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SMART Approach

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SMART Approach

Recurrent Hypertriglyceridemia-Associated Acute Pancreatitis: Etiologic Assessment, Metabolic Susceptibility, and Secondary Prevention

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1. Overview

Hypertriglyceridemia-associated acute pancreatitis (HTG-AP) is increasingly encountered, particularly among patients with metabolic comorbidities. Management extends beyond triglyceride (TG) lowering during the acute episode: clinicians must confirm etiologic attribution, address reversible drivers, assess individual susceptibility, and initiate a sustainable prevention plan before discharge. Recurrence reflects longitudinal TG burden, metabolic and genetic susceptibility, other pancreatic risk factors, and gaps in follow-up. Unlike acute TG-lowering strategies, which focus on the index hospitalization, secondary prevention requires longitudinal assessment of metabolic exposure, individual susceptibility, and treatment durability. Here we describe our SMART approach, which organizes these tasks as Screen and confirm, Modify triggers, Assess susceptibility, Reduce TG burden, and Track and tailor long-term management.

2. Brief Background

HTG-AP is an important cause of acute pancreatitis (AP) and carries a substantial disease burden in China. In a 2025 systematic review of 77 studies including 56,617 patients

with AP, 11,315 patients were diagnosed with HTG-AP (19.99%).¹ Across studies, HTG-AP accounted for 1.6% to 47.6% of AP cases and showed a slight upward temporal trend that was not statistically significant ($P = 0.1081$). In Chinese studies, the proportion ranged from 6.3% to 47.6% and increased significantly over time ($P = 0.0119$), underscoring both its growing clinical relevance in China and marked geographic and between-study heterogeneity.

Recurrence estimates vary with study design, patient selection, follow-up duration, and recurrence definitions. In a prospective cohort after a first HTG-AP episode, cumulative recurrence incidence was 8% at 12 months and 22% at 18 months.² A subsequent multicenter prospective cohort reported recurrence in 23% of patients over a mean follow-up of 31 months.³ By contrast, a single-center retrospective study reported 64.8% recurrence during 1 year of follow-up, although the authors acknowledged potential selection bias and possible overestimation.⁴ These estimates are not directly comparable, but collectively they show a substantial long-term burden.

Recurrence should also be distinguished from unplanned readmission. In a prospective cohort of 293 patients with a first episode of HTG-AP, 88 patients (30.0%) experienced at least one unplanned readmission

Abbreviations: ACC, American College of Cardiology; AHA, American Heart Association; ALT, alanine aminotransferase; AP, acute pancreatitis; APACHE II, Acute Physiology and Chronic Health Evaluation II; apoB, apolipoprotein B; apoC-III, apolipoprotein C-III; FCS, familial chylomicronemia syndrome; GIP, glucose-dependent insulinotropic polypeptide; GLP-1, glucagon-like peptide-1; HbA1c, glycated hemoglobin; HTG, hypertriglyceridemia; HTG-AP, hypertriglyceridemia-associated acute pancreatitis; ICU, intensive care unit; PUMCH, Peking Union Medical College Hospital; siRNA, small interfering RNA; TG, triglyceride(s).

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during 2 years of follow-up, accounting for 143 readmission events in total. Among the 88 readmitted patients, 77.3% were readmitted for disease recurrence; among those with recurrence, HTG was reported as the etiology in 66%.⁵

3. Current Standards of Care, Evidence Gaps, and the Chinese Context

Acute care follows international pancreatitis guidance. Most comparative TG-lowering studies cited below are Chinese multicenter studies, whereas long-term management draws on international dyslipidemia and chylomicronemia guidance.

Acute management of HTG-AP should follow general principles of AP care, including appropriate intravenous fluid resuscitation, analgesia, early oral feeding in mild disease or enteral nutrition in moderately severe or severe disease, and close monitoring for progression to severe disease and organ failure.⁶ In parallel, clinicians should identify uncontrolled diabetes, alcohol exposure, TG-raising medications, pregnancy-related metabolic changes, and other secondary causes.

The clinical benefit of rapid TG lowering during acute HTG-AP remains uncertain. In one multicenter prospective cohort study, achieving TG ≤ 500 mg/dL by day 3 was not associated with more organ failure-free days after adjustment; a sensitivity analysis using the early TG-decline slope also showed no significant association.⁷ In a separate secondary analysis, exploratory subgroup analyses showed that target achievement was associated with a lower proportion of patients with organ failure at day 14 among those with organ failure at enrollment (7.8% vs 22.0%) and among those with an APACHE II score ≥ 8 (5.8% vs 17.7%), but confirmatory trials are needed.⁸

Recent interventional and comparative data further inform practice. In a 13-center open-label randomized trial of 533 patients admitted within 48 hours of symptom onset with baseline TG of 1000–3550 mg/dL, low-molecular-weight heparin plus insulin was not superior to insulin alone in reducing new-onset organ failure or death (25.0% vs 28.3%; risk ratio, 0.89); both groups reached TG < 500 mg/dL in a median of 2 days.⁹ In a multicenter prospective cohort of 267 patients, plasmapheresis was not associated with more organ failure-free days after adjustment and was associated with a greater need for ICU admission.¹⁰ Thus, TG lowering should complement rather than replace standard supportive care. Current comparative evidence does not support routinely adding heparin to insulin or the routine use of plasma exchange.

After the acute episode, recurrence prevention rests on lifestyle and dietary intervention, glycemic optimization, avoidance of alcohol and TG-raising medications, and indicated pharmacologic therapy. For persistent severe HTG (≥ 500 mg/dL), fibrates and prescription omega-3 fatty acids are guideline-supported TG-lowering options, but direct randomized trial evidence that they prevent pancreatitis is limited. Statins remain primarily directed

toward atherosclerotic cardiovascular disease risk reduction rather than AP prevention.¹¹

TG thresholds serve different clinical purposes. The 2026 ACC/AHA dyslipidemia guideline provides a pancreatitis-risk management pathway for fasting TG ≥ 500 mg/dL and places particular emphasis on TG-lowering therapy when levels are ≥ 1000 mg/dL.¹¹ Definitions and clinical assessment of familial chylomicronemia syndrome (FCS) may use 10 mmol/L (approximately 885 mg/dL) or 1000 mg/dL, depending on regional and unit conventions.¹² We therefore use ≥ 1000 mg/dL as a pragmatic marker of extreme HTG and likely chylomicronemia, while acknowledging the 10 mmol/L convention commonly used in FCS assessment.

Current guidelines provide specific recommendations for HTG-AP, including maintaining TG < 500 mg/dL after discharge. However, no validated pathway yet integrates etiologic reassessment, susceptibility assessment, recurrence-risk evaluation, TG reduction, and longitudinal secondary prevention. SMART is intended to organize these tasks, not to replace pancreatitis or dyslipidemia guidelines.

4. Unresolved Management Questions

Despite advances in the management of severe HTG, several questions remain in HTG-AP, particularly after the acute episode, when recurrence risk and long-term management must be defined.

How should HTG causality be assigned when TG are measured late or competing etiologies coexist? TG levels may fall rapidly after fasting and treatment, while gallstones, alcohol, medications, pregnancy, or structural pancreatic disease may coexist. A validated approach for assigning the dominant etiology is lacking.

Which TG measure best predicts recurrence, and what should the long-term target be? Admission TG alone may not capture cumulative exposure. The prognostic value of peak, discharge, rebound, and longitudinal TG levels, as well as the optimal target for secondary prevention, remains unclear.

Who should undergo genetic evaluation? Genetic testing may identify monogenic chylomicronemia or pancreatitis susceptibility, but criteria for selecting patients remain undefined.

Who may benefit from apoC-III-directed therapy? These therapies markedly lower TG and reduce pancreatitis risk in selected patients, but their long-term benefit, optimal patient selection, and specific role in recurrent HTG-AP remain to be established.

Can structured follow-up reduce recurrence? Early recognition of TG rebound, worsening glycemia, treatment interruption, or recurrent symptoms may improve secondary prevention, but optimal follow-up strategies require prospective evaluation.

5. How We Do It: The “SMART” Approach

The SMART approach was developed from clinical practice at Peking Union Medical College Hospital (PUMCH), a tertiary pancreatology referral center in China. Our online multimodal acute pancreatitis registry has accumulated data from more than 200,000 cases. Preliminary enrollment in our prospective AP biobank includes approximately 140 patients, 50–60% of whom have HTG-AP (unpublished institutional data). Because this is a selected referral population, these figures should not be interpreted as prevalence. In our clinical practice, we frequently encounter patients with diabetes, obesity, recurrent severe TG elevations, or mixed etiologies. During hospitalization we clarify etiology, address modifiable

drivers, establish a sustainable TG-lowering strategy, and define responsibility for follow-up. We are developing a dedicated AP registry and structured interviews to characterize recurrence and metabolic susceptibility. The SMART approach (**Figure 1**) distinguishes guideline-supported care, published trial and cohort evidence, and pragmatic institutional practice. The proposed follow-up intervals, etiologic-confidence classification, and selected escalation decisions remain expert practice recommendations requiring prospective validation.

For clarity and conciseness in the following sections, guideline or consensus-based recommendations are abbreviated as GR, pragmatic recommendations as PR, and recommendations supported by cohort or trial evidence as CR.

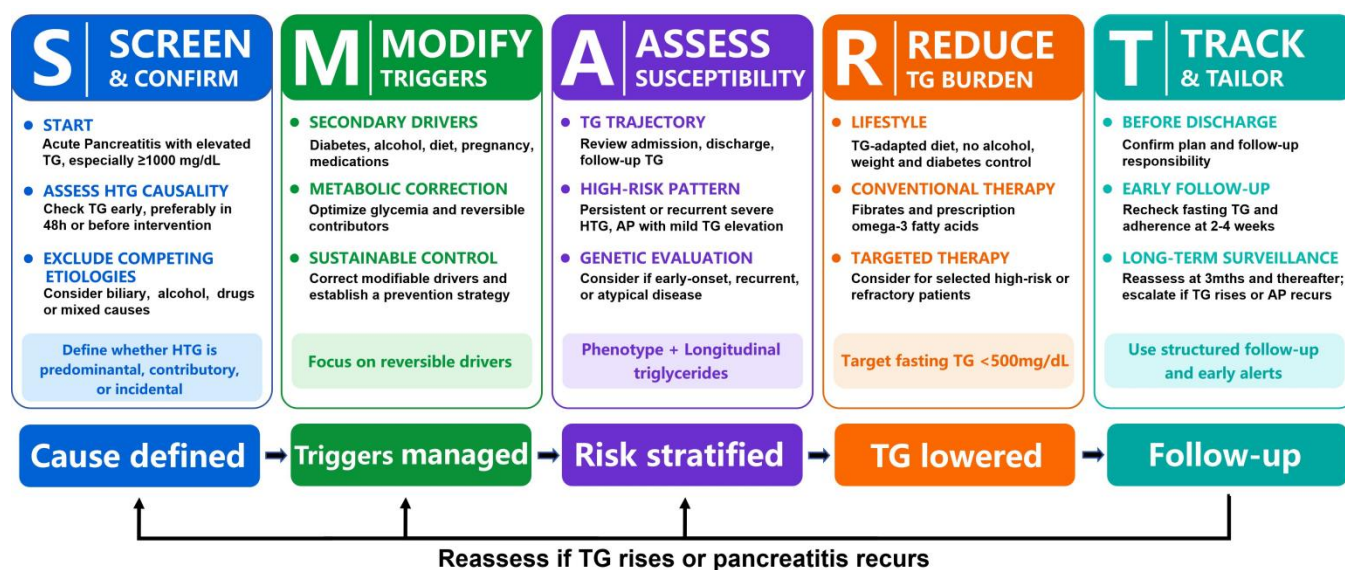


Figure 1. The SMART (Screen and confirm, Modify triggers, Assess susceptibility, Reduce TG burden, Track and tailor) iterative pathway for secondary prevention after HTG-AP. This flexible clinical framework provides a stepwise approach to individualized secondary prevention by assessing the causal contribution of HTG and excluding competing etiologies, correcting reversible secondary drivers and assessing long-term susceptibility through TG trajectories and consideration of genetic or metabolic predisposition. TG reduction integrates lifestyle intervention and conventional pharmacological therapy, with consideration of emerging targeted therapies in selected high-risk patients with persistent severe HTG and appropriate clinical phenotypes. Structured follow-up after discharge, including early reassessment and long-term monitoring, enables timely treatment adjustment and re-evaluation if TG levels rise or pancreatitis recurs.

S — Screen and Confirm

IF TG are markedly elevated early, THEN determine whether HTG is the predominant etiology (PR). We obtain serum TG as early as possible, ideally within 48 hours of symptom onset and, when feasible, within the first 24 hours of symptom onset when feasible preferably before TG-lowering intervention without delaying necessary treatment. Because TG levels may decline rapidly over time and after treatment, later measurements may underestimate the TG burden present at disease onset.¹³

IF an early TG level is ≥ 1000 mg/dL, particularly with evidence of chylomicronemia and no stronger alternative etiology, THEN we consider HTG the predominant cause (GR+PR).⁶ Evidence supporting chylomicronemia includes extreme or persistent fasting hypertriglyceridemia, particularly TG ≥ 1000 mg/dL, a lipemic sample, and, when specifically assessed, the presence of chylomicrons after an overnight fast.^{12,14} A very high TG-to-total-cholesterol ratio with relatively low apolipoprotein B (apoB), together with a compatible phenotype such as early-onset severe HTG, recurrent pancreatitis, eruptive xanthomas, lipemia retinalis, or a

suggestive family history, further raises suspicion for FCS.¹² Lipemic appearance is supportive, not diagnostic, and chylomicronemia is not synonymous with FCS.

IF the early TG level is 500–999 mg/dL, THEN we consider HTG a possible contributor rather than a definitive cause of AP (GR+PR).^{6,11} We review prior TG levels and HTG-AP episodes, evidence of chylomicronemia, major metabolic triggers, and competing etiologies. If competing causes are excluded and the presentation is compatible, we consider HTG a likely contributory factor. The ≥ 500 mg/dL threshold used to define and manage severe HTG reflects increased pancreatitis risk and should not, by itself, be interpreted as evidence that HTG caused the presenting episode of AP.

IF TG were measured late, THEN reassess causality using historical information (PR). A post-treatment TG < 1000 mg/dL does not reliably exclude HTG-AP. We therefore integrate the earliest available value, prior lipid profiles, documented chylomicronemia, major secondary triggers, and competing etiologies. We then assign both an etiologic impact (predominant, contributory, or incidental) and a confidence level (high, intermediate, or low). Documenting this assessment in the discharge summary may help guide individualized secondary prevention and future etiologic reassessment. High confidence requires early extreme elevation, supportive evidence of chylomicronemia, and no stronger alternative. Intermediate confidence includes an early level of 500–999 mg/dL, a lower post-treatment level with strong prior evidence, or a plausible coexisting cause. Low confidence applies when supporting evidence is lacking and a stronger alternative is established. This three-tier classification is a pragmatic documentation aid proposed within the SMART approach and has not been prospectively validated.

IF biliary pancreatitis remains plausible, THEN evaluate for a biliary or mixed etiology rather than attributing the episode to HTG alone (GR+PR).¹⁵ Gallstones and marked HTG may coexist, and HTG may represent an additional metabolic stressor in patients with other pancreatic insults. Early liver biochemistry and biliary imaging are therefore important. An ALT ≥ 150 U/L within 48 hours of symptom onset strongly supports a biliary origin, while common bile duct dilation (> 6 mm with the gallbladder in situ) raises suspicion for a biliary cause and warrants interpretation alongside bilirubin levels and other imaging findings.¹⁵ When convincing biliary etiology is present, the episode should not be attributed to HTG alone; within the SMART approach, we classify such cases as biliary or mixed according to the relative strength of the available etiologic evidence.

IF another established cause coexists, THEN consider multiple plausible etiologies rather than forcing a single label (PR). We assess the strength and temporal plausibility of each factor and address all clinically relevant and modifiable causes.

ELSE (PR), when TG elevation is limited or measured late and a stronger alternative etiology is well established, we regard HTG as a contributory metabolic abnormality rather than the predominant cause of AP.

M — Modify Triggers

Once HTG is established as a major contributor, we systematically identify and correct secondary factors that may drive recurrent severe HTG. In most patients, these factors are as important as the choice of TG-lowering therapy.

IF diabetes, insulin insufficiency, insulin resistance, or deteriorating glycemic control is present, THEN identify and address these metabolic drivers as a central component of sustained TG control and recurrence prevention (GR+CR+PR).^{11,16} Poor glycemic control can substantially exacerbate hypertriglyceridemia, and optimization of glycemic control may improve TG levels, particularly in patients with HTG.^{11,16} In practice, we assess HbA1c, recent glucose trends, and current diabetes treatment and involve endocrinology when diabetes or suspected insulin deficiency is difficult to control. During AP, hyperglycemia and insulin insufficiency should be treated when clinically indicated; insulin may also facilitate TG lowering. Glycemic status should also be reassessed after HTG-AP, as recurrent episodes have been associated with a higher likelihood of post-AP diabetes, with risk increasing with the number of recurrences.¹⁷ Incretin-based therapies, including GLP-1 receptor agonists and dual GIP/GLP-1 receptor agonists, may be considered when otherwise indicated for type 2 diabetes or obesity; improved glycemia and weight may reduce metabolic drivers of HTG, but their role in patients with previous HTG-AP remains uncertain, and these agents are not established therapies for preventing recurrent HTG-AP.

IF alcohol contributes, THEN recommend abstinence rather than moderation (GR).⁶ Alcohol may both increase TG and provide an independent pancreatic insult, particularly in patients with previous HTG-AP.

IF a TG-raising medication is present, THEN determine whether it can be withdrawn or replaced (GR).¹¹ Evaluation and correction of secondary causes, including medication-related contributors, are recommended components of the management of hypertriglyceridemia. Medications associated with increased TG include β -blockers, thiazide and loop diuretics, bile acid sequestrants, glucocorticoids, oral estrogens, human immunodeficiency virus (HIV) protease inhibitors, immunosuppressants (cyclosporine, tacrolimus, and sirolimus), atypical antipsychotic agents (e.g., olanzapine and clozapine), isotretinoin, tamoxifen, L-asparaginase,

cyclophosphamide, and propofol.¹¹ In practice, we review these and other potential pharmacologic contributors and, when clinically feasible, discontinue, reduce, or substitute TG-raising medications as part of secondary-cause management.

IF other secondary or metabolic drivers are present, THEN address them before labeling the patient refractory (GR).¹⁶ Hypothyroidism, renal disease, obesity, excess caloric intake, and pregnancy may substantially increase TG burden. Pregnancy requires particular caution because TG may rise markedly and treatment options differ.

Dietary intervention should be individualized, with attention to total caloric intake, dietary fat, refined carbohydrates, fructose-containing foods and beverages from all sources, body weight, alcohol exposure, and glycemic control. Detailed nutritional guidance has been summarized in a recent review.¹⁸

A — Assess Susceptibility

Patients with similar TG levels may differ substantially in pancreatitis risk. We therefore assess three domains of susceptibility: longitudinal TG exposure, inherited lipid-metabolic susceptibility, and susceptibility to pancreatic injury.

IF TG remain elevated after the acute episode, THEN assess the longitudinal trajectory rather than relying on the admission value alone (GR+PR).¹⁹ TG levels vary with the numerous factors mentioned above. We review the earliest or peak level, the level near discharge, early post-discharge measurements, and subsequent fasting levels. Persistent TG ≥ 500 mg/dL after a first HTG-AP episode has been associated with higher recurrence risk.² Current guidelines conditionally recommend maintaining TG consistently below 500 mg/dL after discharge to reduce recurrence risk, based on low-quality evidence.¹⁹ Persistent, recurrent, or rapidly rebounding severe HTG therefore prompts intensified secondary prevention; decisions should rely on repeated measurements and trajectories rather than an isolated value.

IF HTG is early-onset, persists despite secondary-factor correction, responds poorly to conventional therapy, or is accompanied by recurrent pancreatitis or classic stigmata, THEN evaluate for FCS (GR).^{11,12} The North American FCS score is a useful adjunct to prioritize genetic testing.²⁰ It complements rather than replaces comprehensive clinical assessment. If FCS is suspected, genetic testing, when available, can help confirm the diagnosis and should cover the five canonical FCS genes: *LPL*, *APOC2*, *APOA5*, *GPIHBP1*, and *LMF1*.¹² The diagnostic yield and clinical utility of lipid genetic testing may vary across populations, and data from Chinese cohorts remain limited.

IF pancreatitis recurs despite sustained TG control, THEN reassess whether HTG is the sole driver (GR+PR).²¹ Evaluate additional structural, obstructive, or genetic causes, particularly with unexplained recurrent attacks, early-onset disease, or a family history of pancreatitis. In selected patients, testing may include pancreatitis-susceptibility genes such as *PRSS1*, *SPINK1*, *CFTR*, *CTRC*, and *CPA1*.²² Lipid-gene testing addresses severe HTG, whereas pancreatitis-gene testing addresses susceptibility to recurrent pancreatic injury. Testing should therefore be targeted to results likely to affect counseling, family evaluation, or specialist management.

R — Reduce TG Burden

Our objective is sustained reduction of TG exposure rather than normalization of a single laboratory measurement during hospitalization.

IF TG remain in the severe range, THEN intensify conventional management first (GR+CR+PR).^{2,11} The guideline highlights fasting TG ≥ 500 mg/dL as a threshold for pancreatitis-risk management.¹¹ After HTG-AP, we use TG < 500 mg/dL as the minimum target for secondary prevention, while favoring lower and more stable levels in patients with recurrent disease. This is supported by observational evidence that post-attack TG ≥ 500 mg/dL is associated with higher recurrence risk.²

IF fasting TG remain ≥ 500 mg/dL despite optimization of lifestyle interventions and management of secondary causes, THEN initiate or intensify TG-lowering therapy to achieve sustained TG reduction and mitigate the risk associated with severe HTG (GR).^{11,16} Fibrates (commonly fenofibrate in clinical practice) and prescription omega-3 fatty acids (e.g., icosapent ethyl or omega-3 acid ethyl esters) are guideline-supported TG-lowering options for severe HTG, but direct evidence that either prevents pancreatitis is limited.¹⁶ Statins lower TG modestly and should not be used alone when pancreatitis risk is the primary concern, although they remain important for cardiovascular prevention.¹¹ Niacin is not routinely recommended.

IF severe HTG persists despite correction of secondary drivers and optimized conventional therapy, THEN consider apoC-III-directed therapy according to phenotype and locally approved indications (CR). Olezarsen, a monthly antisense oligonucleotide targeting APOC3, produced placebo-adjusted least-squares mean TG reductions of 49.2%–72.2% at 6 months in CORE-TIMI 72a and CORE2-TIMI 72b ($n = 1,061$) and was associated with fewer AP events.²³ Under the June 2026 U.S. label, adults with severe HTG start at 50 mg monthly, with escalation to 80 mg if tolerated and additional TG reduction is clinically indicated, whereas adults with FCS receive 80 mg monthly. Liver enzyme testing should be considered before

treatment initiation and dose escalation and performed thereafter as clinically indicated; changes in hepatic fat, platelet count, and glycemic measures were observed in trials.

Plozasiran, an apoC-III-directed siRNA given every 3 months, reduced TG and pancreatitis events in PALISADE, which enrolled patients with persistent chylomicronemia with or without a genetic diagnosis.²⁴ The U.S. indication is limited to adults with FCS at 25 mg subcutaneously every 3 months as an adjunct to a low-fat diet; hyperglycemia is a relevant safety consideration. China approved plozasiran for adults with FCS in 2026.

No head-to-head trial has established superiority of either agent. Selection should reflect phenotype, approved indication, safety, dosing schedule, and access. Randomized evidence now supports apoC-III-directed therapy in severe HTG and selected persistent-chylomicronemia phenotypes, but benefits in specific recurrent HTG-AP subgroups and long-term safety remain uncertain.

T — Track and Tailor

The final step is to prevent loss of metabolic control after discharge. Recurrence risk is dynamic; a patient who is stable at discharge may become high risk again with worsening glycemic control, weight gain, alcohol exposure, treatment interruption, pregnancy, or recurrent TG elevation.

IF the patient is discharged after HTG-AP, THEN establish a follow-up plan with fasting TG at 2–4 weeks, 3 months, 6 months, and every 6–12 months once control is stable (PR). Reassess earlier after treatment changes, worsening glycemia, pregnancy, alcohol exposure, or symptoms. Routine serial lipase monitoring is not recommended after the diagnosis of AP has been established, because lipase levels do not correlate with disease severity, prognosis, or discharge decisions.⁶ In the secondary-prevention setting, repeat lipase testing should be reserved for patients with new symptoms suggestive of recurrent AP rather than used to monitor TG control. This proposed follow-up schedule has not been prospectively validated and should be individualized.

IF TG remain or return to ≥ 500 mg/dL, THEN reassess the drivers before escalating therapy (GR+PR).^{11,14,16} Review adherence, glycemic control, alcohol exposure, diet, recent weight change, secondary diseases, and TG-raising medications. If TG rebound to ≥ 1000 mg/dL, particularly after HTG-AP, this represents a high-risk state associated with chylomicronemia and increased pancreatitis risk and should prompt timely reassessment and treatment intensification.¹⁴ Marked TG elevation with recurrent abdominal pain or other concerning symptoms warrants urgent assessment for AP.

IF metabolic circumstances change, THEN reassess risk outside the routine schedule (GR).¹⁶ Worsening

diabetes, discontinuation of lipid-lowering treatment, initiation of a TG-raising medication, pregnancy, substantial weight gain, recurrent alcohol exposure, or new abdominal symptoms should trigger earlier reassessment. Patients with recurrent disease, poor adherence, difficult-to-control diabetes, FCS or persistent chylomicronemia, or repeated TG rebound may benefit from multidisciplinary care.

IF digital support is available, THEN use it to close the follow-up loop (PR). At PUMCH, a digital platform integrates online follow-up, patient education, laboratory monitoring, and structured interviews for high-risk patients to identify TG rebound, worsening glycemic control, treatment interruption, and poor adherence, and to enable timely clinical intervention. We are prospectively evaluating whether this pathway improves metabolic control and adherence and ultimately reduces recurrence. Digital follow-up remains a promising implementation strategy rather than an established intervention for recurrence prevention.

6. Putting SMART Together

The SMART framework is intended to be iterative rather than linear. A patient may return from T (Track) to M (Modify) when diabetes worsens, from T to A (Assess) when recurrent pancreatitis occurs despite apparently adequate TG control, or from T back to S (Screen) when a subsequent episode raises doubt about the original etiologic assignment. The practical objective is not simply to achieve a TG value below a predefined threshold, but to maintain durable metabolic control while continually reassessing the factors that determine an individual patient's risk of another attack.

7. Future Directions

First, HTG causality and metabolic rebound need to be identified earlier and more reliably. Future diagnostic approaches should integrate the timing and trajectory of TG, evidence of chylomicronemia, competing etiologies, and prior metabolic history. Point-of-care TG testing using finger-prick blood and portable or smartphone-based analyzers may facilitate rapid TG assessment, although its clinical utility in HTG-AP remains to be established.²⁵ Second, the optimal TG target for secondary prevention remains uncertain. Higher post-attack TG levels are associated with recurrence,^{2,4} but whether more intensive lowering provides additional protection is unknown. The REDUCE trial was designed to compare TG targets of <150 mg/dL and <500 mg/dL and may help clarify this question.²⁶ In acute HTG-AP, current evidence has not demonstrated clear clinical benefit from routine plasmapheresis or from adding heparin to insulin-based therapy.^{9,10} Future studies should determine whether selected high-risk phenotypes may nevertheless benefit from rapid extracorporeal TG removal.

Finally, prevention should become increasingly phenotype- and genotype-directed. Clinical phenotype—including age at onset, persistence and severity of HTG, recurrent pancreatitis, secondary metabolic drivers, and response to conventional therapy—should guide further evaluation. Genetic testing may help confirm FCS or identify other inherited susceptibility and, together with phenotype, may inform the use of conventional therapy and targeted approaches such as apoC-III inhibition. Future studies should determine whether phenotype- and

genotype-guided treatment, structured follow-up, and earlier detection of metabolic rebound can reduce recurrent HTG-AP. In Chinese populations, the prevalence and clinical significance of lipid-associated variants remain incompletely characterized; large genomic cohorts linking genotype with longitudinal TG trajectories, metabolic phenotype, and recurrence are needed to identify who benefits from testing and whether the genetic architecture differs from that of predominantly Western cohorts.

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Conflict of Interest Statement

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