



CAGRISEMA (SEMAGLUTIDE + CAGRILINTIDE): PROTOCOL FOR A SCOPING REVIEW OF CLINICAL EFFICACY, SAFETY, AND IMPLICATIONS FOR OBESITY MANAGEMENT

General Medicine

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KEYWORDS

Background and Rationale

Obesity remains a persistent global health crisis, and there is an urgent need for therapies that deliver clinically meaningful and sustainable weight loss. CagriSema, the fixed-dose combination of semaglutide (a GLP-1 receptor agonist) and cagrilintide (an amylin analogue), has emerged as a potential game-changer based on recent randomized controlled trials. Given the rapid evolution of this therapeutic area and anticipated regulatory changes, a scoping review is necessary to map all available evidence regarding the clinical efficacy, safety, mechanistic rationale, and health care implications of CagriSema in the management of overweight and obesity.

2. OBJECTIVES

Primary: To systematically map the breadth and nature of published evidence on CagriSema's clinical efficacy and safety in overweight/obese adults.

Secondary: To identify evidence gaps, explore the mechanistic and practical significance, and assess the real-world and policy implications for the management of obesity.

3. REVIEW QUESTIONS

- What clinical trials and real-world studies have assessed the effects of CagriSema on weight loss, metabolic endpoints, and safety?
- What are the key findings regarding efficacy and tolerability compared to other anti-obesity treatments?
- What are the implications for future clinical practice, patient selection, and health policy?

4. ELIGIBILITY CRITERIA

Randomised Controlled trials done on Adults (≥ 18 years) with overweight or obesity

Exclusion: Paediatrics, animals, and in vitro studies will be excluded.

5. SEARCH STRATEGY

- We will search in PubMed/MEDLINE, Embase, CENTRAL, Scopus, Web of Science, ClinicalTrials.gov, WHO ICTRP.
- Other sources: Reference and citation checks of included articles, hand-searching recent meetings (ADA, EASD, Obesity Society).

Study selection will be in two phases: title/abstract screening and full-text review by two independent reviewers, with third-party resolution for disputes.

6. DATA CHARTING AND EXTRACTION

A standardised data extraction form will capture:

- Study characteristics: author, year, design, setting, population, intervention details, comparator, sample size, duration
- Outcomes: efficacy (mean % weight loss, categorical responders, metabolic parameters), adverse events (frequency and severity), withdrawals, QOL, cost or implementation data
- Other: Funding, conflicts of interest, study limitations, regulatory status, practice recommendations

7. DATA SYNTHESIS

- Qualitative synthesis: Narrative mapping of available evidence, grouped by study type and outcome domain (efficacy, safety/tolerability, quality of life, economic/implementation).
- Tabulation: Main features/results displayed in summary tables.
- Gaps: Highlighting research/implementation/evidence gaps and future directions.

8. REPORTING

The review will adhere to the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) guidelines, with a PRISMA flow diagram. 9. Dissemination

Findings will be:

- Submitted to a high-impact endocrinology or obesity journal
- Presented at relevant scientific meetings and webinars
- Shared with guideline committees and policymakers

10. TIMELINE

- Protocol submission: August 2025
- Data collection: August–October 2025
- Synthesis and manuscript preparation: November–December 2025
- Anticipated submission: January 2026

11. PICO FRAMEWORK

Component	Description
Population	Adults with overweight or obesity (BMI ≥ 27 kg/m ²)
Intervention	CagriSema (semaglutide + cagrilintide, any dose/regimen)
Comparison	Placebo, monotherapy (semaglutide or cagrilintide), other anti-obesity agents
Outcomes	Efficacy (weight loss, metabolic), safety/tolerability, patient-centric and system-level outcomes

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