



A Proposed Stepwise Pathway for Evaluating Refractory Gastroparesis Following Incretin-Based Weight Loss Therapy in Middle-Aged Women

Zarina Hakobyan^{1*}, Bruno Petrosyan², Omar Lindo³

¹Department of Medical Sciences, Danube Institute of Medical Sciences, Malaysia

²Department of Medical Sciences, Douro Center for Medical Sciences, United Arab Emirates

³Department of Medical Sciences, Tamiraparani University Centre for Medical Sciences, Iceland

Article Info

Volume 1, Issue 1, 2026

doi: [10.62715/ijg.2026.v1.i1.pp15-20](https://doi.org/10.62715/ijg.2026.v1.i1.pp15-20)

Received: 01 April 2026

Accepted: 16 May 2026

Published: 01 July 2026

Abstract

Glucagon-like peptide-1 receptor agonists and related incretin-based drugs slow gastric emptying as part of their pharmacology, and nausea, vomiting and early fullness are their commonest adverse effects. A small number of people report symptoms that persist and resist first-line treatment, and observational data link these drugs to a diagnosis of gastroparesis. Middle-aged women deserve particular attention because they form a large share of those treated for obesity and are also the group in which idiopathic gastroparesis and functional dyspepsia are most often diagnosed, so attribution to the drug is easily made and easily mistaken. This article proposes a seven-step pathway for evaluating such a patient: reconstruct the timeline of exposure and symptoms, exclude obstruction and mimics, withdraw the drug and allow for its long half-life, measure gastric emptying by a standardised method while off the drug, classify the syndrome and grade the likelihood of a causal link, manage symptoms and nutrition in steps, and decide on future weight therapy while reporting the event. Each step is described with its rationale and the record it should leave. The pathway is assembled from published guidelines and pharmacology. It is a proposal that has not been applied to patients or validated here, and the article states what would have to be shown before it could be recommended.

Keywords: *Gastroparesis, GLP-1 receptor agonists, Semaglutide, Gastric emptying scintigraphy, Adverse drug reaction, Obesity pharmacotherapy*

© 2026 Zarina Hakobyan et al. This is an open access article under the CC BY license (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.

1. Introduction

Incretin-based drugs have changed the medical treatment of obesity. Once-weekly semaglutide and the dual agonist tirzepatide produce weight loss on a scale previously seen only after surgery (Wilding et al., 2021; Jastreboff et al., 2022), and their use has spread far beyond specialist clinics. Gastrointestinal symptoms are the price most often paid. In the registration trials nausea, vomiting, diarrhoea and constipation were common, usually mild to moderate, and concentrated in the period of dose escalation.

* Corresponding author: Zarina Hakobyan, Department of Medical Sciences, Danube Institute of Medical Sciences, Malaysia. E-mail: zarina.hakobyan@danube.edu

© 2026 Zarina Hakobyan et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

For most people these effects fade. Gastroenterologists are now asked to see the exceptions: patients with weeks or months of vomiting, early satiety and bloating, some of whom say that the symptoms continued after the drug was stopped. A pharmacoepidemiological analysis found that agonists prescribed for weight loss were associated with a higher risk of gastroparesis than a comparator weight loss drug (Sodhi *et al.*, 2023). Such an association does not show how often true, lasting gastric motor failure occurs, and published guidance on how to investigate an individual patient is thin.

This article proposes a structured pathway for that investigation, written with one common presentation in mind: a middle-aged woman with apparently refractory gastroparesis after incretin-based weight loss therapy. It is a methodological proposal built from existing guidelines on gastroparesis and from the known pharmacology of the drugs. It describes no patient and reports no outcomes, and it has not been validated.

2. Background

Three bodies of knowledge inform the design: how these drugs affect the stomach, how gastroparesis is defined and measured, and why the demographic group in question is prone to diagnostic confusion.

2.1. Incretin drugs and gastric emptying

Glucagon-like peptide-1 delays gastric emptying through vagally mediated effects on fundic tone, antral contraction and pyloric resistance, and this contributes to its effect on glucose after meals (Drucker, 2018). The delay is subject to tachyphylaxis: with continuous exposure it weakens within hours to days (Nauck *et al.*, 2011). Long-acting agonists therefore slow the stomach less at steady state than at the start of treatment, although a measurable delay can persist. In a trial of liraglutide in obesity, emptying of solids was clearly slowed after several weeks and less so after several months (Halawi *et al.*, 2017). The practical consequence is that a delayed emptying test in someone still exposed to the drug shows an expected drug effect and says nothing about underlying gastric function.

2.2. Defining and measuring gastroparesis

Gastroparesis is defined by upper gastrointestinal symptoms together with objectively delayed gastric emptying in the absence of mechanical obstruction (Camilleri *et al.*, 2022). The reference test is scintigraphy of a standard low-fat, egg-white meal with imaging to four hours, and retention of more than ten per cent of the meal at four hours is the accepted criterion for delay (Tougas *et al.*, 2000; Abell *et al.*, 2008). Shorter protocols and non-standard meals misclassify patients in both directions. Symptom severity is commonly recorded with the Gastroparesis Cardinal Symptom Index (Revicki *et al.*, 2003). European consensus adds that symptoms correlate only loosely with the degree of delay (Schol *et al.*, 2021).

2.3. Why middle-aged women are a difficult group

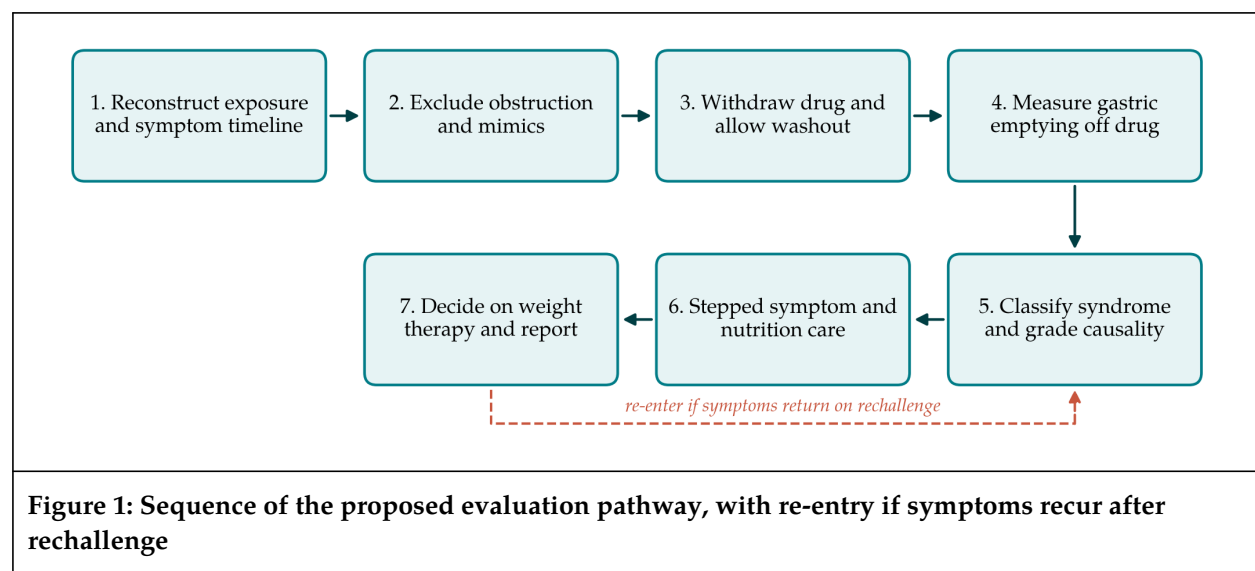
Women make up the great majority of patients with idiopathic gastroparesis in registry data (Parkman *et al.*, 2011), and healthy women empty solids more slowly than men (Datz *et al.*, 1987). Functional dyspepsia, defined by the Rome IV criteria (Stanghellini *et al.*, 2016), produces the same symptoms, is also more frequent in women, and overlaps with gastroparesis to the point that the two have been described as interchangeable syndromes in tertiary care (Pasricha *et al.*, 2021). A woman in midlife who starts weight loss therapy may thus have had mild, unrecognised symptoms beforehand. Rapid weight loss adds its own hazards, among them gallstone disease. Any pathway has to separate a drug effect from a coincident or unmasked disorder.

3. The Proposed Pathway

The pathway has seven steps, listed in Table 1 with the record each should leave in the notes. Figure 1 shows the sequence. The steps are intended to be taken in order, since each depends on information from the one before, but the first three can overlap in time.

Table 1: Steps of the proposed pathway, the question each answers and the record to be kept

Step	Question answered	Record kept
1. Timeline	Did symptoms begin, worsen or change with drug exposure?	Dated chart of doses, symptoms and weight
2. Exclusion	Is there obstruction or another cause of vomiting?	Endoscopy, imaging and medication review
3. Withdrawal and washout	Do symptoms improve when the drug is cleared?	Stop date and serial symptom scores
4. Emptying test	Is emptying delayed when measured off the drug?	Standard four-hour scintigraphy report
5. Classification	Which syndrome is present, and how likely is a drug cause?	Diagnosis and causality grade
6. Stepped care	What controls symptoms and protects nutrition?	Treatments tried, response, weight
7. Decision and reporting	Should weight therapy resume, and in what form?	Shared decision note; adverse event report



3.1. Step 1: Reconstruct the timeline

The clinician draws up a dated record of the drug, its dose escalations, missed and final doses, and the onset and course of each symptom, set beside body weight. Symptoms that appeared at a dose increase and eased between increases suggest a pharmacological effect. Symptoms present before the first injection suggest a pre-existing disorder. The history should also establish whether the patient has diabetes, since long-standing diabetes is itself a cause of gastroparesis, and should record previous gastric or bariatric surgery, thyroid disease, and the use of opioids, anticholinergic drugs and cannabis.

3.2. Step 2: Exclude obstruction and mimics

Guidelines require mechanical obstruction to be excluded before gastroparesis is diagnosed (Camilleri et al., 2022). Upper endoscopy is the usual means, with cross-sectional imaging when small bowel obstruction is possible. In this setting the differential diagnosis is wider than usual. Gallstones and pancreatitis should be considered in anyone with pain after rapid weight loss, and pancreatitis and bowel obstruction were among the events associated with these drugs in the analysis by Sodhi et al. (2023). Rumination syndrome, cyclic vomiting and cannabinoid hyperemesis can each be mistaken for

gastroparesis, and each is managed differently. Marked weight loss can, rarely, lead to compression of the duodenum by the superior mesenteric artery.

3.3. Step 3: Withdraw the drug and allow washout

If the drug has not already been stopped, it is stopped in agreement with the prescriber. The length of observation must respect pharmacokinetics. Semaglutide has an elimination half-life of about one week, so meaningful concentrations remain for more than a month after the last dose, and the picture for other weekly agents is similar. Symptoms are scored at regular intervals with a validated instrument through this period. Improvement that follows the expected clearance of the drug supports a drug effect. Persistence well beyond it is the finding that makes the label refractory worth using, and it is the point at which formal testing becomes informative.

3.4. Step 4: Measure gastric emptying under standard conditions

Scintigraphy is performed according to the consensus protocol, with the standard meal, imaging to four hours and prior withdrawal of other drugs that alter motility ([Abell et al., 2008](#)). In patients with diabetes the blood glucose is checked beforehand, because marked hyperglycaemia slows emptying. A test done while the incretin drug is still active should be labelled as such and not used to diagnose gastroparesis. Where scintigraphy is unavailable, a validated breath test is an accepted alternative ([Camilleri et al., 2022](#)).

3.5. Step 5: Classify the syndrome and grade causality

Three outcomes are possible. Delayed emptying with compatible symptoms after washout meets the definition of gastroparesis. Normal emptying with persistent symptoms points to functional dyspepsia or another disorder identified at Step 2. Resolution of symptoms before testing indicates a reversible drug effect. For the first two, the probability that the drug was responsible is graded with a structured instrument such as the adverse drug reaction probability scale of [Naranjo et al. \(1981\)](#), which weighs timing, response to withdrawal, alternative causes and rechallenge. The grade is recorded in words. In most cases it will be no stronger than possible or probable, and the notes should say so.

3.6. Step 6: Stepped symptom and nutritional care

Management follows existing guidance for gastroparesis and does not differ because of the suspected cause ([Camilleri et al., 2022](#); [Schol et al., 2021](#)). It begins with dietary change towards small, low-fat, low-residue meals and with attention to hydration and micronutrients, which matter particularly after substantial weight loss. Antiemetic and prokinetic drugs are added according to licensed indications and local practice. For patients who remain symptomatic, the expert review by [Lacy et al. \(2022\)](#) describes the options, including neuromodulators, pyloric intervention in carefully selected patients with confirmed delay, and enteral feeding when oral intake fails. This article proposes no new treatment and no dosing.

3.7. Step 7: Decide on future weight therapy and report

The final step is a shared decision about obesity treatment, since the condition that prompted therapy remains. Options include no further incretin-based drug, a cautious retrial, or a different approach altogether. Rechallenge gives the strongest evidence on causality but exposes the patient to recurrence, and it should be considered only when symptoms resolved fully and the patient wishes it. A suspected serious reaction is reported to the national pharmacovigilance scheme whatever the causality grade.

4. Fitting the Pathway to Practice

The pathway asks for nothing that a general gastroenterology service does not already have, with the possible exception of four-hour scintigraphy, which many centres still shorten. Its main demand is patience: the washout period is long, and both patient and clinician will be tempted to test early. A shared record between the prescriber, who is often in primary care or a weight management service, and the gastroenterologist avoids repeated or contradictory advice. Anaesthetic colleagues should be told when endoscopy is planned for a patient recently exposed to these drugs, because retained gastric contents are a

recognised concern.

5. Limitations and What Remains to Be Shown

The pathway is a proposal and has not been tested. Its central assumption, that delay persisting after washout identifies a distinct and clinically meaningful group, is unproven: the proportion of symptomatic patients who have delayed emptying once the drug has cleared is not known, nor is their long-term course. The suggested washout rests on half-life and not on direct studies of how quickly gastric function recovers. Causality scales were designed for adverse reactions in general and may perform poorly for a symptom complex as common as dyspepsia in the background population.

Validation would require a prospective series in which the pathway is applied consistently, with emptying measured by the standard method at defined intervals after withdrawal, and with comparison against patients who have similar symptoms and no drug exposure. The focus on middle-aged women reflects who is most often affected by diagnostic overlap. Nothing in the steps is specific to sex or age, and whether the pathway performs differently in other groups is a further open question.

6. Conclusion

Persistent vomiting and fullness after incretin-based weight loss therapy may be a prolonged drug effect, an unmasked functional disorder or, perhaps, lasting gastroparesis, and these cannot be told apart by a single emptying test done at the wrong time. The seven steps proposed here put the timeline first, insist on an adequate washout before standardised testing, make the grading of causality explicit and leave treatment to established guidance. Whether the approach improves diagnosis or outcomes remains to be demonstrated in prospective work.

Conflict of interest

To be declared by the author(s) before publication.

Funding

To be declared by the author(s) before publication.

References

- Abell, T.L., Camilleri, M., Donohoe, K., Hasler, W.L., Lin, H.C., Maurer, A.H., et al. (2008). [Consensus recommendations for gastric emptying scintigraphy: A joint report of the American Neurogastroenterology and Motility Society and the Society of Nuclear Medicine](#). *American Journal of Gastroenterology*, 103(3): 753-763. <https://doi.org/10.1111/j.1572-0241.2007.01636.x>
- Camilleri, M., Kuo, B., Nguyen, L., Vaughn, V.M., Petrey, J., Greer, K., Yadlapati, R. and Abell, T.L. (2022). [ACG clinical guideline: Gastroparesis](#). *American Journal of Gastroenterology*, 117(8): 1197-1220. <https://doi.org/10.14309/ajg.0000000000001874>
- Datz, F.L., Christian, P.E. and Moore, J. (1987). [Gender-related differences in gastric emptying](#). *Journal of Nuclear Medicine*, 28(7): 1204-1207.
- Drucker, D.J. (2018). [Mechanisms of action and therapeutic application of glucagon-like peptide-1](#). *Cell Metabolism*, 27(4): 740-756. <https://doi.org/10.1016/j.cmet.2018.03.001>
- Halawi, H., Khemani, D., Eckert, D., O'Neill, J., Kadouh, H., Grothe, K., et al. (2017). [Effects of liraglutide on weight, satiation, and gastric functions in obesity: A randomised, placebo-controlled pilot trial](#). *The Lancet Gastroenterology & Hepatology*, 2(12): 890-899. [https://doi.org/10.1016/S2468-1253\(17\)30285-6](https://doi.org/10.1016/S2468-1253(17)30285-6)
- Jastreboff, A.M., Aronne, L.J., Ahmad, N.N., Wharton, S., Connery, L., Alves, B., et al. (2022). [Tirzepatide once weekly for the treatment of obesity](#). *New England Journal of Medicine*, 387(3): 205-216. <https://doi.org/10.1056/NEJMoa2206038>
- Lacy, B.E., Tack, J. and Gyawali, C.P. (2022). [AGA clinical practice update on management of medically refractory gastroparesis: Expert review](#). *Clinical Gastroenterology and Hepatology*, 20(3): 491-500.

<https://doi.org/10.1016/j.cgh.2021.10.038>

- Naranjo, C.A., Busto, U., Sellers, E.M., Sandor, P., Ruiz, I., Roberts, E.A., Janecek, E., Domecq, C. and Greenblatt, D.J. (1981). [A method for estimating the probability of adverse drug reactions.](#) *Clinical Pharmacology & Therapeutics*, 30(2): 239-245. <https://doi.org/10.1038/clpt.1981.154>
- Nauck, M.A., Kemmeries, G., Holst, J.J. and Meier, J.J. (2011). [Rapid tachyphylaxis of the glucagon-like peptide 1-induced deceleration of gastric emptying in humans.](#) *Diabetes*, 60(5): 1561-1565. <https://doi.org/10.2337/db10-0474>
- Parkman, H.P., Yates, K., Hasler, W.L., Nguyen, L., Pasricha, P.J., Snape, W.J., et al. (2011). [Clinical features of idiopathic gastroparesis vary with sex, body mass, symptom onset, delay in gastric emptying, and gastroparesis severity.](#) *Gastroenterology*, 140(1): 101-115. <https://doi.org/10.1053/j.gastro.2010.10.015>
- Pasricha, P.J., Grover, M., Yates, K.P., Abell, T.L., Bernard, C.E., Koch, K.L., et al. (2021). [Functional dyspepsia and gastroparesis in tertiary care are interchangeable syndromes with common clinical and pathologic features.](#) *Gastroenterology*, 160(6): 2006-2017. <https://doi.org/10.1053/j.gastro.2021.01.230>
- Revicki, D.A., Rentz, A.M., Dubois, D., Kahrilas, P., Stanghellini, V., Talley, N.J. and Tack, J. (2003). [Development and validation of a patient-assessed gastroparesis symptom severity measure: The Gastroparesis Cardinal Symptom Index.](#) *Alimentary Pharmacology & Therapeutics*, 18(1): 141-150. <https://doi.org/10.1046/j.1365-2036.2003.01612.x>
- Schol, J., Wauters, L., Dickman, R., Drug, V., Mulak, A., Serra, J., et al. (2021). [United European Gastroenterology \(UEG\) and European Society for Neurogastroenterology and Motility \(ESNM\) consensus on gastroparesis.](#) *United European Gastroenterology Journal*, 9(3): 287-306. <https://doi.org/10.1002/ueg2.12060>
- Sodhi, M., Rezaeianzadeh, R., Kezouh, A. and Etminan, M. (2023). [Risk of gastrointestinal adverse events associated with glucagon-like peptide-1 receptor agonists for weight loss.](#) *JAMA*, 330(18): 1795-1797. <https://doi.org/10.1001/jama.2023.19574>
- Stanghellini, V., Chan, F.K.L., Hasler, W.L., Malagelada, J.R., Suzuki, H., Tack, J. and Talley, N.J. (2016). [Gastrooduodenal disorders.](#) *Gastroenterology*, 150(6): 1380-1392. <https://doi.org/10.1053/j.gastro.2016.02.011>
- Tougas, G., Eaker, E.Y., Abell, T.L., Abrahamsson, H., Boivin, M., Chen, J., et al. (2000). [Assessment of gastric emptying using a low fat meal: Establishment of international control values.](#) *American Journal of Gastroenterology*, 95(6): 1456-1462.
- Wilding, J.P.H., Batterham, R.L., Calanna, S., Davies, M., Van Gaal, L.F., Lingvay, I., et al. (2021). [Once-weekly semaglutide in adults with overweight or obesity.](#) *New England Journal of Medicine*, 384(11): 989-1002. <https://doi.org/10.1056/NEJMoa2032183>