

Le Obesità: aspetti psico-nutrizionali e aggiornamenti terapeutici

Terapia dell'obesità in menopausa

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Dipartimento di Eccellenza MUR 2023 – 2027.

I have no conflicts of interest to disclose.

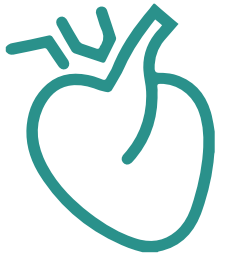


Menopausa: una transizione cardiometabolica

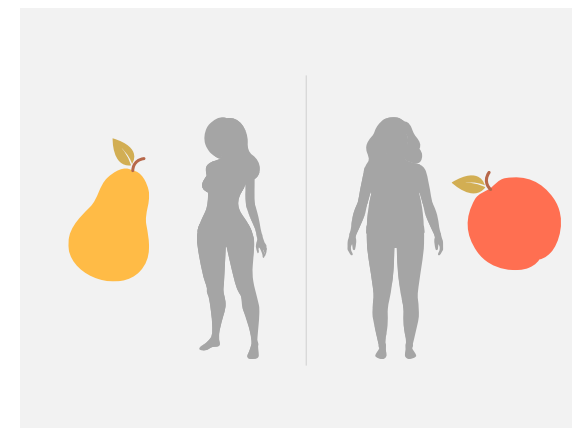
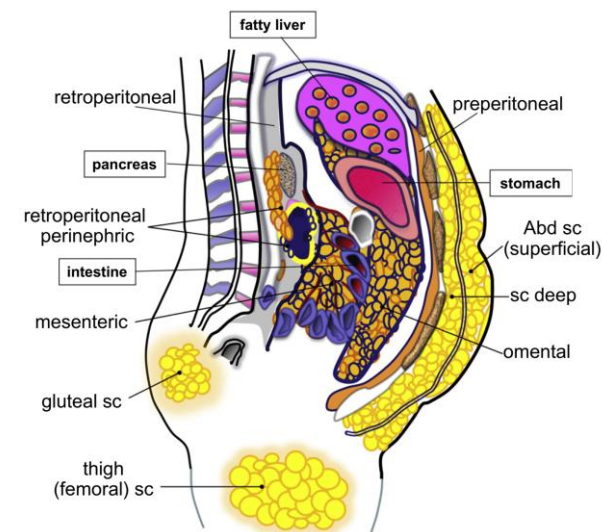
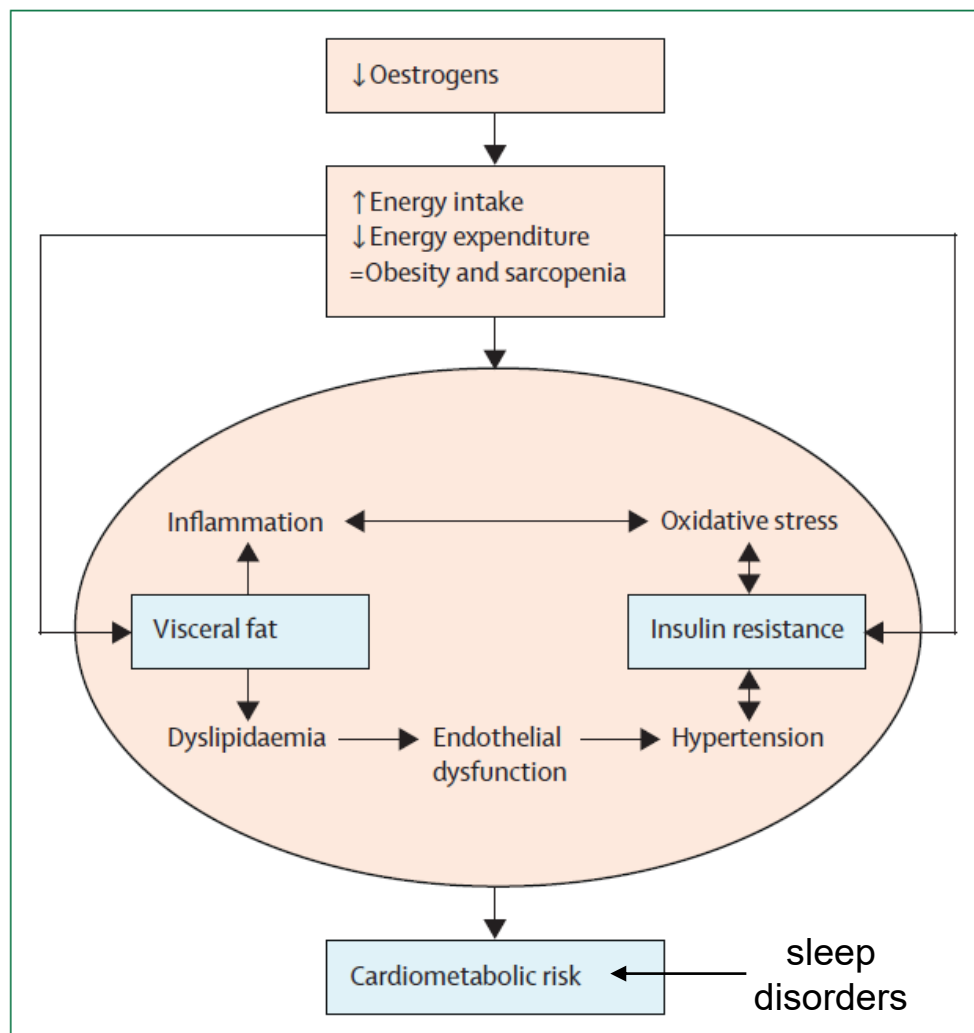
La menopausa è definita come la cessazione permanente delle mestruazioni, confermata retrospettivamente dopo 12 mesi consecutivi di amenorrea, in assenza di altre cause patologiche o fisiologiche.

Review article

Menopause transition and cardiovascular disease risk



Cambiamento della composizione corporea



Cambiamento della composizione corporea

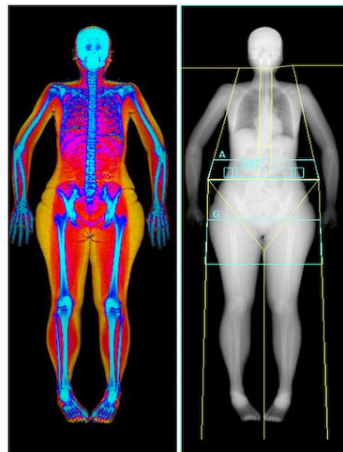
Universita' degli Studi di Ferrara
Centro di Ricerca per lo Studio della Menopausa e dell'Osteoporosi
Via Boschetto, 31, Ferrara 44124

Telefono: 800229394

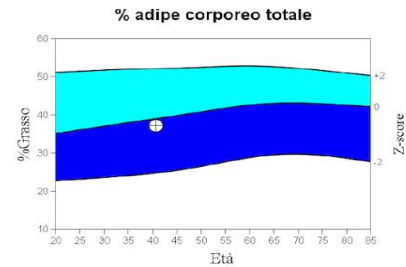
E-mail: cmo@unife.it

Fax: 0532747038

Nome: [redacted] Sesso: Femminile Height: 165.8 cm
ID paziente: [redacted] Etnia: Bianco Peso: 61.2 kg
Data di: [redacted] Età: 40

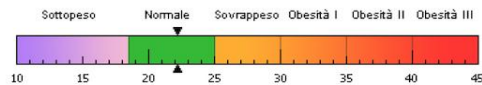


Grasso Inclinato Osso



Origine: 2008 NHANES Femmina bianca

Classificazione dell'indice di massa corporea (BMI) secondo l'Organizzazione Mondiale della Sanità
BMI = 22.3 WHO Classification Normal



Il BMI presenta alcuni limiti e una diagnosi effettiva di sovrappeso o di obesità deve essere effettuata da un medico. L'obesità è associata a cardiopatie, determinati tipi di cancro, diabete di tipo 2 e altri rischi per la salute. Più il BMI di un individuo è superiore a 25, tanto maggiori sono i loro rischi correlati al peso.

Risultati della composizione corporea

Regione	Grasso	Inclinato + Massa (g)	Totale Massa (g)	%Grasso	Percentile SN	% adiposo AM
Braccio Sx	1221	1692	2913	41.9	60	46
Braccio Dx	1120	1960	3081	36.4	38	25
Tronco	9033	18166	27199	33.2	52	33
Gamba Sx	5069	6510	11579	43.8	64	56
Gamba Dx	5242	6884	12126	43.2	59	50
Subtotale	21685	35213	56898	38.1	56	40
Testa	905	2814	3719	24.3		
Totale	22590	38027	60617	37.3	57	40
Androide (A)	1516	3025	4542	33.4		
Ginoide (G)	5004	6611	11615	43.1		

Data scansione: 10 Marzo 2021 ID: A03102107

Tipologia di scansione: a Corpo Intero

Analisi: 10 Marzo 2021 12:14 Versione 13.6.0.5

Auto Whole Body

Operatore: MR

Modello: Horizon W (S/N 301644M)

Indici adiposi

Misura	Risultato	SN	Percentuale AM
% adiposo corporeo totale	37.3	57	40
Massa grassa (kg/m²)	8.33	43	28
Rapporto androide/ginoide	0.78		
% adiposo tronco/arti	0.70	45	30
Rapporto massa adiposa tronco/arti	0.71	34	19
Est. VAT Mass (g)	296		
Est. VAT Volume (cm³)	320		
Est. VAT Area (cm²)	61.5		

Lean Indices

Misura	Risultato	SN	Percentuale AM
Lean/Height² (kg/m²)	13.1	13	10
Appen. Lean/Height² (kg/m²)	5.85	26	25

Est. VAT = Estimated Visceral Adipose Tissue

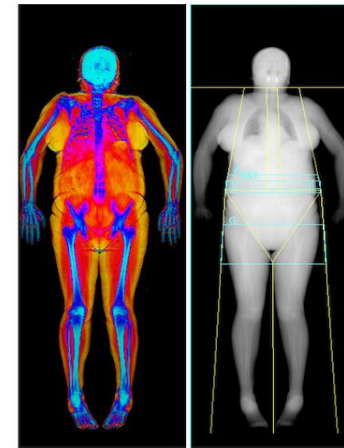
Centro di Ricerca per lo Studio della Menopausa e dell'Osteoporosi
Via Boschetto, 31, Ferrara 44124

Telefono: 800229394

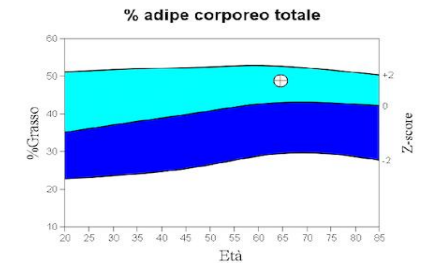
E-mail: cmo@unife.it

Fax: 0532747038

Nome: [redacted] Sesso: Femminile Height: 160.7 cm
ID paziente: [redacted] Etnia: Bianco Peso: 71.5 kg
Data di: [redacted] Età menopausa: 51 Età: 64

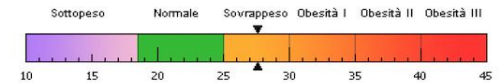


Grasso Inclinato Osso



Origine: 2008 NHANES Femmina bianca

Classificazione dell'indice di massa corporea (BMI) secondo l'Organizzazione Mondiale della Sanità
BMI = 27.7 WHO Classification Overweight



Il BMI presenta alcuni limiti e una diagnosi effettiva di sovrappeso o di obesità deve essere effettuata da un medico. L'obesità è associata a cardiopatie, determinati tipi di cancro, diabete di tipo 2 e altri rischi per la salute. Più il BMI di un individuo è superiore a 25, tanto maggiori sono i loro rischi correlati al peso.

Risultati della composizione corporea

Regione	Grasso	Inclinato + Massa (g)	Totale Massa (g)	%Grasso	Percentile SN	% adiposo AM
Braccio Sx	2289	1615	3904	58.6	98	95
Braccio Dx	2511	1966	4477	56.1	97	90
Tronco	18638	18199	36837	50.6	96	93
Gamba Sx	5102	5472	10573	48.3	86	68
Gamba Dx	5062	5872	10935	46.3	76	52
Subtotale	33602	33124	66726	50.4	95	88
Testa	1058	3171	4229	25.0		
Totale	34660	36294	70955	48.8	95	87
Androide (A)	3562	3062	6625	53.8		
Ginoide (G)	4837	5761	10597	45.6		

Data scansione: 10 Marzo 2021 ID: A03102107

Tipologia di scansione: a Corpo Intero

Analisi: 10 Marzo 2021 12:26 Versione 13.6.0.5

Auto Whole Body

Operatore: MR

Modello: Horizon W (S/N 301644M)

Commento:

Indici adiposi

Misura	Risultato	SN	Percentuale AM
% adiposo corporeo totale	48.8	95	87
Massa grassa (kg/m²)	12.4	81	62
Rapporto androide/ginoide	1.18		
% adiposo tronco/arti	1.07	95	84
Rapporto massa adiposa tronco/arti	1.25	96	80
Est. VAT Mass (g)	1391		
Est. VAT Volume (cm³)	1503		
Est. VAT Area (cm²)	288		

Lean Indices

Misura	Risultato	SN	Percentuale AM
Lean/Height² (kg/m²)	13.4	17	16
Appen. Lean/Height² (kg/m²)	5.48	14	19

Est. VAT = Estimated Visceral Adipose Tissue

YN = Giovane normale

AM = Corrispondente per età

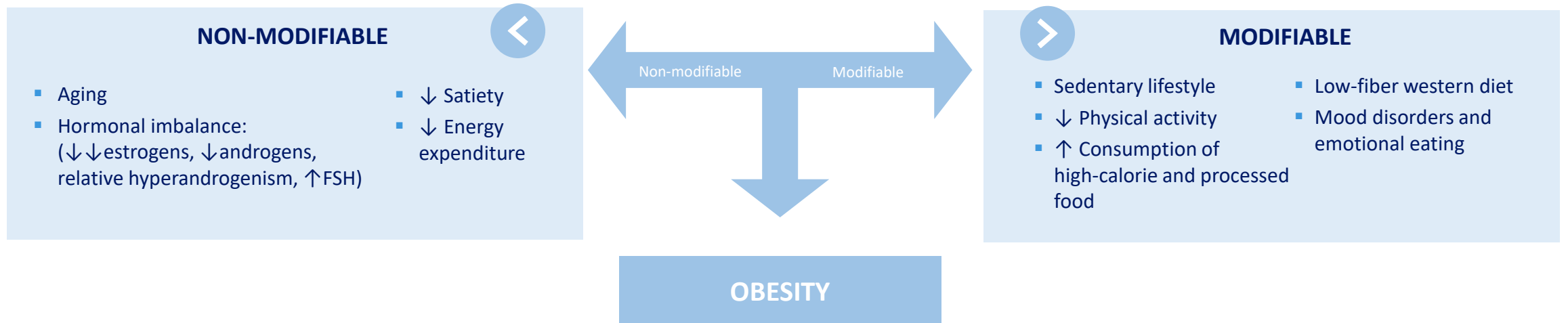
Incremento ponderale



Review

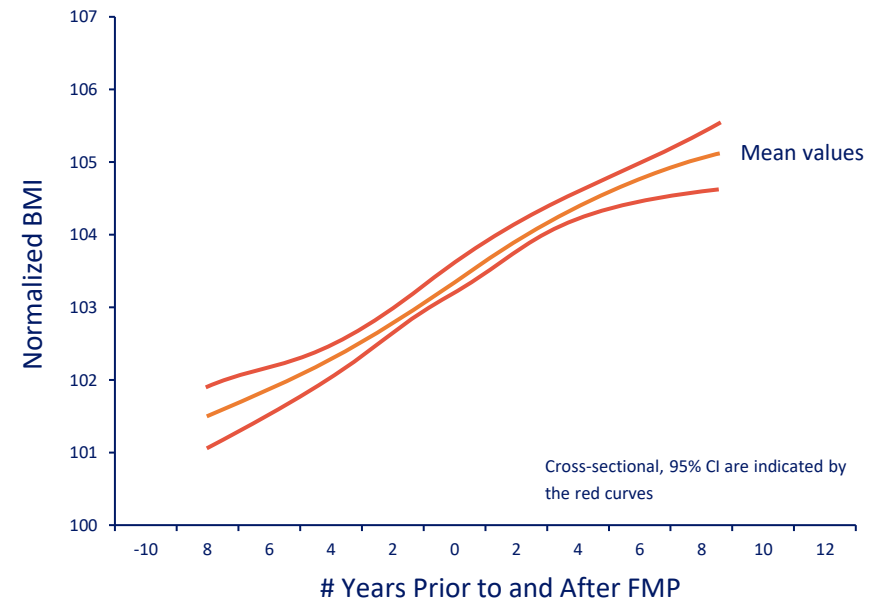
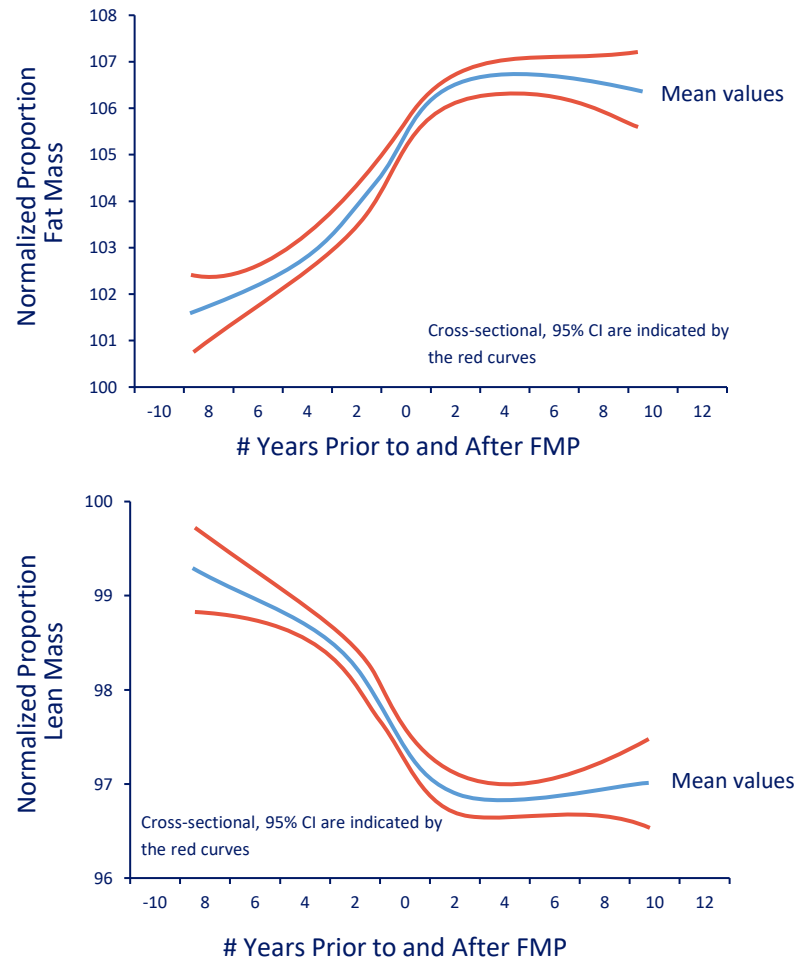
> [Climacteric](#). 2012 Oct;15(5):419-29. doi: 10.3109/13697137.2012.707385.

Understanding weight gain at menopause



Changes in body composition and weight during the menopause transition

Analysis of body composition of 1246 women with mean baseline age of 47 years.



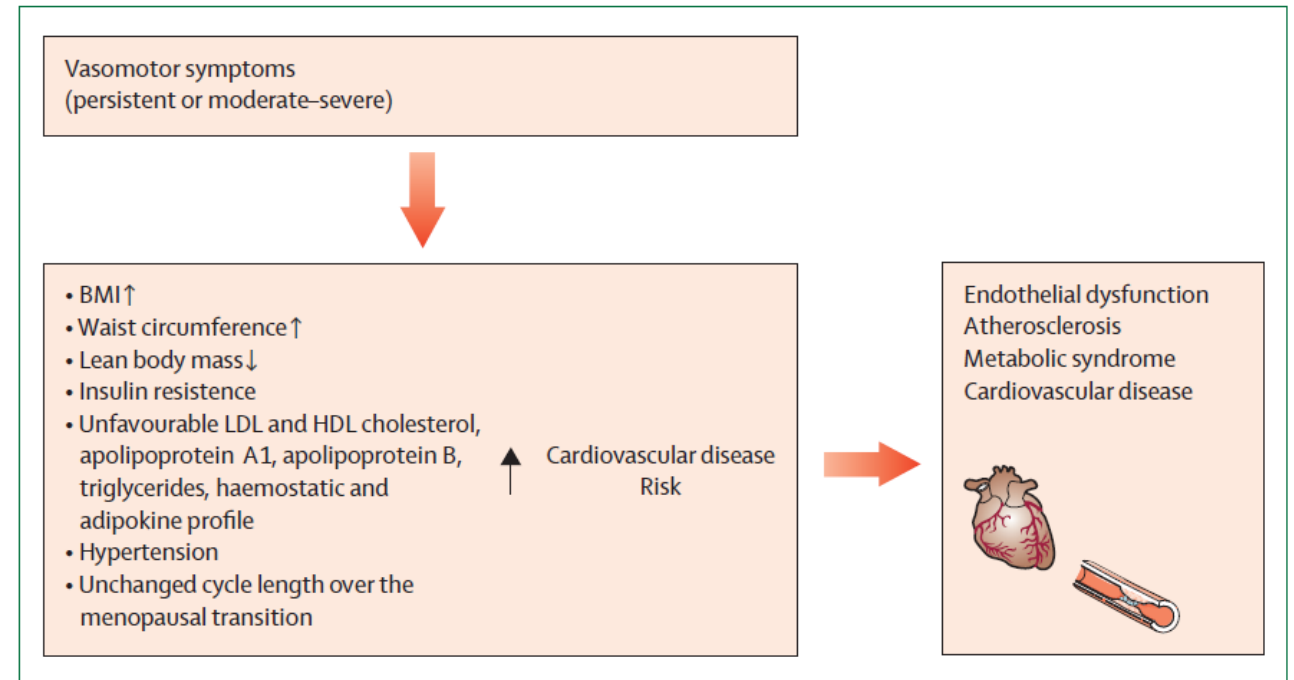
Sindrome menopausale

Journal of the American Heart Association

ORIGINAL RESEARCH

Menopausal Vasomotor Symptoms and Risk of Incident Cardiovascular Disease Events in SWAN

Rebecca C. Thurston , PhD; Helen E. Aslanidou Vlachos, MSc; Carol A. Derby, PhD; Elizabeth Maria Mori Brooks, PhD; Karen A. Matthews, PhD; Sioban Harlow, PhD; Hadine Joffe, MD, Samar R. El Khoudary, PhD, MPH



Obesità in menopausa

43%

Over 43% of menopausal women have obesity



The challenges that promote obesity in menopausal women and barriers to effective treatment are **multifactorial**

Knight MG et al., Menopause. 2021 May 24;28(8):960-965.

1.5x

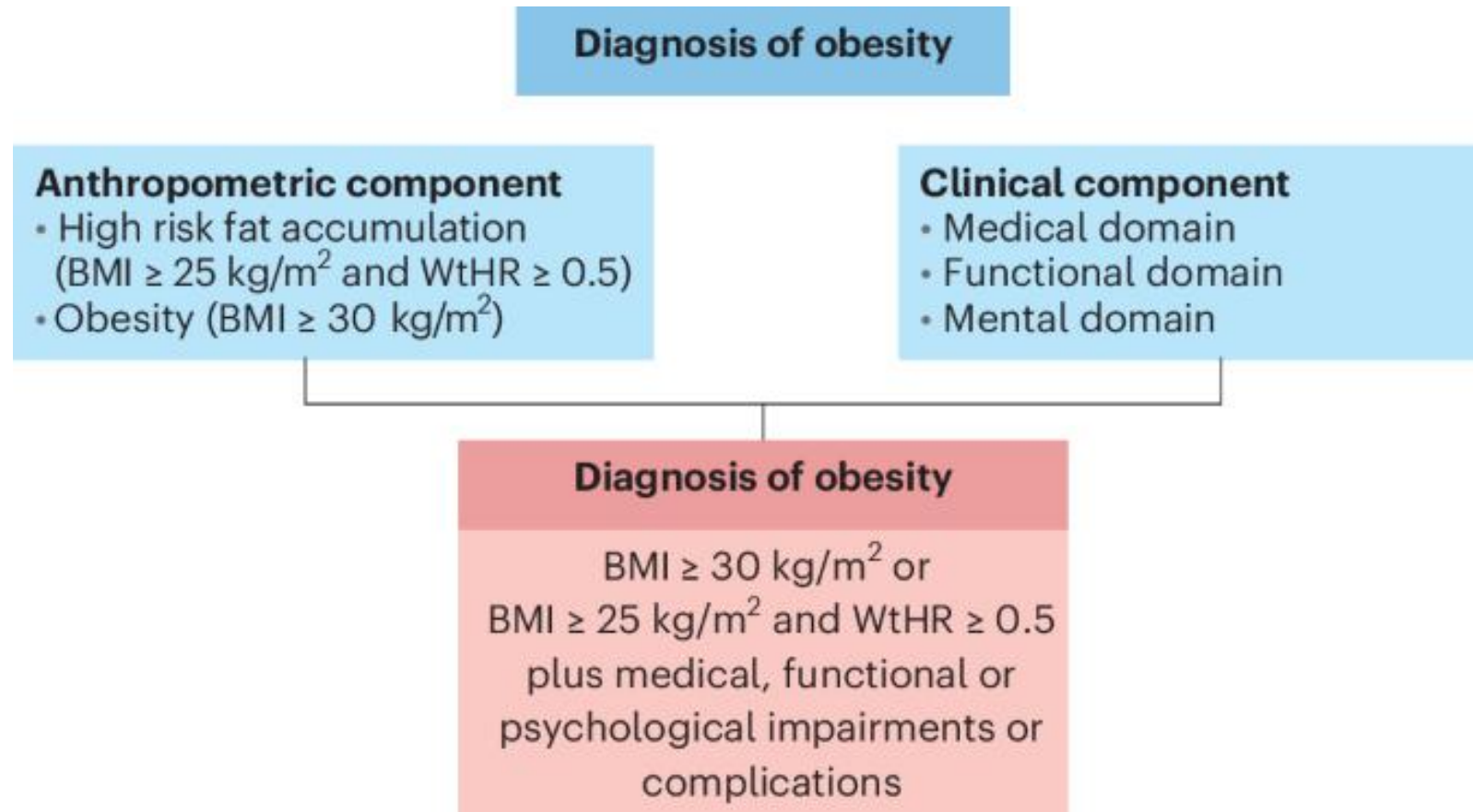
Compared with those with normal BMI (18.5–24.9 kg/m²), women with overweight or obesity were **~1.5 times more likely to experience late menopause**



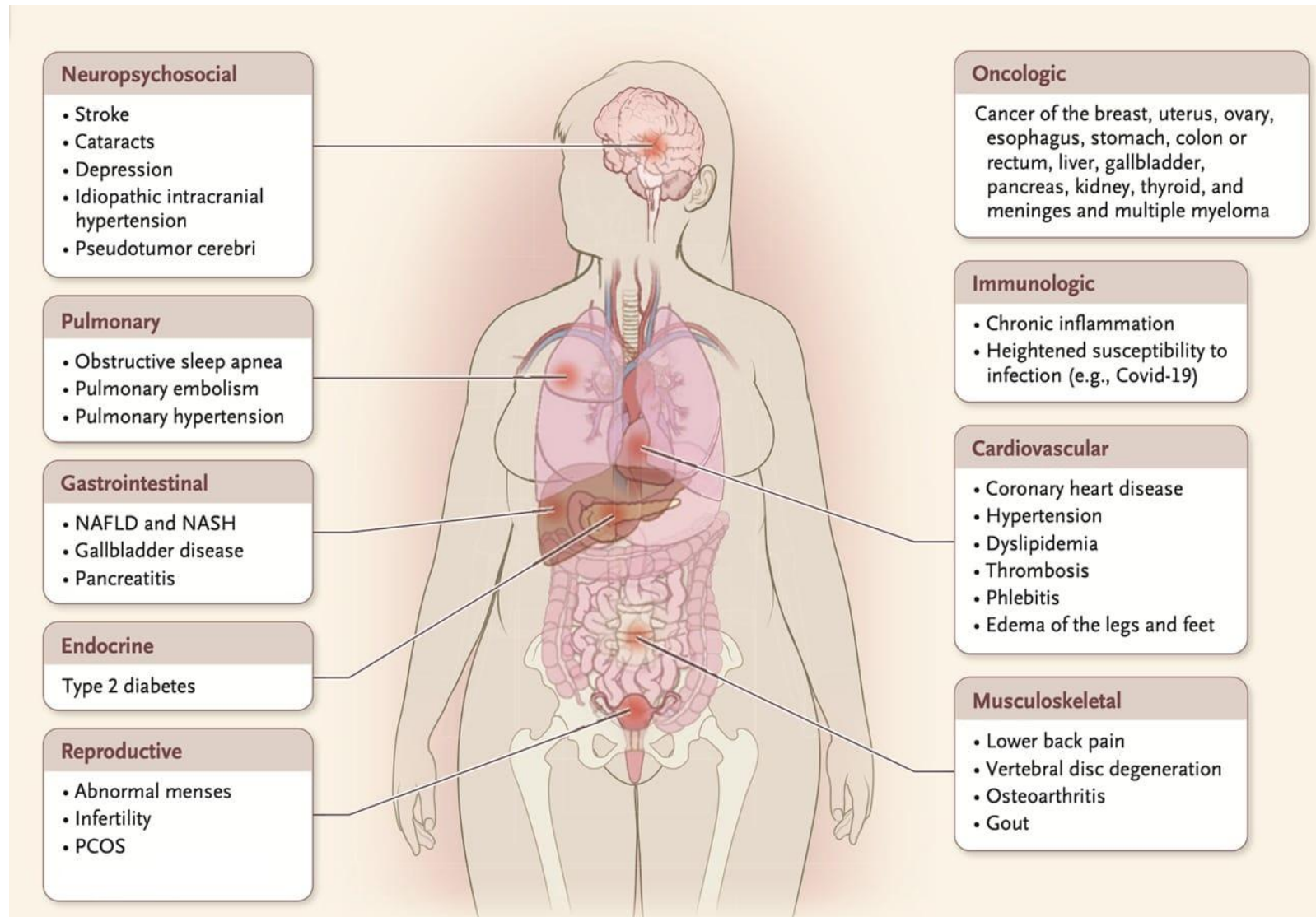
Overweight and obesity are significantly associated with **~20% increased risk** of menopause at ages 52–53 and 54–55 years

D. Zhu, et al., Eur J Epidemiol. 2018 Aug;33(8):699-710.

Nuovi criteri diagnostici di obesità

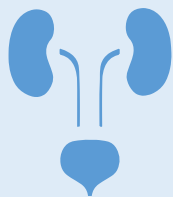


Complicanze dell'obesità



Potenziali benefici del calo ponderale

Urinary incontinence¹



Weight loss of at least 5% is recommended for improvement of urinary incontinence in postmenopausal women with obesity

Cardiovascular disease²



Weight loss in postmenopausal women with overweight and obesity lead to improvement in several cardiovascular risk factors including systolic blood pressure, diastolic blood pressure, total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides

Insulin sensitivity³



Glucose utilization and insulin sensitivity increased by 16% following weight loss in postmenopausal women with overweight and obesity

Breast cancer⁴



Postmenopausal women who lose weight have lower breast cancer risk than those with stable weight.

Vasomotor symptoms⁵



Postmenopausal women with overweight and obesity who lost weight reported greater reductions in self-reported hot-flashes

1. Kolodynska G et al., Prz Menopauzalny 2019; 2. Beavers DP et al., J Gerontol A Biol Med Sci 2013;
3. Ryan A et al., Diabetes care; 4. Chlebowski R et al., Cancer 2018; 5. Thurston R et al., Menopause 2015.

Terapia dell'obesità in menopausa

REVIEW ARTICLE

Management of obesity in menopause

Santiago Palacios^{a*}, Peter Chedraui^{b*}, Rafael Sanchez-Borrego^c, Pluvio Coronado^d, Tommaso Simoncini^e, Katrin Schauding^f, Tim Hillard^g and Rossella E. Nappi^{h,j}

Panel 2: Non-hormonal management of women transitioning to menopause in the context of cardiometabolic health

Diet

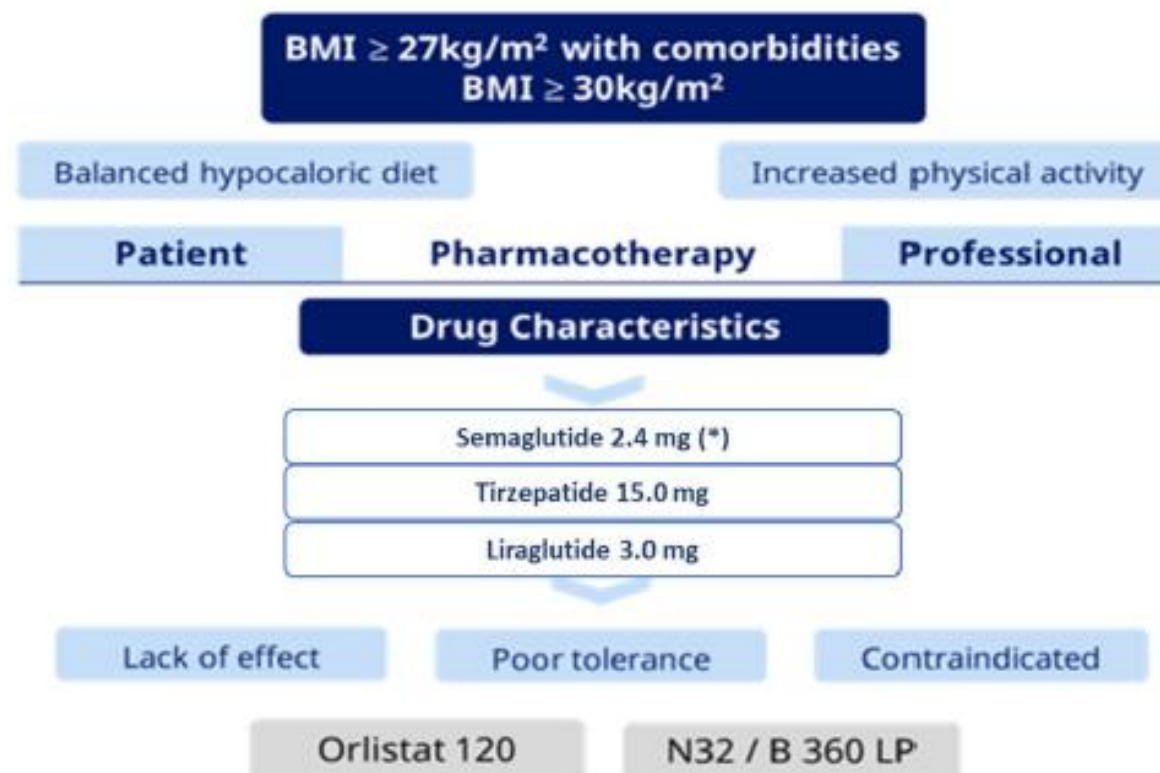
- High intake of fruit, vegetables, nuts, fish, whole grains, and olive oil
- Low consumption of red and processed meat, sweet foods and beverages, and refined grains
- Alcohol intake in moderation

Exercise

- Aerobic exercise five times a week, for at least 10–15 min
- Muscle strengthening activities at least twice a week
- Older adults should aim to be as physically active as possible
- Aim to increase the duration of moderate-intensity aerobic activity to 300 min a week, or engage in 150 min of vigorous-intensity aerobic exercise, or a combination of both

Other behaviours

- Stop smoking
- Adequate sleep
- Promotion of psychological wellbeing





Liraglutide 3 mg

Obesidad en la mujer: prevalencia, riesgos específicos y tratamiento. Experiencia con Liraglutide 3.0 en mujeres menopáusicas

Vázquez C, Luca BL, Cárdenas J, Montoya T, Silva MJ, Martin C, Hoyas I, Sierra R, Fernández Y, Meneses D

	6 meses	12 meses
Pérdida de peso, kg (SD)	6.6 (5)	8.3 (7.8)
Pérdida del 5% del peso corporal, n (%)	54 (68.4)	26 (72.2)
Pérdida del 10% del peso corporal, n (%)	22 (27.8)	15 (41.7)

	Inicial (N = 123)	6 meses (n = 79)	12 meses (n = 36)	Valor p†
Peso, kg	92 (82.3 – 102)	84.7 (12.6)	85.3 (11.6)	0.003*
IMC, kg/m ²	36.1 (5.1)	32.4 (5.2)	33.2 (4.9)	0.004*
Cintura, cm	111.3 (12.8)	103.7 (14)	104.1 (10.6)	0.109
Grasa corporal‡, %	44.9 (5.6)	41.3 (6.9)	42.5 (4.9)	0.192
TAS, mmHg	132.4 (15.4)	123.9 (13.5)	132.5 (6.4)	—
TAD, mmHg	82.2 (9.8)	78.3 (6.7)	79.8 (6.02)	—
FC, LPM	75 (14)	76.7 (12.9)	—	—
Glucosa basal, mg/dL	96.2 (10.8)	90.2 (9.2)	93.2 (11.1)	0.201
HbA1c, %	5.5 (0.3)	5.3 (0.3)	5.3 (0.3)	0.002*
Colesterol total, mg/dL	202.9 (34.1)	186.5 (38.9)	176.8 (26)	0.000*
Colesterol LDL, mg/dL	120.6 (31.6)	109.6 (33)	99.6 (30)	0.003*
Colesterol HDL, mg/dL	58.5 (18.1)	42.5 (11.9)	60 (19.7)	0.704
Triglicéridos, mg/dL	120.9 (42.6)	118.3 (39.4)	104 (43.1)	0.077

*p significativa
†Variables iniciales vs 12 meses
‡Estimada mediante bioimpedancia eléctrica



Semaglutide 1 mg

Effectiveness of Low Doses of Semaglutide on Weight Loss and Body Composition Among Women in Their Menopause

TABLE 1. BASELINE ANTHROPOMETRIC PARAMETERS IN PREMENOPAUSAL AND WOMEN IN THEIR POSTMENOPAUSAL PERIOD

	<i>Premenopausal women (N = 55)</i>	<i>Postmenopausal women (N = 45)</i>	P
Age (years)	38.4 ± 7.9	53.6 ± 5.9	<0.0001
Initial weight (kg)	86.4 ± 12.8	95 ± 23.4	0.02
Initial BMI (kg/m ²)	32.9 ± 4.7	35.9 ± 7.3	0.03
Waist circumference (cm)	99.9 ± 9.1	111.5 ± 12.6	<0.0001
Fat mass (%)	40.9 ± 7.1	43.2 ± 8.1	0.2
Fat mass (kg)	38.2 ± 9.8	45.2 ± 17.1	0.03
Lean mass (kg)	32.4 ± 8.4	29.6 ± 5.5	0.08

TABLE 2. CHANGES IN ANTHROPOMETRIC PARAMETERS IN PREMENOPAUSAL AFTER 4 MONTHS OF TREATMENT WITH SEMAGLUTIDE 1 MG

<i>Premenopausal women (N = 56)</i>	<i>Baseline</i>	<i>4 months</i>	P
Initial weight (kg)	86.1 ± 17.1	75.8 ± 13.7	<0.0001
Initial BMI (kg/m ²)	32.4 ± 5	28.5 ± 3.9	<0.0001
Waist circumference (cm)	101.9 ± 10.1	94.3 ± 9.2	<0.0001
Hip perimeter (cm)	112.6 ± 9.3	107.8 ± 8.7	<0.0001
Fat mass (%)	41.2 ± 5.6	37.3 ± 5.5	<0.0001
Fat mass (kg)	35.7 ± 11.8	28.4 ± 9.5	<0.0001
Lean mass (kg)	46.6 ± 5.1	44.9 ± 4.6	<0.0001

TABLE 3. CHANGES IN ANTHROPOMETRIC PARAMETERS IN POSTMENOPAUSAL AFTER 4 MONTHS OF TREATMENT WITH SEMAGLUTIDE 1 MG

<i>Postmenopausal women (N = 44)</i>	<i>Baseline</i>	<i>4 months</i>	P
Initial weight (kg)	88.7 ± 19.4	78.8 ± 17.2	<0.0001
Initial BMI (kg/m ²)	34.1 ± 6.6	30.5 ± 6.1	<0.0001
Waist circumference (cm)	110.2 ± 12.7	102.4 ± 11.4	<0.0001
Hip perimeter (cm)	111.3 ± 11.4	106.9 ± 10.4	<0.0001
Fat mass (%)	43.8 ± 5.4	40.8 ± 5.1	<0.0001
Fat mass (kg)	39.1 ± 12.7	32.3 ± 10.9	<0.0001
Lean mass (kg)	45.9 ± 6.4	44.2 ± 6.2	<0.0001



Semaglutide 1 mg

1 mg weekly semaglutide as adjunctive therapy to lifestyle interventions among women in their menopause period is as effective as in premenopausal women in reducing body weight and fat mass, without losing significant lean mass.

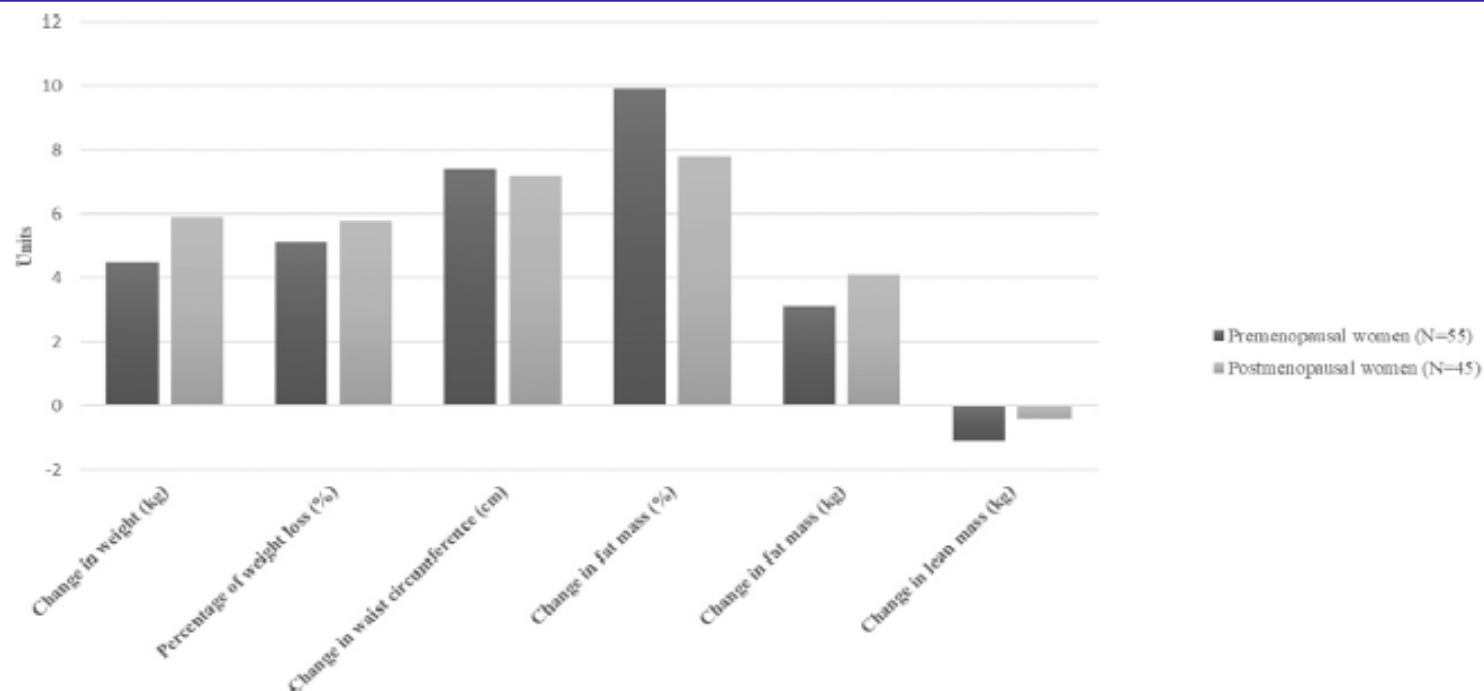
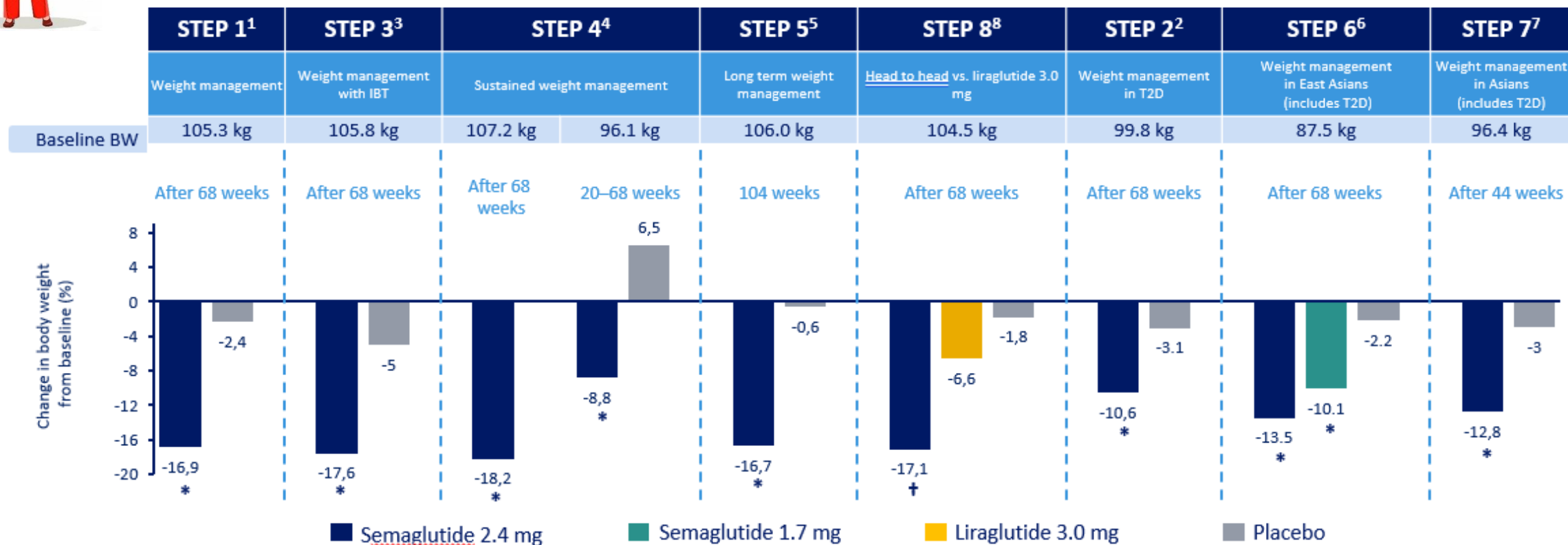


FIG. 1. Changes in anthropometric parameters between pre- and postmenopausal women after 4 months of treatment with semaglutide 1 mg: *No significant differences were seen between pre- and postmenopausal women.



Semaglutide 2.4 mg

There are no specific studies in the menopausal population



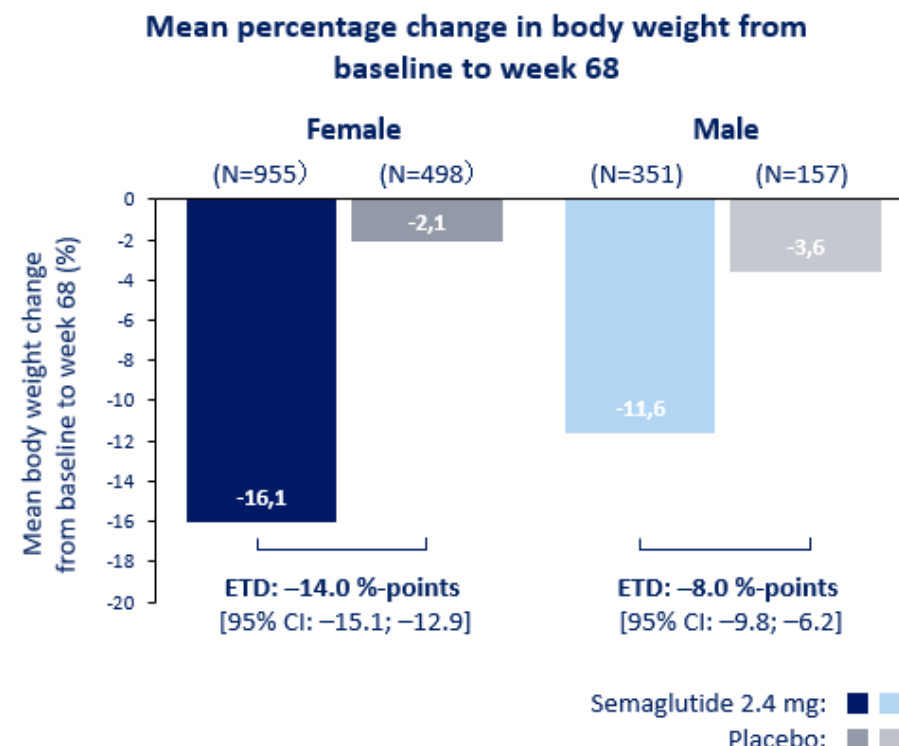
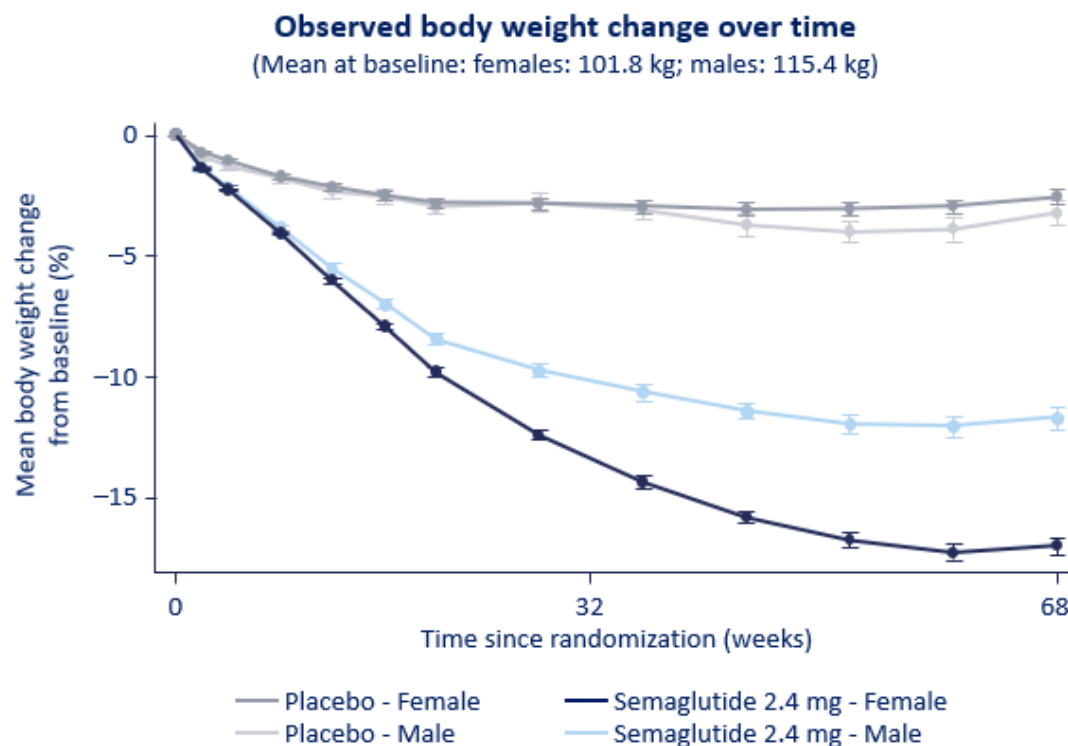
1. Wilding et al. N Engl J Med 2021;
2. Davies et al. Lancet, 2021;
3. Wadden et al. JAMA;
4. Rubino et al. JAMA.2021;
5. Garvey et al. Nat Med 28, 2083–2091 (2022);
6. Kadowaki et al. The Lancet Diabetes & Endocrinology 2022;
7. Mu, Y., et al. The Lancet Diabetes & Endocrinology, 2024;
8. Rubino et al. JAMA 2022.



Semaglutide 2.4 mg

STEP 1

Body weight changes by sex



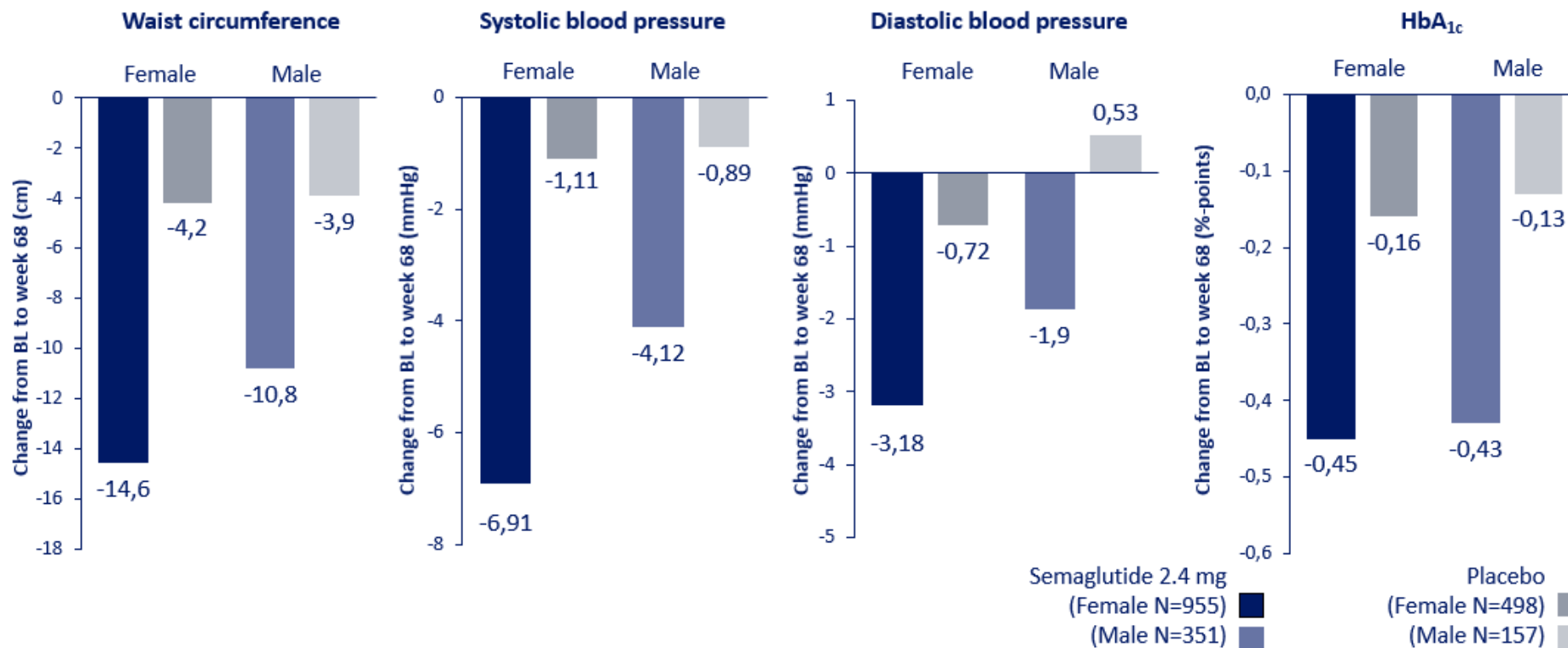
Body weight reductions from baseline to week 68 appeared greater in semaglutide-treated females than males.



Semaglutide 2.4 mg

STEP 1 Changes in CV risk parameters by sex

From baseline to week 68



Reduction in waist circumference, in blood pressure and in HbA_{1c} from baseline to week 68 appeared greater in semaglutide-treated females than males.

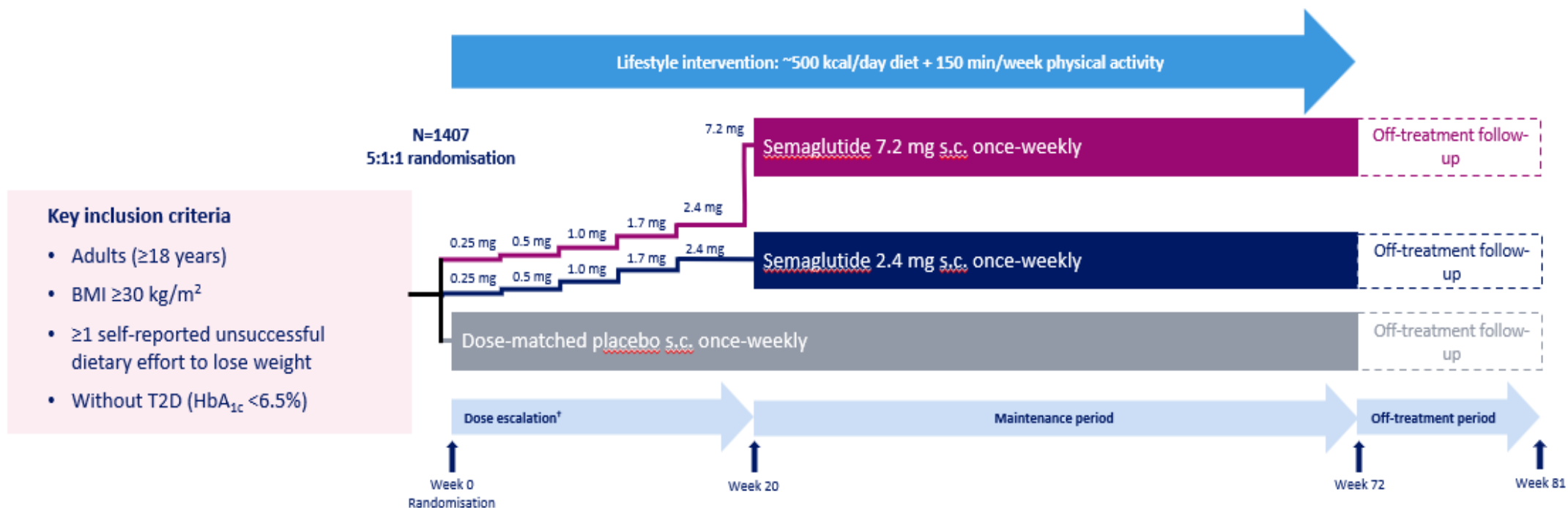


Semaglutide 7.2 mg

There are no specific studies in the menopausal population

STEP UP trial design

Randomised, double-blind, multinational, placebo- and active-controlled trial

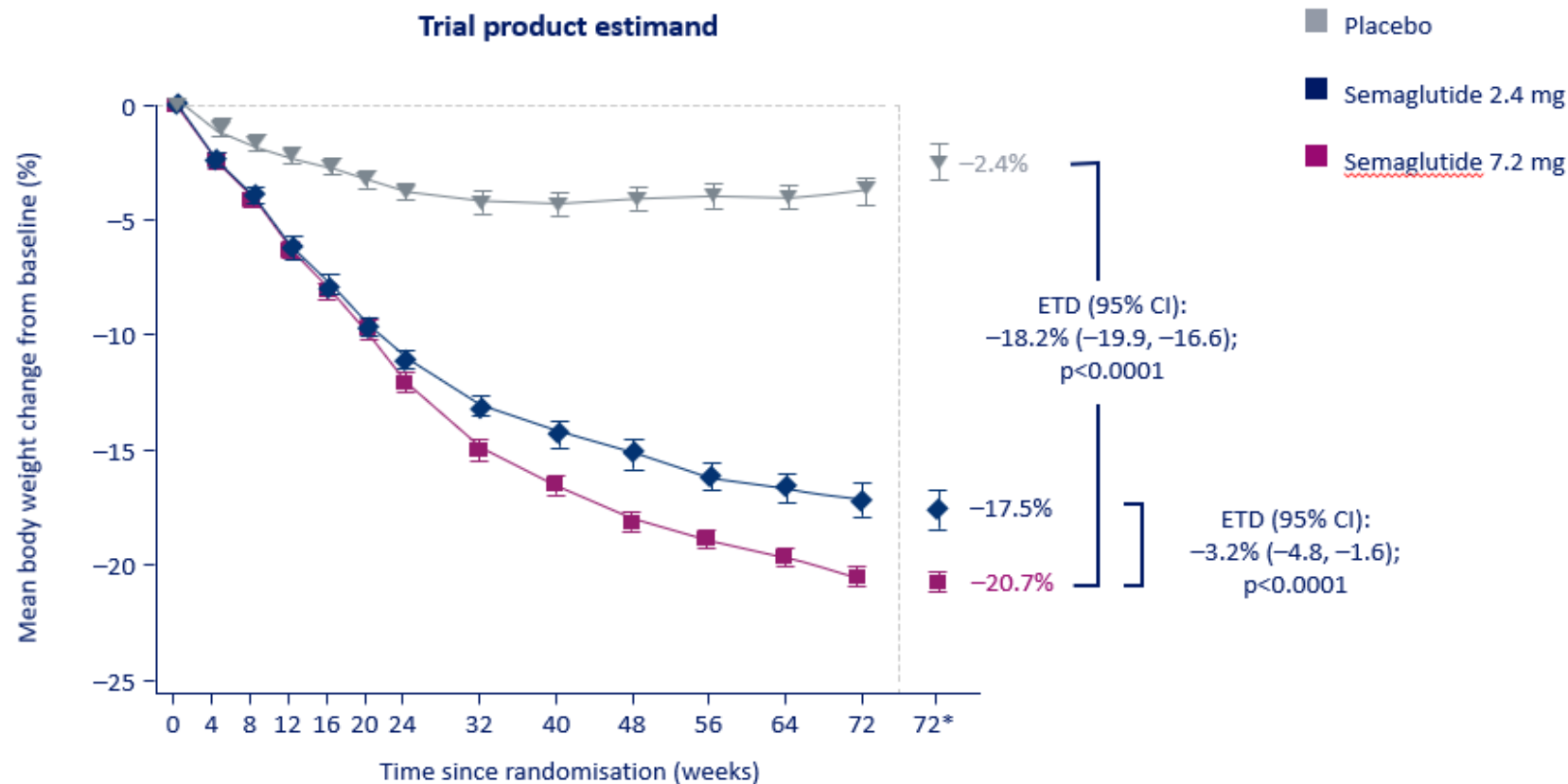




Semaglutide 7.2 mg

STEP UP

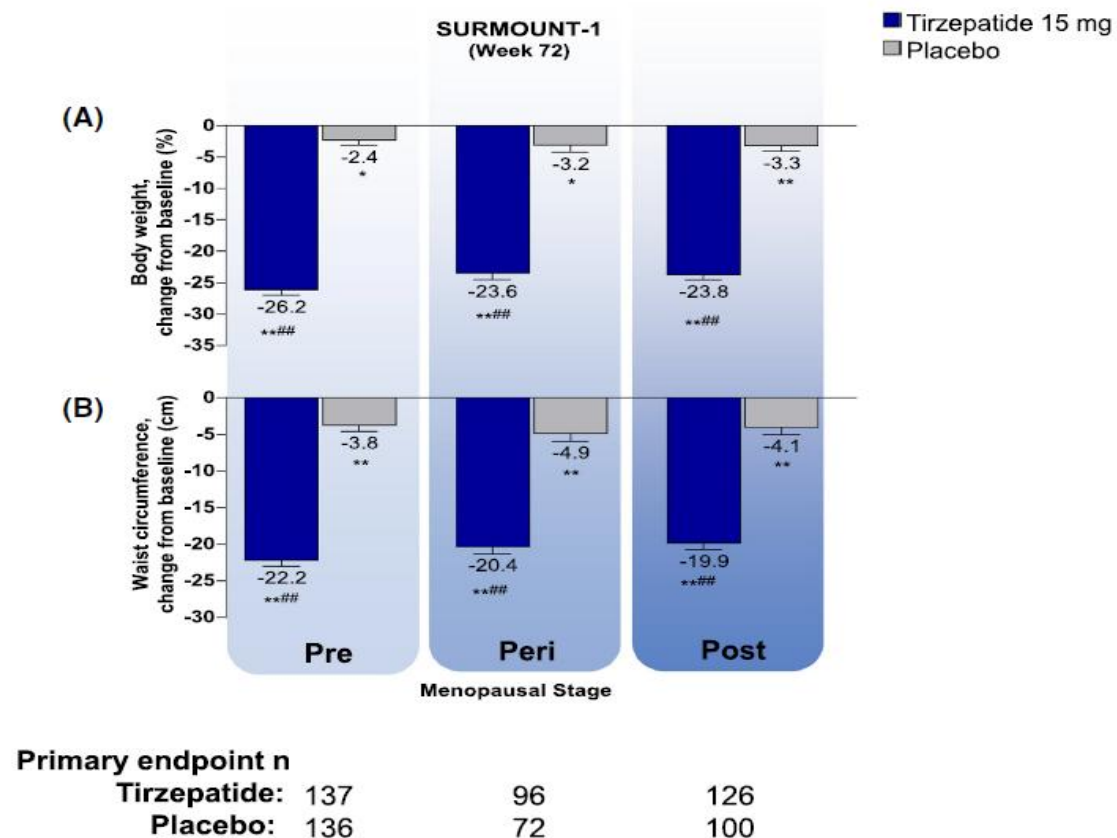
Change in body weight (%)



Semaglutide 7.2 mg was superior to placebo and 2.4 mg for body weight reduction in adults with obesity, while retaining a favourable risk–benefit profile.



Tirzepatide 15 mg



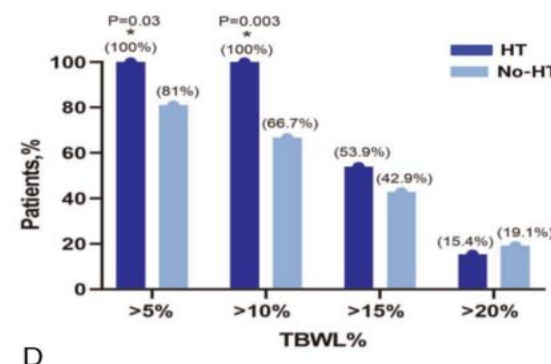
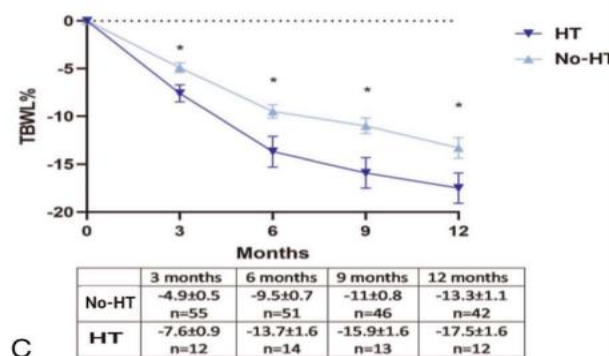
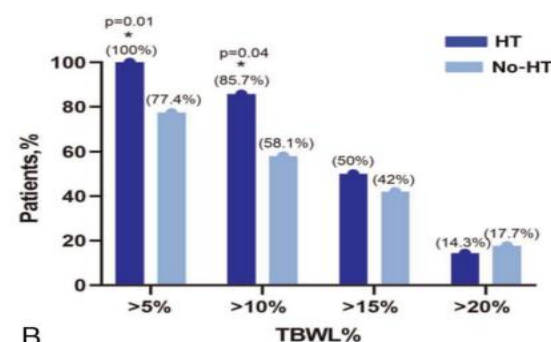
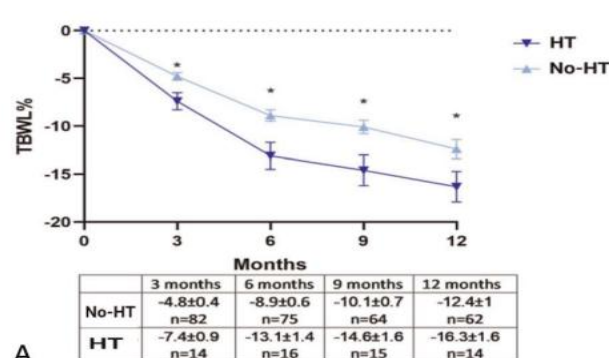
In this post hoc analysis, tirzepatide treatment was associated with significant body weight, waist circumference, and WHtR reductions versus placebo in women living with obesity or overweight and without type 2 diabetes, irrespective of reproductive stage.



Semaglutide + HRT



Weight Loss Response to Semaglutide in Post-menopausal Women with and without Hormone Therapy Use



In this study, HT use in post-menopausal women was associated with a greater weight loss with semaglutide. Larger studies are needed to confirm these results.



Sarcopenia



Obesity and sarcopenia after menopause are reversed by sex hormone replacement therapy

Table 2. Changes in body composition and oestradiol during HRT and placebo

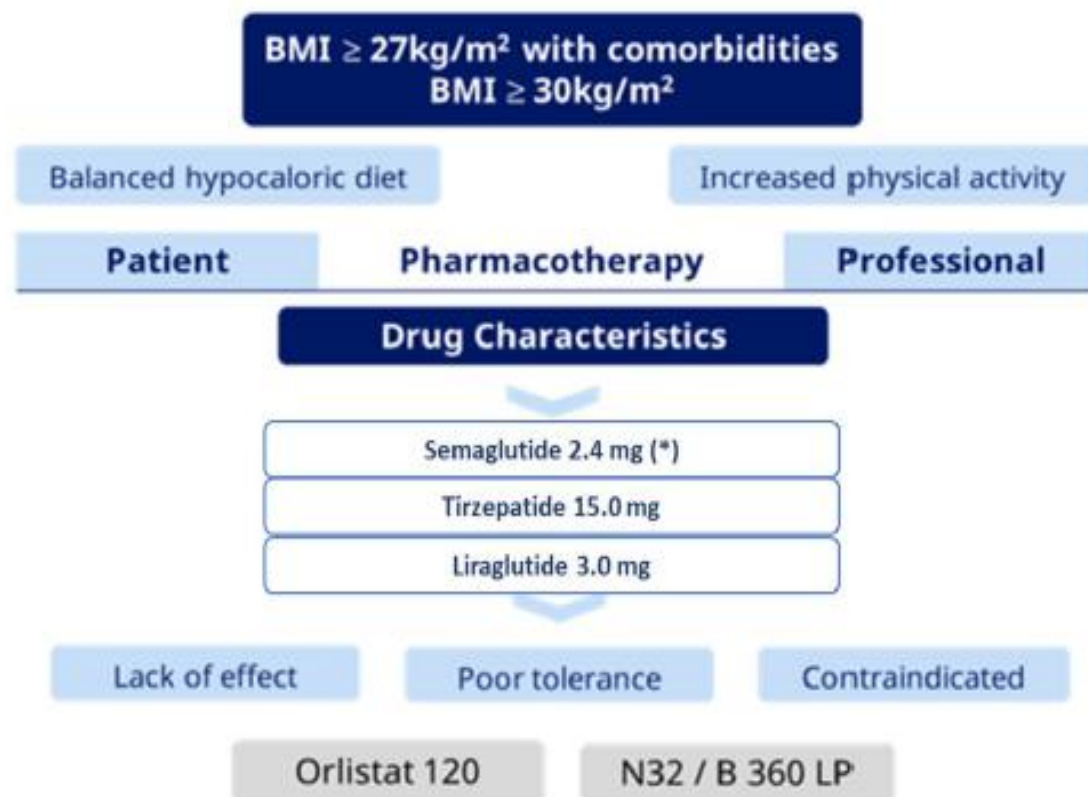
	Change during placebo	Change during HRT
Weight (kg)	-0.164 ± 1.40	-0.025 ± 2.14
Lean body mass (kg)	$-0.996 \pm 1.58^*$	$+0.347 \pm 0.858^\dagger$
Total BMC (g)	-4.38 ± 58.7	$+28.9 \pm 30.1^\dagger$
Total BMD (mg/cm)	-3.88 ± 20.4	$+8.63 \pm 29.0$
Abdominal fat mass (kg)	$+0.253 \pm 0.641$	$-0.185 \pm 0.594^\dagger$
Total fat mass (kg)	$+0.836 \pm 1.34^*$	-0.401 ± 1.98
Percentage of fat mass (%)	$+1.24 \pm 1.66^*$	$-0.50 \pm 1.63^\dagger$
Estradiol (pmol/liter)	$+40.4 \pm 153$	$+673 \pm 407^\dagger$

HRT is linked to the reversal of both menopause-related obesity and loss of lean mass, without overall change in body weight.





Terapia dell'obesità in menopausa



Pharmacologic options for the treatment of overweight and obesity

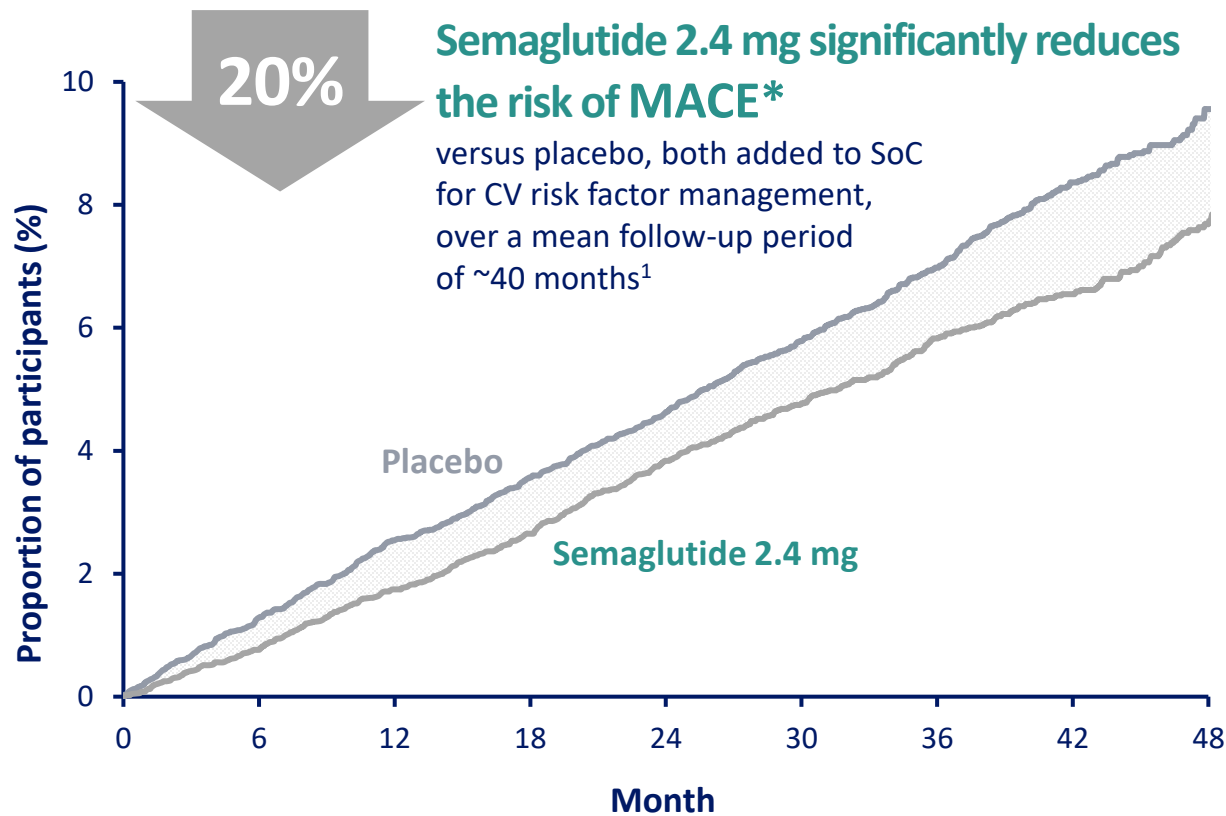
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Remarkably, semaglutide is the first and only antiobesity medication approved for CVD risk reduction based on its cardiovascular outcomes data showing that, in persons with obesity and preestablished cardiovascular disease, it reduces cardiovascular events by 20%.⁹ As such, although tirzepatide may be associated with better weight loss outcomes, women with preestablished CVD may benefit from semaglutide for now.



Semaglutide 2.4 mg

SELECT



only 27.7% were women

In patients with preexisting cardiovascular disease and overweight or obesity but without DM, semaglutide 2.4 mg/week was superior to placebo in reducing the incidence of MACE at a mean follow-up of 39.8 months.



Take Home Messages

La menopausa rappresenta una fase di transizione cardiometabolica per la donna.

Il calo estrogenico provoca variazioni metaboliche con conseguente incremento del rischio cardiovascolare, specialmente in presenza di una sindrome menopausale.

L'obesità, in particolare in menopausa, è una patologia da individuare e da trattare.

Le evidenze, seppur scarse, dimostrano che i GLP1RA, in prima linea Semaglutide 2.4 mg/sett, sono efficaci nel determinare un calo ponderale e nel ridurre il rischio cardiovascolare anche nella donna in menopausa.

La HRT non va intesa come terapia per l'obesità, ma, se abbinata al GLP1RA, può contribuire al calo ponderale e alla preservazione della massa muscolare.



Determinare un calo ponderale significa ridurre l'incidenza delle comorbidità legate all'obesità, tra cui il rischio di cancro.



Grazie per l'attenzione

