SMART-MD

Volume 3 / Issue 3
Summer 2026

Journal of

# Precision Medicine

*Topic:* **Pancreatitis**

*Editor:* **David C. Whitcomb, MD PhD**


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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 had HTG-AP (19.99%).[1] Across studies, HTG-AP accounted for 1.6% to 47.6% of AP cases and showed no significant overall temporal increase ($P$ = 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 within 1 year, 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 followed for 2 years after a first HTG-AP episode, 30.0% had an unplanned readmission. Disease recurrence accounted for 77.3% of readmissions, and HTG was the etiology in 66% of recurrent episodes.[5]

*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; ApoC3 / ApoC-III, apolipoprotein C3; ASO, antisense oligonucleotide; CI, confidence interval; 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; NMPA, National Medical Products Administration (China); PUMCH, Peking Union Medical College Hospital; RCT, randomized controlled trial; sHR, sub-distribution hazard ratio; siRNA; small interfering RNA; TG, triglyceride(s); ULN, upper limit of normal.


**ISSN** 2997-2876 (online)
**ISSN** 2997-2868 (print)
**DOI**: 10.69734/b2mjdg03
Website: www.SMART-MD.org

*Keywords*: hypertriglyceridemia (HTG); acute pancreatitis; recurrent acute pancreatitis; chylomicronemia; secondary prevention; SMART approach

## 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 include appropriate intravenous fluid resuscitation, analgesia, early oral or enteral nutrition as tolerated, and close monitoring for organ failure and local or systemic complications.[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, 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 was also negative.[7] A secondary analysis of 413 patients found no significant overall difference in organ failure at day 14 (3.1% vs 6.8%; $P$ = 0.091). Exploratory subgroups with organ failure at enrollment (7.8% vs 22%; $P$ = 0.039) or an APACHE II score ≥8 showed an association favoring target achievement, 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 did not reduce new-onset organ failure or death compared with insulin alone (25.0% vs 28.3%; risk ratio, 0.89; $P$= 0.40)HT 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 higher 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 trial evidence that they prevent pancreatitis is limited. Statins remain primarily directed toward atherosclerotic cardiovascular disease risk reduction.[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] Some definitions and clinical assessment tools for familial chylomicronemia syndrome (FCS) instead use 10 mmol/L (approximately 885 mg/dL).[12] We therefore use ≥1000 mg/dL as a pragmatic marker of extreme HTG and likely chylomicronemia, while acknowledging the 10 mmol/L convention in FCS assessment.

No dedicated evidence-based guideline yet integrates etiologic reassessment, metabolic and genetic susceptibility, recurrence-risk evaluation, and longitudinal secondary prevention after HTG-AP. “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 ApoC3-directed therapy?** These therapies markedly lower TG and may reduce pancreatitis risk in selected patients, but their impact in recurrent HTG-AP and multifactorial chylomicronemia remains 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. 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. "SMART" 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.

## S — Screen and Confirm

**IF TG are markedly elevated early, THEN determine whether HTG is the predominant etiology** *(pragmatic recommendation)*. We obtain serum TG as early as possible, preferably within the first 24–48 hours after symptom onset. Because fasting and treatment can lower TG rapidly, later measurements may underestimate the metabolic burden at 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** *(guideline-supported and pragmatic recommendation)*. Evidence of chylomicronemia includes extreme or recurrent fasting HTG consistent with

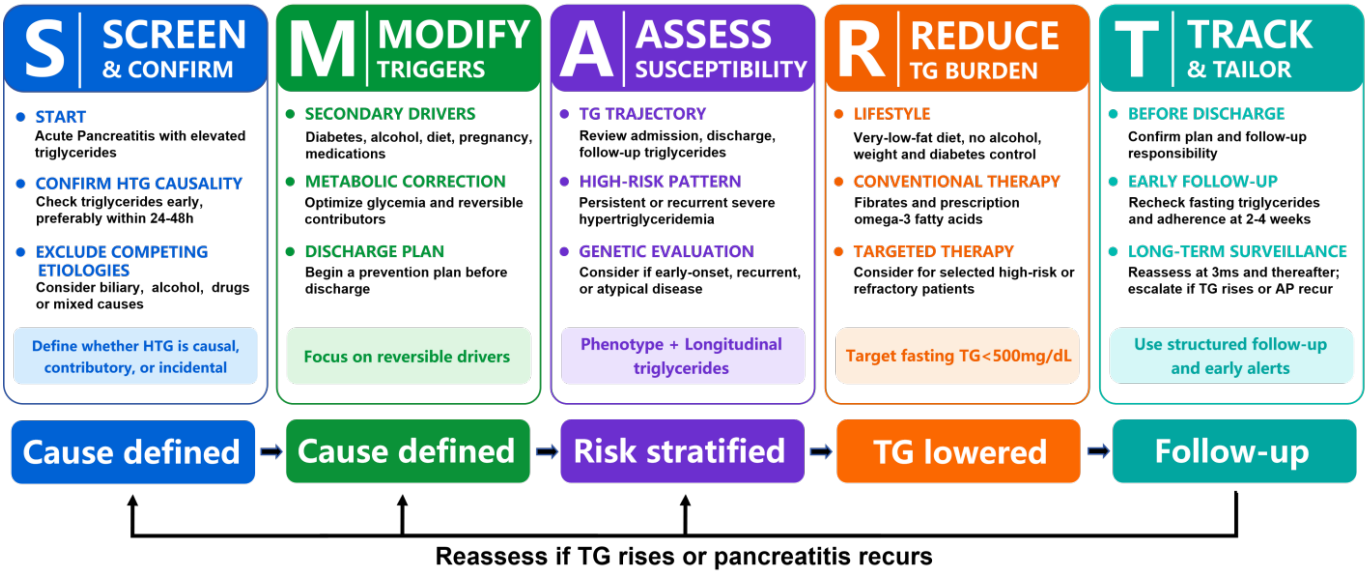


**Figure 1.** The SMART (Screen and confirm, Modify triggers, Assess susceptibility, Reduce TG burden, Track and tailor) iterative pathway for secondary prevention after hypertriglyceridemia-associated acute pancreatitis (HTG-AP). This flexible clinical framework provides a stepwise approach to individualized secondary prevention by assessing the causal contribution of HTG and excluding competing etiologies, correcting reversible secondary drivers (including diabetes, alcohol exposure, dietary factors, and medications), 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 (e.g., ApoC3-directed approaches) 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 triglycerides rise or pancreatitis recurs.

circulating chylomicrons, supported by a lipemic sample, fasting chylomicrons on lipoprotein analysis, persistent fasting TG levels in the range associated with chylomicronemia, a high TG-to-total-cholesterol ratio with relatively low apolipoprotein B (apoB), or a compatible phenotype (eruptive xanthomas, lipemia retinalis, early-onset severe HTG, recurrent pancreatitis, or a suggestive family history).[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** *(pragmatic recommendation)*. 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 manage severe HTG should not be interpreted as proof of causality.[6,11]

**IF TG were measured late, THEN reassess causality using historical information** *(pragmatic recommendation)*. A post-treatment TG <1000 mg/dL does not reliably exclude HTG-AP. We integrate the earliest available value, prior lipid profiles, documented chylomicronemia, and major secondary triggers, then assign both an etiologic impact (predominant, mixed, or contributory) and a confidence level (high, intermediate, or low). Documenting this classification in the discharge summary can guide secondary prevention. 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 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** *(guideline-supported)*. 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) should raise suspicion for a biliary cause. When convincing biliary features are present, the episode should be considered biliary or mixed in etiology rather than HTG alone.[14]

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

**ELSE**, 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 lipid-lowering therapy.

**IF insulin resistance, relative insulin deficiency, diabetes, or deteriorating glycemic control is present, THEN make metabolic management a central component of recurrence prevention** *(guideline-supported and clinical recommendation)*. Severe HTG can reflect increased hepatic production and impaired clearance of TG-rich lipoproteins, including before overt hyperglycemia. We assess HbA1c, recent glucose trends, and current diabetes treatment, and involve endocrinology when difficult-to-control diabetes or insulin deficiency is suspected.[15] During AP, insulin is used when clinically indicated for hyperglycemia and may also lower TG; randomized evidence does not support routinely adding low-molecular-weight heparin to insulin.[9] Glycemic status should also be reassessed after AP, as recurrent pancreatic injury may further impair glucose metabolism.[16] 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 these agents are not established for preventing recurrent HTG-AP.

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

**IF a TG-raising medication is present, THEN determine whether it can be withdrawn or replaced** *(guideline-supported)*. We review potential pharmacologic contributors and, when clinically feasible, discontinue, reduce, or substitute TG-raising medications as part of secondary-cause management. Common culprits include nonselective β-blockers (e.g., propranolol), thiazide diuretics, bile acid sequestrants, glucocorticoids, oral estrogens (contraceptives or hormone replacement therapy), HIV protease inhibitors (especially ritonavir), and immunosuppressants (cyclosporine, tacrolimus, sirolimus). Additional agents reported to raise triglycerides include atypical antipsychotics (clozapine, olanzapine), oral retinoids (isotretinoin), certain chemotherapeutics (asparaginase, tamoxifen), and prolonged propofol infusion.[15]

**IF other secondary or metabolic drivers are present, THEN address them before labeling the patient refractory** *(guideline-supported)*. Hypothyroidism, renal disease, obesity, excess caloric intake, and pregnancy may substantially increase TG burden.[15] 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 recent reviews.[17]

## 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 consider the longitudinal trajectory rather than the admission value alone** *(guideline- and trial-supported and pragmatic recommendation)*. TG varies with fasting status, glycemic control, alcohol exposure, acute illness, pregnancy, diet, and adherence.[15] We review the earliest or peak level, the level near discharge, early post-discharge values, and subsequent fasting levels. Persistent TG ≥500 mg/dL after a first HTG-AP episode has been associated with higher recurrence risk (sub-distribution hazard ratio 2.00).[2] 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 in patients in whom HTG has been established as the predominant cause** *(consensus-supported and pragmatic recommendation)*. The TG-to-cholesterol ratio, apoB level, and the North American FCS score are useful adjuncts to prioritize genetic testing,[12,18,19] but they do not replace clinical assessment or molecular confirmation. If FCS is suspected, genetic testing 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** *(consensus-informed approach)*. 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*.[14,20] 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** *(guideline-supported)*. The 2026 ACC/AHA dyslipidemia guideline highlights fasting TG ≥500 mg/dL as a threshold for pancreatitis-risk management.[11] In our practice, TG <500 mg/dL is the minimum post–HTG-AP target, with lower and more stable levels favored after recurrent disease. This is a pragmatic target, supported by observational evidence that post-attack TG ≥500 mg/dL is associated with higher recurrence risk.[2,11]

**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** *(guideline-supported)*. 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.[15] 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 after correction of secondary drivers and optimization of conventional therapy, THEN consider targeted ApoC3 therapy where indicated** *(trial-supported)*. Olezarsen is a monthly antisense oligonucleotide that reduces hepatic ApoC3 mRNA. In CORE-TIMI 72a and CORE2-TIMI 72b (*n* = 1,061 in the primary analysis), placebo-adjusted TG reductions at 6 months ranged from 49.2% to 72.2%; acute pancreatitis was also less frequent (mean rate ratio 0.15; 95% CI, 0.05–0.40).[21]

Under the U.S. prescribing information revised in June 2026, olezarsen has expanded therapeutic options for severe HTG (≥500 mg/dL); however, clinical decision-making should remain phenotype-based, considering the strength of evidence, approved indications, persistent chylomicronemia, pancreatitis history, and access. Recommended treatment is initiated at 50 mg subcutaneously once monthly and may be increased to 80 mg monthly when additional TG reduction is clinically indicated and the 50 mg dose is tolerated. Liver-enzyme testing should be considered before initiation or dose escalation and thereafter when clinically indicated. ALT elevations ≥3 times the ULN occurred in 7% with 80 mg, 3% with 50 mg, and 3% receiving placebo. Olezarsen is preventive therapy and should not be regarded as treatment for an established AP episode.

Plozasiran is an ApoC3-directed siRNA administered every 3 months. In patients with persistent chylomicronemia due to FCS, plozasiran reduced TG levels and was associated with fewer pancreatitis events compared with placebo.[22] The U.S. label indicates 25 mg every 3 months as an adjunct to diet for adults with FCS.

China's NMPA approved plozasiran for reducing TG in adults with FCS in January 2026. Importantly, current evidence and approved indications for plozasiran should not yet be extrapolated to broader severe HTG populations, particularly those without FCS or persistent chylomicronemia.

No head-to-head trial has established superiority of plozasiran or olezarsen. Selection should reflect the locally approved indication and dosing schedule. Safety considerations are important when selecting ApoC3-directed therapies. Olezarsen and plozasiran are generally well tolerated in clinical trials,[21,22] but monitoring remains necessary. Long-term safety data, particularly in broader severe HTG populations beyond current approved indications, remain limited.

### 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** *(pragmatic recommendation)*. 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. These follow-up intervals are not validated recurrence-risk models and should be individualized.

**IF TG remain or return to ≥500 mg/dL, THEN reassess the drivers before escalating therapy** *(guideline-supported)*. 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 clinically concerning state associated with increased pancreatitis risk that may warrant prompt treatment intensification based on clinical judgment.[15,23] 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** *(guideline-supported)*. 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.[15] 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** *(pragmatic recommendation)*. At our center 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, adherence, and ultimately 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. Bedside point-of-care TG testing may improve early assessment, whereas home or wearable TG monitoring remains investigational.[24]

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 ongoing REDUCE trial comparing targets of <150 mg/dL and <500 mg/dL may help clarify this question.[25] 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 ApoC3 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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**Author Contributions**

F.K. was responsible for drafting the manuscript. D.W. conceived the SMART framework, provided the core concept and clinical expertise, critically revised the manuscript, and supervised the work. J.L. contributed to critical revision of the manuscript. Y.D. and Y.L. performed the literature search and contributed to the literature review. All authors reviewed and approved the final version of the manuscript.

**Conflict of Interest Statement**

The authors declare no conflicts of interest related to this manuscript.

**Financial Support**

This work was supported by National Key Research and Development Program of China(2024YFA0918504), National Natural Science Foundation of China (82460135), BeijingNatural Science Foundation (L248074 to D.W., QG26031 to J.L.), Non-profit CentralResearch Institute Fund of Chinese Academy of Medical Sciences (2024-RW320-01),Special Program for Clinical and Translational Medicine Research of Chinese Academy ofMedical Sciences (2024-I2M-C&T-B-008), and the Young Reserve Talent DevelopmentProgram of Peking Union Medical College Hospital (UHB11699).