INTERNATIONAL ACADEMIC PUBLICATION SERIES

VIEN GUT MODEL

Integrated Outpatient Care for Complex Chronic Multimorbidity

Part C – Management of the Main Disease Axis and Comorbidities

DOCUMENT C.1

MANAGING THE GOUT AXIS AND ITS COMORBIDITIES

Applying the A–B architecture of the Vien Gut Model to the gout disease axis in the setting of complex chronic multimorbidity

Vien Gut Model – International Academic Publication Series

First systematized compilation – March 2026

Ho Chi Minh City, Vietnam

C.1 – Management of Gout and ComorbiditiesAUTHORS AND ACADEMIC LEAD

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TEAM INVOLVED IN DESIGNING HOW AND DATA-TO-OPERATE – VIEN GUT

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ACADEMIC SUPPORT AND WHAT (GUIDELINE) BENCHMARKING – INTERNATIONAL EXPERT GROUP

Thomas Bardin, Pascal Richette Co-authors of the EULAR recommendations, together with French experts, transferred the WHAT of gout and comorbidity treatment guidelines and helped benchmark WHAT against international standards.

TREATING PHYSICIANS + MULTIDISCIPLINARY TEAM OF VIEN GUT GENERAL CLINIC

Clinical HOW in practice – risk stratification, opportunity-window assessment, longitudinal follow-up, risk control, polypharmacy management, and activation of the safety referral valve.

STUDY SITE

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ABSTRACT

Patients with severe complicated gout together with complex chronic multimorbidity—such as chronic kidney disease, heart failure, decompensated cirrhosis, and adrenal insufficiency—are usually excluded from international clinical studies. High treatment targets have been shown to be achievable, including dissolution of urate crystals [4–11], dialysis deferral [12,13], reduction of heart-failure decompensation [14–16], and hepatic recompensation [17,20]. But these results mostly come from selected populations in research settings that are very different from real-world practice.

Even in the 100 patients included in the Vien Gut study series, published at ACR 2017 [4], EULAR 2019 [5], ACR 2020 [6], and Seminars in Arthritis and Rheumatism 2022 [7] with Professor Thomas Bardin as co-author, the population was not a broad severe multimorbidity gout population. Although it included hypertension, type 2 diabetes, dyslipidemia, coronary disease, and long-term steroid dependence, the study required eGFR > 60 mL/min in order to avoid the renal effects of anti-inflammatory pain medicines.

This created an important clinical and academic question for Vien Gut: how can patients who are excluded from studies still be helped to regain treatment goals similar to those achieved in Vien Gut studies and in other international studies?

Document C.1 answers that question. It explains how Vien Gut organizes urate crystal dissolution in patients who are still within guideline-covered zones, and also in patients with CKD stage 3 to end stage, from ischemic heart disease to heart failure with reduced ejection fraction, from liver fibrosis F2–F3 to decompensated cirrhosis, and in other severe chronic diseases. It presents the process of measurement, longitudinal follow-up, and confirmation of crystal-free status at the assessment time point. It also explains the role of surgery in gout, and the guideline-based principle that gout can be cured, which is the basis for confirming gout-free status at the assessment time point.

From July 2024 to March 2026, 155 patients were confirmed as crystal-free. This is single-center data and still needs further standardization and multicenter verification. The first step is the ReViGore40 study (NCT06669000) [23], led by Professor Pascal Richette.

The other major comorbidity axes are presented separately: C.2 for dialysis deferral, including patients with severe gout complications; C.3 for reducing heart-failure decompensation, including patients whose underlying disease is a complication of gout; and C.4 for hepatic recompensation, including patients whose underlying disease is also a complication of gout.

BACKGROUND

Vien Gut was founded in 2007 to find practical solutions for patients with severe complicated gout who were living with prolonged pain, deadlock, and despair.

In 2014, a research collaboration with Professor Thomas Bardin of Paris 7 University, France, and his colleagues helped Vien Gut clarify its treatment strategy for gout and comorbidities. Recommendation 8 of the 2006 EULAR guideline [1] stated a core principle:

“Gout is a crystal deposition disease. It can exist only when urate crystals are present. If further crystal formation is prevented and existing crystals are dissolved, the patient is essentially cured.”

Results from Vien Gut’s treat-to-target allopurinol study in 100 patients with severe gout, published with Professor Thomas Bardin and colleagues at ACR 2017 [4], EULAR 2019 [5], and ACR 2020 [6], changed how Vien Gut defined its treatment goal. While guidelines emphasized lowering and maintaining serum uric acid below the

saturation threshold, Vien Gut set a more central task: dissolve all deposited urate crystals. Lowering uric acid for long enough is mandatory, but dissolving the crystal burden is the main mission.

Once Vien Gut made complete urate crystal dissolution the central mission, that goal was applied to all patients. EULAR and ACR guidance on allopurinol or febuxostat, colchicine, NSAIDs, and corticosteroids was still used, but adapted to each real clinical situation.

The real-world challenge then became clear: how to measure the urate crystal burden, how to lower uric acid and manage flares in very different patients—from uncomplicated disease to severe complications—how to combine treatment for comorbid diseases using their own guidelines, and how to change patient and family understanding so that goals, methods, and treatment management are followed correctly.

These kinds of tasks are hard to achieve in fragmented or cross-sectional care models. But they are routine work for physicians and multidisciplinary teams in an integrated multimorbidity care model such as Vien Gut.

FIRST VISIT FOR PATIENTS WITH GOUT

While Document B.1 describes the operational design of the first visit for patients with complex chronic multimorbidity in the Vien Gut model, Section 1 of Document C.1 describes the first-visit design specifically for management of the gout axis and its comorbidities.

1.1. Measuring the urate crystal burden by ultrasound

1.1.1. Role of ultrasound and international basis

At the first visit for a patient with gout, Vien Gut uses joint ultrasound mainly to establish a baseline of deposited urate crystals. This allows the physician and the care team to follow crystal dissolution over time during treatment. This fits the logic of C.1: gout treatment should not stop at lowering serum uric acid; it must also dissolve the pool of urate crystals already deposited in joints and surrounding tissues.

OMERACT [25] standardized four ultrasound lesions in gout: the double contour sign, tophus, aggregates, and erosion. The 2023 EULAR imaging recommendations [24] confirmed that ultrasound can follow both crystal deposits and inflammation, adding useful information beyond clinical and biochemical assessment.

1.1.2. Why ultrasound was chosen instead of DECT

At Vien Gut, ultrasound was chosen instead of DECT because it meets several needs at once: no radiation, repeated use over many years, lower cost, real-time results, feasibility in low- and middle-income settings, and the ability to see the double contour sign, which DECT cannot distinguish directly. Vien Gut began studying joint ultrasound in 2012, comparing it with gross findings during tophus surgery and with DECT in 2014. Ultrasound became not only a diagnostic tool, but also an operational tool for treatment management and long-term adherence.

1.1.3. Measurement method and target-tophi strategy

The first ultrasound study at Vien Gut answers four questions: where are the crystals located (cartilage, joints, tendons, soft tissue), where is the heaviest burden, how large are the tophi, and how strong is the double contour sign? Vien Gut measures tophi with a two-dimensional caliper method (mm^2). This method covers the full range of disease, is practical in daily work, and is sensitive to change. The double contour sign is recorded by severity grade.

Vien Gut uses ultrasound as a treatment-management measurement system. In patients with many tophi, scanning every site at every follow-up is not practical. So from the first visit, Vien Gut sets a target-tophi strategy:

choose priority sites—often both first metatarsophalangeal joints—as fixed longitudinal targets. When one target tophus has dissolved, the team moves to a new target and continues step by step until the crystal burden is exhausted.

1.1.4. Ultrasound schedule and its complementary role with serum uric acid

Vien Gut uses ultrasound every 3 months. This is early enough to show target tophi shrinking, close enough to support adherence, and still realistic in cost. Ultrasound is the 'eye' that sees the crystal burden. Serum uric acid is the 'biochemical clock' used to adjust treat-to-target therapy according to ACR 2020 [3]. The two tools support each other; they do not replace each other.

From the first visit onward, ultrasound establishes the starting crystal burden, selects the longitudinal target, and gives visual proof that helps patients understand and believe in the treatment goal. This becomes the basis for later steps: uric acid control, flare management, target-tophi follow-up, and confirmation of crystal-free status.

1.2. Detecting tophus-related joint damage by X-ray

1.2.1. The role of X-ray in the three-layer imaging system

X-ray is used to detect and standardize the degree of bone and joint structural damage caused by tophi. It is the second imaging layer in the model: ultrasound shows the crystal burden that is being deposited or dissolved, while X-ray shows the structural consequences left by long-term deposition. Appendix 6 defines X-ray as part of a three-layer imaging system, with a role in following bone defects, structural recovery, and the shrinking-toe sign.

Among 8,001 gout patients seen from January 2020 to March 2026, 2,543 had joint-destroying tophi (31.78%) and 4,558 had tophi without joint destruction (56.97%). Vien Gut therefore performs X-ray from the first visit to separate two very different clinical situations.

1.2.2. Improvement of erosive damage under urate-lowering therapy – SAT0410, EULAR 2019 [5]

At EULAR 2019, the Vien Gut group, together with Professor Thomas Bardin and colleagues, presented abstract SAT0410 [5], a prospective study of 100 patients with gout starting allopurinol. The median maintenance dose was 520 mg/day. Seventy-one patients had urate arthropathy on baseline X-ray. The X-ray erosion score improved by 0.7 at month 6, 1.4 at month 12, and 4.2 at month 24. The improvement correlated with reduction of the double contour sign. Importantly, the study also noted bone repair, reappearance of bone margins, and joint fusion in 4 patients.

This finding means that, in severe gout, X-ray is more than a tool to confirm damage. It can also follow improvement of erosions and return of bone contours, showing that bone and joint damage in severe gout is not fixed forever and can change if crystals are dissolved.

1.2.3. Shrinking toe – ACR 2020 [6]

At ACR 2020, the Vien Gut group presented Abstract 0684 [6], which described the shrinking-toe sign in 12 toes from 10 patients with severe tophaceous gout. The mechanism is collapse of the subchondral bone area after crystal dissolution. It appeared on average 22.9 months after the serum urate goal of <300 µmol/L had been reached.

Without serial X-rays, shrinking toe can easily be misunderstood as treatment failure. The report emphasized the need to treat gout early, before tophi destroy the bone framework so severely that, once crystals dissolve, the joint structure is no longer strong enough to preserve its shape.

1.2.4. Standardized clinical photography and the three-image combination

At Vien Gut, X-ray does not work alone. Its full value appears when it is combined with joint ultrasound and standardized clinical photography in one unified longitudinal follow-up system. Appendix 6 describes the third imaging layer as standardized clinical photographs taken at every visit with the same angle, distance, background, and lighting, so they can be matched against ultrasound and X-ray, document progression, and support visual medicine.

In this system, ultrasound shows the changing crystal burden, X-ray records bone defects, reconstruction, and shrinking toe, and standardized photographs show the visible external form over time, including subcutaneous tophi and deformities of the feet or elbows. This visual layer links specialist imaging to what the patient can actually see.

Together, the three layers give a full picture: crystals dissolving, bone and joint structure recovering, and external clinical appearance changing over time.

1.3. Diagnosis and treatment stratification of gout and comorbidities

1.3.1. Why international guidelines require stratification

The next step of the first visit at Vien Gut is diagnosis and treatment stratification across both the gout axis and the comorbidity axes. Clinical decisions must be based on multi-organ assessment: kidneys, cardiovascular system, liver, metabolism, endocrine system, and hematology.

International guidelines already point in this direction. EULAR [1,2] recommends systematic screening for comorbidities and cardiovascular risk factors in all patients with gout, including impaired kidney function, cardiovascular disease, diabetes, dyslipidemia, obesity, and lifestyle-related risks. ACR 2020 [3] also stresses that gout treatment must be planned in the setting of comorbidity. Drug choice, anti-inflammatory therapy, and dose escalation all have to be judged against the safety of each disease axis. Allopurinol remains the preferred first-line urate-lowering therapy in many patients, including those with CKD, but it should be started low and increased carefully.

KDIGO 2024 [12] classifies CKD by cause, eGFR, and albuminuria. AHA/ACC/HFSA [14,15] classifies heart failure by ejection fraction. ADA [28] defines diabetes using HbA1c ≥6.5%. Baveno VII [17,20] distinguishes compensated from decompensated cirrhosis and introduces the concept of recompensation. So the question is no longer just 'How should gout be treated?' but 'How should gout be treated on top of which CKD stage, which EF, which cirrhosis stage, which HbA1c level, and under what safety limits?'

1.3.2. Comorbidity structure at Vien Gut

Vien Gut treated 8,001 patients with gout between January 2020 and March 2026: 900 without tophi, 7,101 with tophi, including 2,543 with joint destruction. The cohort also included 749 patients with chronic kidney disease, 757 with liver disease (674 with F2–F3 fibrosis and 83 with decompensated F4 cirrhosis), 624 with cardiovascular disease or heart failure, 3,272 with low cortisol or steroid withdrawal, 1,148 with HbA1c > 6.5%, and 4,232 with hypertension. This is gout inside a dense matrix of comorbid disease.

No.	Disease group	Number of patients	Rate
1	Gout without tophi	900	11.25%
2	Gout with tophi but no joint destruction	4,558	56.97%
3	Tophaceous gout with joint destruction	2,543	31.78%
4	Chronic kidney disease	749	9.36%
5	Liver disease (F2–F3: 674; decompensated F4: 83)	757	9.46%

6	Ischemic heart disease, arrhythmia, or heart failure	624	7.80%
7	Low cortisol / steroid withdrawal	3,272	40.89%
8	HbA1c > 6.5%	1,148	14.35%
9	Hypertension	4,232	52.89%

1.3.3. Four practical questions for stratification

Vien Gut asks four stratification questions: (1) how severe is the gout axis—no tophi, tophi without joint destruction, or joint-destructive tophi? (2) What is the stage of the comorbid disease? (3) Which axis is currently the main survival threat? (4) What should be the immediate priority goal?

This stratification determines whether colchicine or NSAIDs can be used, which urate-lowering therapy should be chosen, what dose and speed of escalation are safe, how dense the follow-up should be, which laboratory tests or consultations should be prioritized, and when the referral safety valve should be activated. Stratifying by comorbidity is how WHAT becomes safe operational HOW in real life.

1.3.4. From stratification to treatment decisions and phase-specific goals

At Vien Gut, stratification sets phase-specific goals. In some patients, the near goal is flare control and safe initiation of urate-lowering therapy. In others, the first priority is to keep the kidneys off dialysis, stabilize heart failure, or break the alcohol–cirrhosis–adrenal insufficiency loop before pushing crystal dissolution faster.

The general rule is that comorbidities are not just a background issue. They directly decide urate-lowering strategy, flare treatment, follow-up rhythm, and the threshold for referral. At the first visit, stratification decides who is still within the guideline-covered zone, who is in the borderline zone, and who is already outside guideline coverage. It also decides who can move faster toward crystal-free and who must move more slowly to protect safety.

OUTPATIENT MANAGEMENT OF GOUT AND COMORBIDITIES

2.1. Goals of the outpatient treatment plan

The outpatient treatment plan at Vien Gut is built on three goal layers: (1) dissolve the deposited urate crystal burden—this is the central goal for every patient; (2) protect vital organs—do not worsen kidney failure, do not push heart failure into decompensation, do not worsen cirrhosis, and do not trigger adrenal crisis; and (3) keep treatment going for long enough and steadily enough to reach crystal-free status while an opportunity window still exists.

These three layers are not always ranked in the same order. In patients still well within the guideline zone, the first layer dominates. In patients with severe kidney disease or decompensated heart failure, the second layer may temporarily come first. In patients with several severe overlapping diseases, all three layers have to be balanced continuously at each follow-up visit.

2.2. Core principles and patient zones

Vien Gut uses five core principles: (1) treatment always follows two tracks at once—the gout axis and the comorbidity axis; (2) when crystal dissolution speed conflicts with the safety of vital organs, organ safety comes first; (3) urate lowering must go together with flare control and polypharmacy management; (4) treatment is organized by phases, not by one fixed prescription; and (5) outpatient treatment continues only while a safe opportunity window remains—when the window closes, Vien Gut actively refers the patient.

Based on the stratification described above, patients are divided into three zones: the guideline-covered zone (normal or mildly reduced kidney function, no heart failure, no severe cirrhosis, no steroid dependence); the borderline zone (one or two comorbid diseases at a moderate level); and the outside-coverage zone (CKD stage 4–5, reduced-EF heart failure, decompensated cirrhosis, adrenal insufficiency, or several severe axes overlapping at once).

2.3. The four treatment phases, monitoring rhythm, and follow-up

Vien Gut organizes treatment into four phases: Phase 1 – Acute stabilization (control inflammation and pain, evaluate comorbidities, and build the baseline; this may last 1–2 weeks in the guideline zone and several weeks to months outside it); Phase 2 – Titration (start urate-lowering therapy, increase dose step by step, and control flares; the speed depends on the zone); Phase 3 – Maintenance (keep serum urate below saturation long enough for the crystal burden to continue dissolving; this is the longest phase, and poor adherence becomes the main risk); and Phase 4 – Crystal-free assessment (confirm absence of crystals by imaging, clinical status, and biochemistry, and then move to Sections 3 and 5). Patients may move backward between phases if comorbid disease becomes unstable again.

No.	Phase	Main content	Follow-up rhythm
1	Phase 1	Acute stabilization: control inflammation and pain, assess comorbidities, build the baseline	Monthly or more often
2	Phase 2	Titration: start ULT, increase dose step by step, control flares	Monthly
3	Phase 3	Maintenance: keep serum urate below saturation long enough for the crystal burden to continue dissolving	Every 2–3 months, aligned with ultrasound
4	Phase 4	Crystal-free assessment: confirm absence of crystals by imaging, clinical status, and biochemistry	Every 3–6 months

At Vien Gut, Phases 1 and 2 usually require monthly or even denser visits. Phase 3 can stretch to every 2–3 months, usually aligned with ultrasound. Phase 4 can extend to every 3–6 months. X-rays are repeated every 6–12 months. Standardized clinical photographs are taken at each visit. Vien Gut also triggers unscheduled early visits when severe flares occur, creatinine rises more than 30%, symptoms of heart or liver decompensation appear, adrenal symptoms appear, or the patient stops medication on their own.

2.4. Treatment plan for gout patients still within the guideline-covered zone

2.4.1. Choice of urate-lowering therapy and dose-escalation process

Vien Gut uses allopurinol in patients with eGFR of 60 mL/min or higher, and febuxostat when eGFR is below 60. If a patient is allergic to one drug, the other is used. In a retrospective review of 1,000 new patients seen in 2025, there were 27 mild allergic reactions to allopurinol (2.7%): 11 at the start, 13 during the first 3 months of dose escalation, and 3 only after escalation to 800 mg. Since Vien Gut adopted gradual treat-to-target dose escalation in 2015, no Stevens–Johnson syndrome or toxic epidermal necrolysis has been recorded. This is consistent with the HLA-B*5801 study done with Professor Bardin in 2019 [22], where all 10 severe skin reactions occurred in patients who had not been escalated slowly. High dose itself was not the key risk factor; lack of slow escalation was statistically significant ($p<0.0001$).

At Vien Gut, allopurinol is usually started at 150 mg for 15 days, increased to 300 mg on day 16, and checked again on day 31. If the target is not reached, the dose is increased to 450 mg, and then continued upward by the

same logic to a maximum of 800 mg/day. Febuxostat is started at 40 mg when eGFR ≥30, or 20 mg when eGFR <30, with a maximum of 120 mg/day.

2.4.2. Serum uric acid target

Vien Gut uses <300 µmol/L as the treatment target for all patients. Since 2020, many patients have been brought below 240 µmol/L, and in some safe cases even below 200 µmol/L. The uric-acid target is always linked to target-tophi ultrasound every 3 months. If uric acid reaches target but the tophus does not shrink, the team reviews adherence, drug interactions, and whether a lower uric acid level is needed.

2.4.3. Flare treatment and polypharmacy management

Vien Gut prevents flares with low-dose colchicine or low-dose NSAIDs for at least 3–6 months after starting urate-lowering therapy. Short-course corticosteroids are used when both are not suitable. All gout patients are warned from the start that worse pain early in treatment may simply mean crystals are dissolving. Polypharmacy is reviewed at every follow-up visit. Vien Gut prefers medicines with double benefit, such as losartan and SGLT2 inhibitors, and removes unnecessary drugs before adding new ones.

2.5. Adjusting the plan for each comorbidity

Each subsection below explains what must change compared with the standard framework in 2.4, using four questions: what is the main risk, what must be avoided, what must be prioritized, and how should urate-lowering therapy and flare treatment be modified?

No.	Disease axis	Avoid	First-line ULT	Flare management	Extra follow-up	Guideline
1	Chronic kidney disease	NSAIDs (CKD 4–5)	Febuxostat 20–40 mg	Short-course corticosteroid	Creatinine, potassium, eGFR	KDIGO 2024 [12]
2	Cardiovascular disease / heart failure	NSAIDs (any EF)	Allopurinol; SGLT2i with dual benefit	Short-course corticosteroid	NT-proBNP, weight, edema	AHA/ACC/HFSA [14–16]
3	Liver disease / cirrhosis	NSAIDs; colchicine in Child B–C	Low dose, slow escalation	Short-course corticosteroid	Albumin, bilirubin, INR	Baveno VII [17,20]
4	Steroid dependence	Abrupt steroid withdrawal	Start ULT alongside tapering	Stronger flare prevention	Morning cortisol every 4–6 weeks	Vien Gut HOW
5	Diabetes	Long corticosteroid courses	No major change	Prefer colchicine	HbA1c every 3 months	ADA 2025 [28]
6	Anemia, electrolytes	—	Correct instability before or together with ULT	—	CBC, electrolytes, iron, ferritin, vitamin D	—

2.5.1. On the background of chronic kidney disease

At Vien Gut, the main risks are oxypurinol accumulation, NSAID nephrotoxicity, and the possibility that every flare treated with NSAIDs may push creatinine upward in a non-reversible way. NSAIDs are avoided in CKD stage 4–5, and standard-dose colchicine is avoided when eGFR is below 30. The main priority is to keep the patient off dialysis. Febuxostat is often the first choice, usually starting at 20–40 mg and increasing every 4–6 weeks. Flares are treated with short-course corticosteroids; colchicine 0.5 mg every other day can be used in CKD stage 3. Creatinine and potassium are followed every 2–4 weeks during titration, and eGFR every 3 months in maintenance. Referral is triggered by rapid eGFR decline (>5 mL/min/year), persistent potassium >5.5, or symptoms of advanced uremia. The framework is coordinated with KDIGO 2024 [12].

2.5.2. On the background of cardiovascular disease and heart failure

At Vien Gut, the main risk is that NSAIDs retain fluid and can precipitate heart-failure decompensation. Febuxostat was also questioned for cardiovascular safety after CARES 2018 [27]. NSAIDs are therefore avoided in heart failure regardless of EF, and colchicine is used carefully when interacting drugs such as amiodarone or digoxin are present. The main priority is to keep EF and hemodynamic stability. Allopurinol is preferred when kidney function allows, and SGLT2 inhibitors are valuable because they help both the heart and other axes. Flares are usually treated with short-course corticosteroids. Extra follow-up includes NT-proBNP every 3 months and weight plus edema assessment at every visit. Referral is triggered by acute decompensation, EF <30%, or uncontrolled arrhythmia. The plan follows AHA/ACC/HFSA 2022 [14–16].

2.5.3. On the background of liver disease and cirrhosis

At Vien Gut, the risks include liver-enzyme rise with allopurinol, the contraindication of colchicine in advanced cirrhosis (Child–Pugh B–C), and the fluid retention or bleeding risk of NSAIDs. NSAIDs are avoided in cirrhosis, and colchicine is avoided in Child–Pugh B–C. The priority is to keep the liver stable; Baveno VII recompensation goals [17,20] must be stabilized before pushing crystal dissolution faster. Alcohol abstinence is a prerequisite. Urate-lowering therapy starts at low dose with AST, ALT, and GGT followed every 2–4 weeks. In decompensated cirrhosis, the lowest effective dose is used. Extra follow-up includes albumin, bilirubin, and INR. Referral is triggered by new ascites, bilirubin >50 μmol/L, INR >1.7, gastrointestinal bleeding, or rising MELD score.

2.5.4. On the background of steroid dependence and secondary adrenal insufficiency

At Vien Gut, the risk is suppression of the hypothalamic–pituitary–adrenal axis. Abrupt steroid withdrawal can cause acute adrenal crisis. Sudden cessation must be avoided, and high-dose corticosteroids for flares are avoided until the baseline cortisol status is known. Morning cortisol and ACTH are checked at the first visit, and a structured steroid-taper plan is created using stepwise dose reduction. If the patient is otherwise stable, urate-lowering therapy is started in parallel with steroid tapering, but flare prevention is often intensified because the patient is losing the anti-inflammatory effect of chronic steroids. Morning cortisol is followed every 4–6 weeks during tapering. No gout guideline directly covers this group; the integrated steroid-tapering protocol used by Vien Gut is part of its own HOW, built from practice in 3,272 steroid-dependent patients.

Vien Gut has a structured tapering protocol using Medrol 4 mg to safely restore adrenal function in gout patients who are steroid dependent and also have type 2 diabetes, hypertension, and CKD stages 3–5. This is a particularly difficult group because even low-dose Medrol can worsen hyperglycemia, fluid retention, hypertension, and the burden of reduced kidney function. The Vien Gut protocol uses Medrol 4 mg as the basic step-down unit. Each tapering step is linked to morning cortisol, glucose, blood pressure, creatinine, and potassium monitoring. If adrenal symptoms or instability in a comorbid axis appears, the dose is held or returned to the previous step. The aim is to stop steroids fully and recover the hypothalamic–pituitary–adrenal axis while keeping all comorbid axes safe. This process is not described in any gout or endocrine guideline; it is an integrated Vien Gut HOW built from practice.

2.5.5. On the background of diabetes and metabolic disease

At Vien Gut, the main risk is loss of glycemic control when corticosteroids are used for flare treatment. Long corticosteroid courses are avoided in uncontrolled diabetes. HbA1c control is pursued in parallel with urate lowering. There is usually no major change in ULT choice, and losartan plus SGLT2 inhibitors are seen as medicines with double or triple benefit. Colchicine is preferred for flare treatment because it does not worsen glucose. If corticosteroids must be used, blood glucose is followed daily for 7–10 days. HbA1c is checked every 3 months, in line with ADA 2025 [28].

2.5.6. On the background of anemia, electrolyte disorders, and hidden biological instability

At Vien Gut, many gout patients with multimorbidity carry biological instability that does not belong neatly to one named comorbidity axis but still directly affects treatment safety. Examples include chronic anemia, potassium disorders, hyponatremia, persistent high GGT, and vitamin D deficiency. The first-visit laboratory panel therefore includes CBC, electrolytes, iron, ferritin, vitamin D, and morning cortisol so that these unstable factors can be corrected before or alongside urate-lowering therapy.

2.6. Gout patients with overlapping severe multimorbidity

When a patient carries two, three, or four severe disease axes at the same time, drug constraints and safety thresholds often conflict directly. The four treatment phases then become distorted: Phase 1 becomes longer because several axes must be stabilized together; Phase 2 titration becomes slower; Phase 3 is less stable because the patient may move backward at any time; and Phase 4 still aims at crystal-free status, but in some patients the realistic goal is maximal crystal reduction within safety limits. The third stratification question from Section 1.3—Which axis is the main survival threat right now?—must be answered again at every visit. Follow-up rhythm becomes fully individualized. No international guideline directly explains how to manage this group.

2.7. Referral safety valve and outpatient reintegration

Referral is a built-in operational component, not a sign of failure. Referral thresholds are set by disease axis: kidney—eGFR <15, potassium >6 mmol/L, or eGFR drop >10 mL/min within 3 months; heart—acute decompensation, EF <30%, or uncontrolled arrhythmia; liver—GI bleeding, refractory ascites, hepatic encephalopathy, or MELD >20; adrenal axis—acute adrenal crisis needing inpatient emergency treatment.

No.	Disease axis	Referral trigger threshold
1	Kidney	eGFR <15; potassium >6 mmol/L; eGFR drop >10 mL/min within 3 months
2	Heart	Acute decompensation; EF <30%; uncontrolled arrhythmia
3	Liver	GI bleeding; refractory ascites; hepatic encephalopathy; MELD >20
4	Adrenal axis	Acute adrenal crisis needing inpatient emergency care

When referral is activated, the file sent with the patient includes the stratification summary, recent disease-axis changes, medication list, current serum uric acid, and the most recent crystal-burden measurement. Reintegration back into outpatient care requires that the core disease axis has become stable again, the patient can return to scheduled follow-up, and the opportunity window is still open for ongoing ULT. Section 2.7 links directly to C.2 (dialysis deferral), C.3 (reduced heart-failure decompensation), and C.4 (hepatic recompensation).

THE ROLE OF SURGERY IN GOUT CARE AT VIEN GUT

3.1. The place of surgery in the treatment pathway

In severe complicated gout, surgery does not compete with internal medicine and does not replace urate-lowering therapy. Instead, it addresses mechanical damage that internal medicine alone cannot reverse fast enough: tendon compression, cartilage destruction, bone defects, prolonged ruptured tophi, infection, or major loss of function. In the four-phase pathway described earlier, surgery usually appears in Phase 1 when ruptured or infected tophi need urgent control, or in Phase 3 when very large tophi are not dissolving quickly enough and continue to impair function. After surgery, the patient returns to the same medical pathway at Vien Gut: ULT continues, longitudinal ultrasound continues, and the crystal-free goal does not change.

3.2. Principles, classification, and techniques

The Vien Gut surgical protocol (PL-5.C1) follows three principles: describe the lesion before making the indication, repair according to structure (tendon, capsule, cartilage surface, bone), and restore function. Vien Gut classifies tophus masses by eight dimensions—site, size, number, anatomy, progression, related disease, age group, and lesion pattern—and grades injury across four core anatomic structures, each with three severity levels. Repair follows the same structural logic: tendon lesions require release of adhesion, removal of urate deposits, and tendon repair or grafting; joint lesions require opening the capsule and removing tophi; bone lesions require tophus excision, curettage of bone defects, and bone shortening if a segment has been lost. Full details are in PL-5.C1.

3.3. Indications, contraindications, and process

Surgery is indicated when the mechanical and functional benefit is greater than the total-body risk: ruptured tophi, infected ruptured tophi, tendon/muscle/bone/joint damage, loss of function, or tophi at high risk of rupture or major interference with daily life. Contraindications include unstable severe internal disease, advanced liver or kidney failure, steroid dependence, or severe wasting. Surgery is always judged inside the full-body risk stratification described in Section 1.3. Vien Gut organizes tophus surgery into five stages: preparation, operation, early monitoring, postoperative care, and rehabilitation. If the lesion goes beyond the safe scope of the protocol, transfer is allowed.

3.4. Methodological and research contributions

3.4.1. Gross anatomy–ultrasound correlation

During tophus surgery, surgeons can directly see urate crystals on cartilage surfaces, tendon surfaces, in the joint capsule, or inside bone defects. This gave Vien Gut a structural basis for the double contour sign and tophus appearance on ultrasound. This correlation helped standardize recognition of these lesions at Vien Gut from 2012 onward, even before OMERACT [25] published its formal definitions. In this way, surgery provided an anatomic reference that strengthened the imaging foundation of the model.

3.4.2. CPPD crystals inside gouty tophi

The study by Ea HK, Bardin T, and colleagues (Arthritis & Rheumatology, 2020) [26] analyzed 25 tophus samples from 22 patients who underwent surgery at Vien Gut. It found CPPD crystals in 9 of 25 samples from 6 patients. This suggests that CPPD may form later inside mature tophi and may help explain why some tophi dissolve slowly even when uric acid is already at target, because the CPPD part does not respond to ULT.

3.5. Limitations

The Vien Gut surgical protocol was developed from internal practice data in a population of patients with severe complicated gout. It is therefore a practice-derived protocol: it has a clear practical basis, but it still needs further standardization and external verification before it can be proposed as a broader guideline.

THE ROLE OF PATIENTS AND FAMILY

4.1. Patients and family are part of the operating system

The global medical community increasingly agrees that integrated care must be viewed from the patient's experience—patient-centered and coordinated across services. In long-term outpatient care, the patient is not just a recipient of treatment. The patient helps run the system: taking medicine correctly, recognizing warning signs, controlling alcohol intake, and returning on time. Document B.3 established that the opportunity window

exists only when the necessary system conditions and the sufficient patient conditions are both present. B.4 developed this into eight patient capacities.

4.2. Eight participation capacities applied to gout patients

Vien Gut applies the same eight capacities to gout patients: real commitment (accepting a multi-year path to crystal-free status), correct understanding (knowing that flares during dose escalation may mean crystals are dissolving), practical resources (medicine and follow-up capacity), self-monitoring (seeing warning signs from the heart, liver, kidneys, or adrenal axis), a support system (family or caregiver), cooperation (not adding or stopping medicine independently), structured training (from the first visit and reinforced at each follow-up), and ongoing reassessment. Full details are in B.4.

4.3. Geography and transfer of care

Vien Gut patients come from all 63 provinces and cities of Vietnam, now administratively merged into 34 provinces and cities. Many live more than 2,000 km away. Because of travel reality in Vietnam, many patients who live 100–200 km away can only return every 4–6 months, not at the ideal 2–3 month rhythm described in Section 2.3. This created a real problem that no guideline explains: how can the treatment strategy be maintained when patients cannot return frequently?

Among 8,001 patients seen from January 2020 to March 2026, 613 (7.66%) came once and then stopped; 2,455 (30.68%) were treated for 3–6 months and then stopped; 3,257 (40.71%) were treated for 6–9 months and then asked to continue locally—the largest group, and most had already reached the serum uric acid target; 1,327 (16.59%) were still in active treatment; and 349 (4.36%) were lost to follow-up. Adding 376 patients from before 2020 gives a total of 1,703 still under treatment.

No.	Group	Number (%)	Note
1	One visit only, then stopped	613 (7.66%)	Mostly milder cases
2	Treated 3–6 months, then stopped after pain improved	2,455 (30.68%)	Did not fully understand that pain relief is not cure
3	Treated 6–9 months, then requested transfer to local care	3,257 (40.71%)	Largest group; most had reached the uric acid target
4	Lost to follow-up	349 (4.36%)	
5	Still treated at Vien Gut (from 2020 onward)	1,327 (16.59%)	
6	Still treated at Vien Gut (before 2020)	376	Total still treated: 1,703 cases

For patients who requested local continuation of treatment, Vien Gut provided records and guidance. However, there is still no formal coordination mechanism with local health facilities. The high rate of non-completion at Vien Gut (79.05%) does not mainly reflect abandonment; the largest part reflects conscious transfer of care. Vien Gut therefore needs to move toward a structured transfer mechanism.

The figures above show that the need to transfer the Vien Gut integrated care model for gout and comorbidities to other centers in Vietnam and elsewhere comes from patients themselves: 40.71% actively asked to continue treatment locally after they had reached early goals. But Vien Gut still has no formal partnership mechanism with local facilities. Vien Gut is a private center with strong practical experience, but wider transfer will require technical and academic dialogue with EULAR, ACR, WHO, and related international bodies; multicenter verification such as the first step already underway through ReViGore40 (NCT06669000) [23]; and readiness from other health centers to receive, adapt, and apply the HOW framework in their own settings. Vien Gut developed this model to share 18 years of integrated clinical practice and to invite the international medical community to

test and improve it—because the real goal is not to defend a model, but to help patients with severe complicated gout and complex chronic multimorbidity wherever they live.

4.4. Nutrition, lifestyle, and alcohol withdrawal

Advice on reducing alcohol, reducing high-purine foods, maintaining body weight, and drinking enough water starts at the first visit and is repeated at every follow-up. In patients with heavy alcohol exposure—especially those with liver disease—alcohol cessation is not just a recommendation; it is a prerequisite. Longitudinal ultrasound and standardized photographs help patients see crystals dissolving over time, which improves motivation.

4.5. Cooperation as an operational variable

When a patient becomes less cooperative, the system must ask: what part of HOW should be adjusted, does the plan need to be simplified, and does training need to be repeated? Cooperation is reassessed at every visit as a longitudinal variable. Family—especially spouses and children—are treated as members of the care team: reminding medication, helping reduce alcohol exposure, ensuring follow-up attendance, and reporting symptoms early.

ACADEMIC MEANING OF THE CRYSTAL-FREE ENDPOINT

5.1. The gap between the guideline principle and the practical endpoint

Appendix 1.C1 showed that from 2006 to 2022, 18 guidelines from 14 organizations or countries consistently reaffirmed that gout can be cured when urate crystals are fully dissolved.

But that principle still exists mainly at the WHAT level: it states what should be achieved. International guidelines focus on treat-to-target serum urate below the saturation threshold in order to stop acute attacks, shrink tophi, and control disease in a stable way. No guideline has yet standardized crystal-free status as an imaging endpoint that can be confirmed in routine clinical practice—in other words, they do not answer the practical question: has this individual patient truly reached a state where urate crystals are no longer present at the time of assessment?

Vien Gut started from that gap and developed a practice-based process that turns the principle into a confirmable endpoint, with explicit criteria, a certification process, and longitudinal follow-up.

5.2. Crystal-free: where it sits among gout treatment endpoints

The main treatment endpoints in gout today include reaching the serum urate target, reducing flares, shrinking or removing clinically visible tophi, and improving erosions on imaging. Crystal-free status at the assessment time point—confirmed by ultrasound showing no remaining double contour sign and no tophus lesion on imaging—goes one step deeper: it confirms that the material basis of the disease, monosodium urate crystals, has been removed, not just that symptoms are under control.

Clinically, a patient may reach the serum urate goal but still keep urate crystals in the joints and soft tissues, and may still flare if treatment is stopped or if comorbid disease destabilizes. A patient confirmed as crystal-free has reached the state that EULAR 2006 [1] described, at the principle level, as essentially cured.

So crystal-free does not go against the guidelines. It grows directly from the logic already established by the guidelines and fills in the practice layer that they have not standardized: confirmation criteria (imaging + clinical + biochemical), a 4-phase treatment process, longitudinal follow-up, and an invitation for multicenter verification, beginning with ReViGore40 (NCT06669000) [23].

5.3. Crystal-free versus remission

No.	Aspect	Crystal-free (Vien Gut)	Remission (international literature)
1	Definition	No remaining urate crystals, confirmed by imaging	No symptoms, mainly confirmed clinically
2	Main endpoint	Ultrasound: no DC and no tophus	Clinical: no flares and no clinically visible tophi
3	Can crystals still remain?	No, absence is confirmed	Yes, crystals may still remain despite no symptoms
4	Measurement tools	Ultrasound + clinical + biochemical data	Clinical + biochemical data, imaging not mandatory

Remission reflects the symptom state. Crystal-free confirms that the material substrate of the disease has been removed in the assessed field. At Vien Gut, certification is tied to crystal-free status.

5.4. Clinical data supporting the feasibility of crystal-free as an endpoint

From July 2024 to March 2026, 155 patients at Vien Gut were confirmed as crystal-free at the assessment time point. This is single-center data and still requires standardization and multicenter verification. Longitudinal follow-up in 1,703 ongoing patients makes it possible to evaluate the degree of tophus dissolution across the treatment population. The distribution is shown below:

No.	Tophus dissolution	Cases	Tophus dissolution	Cases
1	0–10%	94	50–60%	192
2	10–20%	122	60–70%	188
3	20–30%	148	70–80%	152
4	30–40%	206	80–90%	124
5	40–50%	190	90–100%	287

The 90–100% dissolution group is the largest single group: 287 cases (16.85%). If we group more broadly, 943 cases (55.37%) have at least 50% tophus dissolution, and 563 cases (33.06%) have at least 70% dissolution. Only 216 cases (12.68%) are still under 20%.

So the 155 crystal-free patients do not stand alone. Behind them is a larger treatment population in which crystals are continuously dissolving in the same direction.

Of the patients certified between July 2024 and March 2026, 89 of 95 who had reached the follow-up time point returned for re-check. Forty-five patients have already completed a second follow-up, and in all of them ULT was maintained and no urate redeposition was found. Detailed data are in Appendix 8.C1.

5.5. Link within the C.1 document system

Section 5 connects with Appendix 1.C1 (the 18 international guidelines that form the WHAT foundation) and Appendix 7.C1 (the Gout-Free Certificate, which turns the principle into practice). Appendix 1.C1 shows the international agreement at the principle level. Section 3 explains the role of surgery. Section 5 establishes the academic meaning and the clinical support data: crystal-free follows directly from guideline logic and is supported by practice data from 1,703 active patients and 155 confirmed cases. Section 6 then describes how Vien Gut turns this endpoint into a structured certification act.

CERTIFICATION OF GOUT-FREE STATUS AT THE ASSESSMENT TIME POINT

6.1. Why certification was needed

Section 5 established that crystal-free is an endpoint derived from international guideline logic and supported by clinical data in 1,703 patients. But an academic endpoint only becomes meaningful when it is turned into a concrete clinical act. The request for certification came from patients themselves.

In 2014, Professor Thomas Bardin transferred to Vien Gut the principle, from EULAR 2006 recommendation 8, that gout can be cured when urate crystals are fully dissolved. Vien Gut then studied a treat-to-target allopurinol strategy in 100 patients with severe gout together with Professor Bardin and colleagues, with publications at ACR 2017, EULAR 2019, and ACR 2020. These studies showed not only crystal dissolution, but also improvement in bone erosion scores. To persuade patients to focus on complete crystal dissolution, Vien Gut used both the EULAR principle that gout can be cured and visual examples of patients whose very large tophi had gradually disappeared after years of treatment.

Once some patients truly reached crystal-free status, they asked the reverse question: if my crystals are gone, why am I not officially certified as gout-free so that I can regain the psychological state of a person who no longer carries the disease? How long do I still need treatment?

During Professor Thomas Bardin's visit to Vietnam in July 2024, some patients asked him directly. If they had previously been told that dissolving all urate crystals means cure, why was there still no official confirmation once that state had been reached? That question forced Vien Gut to create a strict enough set of criteria and a process that could answer the issue both clinically and ethically.

6.2. The three-layer logic behind certification

No.	Layer	Source	Content
1	Layer 1	EULAR 2006 + 18 guidelines	Pathophysiology principle: gout exists only while urate crystals remain; when crystals are fully dissolved, the patient is essentially cured.
2	Layer 2	Vien Gut	Crystal-free verification process: serial ultrasound of target tophi, gradual fall of the double contour sign from grade 3 to 0, plus clinical and biochemical confirmation.
3	Layer 3	Maintenance condition	The patient commits to lifelong ULT and 6-monthly follow-up to prevent new crystal formation.

Layer 1 provides the disease-biology basis. Layer 2 provides the confirmation method. Layer 3 prevents crystal-free status at one assessment point from being misunderstood as permanent cure without conditions.

6.3. Crystal-free confirmation criteria: three axes at the same time

No.	Criterion	Requirement
1	Axis 1 — Ultrasound	Two confirming ultrasound examinations 6 months apart. In all assessed joints, there is no remaining double contour sign on the articular cartilage surface and no remaining tophus on ultrasound.
2	Axis 2 — Clinical	No recurrence of gouty joint inflammation, even mild episodes, for at least 12 months.
3	Axis 3 — Biochemical	Serum uric acid maintained below saturation, with at least 2 measurements <300 µmol/L within 12 months.

All three axes must be met together. If one axis is missing, the patient is not yet eligible for certification. This avoids the mistaken idea that 'pain-free means cured' or 'low uric acid alone means cured.'

6.4. The two conditions for certification

No.	Condition	Content
1	Condition 1 — Crystal-free	The patient meets all 3 confirmation axes at the same time.
2	Condition 2 — Informed agreement	The patient understands that certification at the assessment time point does not mean permanent cure, and commits to lifelong ULT and regular follow-up.

Condition 2 brings adherence directly into the certification decision. The patient understands both the result they have reached and the conditions needed to keep it, which supports long-term ULT adherence.

6.5. Five-step process for issuing the certificate

No.	Step	Content
1	Confirm crystal-free status	The ultrasound physician confirms, twice 6 months apart, that there is no DC and no tophus; the treating physician confirms the clinical and biochemical criteria.
2	Clinical Conductor review	The whole file is reviewed to confirm that all 3 criteria are met together.
3	Patient counseling	Explain that crystal-free at the assessment time point does not mean permanent cure; lifelong ULT and regular follow-up are still required.
4	Signed agreement	The patient signs a commitment to lifelong ULT and regular follow-up.
5	Issue certificate	The certificate is issued and the next check is scheduled every 6 months.

Step 2 is especially important: the Clinical Conductor must review the whole file before certification is granted. This ensures the decision is integrated and not based on only one axis.

6.6. Follow-up after certification

No.	Item	Content
1	Ultrasound check	Confirm maintenance of crystal-free status: no redeposition of the double contour sign and no recurrence of tophi.
2	Biochemistry	Serum uric acid remains <300 µmol/L; kidney and liver function and basic indicators are checked.
3	Clinical review	Assess flares, adherence, and overall status.
4	ULT adherence	Confirm that the patient continues therapy and warn about the risk of redeposition if treatment is stopped.

After certification, the patient moves into a maintenance stage of crystal-free status with follow-up every 6 months.

6.7. The academic boundary of the phrase 'gout-free at the assessment time point'

The certificate does not claim that the patient is permanently cured in every possible circumstance. The phrase 'at the assessment time point' makes two things clear: first, at that moment the material basis of the disease is absent; second, that state continues only if the patient keeps taking ULT and continues regular follow-up. If treatment is stopped, new crystals can form again.

This is therefore a conditional scientific conclusion: it remains faithful to the crystal-based biology of gout while staying cautious within the limits of the available data.

CONCLUSION

Document C.1 explains how Vien Gut organizes treatment to dissolve urate crystals in patients with gout and complex chronic multimorbidity—from patients still within guideline-covered zones to those with end-stage CKD, reduced-ejection-fraction heart failure, decompensated cirrhosis, and adrenal insufficiency.

The central target is crystal-free status at the assessment time point. This target follows directly from the principle established by 18 international guidelines between 2006 and 2022: gout can be cured when urate crystals are completely dissolved. Vien Gut's task has been to turn that principle into a practical endpoint with three-axis confirmation criteria (ultrasound, clinical, and biochemical), a four-phase treatment process, a five-step certification pathway, and longitudinal follow-up after certification.

From July 2024 to March 2026, 155 patients were confirmed as crystal-free. Longitudinal data in 1,703 patients show that 55.37% have achieved at least 50% tophus dissolution, and 287 cases have already reached the 90–100% range.

These are single-center data. Vien Gut publishes C.1 as an invitation to multicenter verification, beginning with the ReViGore40 study (NCT06669000) [23] led by Professor Pascal Richette.

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