

Cost-effectiveness of tirzepatide versus liraglutide, both adjunct to diet and exercise, for patients with obesity or overweight: A UK perspective

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Additional scenario analyses

Table S1. Scenario analyses results for tirzepatide vs. liraglutide (subgroup population)

		Tirzepatide 5 mg	Tirzepatide 10 mg	Tirzepatide 15 mg
Description		INHB (ICER) at WTP threshold of £20,000/QALY gained ^a		
Base Case		0.61 (£5,401)	0.70 (£6,265)	0.71 (£7,864)
1	Efficacy Waning Period Post-Discontinuation: 2 Years assumed (<i>Base Case: 3 Years</i>)	0.65 (£4,766)	0.74 (£5,736)	0.75 (£7,333)
2	Source for Natural Weight Regain Post-Discontinuation: Iyen et al. 2021 (<i>Base Case: Ara et al. 2012</i>)	0.55 (£5,903)	0.64 (£6,683)	0.65 (£8,320)
3	Apply discontinuation due to AEs indefinitely (<i>Base Case: Apply for 3 years only</i>)	0.50 (£2,151)	0.52 (£1,486)	0.55 (£4,377)
4	Risk Equation for Development of T2DM: Framingham Offspring Study (<i>Base Case: QDiabetes</i>)	0.13 (£16,222)	0.20 (£15,281)	0.13 (£17,281)

5	Risk Equation for Development of T2DM: REGARDS (<i>Base Case: QDiabetes</i>)	0.24 (£13,299)	0.34 (£12,390)	0.28 (£14,554)
6	Risk Equation for Initial CVD Event: Framingham Heart Study (<i>Base Case: QRisk3</i>)	0.55 (£5,534)	0.64 (£6,505)	0.66 (£8,022)
7	Risk Equation for Recurrent CVD Events: LIPID Study (<i>Base Case: Framingham Heart Study</i>)	0.62 (£5,308)	0.71 (£6,221)	0.72 (£7,780)
8	Risk Equation for OSA: Young et al. 2002 (<i>Base Case: Erridge et al. 2021</i>)	0.52 (£6,865)	0.60 (£7,595)	0.60 (£9,206)
9	Approach to Combining Utilities: Multiplicative (<i>Base Case: Additive</i>)	0.60 (£5,461)	0.69 (£6,327)	0.69 (£7,937)

Footnote: ^aA positive NHB implies that the health benefits gained outweigh the additional costs incurred by the intervention, at a WTP threshold of £20,000/QALY gained.

Abbreviations: AE: adverse event; CVD: cardiovascular disease; INHB: incremental net health benefit; ICER: incremental cost-effectiveness ratio; OSA: obstructive sleep apnoea; QALY: quality-adjusted life year; T2DM: type 2 diabetes mellitus.

Baseline characteristics

Table S2. Baseline patient characteristics

	Trial population (efficacy estimand)	Subgroup population (treatment regimen estimand)
Parameter	Mean (SD)	
Age (years)	44.9 (12.50)	46.60 (11.80)
Sex (% female)	67.5 (-)	66.4 (-)
BMI (kg/m ²)	38.00 (6.81)	42.56 (6.29)
SBP (mmHg)	123.30 (12.70)	126.46 (13.38)
Total cholesterol (mg/dL)	187.90 (38.14)	158.77 (79.18)
HDL (mg/dL)	47.30 (12.44)	45.34 (11.38)
FPG (mg/dL)	5.41 (0.57)	5.69 (0.56)
Hypertension (%)	32.26 (-)	40.73 (-)
eGFR (ml/min/1.73 m ²)	98.10 (19.62)	96.51 (18.56)
Triglycerides (mg/dL)	128.40 (64.20)	144.08 (64.82)
PCOS (% of female patients)	2.28 (-)	1.10 (-)
Treated hypertension (%)	29.81 (-)	37.80 (-)
COPD (%)	10.52 (-)	1.47 (-)
Hypothyroidism (%)	10.87 (-)	11.74 (-)
Gestational diabetes (%)	0.93 (-)	1.93 (-)

Systemic lupus erythematosus (%)	0.12 (-)	0.00 (-)
Acromegaly (%)	0.04 (-)	0.00 (-)
DBP (mmHg)	79.53 (8.16)	81.34 (8.53)
Erectile dysfunction (%)	4.61 (-)	4.37 (-)
Use of corticosteroids (%)	1.58 (-)	1.83 (-)
Prediabetes (%)	40.65 (-)	100.00 (-)
Use of statins/pravastatin	13.43 (-)	12.66 (-)

Abbreviations: BMI: body mass index; COPD: chronic obstructive pulmonary disease; DBP: diastolic blood pressure; eGFR: estimated glomerular rate; FPG: fasting plasma glucose; HDL: high-density lipoprotein; SBP: systolic blood pressure; SD: standard deviation.

Sources: Jastreboff et al. 2022(1); NMA. Lilly Data on File 2023.

Table S3. Additional baseline patient characteristics for use in risk equations in both populations

Variable	Value	Source
Townsend score	0.5 (3.3)	QDiabetes(2)
Proportion of patients who are smokers ^a	54.3%	
Family/parental history of diabetes	14.9%	
Schizophrenia/BPD	0.8%	
Learning disability	0.7%	

Race or ethnic group (%) ^b		
White	82.30% (-)	
Indian	3.17% (-)	
Pakistani	1.71% (-)	
Bangladeshi	1.38% (-)	
Other Asian	2.07% (-)	
Caribbean	1.36% (-)	
Black African	3.02% (-)	
Chinese	1.11% (-)	
Other	3.88% (-)	
CKD (stage 3, 4 or 5)	Female: 0.5% Male: 0.3%	QRISK3(3)
Family history of CHD	Female: 12.0% Male: 9.3%	
Rheumatoid arthritis	Female: 1.1% Male: 0.5%	
Atrial fibrillation	Female: 0.4% Male: 0.5%	

Migraine	Female: 6.4% Male: 2.7%	
Severe mental illness	Female: 6.8% Male: 4.3%	
Macroalbuminuria	1.9%	UKPDS82(4)
Diagnosis of peripheral vascular disease	0%	Assumption aligned with UKPDS(4)
White blood count	0%	
Previous CHF	0%	
Previous amputation	0%	
Never revascularisation	Female: 64.7% Male: 53.0%	LIPID study(5)
Vascularisation before ACS	Female: 9.7% Male: 14.4%	
Hyperlipidaemia	24.20%	Erridge et al. 2021(6)
GERD	38.26%	
Benzodiazepines	71.01%	

Footnote: ^aThe QRISK3 risk equation requires the following input categories: non-smoker, former smoker, light smoker, moderate smoker and heavy smoker. In this case, patients who do not smoke are divided evenly between the non-smoker and former smoker categories, while patients who smoke are divided evenly between the light, moderate and heavy smoker categories. ^bRace data are available in SURMOUNT-1 however the

categorisation of this characteristic was less relevant to a UK population; therefore, it was decided to use these inputs from an alternative source which are derived from a UK population.

Abbreviations: ACS: acute coronary syndrome; BPD: bipolar disorder; CHD: coronary heart disease; CHF: coronary heart failure; CKD: chronic kidney disease; GERD: gastroesophageal reflux disease; UK: United Kingdom; UKPDS: United Kingdom prospective diabetes study.

Efficacy inputs

Table S4. Change from baseline in surrogate endpoints (72 weeks in SURMOUNT-1 for tirzepatide; 52 weeks in O’Neil et al. 2018 for liraglutide 3 mg in the trial population, 56 weeks in SCALE for liraglutide 3 mg in the subgroup population)

Population	Treatment	Weight (%)			SBP (mmHg)			HDL (%)			Total Cholesterol (%)		
		Mean	L95% CrI	U95% CrI	Mean	L95% CrI	U95% CrI	Mean	L95% CrI	U95% CrI	Mean	L95% CrI	U95% CrI
Trial (efficacy estimand)	Tirzepatide (5 mg)	-15.40%	-18.11%	-8.40%	-7.29	-9.41	-4.83	5.64%	-6.13%	12.50%	-4.12%	-11.48%	6.10%
	Tirzepatide (10 mg)	-20.74%	-23.41%	-13.45%	-8.67	-10.78	-6.17	7.12%	-4.93%	13.89%	-4.79%	-12.14%	5.55%
	Tirzepatide (15 mg)	-21.83%	-24.50%	-14.50%	-7.88	-9.99	-5.40	6.74%	-5.25%	13.53%	-6.46%	-13.54%	4.20%
	Liraglutide (3 mg)	-7.84%	-10.86%	-4.35%	-8.39	-11.97	-4.85	3.15%	-7.06%	11.42%	0.10%	-9.05%	8.65%
Subgroup (treatment)	Tirzepatide (5 mg)	-13.77%	-17.90%	-9.45%	-8.35	-12.01	-4.62	6.09%	-4.03%	16.18%	-2.77%	-12.89%	7.50%

regimen estimand)	Tirzepatide (10 mg)	-18.19%	-22.24%	-13.96%	-7.96	-11.48	-4.39	5.06%	-7.19%	17.16%	-5.49%	-15.72%	4.81%
	Tirzepatide (15 mg)	-19.90%	-23.82%	-15.81%	-6.76	-10.32	-3.14	4.39%	-5.80%	14.51%	-5.03%	-15.12%	5.17%
	Liraglutide (3 mg)	-7.88%	-10.68%	-5.03%	-6.68	-9.44	-3.89	1.80%	-5.53%	9.13%	-1.95%	-10.49%	6.60%

Footnote: all pharmacological therapies are as an adjunct to D&E.

Abbreviations: CrI: credible interval; D&E: diet and exercise; HDL: high-density lipoprotein; NMA: network meta-analysis; SBP: systolic blood pressure.

Sources: Jastreboff et al. 2022(1); O'Neil et al. 2018(7); Pi-Sunyer et al. 2015(8); NMA. Lilly Data on File 2023.

Table S5. Percentage of patients with prediabetes at baseline experiencing glycaemic status reversal, using the treatment regimen estimand

Population	Treatment	Value	L95% CrI	U95% CrI
Trial	Liraglutide (3 mg)	87.97%	69.89%	95.69%
	Tirzepatide (5 mg)	93.62%	80.89%	97.99%
	Tirzepatide (10 mg)	92.46%	77.97%	97.54%
	Tirzepatide (15 mg)	93.75%	81.23%	98.02%
Subgroup	Liraglutide (3 mg)	90.40%	73.92%	96.83%

	Tirzepatide (5 mg)	93.19%	77.62%	98.18%
	Tirzepatide (10 mg)	93.88%	79.72%	98.32%
	Tirzepatide (15 mg)	96.39%	86.28%	99.19%

Footnote: all pharmacological therapies are as an adjunct to D&E.

Abbreviations: CrI: credible interval; D&E: diet and exercise; NMA: network meta-analysis.

Sources: NMA. Lilly Data on File 2023.

Discontinuation inputs

Table S6. AE-related discontinuation in both populations (efficacy estimand; at Week 72 for all tirzepatide doses; at Week 52 for liraglutide 3 mg)

Treatment	Discontinuation	SE
Tirzepatide (5 mg)	4.32%	2.83%
Tirzepatide (10 mg)	7.17%	4.32%
Tirzepatide (15 mg)	6.26%	3.87%
Liraglutide (3 mg)	8.54%	3.58%

Footnote: all doses of tirzepatide are as an adjunct to D&E.

Abbreviations: AE: adverse event; D&E: diet and exercise; SE: standard error; NMA: network meta-analysis.

Sources: NMA. Lilly Data on File 2023.

Table S7. Primary treatment failure discontinuation

Population	Treatment	Discontinuation	Applied time point
Trial (efficacy estimand)	Tirzepatide (5 mg)	10.65%	Week 30, inclusive of a 4-week titration period
	Tirzepatide (10 mg)	3.74%	Week 38, inclusive of a 12-week titration period
	Tirzepatide (15 mg)	3.64%	Week 46, inclusive of a 20-week titration period
	Liraglutide (3 mg)	30.80%	Week 16, inclusive of a 4-week titration period
Subgroup (treatment regimen estimand)	Tirzepatide (5 mg)	14.85%	Week 30, inclusive of a 4-week titration period
	Tirzepatide (10 mg)	11.10%	Week 38, inclusive of a 12-week titration period
	Tirzepatide (15 mg)	8.99%	Week 46, inclusive of a 20-week titration period
	Liraglutide (3 mg)	29.29%	Week 16, inclusive of a 4-week titration period

Footnote: all pharmacological therapies are as an adjunct to D&E.

Abbreviations: D&E: diet and exercise; NMA: network meta-analysis.

Sources: NMA. Lilly Data on File 2023.

Adverse events

Incidence

Table S8. Annual occurrence of severe or serious GIs in both populations (efficacy estimand)

Treatment	% Patients	Source
Tirzepatide (5 mg)	1.23%	Jastreboff et al. 2022(1)
Tirzepatide (10 mg)	2.26%	
Tirzepatide (15 mg)	2.40%	
Liraglutide (3 mg)	2.46%	STEP-8. Rubino et al. 2022(9)

Footnote: all pharmacological therapies are as an adjunct to D&E.

Abbreviations: D&E: diet and exercise; GI: gastrointestinal event.

Disutilities and management costs

AE disutilities and management costs (applied per incidence of AE)

Category	Value	Source
Severe GI event cost	£148.93	NHS Reference Costs 2021/2022(10)
GI event disutility (mean [SE])	-0.04802	Matza et al. 2007; nausea and vomiting(11)

Abbreviations: AE: adverse event; GI: gastrointestinal; NHS: National Health Service; SE: standard error.

Cost inputs

Treatment costs

Table S9. Tirzepatide drug pack acquisition costs

Description/Phase	Number of injections per pack	Vial size (mg/mL)	Pack cost	Source
Tirzepatide 5 mg QW SQ	4.00	10.0	£92.00	BNF 2024(12)
Tirzepatide 10 mg QW SQ		20.0	£107.00	

Tirzepatide 15 mg QW SQ		30.0	£122.00	
Liraglutide 3 mg SQ	5.00	6.0	£196.20	BNF 2023(13)

Abbreviations: BNF: British National Formulary; QW: every week; SQ: subcutaneously.

Table S10. Treatment administration unit costs

Administration method	Unit cost	Source
First SQ injection	£24.00	Hospital based nurse, Band 4. PSSRU 2022; 2 x 20-minute trainings(14)
Subsequent SQ injection pen (self-administration)	£0.00	Assumption

Abbreviations: PSSRU: personal social services research unit; SQ: subcutaneous.

Monitoring and resource use costs

For all patients receiving treatment with D&E (either with tirzepatide or liraglutide), patients are assumed to have weekly 30-minute appointments with the dietician for 4 weeks, followed by every 12 weeks thereafter up to 2 years. Additionally, patients on tirzepatide have a 20-minute initial nurse consultation for a training on the injection pen, a 30-minute nurse consultation at the first dose titration (4 weeks) and 15-minute nurse appointment for each 4-weekly titration thereafter. Patients receiving tirzepatide also have an annual 10-minute GP visit. Finally, patients receiving liraglutide have a 15-minute nurse appointment for each weekly titration, which commences after an initial nurse consultation. Annual costs for Year 1, Year 2 and Year 3+ are summarised in **Error! Reference source not found..**

Table S11. Annual HCRU costs for obesity

Intervention	Year 1	Year 2	Year 3+
Tirzepatide 5 mg	£324.08	£149.76	£41.00
Tirzepatide 10 mg	£379.73		
Tirzepatide 15 mg	£435.38		
Liraglutide 3 mg (only applied in the trial population)	£324.08		

Footnote: all doses are as an adjunct to D&E

Abbreviations: D&E: diet and exercise; HCRU: healthcare resource use.

Table S12. SWMS cost applied to the liraglutide arm in the subgroup analysis

Variable	Cost	Source
Tier 3 service secondary care	£1,796 per patient per year	NICE 2023(15)

Table S13. Annual ongoing resource use costs (excluding event costs)

Complication	Cost	Source
T2DM annual resource use costs (excluding event costs)		

T2DM	£1,770.52	Weighted average cost for number of activity and national average unit costs from Total HRGs tab for Diabetes with Hypoglycaemic Disorders (NHS direct costs): KB01C, KB01D, KB01E, KB01F, KB02G, KB02H, KB02J, KB02K. NHS Reference Costs 2021/2022(10)
Post-MI/angina annual resource use costs (excluding event costs)		
MI, first year	£1,121.30	Alva et al. 2015 ^a (16)
MI, subsequent years	£781.30	
Angina, first year	£1,006.02	
Angina, subsequent years	£761.50	
Post-stroke annual resource use costs (excluding event costs)		
First year	£1,270.34	Alva et al. 2015 ^a (16)
Subsequent years	£880.27	

Footnotes: ^aCosts inflated from 2012/13 (price year used in the source) to 2021/2022 costs using a combination index of NHSCII and pay and price index.

Abbreviations: HRG: healthcare resource group; MI: myocardial infarction; NHS: national health service; NHSCII: national health service cost inflation index; T2DM: type 2 diabetes mellitus.

Clinical event costs

Table S14. Cost of acute clinical events (one-off)

Clinical event	Cost	Source
MI (fatal or non-fatal)	£3,120.22	Weighted average cost for number of FCE's and national average unit costs from Non-Elective Long Stay for acute or suspected MI codes: EB10A, EB10B, EB10C, EB10D, EB10E. NHS Reference Costs 2021/2022(10)
Stroke (fatal or non-fatal)	£6,089.36	Weighted average cost for number of FCE's and national average unit costs from Non-Elective Long Stay for stroke codes: AA35A, AA35B, AA35C, AA35D, AA35E, AA35F. NHS Reference Costs 2021/2022(10)
Knee osteoarthritis	£8,186.07	Weighted average cost for number of FCE's and national average unit costs from Elective Inpatient for very major knee procedures for non-trauma, codes: HN22A, HN22B, HN22C, HN22D, HN22E. NHS Reference Costs 2021/2022(10)
Angina	£2,172.93	Weighted average cost for number of FCE's and national average unit costs from Non-Elective Long Stay for angina codes: EB13A, EB13B, EB13C, EB13D. NHS Reference Costs 2021/2022(10)

Abbreviations: FCE: finished consultant episode; MI: myocardial infarction; NHS: national health service; TIA: transient ischemic attack.

Table S15. Cost of non-acute clinical events (annual)

Clinical event	Cost	Source
OSA	£698.42	Weighted average cost for number of activity and national average unit costs from Total HRGs tab for sleep disorders affecting breathing codes (NHS direct costs): DZ18D, DZ18E, DZ18F, DZ18G. NHS Reference Costs 2021/2022(10)
MAFLD	£3,108.37	Weighted average cost for number of activity and national average unit costs from Total HRGs tab for liver failure disorder codes (NHS direct costs): GC01C, GC01D, GC01E, GC01F. NHS Reference Costs 2021/2022(10)

Abbreviations: HRG: healthcare resource group; OSA: obstructive sleep apnoea; MAFLD: metabolic associated fatty liver disease; NHS: national health service; SE: standard error.

Table S16. Cost of bariatric surgery (one-off)

Category	Cost	Source
RYGB procedure	£8,334.84	Weighted average cost for number of activity and national average unit costs for complex surgical procedures for obesity (FF10Z) and major surgical procedures for obesity (FF11Z). NHS Reference Costs 2021/2022(10)
Sleeve gastrectomy procedure	£6,778.80	National average unit cost for sleeve gastrectomy for obesity (FF12Z). NHS Reference Costs 2021/2022(10)

Gastric band procedure	£4,031.00	National average unit cost for gastric band procedures for obesity (FF13Z). NHS Reference Costs 2021/2022(10)
OAGB/MGB procedure	£8,334.84	Weighted average cost for number of activity and national average unit costs for complex surgical procedures for obesity (FF10Z) and major surgical procedures for obesity (FF11Z). NHS Reference Costs 2021/2022(10)

Abbreviations: MGB: mini gastric bypass; NHS: National Health Service; OAGB: one-anastomosis gastric bypass; RYGB: Roux-en-Y gastric bypass.

Mortality

Table S17. Mortality HR/RRs (applied to clinical events and complications)

Mortality category	Value	95% CI (Lower)	95% CI (Upper)	Source
Prior MI or angina (RR)	1.30	1.04	1.56	Johansson et al. 2017(17)
MAFLD (HR)	1.93	1.86	2.00	Simon et al. 2021(18)
BMI-specific mortality (HR) by BMI category (Reference of BMI 22.5 – 24.9)				
<18.5	1.56	1.52	1.59	Bhaskaran et al. 2018(19)
18.5–19.9	1.29	1.27	1.32	
20.0–22.4	1.11	1.10	1.12	

25.0–27.4	0.98	0.97	0.99	
27.5–29.9	1.01	1.00	1.03	
30.0–34.9	1.12	1.10	1.13	
35.0–39.9	1.36	1.33	1.38	
≥40.0	1.88	1.83	1.93	

Abbreviations: BMI: body mass index; CI: confidence interval; HR: hazard ratio; MI: myocardial infarction; MAFLD: metabolic associated fatty liver disease; RR: relative risk; T2DM: type 2 diabetes mellitus.

Table S18. RR for patients who have experienced a stroke

Age group	Years after stroke	RR (95% CI)		Source
		Male	Female	
25–69 years	>0, ≤1	4.64 (3.71–5.72)	9.27 (6.94–12.1)	Brønnum-Hansen et al. 2001(20)
	>1, ≤5	3.01 (2.63–3.43)	3.52 (2.80–4.35)	
	>5, ≤10	2.75 (2.39–3.15)	3.32 (2.66–4.09)	
	>10, ≤15	2.50 (1.94–3.18)	2.45 (1.60–3.59)	
≥70 years	>0, ≤1	3.70 (3.15–4.32)	5.18 (4.54–5.87)	
	>1, ≤5	1.92 (1.68–2.18)	2.05 (1.81–2.30)	
	>5, ≤10	1.89 (1.56–2.27)	1.99 (1.67–2.36)	

	>10, ≤15	2.49 (1.48–3.93)	1.67 (1.08–2.47)	
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Abbreviations: CI: confidence interval; RR: relative risk.

Utilities

Table S19. Baseline utilities (function for deriving EQ-5D by BMI)

Parameter	BMI 15–35 kg/m ² Mean (SE)		Source
	Male	Female	
Age 25–34	Reference	Reference	Søltøft et al. 2009 with additional precision for BMI ³ from the NICE submissions for semaglutide and liraglutide (Table 35, TA664 and Appendix L Table 71, TA875)(21-23)
Age 35–44	-0.0028 (0.0064)	-0.0213 (0.0059)	
Age 45–54	-0.0081 (0.0071)	-0.0336 (0.0068)	
Age 55–64	-0.0430 (0.0077)	-0.0425 (0.0072)	
Age 65–74	-0.0223 (0.0089)	-0.0619 (0.0092)	
Age 75–100	-0.0565 (0.0121)	-0.0754 (0.0014)	
BMI ³	0.000033 (0.000)	0.00017 (0.0000)	
BMI ²	-0.0032 (0.0009)	-0.0018 (0.0006)	
BMI	0.0990 (0.0265)	0.0572 (0.0183)	
Intercept	-0.0228 (0.2575)	0.4010 (0.1786)	

Abbreviations: BMI: body mass index; EQ-5D: EuroQol-5 Dimension; SE: standard error.

Table S20. Disutilities applied for complications

Health State	Mean (SE)	Source
T2DM	Male: -0.0528 (0.0145) Female: -0.0325 (0.0183)	Søltøft et al. 2009; weighted average of male and females to be applied based on modelled population(21)
Post MI/with angina	-0.037 (0.026)	Sullivan et al. 2011(24)
Post stroke	-0.035 (0.021)	

Abbreviations: AE: adverse event; MI: myocardial infarction; SE: standard error; T2DM: type 2 diabetes mellitus.

Table S21. Disutilities applied to events

Event	Type of Disutility	Mean (SE)	Source
Knee replacement	One-off	Male: -0.1721 (0.0078) Female: -0.2014 (0.0074)	Søltøft et al. 2009; Musculoskeletal problems assumed reflective of knee replacement(21)
OSA	Annual	Male: -0.0242 (0.0084) Female: -0.0430 (0.0097)	
MI/angina	One-off	-0.0626 (0.0132)	Sullivan et al. 2011(24) – ICD-9 Code 410 (acute MI), 433 (acute cerebrovascular disease)^ and 573 (other disorders of the liver)*
Stroke	One-off	-0.0349 (0.0213)	
MAFLD	Annual	-0.0956 (0.0312)	

Bariatric surgery	One-off	-0.22 (-)	Campbell et al. 2010 as per Kim et al. 2022(25, 26)
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Abbreviations: OSA: obstructive sleep apnoea; MI: myocardial infarction; MAFLD: metabolic associated fatty liver disease; SE: standard error.

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