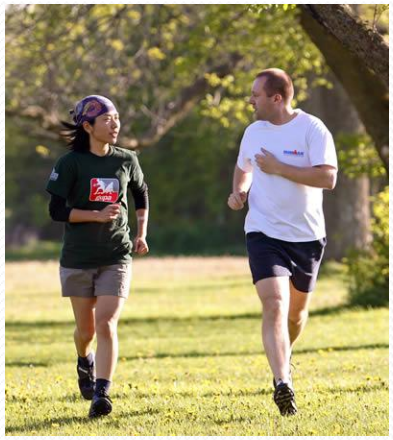
In Metabolic Syndrome with BMI >35kg/m^2 : LSM vs GLP1-RA vs Bariatric Surgery – In Favor of LSM



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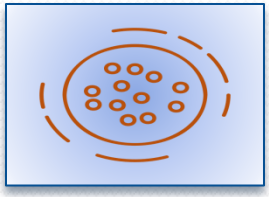
Components of Metabolic Syndrome

The National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) report identified **six** underlying components of the metabolic syndrome in its scientific discussion.

01 Abdominal obesity

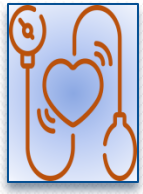
02 Atherogenic dyslipidemia (high TG, low HDL)



Proinflammatory state (high C-rp)

05

03 Raised BP



04

Insulin resistance ± glucose intolerance

Prothrombotic state (high fibrinogen and PAI-1 levels)

06

Circulation Volume 109, Number 3
https://doi.org/10.1161/01.CIR.0000111245.75752.C6
Originally Published 27 January 2004

Definition of Metabolic Syndrome:

(Metabolic syndrome is also called insulin resistance syndrome)

For clinical and epidemiological diagnosis, the ATP III focused on **five** practical, measurable criteria.

- **Elevated waist circumference:** ≥ 102 cm (≥ 40 inches) for men; ≥ 88 cm (≥ 35 inches) for women
- **Elevated triglycerides:** ≥150 mg/dL or on drug treatment
- **Reduced HDL cholesterol:** <40 mg/dL for men; <50 mg/dL for women or on drug treatment
- **Elevated blood pressure:** ≥130/85 mm Hg or on drug treatment
- **Elevated fasting glucose:** ≥100 mg/dL or on drug treatment

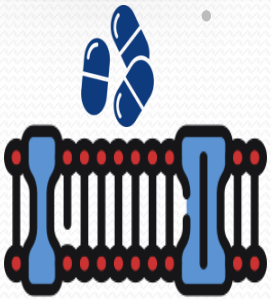
Elevate the risk of atherosclerotic CVD and T2DM

Circulation Volume 109, Number 3
https://doi.org/10.1161/01.CIR.0000111245.75752.C6
Originally Published 27 January 2004

Therapeutic approaches for Met Syndrome with BMI >35kg/m²

1. Lifestyle modification

2. GLP-1 RA



3. Bariatric surgery

Swarup S, et al.InStatPearls [internet] 2024. StatPearls Publishing

LSM

Lifestyle modifications for MetS

The American Heart Association and American College of Cardiology recommend 150 min of moderate-intensity or 70 min of high-intensity physical activity weekly.

Swarup S, et al.InStatPearls [internet] 2024. StatPearls Publishing.

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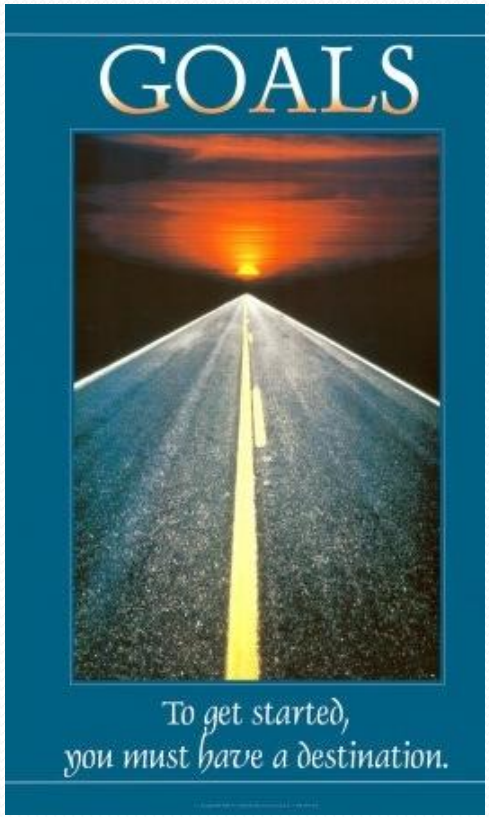
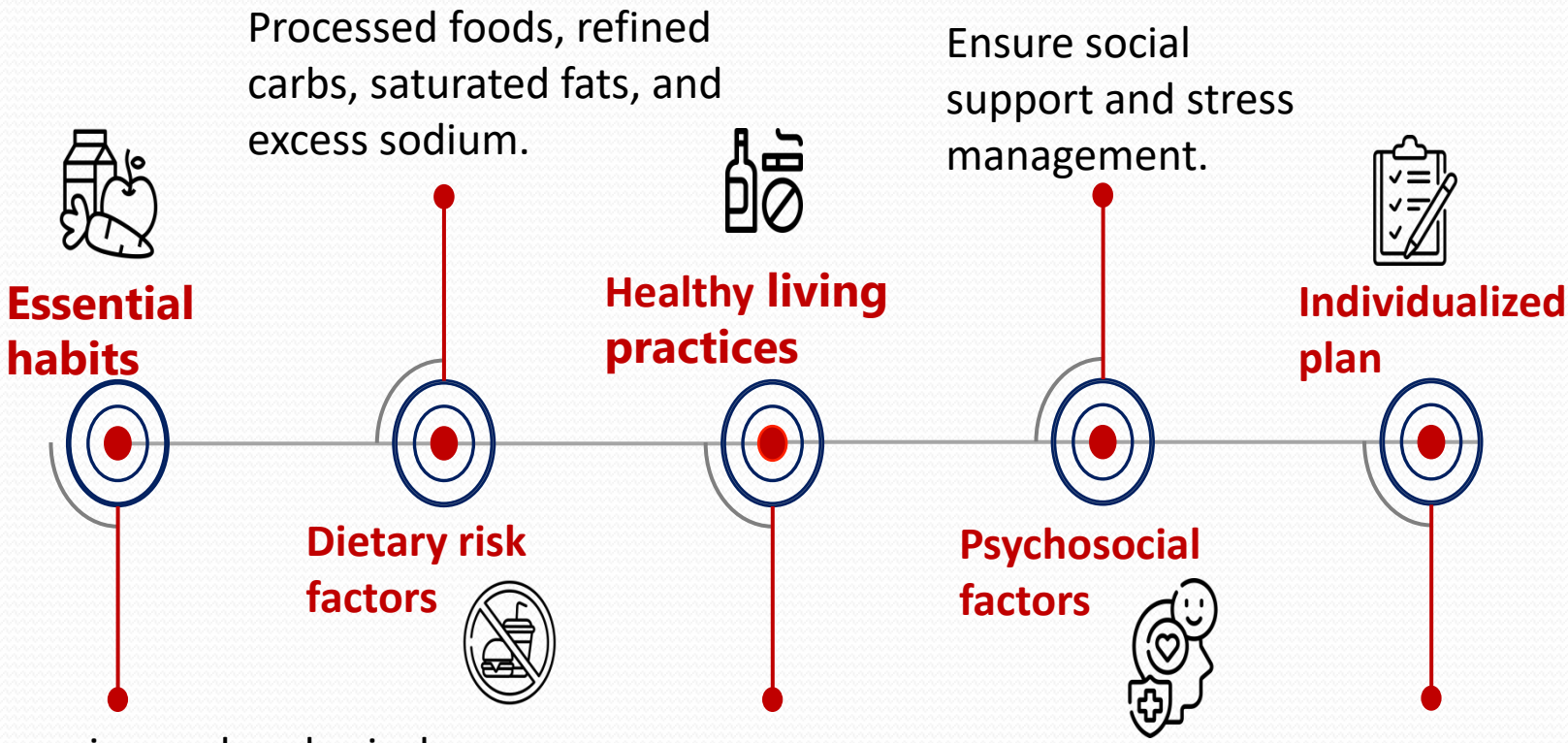


LSM

Target: 7–10% reduction in baseline body weight over 12 months.

Swarup S, et al.InStatPearls [internet] 2024. StatPearls Publishing.

Key recommendations of LSM



Swarup S, et al.InStatPearls [internet] 2024. StatPearls Publishing.

Effects of lifestyle modification on MetS: a systematic review and meta-analysis

Objective:

Evaluate the impact of LSM on:

- **Resolution of MetS**
- **Improvement in MetS components (FBG, HDL, TG, SBP, DBP)**

Methods:

- **Study type:** Systematic review and meta-analysis
- **Data sources:** MEDLINE & Cochrane Database (Jan 1966 – Oct 2011)
- **Comparisons:** LMI vs. control (usual care or no treatment)

Outcomes:

- Relative proportion of resolved MetS
- Mean differences in MetS component values (baseline to 1-year follow-up)

Eleven interventions in eight RCTs were used for the meta-analyses.

Yamaoka K, et al. BMC Med. 2012;10:138.

Effects of lifestyle modification on MetS: a systematic review and meta-analysis (cont..)

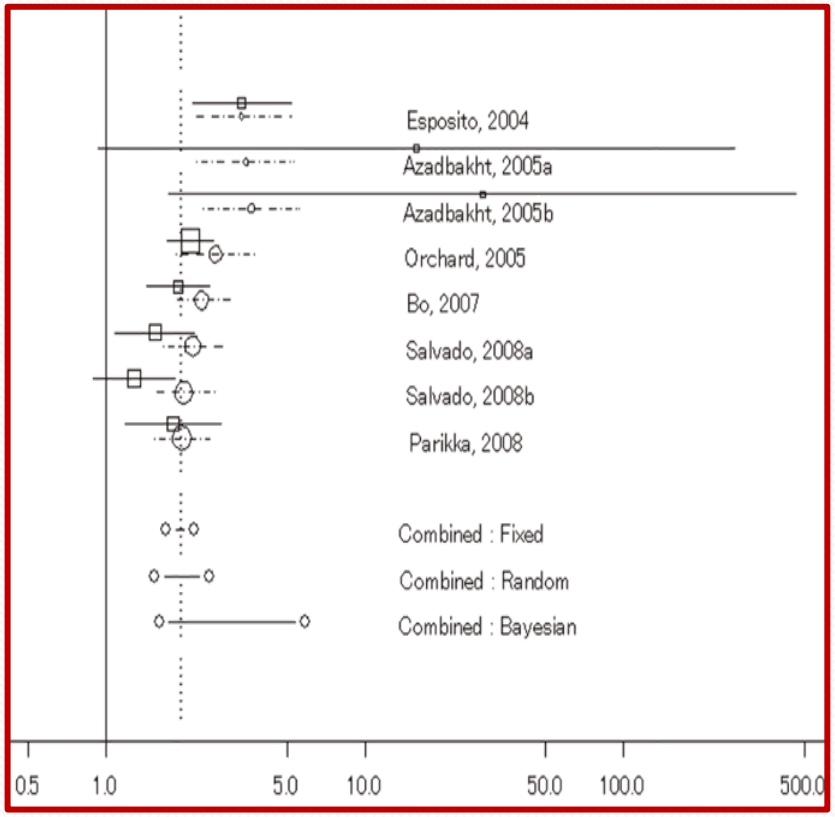
Results

- **MetS resolution:**
  - **The intervention group showed roughly 2-fold higher MetS resolution compared with the control group.**
  - **Intervention group ≈ 2.0× higher resolution rate than control.**

Conclusions

Lifestyle-modification interventions effectively:

- **Resolved MetS**
- **Significantly improve FBG, SBP, DBP, and TG levels.**



Patients with resolved MetS with 95% CI for each study and overall, for several models (eight interventions).

Yamaoka K, et al. BMC Med. 2012;10:138.

Comprehensive lifestyle modification in MetS - a systematic review and meta-analysis

Objective: Examine clinical outcomes and behavioral adherence associated with comprehensive lifestyle modification (CLM) interventions in MetS.

Methods:
Databases searched: CINAHL, PubMed (Medline), PsycINFO, Embase
Included studies: 7 eligible studies.
Intervention type:
Home-based comprehensive lifestyle modification
Core components: Diet + exercise
Duration: 6 months

Park S, et al. J Nurs Scholarsh. 2024;56(2):249-259.

Comprehensive lifestyle modification in MetS- a systematic review and meta-analysis (cont..)

Results

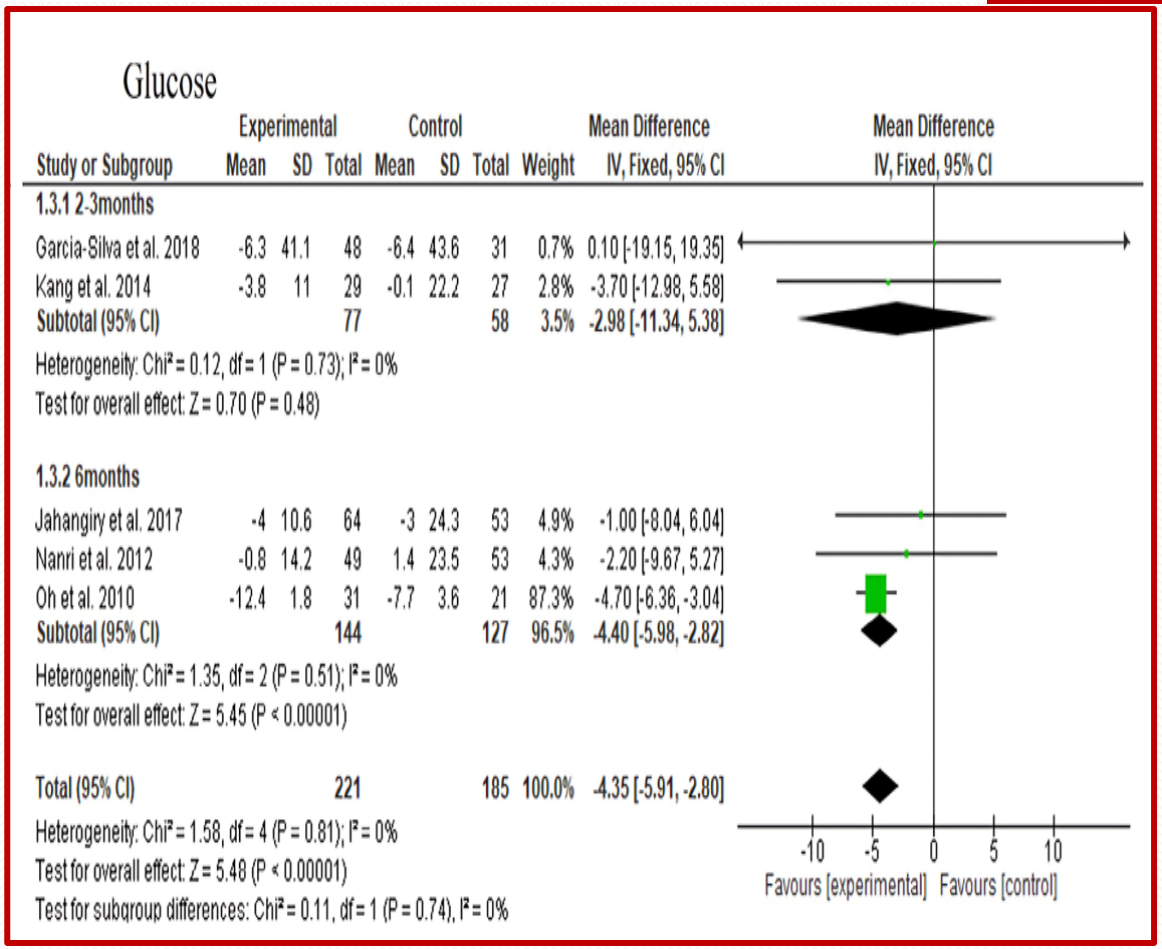
Significant improvements observed:

Glucose levels ↓

Systolic BP↓

Positive behavioural outcomes:

Improved adherence to healthy diet and exercise routines.



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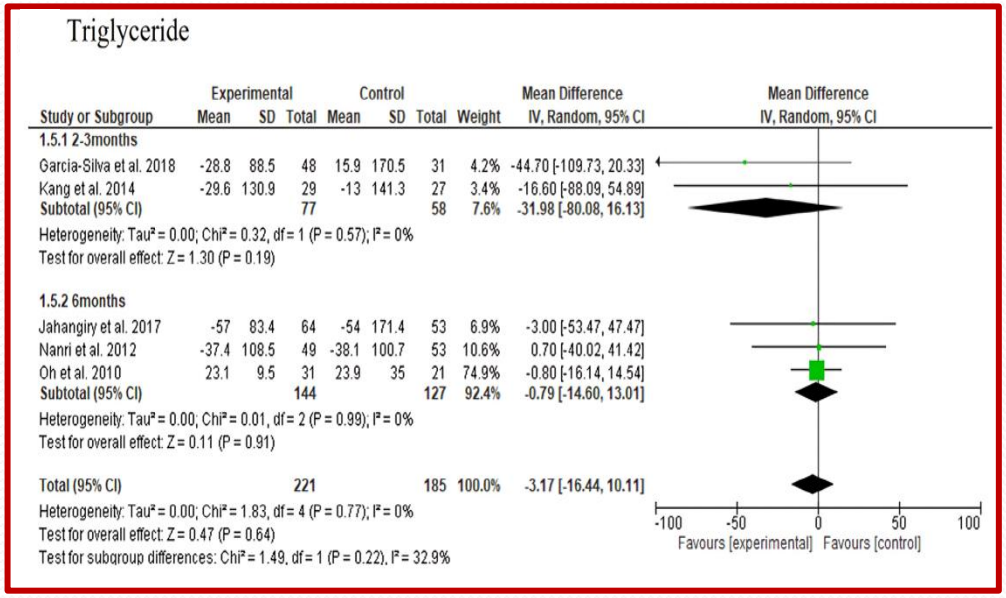
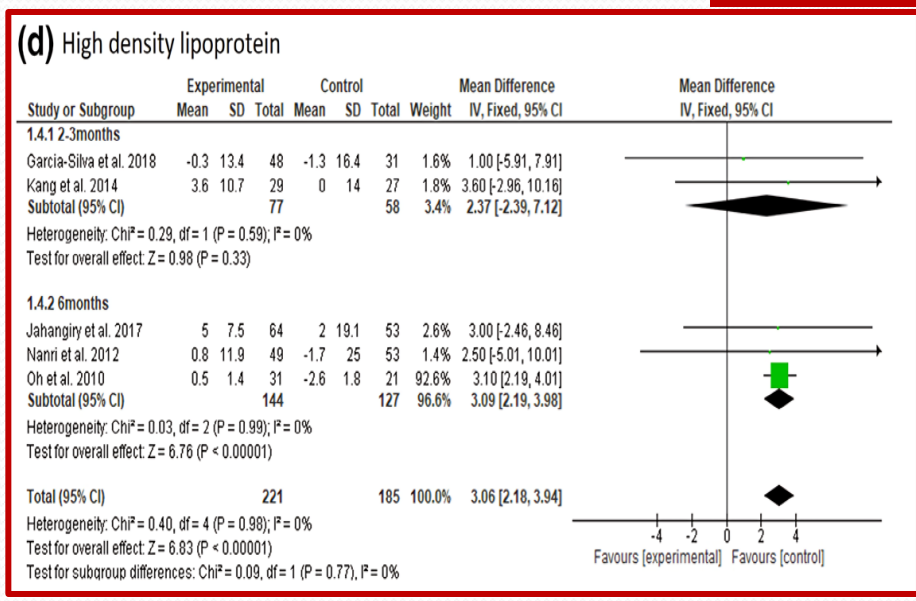
Comprehensive lifestyle modification in MetS- systematic review and meta-analysis (cont..)





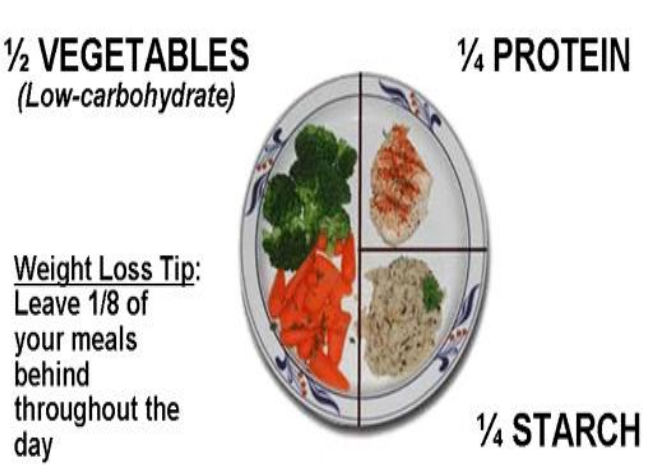
Conclusion

- **Comprehensive Lifestyle Modification**→ Improves both **health behaviour** and a few **clinical parameters** in MetS.
- **6-month interventions** show measurable short-term benefits.

Park S, et al. J Nurs Scholarsh. 2024;56(2):249-259.

Lifestyle modification in the management of obesity: achievements and challenges

- LSM is the first-line treatment for obesity, and that includes exercise, changes in diet, and behavioral therapy.
- LSM can reduce patients' weight by 8% - 10% in approx 30 weeks.
- However maintaining a healthy lifestyle in the long term is difficult, and the approach is associated with not only high failure rate but also weight regain.



Grave R D, Calugi S, El Ghoch M. Lifestyle modification in the management of obesity: achievements and challenges. Eat Weight Disord EWD. 2013;18(4):339-349.

GLP-RA in obesity

- When LSM fail, pharma treatment like GLP1-RA can be used to manage obesity.
- They are recommended for patients with

- **BMI > 30 kg/m²**

- **or >27 kg/m² with co-morbidities.**

Wilding JPH, Batterham RL, Calanna S, et al. Once-weekly semaglutide in adults with overweight or obesity. N Engl J Med. 2021;384(11):989-1002.

Bariatric surgery: a review of procedures and outcomes

- Bariatric surgery is a highly effective option for treating **severe obesity**, typically indicated for individuals

- with a **BMI >40 kg/m²** or

  >35 kg/m² with obesity related co-morbidities

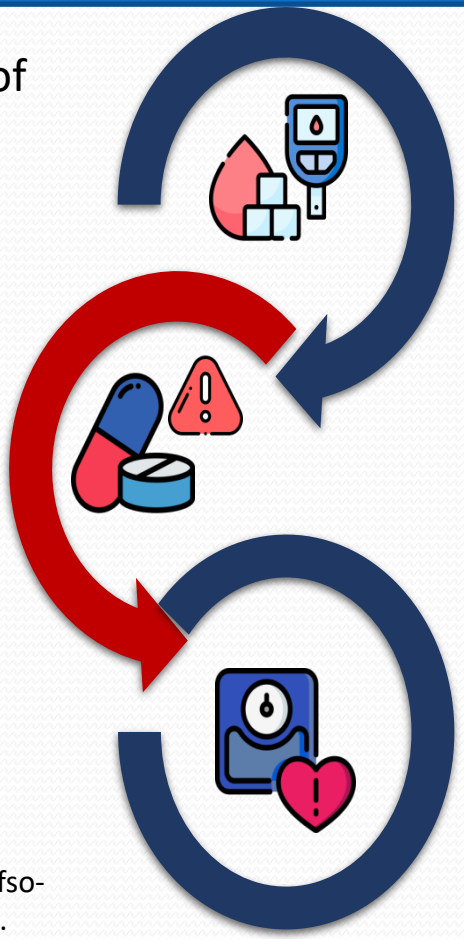
Elder KA, Wolfe BM. Bariatric surgery: a review of procedures and outcomes. Gastroenterology 2007;132:2253–2271.

Revised Indications for MBS

The American Society for Metabolic and Bariatric Surgery recommendations for metabolic and bariatric surgery in MetS

1. **BMI ≥35 kg/m²**, regardless of comorbidity status or severity.

2. **BMI of 30-34.9 kg/m2** with metabolic disease



3. BMI thresholds should be adjusted in the **Asian population** such that a BMI ≥ 25 kg/m2 suggests clinical obesity, and individuals with **BMI ≥ 27.5 kg/m2** should be offered MBS.

4. Appropriately selected children and adolescents should be considered for MBS.

https://asmbs.org/resources/2022-asmbs-and-ifso-indications-for-metabolic-and-bariatric-surgery/.

Bariatric Surgery and Long-term Durability of Weight Loss

- In this study **1787 patients undergoing RYGB** had a mean (SD) **age of 52.1** (8.5) years and 5305 nonsurgical matches had a mean (SD) age of 52.2 (8.4) years.

- Patients undergoing RYGB and nonsurgical matches had a mean **BMI of 47.7** and 47.1, respectively, and were **predominantly male** (1306 [73.1%] and 3911 [73.7%], respectively).

Roux-en-Y gastric bypass (RYGB)

Maciejewski ML, Arterburn DE, Van Scoyoc L, Smith VA, Yancy WS Jr, Weidenbacher HJ, Livingston EH, Olsen MK. Bariatric Surgery and Long-term Durability of Weight Loss. **JAMA Surg. 2016** Nov 1;151(11):1046-1055.

Bariatric Surgery and Long-term Durability of Weight Loss

- All patients undergoing RYGB **lost >21% wt** (95% CI, 11%-31%) of their baseline wt **at 10 yr** than nonsurgical matches.

- Out of that **>20% wt lost in 71.8%** vs 10.8% of non surgical matches
- Out of that **>30% wt lost in 39.7%** vs 3.9% of non surgical matches

- **Only 3.4% regained wt** within 5% of their baseline wt by 10 years.

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Lifestyle management for enhancing outcomes after bariatric surgery

- Postoperative weight loss following any type of bariatric surgery is largely dependent on the extent to which patients can make and sustain changes in eating and activity.

- **Therefore, lifestyle management including diet, exercise, and behavior modification is critical to helping patients achieve long-term weight loss after MBS.**

Kalarchian M, Turk M, Elliott J, Gourash W. Lifestyle management for enhancing outcomes after bariatric surgery. Curr Diab Rep. 2014 Oct;14(10):540.

Future of Bariatric Surgery - Does it need reshaping?

- Though Bariatric surgery is effective, it's also facing challenges from new pharma treatments, necessitating a re-evaluation of its role and accessibility.

Tirzepatide as Compared with Semaglutide for the Treatment of Obesity: SURMOUNT-5 Trial

- Among 751 participants with obesity but without diabetes, treatment with tirzepatide was superior to semaglutide with respect to **reduction in body weight** and **waist circumference** at 72 week.

- The least-squares mean percent change in weight at 72 wk was –20.2% (95% confidence interval [CI], –21.4 to –19.1) with tirzepatide and **–13.7%** (95% CI, –14.9 to –12.6) with semaglutide (P<0.001)

- The least-squares mean **change in waist circumference at 72 wk was –18.4 cm** (95% CI, –19.6 to –17.2) with tirzepatide and **–13.0 cm** (95% CI, –14.3 to –11.7) with semaglutide (P<0.001).

Published May 11, 2025 N Engl J Med 2025; 393:26-36 DOI: 10.1056/NEJMoa2416394

Tirzepatide as Compared with Semaglutide for the Treatment of Obesity: SURMOUNT-5 Trial

- **In the SURMOUNT-5 trial, lifestyle modification (reduced-calorie diet & increased physical activity) was a crucial *foundation*,**
- LSM acting as a lead-in phase before comparing tirzepatide (Mounjaro/Zepbound) with semaglutide (Wegovy) for obesity.
- **showing medication added significant weight loss *on top* of intensive lifestyle efforts.**

Published May 11, 2025 N Engl J Med 2025; 393:26-36 DOI: 10.1056/NEJMoa2416394

Patient selection criteria for MBS vs GLP-RA vs LSM

	Bariatric surgery	GLP-RA	LSM
Age	1. Consider for all adults who meet the criteria. 2. **Special consideration for patients under the age of 18 with morbid obesity who have gone through rigorous evaluation with a pediatrician and with parental involvement.** 3. **Also, special consideration for patients above the age of 60 years but there is a higher risk of peri-operative complications .** 4. It is important to consider long-term effects of bariatric surgery performed in children, including vitamin deficiencies from absorption complications and surgical complications.	Special consideration for GLP1-RA for children 18 years old and younger.	**No age restriction for lifestyle modification.**

1. Boyers D, Retat L, Jacobsen E, et al.: Cost-effectiveness of bariatric surgery and non-surgical weight management programmes for adults with severe obesity: a decision analysis model. Int J Obes (Lond). 2021, 45:2179-90. 10.1038/s41366-021-00849-8
2. Docimo S Jr, Shah J, Warren G, Ganam S, Sujka J, DuCoin C: A cost comparison of GLP-1 receptor agonists and bariatric surgery: What is the break even point?. Surg Endosc. 2024, 38:6560-5. 10.1007/s00464-024-11191-1

Patient selection criteria for MBS vs GLP-RA vs LSM

	Bariatric surgery	GLP-RA	LSM
Cost	Higher upfront cost but more cost-effective in the long term [1]	Lower initial cost but with long-term expenses with medications [2]	**No cost for LSM.**

1. Boyers D, Retat L, Jacobsen E, et al.: Cost-effectiveness of bariatric surgery and non-surgical weight management programmes for adults with severe obesity: a decision analysis model. Int J Obes (Lond). 2021, 45:2179-90. 10.1038/s41366-021-00849-8
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In Metabolic Syndrome with BMI >35kg/m² : LSM vs GLP1-RA vs Bariatric Surgery – In Favor of LSM

Summary

MetS is characterized by obesity, dyslipidemia, hypertension, and insulin resistance and rising global prevalence contributes significantly to cardiometabolic morbidity and healthcare costs.

Three main strategies- LSM, GLP-1 RA, and MBS- target weight reduction, improved insulin sensitivity, and cardiovascular risk mitigation.

LSM offers sustainable, low-risk improvement; GLP-1 RAs provide moderate short-term benefits; surgery achieves maximal weight loss but with higher risk and lifelong follow-ups.

Meta-analyses and major trials show LSM improves metabolic health and quality of life sustainably, but further research is warranted.

LSM remains the cornerstone of metabolic syndrome management while pharmacologic and surgical options should complement LSM, not replace, sustained LSM.

Thank you

Please visit Tripura