MANEJO DEL RIESGO METABOLICO EN LA TRANSICION A LA MENOPAUSIA

Gladys Isabel Fernández

ARKHËN

Paciente de 51 años. No fuma. Odontóloga.

MC: Alteraciones del ciclo y leves sofocos de 10 meses de evolución

AC: Hipotiroidismo en tratamiento con 100 µg T4 desde los 48 años

AQ: Peritonitis apendicular a los 25 años

ATG: Menarca: 12a RM: 4/40 0+ (hasta primer hijo, luego 4/28) MAC: condón (uso correcto)

G:2 1 PN (19 años) con inducción de ovulación, RN femenino, 3890 g. Lactancia 4 meses

1 HMR a los 24 años, con legrado evacuador

Refiere que hace 10 meses inició alteraciones del ciclo, con atrasos de hasta 40 días asociados a leves sofocos.

Madre y hermana con DM2, no refiere antecedentes de tiroideopatía ni de cánceres gineco-mamarios.

Siempre tuvo sobrepeso pero en los últimos cinco años aumentó 8 kilos .

Al examen clínico tiroides palpable s/p. FC 80 lpm, TA 150/90 mmHg. Severa AN en nuca (grado 4).

Peso 85 Kg. Talla 1.67 BMI 31.4

Cintura 110 cadera 118 cociente c/c 0.93

Trae estudios recientes:

- **Mamografía y ecografía mamaria normales**
- **Hemograma normal**
- **Hepatograma patológico con leve elevación de ambas transaminasas y de γ-GT**

- col t 248
- LDLc 194
- HDLc 35
- TG 280
- SHBG 23
- glucemia 82 mg%
- insulina 34 mUI/ml
- HOMA 6.88

Maintaining postreproductive health: A care pathway from the European Menopause and Andropause Society (EMAS)

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Maturitas 2016;89:63-72

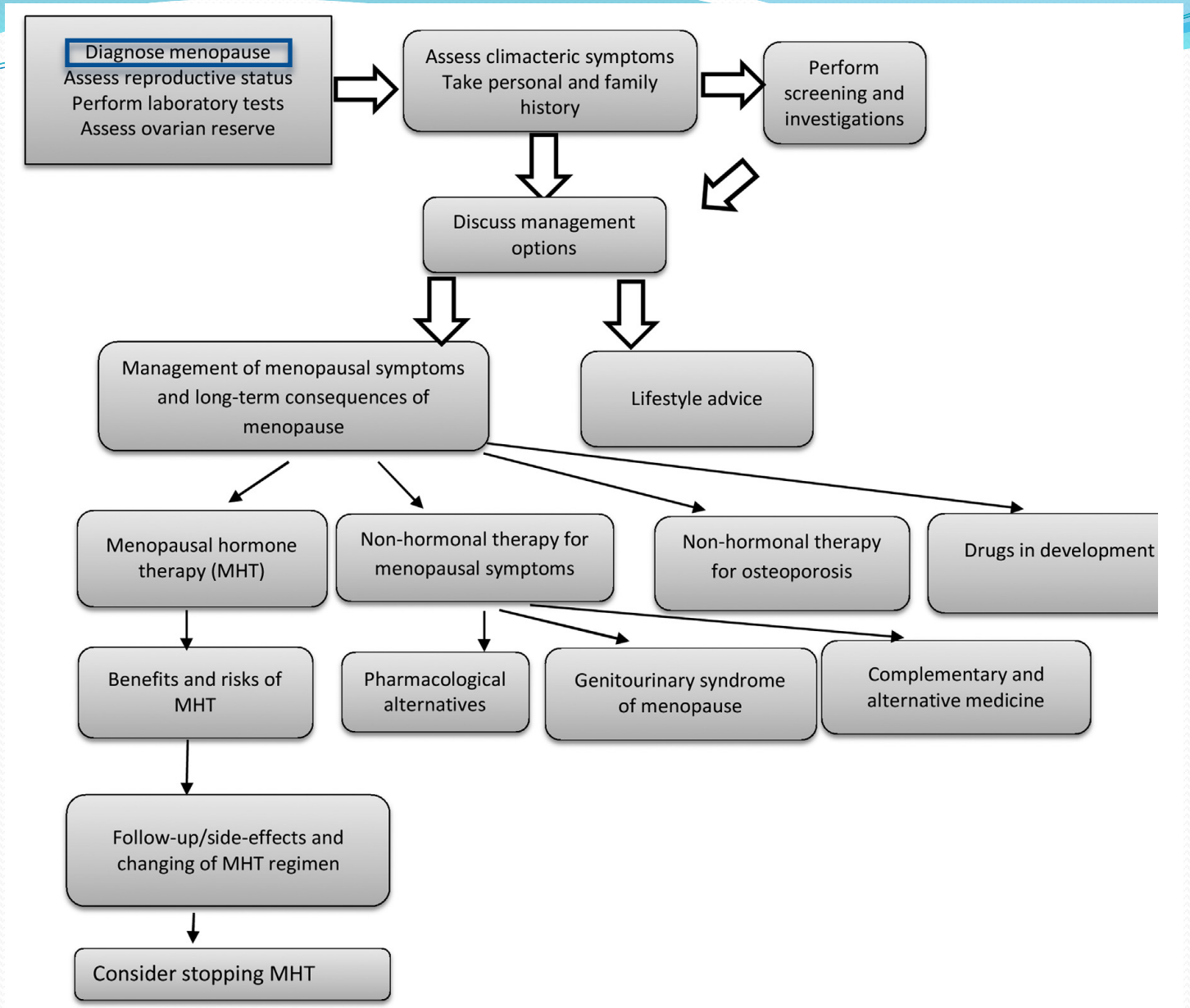


Fig. 1. A care pathway for the maintenance of women's postreproductive health.

Ante esta paciente nos preguntamos:

1-¿En que estadío del aging reproductivo se encuentra?

2-¿Cuál es el diagnóstico de la paciente desde el punto de vista metabólico?

3-¿Cuál cree que es la mejor aproximación terapéutica en esta paciente?

Menarche

FMP (0)

Stage	-5	-4	-3b	-3a	-2	-1	+1 a	+1b	+1c	+2
Terminology	REPRODUCTIVE				MENOPAUSAL TRANSITION		POSTMENOPAUSE			
	Early	Peak	Late		Early	Late	Early			Late
					Perimenopause					
Duration	*variable*				*variable*	1-3 years	2 years (1+1)		3-6 years	*Remaining lifespan*
PRINCIPAL CRITERIA										
Menstrual Cycle	Variable to regular	Regular	Regular	Subtle changes in Flow/ Length	*Variable Length* Persistent ≥7- day difference in length of consecutive cycles	Interval of amenorrhea of >=60 days				
SUPPORTIVE CRITERIA										
Endocrine FSH AMH Inhibin B			Low Low	Variable* Low Low	↑ Variable* Low Low	↑ >25 IU/L** Low Low	↑ Variable Low Low		Stabilizes Very Low Very Low	
Antral Follicle Count			Low	Low	Low	**Low**	Very Low		Very Low	
DESCRIPTIVE CHARACTERISTICS										
Symptoms						Vasomotor symptoms *Likely*	Vasomotor symptoms *Most Likely*			*Increasing* symptoms of urogenital atrophy

* Blood draw on cycle days 2-5 ↑ = elevated

**Approximate expected level based on assays using current international pituitary standard[67-69]

J Clin Endocrinol Metab 2012;97(4):1159-1168

2. Diagnose menopause

- **Early menopause** describes menopause in women aged 40–45 years.
- **Premature menopause** denotes definitive loss of ovarian function (e.g. through bilateral oophorectomy) before the age of 40.
- **Premature ovarian insufficiency (POI)** describes transient or permanent loss of ovarian function in women before the age of 40. A substantial proportion of these women have spontaneous resumption of ovulation, menstruation and successful spontaneous pregnancy.
- **Menopause transition** is the time when there are changes to the menstrual cycle and endocrine levels. According to STRAW + 10 the transition begins with variation in the length of the menstrual cycle and ends with the final menstrual period [10].

Maturitas 2016;89:63-72

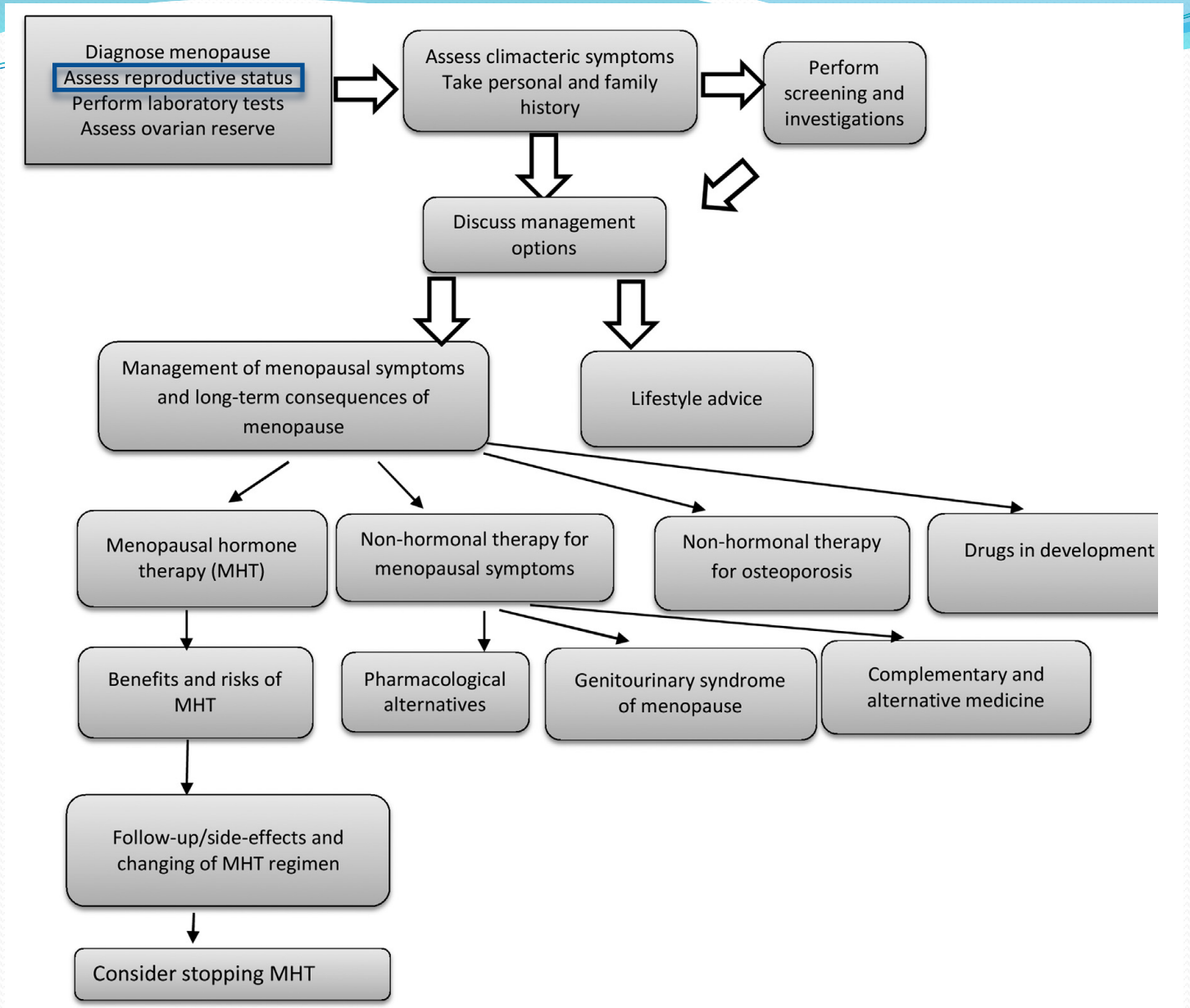


Fig. 1. A care pathway for the maintenance of women's postreproductive health.

3. Investigations and assessment of ovarian reserve

3.1. Endocrine investigations

3.1.1. Follicle stimulating hormone (FSH)

There is no need to measure FSH levels to diagnose menopause in otherwise healthy women (who are not using hormonal contraception) over the age of 45 who have not had a period for at least 12 months or in perimenopausal women with vasomotor symptoms and irregular periods. Nor should FSH levels be used to diagnose menopause in hysterectomised women with menopausal symptoms. However, FSH and E2 measurements should be undertaken in younger women and considered in those with polycystic ovary syndrome (PCOS), endometrial ablation or in women needing a differential diagnosis of amenorrhoea [5].

3.1.2. Thyroid function tests

Symptoms of thyroid dysfunction can often mimic those of menopause. Thyroid function should therefore be checked when the relevant signs and symptoms are present or when there is a lack of response to menopausal hormone therapy.

3.1.3. Exclusion of other causes of amenorrhoea

Pregnancy and hyperprolactinaemia need to be excluded, especially in women under the age of 45

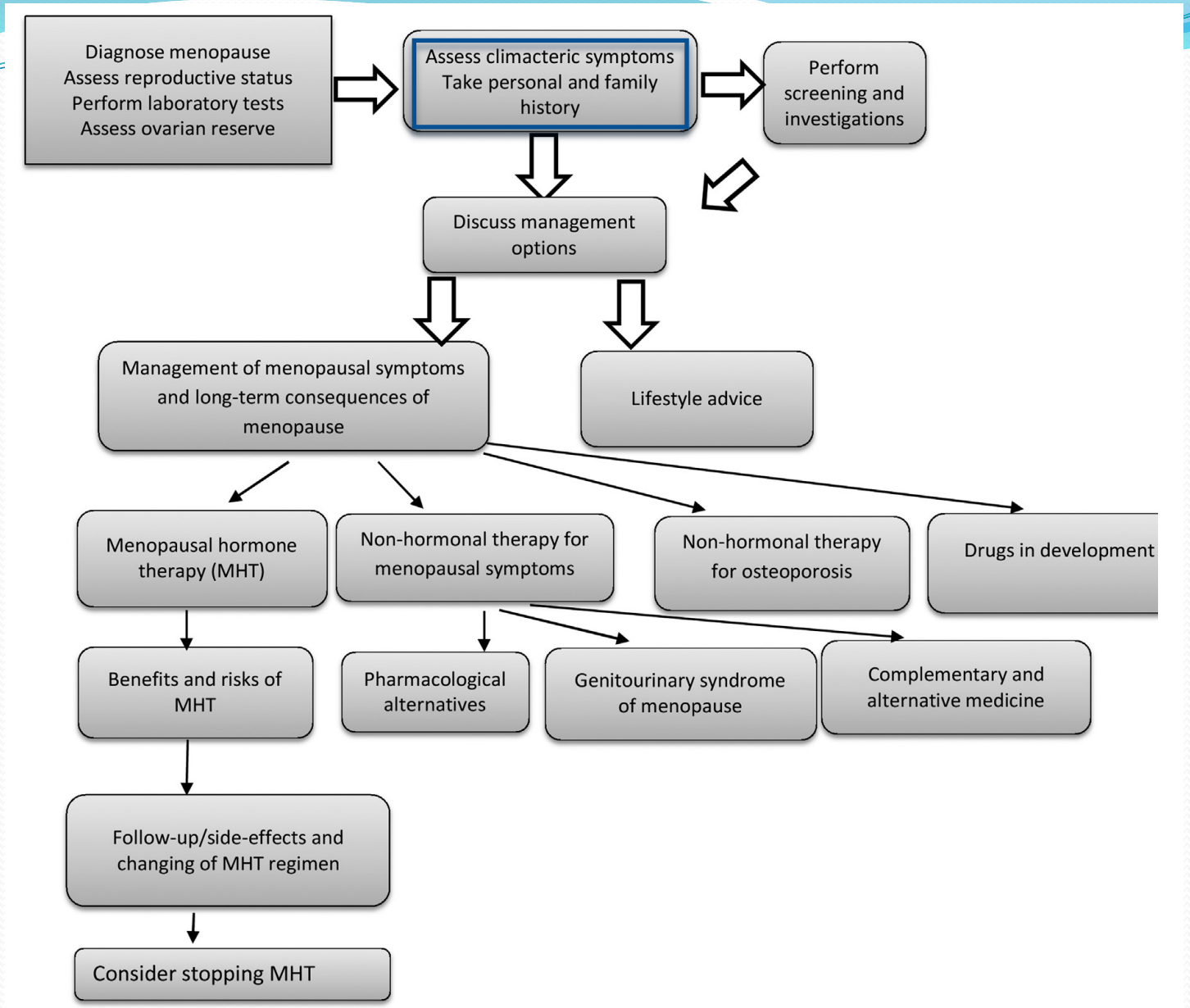


Fig. 1. A care pathway for the maintenance of women's postreproductive health.

4. Assessment of climacteric symptoms, personal and family history

4.1. Climacteric symptoms

4.2. Personal history

4.3. Family history

Maturitas 2016;89:63-72

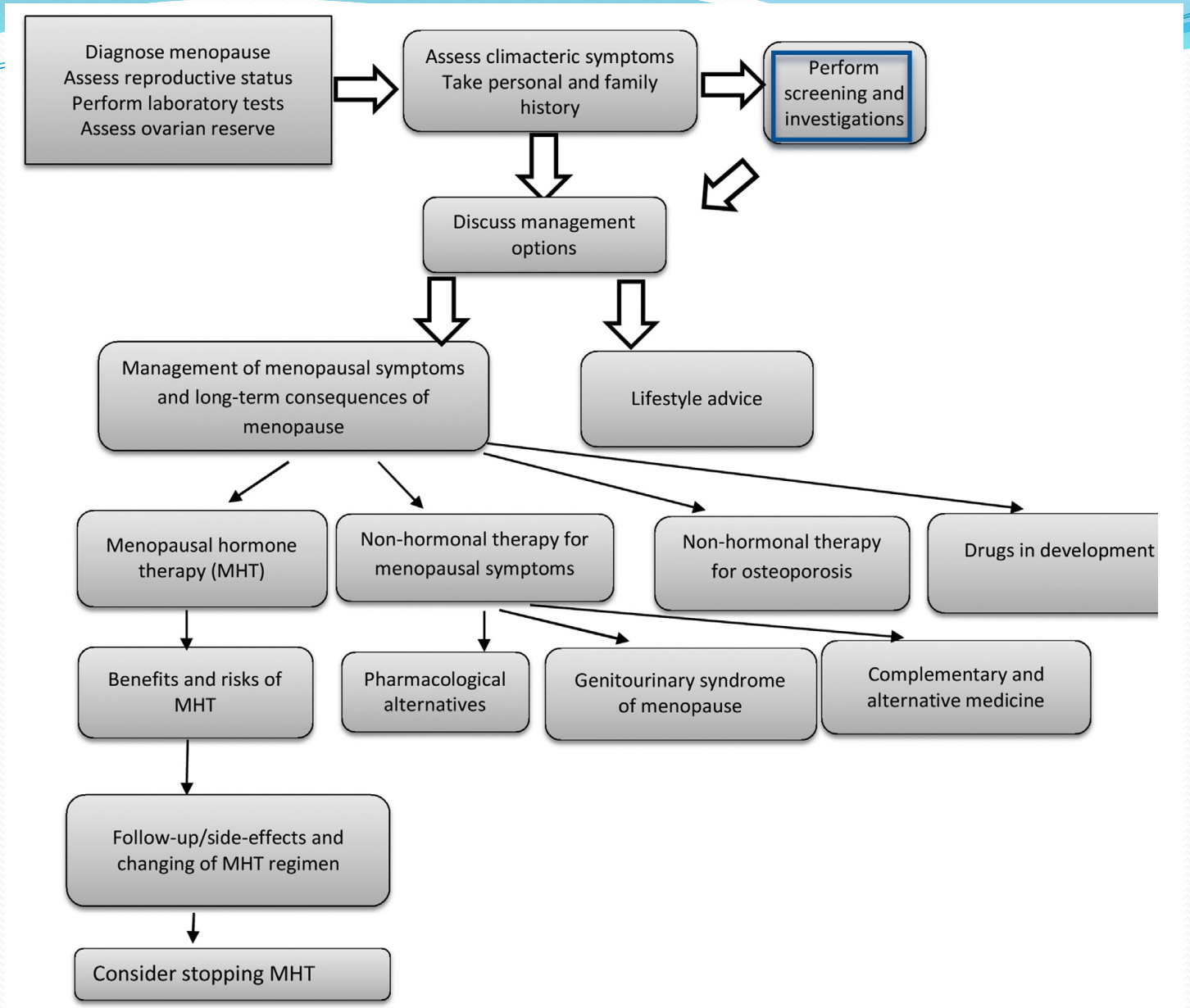


Fig. 1. A care pathway for the maintenance of women's postreproductive health.

Treatment of Symptoms of the Menopause: An Endocrine Society Clinical Practice Guideline

Cynthia A. Stuenkel, Susan R. Davis, Anne Gompel, Mary Ann Lumsden, M. Hassan Murad, JoAnn V. Pinkerton, and Richard J. Santen

2.0 Health considerations for all menopausal women

2.1 When women present during the menopausal transition, we suggest using this opportunity to address bone health, smoking cessation, alcohol use, cardiovascular risk assessment and management, and cancer screening and prevention. (Ungraded best practice statement)

J Clin Endocrinol Metab 2015;100(11):3975-4011

5. Screening and investigations

5.1. Cardiovascular assessment

Evaluation of anthropometric indices, measurement of blood pressure and estimation of cardiovascular risk should be performed in accordance with national and international guidelines.

5.1.1. Anthropometric indices

Records of weight, height, waist and hip circumference should be kept for reference and comparison with follow-up data. Body mass index (BMI) and waist-to-hip ratio (WHR) should be calculated according to standard formulae: BMI = body weight (kg)/height^2 (m^2) and WHR = waist circumference (cm)/hip circumference (cm) [20,21].

TABLE 1

Categories of obesity by body mass index.[a]

Category	BMI (kg/m^2)
Underweight	Less than 18.5
Normal	18.5 to 24.9
Overweight	25.0 to 29.9
Obesity, Grade I	30.0 to 34.9
Obesity, Grade II	35.0 to 39.9
Obesity, Grade III	≥40.0

Note: BMI = body mass index.
[a] WHO 2004.

Practice Committee. Obesity and reproduction. Fertil Steril 2015.

Fertil Steril 2015;104(5):1116-1126

Instructions for Measuring Waist Circumference, According to NHANES III Protocol

To define the level at which waist circumference is measured, a bony landmark is first located and marked. The subject stands and the examiner, positioned at the right of the subject, palpates the upper hip bone to locate the right iliac crest. Just above the uppermost lateral border of the right iliac crest, a horizontal mark is drawn, then crossed with a vertical mark on the midaxillary line. The measuring tape is placed in a horizontal plane around the abdomen at the level of this marked point on the right side of the trunk. The plane of the tape is parallel to the floor and the tape is snug, but does not compress the skin.

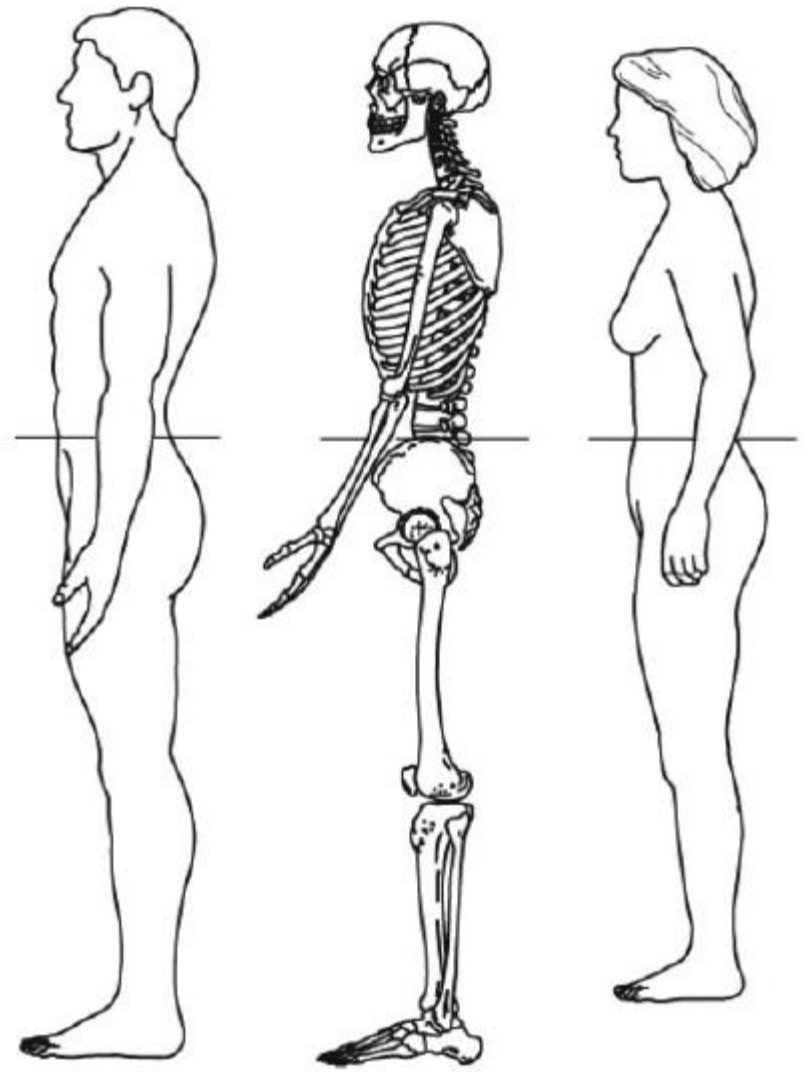
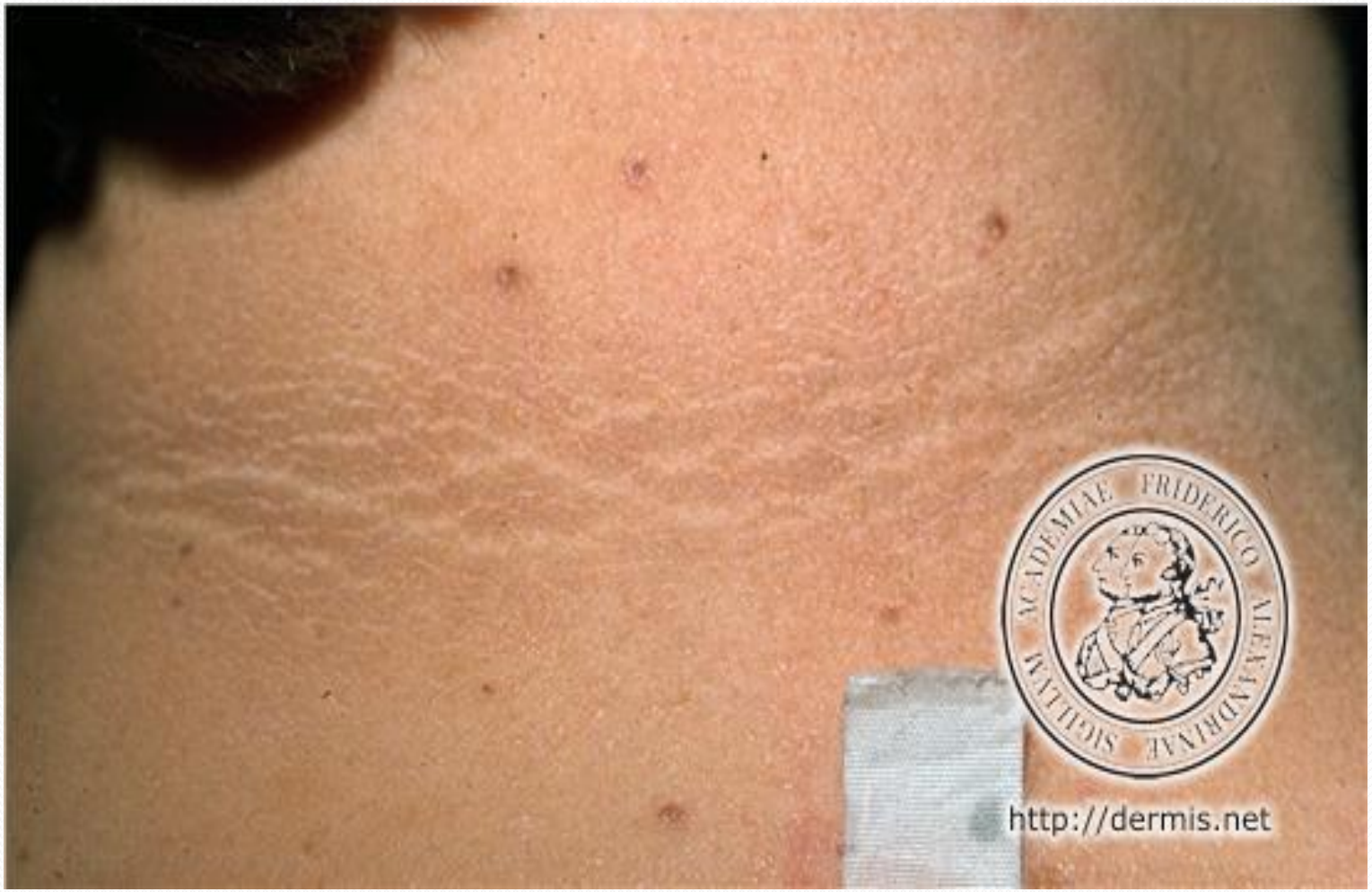


FIG. 1. Measuring waist circumference according to the National Health Information Survey III protocol.
http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=obesity.figgrp.237.

J Clin Endocrinol Metab 2008;93(9):3671-3689

ACANTOSIS NIGRICANS



ACANTOSIS NIGRICANS

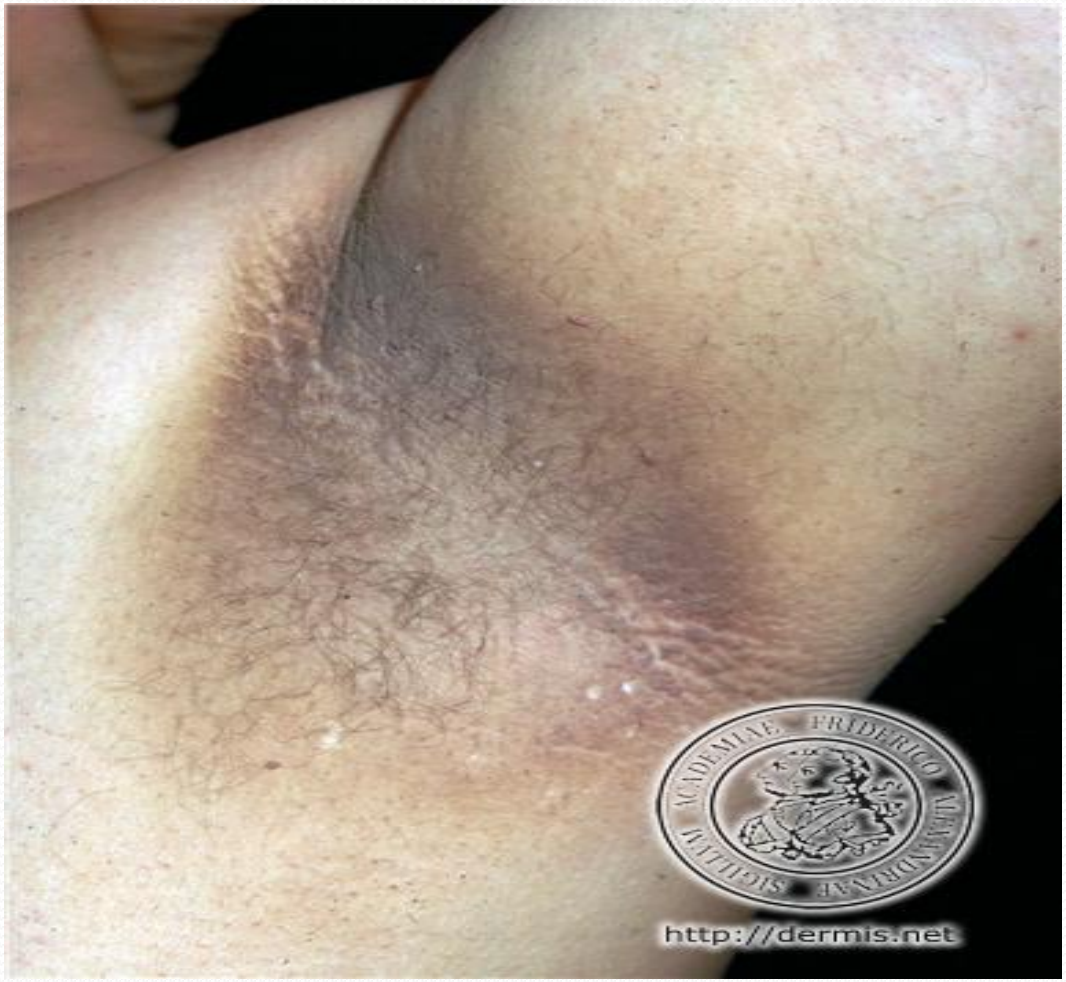


Table 1—*Scale for acanthosis nigricans*

Location and score	Description
Neck severity	
0	Absent: not detectable on close inspection.
1	Present: clearly present on close visual inspection, not visible to the casual observer, extent not measurable.
2	Mild: limited to the base of the skull, does not extend to the lateral margins of the neck (usually <3 inches in breadth).
3	Moderate: extending to the lateral margins of the neck (posterior border of the sternocleidomastoid) (usually 3–6 inches), should not be visible when the participant is viewed from the front.
4	Severe: extending anteriorly (>6 inches), visible when the participant is viewed from the front.
Axilla	
0	Absent: not detectable on close inspection.
1	Present: clearly present on close visual inspection, not visible to the casual observer, extent not measurable.
2	Mild: localized to the central portion of the axilla, may have gone unnoticed by the participant.
3	Moderate: involving entire axillary fossa, but not visible when the arm is against the participant's side.
4	Severe: visible from front or back in the unclothed participant when the arm is against the participant's side.
Neck texture	
0	Smooth to touch: no differentiation from normal skin to palpation.
1	Rough to touch: clearly differentiated from normal skin.
2	Coarseness can be observed visually, portions of the skin clearly raised above other areas.
3	Extremely coarse: "hills and valleys" observable on visual examination.
Knuckles	Present
	Absent
Elbows	Present
	Absent
Knees	Present
	Absent

James P. Burke et al. Diabetes Care 1999;22:1655-1659

5.1.2. *Blood pressure*

Blood pressure should be measured twice during a clinic visit and the average value of systolic and diastolic blood pressure should be recorded [22].

5.1.3. *Estimation of cardiovascular risk*

Estimation of cardiovascular risk may be undertaken using traditional algorithms of cardiovascular risk stratification such as the Systemic Coronary Risk Evaluation (SCORE) risk charts of the European Society of Cardiology (http://www.heartscore.org) or the Framingham score in the USA (http://cvdrisk.nhlbi.nih.gov) [23,24]. Classification in the following categories is used in the European guidelines [23]: low risk, moderate risk, high risk and very high risk. A therapeutic intervention is warranted for women at moderate or greater risk.

Clasificación del riesgo cardiovascular por FRAMINGHAM

Risk Assessment Tool for Estimating Your 10-year Risk of Having a Heart Attack

The risk assessment tool below uses information from the Framingham Heart Study to predict a person's chance of having a heart attack in the next 10 years. This tool is designed for adults aged 20 and older who do not have heart disease or diabetes. To find your risk score, enter your information in the calculator below.

Age: ☐ years

Gender: ○ Female ○ Male

Total Cholesterol: ☐ mg/dL

HDL Cholesterol: ☐ mg/dL

Smoker: ○ No ○ Yes

Systolic Blood Pressure: ☐ mm/Hg

Are you currently on any medication to treat high blood pressure. ○ No ○ Yes

Calculate Your 10-Year Risk

http//cvdrisk.nhlbi.nih.gov

Clasificación del riesgo cardiovascular por FRAMINGHAM

Clasificación del riesgo de padecer un evento cardiovascular en los próximos 10 años:

- **Muy bajo <5%**
- **Bajo 5-10%**
- **Moderado 10-20%**
- **Alto >20%**

http//cvdrisk.nhlbi.nih.gov

Ante esta paciente nos preguntamos:

1-¿En que estadío del aging reproductivo se encuentra?

2-¿Cuál es el diagnóstico de la paciente desde el punto de vista metabólico?

3-¿Cuál cree que es la mejor aproximación terapéutica en esta paciente?

Las características que reúne esta paciente son:

- **Acantosis Nigricans grado 4 de Burke**
- **Obesidad troncular (cc 110 cm)**
- **HTA**
- **HDL <50 mg%**
- **TG >150 mg%**

Metabolic Syndrome

Susan L. Samson, MD, PhD[a], Alan J. Garber, MD, PhD[b,c,d,*]

KEY POINTS

- Metabolic syndrome is a clustering of clinical findings made up of abdominal obesity, high glucose, high triglyceride, and low high-density lipoprotein cholesterol levels, and hypertension.
- Several definitions of metabolic syndrome have been proposed, with varied requirements, including those by the International Diabetes Federation and the National Cholesterol Education Program Adult Treatment Panel III.

Endocrinol Metab Clin N Am 2014;43(1):1-23

Table 1
Comparison of definitions of MetS

	WHO	EGIR	NCEP/ATPIII	AACE	AHA/NHLBI/ADA Updated NCEP/ ATPIII	IDF	Harmonized Definition[a]
Year	1999	1999	2001	2003	2004	2005	2009
Number of risk factors	IFG/IGT/T2DM or insulin resistance[b] and 2 of…	Insulin resistance[c] and 3 or more of…	Three or more of….	IGT/IFG with any of the following…	Three or more of…	Obesity and 2 of…	Three or more of…
Obesity	Waist/hip ratio >0.9 M, >0.85 F or BMI >30 kg/m^2	Waist circumference ≥94 cm M ≥80 cm F	Waist circumference ≥102 cm M ≥88 cm F	BMI ≥25 kg/m^2	Waist circumference ≥102 cm M ≥88 cm F	Waist circumference ≥94 cm M ≥90 (Asian M) ≥80 cm F	Waist circumference[d] Geographic and ethnic specific
Dyslipidemia	HDL-C <0.91 mmol/L M (35 mg/dL) <1.0 mmol/L F (<39 mg/dL) TG ≥1.7 mmol/L (150 mg/dL)	HDL-C <1.0 mmol/L (39 mg/dL) TG ≥2.0 mmol/L (177 mg/dL) or treated	HDL-C <1.0 mmol/L M (40 mg/dL) <1.3 mmol/L F (50 mg/dL) TG ≥1.69 mmol/L (150 mg/dL)	HDL-C <1.0 mmol/L M (40 mg/dL) <1.3 mmol/L F (50 mg/dL) TG ≥1.69 mmol/L (150 mg/dL)	HDL-C <1.0 mmol/L M (40 mg/dL) <1.3 mmol/L F (50 mg/dL) TG ≥1.69 mmol/L (150 mg/dL) or treated	HDL-C <1.0 mmol/L M (40 mg/dL) <1.3 mmol/L F (50 mg/dL) TG ≥1.7 mmol/L (150 mg/dL) or treated	HDL-C <1.0 mmol/L M (40 mg/dL) <1.3 mmol/L F (50 mg/dL) TG ≥1.7 mmol/L (150 mg/dL) or treated
Hyperglycemia	T2DM FPG >6.1 mmol/L (110 mg/dL) 2 h OGT >7.7 mmol/L (140 mg/dL)	Not T2DM FPG >6.1 mmol/L (110 mg/dL)	T2DM FPG ≥110 mg/dL (6.1 mmol/L)	Not T2DM FPG ≥110 mg/dL (6.1 mmol/L) 2 h OGT >7.7 mmol/L (140 mg/dL)	T2DM FPG ≥5.6 mmol/L (100 mg/dL)	T2DM FPG ≥5.6 mmol/L (100 mg/dL)	FPG ≥5.6 mmol/L (100 mg/dL) or treated
Hypertension	SBP ≥140 DBP ≥90	SBP ≥140 DBP ≥90 or treated	SBP ≥130 DBP ≥85	SBP ≥130 DBP ≥85	SBP ≥130 DBP ≥85 or treated	SBP ≥130 DBP ≥85 or treated	SBP ≥130 DBP ≥85 or treated
Additional components	Microalbuminuria ≥20 μg/min Albumin/creatinine ≥30 mg/g	—	—	Insulin resistance (family history T2DM, age, ethnicity, sedentary, lifestyle, PCOS)	—	—	—

SINDROME METABOLICO

Criterios diagnósticos (ATP III)

Factor de riesgo	*Nivel de corte*
Circunferencia cintura	
Hombre	**>102 cm**
Mujer	**> 88 cm**
Triglicéridos	**≥150 mg/dl**
HDL	
Hombre	**<40 mg/dl**
Mujer	**<50 mg/dl**
Presión arterial	**≥130/85**
Glucemia en ayuno	**≥110 mg/dl**

JAMA 2001;285:2486

Diagnosis and Management of the Metabolic Syndrome

An American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement

Executive Summary

Scott M. Grundy, MD, PhD, Chair; James I. Cleeman, MD, Co-Chair; Stephen R. Daniels, MD, PhD; Karen A. Donato, MS, RD; Robert H. Eckel, MD; Barry A. Franklin, PhD; David J. Gordon, MD, PhD, MPH; Ronald M. Krauss, MD; Peter J. Savage, MD; Sidney C. Smith, Jr, MD; John A. Spertus, MD; Fernando Costa, MD

Circulation 2005;112:2735-2752

TABLE 1. Diagnostic Criteria for Metabolic Syndrome

Measure (Any 3 of 5 Criteria Constitute Diagnosis of Metabolic Syndrome)	Categorical Cut Points
Elevated waist circumference*†	≥102 cm (≥40 inches) in men ≥88 cm (≥35 inches) in women
Elevated TG	≥150 mg/dL (1.7 mmol/L) or Drug treatment for elevated TG‡
Reduced HDL-C	<40 mg/dL (1.03 mmol/L) in men <50 mg/dL (1.3 mmol/L) in women or Drug treatment for reduced HDL-C‡
Elevated BP	≥130 mm Hg systolic BP or ≥85 mm Hg diastolic BP or Drug treatment for hypertension
Elevated fasting glucose	≥100 mg/dL or Drug treatment for elevated glucose

Circulation 2005;112:2735-2752

INTERNATIONAL DIABETES FEDERATION CONSENSUS

June 10, 2005

According to the new IDF definition, for a person to be defined as having the metabolic syndrome they must have:

Central obesity *(defined as waist circumference* ≥ 94cm for Europid men and ≥ 80cm for Europid women, *with ethnicity specific values for other groups)*

plus any two of the following four factors:

- ***raised TG level*****:** ≥ 150 mg/dL (1.7 mmol/L), *or* ***specific treatment for this lipid abnormality***
- ***reduced HDL cholesterol***: < 40 mg/dL (1.0 mmol/L) in males and < 50 mg/dL (1.3 mmol/L) in females, ***or specific treatment for this lipid abnormality***
- ***raised blood pressure:*** systolic BP ≥ 130 or diastolic BP ≥ 85 mm Hg, ***or treatment of previously diagnosed hypertension***
- ***raised fasting plasma glucose*** (FPG) ≥ 100 mg/dL (5.6 mmol/L), ***or previously diagnosed type 2 diabetes***
  If above 5.6 mmol/L or 100 mg/dL, OGTT is strongly recommended but is not necessary to define presence of the syndrome.

“La obesidad central es un pre-requisito para el diagnóstico del síndrome metabólico en la nueva definición”

The IDF consensus worlwide of the Metabolic Syndrome
10/6/2005

Country/Ethnic group		Waist circumference*
Europids *In the USA, the ATP III values (102 cm male; 88 cm female) are likely to continue to be used for clinical purposes*	Male	≥ 94 cm
	Female	≥ 80 cm
South Asians *Based on a Chinese, Malay and Asian-Indian population*	Male	≥ 90 cm
	Female	≥ 80 cm
Chinese	Male	≥ 90 cm
	Female	≥ 80 cm
Japanese	Male	≥ 85 cm
	Female	≥ 90 cm
Ethnic South and Central Americans	*Use South Asian recommendations until more specific data are available*	
Sub-Saharan Africans	*Use European data until more specific data are available*	
Eastern Mediterranean and Middle East (Arab) populations	*Use European data until more specific data are available*	

Harmonizing the Metabolic Syndrome

A Joint Interim Statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity

Circulation 2009;120:1640-1645

Table 1. Criteria for Clinical Diagnosis of the Metabolic Syndrome

Measure	Categorical Cut Points
Elevated waist circumference*	Population- and country-specific definitions
Elevated triglycerides (drug treatment for elevated triglycerides is an alternate indicator†)	≥150 mg/dL (1.7 mmol/L)
Reduced HDL-C (drug treatment for reduced HDL-C is an alternate indicator†)	<40 mg/dL (1.0 mmol/L) in males; <50 mg/dL (1.3 mmol/L) in females
Elevated blood pressure (antihypertensive drug treatment in a patient with a history of hypertension is an alternate indicator)	Systolic ≥130 and/or diastolic ≥85 mm Hg
Elevated fasting glucose‡ (drug treatment of elevated glucose is an alternate indicator)	≥100 mg/dL

HDL-C indicates high-density lipoprotein cholesterol.

*It is recommended that the IDF cut points be used for non-Europeans and either the IDF or AHA/NHLBI cut points used for people of European origin until more data are available.

Table 2. Current Recommended Waist Circumference Thresholds for Abdominal Obesity by Organization

Population	Organization (Reference)	Recommended Waist Circumference Threshold for Abdominal Obesity	
		Men	Women
Europid	IDF (4)	≥94 cm	≥80 cm
Caucasian	WHO (7)	≥94 cm (increased risk)	≥80 cm (increased risk)
		≥102 cm (still higher risk)	≥88 cm (still higher risk)
United States	AHA/NHLBI (ATP III)* (5)	≥102 cm	≥88 cm
Canada	Health Canada (8,9)	≥102 cm	≥88 cm
European	European Cardiovascular Societies (10)	≥102 cm	≥88 cm
Asian (including Japanese)	IDF (4)	≥90 cm	≥80 cm
Asian	WHO (11)	≥90 cm	≥80 cm
Japanese	Japanese Obesity Society (12)	≥85 cm	≥90 cm
China	Cooperative Task Force (13)	≥85 cm	≥80 cm
Middle East, Mediterranean	IDF (4)	≥94 cm	≥80 cm
Sub-Saharan African	IDF (4)	≥94 cm	≥80 cm
Ethnic Central and South American	IDF (4)	≥90 cm	≥80 cm

*Recent AHA/NHLBI guidelines for metabolic syndrome recognize an increased risk for CVD and diabetes at waist-circumference thresholds of ≥94 cm in men and ≥80 cm in women and identify these as optional cut points for individuals or populations with increased insulin resistance.

Optimal waist circumference cutoff value for defining the metabolic syndrome in postmenopausal Latin American women

Juan E. Blümel, MD, PhD, Deborah Legorreta, MD, Peter Chedraui, MD, MSc, Felix Ayala, MD, Ascanio Bencosme, MD, Luis Danckers, MD, Diego Lange, MD, Maria T. Espinoza, MD, Gustavo Gomez, MD, Elena Grandia, MD, Humberto Izaguirre, MD, MSc, Valentin Manriquez, MD, Mabel Martino, MD, Daysi Navarro, MD, PhD, Eliana Ojeda, MD, MSc, William Onatra, MD, MSc, Estela Pozzo, MD, Mariela Prada, MD, Monique Royer, MD, PhD, Javier M. Saavedra, MD, Fabiana Sayegh, MD, Konstantinos Tserotas, MD, Maria S. Vallejo, MD, and Cristina Zuñiga, MD, from the Collaborative Group for Research of the Climacteric in Latin America (REDLINC)

Un total de 3965 mujeres postmenopáusicas (45-64 años) de 12 centros ginecológicos de América Latina fueron incluidas en el estudio para establecer el valor de corte óptimo de la circunferencia de cintura para predecir SM.

Menopause 2012;19(4):433-437

CONCLUSIONS

According to the results of this multicenter study, it can be concluded that a WC cutoff value of 88 cm is optimal for defining the METS among postmenopausal Latin American woman. This cutoff value is the same as that set for occidental women and not similar to that set for Asians (range, 80-85 cm) as was previously thought.

Menopause 2012;19(4):433-437

SINDROME METABOLICO

Entidad caracterizada por:

- **Poseer distintos criterios diagnóstico (WHO, ATP-III, IDF)**
- **Incrementado riesgo de desarrollar enfermedad cardiovascular**
- **Incrementado riesgo de desarrollar DM2**

Maturitas 2008;60:10-18

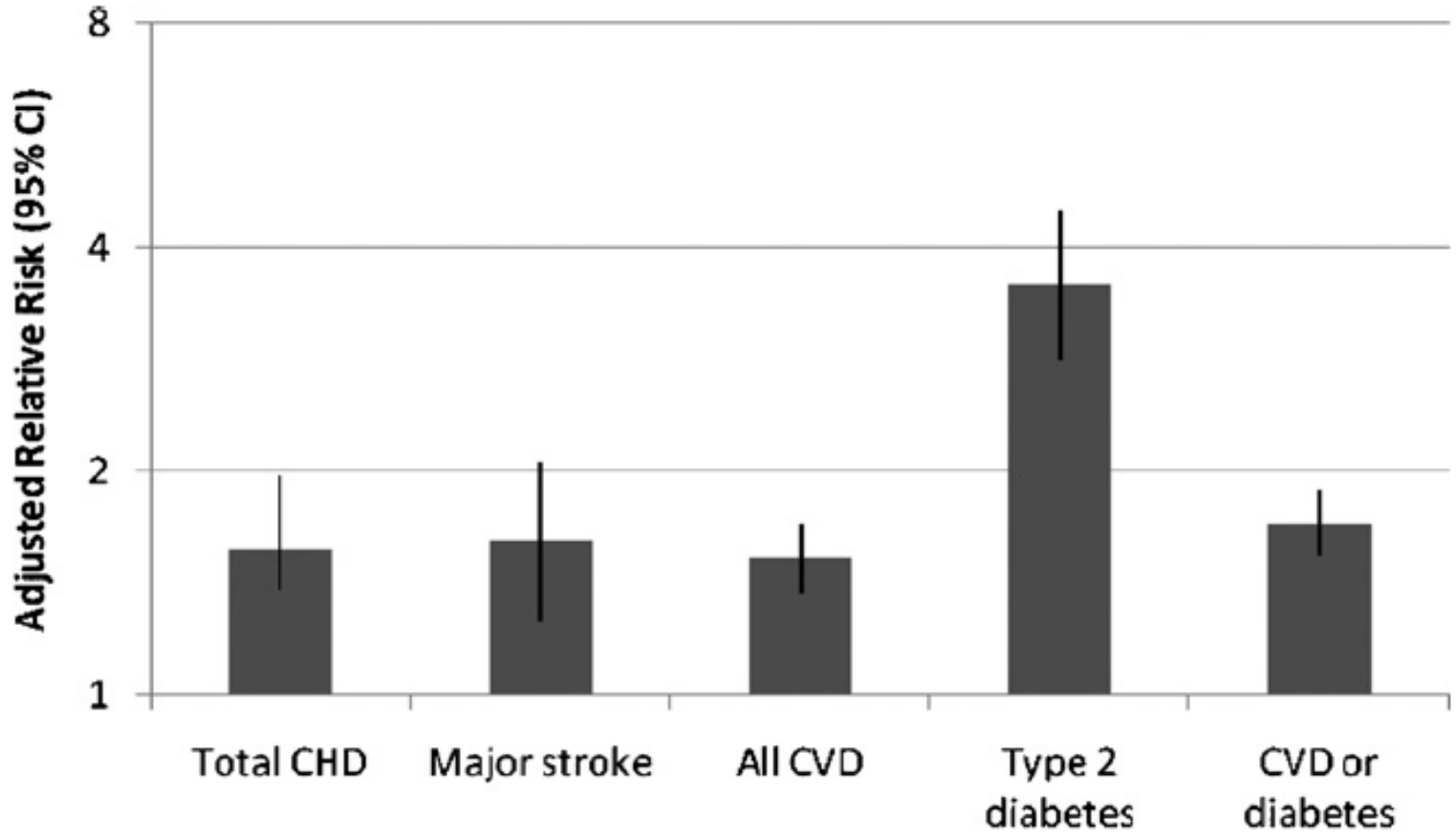


Fig. 1. Relative risk for CVD and diabetes associated with the metabolic syndrome (adapted from Wannamethee, 2008) [15].

Maturitas 2010;65:117-121

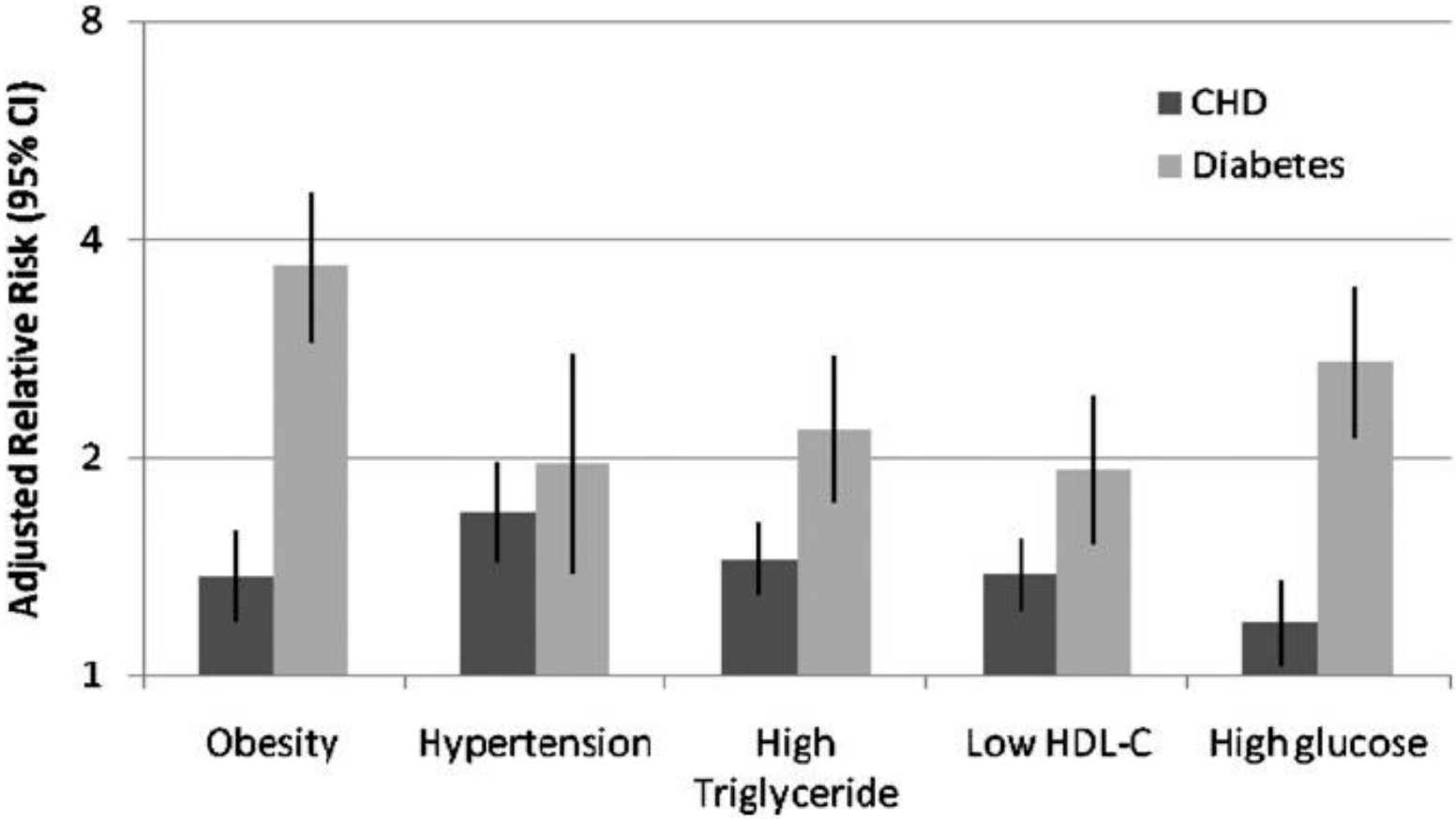


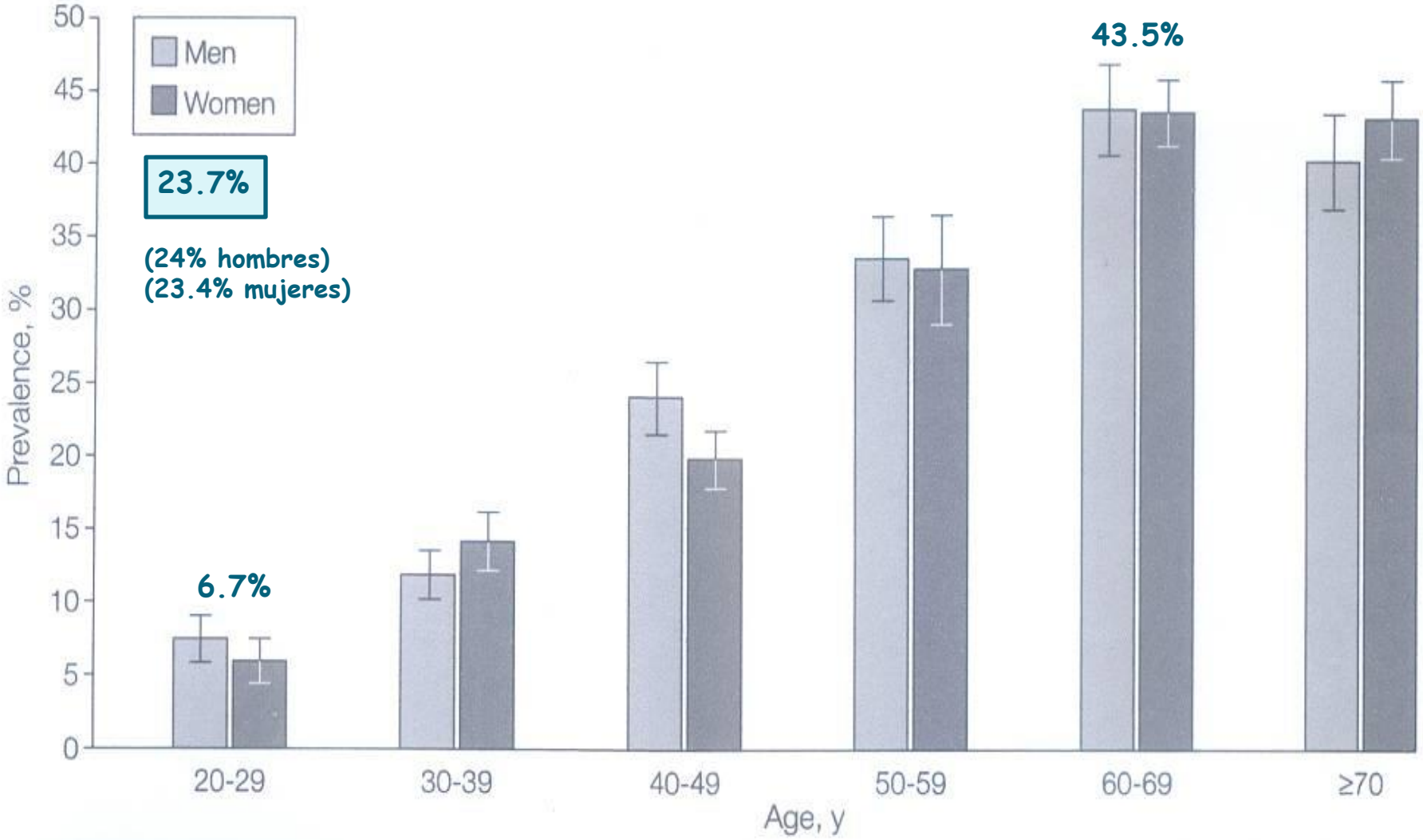
Fig. 2. Relative risk for CHD and diabetes associated with components of the metabolic syndrome (adapted from Wannamethee, 2008) [15].

Maturitas 2010;65:117-121

“Prevalence of the Metabolic Syndrome Among US Adults. Findings From the Third National Health and Nutrition Examination Survey”

JAMA 2002;287(3):356-359

Figure 1. Age-Specific Prevalence of the Metabolic Syndrome Among 8814 US Adults Aged at Least 20 Years, by Sex, National Health and Nutrition Examination Survey III, 1988-1994



Data are presented as percentage (SE).

JAMA 2002;287(3):356-359

“Prevalence of the Metabolic Syndrome Among US Adults. Findings From National Health and Nutrition Examination Survey (NHANES) 2003-2006”

Circulation 2010;121(7):e-45-e-215

NHANES 2003-2006

De un total de 3423 adultos de ≥ 20 años se observa una prevalencia de SM (según ATP III) de 34% con

- **35.1% para hombres**
- **32.6% para mujeres**
  - **15.6% de 20-39 años**
  - **37.2% de 40-59 años**
  - **54.4% ≥ de 60 años**

Circulation 2010;121(7):e-45-e-215

Metabolic syndrome throughout the menopausal transition: influence of age and menopausal status

V. R. Mesch, L. E. Boero, N. O. Siseles, M. Royer*, M. Prada*, F. Sayegh*, L. Schreier, H. J. Benencia and G. A. Berg*

Climateric 2006;9:40-48

Table 1 General features of the study sample. Data are expressed as mean ± standard deviation

	Premenopausal women (n = 29)	*Menopausal transition women with menstrual bleeding (n = 35)*	*Menopausal transition women with 3–6 months amenorrhea (n = 29)*	*Postmenopausal women (n = 31)*	*ANOVA p*
Age (years)	33 ± 5.6	47 ± 3.3	49 ± 3.0	55 ± 5.6	0.0001
FSH (mUI/ml)	6.7 ± 2.5	28.3 ± 25.1	45.2 ± 29.7	64.7 ± 19.8	0.01
Body mass index (kg/m^2)	23.3 ± 4.5	27.0 ± 3.8	27.7 ± 4.0	25.8 ± 3.8	0.0005
Waist circumference (cm)	77.8 ± 12	88.0 ± 10.9	90.6 ± 10.2	88.1 ± 10.8	0.0002
Waist-to-hip ratio	0.78 ± 0.08	0.84 ± 0.08	0.85 ± 0.06	0.86 ± 0.08	0.024
Systolic BP (mmHg)	110 ± 32	127 ± 18	129 ± 14	125 ± 10	0.03
Diastolic BP (mmHg)	72.3 ± 9.3	80 ± 9.2	84.8 ± 13.5	78.3 ± 7.0	0.008
Triglycerides (mmol/l)	0.75 ± 0.28	1.19 ± 0.59	1.28 ± 0.71	1.42 ± 0.50	0.0001
HDL cholesterol (mmol/l)	1.47 ± 0.28	1.41 ± 0.33	1.54 ± 0.42	1.48 ± 0.34	0.49
Triglycerides/HDL cholesterol	0.53 ± 0.27	0.97 ± 0.67	0.96 ± 0.77	1.03 ± 0.52	0.007
Fasting glucose (mmol/l)	4.6 ± 1.4	4.8 ± 0.4	4.9 ± 0.4	5.2 ± 0.7	0.04
Fasting insulin (μUI/ml)	9.3 ± 4.9	10.7 ± 5.4	13.3 ± 6.2	12.5 ± 9.2	0.09
HOMA	2.03 ± 1.14	2.23 ± 1.34	2.92 ± 1.41	2.86 ± 2.39	0.09
QUICKI	0.35 ± 0.02	0.34 ± 0.02	0.33 ± 0.02	0.34 ± 0.03	0.06
McAuley index	8.7 ± 1.7	7.4 ± 1.6	6.8 ± 1.4	6.8 ± 1.4	0.0001

Climateric 2006;9:40-48

Frecuencia relativa de síndrome metabólico en los 4 grupos de pacientes

	Mujeres premenopáusicas (n=29)	Mujeres en transición con sangrado menstrual (n=35)	Mujeres en transición con 3-6 meses de amenorrea (n=29)	Mujeres postmenopásicas (n=31)
Síndrome metabólico	0%	20%*	21%*	22%*

* p<0.001 vs mujeres premenopáusicas

Climateric 2006;9:40-48

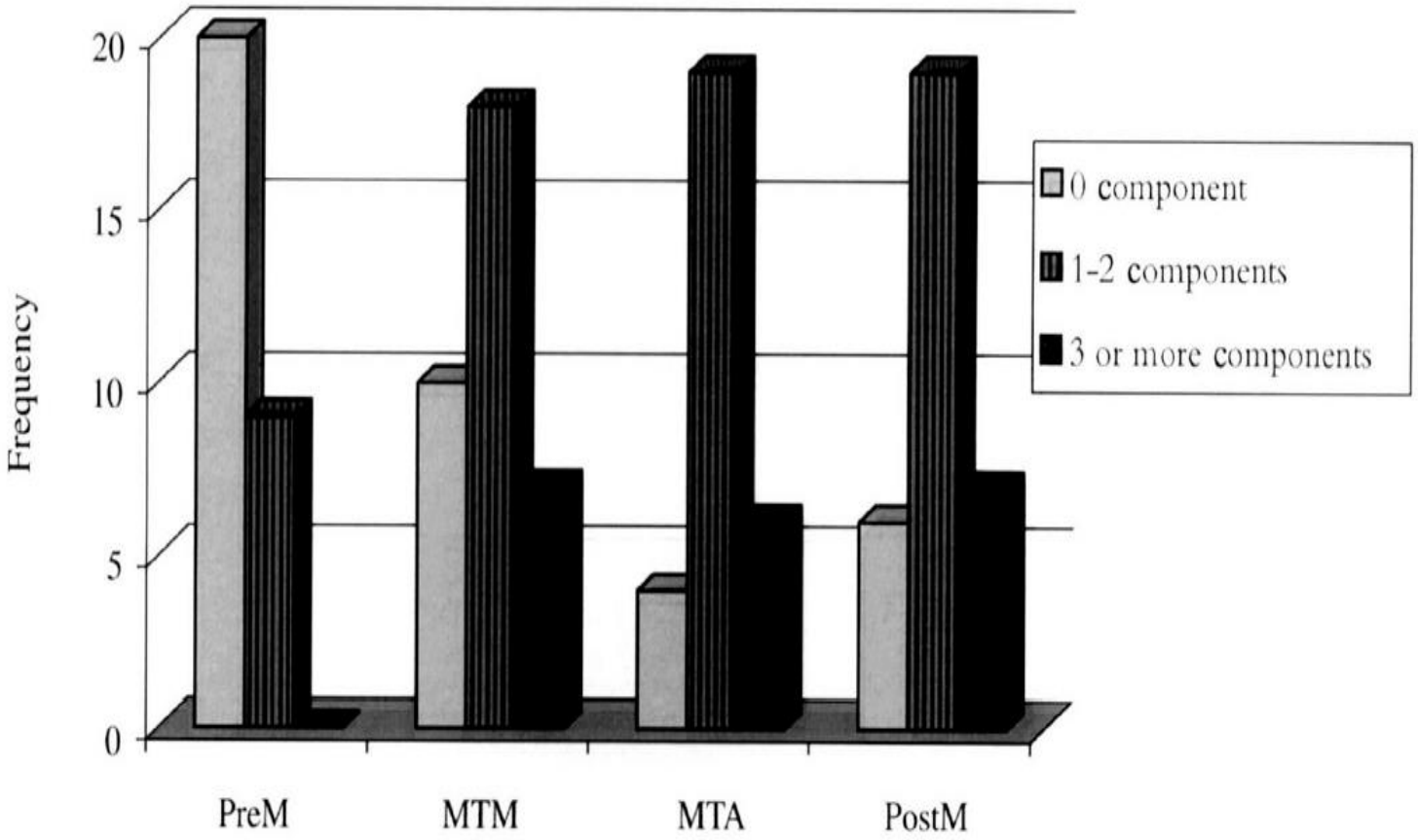


Figure 1 Frequency distribution according to the number of components of the metabolic syndrome (see Methods) in premenopausal women (PreM, $n = 29$), menopausal transition women with menstrual bleeding (MTM, $n = 35$), menopausal transition women with 3–6 months amenorrhea (MTA, $n = 29$) and postmenopausal women (PostM, $n = 31$). χ^2, $p < 0.001$

Climateric 2006;9:40-48

The US National Cholesterol Education Programme Adult Treatment Panel III (NCEP ATP III): prevalence of the metabolic syndrome in postmenopausal Latin American women

M. Royer, C. Castelo-Branco, J. E. Blümel, P. A. Chedraui, L. Danckers, A. Bencosme, D. Navarro, S. Vallejo, M. T. Espinoza, G. Gómez, H. Izaguirre, F. Ayala, M. Martino, E. Ojeda, W. Onatra, J. Saavedra, K. Tserotas, E. Pozzo, V. Manriquez, M. Prada, E. Grandia, C. Zuniga, D. Lange and F. Sayegh for the Collaborative Group for Research of the Climacteric in Latin America

Climateric 2007;10:164-170

Table 1 Demographic characteristics of the women included in this survey

Center	*n*	*Age ± SD* (years)	*Time elapsed since menopause* (years)	*Smokers* (%)	*HT use* (%)
Bogota (Colombia)	336	56.0 ± 4.7	6.8 ± 4.7	7.1	14.6
Buenos Aires (Argentina)	345	56.5 ± 4.6	7.5 ± 5.1	21.9	15.9
Cali (Colombia)	313	53.9 ± 5.4	7.1 ± 6.8	6.3	31.5
Cochabamba (Bolivia)	337	53.8 ± 5.5	6.2 ± 5.3	41.8	69.9
Cuzco (Peru)	350	53.8 ± 5.0	6.6 ± 4.4	3.1	21.7
Ciudad de la Habana (Cuba)	339	50.9 ± 4.5	4.6 ± 3.9	77.3	58.8
Lima (Peru)	312	52.2 ± 5.2	5.2 ± 4.5	1.3	12.7
Mendoza (Argentina)	321	54.3 ± 5.1	6.6 ± 5.2	18.2	20.1
Rosario (Argentina)	311	55.4 ± 4.9	6.9 ± 5.2	14.8	16.4
Salta (Argentina)	321	55.8 ± 4.2	7.7 ± 4.9	18.3	28.6
Santiago (Dominican Republic)	336	55.3 ± 5.8	7.7 ± 5.3	29.7	3.6
Santiago (Chile)	344	54.0 ± 4.1	6.7 ± 4.7	8.6	8.8
Total	3965	54.3 ± 5.1	6.6 ± 5.0	11.8	24.7

SD, standard deviation; HT, hormone therapy

Climateric 2007;10:164-170

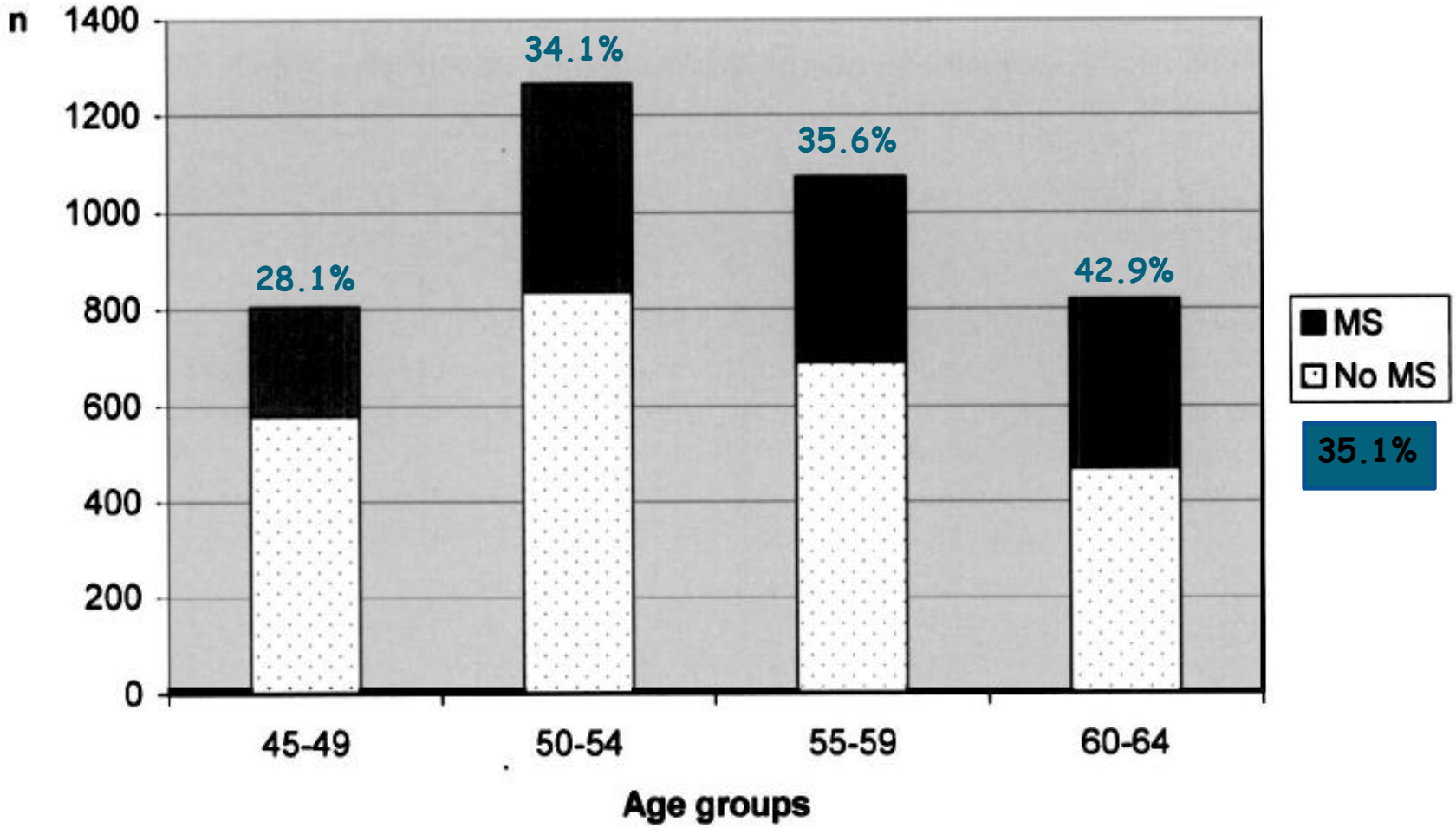


Figure 1 Age group prevalence of metabolic syndrome. Regarding the effect of age on the prevalence of METS, women between 45 and 49 years old showed the lowest prevalence of METS

Climateric 2007;10:164-170

Table 4 Metabolic syndrome risk factors: logistic regression analysis (multivariate)

Risk factor	*Risk (odds ratio)*	*95% Confidence interval*
Current cigarette consumption	1.40	1.19–1.65
Age ≥55 years	1.22	1.03–1.43
>5 years since menopause	1.18	1.00–1.38
Current hormone therapy use	0.59	0.51–0.70

Climateric 2007;10:164-170

Metabolic syndrome in Argentine women: ATPIII, IDF, IDF/AHA/NHLBI; What criterion should be used?

JIMENA SOUTELO, MELINA SABAN, VIRGINIA QUEVEDO, EUGENIA GANDUR, ANALIA PARIS, PAOLA ALBA, JULIA GONZALEZ, MARIA BARBERO, CLARA FRIZT, & GABRIEL FARAJ

Endocrinology Service Medical Complex (PFA), (Argentine Federal Police) Churruca - Visca Hospital, Buenos Aires, Argentina

(Received 16 April 2010; accepted 14 June 2010)

Evaluaron la prevalencia de SM (usando los 3 criterios) en 120 mujeres premenopáusicas y 133 postmenopáusicas que consultaron al Servicio de Endocrinología del Hospital Churruca-Visca.

Gynecol Endocrinol 2011;27(6):448-451

Table III. Components of the metabolic syndrome present in pre-menopausal and post-menopausal women with MS diagnosis according to each criteria.

Components	Pre-menopausal (*n*)	Post-menopausal (*n*)
IDF	34	67**
IDF/AHA/NHLBI	34	67**
ATPIII	31	59*

**$p < 0.05$; *$p < 0.01$.

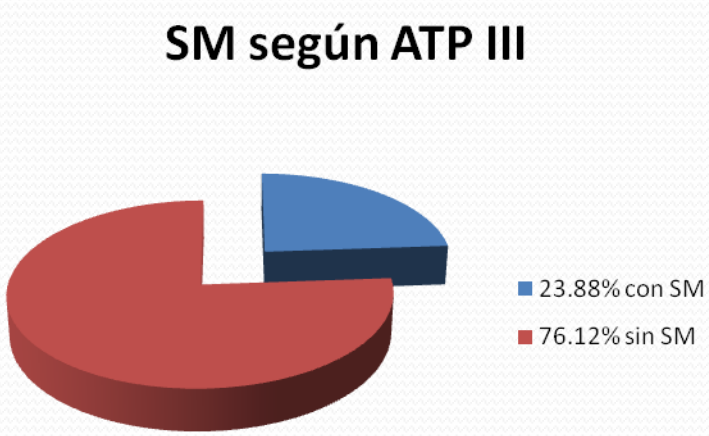
Gynecol Endocrinol 2011;27(6):448-451

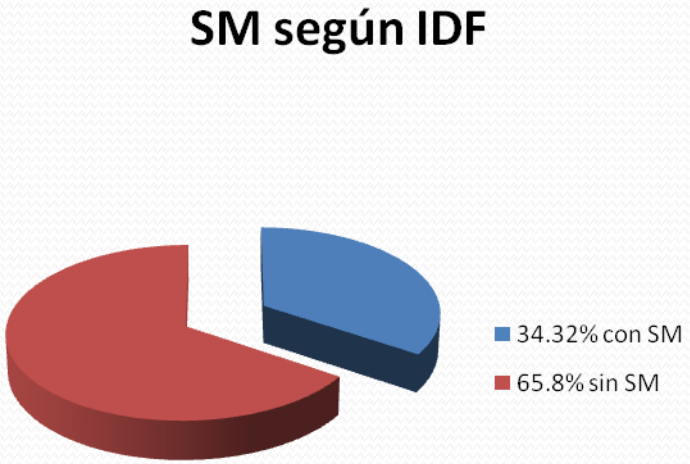
PREVALENCIA DE SINDROME METABOLICO SEGUN ATP III (ADULT TREATMENT PANEL III) E IDF (INTERNATIONAL DIABETES FEDERATION) EN UNA POBLACION DE MUJERES POSTMENOPAUSICAS

S. Leiderman; J. Dome; G. Fernández; L. Pacienza; J. Schweizer; P. Szeinberg.

Hospital Municipal de Vicente López, Prof. B. A. Houssay. Servicio de Ginecología, Jefe de servicio Dr. Roberto Sainz, Vicente López, AR

67 mujeres postmenopáusicas que concurrieron espontáneamente al consultorio de climaterio del Hospital Vicente López





RIESGO FRAMINGHAM SEGÚN SM POR ATP III Y POR IDF

	SM SEGÚN ATP III	SM SEGÚN IDF
RIESGO NORMAL Y BAJO	25% (4/16)	30.42% (7/23)
RIESGO ALTO	75% (12/16)	69.56% (16/23)

PREVALENCIA DE SINDROME METABOLICO SEGUN ATP III (ADULT TREATMENT PANEL III) E IDF (INTERNATIONAL DIABETES FEDERATION) EN UNA POBLACION DE MUJERES POSTMENOPAUSICAS

CONCLUSIONES:

La diferencia en la prevalencia de SM según se aplique el criterio de ATP III o de IDF es del 10.44%. Durante la menopausia, la ausencia de estrógenos asociada a un medio más androgénico, tienden a redistribuir la masa grasa hacia el tronco, aumentando la circunferencia de cintura y esto podría sobreestimar la cantidad de mujeres con SM. Concluimos que en el período postmenopáusico, el criterio diagnóstico de riesgo cardiometabólico es mejor a través del ATP III.

SINDROME METABOLICO

“Afecta 20-30% de población de edad media, y hasta 60% de mujeres postmenopáusicas”

J Clin Endocrinol Metab 2003;88:2404

¿A qué obedece el mayor riesgo de desarrollar S.M. en la transición a la menopausia?

CAMBIOS METABOLICOS DE LA POSTMENOPAUSIA

- **Cambios producidos por el “aging”**
- **Secundarios al déficit de esteroides sexuales**

MENOPAUSIA

La menopausia se asocia con:

- **perfil lipídico adverso**
- **alteración del metabolismo de HdeC**
- **mayor trombogénesis e inflamación**
- **afectación del endotelio vascular**
- **aumento del peso corporal**
- **variación de la composición corporal**

MENOPAUSIA

PERFIL LIPIDICO ADVERSO

- ↑ col t 15%
- ↑ LDLc 10-20%
- ↑ LDL densas
- ↓ HDLc (ppal HDL_2)
- ↑ apo B
- ↑ triglicéridos 16%
- ↑ Lp(a) 25-50%

"MAYOR RIESGO DE ENFERMEDAD CARDIOVASCULAR"

J Clin Endocrinol Metab 2003;88:2404

TABLE 4. Percentage of women who maintain or change LDL size with menopause

	Premenopause		Postmenopause
51%	lbLDL	⇨	lbLDL
36%	lbLDL	⇨	sdLDL
13%	sdLDL	⇨	sdLDL

Data are from Austin *et al.* (43). lbLDL, Large, buoyant LDL; sdLDL, small, dense LDL.

J Clin Endocrinol Metab 2003;88:2404

CAMBIOS LIPOPROTEICOS DE LA POSTMENOPAUSI

- ↑ IDL
-
-
- da en postmenopausia
- no cambia sustancialmente

"EL RIESGO LIPIDICO EN LA POSTMENOPAUSIA PARECE SER POR AUMENTO DE LDL Y OTRAS LIPOPROTEINAS CON APO B MODIFICADAS Y NO POR DESCENSO DE HDL"

SAEGRE 2003;10(1):14-21

CAMBIOS LIPOPROTEICOS DE LA TRANSICION

Estudiaron 2659 mujeres pre/perimenopáusicas del SWAN seguidas longitudinalmente, a quienes se les realizó dosajes anuales y se observó que colesterol total, LDLc, Lpa, TG y apoB

-Iniciaron aumentos ya en la TM temprana

-Con picos máximos durante la TM tardía y la postmenopausia temprana

Endocrinol Metab Clin N Am 2016;45(1):65-85

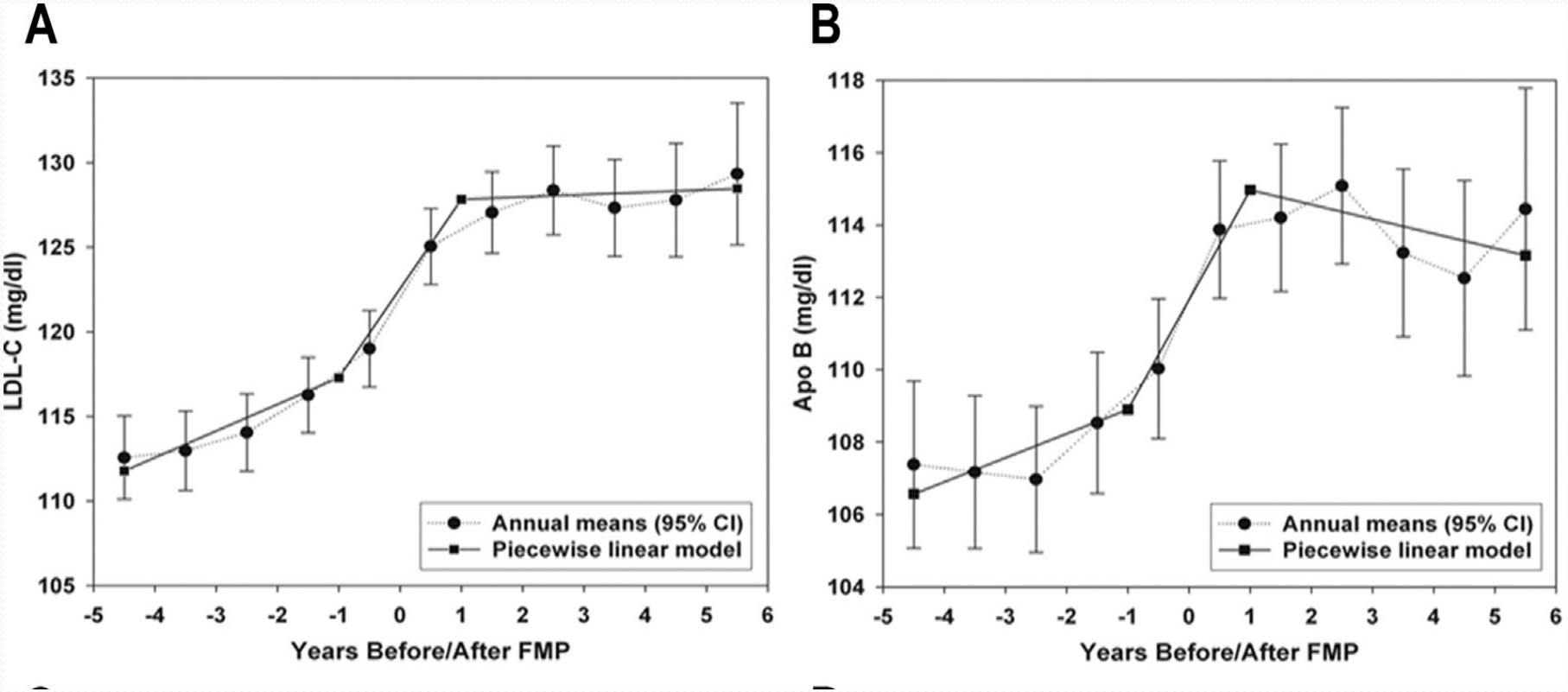


Fig. 5. Lipids annual and estimated means patterns of LDL-C (*A*), apolipoprotein (Apo) B (*B*), HDL-C (*C*), and Apo A1 (*D*) across the SWAN study follow-up period. FMP, final menstrual period. (*From* Matthews KA. Are changes in cardiovascular disease risk factors in midlife women due to chronological aging or to the menopausal transition? J Am Coll Cardiol 2009;54(25):2366–73; with permission.)

POSTMENOPAUSIA

METABOLISMO HIDROCARBONADO

El metabolismo de H. de C. se altera por:

- ↓ estrógenos
- aging
  - ↑ peso corporal
  - ↑ grasa corporal
  - ↓ SDHEA
  - ↑ TNF
  - ↑ IL6

POSTMENOPAUSIA
METABOLISMO HIDROCARBONADO

- **Reducción en la producción pancreática de insulina**
- **Reducción de la captación hepática de insulina (tal vez 2º a ↑ de NEFA y ↓ de Estrógenos)**
- **Reducción de la sensibilidad a la insulina (progresivo con el incremento de la edad en mujer postmenopáusica)**
- **Deterioro en la tolerancia de glucosa**

Aproximadamente 5% de mujeres postmenopáusicas desarrollarán DM2

POSTMENOPAUSIA

AUMENTO DEL PESO CORPORAL

En la mujer, un incremento significante del peso corporal es observado entre los 38-47 años, que continúa elevándose con el avance de la edad.

- **Cambios metabólicos (lípidos y glúcidos)**
- **Cambios hormonales (reducida función tiroidea)**
- **Reducción del gasto energético (actividad física reducida)**
- **Aumento de la ingesta alimentaria**

POSTMENOPAUSIA

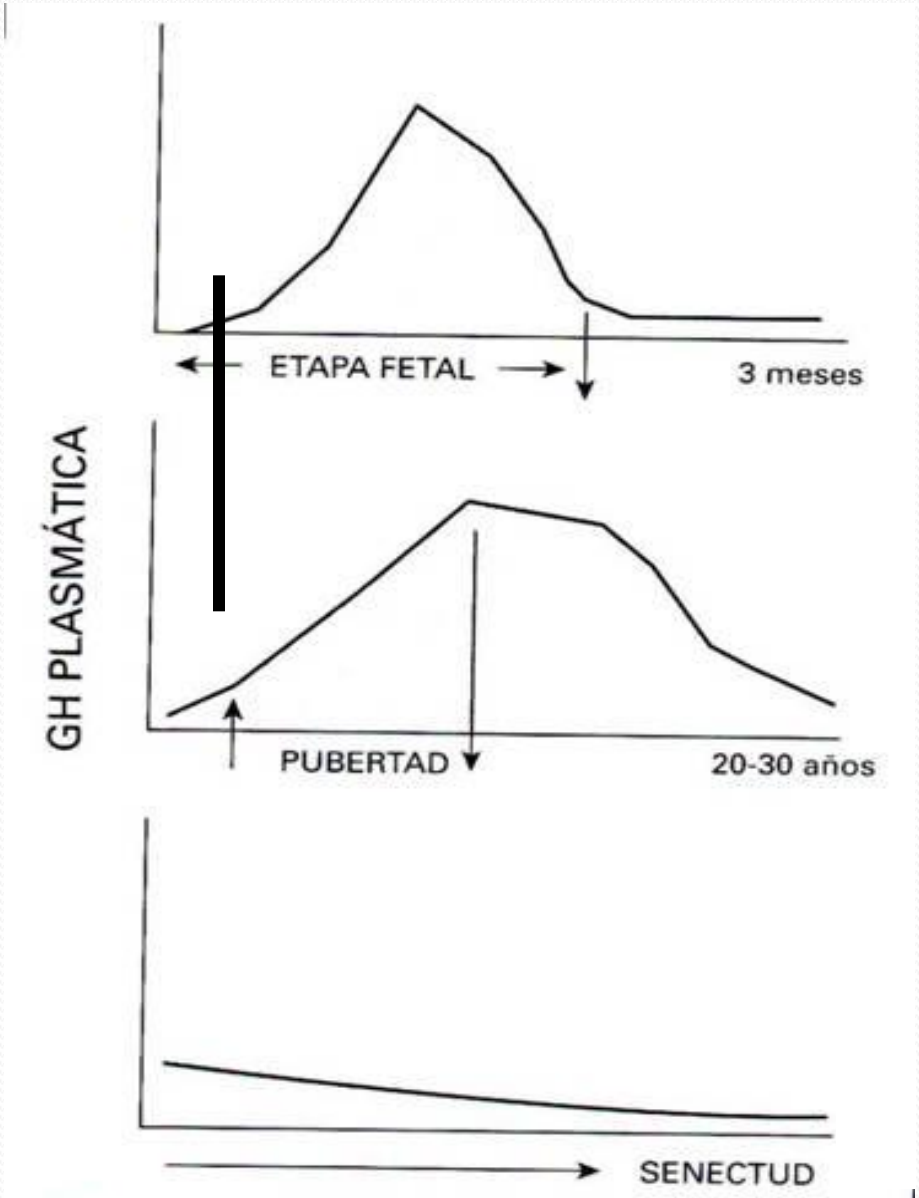
AUMENTO DEL PESO CORPORAL

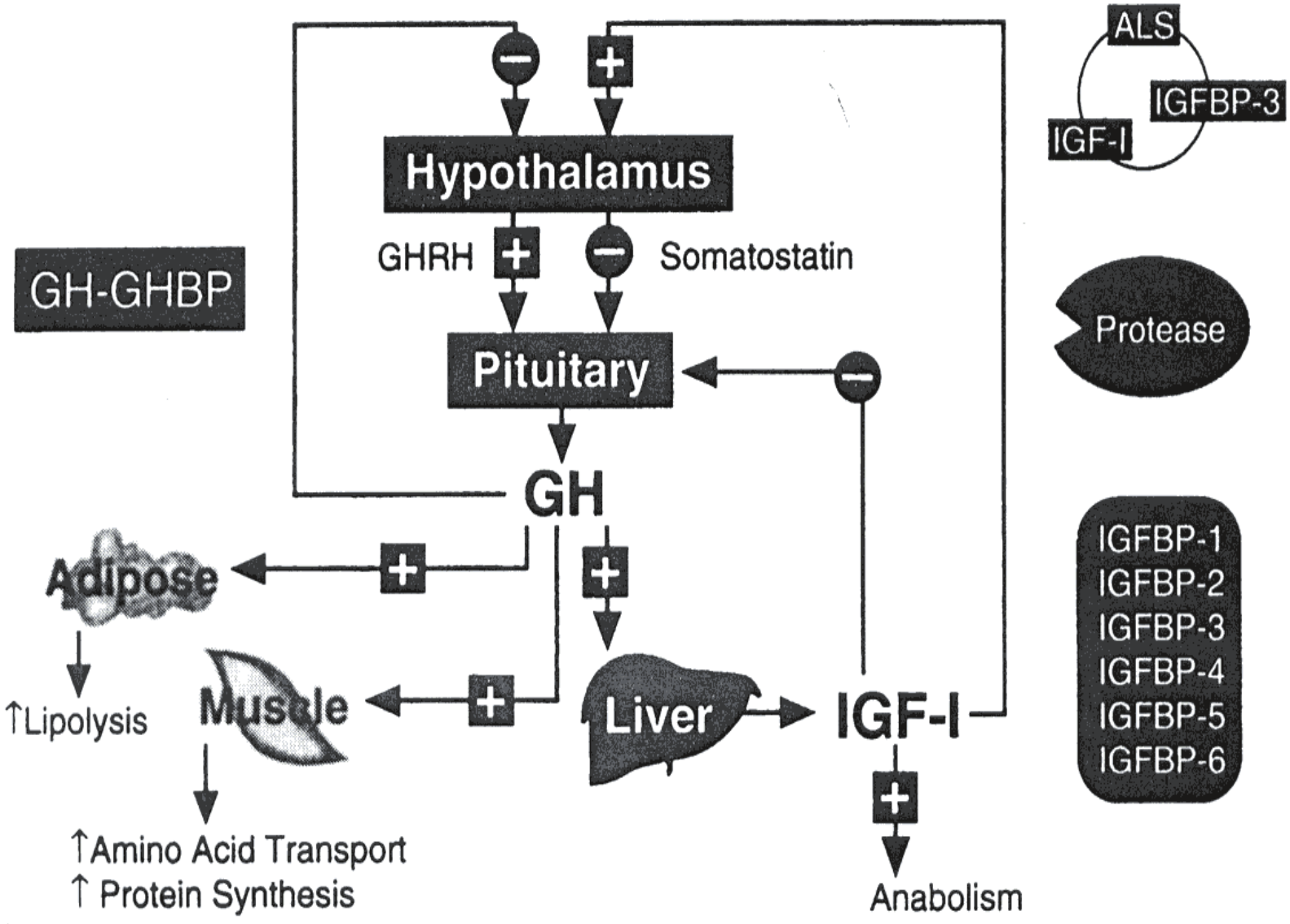
Un promedio de 0.9 Kg total de ganancia anual de peso corporal se asoció con:

- **↑ de 1.4 Kg de compartimiento graso**
- **↓ de 0.5 Kg de compartimiento magro**

Sowers.Am J Epidemiol 1999;149:47-54

GH durante distintas edades




ALS
IGFBP-3
IGF-I
Hypothalamus
GHRH
Somatostatin
GH-GHBP
Protease
Pituitary
GH
Adipose
IGFBP-1
IGFBP-2
IGFBP-3
IGFBP-4
IGFBP-5
IGFBP-6
↑Lipolysis
Muscle
Liver
IGF-I
↑Amino Acid Transport
↑ Protein Synthesis
Anabolism

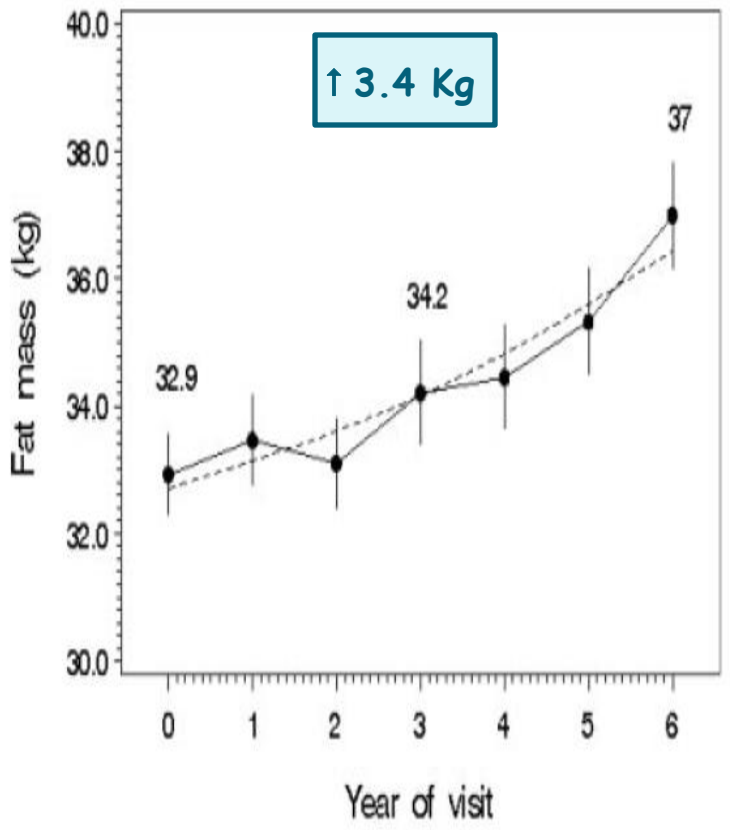
Changes in Body Composition in Women over Six Years at Midlife: Ovarian and Chronological Aging

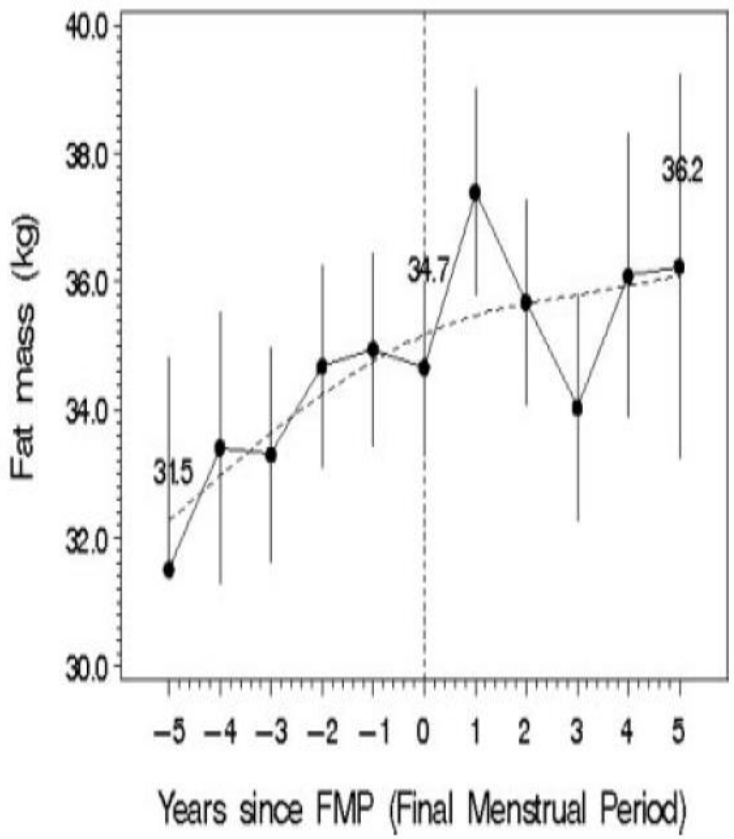
MaryFran Sowers, Huiyong Zheng, Kristin Tomey, Carrie Karvonen-Gutierrez, Mary Jannausch, Xizhao Li, Matheos Yosef, and James Symons

Department of Epidemiology, University of Michigan School of Public Health, Ann Arbor, Michigan 48104

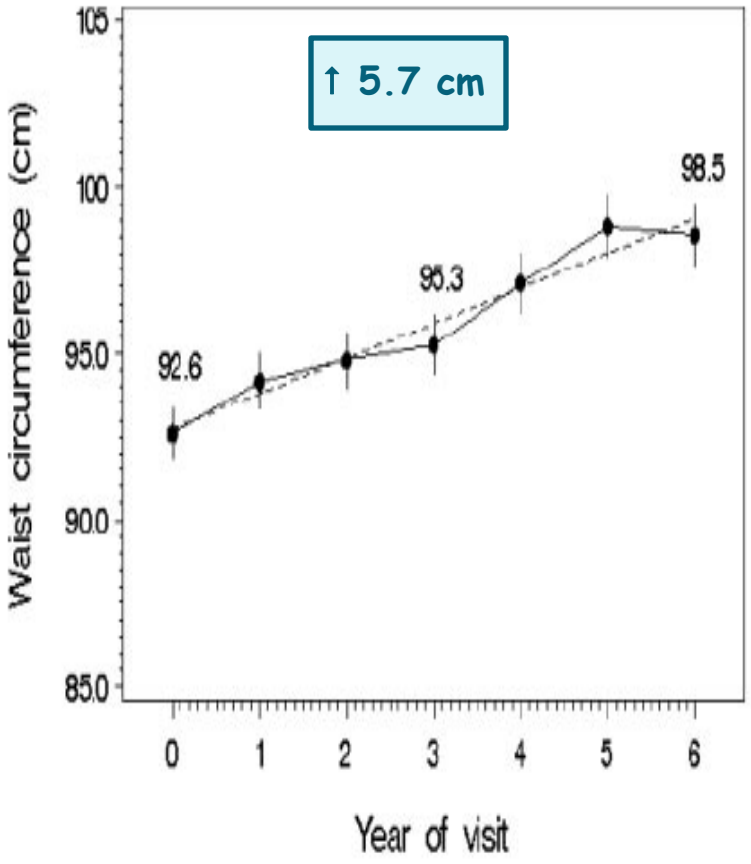
Estudio longitudinal de 543 mujeres pre o perimenopáusicas tempranas del SWAN seguidas longitudinalmente por 6 años para evaluar efecto de edad cronológica y edad ovárica sobre la composición corporal.

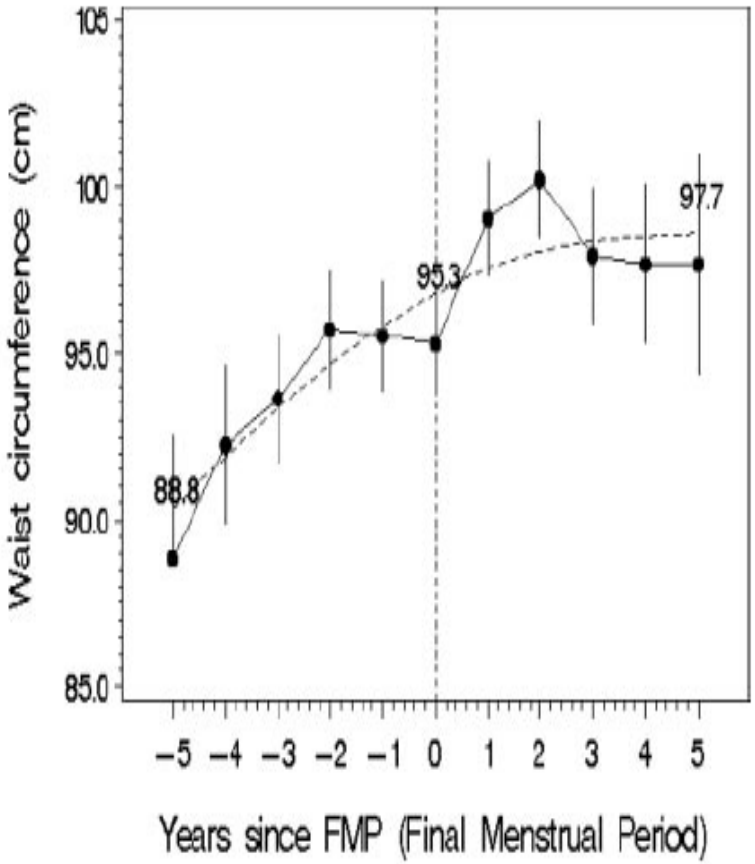
J Clin Endocrinol Metab 2007;92:895-901



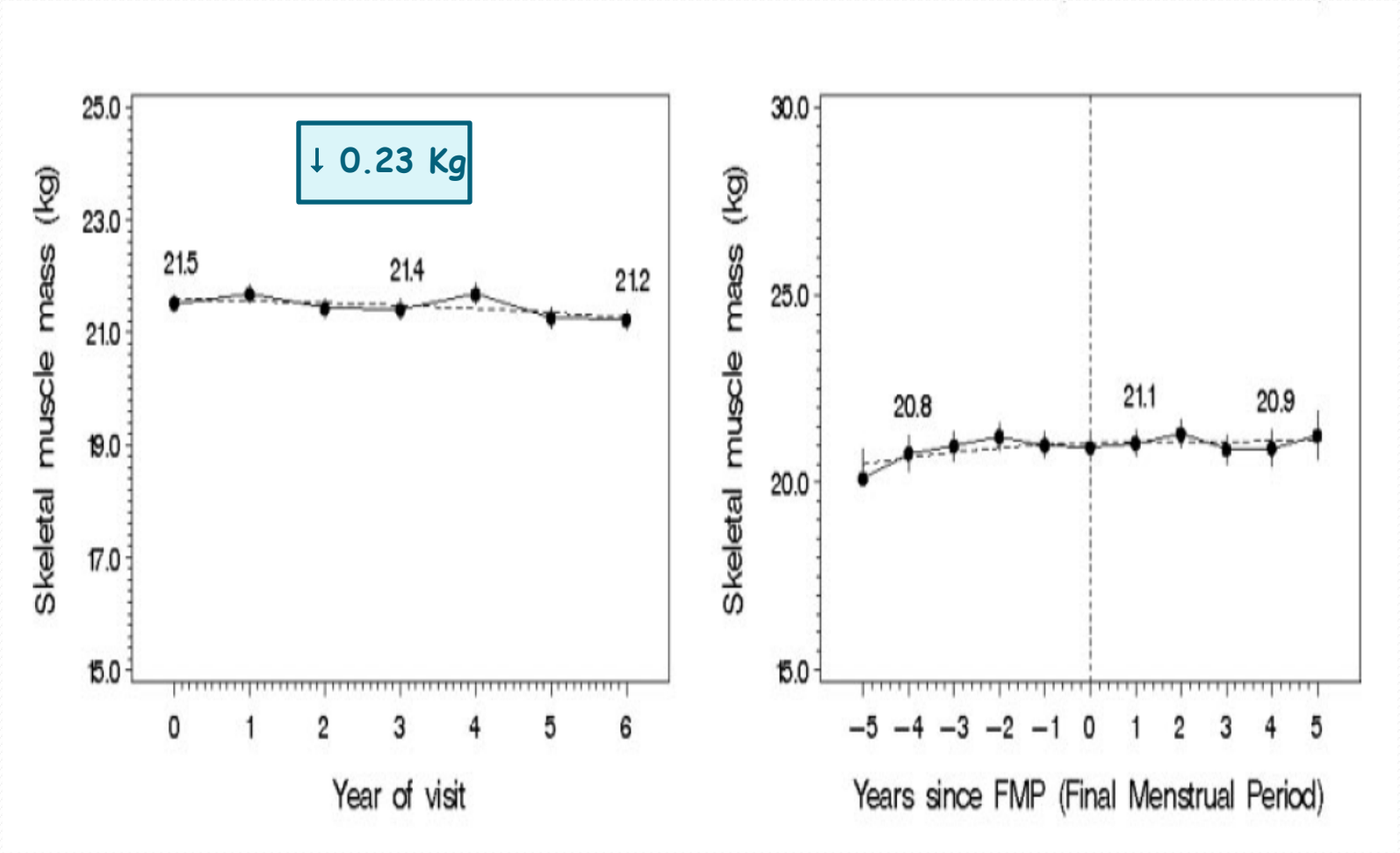


J Clin Endocrinol Metab 2007;92:895-901





J Clin Endocrinol Metab 2007;92:895-901



J Clin Endocrinol Metab 2007;92:895-901

“Tanto la edad cronológica como el envejecimiento ovárico contribuyen en los cambios de la composición corporal”

J Clin Endocrinol Metab 2007;92:895-901

Understanding weight gain at menopause

S. R. Davis, C. Castelo-Branco, P. Chedraui†, M. A. Lumsden‡, R. E. Nappi**, D. Shah†† and P. Villaseca‡‡*
as the Writing Group of the International Menopause Society for World Menopause Day 2012

Women's Health Research Program, Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia; *Unit of Endocrinological Gynaecology, Department of Gynaecology, ICGON, Hospital Clínic de Barcelona, Universitat de Barcelona, IDIBAPS, Barcelona, Spain; †Institute of Biomedicine, Facultad de Ciencias Médicas, Universidad Católica de Santiago de Guayaquil, Guayaquil, Ecuador; ‡Head of Reproductive & Maternal Medicine, School of Medicine, University of Glasgow, Scotland, UK; **Research Centre for Reproductive Medicine, Department of Obstetrics and Gynecology, IRCCS S. Matteo Foundation, University of Pavia, Italy; ††Department of Obstetrics and Gynecology, Breach Candy Hospital and Research Center, Jaslok Hospital and Research Center, Sir Hurkisondas Hospital and Research Center, Mumbai, India; ‡‡Department of Endocrinology, Faculty of Medicine, Pontificia Universidad Católica de Chile, Santiago, Chile

KEY POINTS

- Weight gain is a major health concern for women at midlife.
- Weight gain *per se* does not appear to be affected by the hormonal changes of the menopause.
- The fall in estrogen at menopause favors central abdominal fat accumulation.

Climateric 2012;15(5):419-429

POSTMENOPAUSIA
COMPOSICION CORPORAL

- **Aumento de la masa grasa corporal.**
- **Redistribución de la masa grasa corporal, con aumento de la grasa abdominal (que contribuye a las alteraciones lipídicas y a la Ri).**

PATRONES DE DISTRIBUCION GRASA CORPORAL

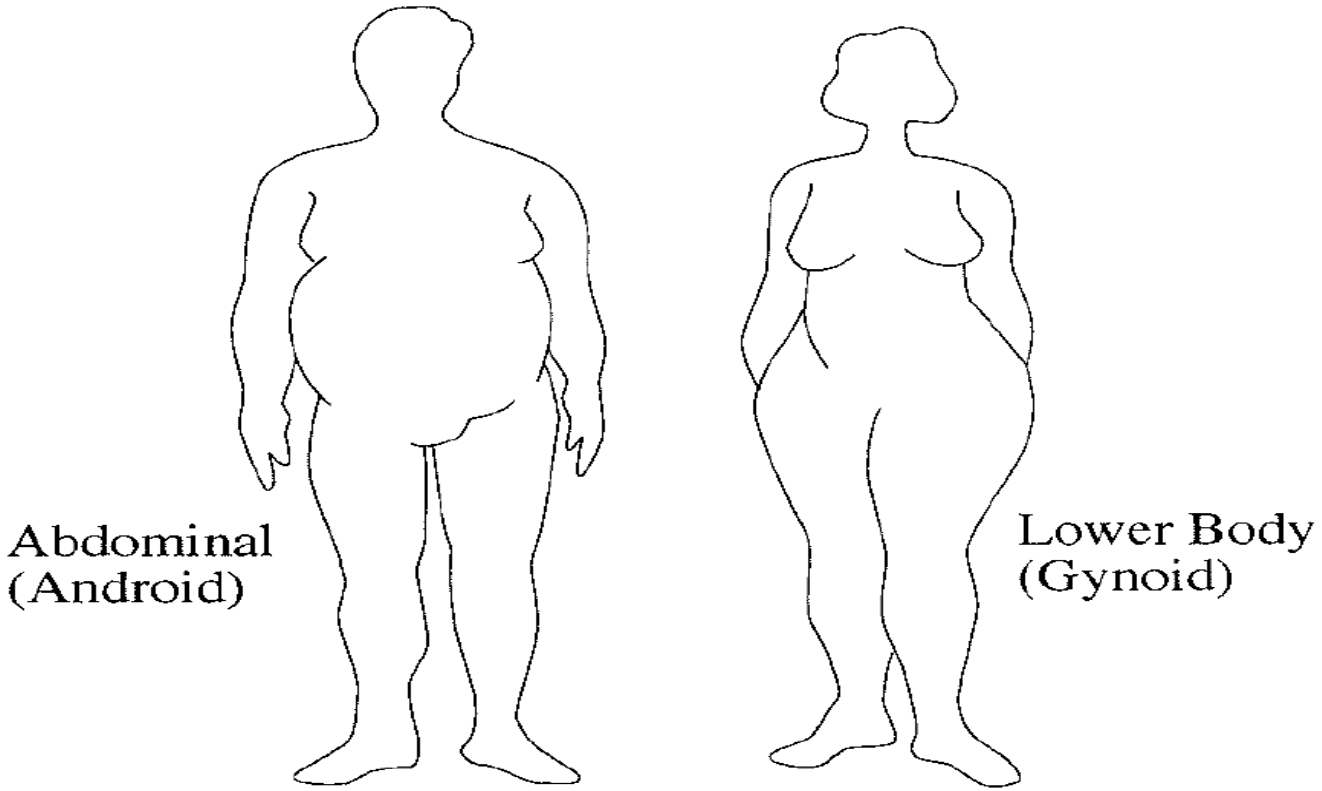
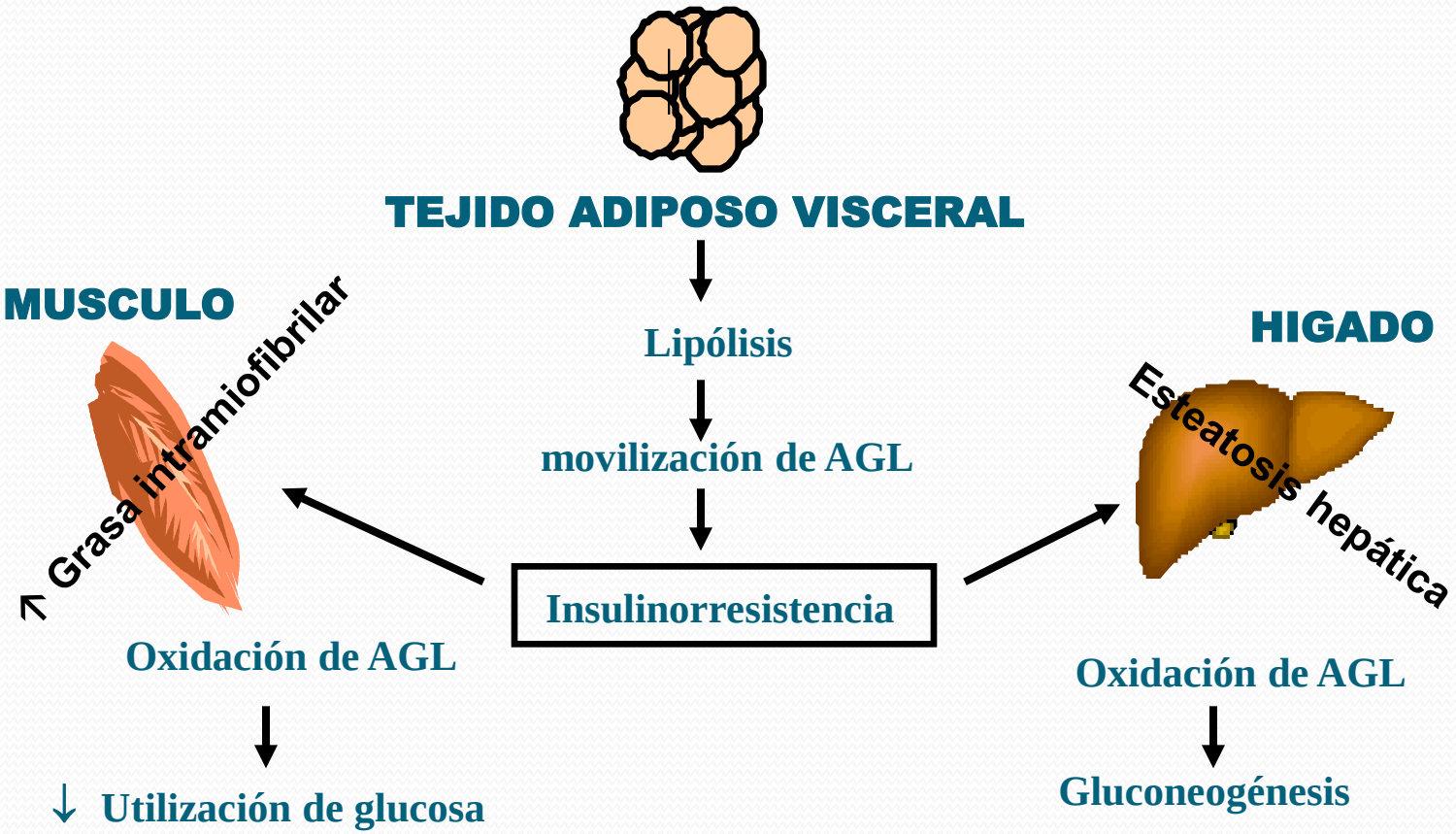
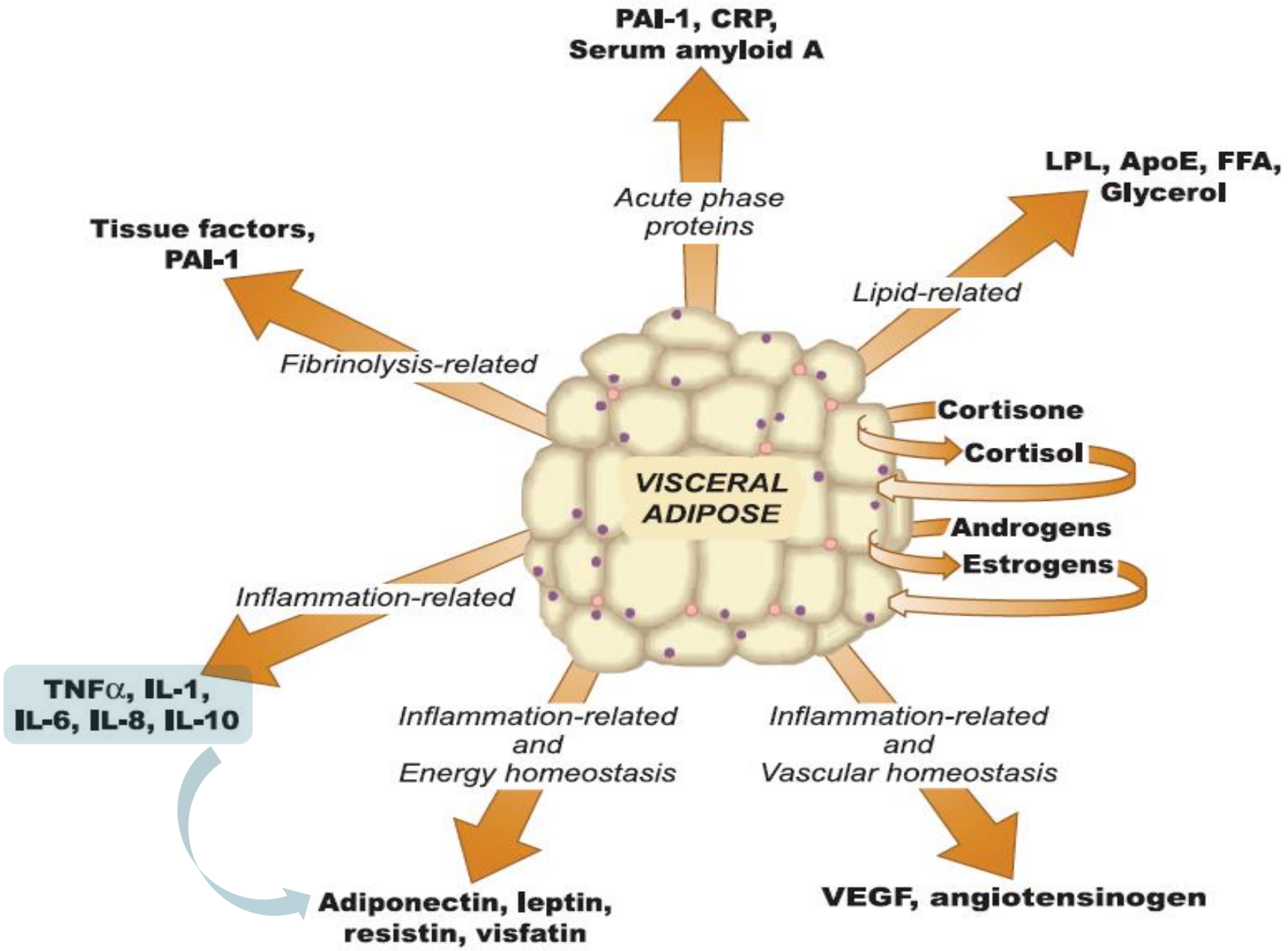


FIG. 1. Patterns of body fat distribution.

J Clin Endocrinol Metab 2003;88:2404

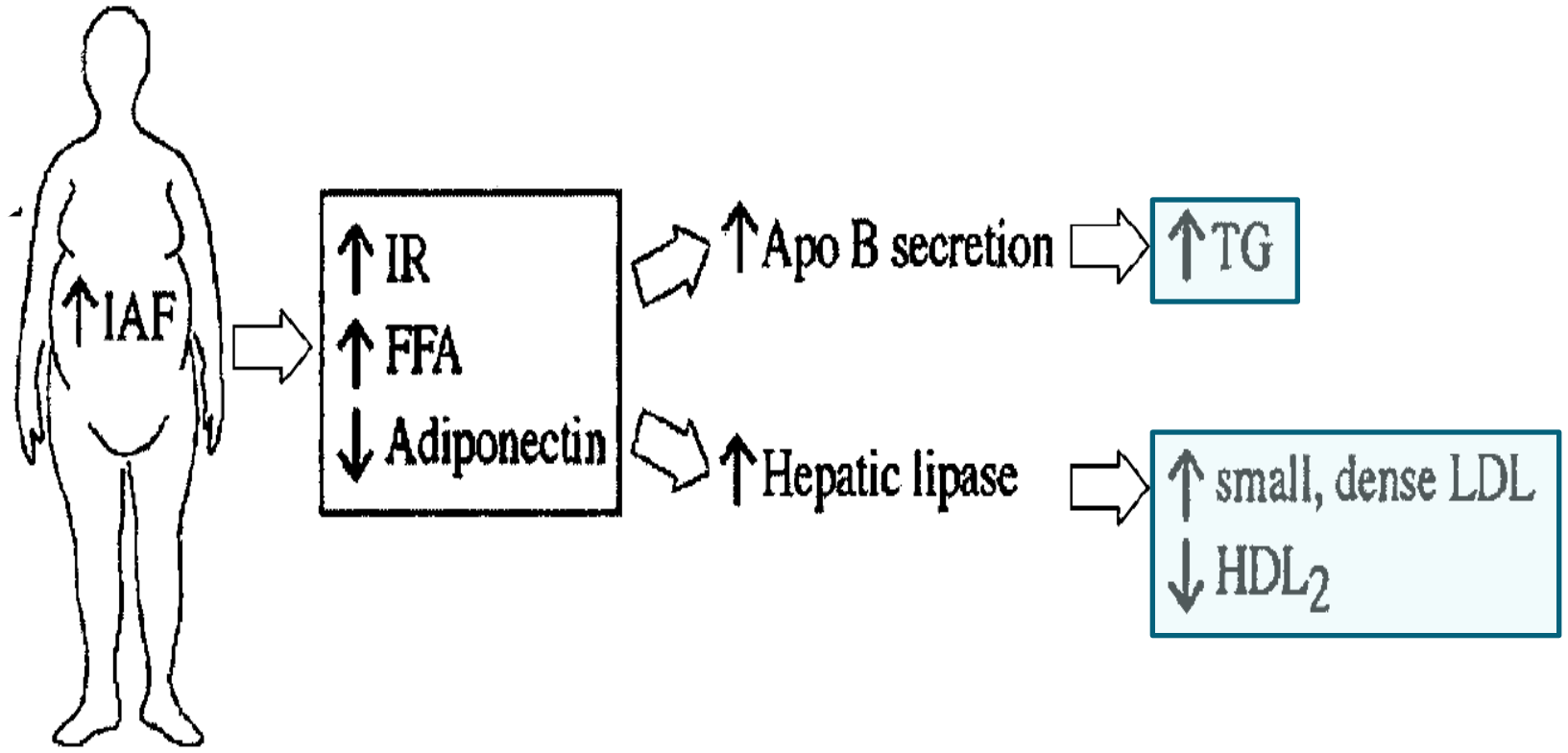
Rol de AG libres en la insulinorresistencia





Turgeon J. et al. Endocrine Review, Junio 2006

AUMENTO DE GRASA ANDROIDE



J Clin Endocrinol Metab 2003;88:2404

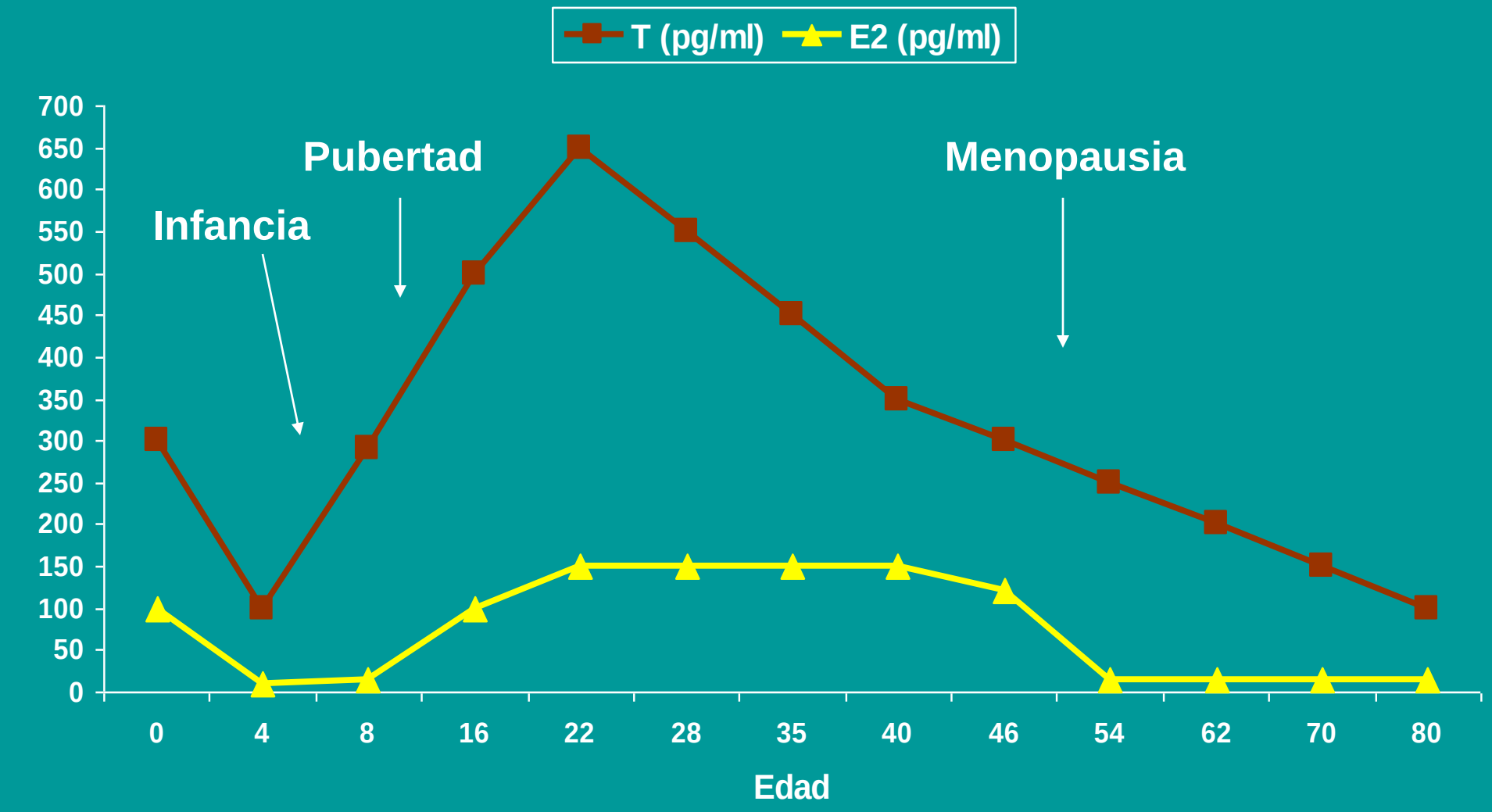
“Body fat mass and lean mass distribution in a group of pre and postmenopausal women”

Centros de Endocrinología del Hospital Francés y Hospital Churruca-Visca

THE ENDOCRINE SOCIETY´S 88th ANNUAL MEETING. ENDO 2006.BOSTON.

	Pre-menopausal (n=15)	*Post-menopausal (n=35)*	P
Age	37.4 ± 5.92	55.62 ± 4.95	<0.0001
YSM	---	6,59 ± 5,24	---
BMI (kg/m^2)	23.6 ± 6.28	25.78 ± 4.09	ns
BMD (g/cm^2)	1.121 ± 0.067	1.096 ± 0.081	ns
%Fat Mass (FM)	31.68 ± 10.59	38.26 + 6.21	<0.05
TFM (g)	19505 ± 12298	23673 ± 7484	ns
TLM (g)	38244 ± 5623	36891 ± 3466	ns
% Central FM	33.72 ± 11	41.34 ± 6.3	<0.05
Central FM (g)	4784 ± 3283	6188 ± 2207	ns
Central LM (g)	8340 ± 1267	8391 ± 1088	ns
% Peripheral FM	34.74 ± 10.11	39.41 ± 7.11	ns
Peripheral FM (g)	7352 ± 3854	8150 ± 2702	ns
Peripheral LM (g)	12951 ± 2221	12058 ± 1261	ns
C/P fat mass	0.62 ± 0.12	0.75 ± 0.22	<0.02
C/P lean mass	0.65 ± 0.08	0.67 ± 0.14	ns

Cambios Relacionados a la Edad



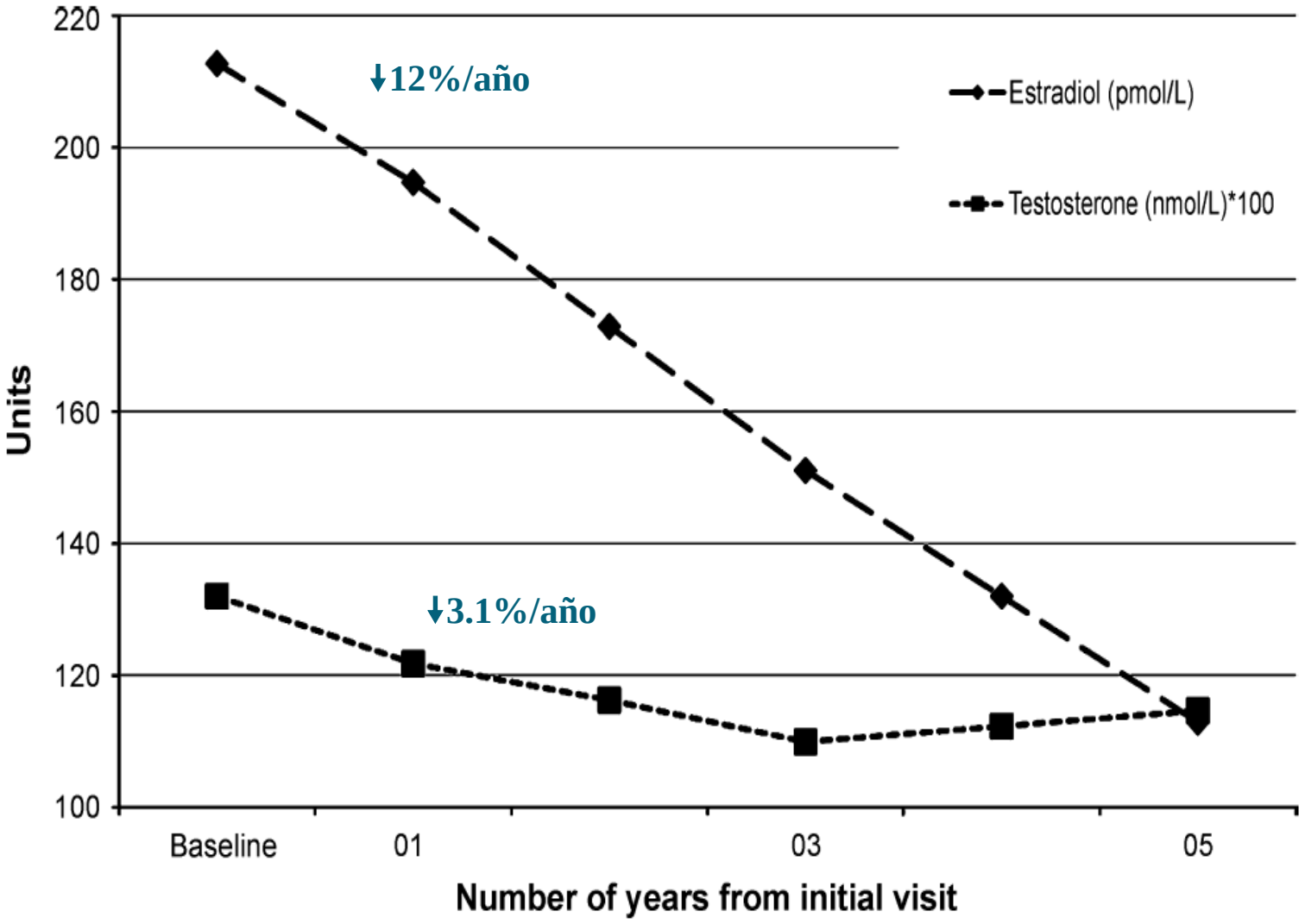
- La tasa de declinación de la Testosterona se relaciona con la edad. No se asocia con la menopausia.

Relative androgen excess during the menopausal transition predicts incident metabolic syndrome in midlife women: Study of Women's Health Across the Nation

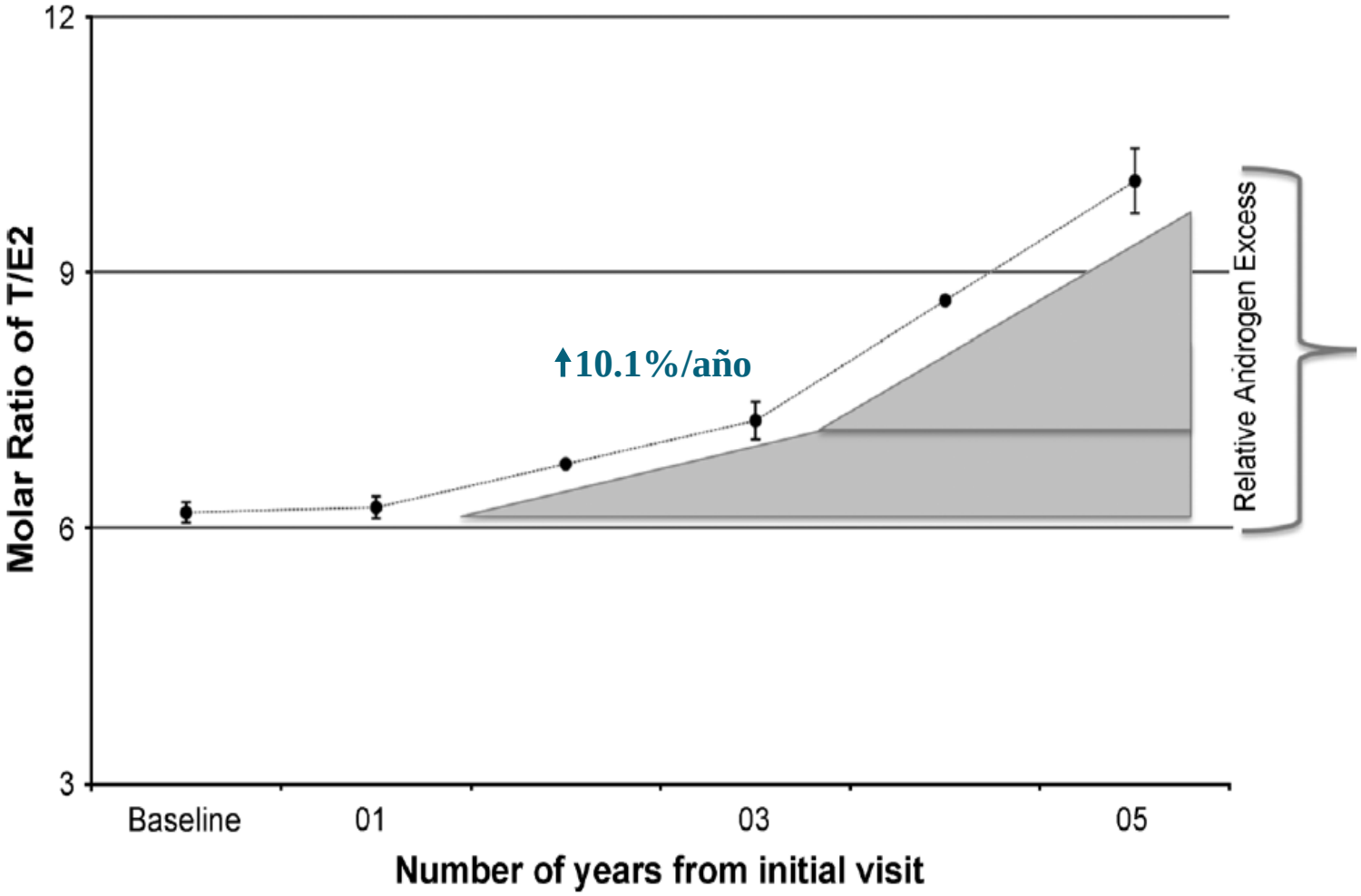
Javier I. Torréns, MD,[1] Kim Sutton-Tyrrell, PhD,[2] Xinhua Zhao, PhD,[2] Karen Matthews, PhD,[2] Sarah Brockwell, PhD,[2] MaryFran Sowers, PhD,[3] and Nanette Santoro, MD[4]

Se evaluaron los datos prospectivos de 1862 mujeres pre o perimenopáusicas tempranas del estudio SWAN, con muestras basales y 1- 3 y 5 años del seguimiento para valorar si cambios en la relación T/E2 en la transición predicen SM.

Menopause 2009;16(2):257-264



Menopause 2009;16(2):257-264

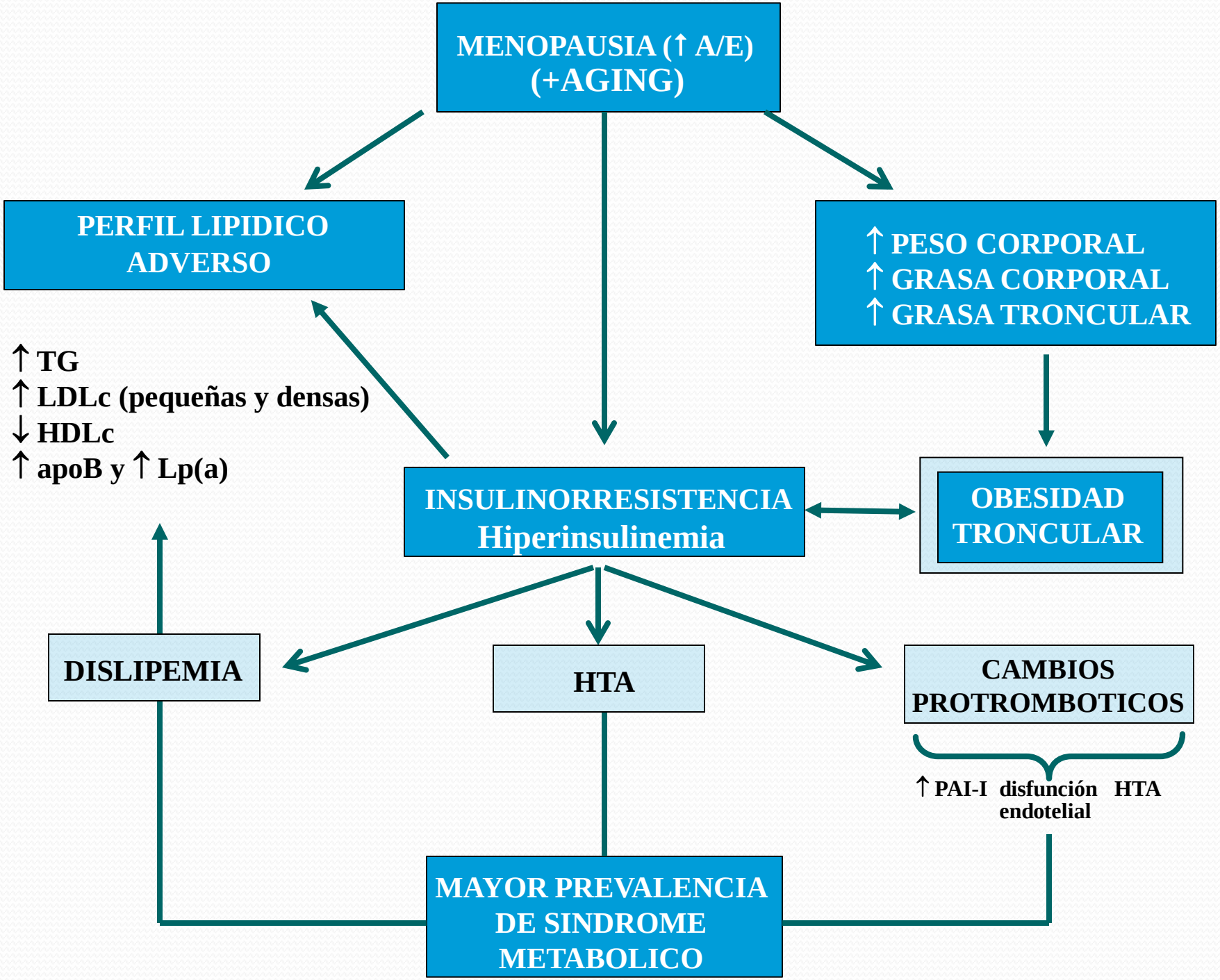


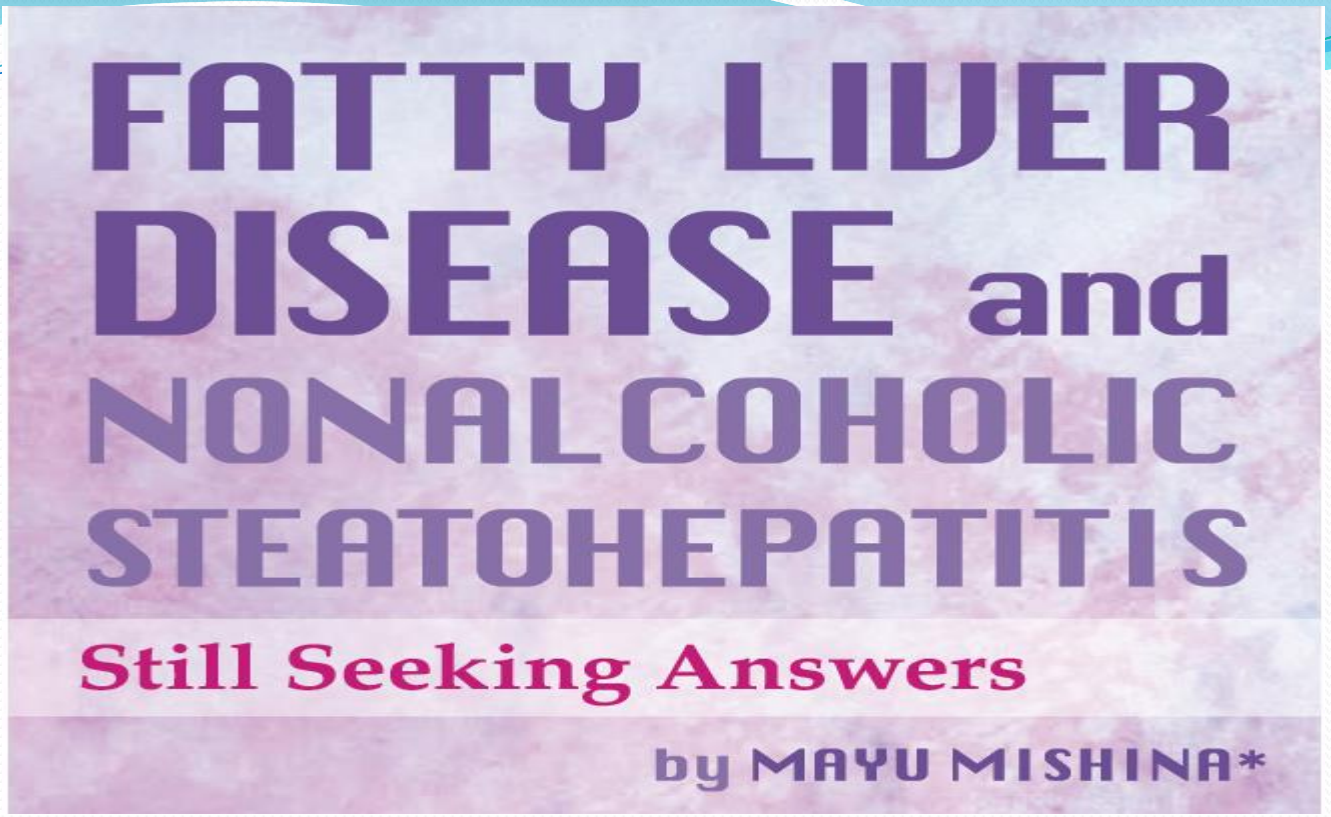
Menopause 2009;16(2):257-264

TABLE 3. *Results from multivariate models*

Models	Baseline hormone		Change in hormone from baseline	
	Risk ratio (95% CI)	*P*	Risk ratio (95% CI)	*P*
Model 1: E_2	0.85 (0.69-1.05)	0.13	0.90 (0.73-1.11)	0.32
Model 2: T	2.04 (1.45-2.86)	<0.001	1.28 (0.81-2.02)	0.29
Model 3: SHBG	0.58 (0.48-0.70)	<0.001	0.80 (0.58-1.10)	0.20
Model 4: FAI	1.77 (1.50-2.09)	<0.001	1.22 (0.93-1.60)	0.16
Model 5: RAE	1.41 (1.17-1.69)[a]	0.001	1.24 (1.01-1.52)	0.04

Menopause 2009;16(2):257-264


MENOPAUSIA (↑ A/E)
(+AGING)
PERFIL LIPIDICO
ADVERSO
↑ PESO CORPORAL
↑ GRASA CORPORAL
↑ GRASA TRONCULAR
↑ TG
↑ LDLc (pequeñas y densas)
↓ HDLc
↑ apoB y ↑ Lp(a)
INSULINORRESISTENCIA
Hiperinsulinemia
OBESIDAD
TRONCULAR
DISLIPEMIA
HTA
CAMBIOS
PROTROMBOTICOS
↑ PAI-I
disfunción
endotelial
HTA
MAYOR PREVALENCIA
DE SINDROME
METABOLICO



ESTEATOSIS HEPATICA NO ALCOHOLICA O NAFLD:

Se ve en el 71% de pacientes con SM.

Si bien NAFLD es un desorden benigno, 10% desarrollan daño hepático y severa inflamación con NASH (Esteatohepatitis no alcohólica). Más del 20% de NASH progresan a Cirrosis.

La secuencia de progresión es:

Hígado normal → ***NAFLD*** → ***NASH*** → ***Cirrosis***

Endocrine News September 2009:19-20

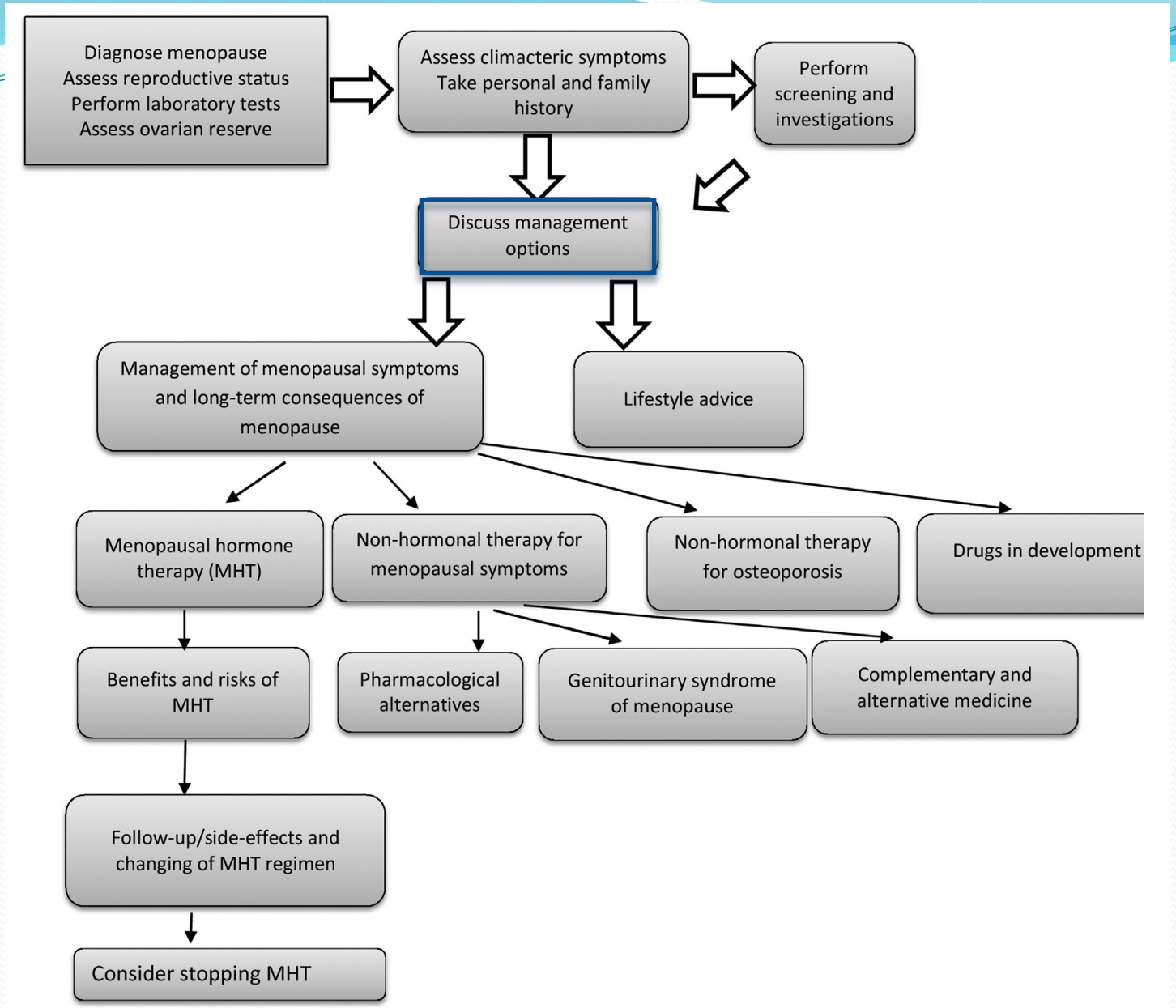


Fig. 1. A care pathway for the maintenance of women's postreproductive health.

Ante esta paciente nos preguntamos:

1-¿En que estadío del aging reproductivo se encuentra?

2-¿Cuál es el diagnóstico de la paciente desde el punto de vista metabólico?

3-¿Cuál cree que es la mejor aproximación terapéutica en esta paciente?

La paciente presenta diagnóstico de:

- **“Sindrome metabólico”**
- **Alteraciones del ciclo y sofocos leves**

“La paciente debería ser tratada conjuntamente por el médico clínico o el endocrinólogo por la coexistencia de sindrome metabólico”

- **Primary intervention**

IDF recommends that primary management for the metabolic syndrome is healthy lifestyle promotion. This includes:

  - moderate calorie restriction (to achieve a 5–10 per cent loss of body weight in the first year)
  - moderate increase in physical activity
  - change in dietary composition

The results of Finnish and American prevention of diabetes studies have shown the marked clinical benefits associated with a small weight loss in terms of preventing (or at least delaying by several years) the conversion to type 2 diabetes among high-risk individuals with glucose intolerance who were, generally, obese.[12,13]

- **Secondary intervention**

In people for whom lifestyle change is not enough and who are considered to be at high risk for CVD, drug therapy may be required to treat the metabolic syndrome. While there is a definite need for a treatment that can modulate the underlying mechanisms o the metabolic syndrome as a whole and thereby reduce the impact of all the risk factors and the long term metabolic and cardiovascular consequences, these mechanisms are currently unknown and specific pharmacological agents are therefore not yet available. As defined in Table 4, it is currently necessary instead to treat the individual components of the syndrome in order that a reduction in the individual risk associated with each one will reduce the overall impact on CVD and diabetes risk.

IDF Consensus, 2005

Metabolic Syndrome

David W Lam and Derek LeRoith, M.D., PhD.

Lifestyle modification is perhaps the most important intervention in treatment of MetS. The Diabetes Prevention Program demonstrated that lifestyle intervention reduced the incidence of MetS by 41% compared with placebo. The intensive lifestyle intervention involved a healthy low-calorie, low fat diet and moderate physical activity of at least 150 minutes/week, resulting in a weight reduction of 7% (230). The recommended diet should include < 200 mg/day of cholesterol, < 7% saturated fat, with total fat comprising 25-35% of calories, low simple sugars and increased fruits, vegetables and whole grains(11). Smoking cessation should be instituted in all patients with MetS. Additionally, low dose aspirin is recommended in cases of moderate to high cardiovascular risk where no contraindication to aspirin therapy exists (11).

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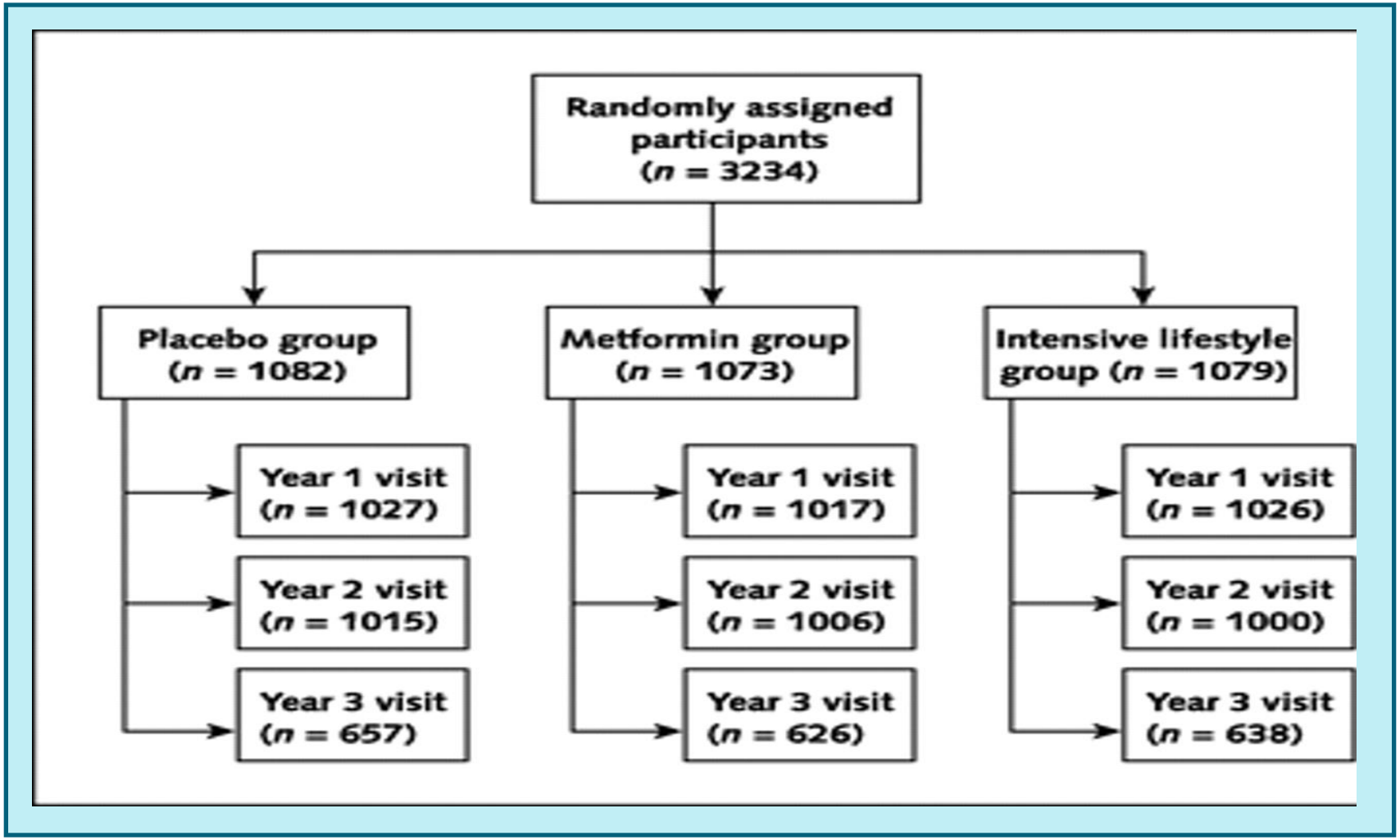
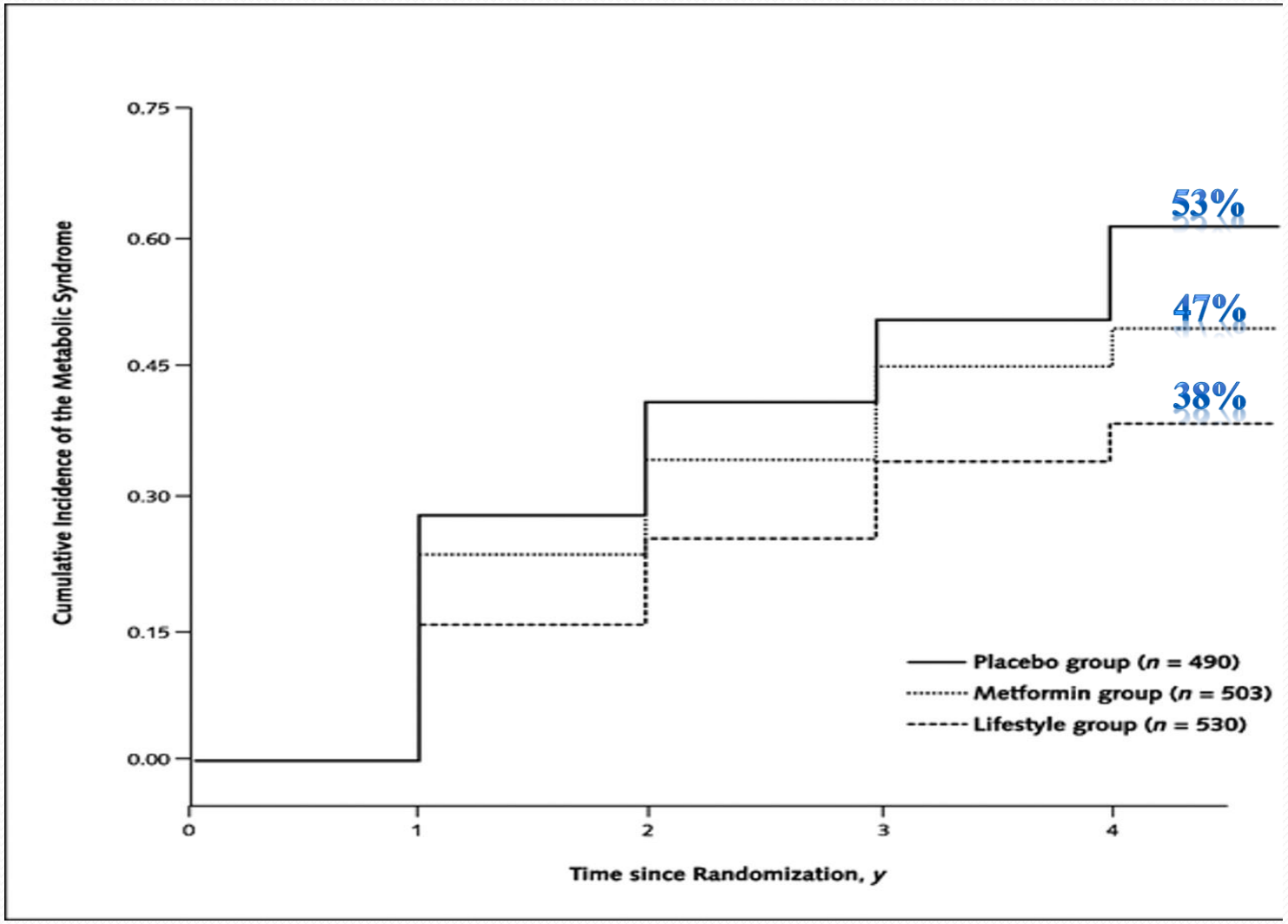
Last Update: May 19, 2015.

The Effect of Metformin and Intensive Lifestyle Intervention on the Metabolic Syndrome: The Diabetes Prevention Program Randomized Trial



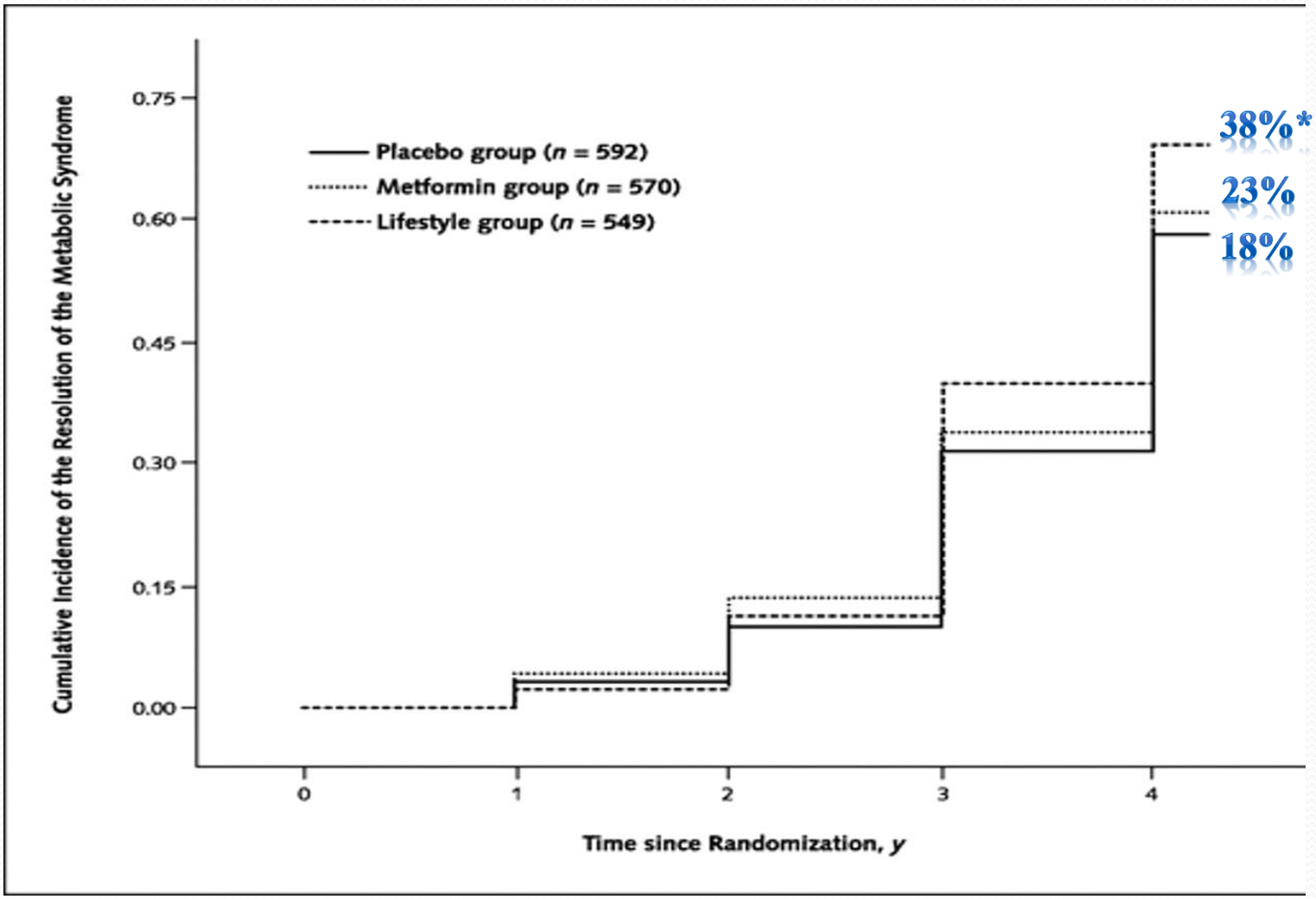
Orchard, T. J. et. al. Ann Intern Med 2005;142:611-619

Development of the metabolic syndrome by intervention group in the Diabetes Prevention Program



Orchard, T. J. et. al. Ann Intern Med 2005;142:611-619

Resolution of the metabolic syndrome by intervention group in the Diabetes Prevention Program



Orchard, T. J. et. al. Ann Intern Med 2005;142:611-619

The Effect of Metformin and Intensive Lifestyle Intervention on the Metabolic Syndrome: The Diabetes Prevention Program Randomized Trial

Los cambios de estilo de vida provocaron reducción de TODOS los factores de riesgo simultaneamente del síndrome metabólico (SM) y es la conducta que más efecto benéfico a largo plazo ofrece.

Orchard, T. J. et. al. Ann Intern Med 2005;142:611-619

Table 4: IDF recommended treatment of the individual components of the metabolic syndrome

Atherogenic dyslipidaemia
Primary aims for therapy: • Lower TG (as well as lowering ApoB and non-HDL cholesterol) • Raise HDL-c levels • Reduce LDL-c levels (elevated levels represent a high risk in the metabolic syndrome) Options: • Fibrates (PPAR alpha agonists) improve all components of atherogenic dyslipidaemia and appear to reduce the risk for CVD in people with metabolic syndrome. The Veterans Affairs High-Density Lipoprotein Intervention Trial (VA-HIT) showed that raising HDL-c concentrations using a fibrate in patients with well-established CHD and both a low HDL-c and a low LDL-c level will significantly reduce the incidence of major coronary events.[8] • Statins to reduce all ApoB-containing lipoproteins and to achieve ATP III goals for LDL-c as well as for non-HDL-c (ATP III, 2001). Several clinical studies have confirmed the benefits of statin therapy.[14–16]

IDF Consensus, 2005

- Fibrates in combination with statins but may be complicated by side effects

Elevated blood pressure

- Categorical hypertension (BP ≥ 140/≥ 90 mm Hg) should be treated according to the USA Seventh Report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure (JNC 7) recommendations.[17]
- In patients with established diabetes, antihypertensive therapy should be introduced at BP ≥ 130/≥ 80 mm Hg.

Options:

- Angiotensin converting enzyme inhibitors and angiotensin receptor blockers are useful antihypertensive drugs, with some clinical trials (but not all) suggesting they carry advantages over other drugs in patients with diabetes. At this time, however, the majority of clinical trials suggest that the risk reduction associated with antihypertensive drugs is the result of blood pressure lowering per se and not due to a particular type of drug.
- No particular agents have been identified as being preferable for hypertensive patients who also have the metabolic syndrome.

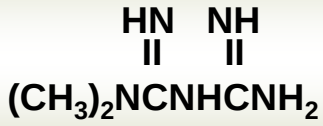
Insulin resistance and hyperglycaemia

There is growing interest in the possibility that drugs that reduce insulin resistance will delay the onset of type 2 diabetes and will reduce CVD risk when metabolic syndrome is present. The Diabetes Prevention Program (DPP) showed that metformin therapy in patients with prediabetes will prevent or delay the development of diabetes and recent thiazolidinedione studies have also demonstrated efficacy in delaying or preventing type 2 diabetes in patients with impaired glucose tolerance (IGT) and insulin resistance.[18,19,20] Similarly, other studies have shown that both acarbose and orlistat can be used to delay the development of type 2 diabetes in patients with IGT.[21,22]

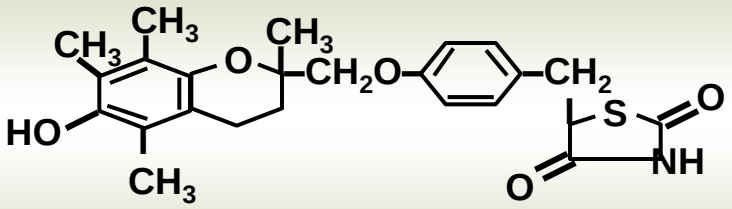
Data do not yet exist to show whether any of the currently available thiazolidinediones reduce the risk of CVD in those with the metabolic syndrome, IGT or diabetes.

INSULINOSENSIBILIZADORES

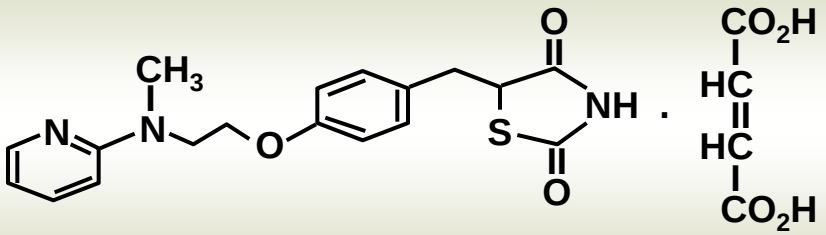
Metformin



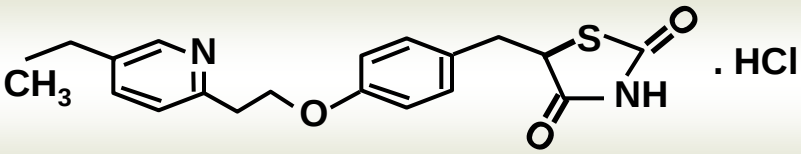
Troglitazone



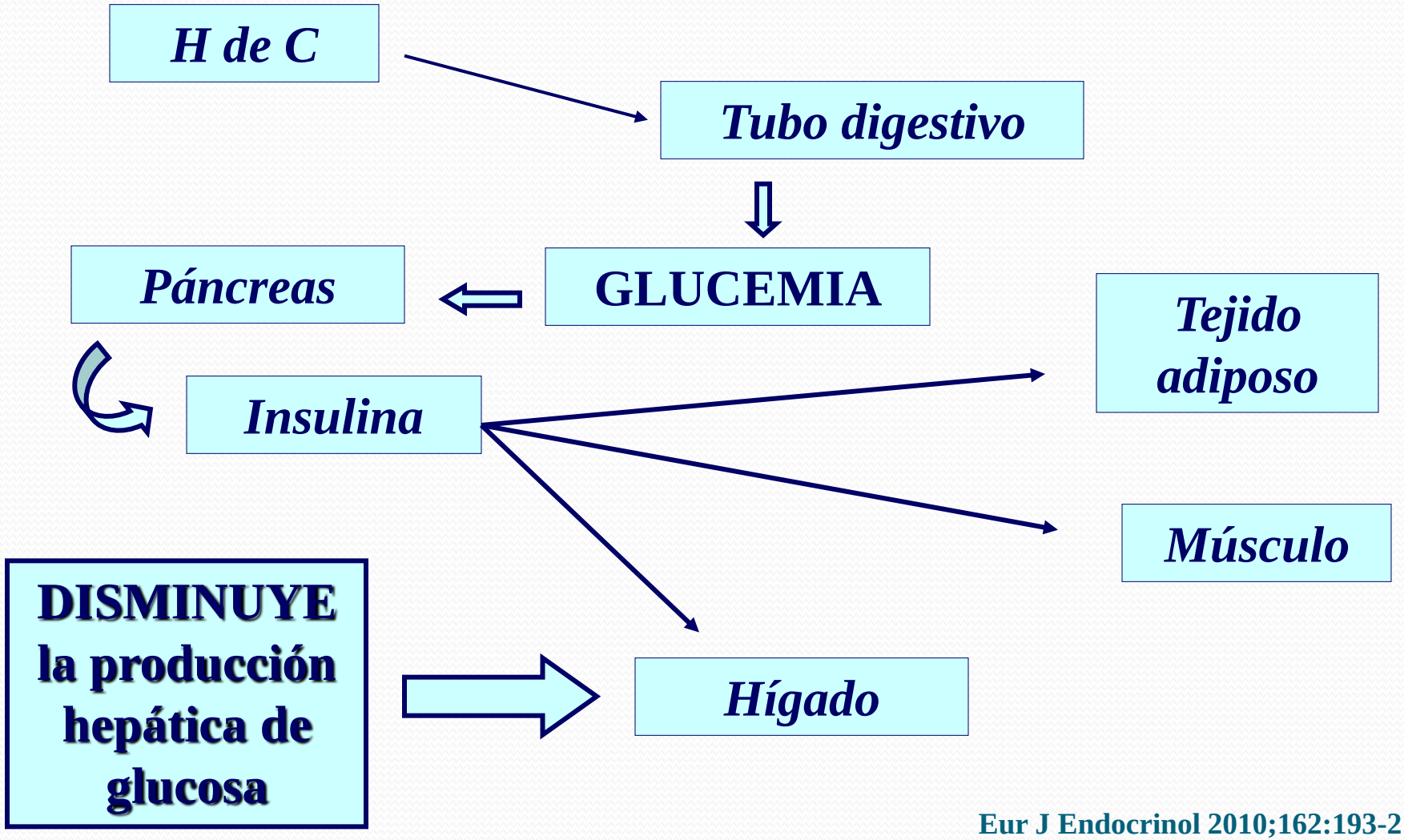
Rosiglitazone



Pioglitazone



Metformina: sitio de acción



Eur J Endocrinol 2010;162:193-212

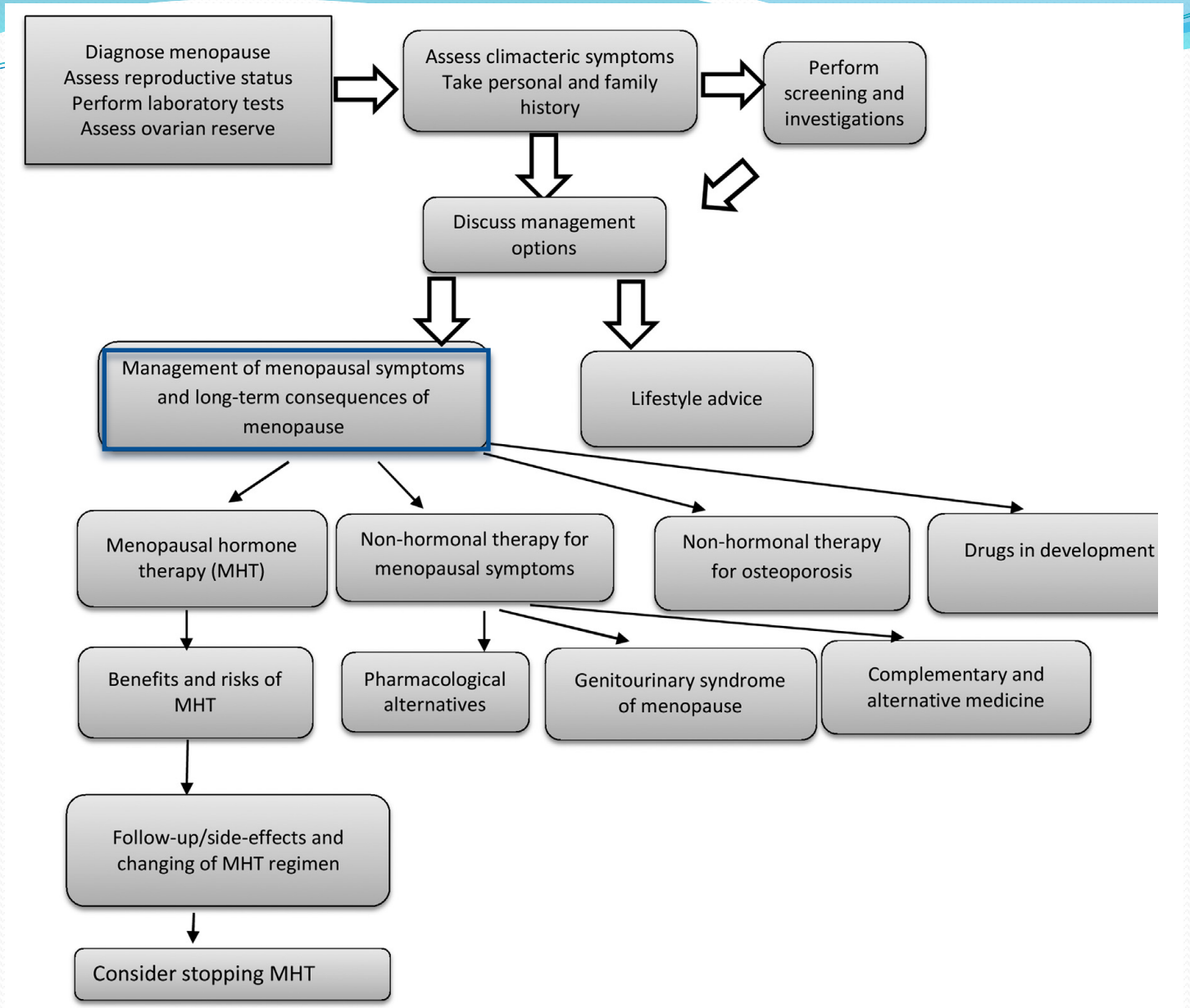


Fig. 1. A care pathway for the maintenance of women's postreproductive health.

2016 IMS Recommendations on women's midlife health and menopause hormone therapy

R. J. Baber, N. Panay & A. Fenton the IMS Writing Group

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To link to this article: http://dx.doi.org/10.3109/13697137.2015.1129166

IMS governing principles on MHT

- MHT remains the most effective therapy for vasomotor symptoms and urogenital atrophy.

- Consideration of MHT should be part of an overall strategy including lifestyle recommendations regarding diet, exercise, smoking cessation and safe levels of alcohol consumption for maintaining the health of peri- and postmenopausal women.

Climateric 2016;19(2):109-150

- MHT must be individualized and tailored according to symptoms and the need for prevention, as well as personal and family history, results of relevant investigations, the woman's preferences and expectations.

- The risks and benefits of MHT differ for women during the menopause transition compared to those for older women.

Climateric 2016;19(2):109-150

Treatment of Symptoms of the Menopause: An Endocrine Society Clinical Practice Guideline

Cynthia A. Stuenkel, Susan R. Davis, Anne Gompel, Mary Ann Lumsden, M. Hassan Murad, JoAnn V. Pinkerton, and Richard J. Santen

University of California, San Diego, Endocrine/Metabolism (C.A.S.), La Jolla, California 92093; Monash University, School of Public Health and Preventive Medicine (S.R.D.), Melbourne 03004, Australia; Université Paris Descartes, Hôpitaux Universitaires Port Royal-Cochin Unit de Gynécologie Endocrnienne (A.G.), Paris 75014, France; University of Glasgow School of Medicine (M.A.L.), Glasgow G31 2ER, Scotland; Mayo Clinic, Division of Preventive Medicine (M.H.M.), Rochester, Minnesota 55905; University of Virginia, Obstetrics and Gynecology (J.V.P.), Charlottesville, Virginia 22908; and University of Virginia Health System (R.J.S.), Charlottesville, Virginia 22903

J Clin Endocrinol Metab 2015;100(11):3975-4011

3.0 Hormone therapy for menopausal symptom relief

3.1 Estrogen and progestogen therapy

3.1a For menopausal women < 60 years of age or < 10 years past menopause with bothersome VMS (with or without additional climacteric symptoms) who do not have contraindications or excess cardiovascular or breast cancer risks and are willing to take menopausal hormone therapy (MHT), we suggest initiating estrogen therapy (ET) for those without a uterus and estrogen plus progestogen therapy (EPT) for those with a uterus. (2⊕⊕◯◯)

J Clin Endocrinol Metab 2015;100(11):3975-4011

Cardiovascular risk

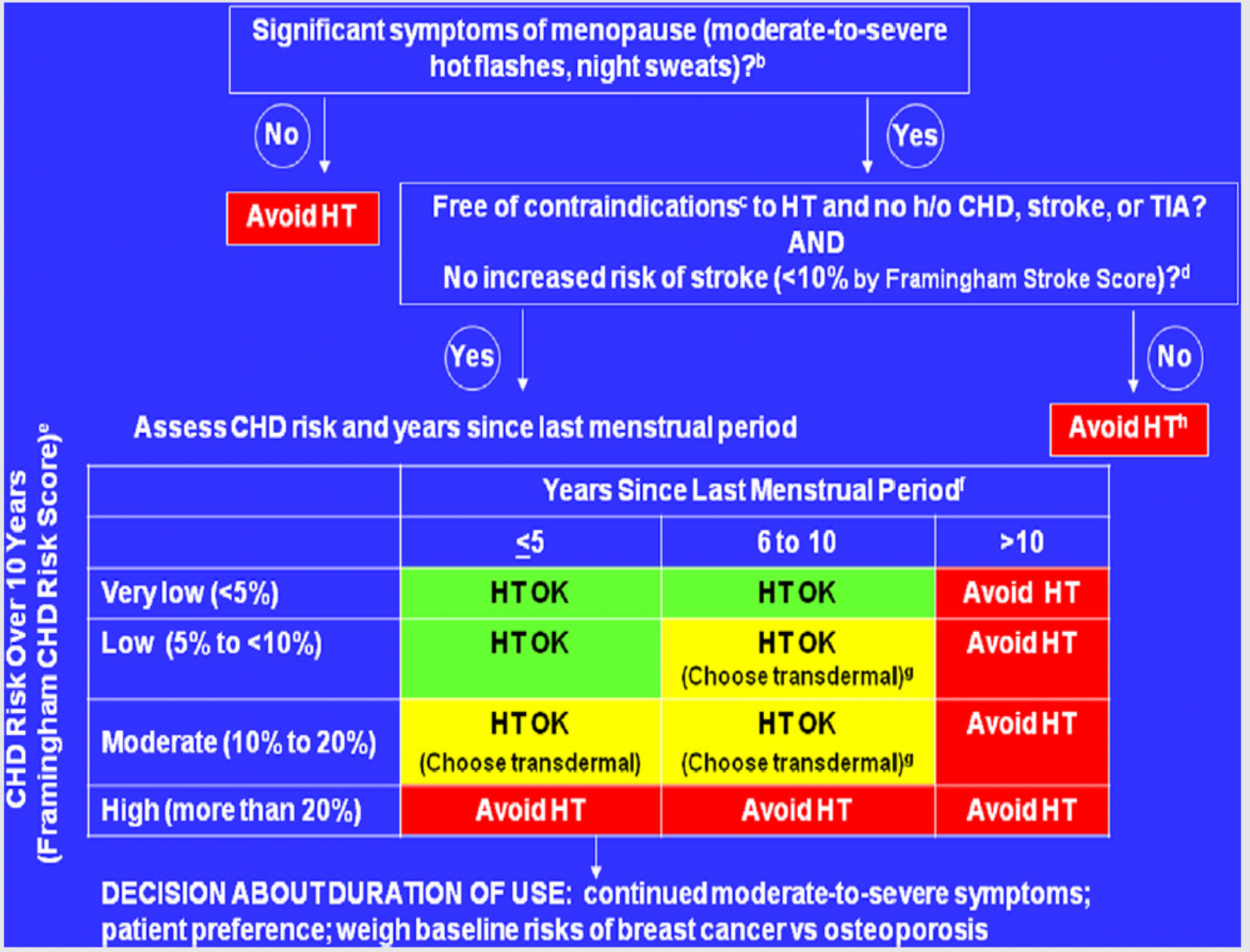
3.1b For women < age 60 or < 10 years past menopause onset considering MHT for menopausal symptom relief, we suggest evaluating the baseline risk of cardiovascular disease (CVD) and taking this risk into consideration when advising for or against MHT and when selecting type, dose, and route of administration. (2|⊕⊕◯◯)

3.1c For women at high risk of CVD, we suggest initiating nonhormonal therapies to alleviate bothersome VMS (with or without climacteric symptoms) over MHT. (2|⊕⊕◯◯)

J Clin Endocrinol Metab 2015;100(11):3975-4011

3.1d For women with moderate risk of CVD, we suggest transdermal estradiol as first-line treatment, alone for women without a uterus or combined with micronized progesterone (or another progestogen that does not adversely modify metabolic parameters) for women with a uterus, because these preparations have less untoward effect on blood pressure, triglycerides, and carbohydrate metabolism. (2⊕⊕◯◯)

J Clin Endocrinol Metab 2015;100(11):3975-4011



Fertil Steril 2014;101(4):916-921

Coronary heart disease events in the Women's Health Initiative hormone trials: effect modification by metabolic syndrome: A nested case-control study within the Women's Health Initiative randomized clinical trials

Robert A. Wild, MD, MPH, PhD,[1] Chunyuan Wu, MS,[2] J. D. Curb, MD, MPH,[3]† Lisa W. Martin, MD,[4] Lawrence Phillips, MD,[5] Marcia Stefanick, PhD,[6] Maurizio Trevisan, MD,[7] and JoAnn E. Manson, MD, DrPH[8]

Conclusions: MetS at baseline in women without prior cardiovascular disease, diabetes, or hypertension at baseline identifies women who are more likely to have had adverse coronary outcomes on HT. CHD risk stratification is recommended before initiating HT. The basis for the greater risk of CHD events with HT among women with MetS requires further study.

Menopause 2013;20(3):254-260

SINDROME METABOLICO Y RIESGO DE EVENTOS CORONARIOS:

- **En WHI combinado (E y E/P): 1.29**
  - **Sin SM: 0.97**
  - **Con SM: 2.26**
- **WHI E-P: 1.42**
  - **Sin SM: 1.13**
  - **Con SM: 2.26**
- **WHI E: 1.15**
  - **Sin SM: 0.62**
  - **Con SM: 1.66**

Menopause 2013;20(3):254-260

Effect of menopausal hormone therapy on components of the metabolic syndrome

Dragana Lovre, Sarah H. Lindsey and Franck Mauvais-Jarvis

Ther Adv Cardiovasc Dis 2016;DOI:10.1177

Table 1. Summary of RCTs.

Trial	Study Design	Population	Number of subjects	Hormone therapy	Effect on adiposity	Effect on lipids	Effect on blood pressure	Effect on glucose homeostasis
PEPI [Miller *et al.* 1995]	3-year RCT	Postmenopausal women aged 45–64 years, mean weight 68–74 kg	875	(1) Placebo; (2) CE 0.625 mg; (3) CE, 0.625 mg plus cyclic MPA 10 mg for 12 days/month; (4) CE, 0.625 mg plus consecutive MPA, 2.5 mg; or (5) CE, 0.625 mg plus cyclic MP 200 mg for 12 days/month.	↑Weight, less weight gain with HRT	↓LDL ↑TG ↑HDL	↔SBP ↔DBP	↓FBG, ↓Fasting Insulin
HERS [Kanaya *et al.* 2003]	4. 1 year RCT	Postmenopausal women with known heart disease, age 67 ± 7 years, mean BMI 28.6 ± 5.5, WC 92 ± 13 cm	2763	Placebo or CE 0.625 mg + MPA2.5 mg	↓Weight, ↓WC, ↓WHR	↓LDL ↑TG ↑HDL	↔BP	35% lower risk for diabetes
WHI [Margolis *et al.* 2004]	5.2 year RCT	Postmenopausal women aged 50 –79 years, mean BMI 28.5	16,608	Placebo or CE0.625mg	↓BMI and ↓WC	↓LDL ↑TG ↑HDL	↑SBP by 1–2 mmHg, ↔DBP	↓FBG, ↓IR 21% lower risk for diabetes
DOPS [Jensen *et al.* 2003]	5-year RCT	Postmenopausal women aged 45–58 years, mean BMI 25± 4.3	2016	Estradiol 2 mg and Norethisterone acetate 1 mg	↓ Gain of FM	N/A	N/A	N/A
SMART-1 [Lobo *et al.* 2009]	2-year ACT	Postmenopausal women, age 40 - 75years, mean BMI 25± 3.5	3397	Placebo; BZA (10, 20, or 40 mg) each with CE (0.625 or 0.45 mg);or raloxifene 60 mg	See Section 4 of the text.	↓LDL ↑TG ↑HDL	See Section 4 of the text.	See Section 4 of the text.

RCT, randomized controlled trial; ACT, active controlled trial; HRT, hormone replacement therapy; CEE, conjugated equine estrogen; CE, conjugated estrogen; MPA, medroxyprogesterone acetate; MP, micronized progesterone; BZA, bazedoxifene; FM, fat mass; WC, waist circumference; FBG, fasting blood glucose; IR, insulin resistance; WHR, waist-to-hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglycerides; BMI, body mass index; ↑, increased; ↓, decreased; ↔ , no effect.
WHI, Women's Health Initiative; HERS, Heart and Estrogen/Progestin Replacement Study; PEPI, The Postmenopausal Estrogen/Progestin Interventions; SMART-1, Selective estrogens, Menopause, And Response to Therapy 1 trial; DOPS, The Danish Osteoporosis Prevention Study.

Meta-analysis: effect of hormone-replacement therapy on components of the metabolic syndrome in postmenopausal women

S. R. Salpeter,[1,2] J. M. E. Walsh,[3] T. M. Ormiston,[2] E. Greyber,[2] N. S. Buckley[4] and E. E. Salpeter[5]

Meta-análisis de los estudios randomizados, controlados, de al menos 8 semanas de duración, publicados entre Abril de 1996 y Octubre del 2004, que evaluaron efecto de la T.H. sobre los distintos componentes del SM en mujeres postmenopáusicas sin DM2.

Diabetes, Obesity Metabol 2006;8:538-554

TH comparando con placebo o ausencia de tratamiento:

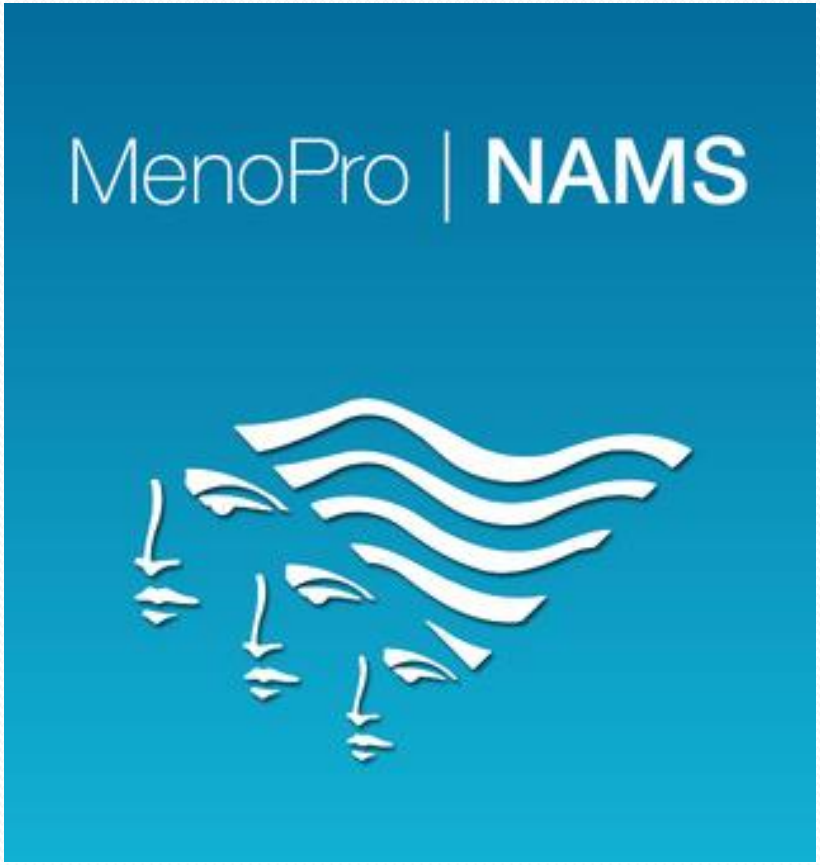
- ↑HDLc 5.1%
- ↓LDLc 11%
- ↓relación LDL/HDL 15.7%
- ↓Lp(a) 25%
- ↑TG 2.1% (no significativo)
- Reducción de la grasa abdominal (6.8%)
- Descenso de IR (12.9%)
- Mejoría del perfil lipídico, de moléculas de adhesión y descenso de factores procoagulantes
- Descenso de la T.A.
- Descenso del número de casos nuevos de DM2

Diabetes, Obesity Metabol 2006;8:538-554

Table 1 Results for hormone-replacement therapy (HRT) combined, and for transdermal and oral agents, in women without known diabetes

Outcome	HRT – all agents (%)	Transdermal agents (%)	Oral agents (%)	p for interaction
HOMA-IR	−12.9* (−4.9 to −13.7)	−6.8 (−17 to 3.5)	−13.5* (−18.3 to −8.8)	NS
LDL/HDL	−11.0* (−12.3 to −9.6)	−8.4* (−13.8 to −2.8)	−17.4* (−20.0 to −14.9)	0.004*
Triglycerides	2.1 (−0.6 to 4.8)	−6.5 (−14.7 to 1.8)	6.0* (4.3 to 7.6)	0.004*
Lp(a)	−25.0* (−32.9 to −17.1)	−22.8* (−44.4 to −1.2)	−25.1* (−33.2 to −17.1)	NS
Mean BP	−1.7* (−2.9 to −0.5)	−0.8 (−3.3 to 1.6)	−2.2* (−4.1 to −0.3)	NS
CRP	37.7* (17.4 to 61.3)	2.0 (−23.0 to 34.0)	47.0* (29.0 to 67.0)	0.02*
E-selectin	−17.3* (−22.4 to −12.1)	−6.0 (−19.8 to 7.9)	−18.6* (−23.9 to −13.3)	NS
Fibrinogen	−5.5* (−7.8 to −3.2)	−4.7* (−7.6 to −1.8)	−5.8* (−8.7 to −2.8)	NS
PAI-1 antigen	−25.1* (−33.6 to −15.5)	−3.0 (−23.0 to 35.0)	−27.0* (−38.0 to −22.0)	0.03*
Protein C	−0.8 (−4.2 to 2.6)	−1.2 (−7.4 to 5.1)	−1.7 (−7.0 to 3.7)	NS
Protein S	−4.8 (−10.7 to 1.2)	−2.2 (−9.9 to 5.6)	−8.6* (−13.1 to −4.1)	0.01*

Diabetes, Obesity Metabol 2006;8:538-554



Endocrine News 2015;November:14-18

ON POINT FROM THE ENDOCRINE SOCIETY

"Postmenopausal Hormone Therapy: An Endocrine Society Scientific Statement" can be downloaded from: http://www.endocrine.org/endocrine-press/scientific-statements.

The Endocrine Society's Hormone Health Network offers an award-winning "Menopause Map" educational tool for patients: www.hormone.org/MenopauseMap.

Endocrine News 2015;November:14-18

Revamped **Menopause Map Now Online**

The Hormone Health Network (HHN) recently released a "new and improved" Menopause Map™, an updated interactive online tool that is essentially a one-stop source for all things relating to menopause.

This new site includes many new features implemented based on feedback from women:

- New and improved design
- Interactive e-magazine
- Print companion magazine
- Conversation starters
- Social media functionality
- Monthly E-newsletter with additional resources and tips
- Microsite with toolkit for health care providers

Endocrine News 2014; August:39

MUCHAS GRACIAS !!

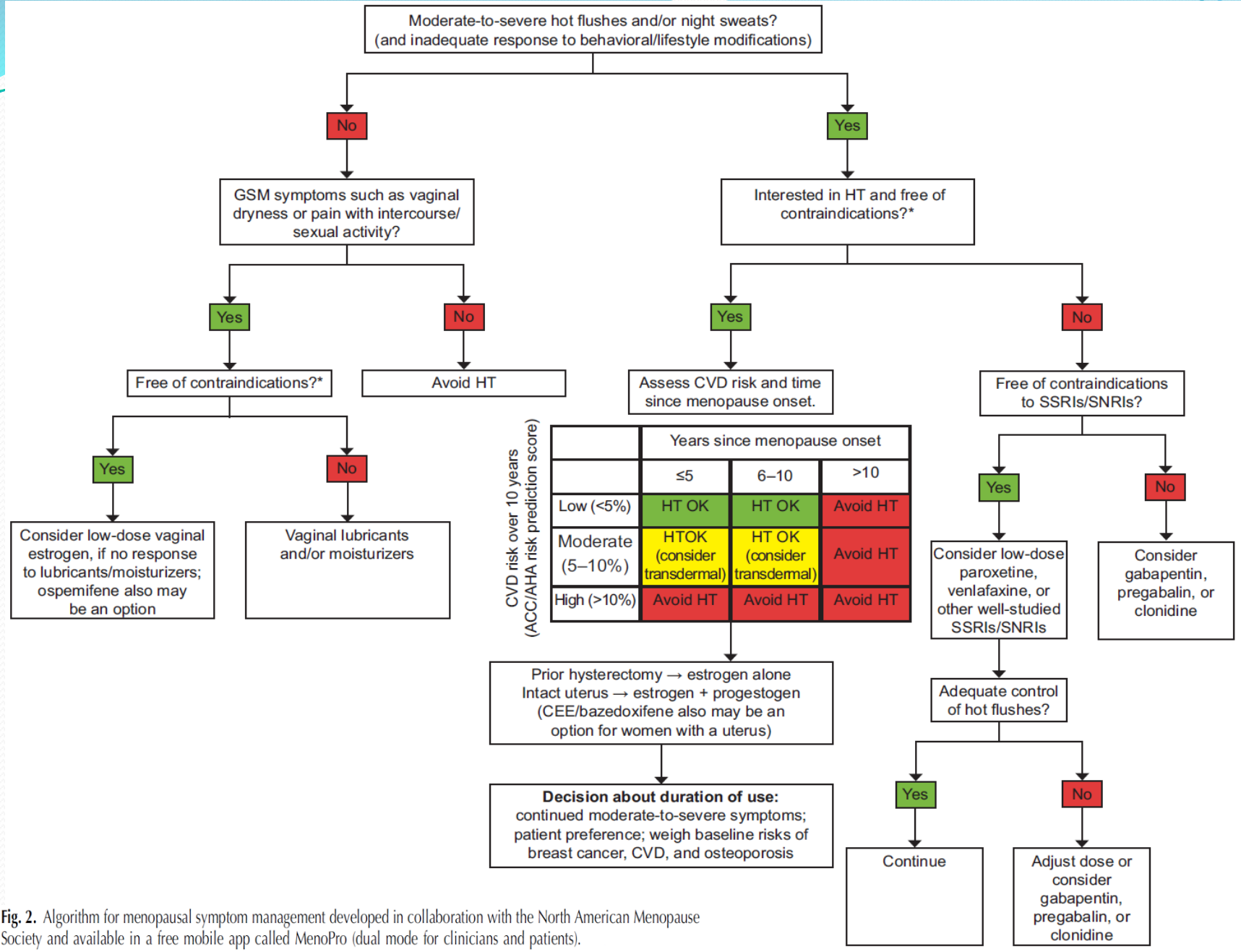


Fig. 2. Algorithm for menopausal symptom management developed in collaboration with the North American Menopause Society and available in a free mobile app called MenoPro (dual mode for clinicians and patients).

Obstet Gynecol 2015;126(4):859-876