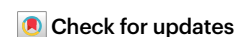


Framework for the pharmacological treatment of obesity and its complications from the European Association for the Study of Obesity (EASO): 2026 update

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This 2026 update integrates emerging trial evidence – particularly for weight loss and liver disease – to refine EASO’s treatment algorithm for obesity management.

The development of obesity-management medications (OMMs), particularly incretin-based therapies, has expanded rapidly over the past few years, which has made it challenging for clinicians to manage a personalized approach in the context of their effect on weight and obesity-related complications. In 2025, the European Association for the Study of Obesity (EASO) published a framework for the pharmacological treatment of obesity and its complications¹. The recommendations were based on the results of a systematic literature review and network meta-analysis based on 56 randomized controlled trials (RCTs) for OMMs approved in Europe that were published by 31 January 2025. Since then, new RCTs on OMMs have been published, which has led to an update of the EASO framework based on a total of 62 RCTs. The updated document retains the original methodology previously published² and incorporates new data, especially for body weight loss and liver disease³ (Table 1).

Obesity pharmacotherapy is advancing at a speed that few other chronic disease areas have experienced. The first EASO algorithm was developed to help clinicians and healthcare professionals interpret the comparative benefits of available medications for total body weight loss (TBWL) and key obesity-related complications, grounded in a systematic review and meta-analysis of randomized trials^{1,2}. The pharmacological framework developed by EASO and published in 2025 (ref. 1) introduced the algorithm as a pragmatic framework for aligning individual goals for the treatment of obesity with the best available comparative evidence at that time, rather than as a prescriptive sequence of treatments. We indicated at that time that the framework will be updated regularly, incorporating new evidence on the OMMs.

Since the publication of the first EASO framework for the pharmacological treatment of obesity and its complications, additional findings from RCTs have emerged, notably on the weight-loss effects of both semaglutide and tirzepatide, as well as new data for semaglutide on liver outcomes in metabolic dysfunction-associated steatohepatitis (MASH)^{3,4}. In parallel, international guidance has begun to incorporate newer medications into recommendations for the pharmacological management of obesity⁵. This Comment represents the updated

EASO framework for the pharmacological treatment of obesity and its complications, incorporating RCT evidence published between 31 January 2025 and 21 November 2025 that met the predefined inclusion criteria, based on an updated systematic literature review and network meta-analysis³.

Body-weight management in obesity

For TBWL, the updated evidence (61 comparisons across 6 new RCTs and 8 linked RCTs) confirms that all medications included in the trials achieved statistically significant and clinically meaningful weight loss versus placebo across trials, with TBWL ranging from 2.9% to 15.4% at study endpoint (Table 1). As the evidence base has expanded, the relative separation between the two most effective weight-lowering medications – tirzepatide and semaglutide – has become clearer. This is consistent with recent head-to-head evidence that provides a direct clinical comparison between tirzepatide and semaglutide⁶. In the updated algorithm (Fig. 1), this is reflected by the fact that tirzepatide is maintained above semaglutide (2.4 mg) in the TBWL domain, with increased confidence in the relative ordering within the time horizons studied, as uncertainty around the estimates has narrowed.

These differences should be interpreted in the context of heterogeneity between clinical trials, including differences in study populations, lifestyle interventions and follow-up duration. Although head-to-head evidence is emerging, many comparisons between treatments remain based on results from separate RCTs rather than direct comparisons. The updated algorithm therefore reflects the best available comparative evidence, with the recognition that treatment decisions must also consider clinical judgement, individual patient characteristics and preferences. Full methodological details are reported in the companion network meta-analysis paper³.

Metabolic dysfunction-associated steatotic liver disease

The most substantive change in this updated algorithm is in the liver domain endpoints. In the first EASO OMM algorithm, this domain was represented by resolution of MASH without worsening of fibrosis, reflective of the available data^{1,2}. Since then, results from the phase 3 ESSENCE trial of semaglutide in non-cirrhotic MASH with fibrosis stage F2–F3 have been reported, providing evidence on both resolution of steatohepatitis and changes in liver fibrosis stage⁴.

For semaglutide, an RCT of compensated cirrhosis (F4) due to MASH remains part of the evidence base⁷. For tirzepatide, an RCT of MASH with F2–F3 fibrosis provides histological evidence on the

Table 1 | Primary endpoints for each subgroup of patients

		Primary endpoint	Orlistat	Naltr-Bupr	Lirag	Phen-Topir	Sema	Tirz		
Body weight management in obesity^a	No complications present	Weight loss at endpoint ^b	2.9	4.4*	4.7*	9.0*	10.5*	15.4*		
		Weight loss at 52 weeks	3.0*	4.4*	4.8*	9.0*	10.7*	15.2*		
		Weight loss at 53–104 weeks	2.6*	4.4*	4.3*	9.0*	10.6*	15.2*		
Obesity management medication decision	Metabolic adiposity	OSAS	OSAS remission (OR)	NA	NA	NA	NA	4.9*		
		KOA	KOA improvement (WMD)	NA	NA	NA	NA	-8.6*	NA	
	Complications management in obesity	Mechanical adiposity	Pre-diabetes	Normoglycemia restoration (OR)	NA	NA	3.2*	NA	19.6*	8.3*
			Type 2 diabetes	Diabetes remission (OR)	NA	2.3*	6.8*	NA	12.3*	15.6*
		Cardiovascular disease	MACE incidence (OR)	NA	0.9	NA	NA	0.8*	NA	
		Heart failure ^c	Hospitalization for heart failure (OR)	NA	NA	NA	NA	0.2*	0.4*	
		MASLD ^d	MASH remission (OR)	NA	NA	NA	NA	3.2*	11.8*	
		MASLD (new in 2026 update) ^d	Liver fibrosis reduction (OR)	NA	NA	NA	NA	0.8 / 1.8 ^e	NA	

Primary endpoints for various subgroups of patients in new RCTs of the OMMs orlistat, naltrexone–bupropion (Naltr-Bupr), liraglutide (Lirag), phentermine–topiramate (Phen-Topir), semaglutide (Sema) and tirzepatide (Tirz), presented as estimates obtained from the network meta-analysis³. * $P < 0.05$ (statistically significant result). ^aBody weight management results are presented as TBWL (%). ^bAt endpoint' indicates end of follow-up for the primary analysis timepoint in the trials included. ^cRCT data reflect people with heart failure with preserved ejection fraction. ^dThese results are based on statistical and non-statistical assessment of study designs, cross-trial strengths and limitations³. ^eNetwork meta-analyses were performed for outcomes with 10 or more RCTs; outcomes with fewer than 10 RCTs used pairwise meta-analysis. For liver fibrosis reduction, 0.8 is the random-effects model estimate (for comparison), and 1.8 is the fixed-effects model estimate (primary). KOA, knee osteoarthritis; MACE, major adverse cardiovascular event; MASLD, metabolic dysfunction-associated steatotic liver disease; NA, not available; OR, subtracted-placebo Mantel–Haenszel odds ratio; OSAS, obstructive sleep apnea syndrome; WMD, subtracted-placebo weighted mean difference.

resolution of MASH and improvement of fibrosis as key study endpoints⁸. Collectively, these data increase the clinical salience of liver outcomes in obesity pharmacotherapy decisions while also highlighting the limits of cross-trial comparability across disease stages, differences in trial populations, endpoint definitions and maturity of evidence.

These new data strengthen the evidence base for histological liver outcomes in non-cirrhotic MASH. Consistent with the predefined methods and inclusion criteria^{2,3}, the updated algorithm expands the liver domain to include two clinically relevant outcomes: resolution of MASH (without worsening of fibrosis), and improvement of fibrosis.

For resolution of MASH, the current trial evidence supports histological benefit for both semaglutide and tirzepatide in the populations studied. Accordingly, Fig. 1 presents semaglutide and tirzepatide side by side for resolution of MASH, with ESSENCE providing the most mature and relevant dataset in patients with non-cirrhotic F2–F3 fibrosis⁴.

For improvement of liver fibrosis, the evidence base remains limited. Current RCT data support the use of semaglutide, while evidence for tirzepatide is less mature and is derived mainly from non-primary fibrosis endpoints in existing RCTs. The algorithm therefore reflects stronger evidence for semaglutide for improvement of liver fibrosis at this stage.

Overall, the liver domain reflects the fact that semaglutide and tirzepatide currently have the most developed RCT evidence for histological liver outcomes in this population, with the strongest data available for the resolution of MASH. Additional trials and longer-term follow-up will help clarify treatment effects on liver outcomes.

Management of complications in obesity: domains beyond liver

Beyond TBWL and liver outcomes, few domains in the OMM algorithm are materially altered by the evidence update. For remission of type 2 diabetes, obstructive sleep apnea, osteoarthritis, cardiovascular outcomes and other complications, the updated systematic review identified limited or no new eligible data compared with our previous analysis, and the relative positions of medications in these domains remain largely unchanged³. Additional endpoints reported in trials – including blood pressure, metabolic parameters and health-related quality of life – were identified during the updated evidence review and are described in the companion methodological paper³, but they are not yet incorporated as distinct domains in the current algorithm.

Doses, licensing scope and jurisdictional relevance

A further practical refinement in the present updated algorithm is the explicit reporting of doses and licensing scope. The algorithm and its underlying meta-analysis focus on pharmacological agents and doses with licenses for chronic weight management in adults in the jurisdictions covered by the framework, which was mainly the European Union at the time of the literature search². Higher doses and new formulations that are under investigation or licensed only in some jurisdictions are acknowledged but are not integrated as separate nodes, to avoid conflation of emerging and established treatment options.

Limitations and methodological considerations

The updated EASO algorithm reflects the best available RCT evidence at the cut-off date of 21 November 2025 and should be interpreted

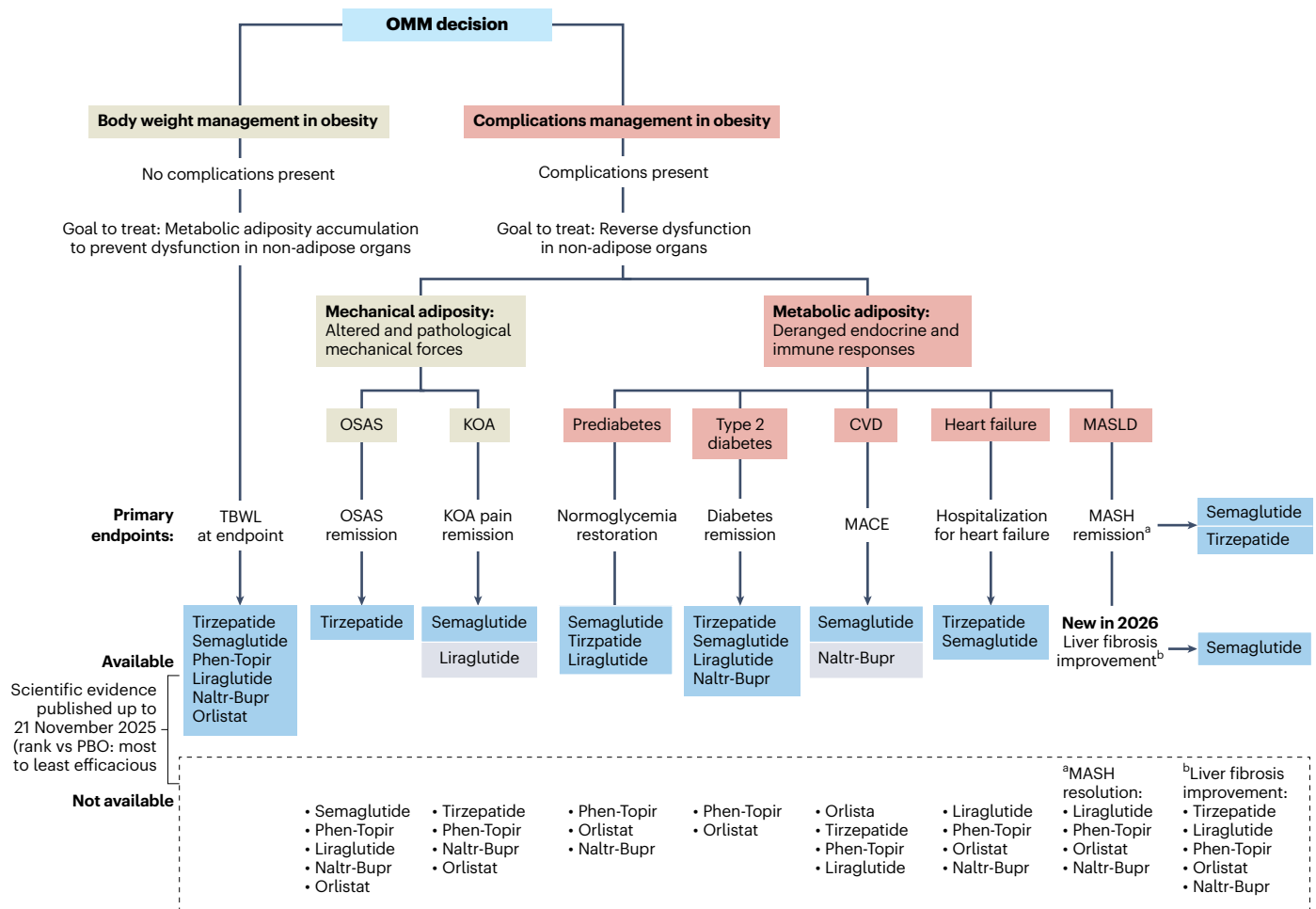


Fig. 1 | Treatment algorithm from the EASO for individuals with obesity: 2026 update. This algorithm is based on the presence or absence of obesity-related complications and RCT evidence available up to 21 November 2025. Medications are listed in order of efficacy for each endpoint indicated. Within each domain, medications are positioned to reflect comparative efficacy for the stated endpoint(s) based on trial evidence available up to the cut-off; this is not a prescribing sequence and should not be interpreted as a universal ranking across domains. Medications shown at the same level have comparable effects for that domain and/or endpoint. Where comparative evidence is indirect or limited, apparent differences should be interpreted alongside uncertainty and evidence maturity. Blue shading indicates statistically significant effects versus control; grey shading indicates no statistically significant effect or no available

evidence for that domain. Algorithm entries reflect doses licensed for chronic weight management in adults in the European Union at the evidence cut-off; higher-dose regimens (for example, semaglutide at 7.2 mg) are acknowledged but are not included as separate nodes. Medications and doses: liraglutide, 3.0 mg; naltrexone–bupropion (Naltr–Bupr), 32 or 360 mg; orlistat, 360 mg; phentermine–topiramate (Phen-Topir), 15 or 92 mg; semaglutide, 2.4 mg; and tirzepatide, 10–15 mg. ^aLimited trial numbers and/or substantial between-study heterogeneity may reduce reliability for selected estimate(s), and clinical judgement is recommended. CVD, cardiovascular disease; HF, heart failure (with preserved ejection fraction); KOA, knee osteoarthritis; MACE, major adverse cardiovascular event; MASLD, metabolic dysfunction-associated steatotic liver disease; OSAS, obstructive sleep apnea; PBO, placebo.

in the context of differences among clinical trial programs, populations, endpoints and evidence maturity^{8,9}. The visual ordering within domains summarizes comparative trial effects for the stated endpoints and pharmacotherapies; it should not be interpreted as a prescribing sequence or overall ranking of pharmacotherapies. Direct head-to-head evidence remains limited for several comparisons, and the strength of evidence varies by domain. TBWL has the most mature evidence base, whereas several complication domains remain sparse or heterogeneous; this imbalance should be kept in mind when using the algorithm for complication-centered decisions¹⁰.

For some outcomes – particularly histological liver endpoints such as improvement of fibrosis – the evidence base is smaller and

conclusions are necessarily made more cautiously^{4,7,8}. Several clinically important outcomes (for example, blood pressure, mental health and health-related quality of life) are not yet represented as distinct domains in the algorithm, despite their relevance to people living with obesity. Full methodological details and sensitivity analyses are reported in the companion network meta-analysis and methods paper³.

Future updates and methodological development

The OMM algorithm is intended as a ‘living framework’ rather than a ‘one-off’ exercise. It reflects the evidence available at the time of the current review and will be updated regularly as new trials, medicines and clinical outcomes emerge. Future updates may incorporate evolving

standards in the definition and management of obesity, broader patient populations and geographic settings, new pharmacotherapies and formulations (including oral agents), and additional clinically relevant endpoints as the evidence base develops. Future updates will consider incorporating a dedicated safety and tolerability domain (for example, discontinuation rates or adverse events), alongside efficacy, to better reflect benefit-risk decision-making in routine care.

Clinical and policy implications

For clinicians, the updated OMM algorithm can be used alongside existing guidance and clinical experience. Importantly, the present algorithm is not intended as clinical guideline and does not prescribe a fixed treatment sequence. Instead, it provides a structured overview of the available evidence across weight loss and obesity-related complications, drawing on published trial data and expert-informed interpretation^{1,2}.

In practice, the algorithm can support clinical decision-making by helping clinicians understand where the evidence is strongest for TBWL and for selected complication outcomes, while also considering safety, obesity-related complications, treatment access, cost and patient preferences. Thus, the framework is intended to complement existing clinical guidance by providing a visual summary of the evolving evidence base across these domains.

Conceptual framing and person-centered care

The algorithm is evolving in parallel with conceptual shifts in how obesity and adiposity are understood^{11,12}. Moving toward more-precise concepts such as metabolic adiposity and mechanical adiposity can help clinicians link pharmacotherapy choices to underlying disease mechanisms and complication profiles – whether the dominant priority is to modify cardiometabolic risk or to alleviate mechanically mediated morbidity¹¹.

By presenting a ‘time-stamped’ evidence map that remains stable across most complication domains while improving precision for TBWL and expanding clinically relevant liver outcomes, this update aims to support more-informed, person-centered and non-stigmatizing conversations about obesity pharmacotherapy in clinical and healthcare settings.

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References

1. McGowan, B. et al. *Nat. Med.* **31**, 3229–3232 (2025).
2. McGowan, B. et al. *Nat. Med.* **31**, 3317–3329 (2025).
3. Ciudin Mihai, A. et al. Preprint at medRxiv <https://doi.org/10.64898/2026.04.19.26351196> (2026).
4. Sanyal, A. J. et al. *N. Engl. J. Med.* **392**, 2089–2099 (2025).
5. American Diabetes Association Professional Practice Committee for Obesity. *BMJ Open Diabetes Res. Care* **13**, e005729 (2026).
6. Aronne, L. J. et al. *N. Engl. J. Med.* **393**, 26–36 (2025).
7. Loomba, R. et al. *Lancet Gastroenterol. Hepatol.* **8**, 511–522 (2023).
8. Loomba, R. et al. *N. Engl. J. Med.* **391**, 299–310 (2024).
9. Hutton, B. et al. *Ann. Intern. Med.* **162**, 777–784 (2015).
10. Dias, S. et al. *NICE Decision Support Unit* <https://go.nature.com/48km3ue> (2014).
11. Busetto, L. et al. *Nat. Med.* **30**, 2395–2399 (2024).
12. Rubino, F. et al. *Lancet Diabetes Endocrinol.* **13**, 221–262 (2025).

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Competing interests

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with Novo Nordisk, Eli Lilly, Rhythm and Regeneron; and is president of the EASO. B.M. has received speaker and/or advisory fees from Novo Nordisk, Eli Lilly, AstraZeneca, Janssen, Pfizer and MSD; has received a research grant from Novo Nordisk; and is a shareholder of Reset Health.