 region§ *§ Regions defined as: forefoot (metatarsophalangeal joints, toes), midfoot (tarsal joints), ankle/hindfoot, knee, hip, fingers, wrist, elbow, shoulder, other* • Acute gout attack involving 3 separate large joints is considered as a form of polyarticular gout for this scheme of management

Case scenarios for defining acute gouty arthritis attack features. These case scenarios were generated by the core expert panel, and therapeutic decision -making options for these scenarios were voted on by the task force panel.

APPENDIX F: Overview of Gout Attack Management



Evidence Grades for Recommendations:
Level A: Supported by multiple (ie, more than one) randomized clinical trials or meta-analyses
Level B: Derived from a single randomized trial, or nonrandomized studies.
Level C: Consensus opinion of experts, case studies, or standard-of-care.

§ Colchicine was recommended as an appropriate option for acute gout if started within 36 hours of symptom onset.

^ Selective COX-2 inhibition with agents available outside the USA such as etoricoxib (Evidence A) was recommended as an option in patients with GI contra-indications or intolerance to NSAIDs, but selective COX-2 inhibition shares many adverse events with NSAID therapy. COX-2 inhibition therapy with celecoxib (Evidence B) requires high doses and has unclear risk-benefit ratio at this time.

¶ ***Inadequate response*** *is defined as*
< 20% *improvement in pain score within* ***24 hours*** *or*
<50% *at ≥* ***24 hours***

>Off-label use of biologic IL-1 inhibitor treatment has been investigated for acute gout when non-biologic therapeutic categories are ineffective or contra-indicated, but this approach is not approved for gout by medical regulatory agencies at the time this is written.

Overview of management of an acute gout attack. This algorithm summarizes the recommendations by the task force panel on the overall approach to management of an acute attack of gouty arthritis, with further details, as expanded in other figures and tables, referenced in the figure and discussed in the text. ULT _ urate-lowering therapy; NSAID _ nonsteroidal antiinflammatory drug; COX-2 _cyclooxygenase 2; GI _ gastrointestinal; IL-1 _ interleukin-1.

APPENDIX G: Informed Consent (English)

INFORMED CONSENT

1. **Project Title: APLAR LONGITUDINAL PROSPECTIVE COHORT STUDY: CLINICAL SCENARIO STAGE ASSOCIATION WITH GOUT**

2. **Research Investigator/Assistant:** *Name:* _____
   Contact details: Contact number: _____
   Email: _____
   *Name (Associate):*_____
   Contact number: _____
   Email: _____
   *Name (Associate):*_____
   Contact number: _____
   Email: _____

3. **What is the purpose of this study?**
   The purpose of this study is pure research. In particular, it aims to determine the demographic profile, clinical characteristics, and Clinical Scenario Stage of patients in the Asia-Pacific region. It will determine the association of Clinical Scenario Stage with uric acid, the risk to develop gout flares and the treatment response among the different stages in gout.

4. **Who can participate in the research? What is the expected duration of my participation? What is the duration of this research?**
   All newly diagnosed and established gout patients seen by doctors of registered APLAR Gout Centers in the Asia-Pacific region can participate in this research. You are expected to participate during your consultations with your doctor within the research period. The research proper will be conducted within a one-year period.

5. **What is the approximate number of participants involved?**
   The number of participants involved in the study is approximately 1,000 and will encompass all consenting gout patients seen in registered APLAR Gout Research Centers in the Asia-Pacific.

6. **What will be done if I take part in this research?**
   You are expected to sign an informed consent document and will be asked a series of questions by your doctor. Your doctor will also conduct a physical examination to ascertain gout tophi and gout flares.

7. **How will my privacy and the confidentiality of my research records be protected?**
   We respect your privacy and confidentiality. Rest assured that your identifiable information (e.g. names) will be coded and known only to the principal investigator. This will not be released to any other person, nor used for publication/presentation. All your identifiable health information and research data will be assigned an alphanumeric code at the earliest possible stage of the research and will be kept in record for a period of 5 years.

8. **What are the possible discomforts and risks for participants?**
   There shall be no discomforts and risks for participants. The survey and physical examination will only take 5 – 15 minutes of your time during your consultation with your doctor.

9. **What is the compensation for any injury?**
   Since only survey forms and physical examination shall be used on you, injury is unlikely. Survey forms will be recording only the form and method of treatment your doctor chooses and will not have any direct connection to the treatment you receive.

10. **Will there be reimbursement for participation?**
    There will be no financial reimbursement for participating in the study.

11. **What are the possible benefits to me and to others?**
    You will not have any direct benefit from this study. However, the results gained from this study will benefit patients, healthcare providers, and the institution by improving the existing knowledge about gout.

12. **Can I refuse to participate in this research?**
    Yes, you can. Your decision to participate in this research is voluntary and completely up to you. You can also withdraw from the study at any time. If you withdraw from the study, no questions will be asked. If you decide to withdraw, consent will be sought and additional consent form be signed if gathered data prior to withdrawal can be included in the study.

13. **Whom should I call if I have any questions or problems?**
    Please contact the Research Assistant/Investigator, Dr. _____ through (cell number/ email address) for all research-related matters. You may also contact the Chairman of the Institutional Review Board of the hospital/center.

Thank you very much in advance for your interest and assistance with this research.

Name (Researcher): _____
Name (Research Associate): _____

CONSENT FORM

Project Title: **APLAR LONGITUDINAL PROSPECTIVE COHORT STUDY: CLINICAL SCENARIO STAGE ASSOCIATION WITH GOUT**

Research Investigator/Assistant:	*Name:* _____
Contact details:	Contact number: _____
	Email: _____
	*Name (Associate):*_____
	Contact number: _____
	Email: _____
	*Name (Associate):*_____
	Contact number: _____
	Email: _____

I hereby acknowledge that:

1. My signature is my acknowledgement that I have agreed to take part in the above research.

2. I have received a copy of this information sheet that explains the use of my data in this research. I understand its contents and agree to donate my data for the use of this research.

3. I can withdraw from the research at any point of time by informing the Principal Investigator and all my data will be discarded. If I withdraw from the study, my data collected prior to withdrawal may be included if I give consent.

* This research has been explained to me in my native language (ie. Filipino), which I understand, by _____ (name of translator) on _____ (date).

_____ _____
Name and Signature (Participant) Date

_____ _____
Name and Signature (Consent Taker) Date

CONSENT FORM ALLOWING USE OF MY DATA
AFTER WITHDRAWAL FROM THE STUDY

Project Title: APLAR LONGITUDINAL PROSPECTIVE COHORT STUDY: CLINICAL SCENARIO STAGE ASSOCIATION WITH GOUT

Research Investigator/Assistant: *Name:* _____
Contact details: Contact number: _____
Email: _____
*Name (Associate):*_____
Contact number: _____
Email: _____
*Name (Associate):*_____
Contact number: _____
Email: _____

This document states the following:

1. I have decided to withdraw from the study.

2. I am allowing the Principal Investigator and his group who are conducting the study to use my data collected, from the start of the study until my withdrawal.

3. My identification and my private data will remain confidential.

* This research has been explained to me in (LOCAL LANGUAGE), which I understand, by _____ (name of translator) on _____ (date).

_____ _____
Name and Signature (Participant) Date

_____ _____
Name and Signature (Consent Taker) Date

APPENDIX H: Informed Consent (Local Language Translation Advised)

APPENDIX I: Patient Characteristics Form

Part I. Patient Characteristics/Gout History
Clinic Number: _____ Patient Number: _____ Birthday: _____
Province*: _____ Age: _____ Sex: _____ Height: _____ Weight: _____

Medical History:
___ None
___ Blood Dyscrasia
___ Cancer
___ Chronic Kidney Disease
Age Dx*: _____
___ Coronary heart disease
Age Dx*: _____
___ Covid-19
___ Diabetes Mellitus
___ Dyslipidemia
___ Hypertension
___ Hypothyroidism
___ Menopause
___ Metabolic syndrome
___ Nephrolithiasis
___ Psoriasis
___ Psoriatic Arthritis
___ Rheumatoid Arthritis
Septic Arthritis
___ Stroke
Age Dx*: _____
___ SLE
___ Tuberculosis
___ Others:

Family History:
___ None
___ Unknown
___ Blood Dyscrasia
___ Cancer
___ Chronic Kidney Disease
___ Coronary heart disease
___ Covid-19
___ Diabetes Mellitus
___ Dyslipidemia
___ Gout
___ Hypertension
___ Hypothyroidism
___ Metabolic syndrome
___ Nephrolithiasis
___ Psoriasis
___ Psoriatic Arthritis
___ Rheumatoid Arthritis
___ Stroke
___ SLE
___ Others:

Personal Social History:
___ Non-smoker
___ Previous Smoker (stopped ≥1 year)
Approximate pack years _____
___ Current Smoker
Approximate pack years _____
___ Non-alcohol beverage drinker
___ Alcohol beverage (most often intake)
___ Beer ___ Wine ___ Spirits

Alcohol Frequency of Intake*:
___ Less than once month
___ Once a month to once a week
___ Two to four times a week
___ Five times a week to once a day
___ Two or more a day
Alcohol Consumption*:
___ 1 – 2 bottles/glasses/shots
___ 3 – 4 bottles/glasses/shots
___ > 4 bottles/glasses/shots

Age first symptoms: _____ Age at first consult: _____ Age at diagnosis: _____

Initial joint involvement (Ask patient to point. Check all involved):
___ Shoulder
___ Elbow
___ Wrist
___ MCP
___ DIP/PIP
___ Hip
___ Knee
___ Ankle
___ Midfoot
___ First MTP
___ Toes
___ Cervical Spine
___ Thoracic Spine
___ Lumbar Spine
___ Sacral Spine

Diagnosed by:
___ Family Medicine
___ General Practitioner
___ Internal Medicine/subspecs
___ OB/Gyne
___ Rheumatologist
___ Surgeon/Orthopedic
___ Other Allied Health Practitioners (Therapist, Nurse, Caregiver, etc.)
___ Non-medical Practitioner (ex. Faith Healer)
___ Unrecalled

Flare Triggers (check all that apply): ___ Unknown

Food:
___ Food (not specified)
___ Alcohol Beverages
___ Sweetened drinks
___ Beans
___ Beef – meat
___ Beef – internal organs
___ Canned goods
___ Pork – meat
___ Pork – internal organs
___ Seafood – fish
___ Seafood – shellfish
___ Other:

Medication:
___ Allopurinol
___ Anti-tuberculosis
___ Aspirin
___ Cyclosporin
___ Febuxostat
___ Herbal/Alt. Medicine
___ Loop diuretics
___ Niacin
___ Thiazide
___ Other:

Activity:
___ Accident/Trauma
___ Blood loss/transfusion
___ Dialysis
___ Diarrhea
___ Diet (excessive)
___ Exercise
___ Heart attack
___ Hospitalization
___ Infection (ex. UTI, CAP)
___ Stroke
___ Surgical procedure
___ Other:

Previous procedures done PRIOR TO INCLUSION in the study (check all that apply):
___ None
___ Arthrocentesis
___ Intra-articular steroid injection
___ Debridement/Debulking/Excision

GOUT Medication PRIOR TO INCLUSION in study (check all that apply):
___ None
___ Unrecalled
___ Colchicine
___ Allopurinol
___ Febuxostat
___ Herbal/Alt. Medicine
___ Celecoxib
___ Diclofenac
___ Etoricoxib
___ Ibuprofen
___ Mefenamic
___ Naproxen
___ Topical NSAID
___ Unrecalled NSAID
___ IA Betamethasone
___ IV Hydroxycortisone
___ Oral Prednisone
___ IA ___ Oral Methylprednisone
___ IA ___ IV ___ Oral (?) steroid
___ Paracetamol
___ Tramadol
___ Paracetamol + Tramadol
___ Other:

Other Medications Taken:
___ None
___ Anti-tuberculosis
___ Aspirin
___ Clopidogrel
___ Statins (Ator/Sim/Rosu/etc.)
___ Fenofibrate
___ Losartan
___ Diuretics
___ Other anti-hypertensives
___ Insulin
___ Other anti-Diabetes Mellitus
___ Other:

Gout Medication Prescription BEFORE INCLUSION IN THE STUDY given by (check all that apply):
___ Family Medicine
___ General Practitioner
___ Internal Medicine/subspecs
___ OB/Gyne
___ Rheumatologist
___ Surgeon/Orthopedic
___ Other Allied Health Practitioners (Therapist, Nurse, Caregiver, etc.)
___ Non-medical Practitioner (Faith Healer, self-medicated)
___ Unrecalled

Part II. Clinical Scenario Staging Form
Date: _____
Number of tophi on physical examination:

___ No tophi
___ 1 joint
___ 2 – 4 joints
___ ≥ 5 joints

If with tophi, are they unstable (drainage, destructive effects (deformity), high risk of infection, rapid growth, severe inflammation)?

___ Yes
___ No

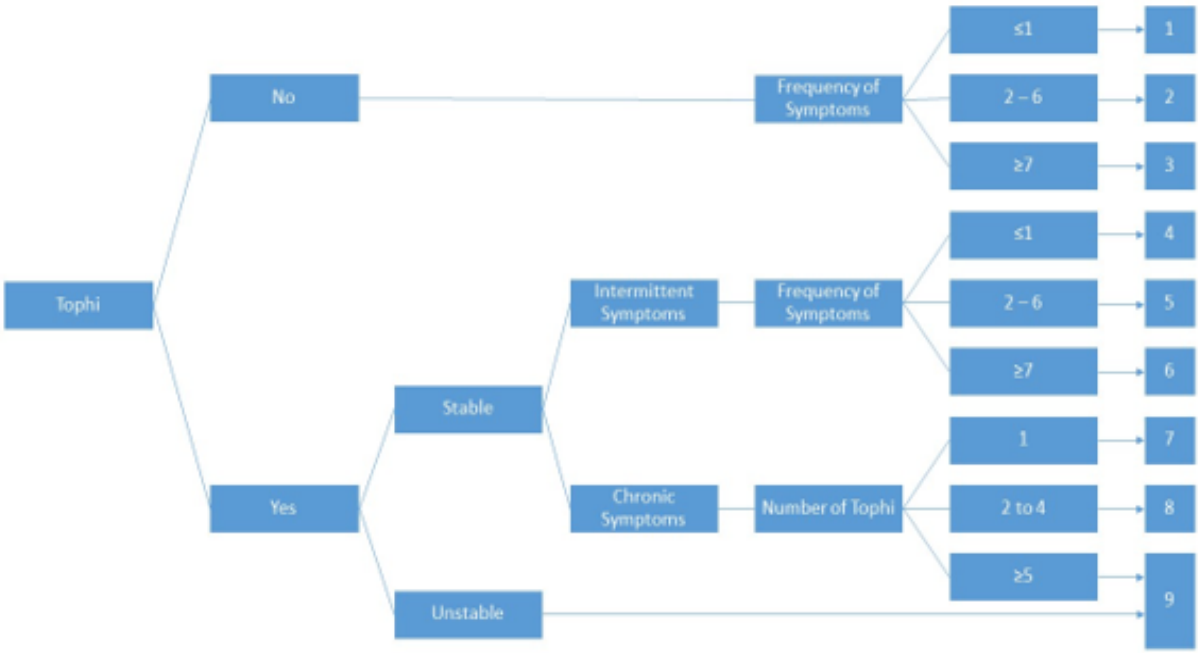
If with stable tophi, describe symptoms experienced by patient:

___ Intermittent (not continuous and can be described as sporadic, isolated or patchy)
___ Chronic (persistent and long standing, lasting 6 or more weeks)

Frequency of symptoms during the PAST YEAR (No need to answer if patient has unstable tophi or with stable tophi but chronic symptoms)?

___ 1 symptom/year
___ 2 – 6 symptoms/year
___ 7 or more symptoms/year

Clinical Scenario: _____



APPENDIX K: Part III. First Consult Form

Part III. First Consultation
Date of Consult: _____ Seen: ___ Inpatient ___ Outpatient BP: _____ Weight: _____

Approximate days since last flare: _____ Days until flare completely resolved: _____
Flare resolution was: ___ Spontaneous ___ Medicated

Patient diagnosis was assisted by:
___ None, clinical examination only
___ Crystal Analysis
___ Ultrasound
___ X-ray imaging
___ Other: _____

Currently in Gouty Arthritis Flare: ___ Yes ___ No
Flare Trigger for this attack (Skip if no flare. Check all that apply): ___ Unknown

Food:	Medication:	Activity:
___ Food (not specified)	___ Allopurinol	___ Accident/Trauma
___ Alcohol Beverages	___ Anti-tuberculosis	___ Blood loss/transfusion
___ Sweetened drinks	___ Aspirin	___ Dialysis
___ Beans	___ Cyclosporin	___ Diarrhea
___ Beef – meat	___ Febuxostat	___ Diet (excessive)
___ Beef – internal organs	___ Herbal/Alt. Medicine	___ Exercise
___ Canned goods	___ Loop diuretics	___ Heart attack
___ Pork – meat	___ Niacin	___ Hospitalization
___ Pork – internal organs	___ Thiazide	___ Infection (ex. UTI, CAP)
___ Seafood – fish	___ Other:	___ Stroke
___ Seafood – shellfish		___ Surgical procedure
___ Other:		___ Other:

Number of joints involved in the current gout flare:
- ____ 1 or few small joints
- ____ 1 or 2 large joints [ankle, knee, wrist, elbow, hip, shoulder]
- ____ Polyarticular [4 or more joints with arthritis involving more than 1 region (forefoot (MTP, toes), midfoot (tarsal), ankle/hindfoot, knee, hip, fingers, wirst elbow, shoulder, other); or, attack involving 3 separtate large joints]

Duration of pain prior to consult:
- ___ Less than 12 hours
- ___ Between 12 – 36 hours
- ___ More than 36 hours

Maximal pain intensity (Scale from 1 to 10) during ENTIRE GOUT FLARE PERIOD:
- ___ Equal or less than 4
- ___ 5 – 6
- ___ 7 or more

Pain intensity (Scale from 1 to 10) during the ACTUAL CONSULTATION:
- ___ Equal or less than 4
- ___ 5 – 6
- ___ 7 or more

GOUT Medication taken PRIOR TO THIS CONSULT (check all that apply):

___ None
___ Unrecalled
___ Colchicine
___ Allopurinol
___ Febuxostat
___ Herbal/Alt. Medicine
___ Celecoxib
___ Diclofenac
___ Etoricoxib
___ Ibuprofen
___ Mefenamic
___ Naproxen
___ Topical NSAID
___ Unrecalled NSAID
___ IA Betamethasone
___ IV Hydroxycortisone
___ Oral Prednisone
___ IA ___ Oral Methylprednisone
___ IA ___ IV ___ Oral (?) steroid
___ Paracetamol
___ Tramadol
___ Paracetamol + Tramadol
___ Other:

Other Medications Taken PRIOR TO THIS CONSULT (check all that apply):

___ None
___ Anti-tuberculosis
___ Aspirin
___ Clopidogrel
___ Statins (Ator/Sim/Rosu/etc.)
___ Fenofibrate
___ Losartan
___ Diuretics
___ Other anti-hypertensives
___ Insulin
___ Other anti-Diabetes Mellitus
___ Other:

GOUT Medication Prescribed by:

___ Family Medicine
___ General Practitioner
___ Internal Medicine/subspecs
___ OB/Gyne
___ Rheumatologist
___ Surgeon/Orthopedic
___ Other Allied Health Practitioners (Therapist, Nurse, Caregiver, etc.)
___ Non-medical Practitioner (Faith Healer, self-medicated)
___ Unrecalled

Is the patient compliant to medication (Self-reported compliance)? ___ Yes ___ No

Recent laboratory exam (tests done within 1-month duration):

Date: _____ Crea (umol/L) _____.
Date: _____ Uric Acid (mg/dL) _____.
Date: _____ AST (IU/L) _____.
Date: _____ ALT (IU/L) _____.
Date: _____ FBS (mmol/L) _____.
Date: _____ HBA1c _____.
Date: _____ Triglycerides (mmol/L) _____.
Date: _____ Total Cholesterol (mmol/L) _____.
Date: _____ HDL (mmol/L) _____.
Date: _____ LDL (mmol/L) _____.

Patient was treated: ___ Inpatient ___ Outpatient

Procedure done during this consult/referral:

___ None
___ Arthrocentesis
___ Intra-articular steroid injection
___ Debridement/Debulking/Excision

Treatment by attending Rheumatologist FOR GOUT (check all that apply):

___ None
___ Colchicine
___ Allopurinol
___ Febuxostat
___ Celecoxib
___ Diclofenac
___ Etoricoxib
___ Naproxen
___ IA Betamethasone
___ IV Hydroxycortisone
___ Oral Prednisone
___ IA ___ Oral Methylprednisone
___ Paracetamol
___ Tramadol
___ Paracetamol + Tramadol
___ Losartan
___ Fenofibrate
___ Other:

Did the patient receive gout education? ___ Yes ___ No

APPENDIX L: Part IV. Follow-up Consult Form

Part IV. Follow-up Consult Form
Date of Consult: _____ Seen: ___ Inpatient ___ Outpatient BP: _____ Weight: _____
*If 1 or more years have passed since the First Consultation/CSS designation, please print and complete PART II CLINICAL SCENARIO STAGING FORM and attach. New CSS: _____

Approximate days since last flare: _____ Days until flare completely resolved: _____
Flare resolution was: ___ Spontaneous ___ Medicated

Any medication adverse effect? * Yes, (medication and short description) _____
If last consult had a flare, symptoms from THAT flare are now (PS – pain scale): PS _____
___ Completely resolved (PS 0/10)
___ No response/Failure (No change in PS/worsening of PS)
___ Improved and on target (PS decreased by ≥half)
___ Improved but off target (PS decreased by ≤half)

Currently in Gouty Arthritis Flare: ___ Yes ___ No
Flare Trigger for this attack (Skip if no flare. Check all that apply): ___ Unknown

Food:	Medication:	Activity:
___ Food (not specified)	___ Allopurinol	___ Accident/Trauma
___ Alcohol Beverages	___ Anti-tuberculosis	___ Blood loss/transfusion
___ Sweetened drinks	___ Aspirin	___ Dialysis
___ Beans	___ Cyclosporin	___ Diarrhea
___ Beef – meat	___ Febuxostat	___ Diet (excessive)
___ Beef – internal organs	___ Herbal/Alt. Medicine	___ Exercise
___ Canned goods	___ Loop diuretics	___ Heart attack
___ Pork – meat	___ Niacin	___ Hospitalization
___ Pork – internal organs	___ Thiazide	___ Infection (ex. UTI, CAP)
___ Seafood – fish	___ Other:	___ Stroke
___ Seafood – shellfish		___ Surgical procedure
___ Other:		___ Other:

Number of joints involved in the current gout flare:
- ____ 1 or few small joints
- ____ 1 or 2 large joints [ankle, knee, wrist, elbow, hip, shoulder]
- ____ Polyarticular [4 or more joints with arthritis involving more than 1 region (forefoot (MTP, toes), midfoot (tarsal), ankle/hindfoot, knee, hip, fingers, wirst elbow, shoulder, other); or, attack involving 3 separtate large joints]

Duration of pain prior to consult:
- ___ Less than 12 hours
- ___ Between 12 – 36 hours
- ___ More than 36 hours

Maximal pain intensity (Scale from 1 to 10) during ENTIRE GOUT FLARE PERIOD:
- ___ Equal or less than 4
- ___ 5 – 6
- ___ 7 or more

Pain intensity (Scale from 1 to 10) during the ACTUAL CONSULTATION:
- ___ Equal or less than 4
- ___ 5 – 6
- ___ 7 or more

GOUT Medication taken PRIOR TO THIS CONSULT (check all that apply):

___ None
___ Unrecalled
___ Colchicine
___ Allopurinol
___ Febuxostat
___ Herbal/Alt. Medicine
___ Celecoxib
___ Diclofenac
___ Etoricoxib
___ Ibuprofen
___ Mefenamic
___ Naproxen
___ Topical NSAID
___ Unrecalled NSAID
___ IA Betamethasone
___ IV Hydroxycortisone
___ Oral Prednisone
___ IA ___ Oral Methylprednisone
___ IA ___ IV ___ Oral (?) steroid
___ Paracetamol
___ Tramadol
___ Paracetamol + Tramadol
___ Other:

Other Medications Taken PRIOR TO THIS CONSULT (check all that apply):

___ None
___ Anti-tuberculosis
___ Aspirin
___ Clopidogrel
___ Statins (Ator/Sim/Rosu/etc.)
___ Fenofibrate
___ Losartan
___ Diuretics
___ Other anti-hypertensives
___ Insulin
___ Other anti-Diabetes Mellitus
___ Other:

GOUT Medication Prescribed by:

___ Family Medicine
___ General Practitioner
___ Internal Medicine/subspecs
___ OB/Gyne
___ Rheumatologist
___ Surgeon/Orthopedic
___ Other Allied Health Practitioners (Therapist, Nurse, Caregiver, etc.)
___ Non-medical Practitioner (Faith Healer, self-medicated)
___ Unrecalled

Is the patient compliant to medication (Self-reported compliance)? ___ Yes ___ No

Recent laboratory exam (test done within 1-month duration):

Date: _____ Crea (umol/L) _____.
Date: _____ Uric Acid (mg/dL) _____.
Date: _____ AST (IU/L) _____.
Date: _____ ALT (IU/L) _____.
Date: _____ FBS (mmol/L) _____.
Date: _____ HBA1c _____.
Date: _____ Triglycerides (mmol/L) _____.
Date: _____ Total Cholesterol (mmol/L) _____.
Date: _____ HDL (mmol/L) _____.
Date: _____ LDL (mmol/L) _____.

Patient was treated: ___ Inpatient ___ Outpatient

Procedure done during this consult/referral:

___ None
___ Arthrocentesis
___ Intra-articular steroid injection
___ Debridement/Debulking/Excision

Treatment by attending Rheumatologist FOR GOUT (check all that apply):

___ None
___ Colchicine
___ Allopurinol
___ Febuxostat
___ Celecoxib
___ Diclofenac
___ Etoricoxib
___ Naproxen
___ IA Betamethasone
___ IV Hydroxycortisone
___ Oral Prednisone
___ IA ___ Oral Methylprednisone
___ Paracetamol
___ Tramadol
___ Paracetamol + Tramadol
___ Losartan
___ Fenofibrate
___ Other:

Did the patient receive gout education? ___ Yes ___ No

ASIA PACIFIC LEAGUE OF ASSOCIATIONS FOR RHEUMATOLOGY (APLAR)
LONGITUDINAL PROSPECTIVE COHORT STUDY:
CLINICAL SCENARIO STAGE ASSOCIATION WITH GOUT

Gout Questionnaire Guide

Thank you for participating in this Cross-sectional, Gout Clinical Scenario Registry. The purpose of this study is pure research. In particular, it aims to determine the demographic profile, clinical characteristics, Clinical Case Scenario/Stage of Asia-Pacific gout patients, management practice, patient compliance, and treatment success. It will only involve data collection via questionnaire and physical examination by a Rheumatologist. It does not obligate the attending Rheumatologist to request laboratories and imaging nor does it require the attending to give specific types of medication. All data collected will be coded and the attending Rheumatologist and their patients‘ privacy and confidentiality will be protected.

All diagnosed gout patients seen by Rheumatologists may be included in this study. Patients will be asked to give and sign informed consent. There is no discomfort and risk for patients. The survey and examination will only take 5 – 15 minutes during their consultation with the Rheumatologist. There will be no financial reinbursements for patients participating in the study.

The Gout Questionnaire is patterned with a Google Forms document. It is synced to Google Spreadsheets and will return processed data. Once the questionnaire is complete, you may connect to Google Forms for data input and uploading (link and QR code located at the bottom). The Google Forms and Spreadshhet will ensure that there are no misplaced or blank data. If there are any questions or clarifications regarding the forms or its answers, please do not hesitate to contact Dr. Ronaldo De Vera at +639399379739. Suggestions are highly appreciated. It is the goal of the questionnaire and online forms to simplify the process. The answer-options listed in the questionnaire and form may increase or decrease depending on the frequent answers given by your patients and your suggestions. Questionnaire and Google Forms may be adjusted according to hospital/institution preferance.

Please answer all questions in the forms. Items marked with an asterix (*) may be left blank but answering them is higly encouraged. The end of the Google Forms has a section where you can include any comments about the patient’s data collection/answers. This is to include patient data that you feel is pertinent about gout but is not part of the current question line-up. Only people involved in the study may use the Google Forms. It is password protected. Please do not share your password with others. Also, please refarian from including unneeded patient identifiers in the forms.

Link: https://forms.gle/V6xedf2BgSGhxLv98 (tentative – plan for APLAR webpage)

QR Code:

Part 1: Patient Characteristics/ Gout History

Medical History – includes patients‘ current illness such as newly diagnosed hypertension, diabetes and Covid-19. If a patient has not been previously diagnosed with illnesses such as hypothyroidism, dyslipidemia or metabolic syndrome, its’ workup or specialist referral is as per the Rheumatologists’ prerogative. If a patient develops or is diagnosed with a new condition (ie. coronary heart disease, stroke), the Rheumatologist is requested to update the q uestionnaire and make the changes to the online Google Forms. This will automatically be reflected on the processed Google Sheets.

Family History – includes the patient’s family history as best to his knowledge.

Personal Social History – asks the patient’s smoking and alcohol beverage drinking habits. Smoking is divided into non-smoker, previous smoker and current smoker. Alcohol beverage drinking will be analyzed according to daily alcohol intake and frequency of intake. Ethanol intake is counted by the number of bottles/glasses/shots taken. Frequency of intake is divided into five categories: less than one per month, one per month to one per week, two to four per week, five per week to one per day, and two or more per day.

Age at first symptoms is defined as the age of the patient when he first experiences and describes symptoms that properly corresponds to gout.

Age at first consult is defined as the age of the patient when he first seeks consult with a medical practitioner for his gouty symptoms. This is irrespective whether or not he was diagnosed with gout or if treatment was given to the patient for his symptoms.

Age at diagnosis is defined as the age of the patient when he was diagnosed with gout by a medical practitioner. This is irrespective whether or not treatment was given to the patient for gout.

Initial joint involvement – please ask the patient to point to all areas that they initially experienced their gouty symptoms.

Diagnosed by – refers to the person who initially diagnosed the patient to have gout. If the patient was previously seen by a different specialty and the patient was diagnosed with gout and given gout medication, that specialty is the one who diagnosed the patient. If a patient is referred for continuing gout care, the referrer is the one who who diagnosed the patient. If a patient is referred to a Rheumatologsit for gout work-up, the receiving Rheumatologist is the who diagnosed the patient.

Flare Triggers – are the food/medication/activities identified by the patient and the doctor. Beans may be included as a flare trigger since it is what the patient perceives to be the cause of their gout attack. Care in explaining to the patient of what the possible gout triggers must be done and future follow-up with the patient may track their identification of triggers.

Previous procedures done PRIOR TO INCLUSION in the study – this pertains to procedures done specifically for gout symptoms/tophi prior to the patient’s inclusion in the study.

GOUT Medication PRIOR TO INCLUSION in the study – this pertains to all medication taken by the patient specifically for gout symptoms/tophi prior to the patient's inclusion in the study. Efficascent oils, bath salts, cummin rubs, ginger/herbal teas are considered part of **Herbal/Alternative Medicine**.

Other Medications Taken – refers to medication that may be correlated to patients' comorbidity that is affected by gout (ex. Tuberculosis, Diabetes, Dyslipidimia, Hypertension, etc.)

Gout Medication Prescription BEFORE INCLUSION IN THE STUDY given by – refers to the person who prescribed the medication taken specifically for gout. More than 1 person may have given a prescription for gout medication.

Part 2: Clinical Scenario Staging Form

Clinical Scenario Staging is based on patient's tophi and the frequency of symptoms experienced in the past year. This form is completed on the first consultation with the Rheumatologist and yearly when it coincides with a consultation.

Unstable - Tophi are considered unstable if one or more tophi present with drainage, aggressive mass or connective tissue destructive effects, high risk of infection, very rapid growth or with severe, tophaceous joint inflammation.

Intermittent symptoms – are defined as gout symptoms of pain and inflammation that occurs at irregular intervals. It is not continuous or steady and can also be described as sporadic, isolated or patchy.

Chronic joint symptoms – due to synovitis attributable to gout are described as persistent and long standing, lasting 6 or more weeks. They are unabating and with long-lasting pain and inflammation even if treated with anti-inflammatory agents.

Frequency of symptoms during the PAST YEAR - No need to answer if patient has unstable tophi or with stable tophi but chronic symptoms. The frequency of symptoms describes the number of symptom-episodes the patient experiences with each symptom-episode having a definite beginning, waning period and end. Symptom-episodes can typically last anywhere from a few hours to up to 2 weeks.

Part 3: First Consultation Form

Approximate days since last flare/ Days until flare completely resolved –
Flare is defined as the fulfillment of at least 3 of 4 criteria (patient defined gout flare, pain at rest score of >3 on a 0–10-point numerical rating scale, presence of at least 1 swollen joint, and presence of at least 1 warm joint). When interviewing a patient regarding historical gout flares (flares not seen by medical practitioners), the Rheumatologist should ask the patient to describe the historical flare to ascertain whether or not the event was gout related.

Flare resolution – considered as spontaneous if the patient did not take any medication (ex. Colchicine, NSAIDs, steroids) for the flare.

Patient diagnosis was assisted by – refers to procedures done in the past/currently that contributed in diagnosing the patient.

Currently in Gouty Arthritis Flare – check if the patient fulfills at least 3 of 4 criteria (patient defined gout flare, pain at rest score of >3 on a 0–10-point numerical rating scale, presence of at least 1 swollen joint, and presence of at least 1 warm joint).

Flare Trigger for this attack (Skip if no flare) – are the food/medication/activities identified by the patient and the doctor. Beans may be included as a flare trigger since it is what the patient perceives to be the cause of their gout attack. Care in explaining to the patient of what the possible gout triggers must be done and future follow-up with the patient may track their identification of triggers.

Number of joints involved in the current gout flare:
Large joints – ankle, knee, wrist, elbow, hip, shoulder
Polyarticular – 4 or more joints with arthritis involving more than 1 region (forefoot (MTP, toes), midfoot (tarsal), ankle/hindfoot, knee, hip, fingers, wirst elbow, shoulder, other); or, attack involving 3 separtate large joints

Duration of pain prior to consult – amount of time in hours since the begining of the of the gouty flare up to the time of consult.

Maximal pain intensity during the ENTIRE GOUT FLARE PERIOD – pain experienced on a scale from 1 to 10 since the beginning of the gout flare until consult.

Pain intensity during the ACTUAL CONSULTATION – pain experienced on a scale from 1 to 10 during the consultation. It may be the same as the maximal pain intensity.

GOUT Medication taken PRIOR TO THIS CONSULT – this pertains to all medication taken by the patient specifically for gout symptoms/tophi prior to the patient's current consultation. Efficascent oils, bath salts, cummin rubs, ginger/herbal teas are considered part of **Herbal/Alternative Medicine**.

Other Medications Taken – refers to medication that may be correlated to patients' comorbidity that is affected by gout (ex. Tuberculosis, Diabetes, Dyslipidimia, Hypertension, etc.)

Gout Medication Prescribed by – refers to the person who prescribed the medication taken specifically for gout. More than 1 person may have given a prescription for gout medication.

Is the patient compliant to medication (Self-reported compliance)? – ask the patient if they have been taking the medication as prescribed by the doctor.

Recent laboratory exam – include tests done within 1-month duration. If the patient consults and laboratory results were sent to the Rheumatologist, this data is included in the first

consultation form. If the patient has a new consultation and follows up with the Rheumatologist with the laboratory results, this may be included in the later follow-up consultation form. Included dates are put to check possible overlapping data.

Patient was treated: Inpatient / Outpatient – if the patient was seen on an outpatient basis and was advised to be admitted, then the patient is labelled as an **Inpatient** treatment. If the patient was seen on an outpatient basis and treated without admission, then the patient is labeled as **Outpatient**. If that same patient treated outpatient but was immediately admitted for whatever reason (hypertension control, blood sugar management, surgery, gouty flare, etc.), then this counts as a new consult and Part 4: Follow-up Consultation Form is filled up. The patient then would be labeled as **Inpatient**. If an admitted patient and was referred right before discharge, and the treatment was to be started after discharge – then that patient is seen as inpatient but treated as **Outpatient**.

Procedure done during this consult/referral – check as indicated. May check more than 1 procedure.

Treatment by attending Rheumatologist FOR GOUT – check all medications given during this consultation period. Example - may check IV steroids and oral steroids if both were given during the inpatient period. Only include medications given by Rheumatologist for treatment of gout. No need to include all medications given (ex. Refill prescription for Diabetes).

Did the patient receive gout education – check if patient received education regarding gout during this consultation.

Part 4: Follow-up Consultation Form

***If 1 or more years have passed since the First Consultation, please print and complete PART II CLINICAL SCENARIO STAGING FORM and attach.**
New CSS: _____
Clinical Scenario Staging is based on patient's tophi and the frequency of symptoms experienced in the past year. This form is completed on the first consultation with the Rheumatologist and yearly when it coincides with a consultation.

Approximate days since last flare/ Days until flare completely resolved –
Flare is defined as the fulfillment of at least 3 of 4 criteria (patient defined gout flare, pain at rest score of >3 on a 0–10-point numerical rating scale, presence of at least 1 swollen joint, and presence of at least 1 warm joint). When interviewing a patient regarding historical gout flares (flares not seen by medical practitioners), the Rheumatologist should ask the patient to describe the historical flare to ascertain whether or not the event was gout related.

Flare resolution – considered as spontaneous if the patient did not take any medication (ex. Colchicine, NSAIDs, steroids) for the flare.

Any medication adverse effect? – Please list any adverse medication effect as reported by the patient.

If last consult had a flare, symptoms from that flare are now – refers response to treatment of the previous flare based on patient's pain scale. First record the patient's pain scale during this consultation – PS. Second, compare the PS now to the previous PS from flare during the last consultation. **Completely resolved** means the PS is now 0. **No response/Failure** means there was no change in PS or there was an increase/worsening of PS. **Improved and on target** means the PS decreased by at least half compared to the previous consult (at least 24 hours ago). **Improved but off target** means PS decreased by less than half compared to the previous consult (at least 24 hours ago).
Sample Scenarios: If the flare has ended and the pain is currently in pain now (from a new flare), then the previous flare is considered – **Completely resolved**. The current pain will be ascribed to a new gouty arthritis flare. If for example, a patient consulted 2 days ago and now consults due to worsening of symptoms then the patient ongoing flare response can be – **No response/Failure**.

Currently in Gouty Arthritis Flare – check if the patient fulfills at least 3 of 4 criteria (patient defined gout flare, pain at rest score of >3 on a 0–10-point numerical rating scale, presence of at least 1 swollen joint, and presence of at least 1 warm joint).

Flare Trigger for this attack (Skip if no flare) – are the food/medication/activities identified by the patient and the doctor. Beans may be included as a flare trigger since it is what the patient perceives to be the cause of their gout attack. Care in explaining to the patient of what the possible gout triggers must be done and future follow-up with the patient may track their identification of triggers.

Number of joints involved in the current gout flare:
Large joints – ankle, knee, wrist, elbow, hip, shoulder
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Duration of pain prior to consult – amount of time in hours since the begining of the gouty flare up to the time of consult.

Maximal pain intensity during the ENTIRE GOUT FLARE PERIOD – pain experienced on a scale from 1 to 10 since the beginning of the gout flare until consult.

Pain intensity during the ACTUAL CONSULTATION – pain experienced on a scale from 1 to 10 during the consultation. It may be the same as the maximal pain intensity.

GOUT Medication taken PRIOR TO THIS CONSULT – this pertains to all medication taken by the patient specifically for gout symptoms/tophi prior to the patient's current consultation. Efficascent oils, bath salts, cummin rubs, ginger/herbal teas are considered part of **Herbal/Alternative Medicine**. This question may be used to check for patient compliance to medication.

Other Medications Taken – refers to medication that may be correlated to patients' comorbidity that is affected by gout (ex. Tuberculosis, Diabetes, Dyslipidimia, Hypertension, etc.)

Gout Medication Prescribed by – refers to the person who prescribed the medication taken specifically for gout. More than 1 person may have given a prescription for gout medication. This question may be used to check if they are seeing more persons for their gout treatment.

Is the patient compliant to medication (Self-reported compliance)? – ask the patient if they have been taking the medication as prescribed by the doctor.

Recent laboratory exam – include tests done within 1-month duration. If the patient consults and laboratory results were sent to the Rheumatologist, this data is included in the first consultation form. If the patient has a new consultation and follows up with the Rheumatologist with the laboratory results, this may be included in the later follow-up consultation form. Included dates are put to check possible overlapping data.

Patient was treated: Inpatient / Outpatient – if the patient was seen on an outpatient basis and was advised to be admitted, then the patient is labelled as an **Inpatient** treatment. If the patient was seen on an outpatient basis and treated without admission, then the patient is labeled as **Outpatient**. If that same patient treated outpatient but was immediately admitted for whatever reason (hypertension control, blood sugar management, surgery, gouty flare, etc.), then this counts as a new consult and Part 4: Follow-up Consultation Form is filled up. The patient then would be labeled as **Inpatient**. If an admitted patient and was referred right before discharge, and the treatment was to be started after discharge – then that patient is seen as inpatient but treated as **Outpatient**.

Procedure done during this consult/referral – check as indicated. May check more than 1 procedure.

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Did the patient receive gout education – check if patient received education regarding gout during this consultation.