The sex gap in cardiometabolic diseases: What we (don't) know and why it matters?

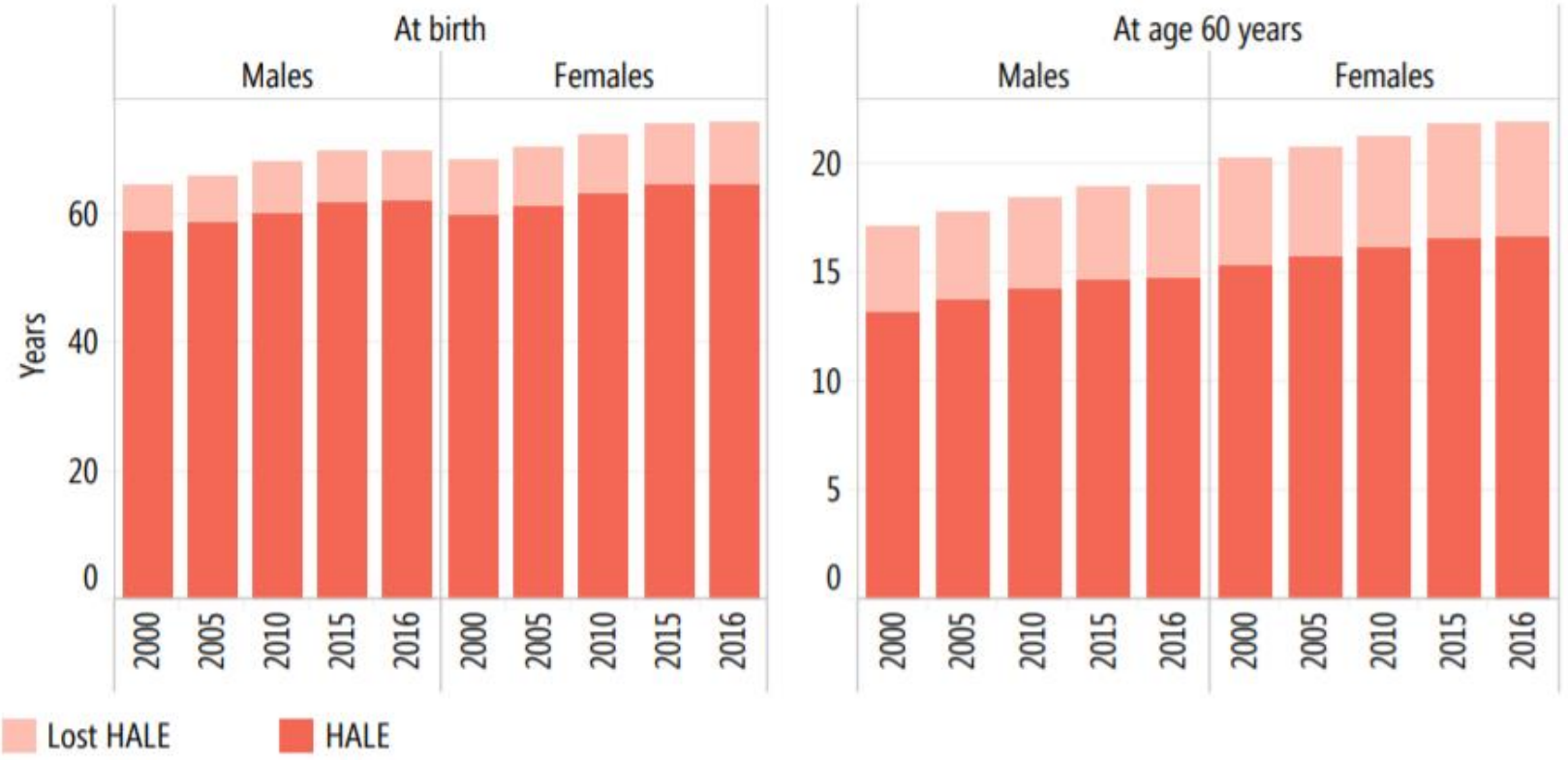
Assoc. Prof Taulant Muka, PD, MD, PhD

Institute of Social and Preventive Medicine (ISPM), University of Bern

taulant.muka@ispm.unibe.ch

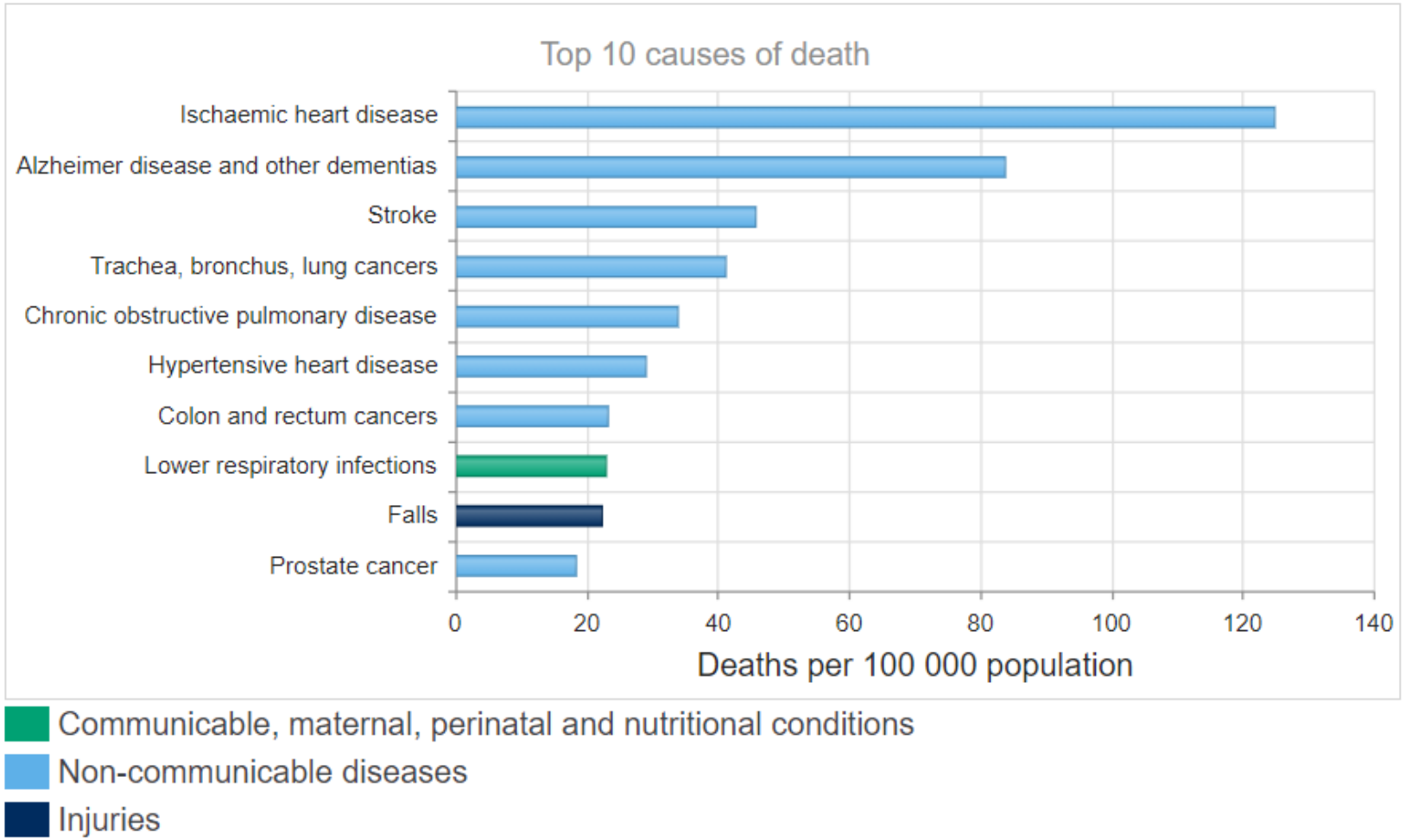
Life expectancy

Fig. 1.3
Global life expectancy and HALE, 2000–2016



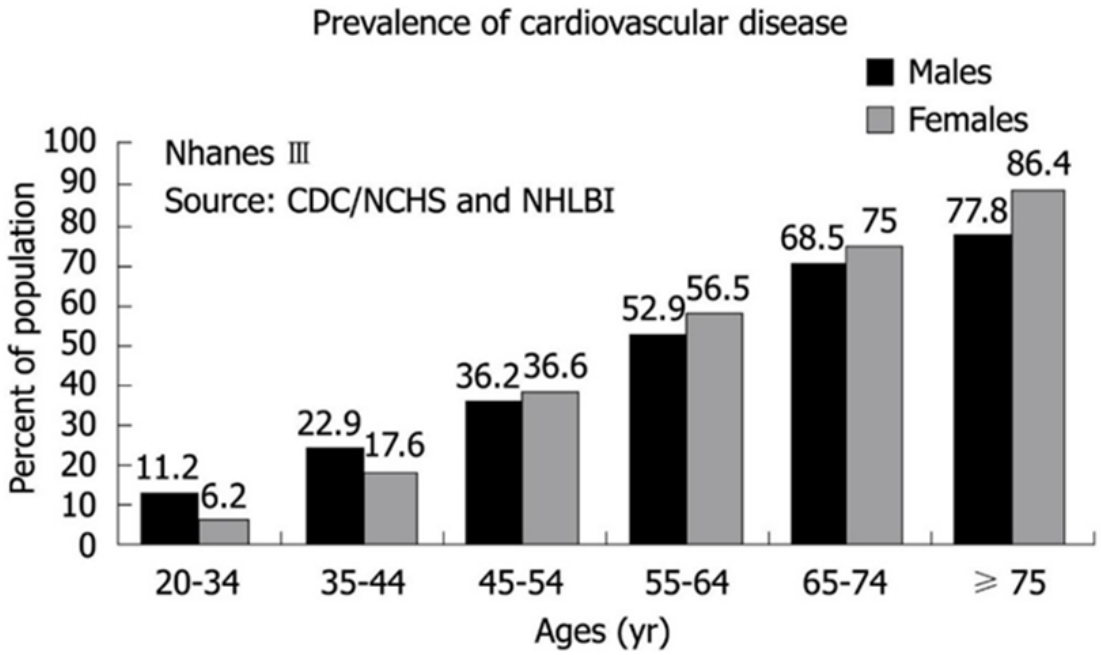
Source: WHO (2018) *(2)*.

Top 10 causes of death, Switzerland



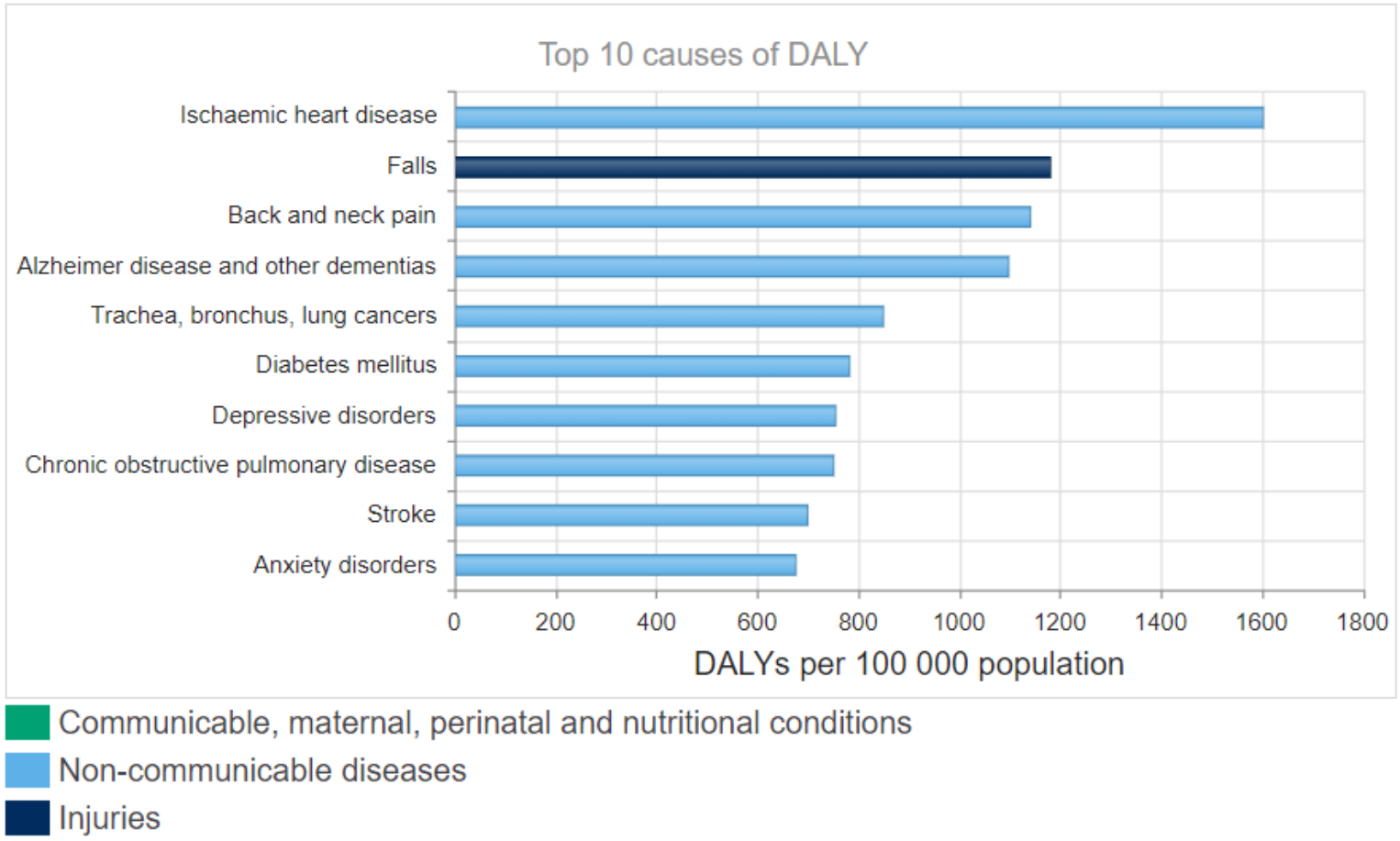
https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-leading-causes-of-death

Sex differences in risk of cardiovascular disease



In Switzerland, CVD is responsible for 37 % of deaths among men and 41% among women

Top 10 causes of DALY, Switzerland



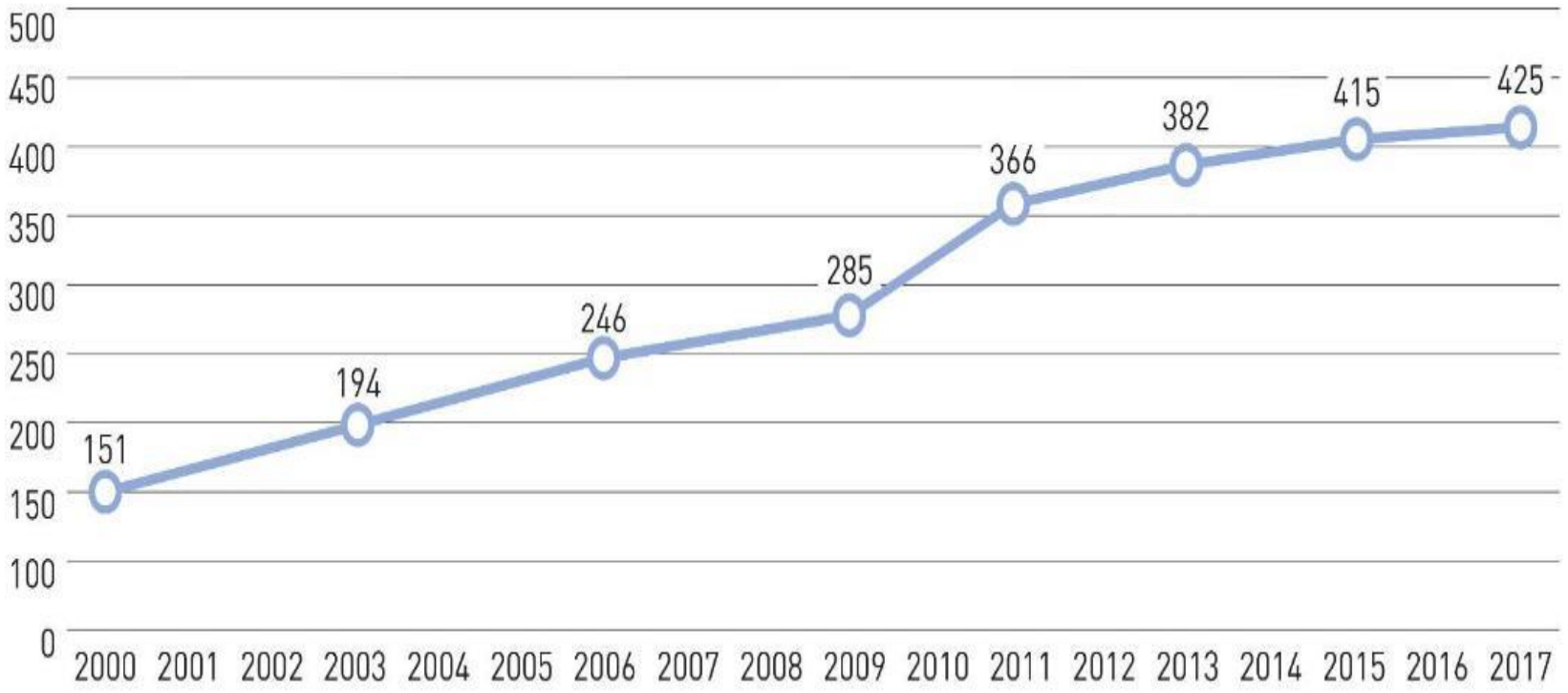
https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-leading-causes-of-death

Total number of adults with diabetes (20-79 years), Globally

In 2017

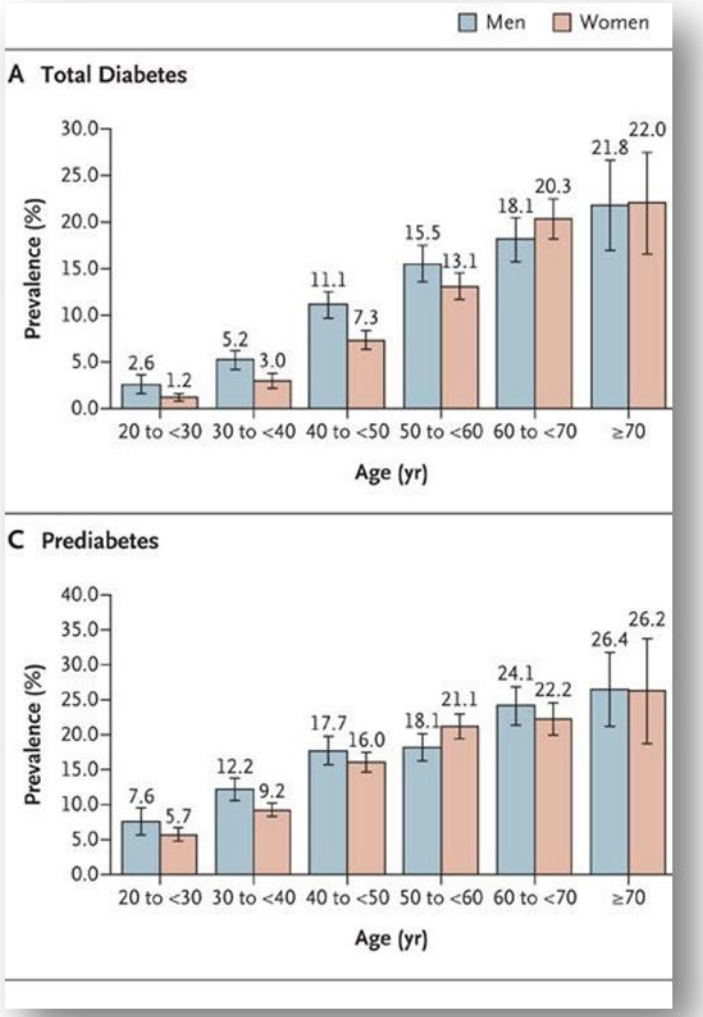
425 million

adults had diabetes



2017 IDF Diabetes Atlas

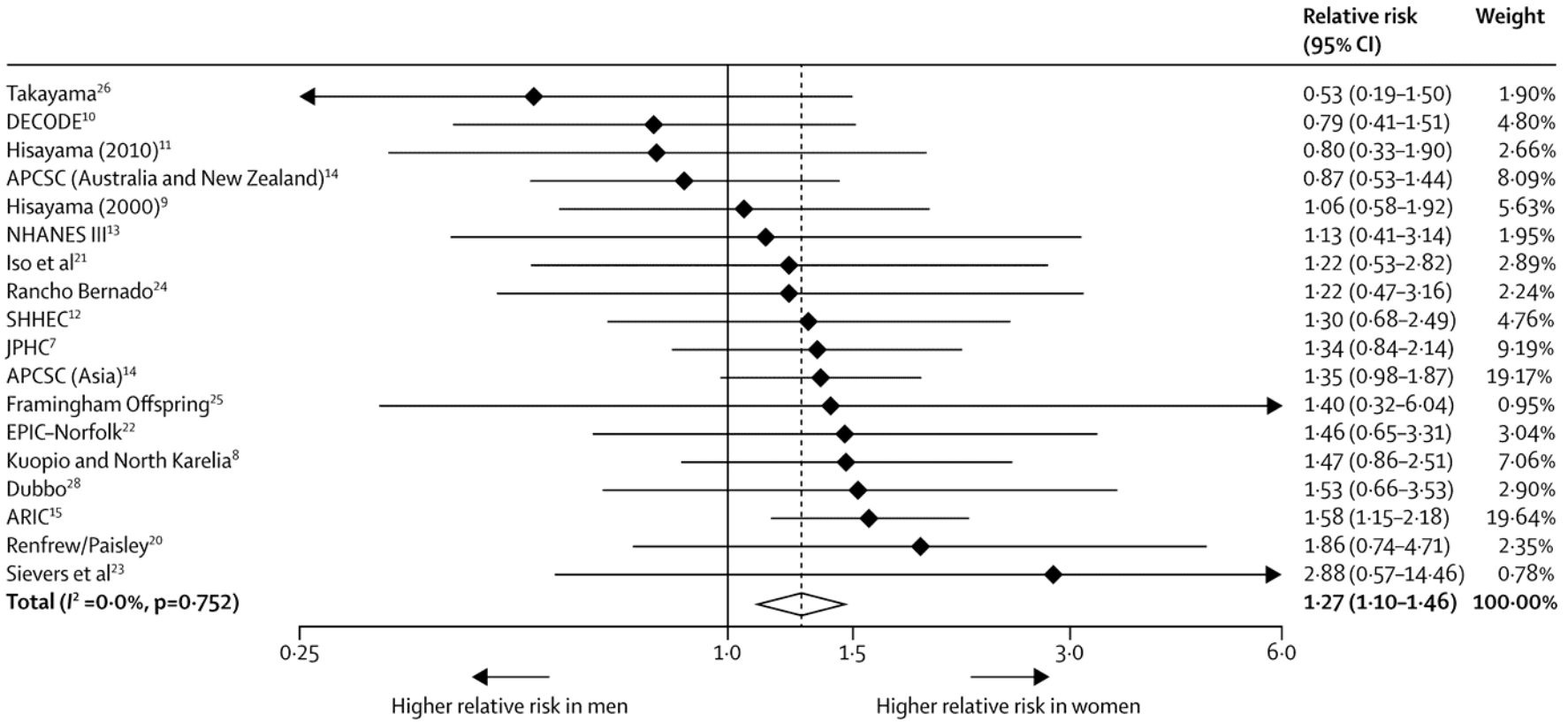
Sex differences in diabetes risk



- The prevalence of prediabetes and diabetes is lower in women than in men aged ≤60 years
- Women in their 60s and 70s have similar prevalence of diabetes or higher than men of the same age

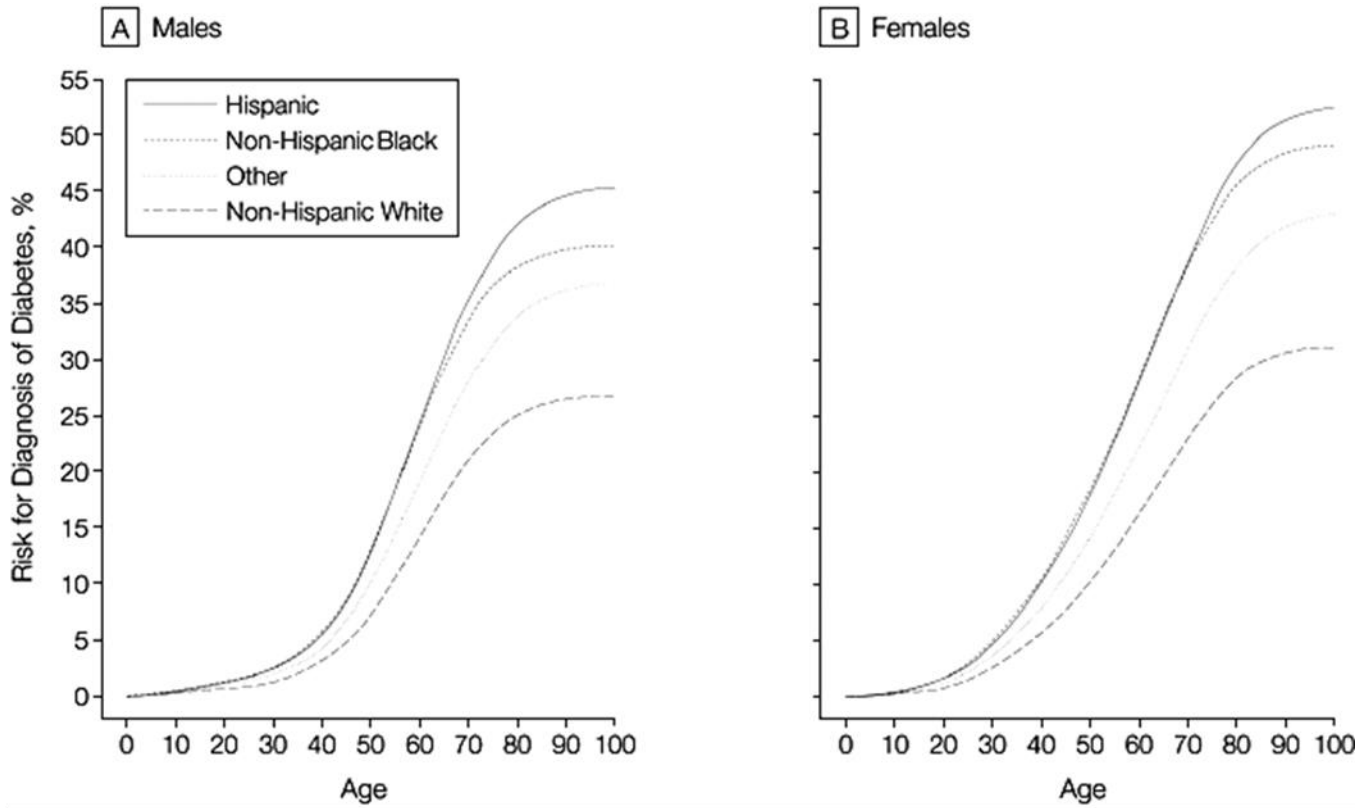
Yang W et al. 2010

Diabetic women to men relative risk for CHD and Stroke



Peters S.A.E et al. 2014

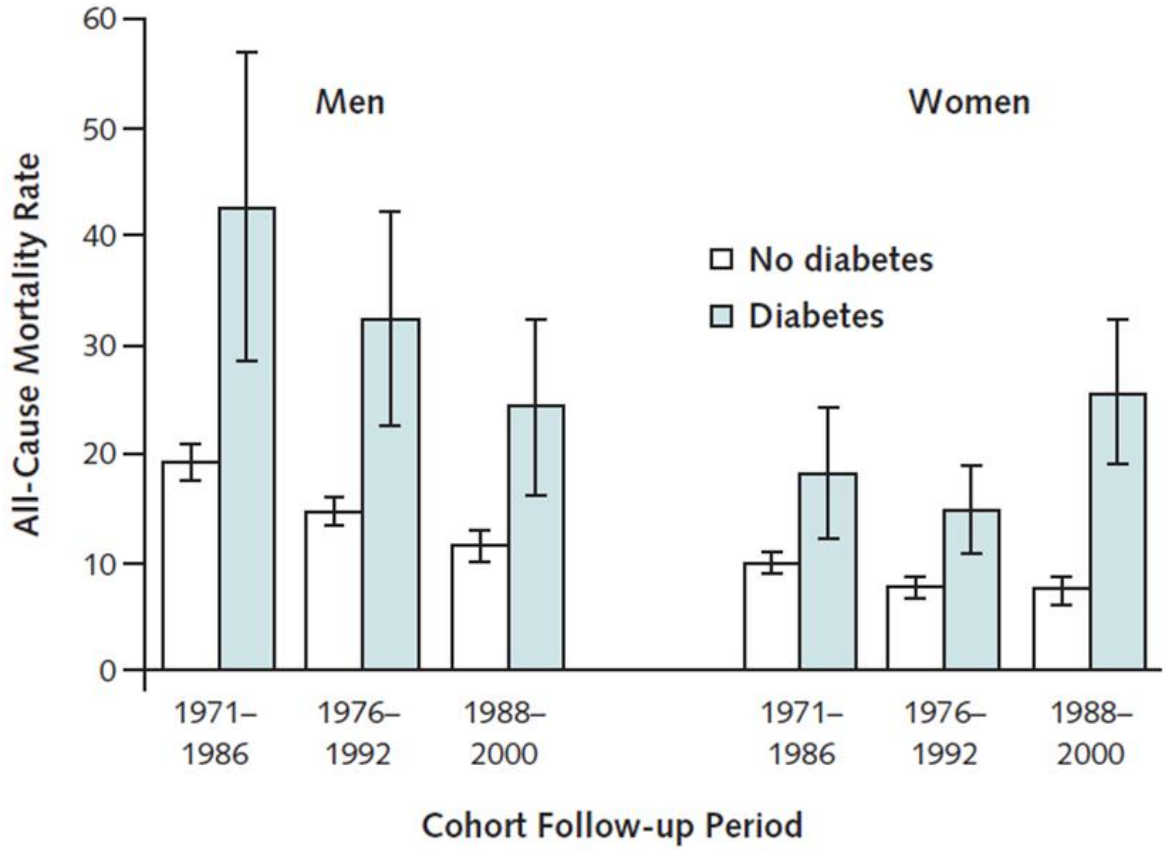
Lifetime risk for diagnosis of diabetes



Narayan et al. 2003

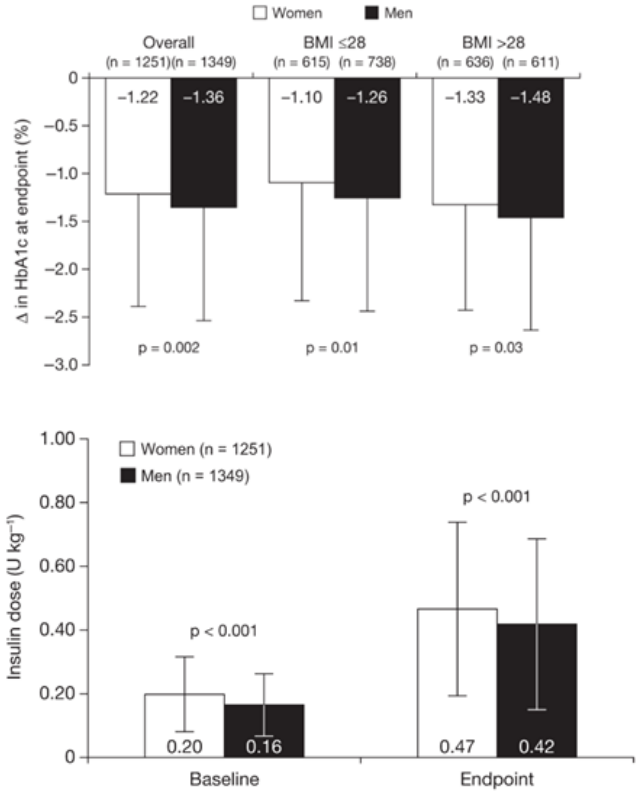
Age-adjusted all-cause mortality

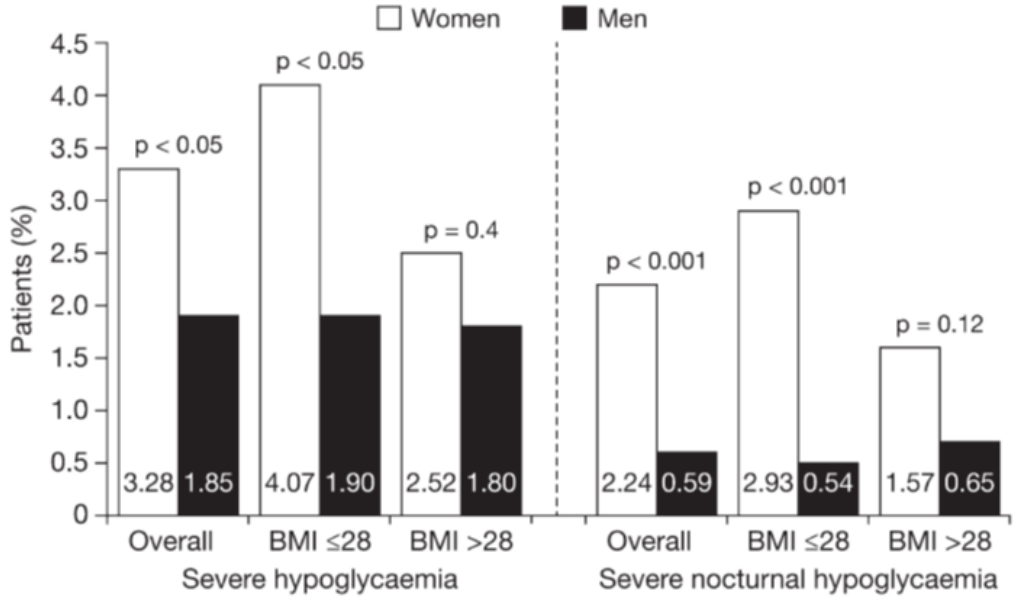
U.S. population age 35 to 74 years with and without diabetes, by cohort and sex



Greg EW et al. 2007

Effect of sex on treatment outcomes in T2D

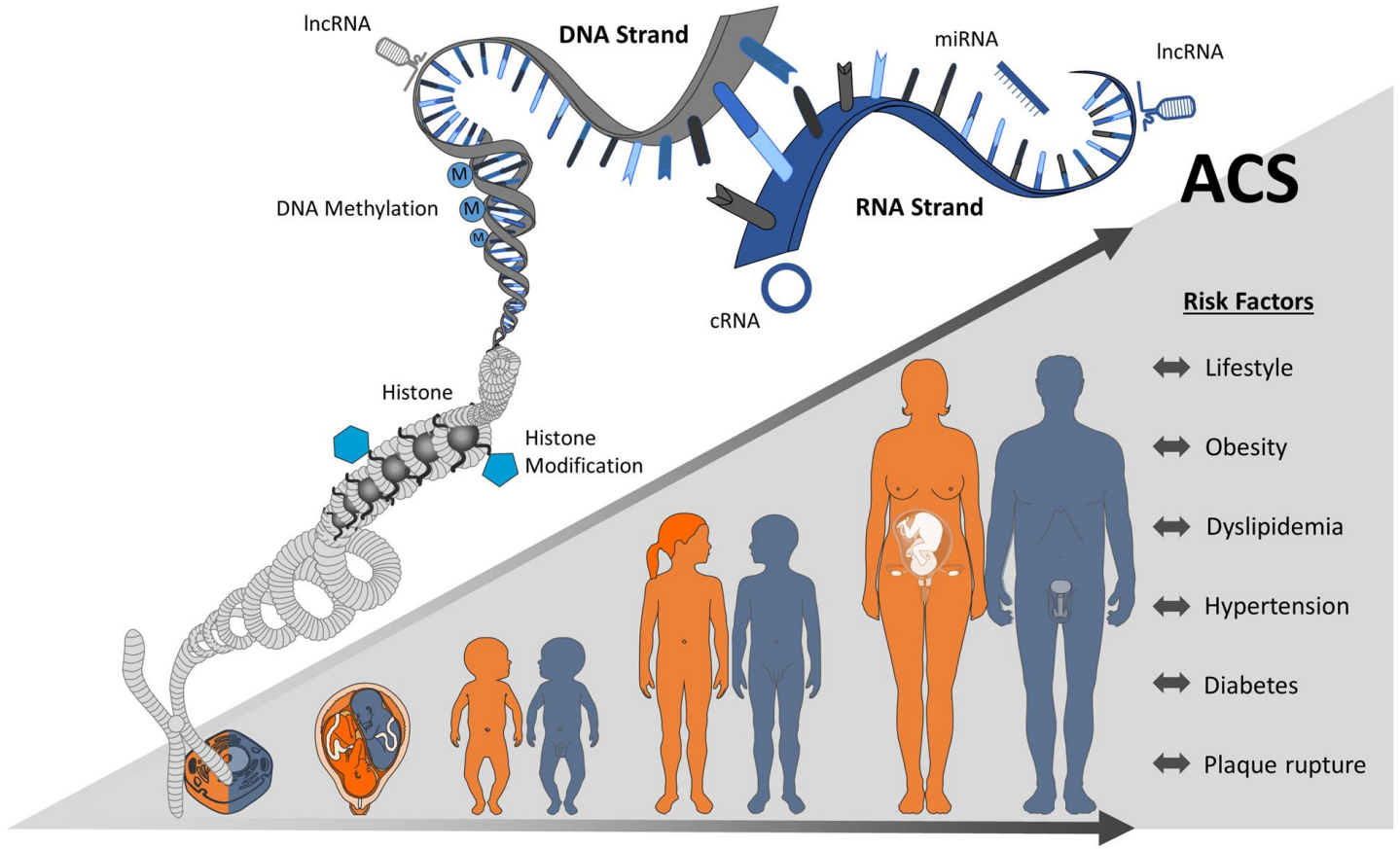




6 RCTs of insulin glargine or NPH insulin

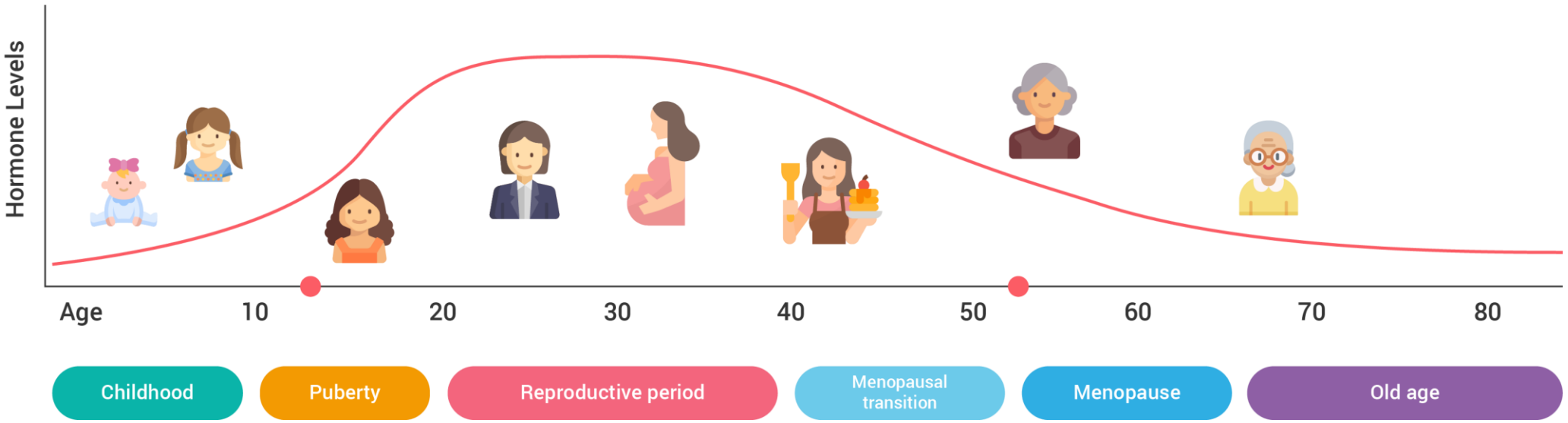
Greg EW et al. 2007

Sex differences in cardiometabolic diseases

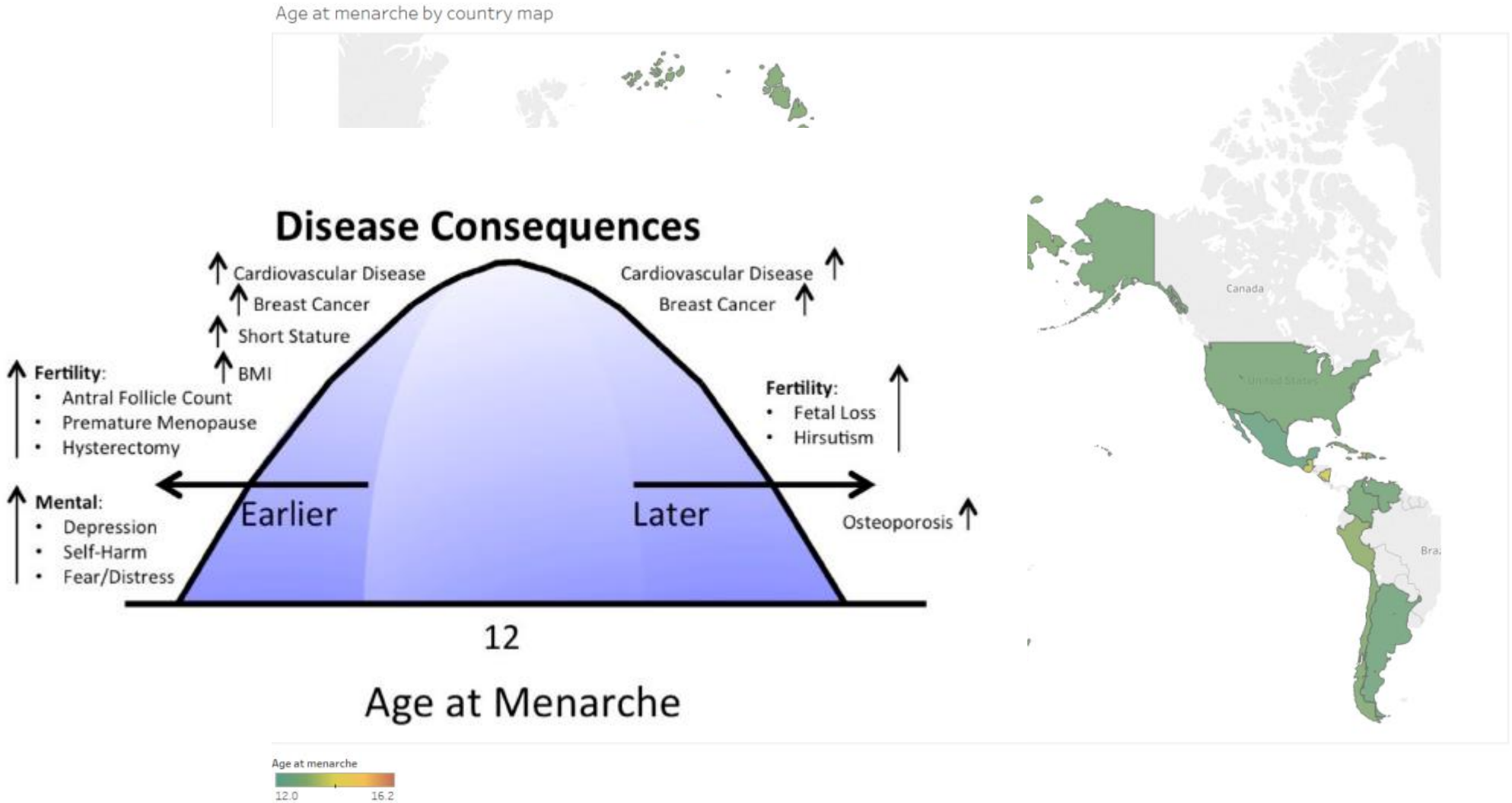


Haider et al. 2020, Muka et al. 2016

Women’s life cycle

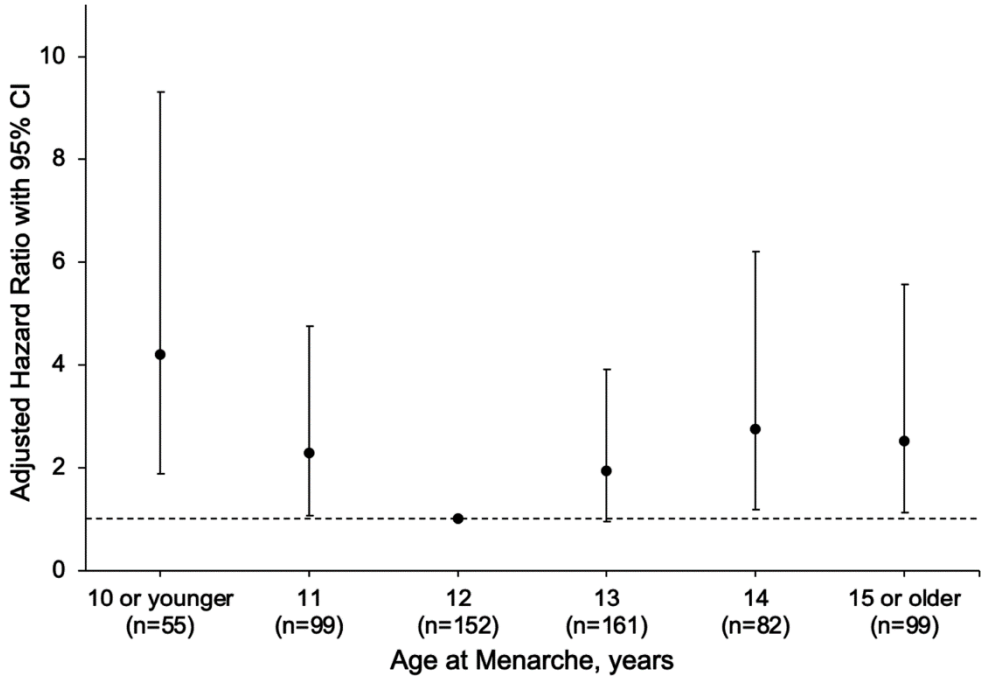


Age at menarche

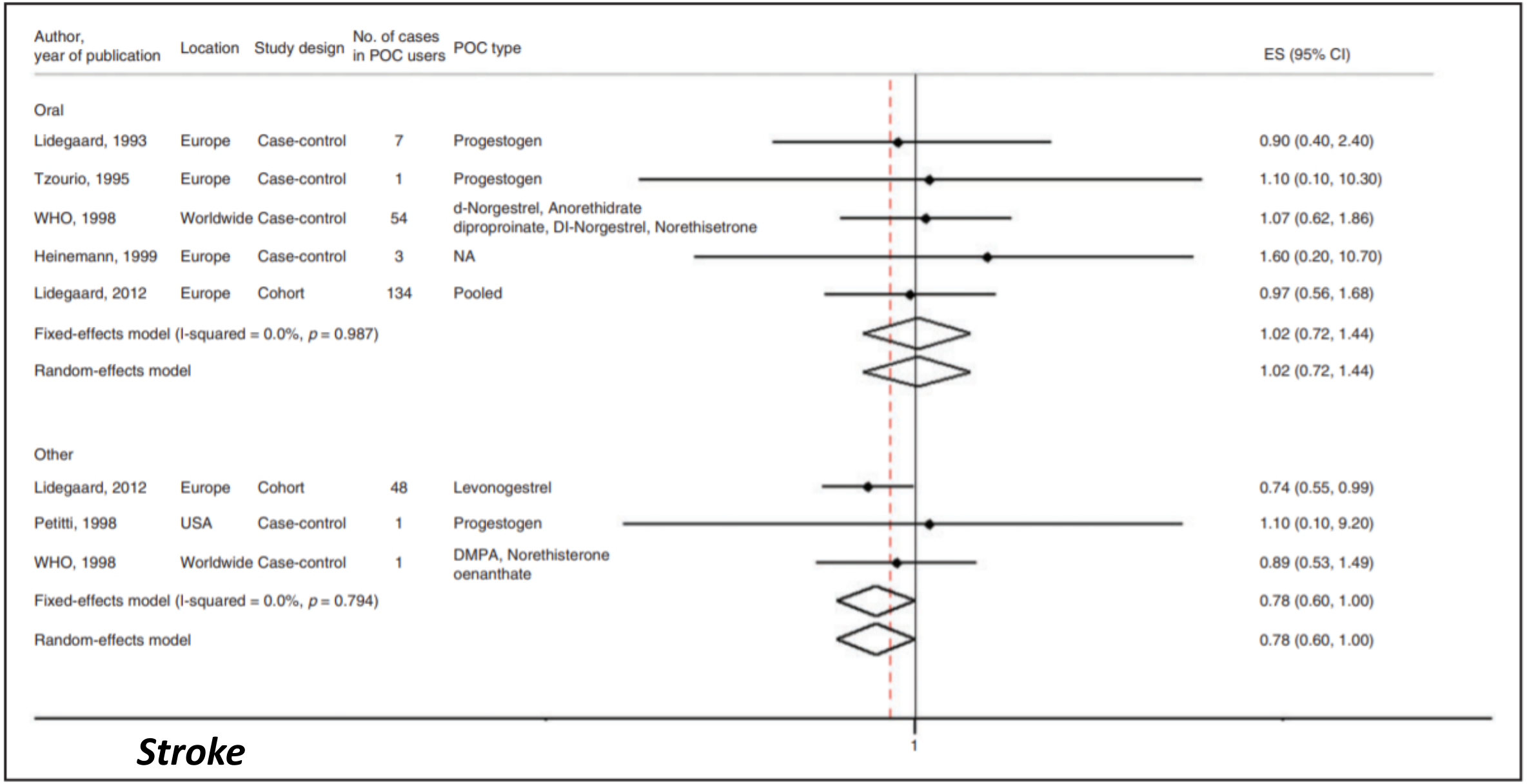


Age at menarche and CVD risk

- The association between the age at menarche and CVD is U-shaped
- Age at menarche could be a potential screening tool for women at risk of adverse CVD events.
- Strong inter-relationship between age at menarche and BMI limits the ability to consider their distinct influences on disease risks in traditional observational studies.



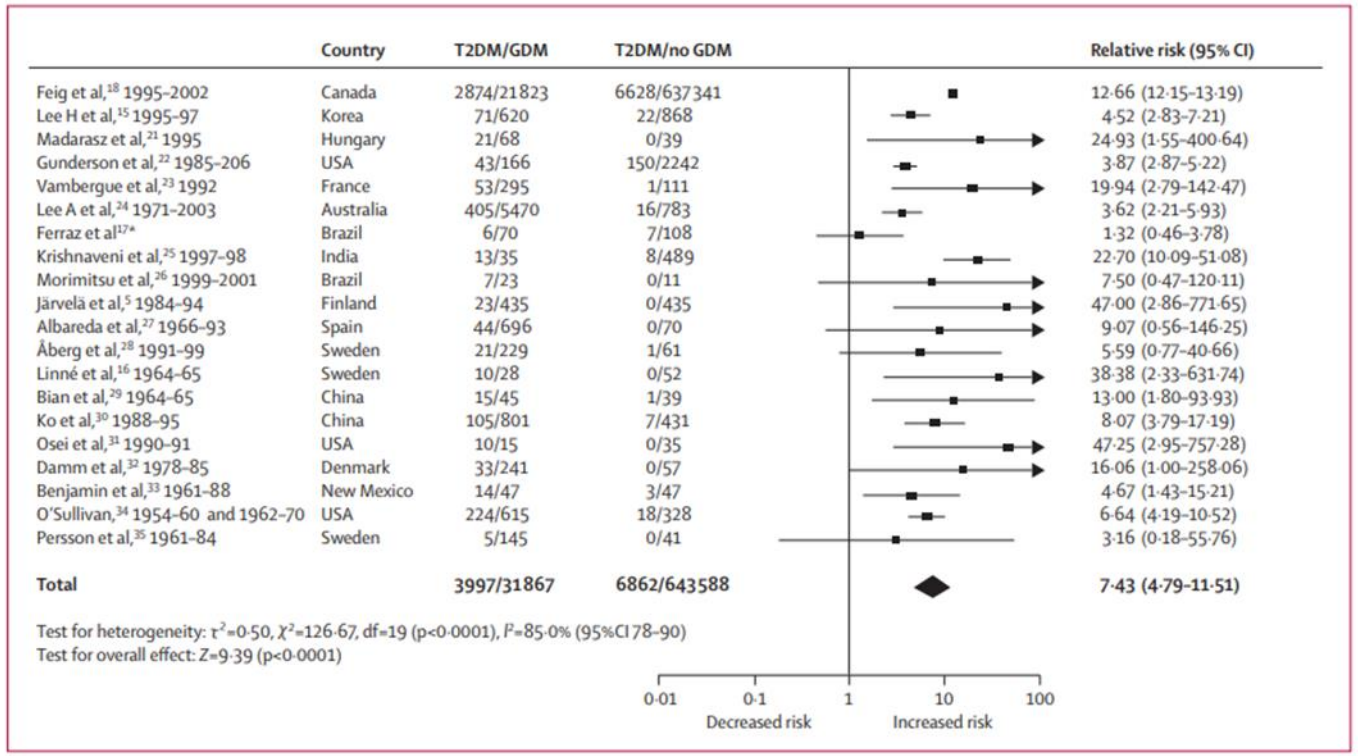
Women's Ischemia Syndrome Evaluation to assess major adverse CVD outcomes (the first occurrence of all-cause death, nonfatal myocardial infarction, nonfatal stroke, or heart failure hospitalization)


Author, year of publication
Location
Study design
No. of cases in POC users
POC type
ES (95% CI)
Oral
Lidegaard, 1993 Europe Case-control 7 Progestogen 0.90 (0.40, 2.40)
Tzourio, 1995 Europe Case-control 1 Progestogen 1.10 (0.10, 10.30)
WHO, 1998 Worldwide Case-control 54 d-Norgestrel, Anorethidrate diproproinate, DI-Norgestrel, Norethisetrone 1.07 (0.62, 1.86)
Heinemann, 1999 Europe Case-control 3 NA 1.60 (0.20, 10.70)
Lidegaard, 2012 Europe Cohort 134 Pooled 0.97 (0.56, 1.68)
Fixed-effects model (I-squared = 0.0%, p = 0.987) 1.02 (0.72, 1.44)
Random-effects model 1.02 (0.72, 1.44)
Other
Lidegaard, 2012 Europe Cohort 48 Levonogestrel 0.74 (0.55, 0.99)
Petitti, 1998 USA Case-control 1 Progestogen 1.10 (0.10, 9.20)
WHO, 1998 Worldwide Case-control 1 DMPA, Norethisterone oenanthate 0.89 (0.53, 1.49)
Fixed-effects model (I-squared = 0.0%, p = 0.794) 0.78 (0.60, 1.00)
Random-effects model 0.78 (0.60, 1.00)
1

Stroke

Gestational diabetes (GDM)

- Hyperglycaemia tha
  pregnancy (late sec
  weeks of gestation)
  trimester (27–40 we
  delivery
- The most common
  pregnancy (1% to >
- Prevalence of undia
  and even overt diab
  increasing.
- Maternal overweigh
  childbearing, previo
  history of type 2 dia
  are major GDM risk

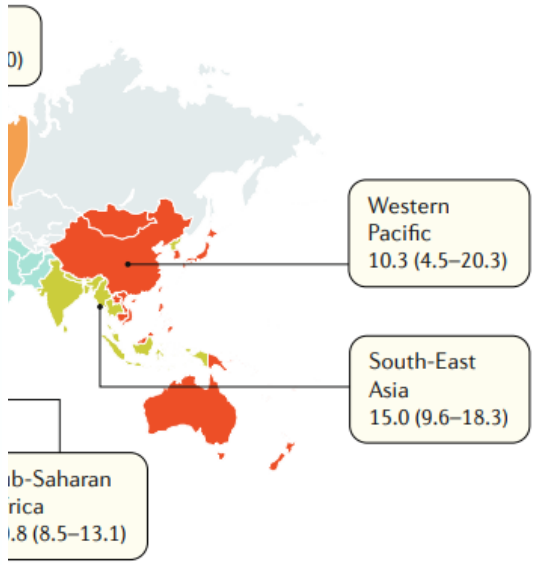


	Country	T2DM/GDM	T2DM/no GDM	Relative risk (95% CI)
Feig et al,[18] 1995–2002	Canada	2874/21823	6628/637341	12·66 (12·15–13·19)
Lee H et al,[15] 1995–97	Korea	71/620	22/868	4·52 (2·83–7·21)
Madarasz et al,[21] 1995	Hungary	21/68	0/39	24·93 (1·55–400·64)
Gunderson et al,[22] 1985–206	USA	43/166	150/2242	3·87 (2·87–5·22)
Vambergue et al,[23] 1992	France	53/295	1/111	19·94 (2·79–142·47)
Lee A et al,[24] 1971–2003	Australia	405/5470	16/783	3·62 (2·21–5·93)
Ferraz et al[17]*	Brazil	6/70	7/108	1·32 (0·46–3·78)
Krishnaveni et al,[25] 1997–98	India	13/35	8/489	22·70 (10·09–51·08)
Morimitsu et al,[26] 1999–2001	Brazil	7/23	0/11	7·50 (0·47–120·11)
Järvelä et al,[5] 1984–94	Finland	23/435	0/435	47·00 (2·86–771·65)
Albareda et al,[27] 1966–93	Spain	44/696	0/70	9·07 (0·56–146·25)
Åberg et al,[28] 1991–99	Sweden	21/229	1/61	5·59 (0·77–40·66)
Linné et al,[16] 1964–65	Sweden	10/28	0/52	38·38 (2·33–631·74)
Bian et al,[29] 1964–65	China	15/45	1/39	13·00 (1·80–93·93)
Ko et al,[30] 1988–95	China	105/801	7/431	8·07 (3·79–17·19)
Osei et al,[31] 1990–91	USA	10/15	0/35	47·25 (2·95–757·28)
Damm et al,[32] 1978–85	Denmark	33/241	0/57	16·06 (1·00–258·06)
Benjamin et al,[33] 1961–88	New Mexico	14/47	3/47	4·67 (1·43–15·21)
O'Sullivan,[34] 1954–60 and 1962–70	USA	224/615	18/328	6·64 (4·19–10·52)
Persson et al,[35] 1961–84	Sweden	5/145	0/41	3·16 (0·18–55·76)
Total		**3997/31867**	**6862/643588**	**7·43 (4·79–11·51)**

Test for heterogeneity: τ^2=0·50, χ^2=126·67, df=19 (p<0·0001), I^2=85·0% (95%CI 78–90)
Test for overall effect: Z=9·39 (p<0·0001)

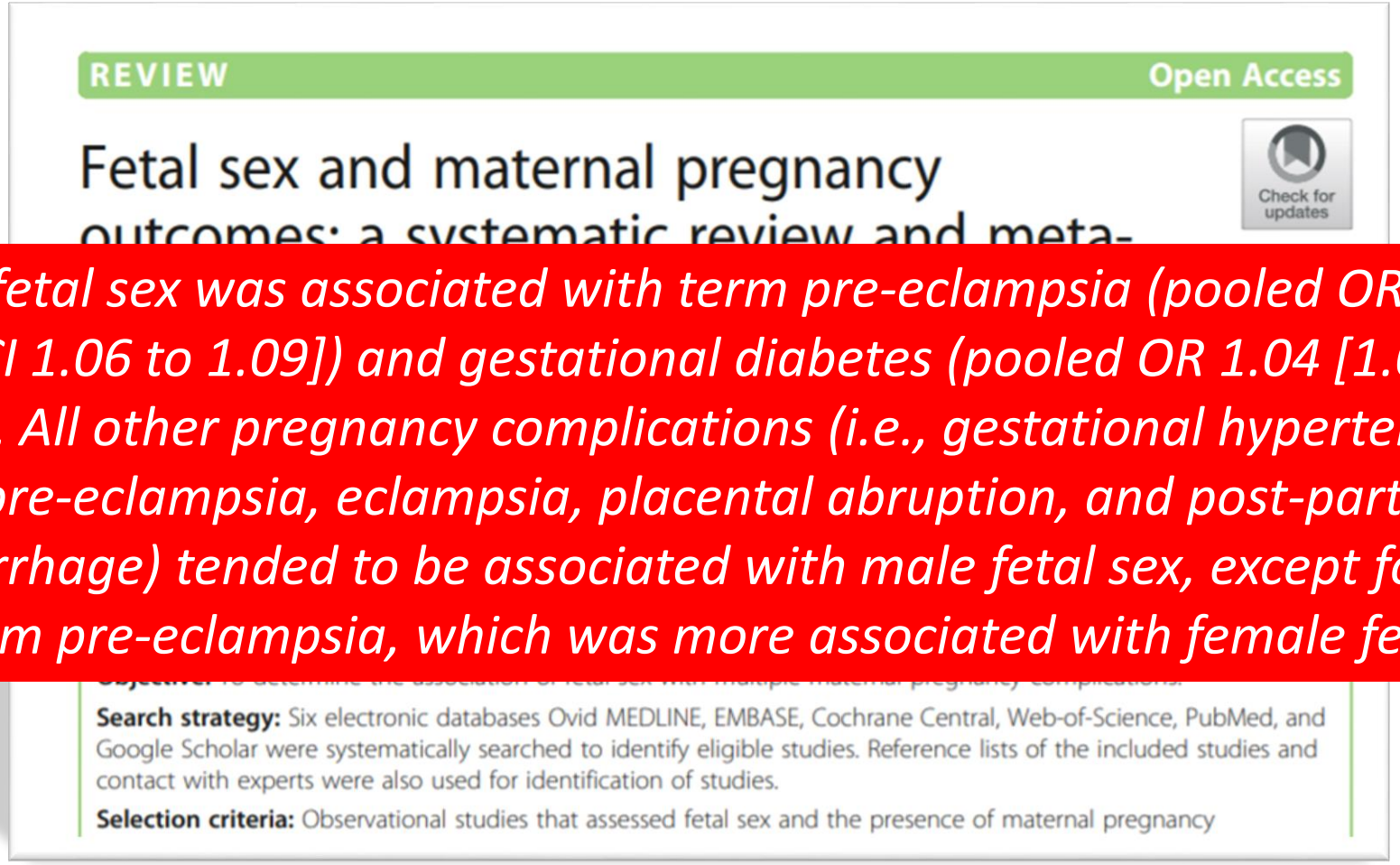
0·01 0·1 1 10 100
Decreased risk Increased risk

Figure 2: **Risk of type 2 diabetes mellitus (T2DM) after gestational diabetes mellitus (GDM)**
x-axis is log scale. Each solid square represents a relative risk. Horizontal lines indicate 95% CIs. df=degrees of freedom. *Dates not available.



le range) prevalence (%) of gestational diabetes
website).

Gestational diabetes (GDM)



REVIEW Open Access

Fetal sex and maternal pregnancy outcomes: a systematic review and meta-

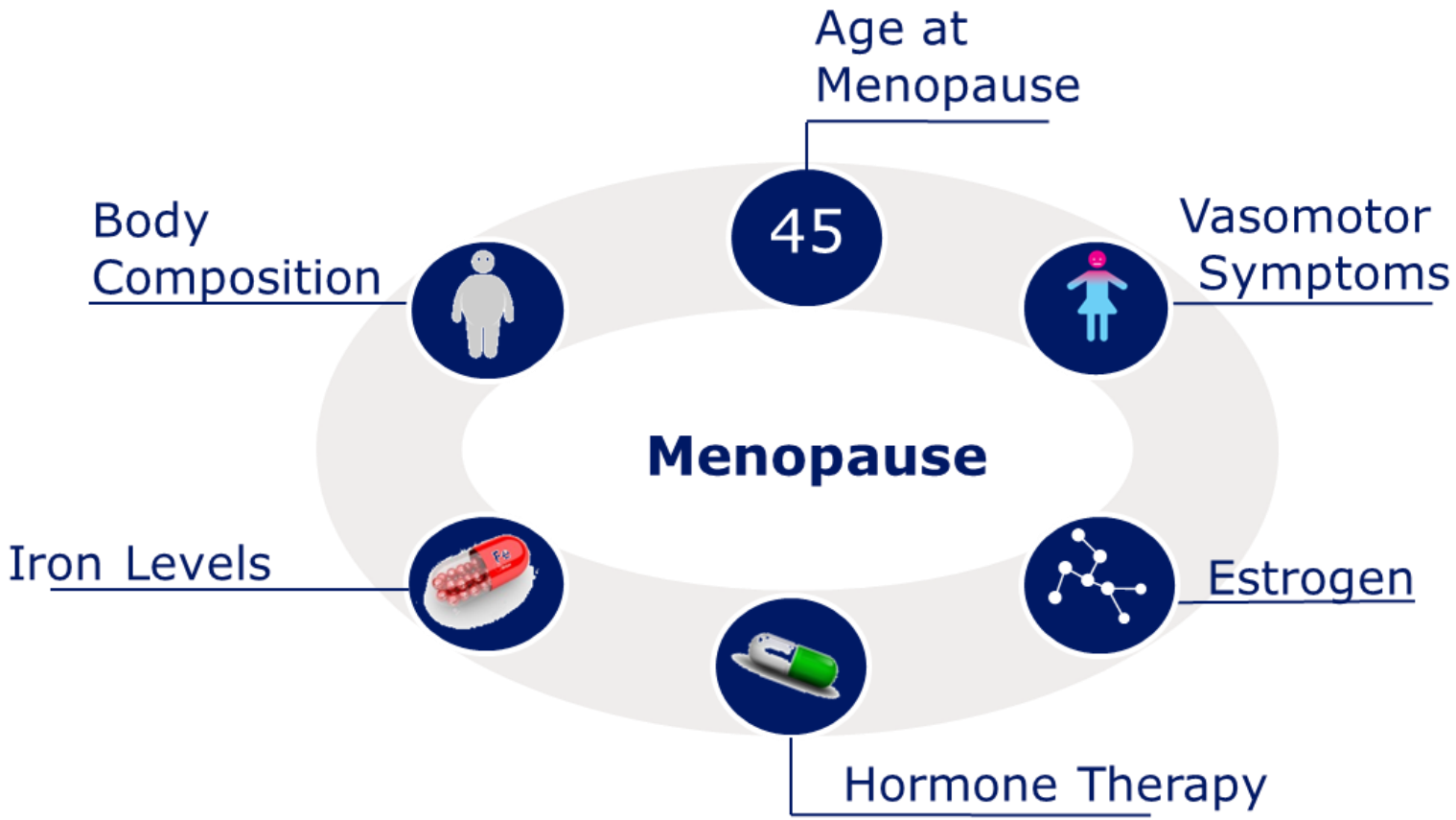
Check for updates

Male fetal sex was associated with term pre-eclampsia (pooled OR 1.07 [95%CI 1.06 to 1.09]) and gestational diabetes (pooled OR 1.04 [1.02 to 1.07]). All other pregnancy complications (i.e., gestational hypertension, total pre-eclampsia, eclampsia, placental abruption, and post-partum hemorrhage) tended to be associated with male fetal sex, except for preterm pre-eclampsia, which was more associated with female fetal sex.

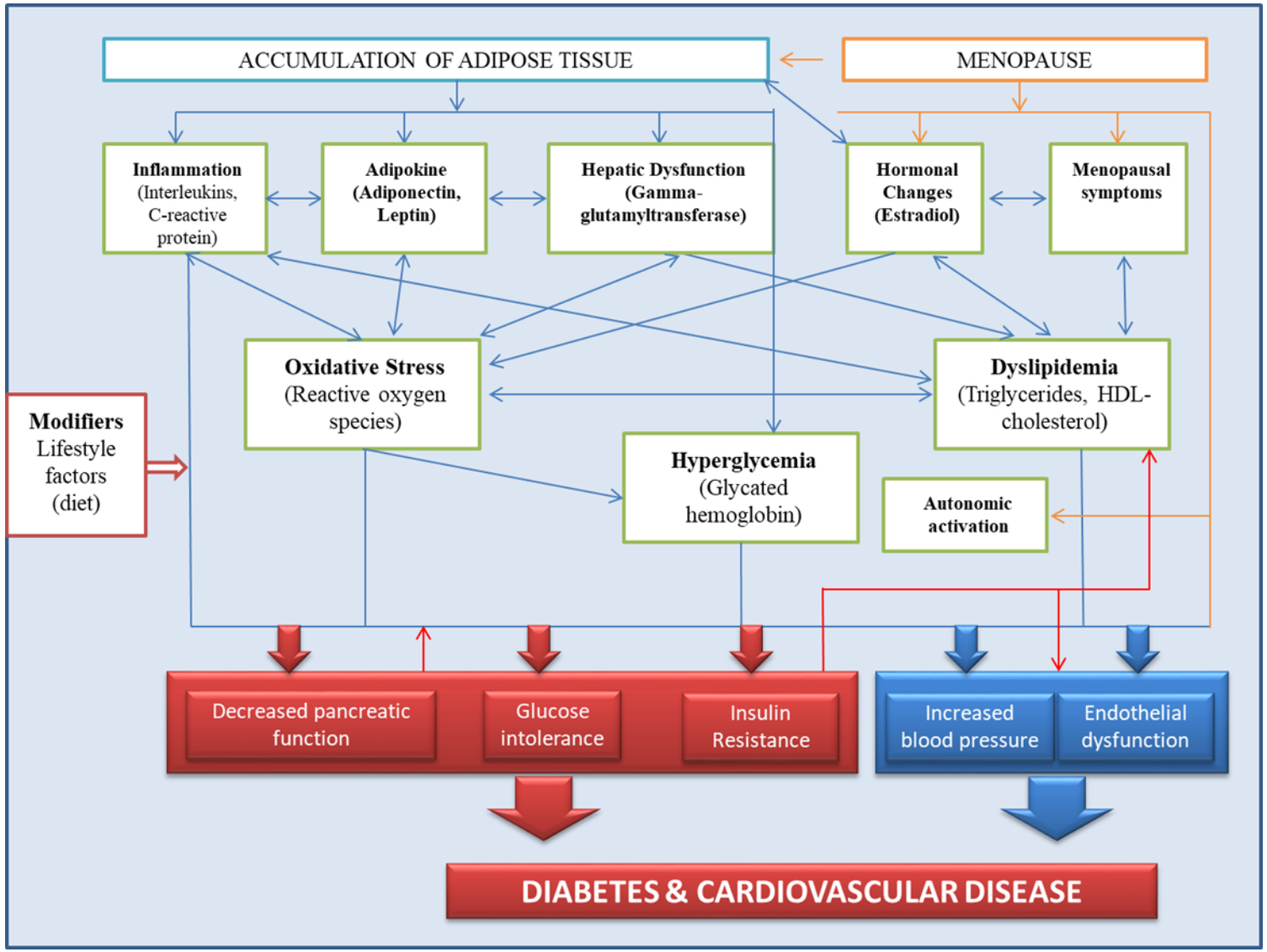
Search strategy: Six electronic databases Ovid MEDLINE, EMBASE, Cochrane Central, Web-of-Science, PubMed, and Google Scholar were systematically searched to identify eligible studies. Reference lists of the included studies and contact with experts were also used for identification of studies.

Selection criteria: Observational studies that assessed fetal sex and the presence of maternal pregnancy

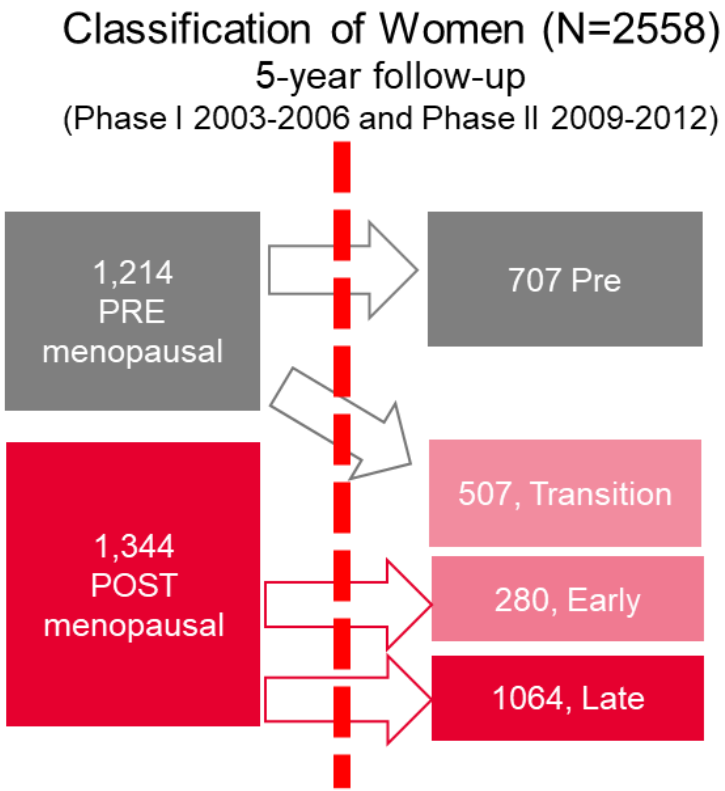
Menopause


Age at Menopause
45
Body Composition
Vasomotor Symptoms
Menopause
Iron Levels
Estrogen
Hormone Therapy

Adverse metabolic changes related to menopause



Is chronological ageing or stage of reproductive aging the dominant factor contributing to cardiometabolic changes in women?



COLAUS Design

Cardiometabolic outcomes

- Blood pressure, serum lipids, glucose level, inflammatory markers, and body mass index

Independent variable

- **Reproductive age** (Pre, Trans, Early, Late) (PRIMARY)
- **Chronologic age** (SECONDARY)

Confounding factors

- Medications and Hormone replacement therapy
- Baseline comorbid CV disease
- Smoking, alcohol, physical activity, education
- Body mass index*

Unpublished data

Is chronological ageing or stage of reproductive aging the dominant factor contributing to cardiometabolic changes in women?

Cross-sectional analysis of risk factors

	PRE	TRANS	Early POST	Late LPOST	p-value
Body mass index (kg/m2)	Ref	0.513 [-0.0814, 0.997]	1.500 [0.722, 2.213]*	2.049 [1.142, 2.845]*	0.000
Systolic blood pressure (mmHg)	Ref	-0.616 [-2.489, 1.257]	-1.663 [-4.259, 0.933]	-0.417 [-3.387,2.554]	0.691
Diastolic blood pressure (mmHg)	Ref	1.950 [0.701, 3.200]*	3.367 [1.635, 5.099]*	3.196 [1.214, 5.178]*	0.001
Total cholesterol (mmol/L)	Ref	0.087 [-0.0275, 0.203]	0.440 [0.280, 0.600]*	0.380 [0.198, 0.563]*	0.000
High-density lipoprotein (mmol/L)	Ref	0.050 [0.0012,0.099]*	0.072 [0.0043, 0.139]*	0.066 [-0.0109, 0.144]	0.104
Triglycerides (mmol/L)	Ref	0.015 [-0.037 ,0.066]*	0.008 [-0.063, 0.0796]	0.057 [-0.0244, 0.139]	0.206
Fasting glucose (mmol/L)	Ref	0.090 [0.0022, 0.177]*	0.143 [0.022, 0.264]*	0.214 [0.075, 0.352]*	0.003
Insulin (microIU/mL)	Ref	-0.031 [-0.099, 0.038]	-0.026 [-0.120, 0.068]	0.067 [-0.0397, 0.175]	0.222
High sensitivity c-reactive protein (mg/L)	Ref	-0.057 [-0.182, 0.068]	-0.126 [-0.298, 0.0472]	0.031 [-0.167, 0.229]	0.866
Leptin (ng/mL)	Ref	-0.019 [-0.098, 0.059]	0.064 [-0.043, 0.171]	0.086 [-0.0371, 0.209]	0.136
Adiponectin (ng/mL)	Ref	-0.004 [-0.085, 0.076]	0.138 [0.0285, 0.247]*	0.173 [0.0479, 0.299]*	0.004
Tumor necrosis factor-alpha (pg/mL)	Ref	-0.007 [-0.125, 0.109]	0.042 [-0.118, 0.203]	0.050 [-0.135, 0.236]	0.536
Interleukin 6 (pg/mL)	Ref	0.164 [-0.0258, 0.353]	0.343 [0.0847, 0.601]*	0.436 [0.138, 0.734]*	0.003
Interleukin 1b (pg/mL)	Ref	-0.170 [-0.402, 0.063]	-0.098 [-0.419, 0.223]	-0.088 [-0.459, 0.284]	0.703

Corrected for use of hypoglycemic drugs, statins and antihypertensive drugs, **AGE**, smoking history, alcohol-use, baseline physical activity, baseline cardiovascular disease, use of hormone replacement therapy, and body mass index

Unpublished data

Is chronological ageing or stage of reproductive aging the dominant factor contributing to cardiometabolic changes in women?

Longitudinal analysis of risk factors

	PRE	TRANS	Early POST	Late POST
Body mass index (kg/m2)	*Ref*	2.927 (-2.762, 8.617)	1.492 (-5.606, 8.591)	0.336 (-4.781, 5.452)
Systolic blood pressure (mmHg)	*Ref*	-1.348 (-19.40, 16.70)	-11.98 (-34.47, 10.52)	7.346 (-8.911, 23.60)
Diastolic blood pressure (mmHg)	*Ref*	2.161 (-9.808, 14.13)	-2.720 (-17.64, 12.20)	4.806 (-5.977,15.59)
Total cholesterol (mmol/L)	*Ref*	0.530 (-0.585, 1.645)	1.112 (-0.279,2.504)	0.984 (-0.0188, 1.987)
High-density lipoprotein (mmol/L)	*Ref*	-0.189 (-0.691, 0.314)	-0.347 (-0.974, 0.280)	0.0465 (-0.405, 0.498)
Triglycerides (mmol/L)	*Ref*	0.440 (-0.0590, 0.940)	0.199 (-0.424, 0.822)	0.0334 (-0.416, 0.482)
Fasting glucose (mmol/L)	*Ref*	0.274 (-0.461, 1.010)	0.0152 (-0.902, 0.932)	0.137 (-0.524, 0.798)
Insulin (microIU/mL)	*Ref*	-0.337 (-0.928, 0.253)	-0.207 (-0.936, 0.523)	-0.0757 (-0.592, 0.440)
High sensitivity c-reactive protein (mg/L)	*Ref*	0.0574 (-1.122, 1.237)	-0.778 (-2.239, 0.684)	-0.0779 (-1.135, 0.979)
Leptin (ng/mL)	*Ref*	0.175 (-0.833, 1.183)	0.715 (-0.494, 1.924)	0.251 (-0.638, 1.139)
Adiponectin (ng/mL)	*Ref*	-0.102 (-0.857, 0.653)	-0.00553 (-0.928, 0.917)	0.330 (-0.332, 0.992)
Tumor necrosis factor alpha (pg/mL)[2]	*Ref*	0.107 (-1.007, 1.220)	0.158 (-1.190, 1.507)	0.222 (-0.766, 1.211)
Interleukin 6 (pg/mL)	*Ref*	0.0159 (-1.825, 1.857)	-0.170 (-2.399, 2.059)	-0.586 (-2.224, 1.053)
Interleukin 1b (pg/mL) [2]	*Ref*	0.133 (-1.742, 2.009)	-1.041 (-3.356, 1.275)	-0.215 (-1.901, 1.471)

Unpublished data

Is chronological ageing or stage of reproductive aging the dominant factor contributing to cardiometabolic changes in women?

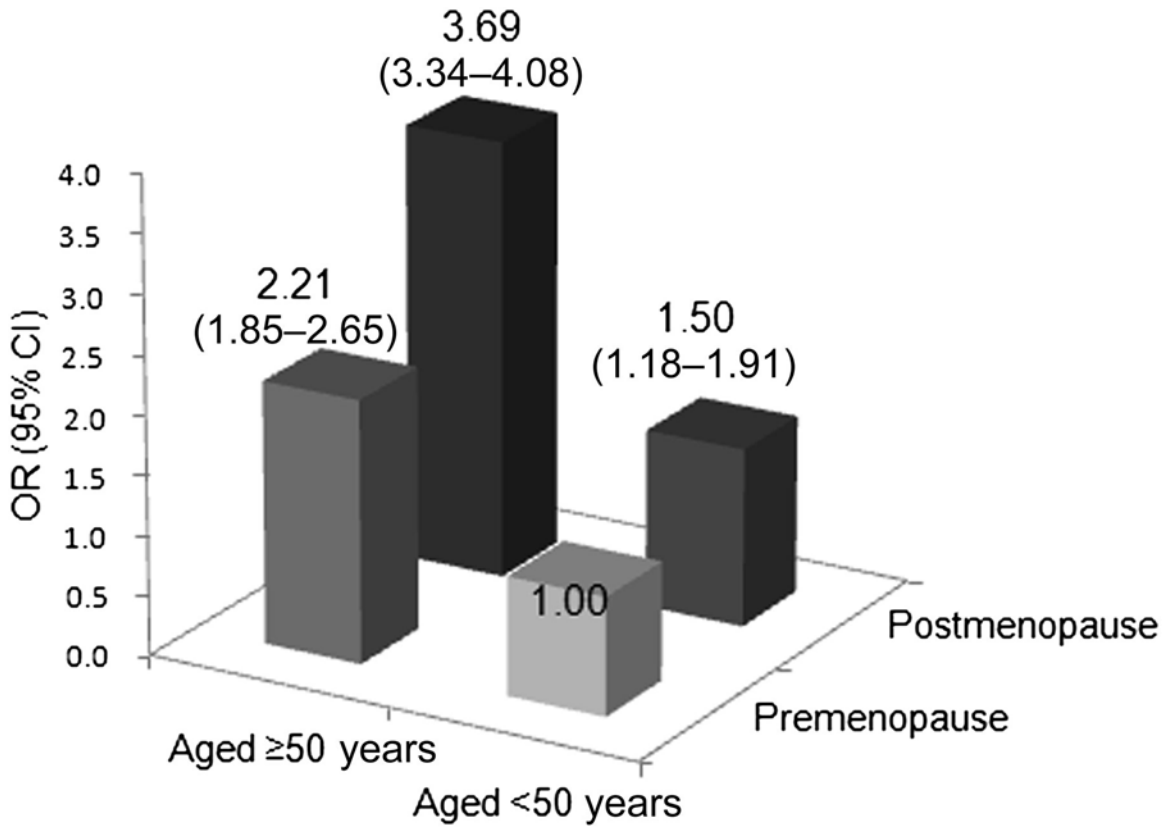
Longitudinal analysis of risk factors (using AGE)

Our findings suggest that the accumulation of deleterious exposures and damage with aging might contribute to menopause-related changes in CVD, and future studies will need to disentangle the relative contribution of effect of age and menopause in CVD risk

	Beta	95% CI	P value
	-0.014	(-0.041, 0.014)	0.330
	0.736	(0.649, 0.824)	<0.000
	0.018	(-0.040, 0.076)	0.541
	0.023	(0.022, 0.032)	<0.000
	0.006	(0.004, 0.009)	<0.000
	0.006	(0.004, 0.008)	<0.000
	0.0038	(0.0002, 0.007)	0.038
	0.0007	(-0.002, 0.003)	0.614
	0.002	(-0.003, 0.008)	0.455
	-0.002	(-0.006, 0.003)	0.422
	0.009	(0.005, 0.012)	<0.000
	0.006	(0.001, 0.011)	0.022
	-0.013	(-0.021, -0.004)	0.004
	-0.007	(-0.014, -0.0002)	0.042

Unpublished data

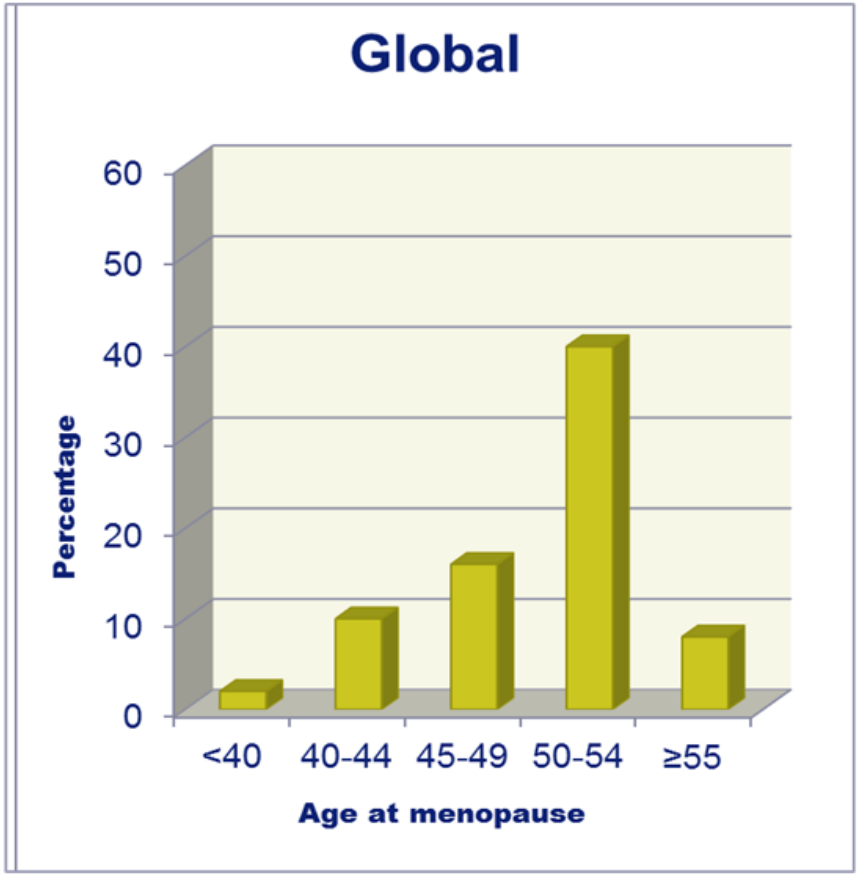
Menopause and Diabetes: independent of age

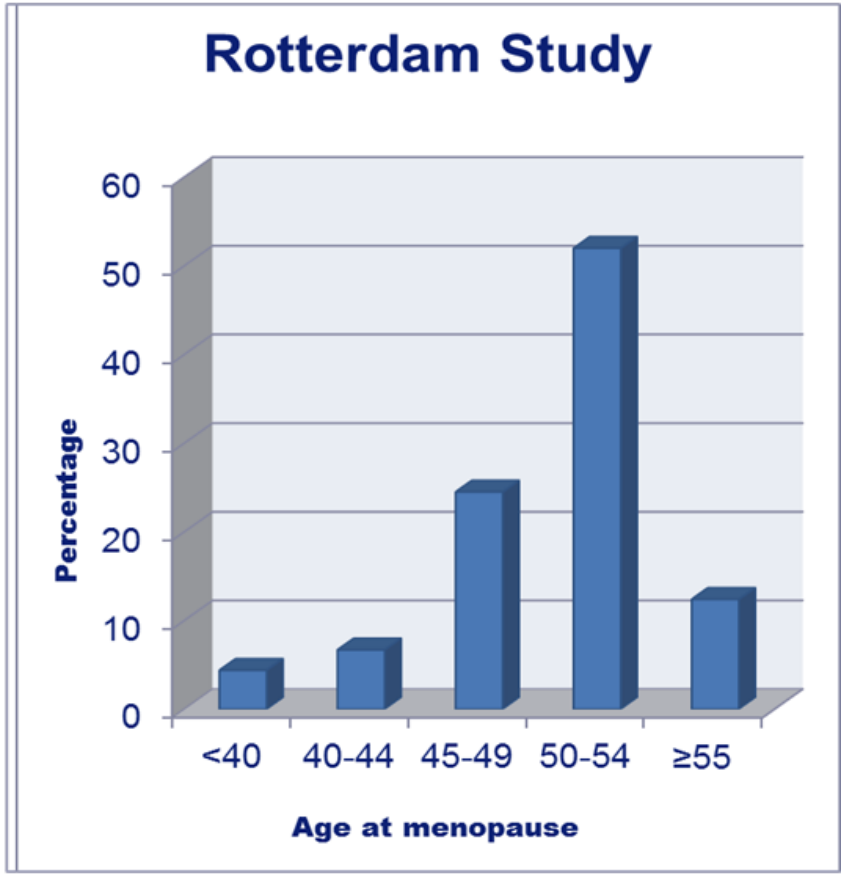


- Older age and postmenopausal status alone significantly associated with an elevated OR for dysglycemia
- The postmenopausal condition and older age additively influence an elevated risk
- Early onset of menopause is associated with increased risk of T2D

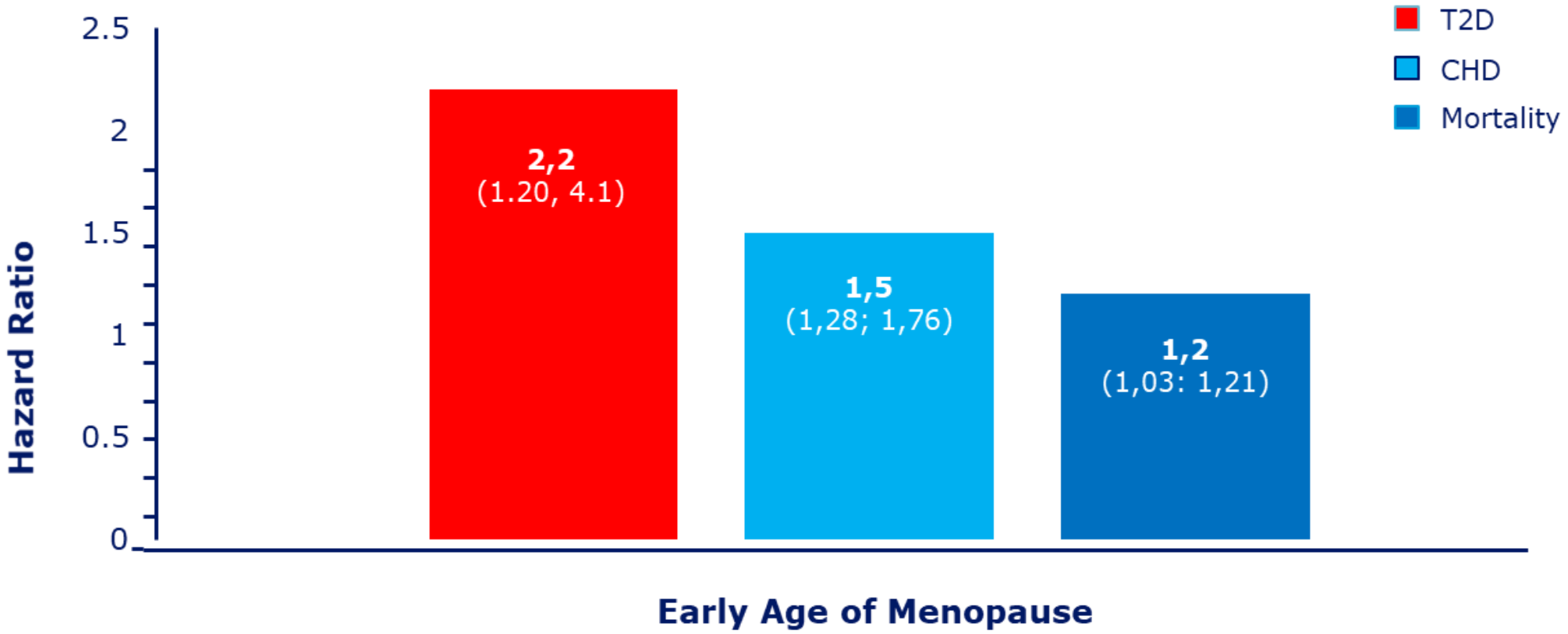
Heianza Y et al. 2013; Muka et al. 2017

Age at menopause



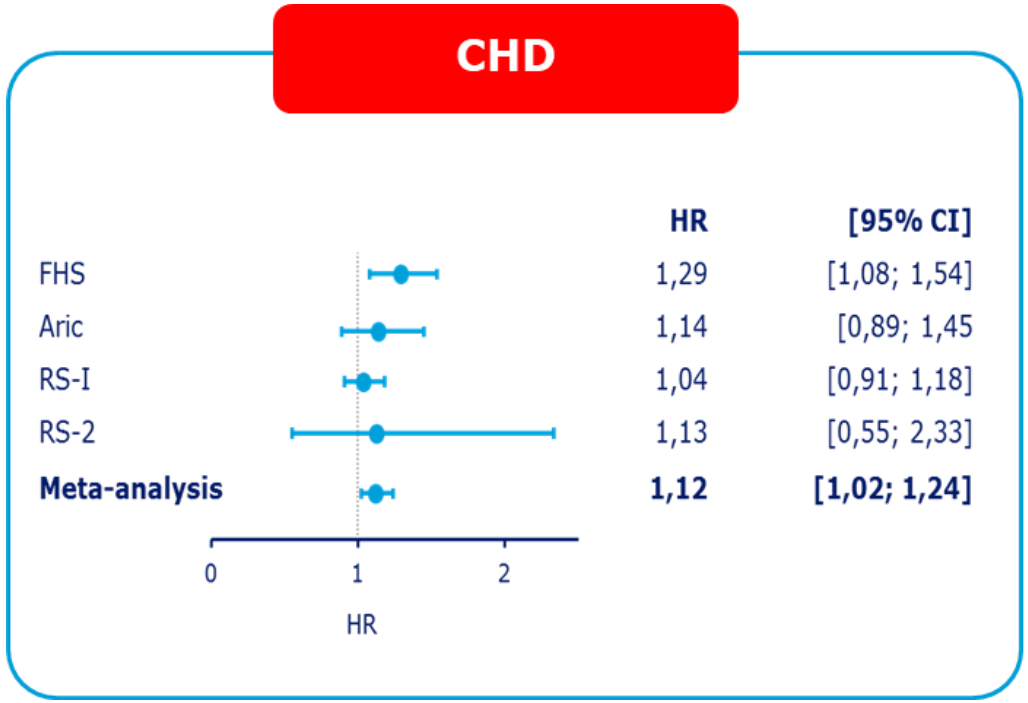


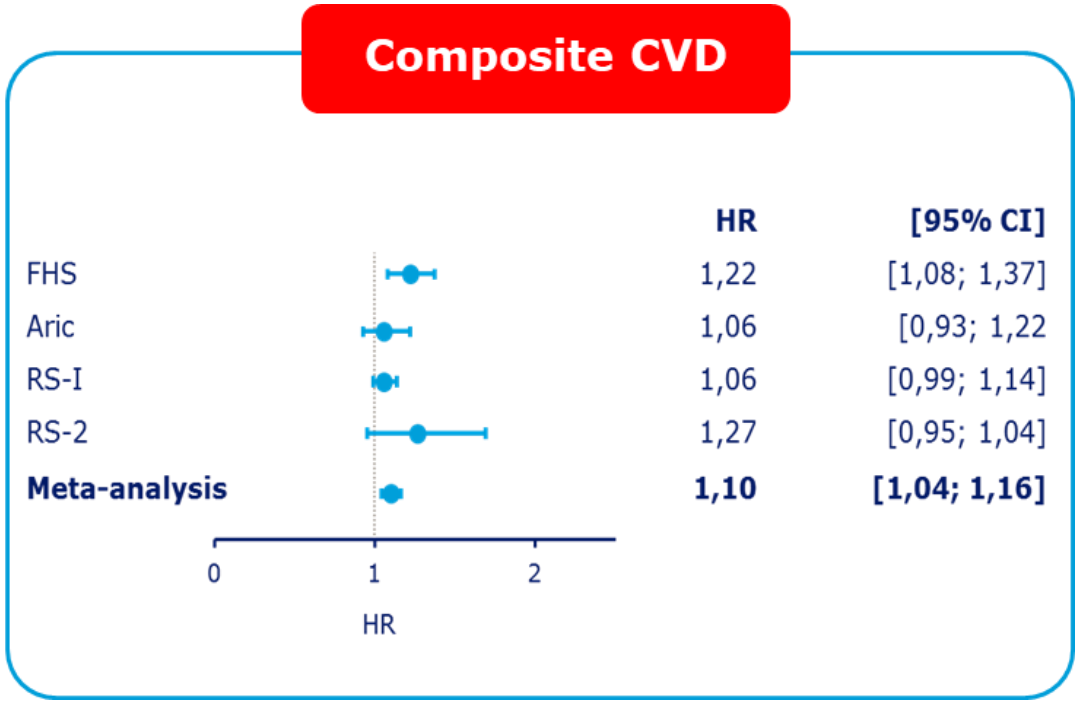
Early menopause and cardiometabolic risk



Muka et al. 2017 Jama Cardiology; Muka et al. 2018 Diabetologia

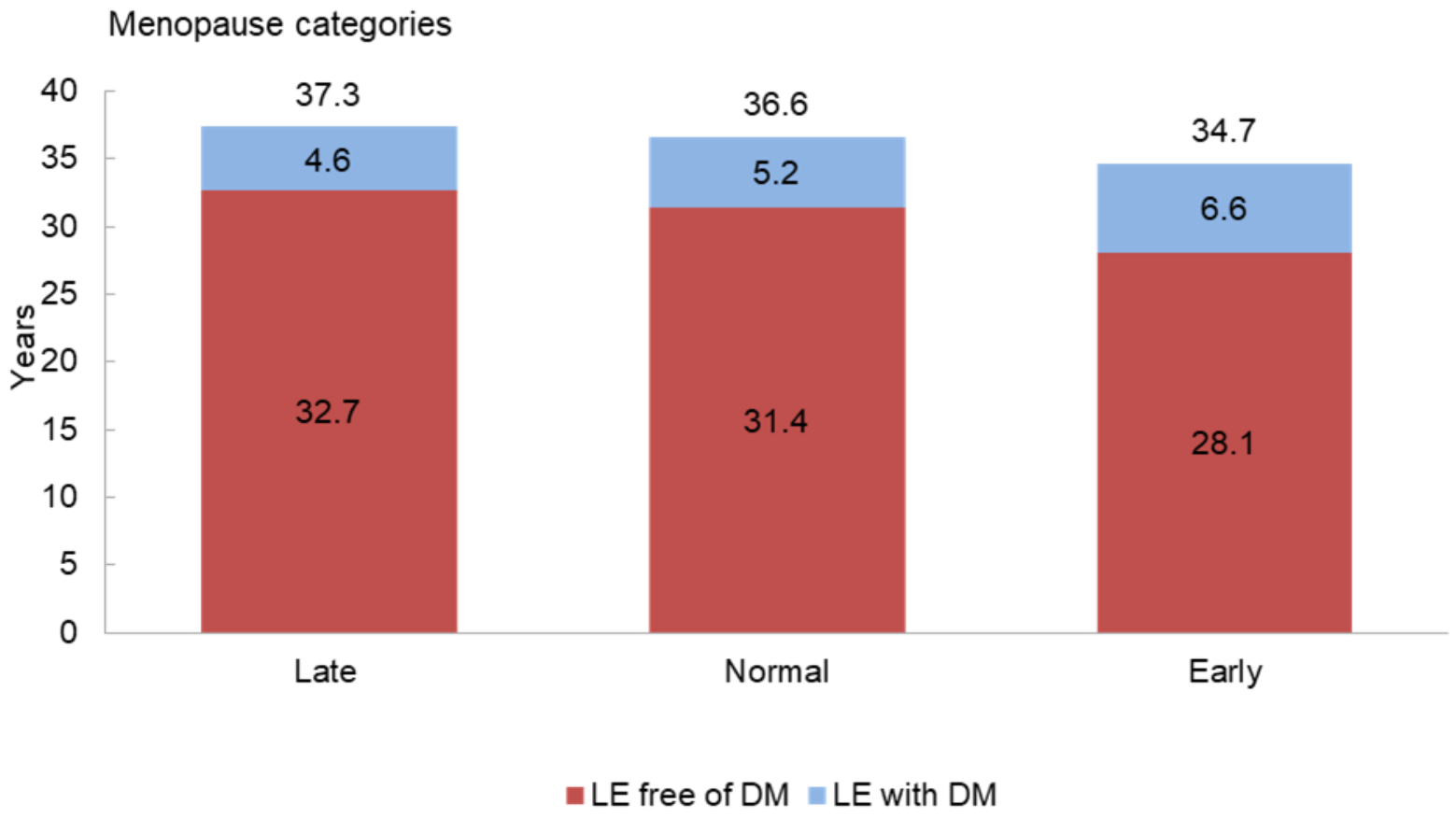
Early menopause and cardiometabolic risk





Sarnowski et al. 2017 Menopause

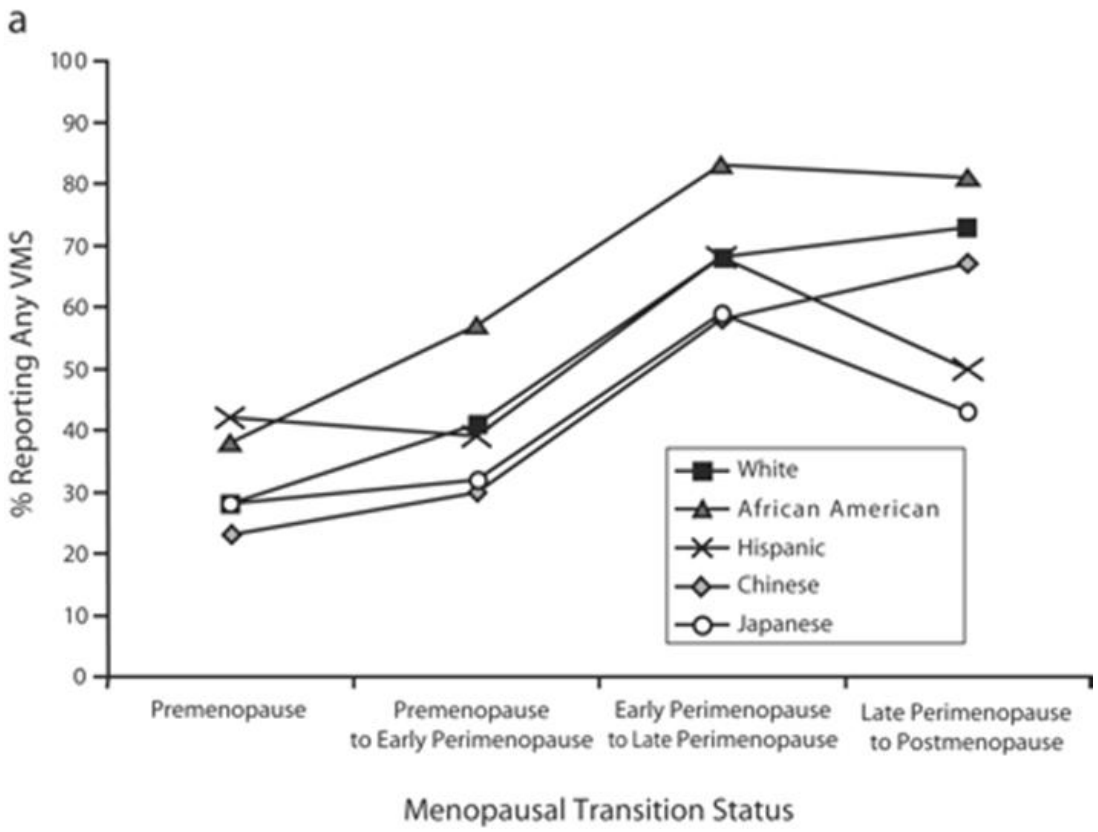
Early menopause and life expectancy



Asllanaj et al. 2019 Diabetologia

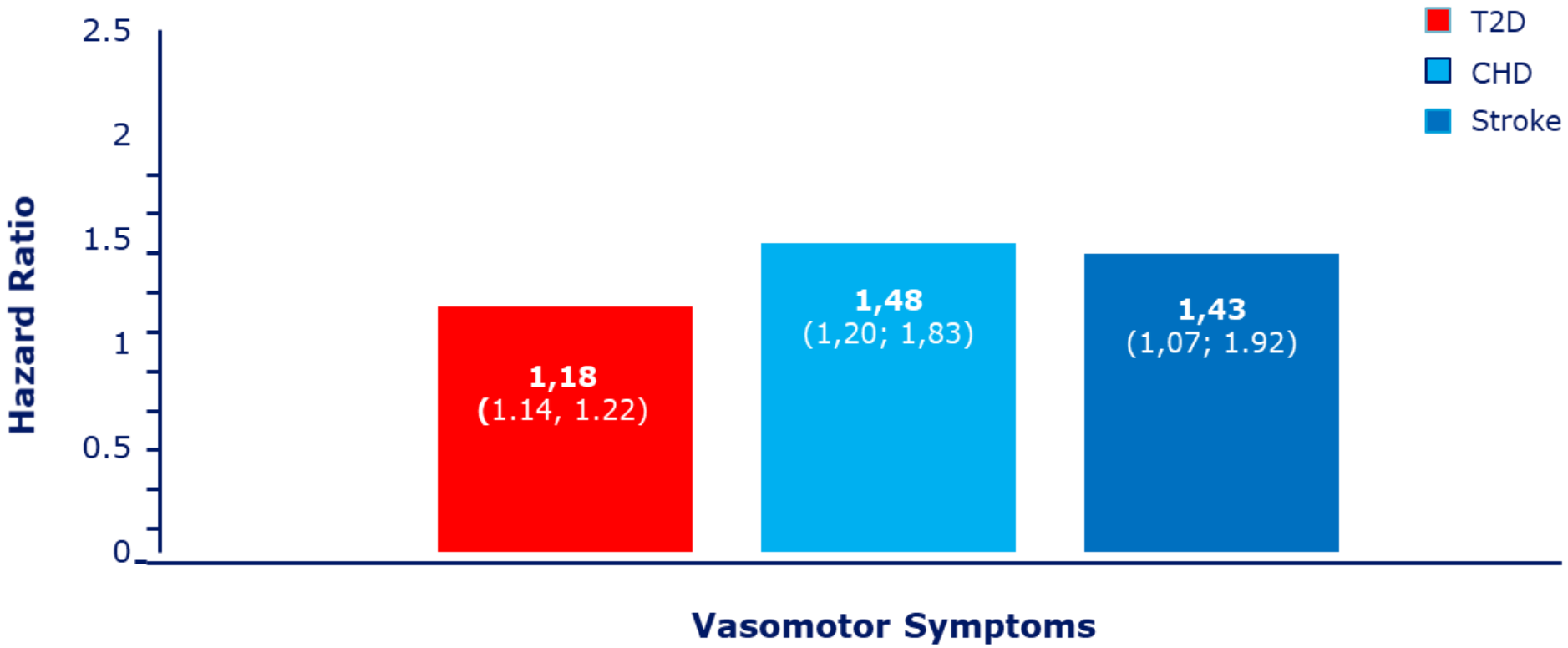
Menopausal symptoms

- **Vasomotor symptoms**
  - Hot flashes and night sweats
- **Other menopausal symptoms**
  - Anxiety
  - Depression
  - Irritability
  - Fatigue
  - Decreased libido
  - Insomnia



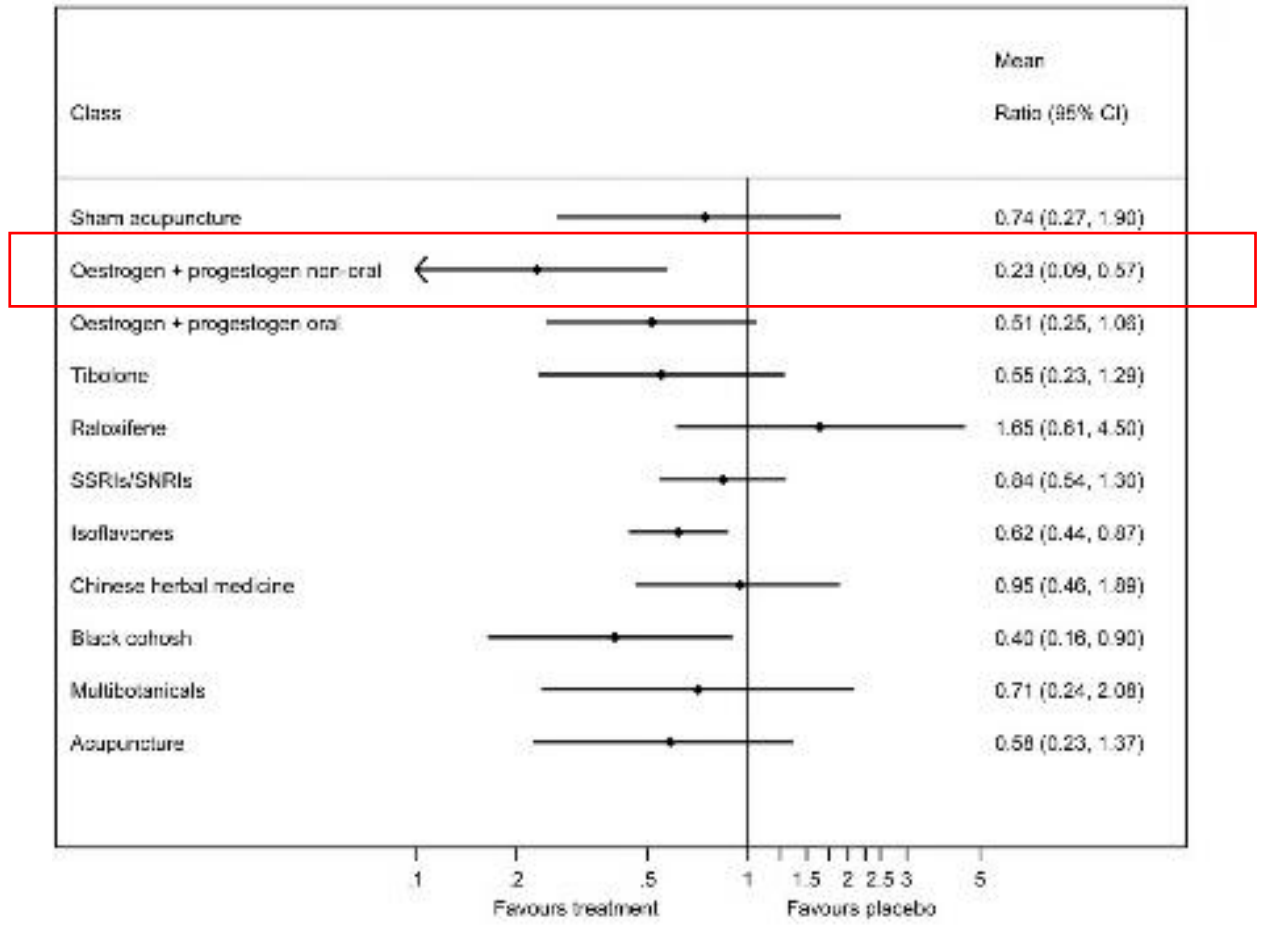
Gold EB et al. 2006

Vasomotor symptoms



Muka et al. 2017 Plos One; Kristen et al. 2018 Menopause

Treatment of menopausal symptoms



G Sarri et al. 2017

Hormone therapy and cardiovascular disease

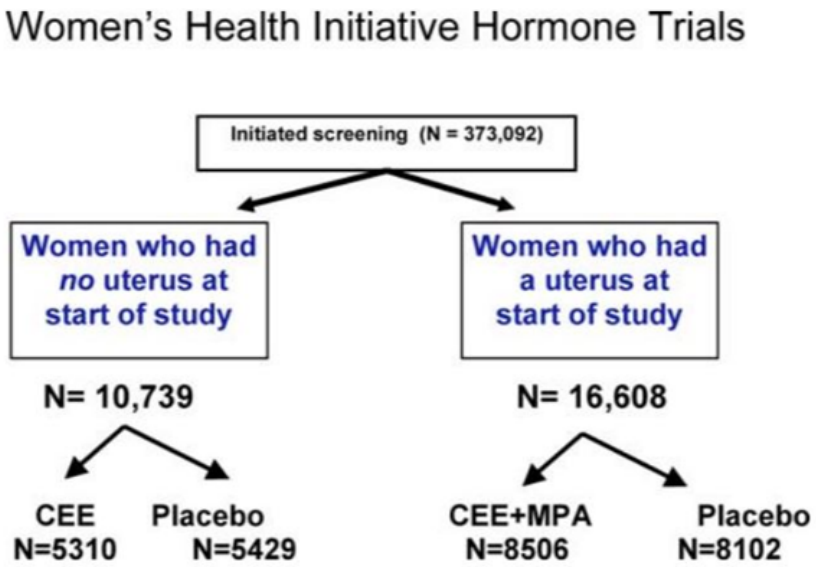


Figure 1. Women's Health Initiative Hormone Trials

CEE, conjugated equine estrogens; MPA, medroxyprogesterone acetate.
DOI: 10.1371/journal.pctr.0010026.g001

Coronary Heart Disease

- For every 10,000 women in their 50s on HT for 1 year, **5 extra cases**
- For every 10,000 women in their 70s on HT for 1 year, **19 extra cases**

Stroke

- For every 10,000 women, **9 extra cases**

Bod clots

- For every 10,000 women on HT for 1 year, **3 extra cases**

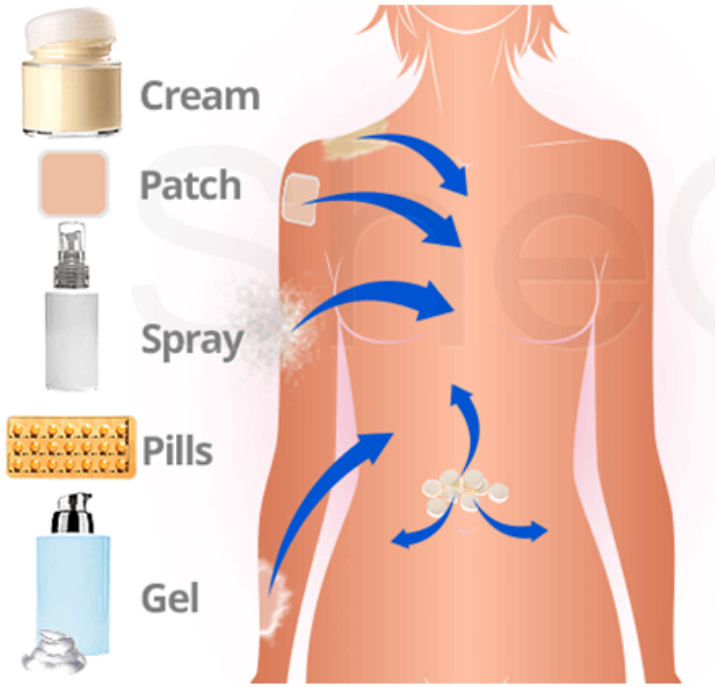
Hormone therapy and cardiovascular disease

Table 5. Cardiovascular and Global Index Events by Years Since Menopause at Baseline

	Years Since Menopause									
	<10			10-19			≥20			
	No. of Cases			No. of Cases			No. of Cases			
	Hormone Therapy (n = 3608)	Placebo (n = 3529)	HR (95% CI)*	Hormone Therapy (n = 4483)	Placebo (n = 4494)	HR (95% CI)*	Hormone Therapy (n = 4081)	Placebo (n = 4122)	HR (95% CI)*	*P* Value for Trend†
	Combined Trials									
CHD‡	39	51	0.76 (0.50-1.16)	113	103	1.10 (0.84-1.45)	194	158	1.28 (1.03-1.58)	.02
Stroke	41	23	1.77 (1.05-2.98)	100	79	1.23 (0.92-1.66)	142	113	1.26 (0.98-1.62)	.36
Total mortality	53	67	0.76 (0.53-1.09)	142	149	0.98 (0.78-1.24)	267	240	1.14 (0.96-1.36)	.51
Global index§	222	203	1.05 (0.86-1.27)	482	440	1.12 (0.98-1.27)	675	632	1.09 (0.98-1.22)	.82
	Estimated Absolute Excess Risk per 10000 Person-Years			Estimated Absolute Excess Risk per 10000 Person-Years			Estimated Absolute Excess Risk per 10000 Person-Years			

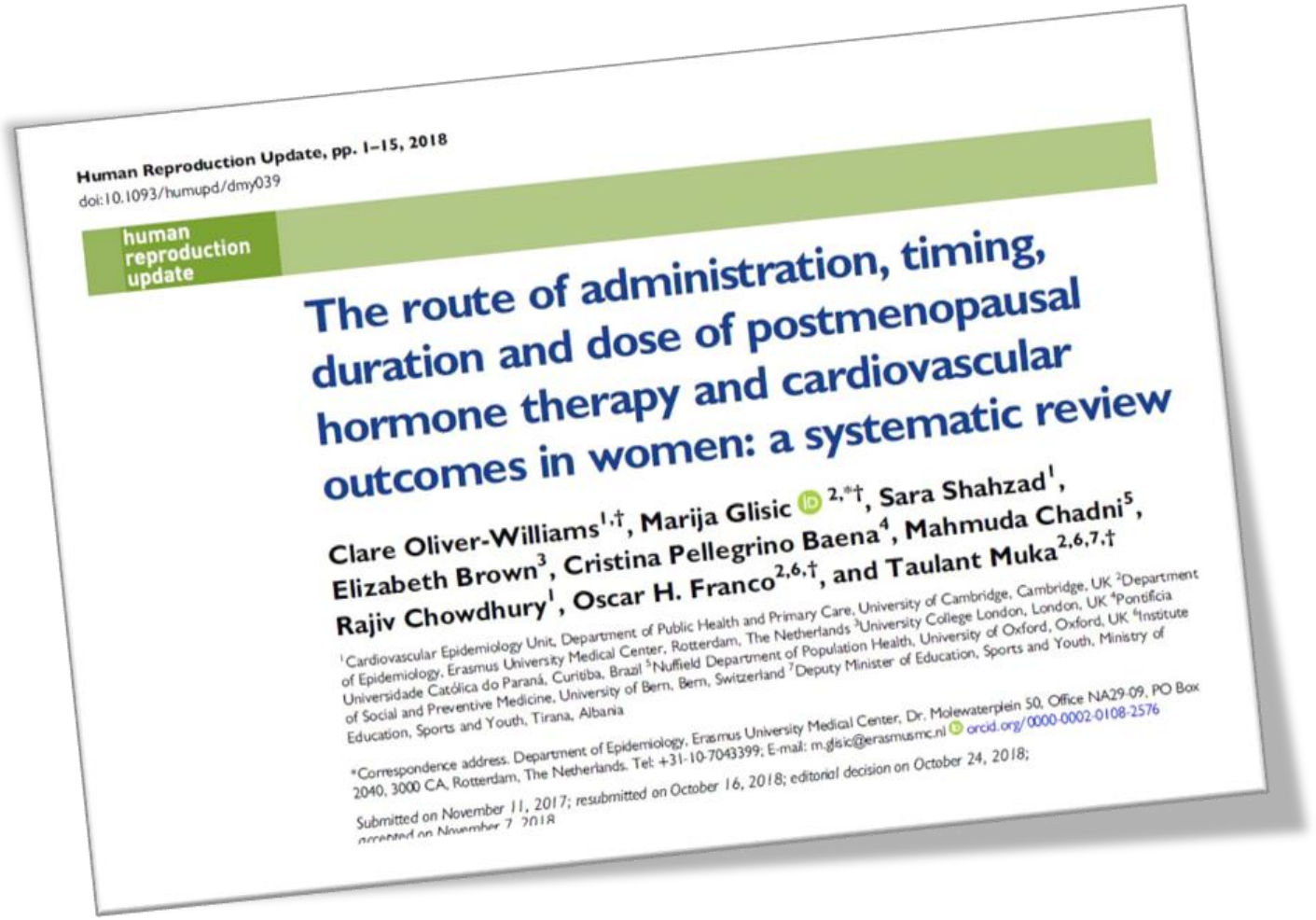
Rossouw et al. 2007

Hormone therapy and cardiovascular disease



- **Route of administration**
  - The most commonly prescribed is oral HT
- **Formula**
  - Conjugated equine estrogen (CEE), the most common
  - Synthetic conjugated estrogens
  - Micronized 17b-estradiol and ethinyl estradiol
  - Progestins: medroxyprogesterone, acetate (MPA), norethindrone acetate and native progesterone

Hormone therapy and cardiovascular disease



Human Reproduction Update, pp. 1–15, 2018
doi:10.1093/humupd/dmy039

human reproduction update

The route of administration, timing, duration and dose of postmenopausal hormone therapy and cardiovascular outcomes in women: a systematic review

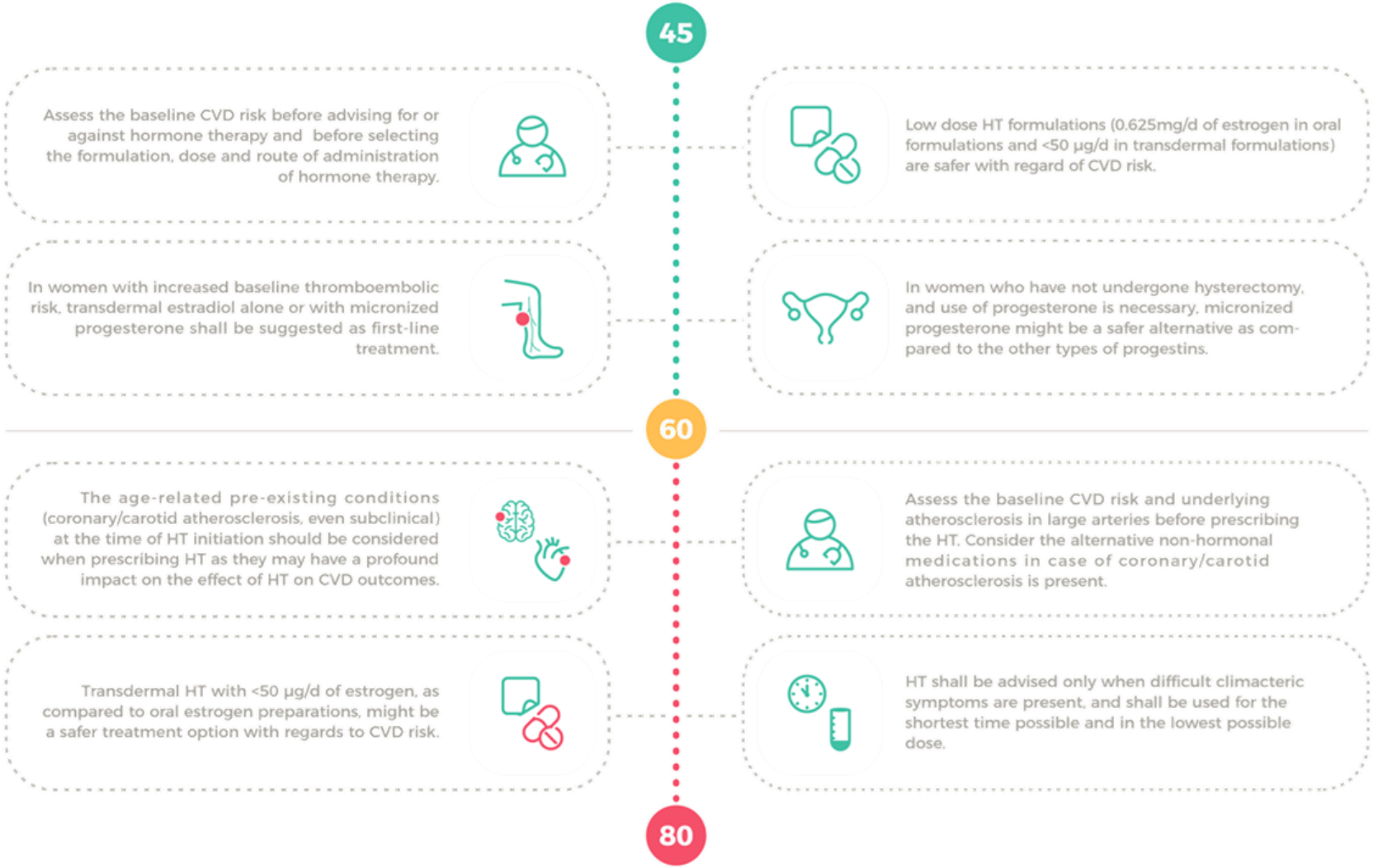
Clare Oliver-Williams[1,†], Marija Glisic[2,*†], Sara Shahzad[1], Elizabeth Brown[3], Cristina Pellegrino Baena[4], Mahmuda Chadni[5], Rajiv Chowdhury[1], Oscar H. Franco[2,6,†], and Taulant Muka[2,6,7,†]

[1]Cardiovascular Epidemiology Unit, Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK [2]Department of Epidemiology, Erasmus University Medical Center, Rotterdam, The Netherlands [3]University College London, London, UK [4]Pontificia Universidade Católica do Paraná, Curitiba, Brazil [5]Nuffield Department of Population Health, University of Oxford, Oxford, UK [6]Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland [7]Deputy Minister of Education, Sports and Youth, Ministry of Education, Sports and Youth, Tirana, Albania

*Correspondence address. Department of Epidemiology, Erasmus University Medical Center, Dr. Molewaterplein 50, Office NA29-09, PO Box 2040, 3000 CA, Rotterdam, The Netherlands. Tel: +31-10-7043399; E-mail: m.glisic@erasmusmc.nl orcid.org/0000-0002-0108-2576

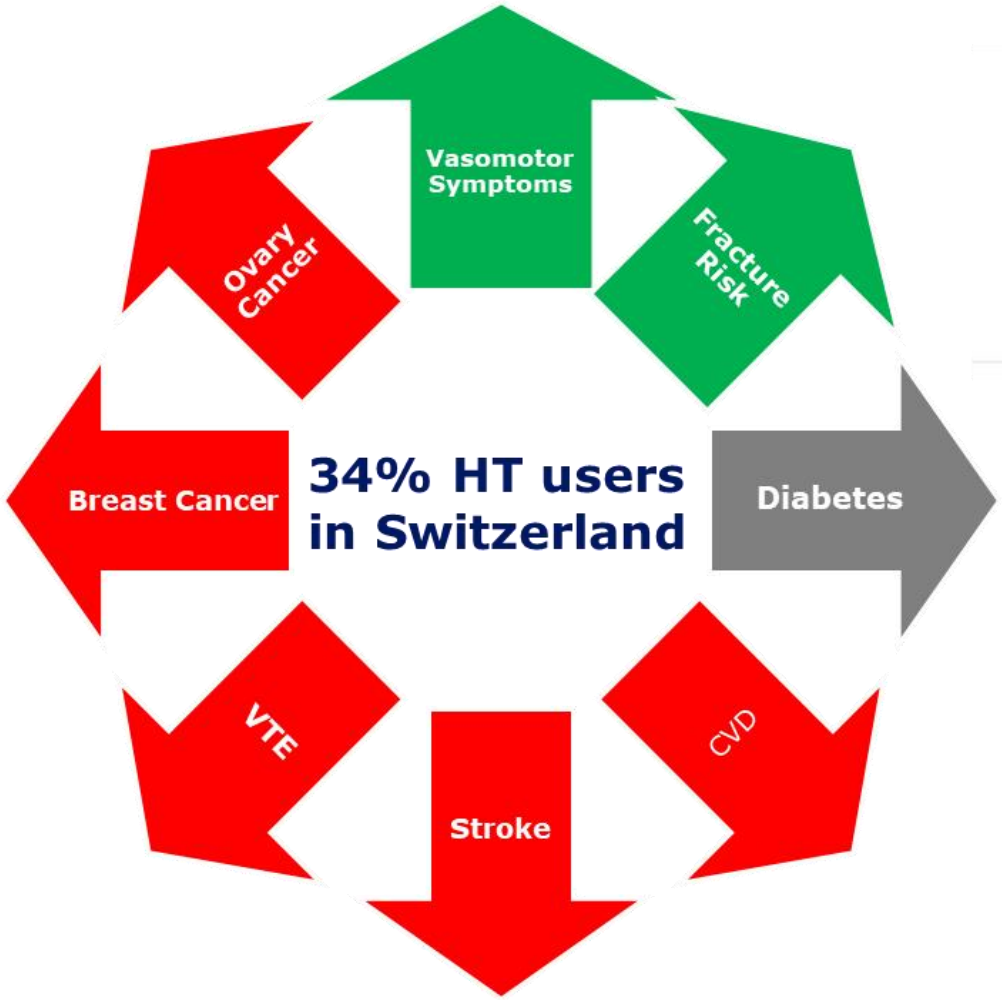
Submitted on November 11, 2017; resubmitted on October 16, 2018; editorial decision on October 24, 2018; accepted on November 7, 2018

Hormone therapy and cardiovascular risk



UNIVERSITÄT BERN

Hormone therapy: benefits and harms



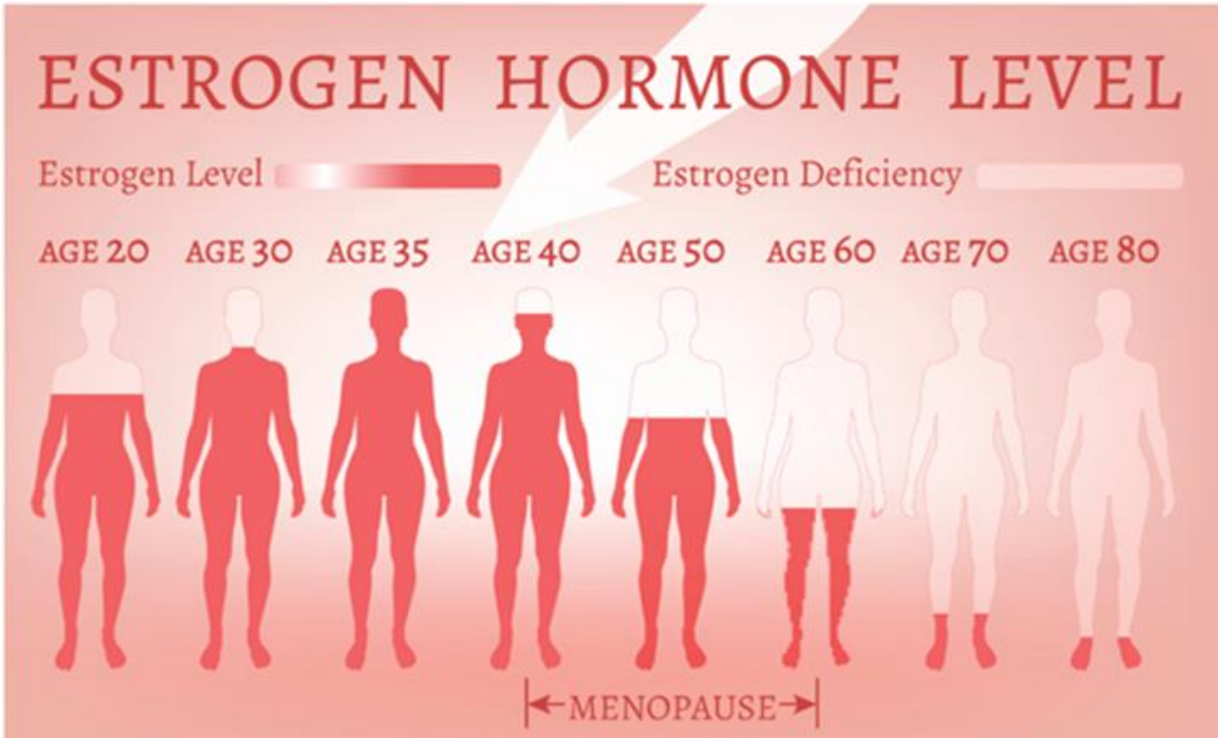
Four in ten women on hormone replacement therapy can't get their medication amid mass shortages

- HRT shortage is forcing some women to go 'cold turkey' on the advice of GPs
- Others are flying to Greece or Spain to get the drugs or rationing the medication
- Survey of 1,500 women found 40 per cent told the medication is not available

HRT shortage in UK expected to continue until next year

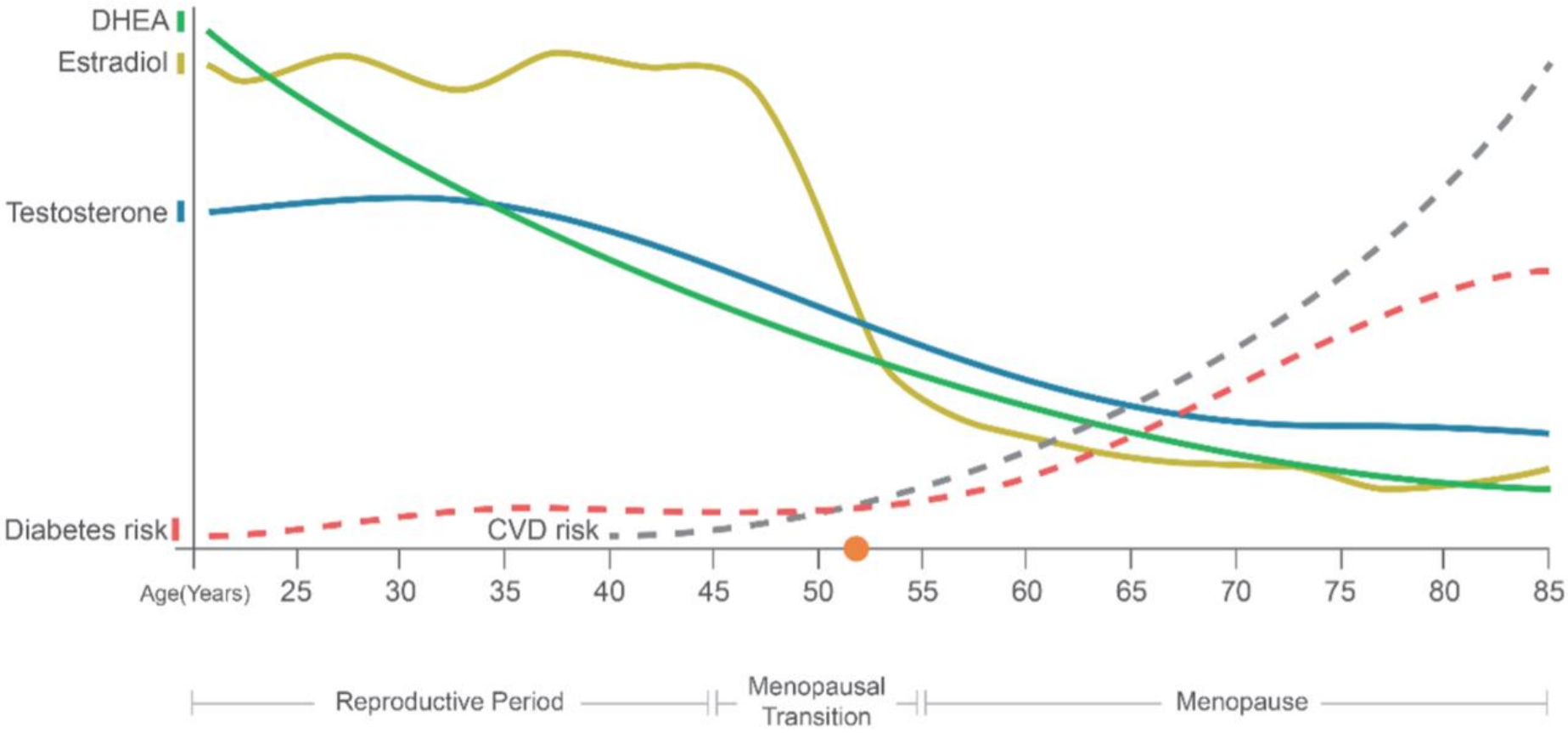
Around half of HRT products have been reported as out of stock in UK pharmacies due to supply issues in China, leading to a shortage.

Estrogen hypothesis:
the evidence is amenable to alternative explanations



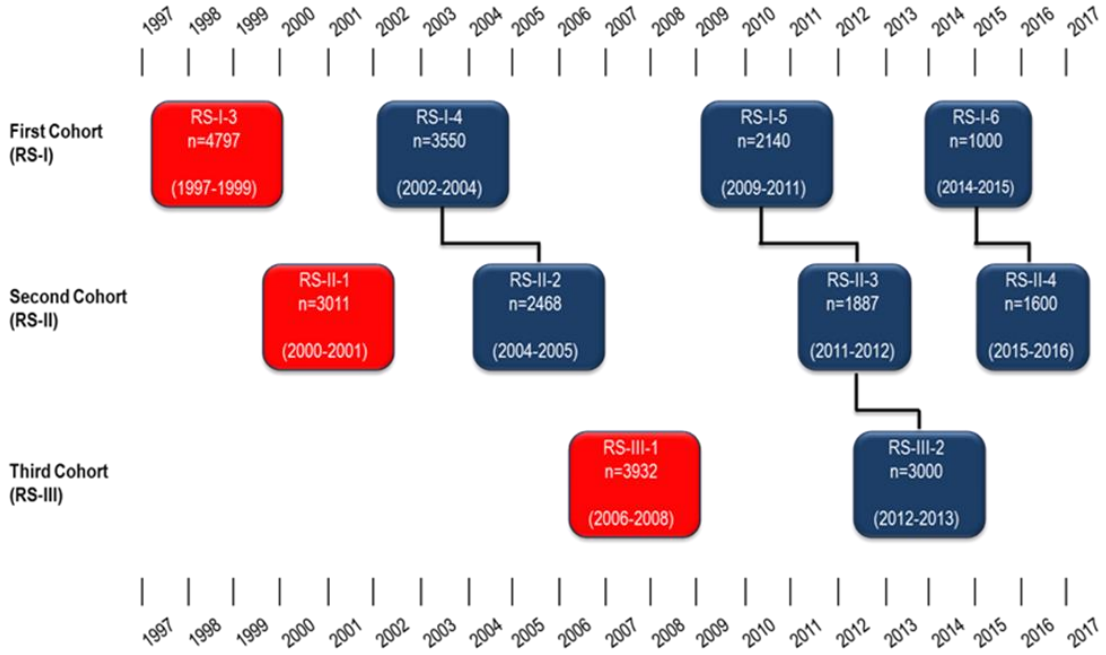
Anagnostis et al. 2019 Endocrine

Adverse metabolic changes related to menopause



al., 2018; Glisic et al., 2019

Sex hormones and risk of type 2 diabetes



384 women developed diabetes over a median follow-up of 11.1 years

Muka et al. 2017. Diabetes


Diabetes Volume 66, March 2017

Taulant Muka,[1,2] Jana Nano,[1] Loes Jaspers,[1] Cindy Meun,[3] Wichor M. Bramer,[4] Albert Hofman,[1,2] Abbas Dehghan,[1] Maryjam Kavousi,[1] Joop S.E. Laven,[2] and Oscar H. Franco[1]

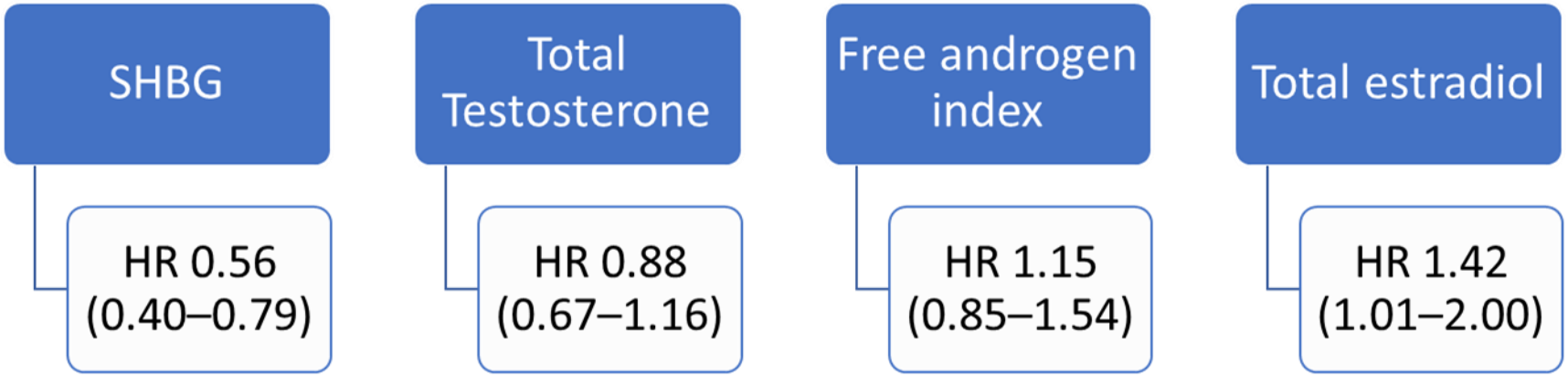
Associations of Steroid Sex Hormones and Sex Hormone–Binding Globulin With the Risk of Type 2 Diabetes in Women: A Population-Based Cohort Study and Meta-analysis

Diabetes 2017;66:577–586 | DOI: 10.2337/db16-0473

Table 1—Selected characteristics of study participants, the Rotterdam Study

	Women (n = 3,117)	% missing values
Age (years)	69.7 ± 8.7	0
Years since menopause (years)	20.9 ± 10.0	4.4
Age of menopause (years)	48.9 ± 5.2	4.4
Number of pregnancies of at least 6 months	2.3 ± 2	12.4
Natural menopause, n (%)	2,433 (78.1)	0
Current smokers, n (%)	218 (9.2)	1.8
Alcohol intake (g/day)	1.3 (10)[a]	26.5
BMI (kg/m^2)	27.0 ± 4.3	2.3

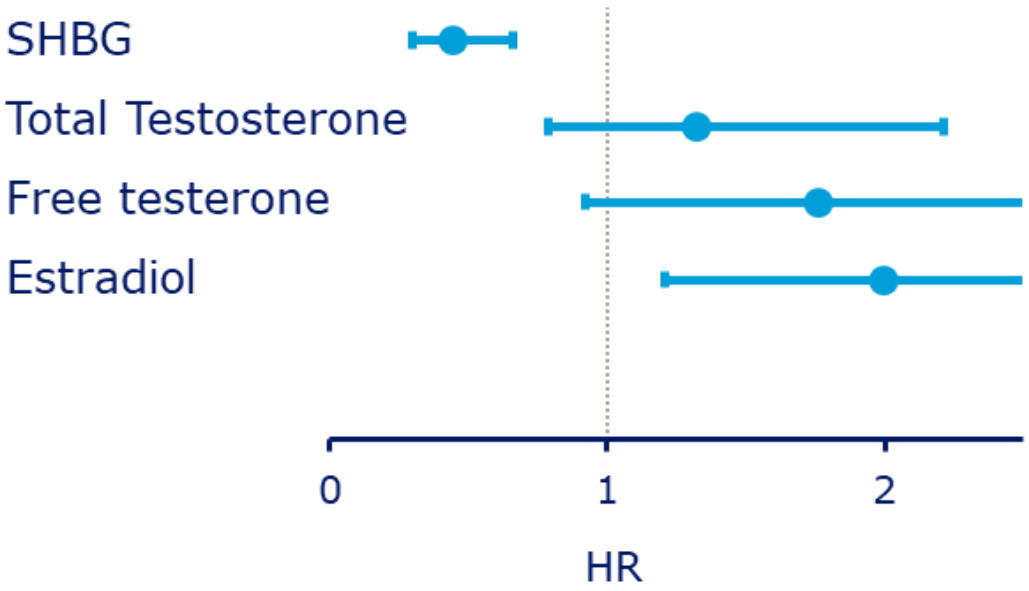
3rd vs. 1st tertiles of steroid sex hormones and type 2 diabetes



Models adjusted for age, cohort, fasting status, insulin, glucose, and BMI, alcohol intake, smoking status, coronary heart disease, serum total cholesterol, statin use, systolic blood pressure, treatment for hypertension, hormone replacement therapy, age of menopause, CRP, and sex hormones for each other

Muka et al. 2017. Diabetes

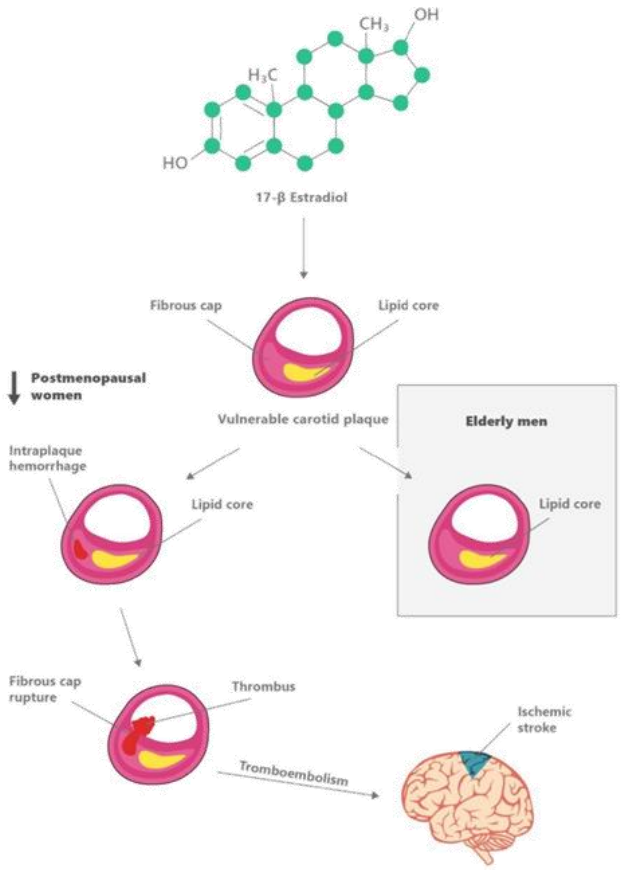
Sex hormones and risk of type 2 diabetes



	HR	[95% CI]
SHBG	0,44	[0,14; 0,22]
Total Testosterone	1,32	[0,79; 2,21
Free testerone	1,76	[0,92; 3,30]
Estradiol	1,99	[1,21; 3,27]

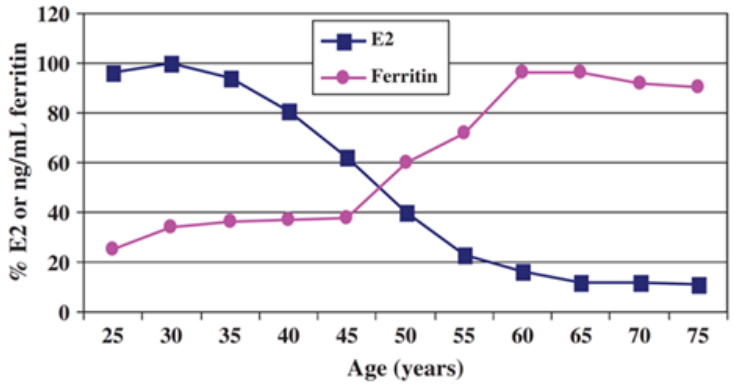
Muka et al. 2017. Diabetes

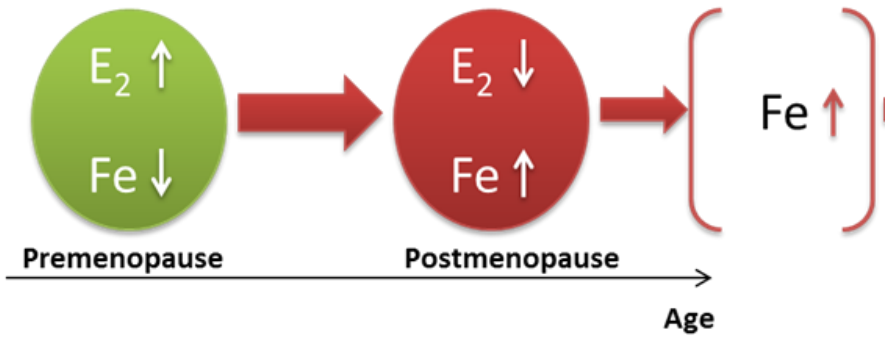
Sex hormones and stroke risk

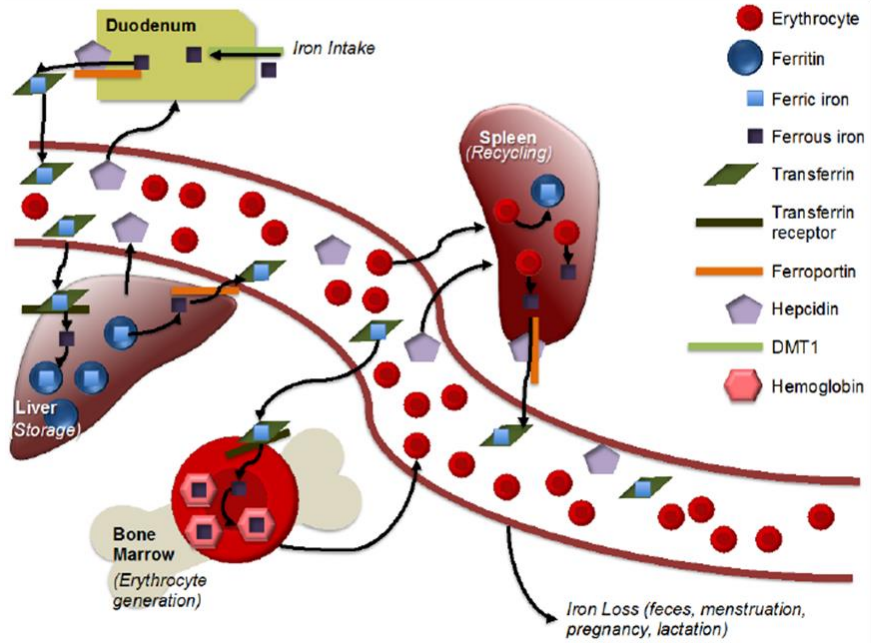


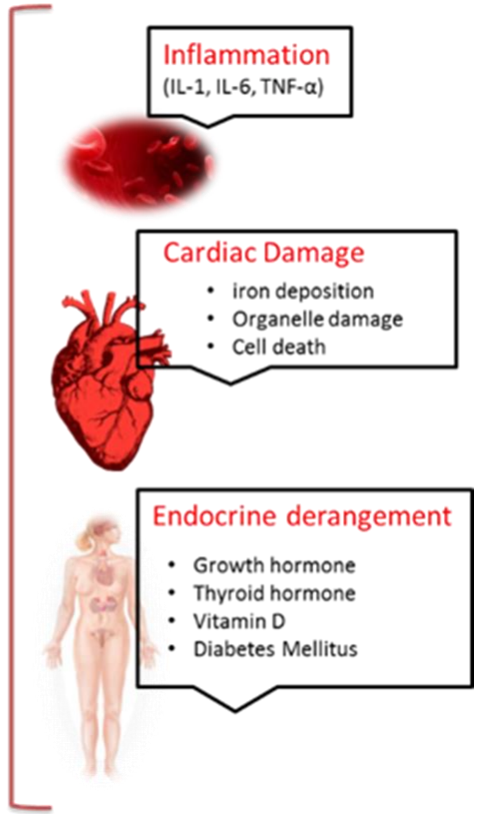
Glisic et al. 2019. Circulation Research

Time to shift from estrogen to iron hypothesis?

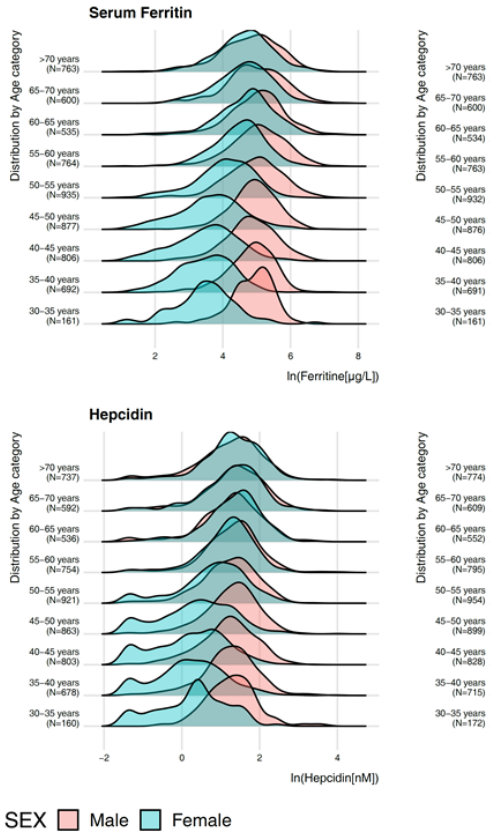


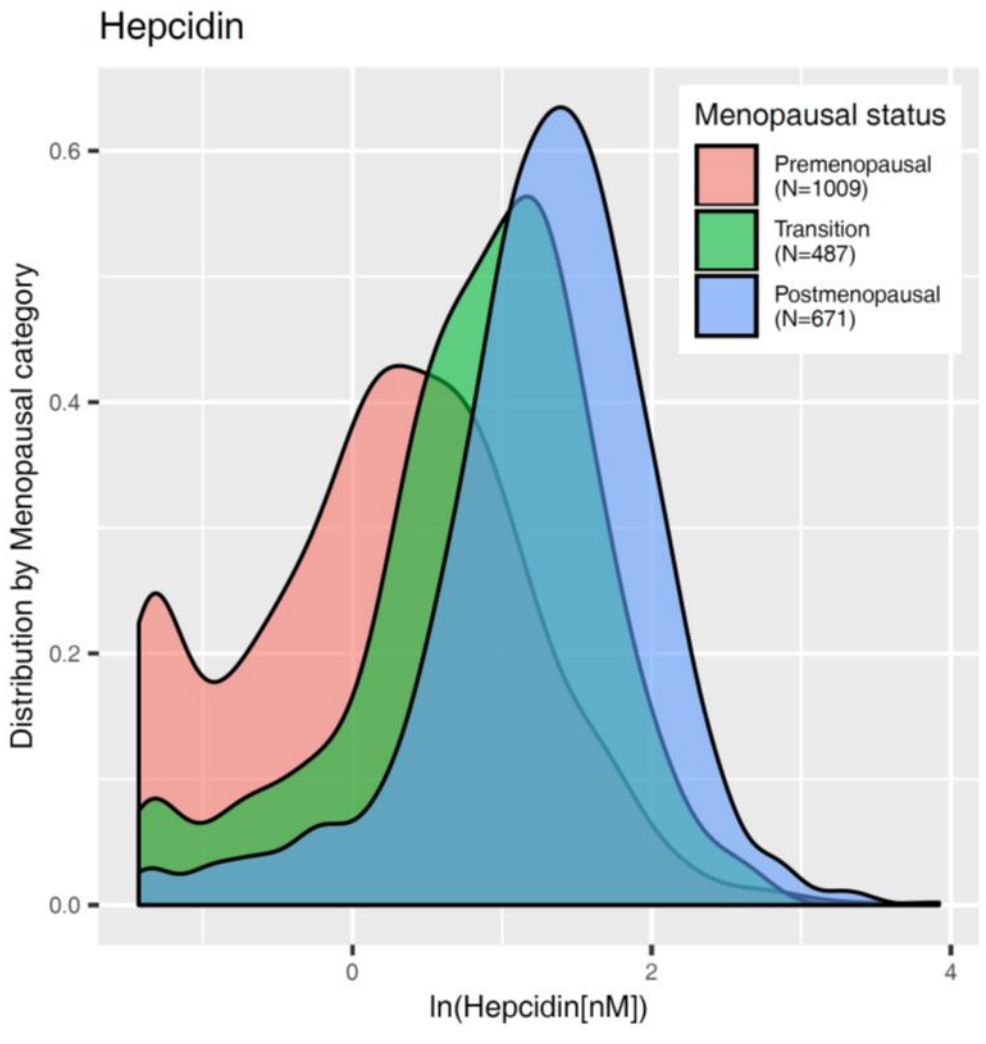


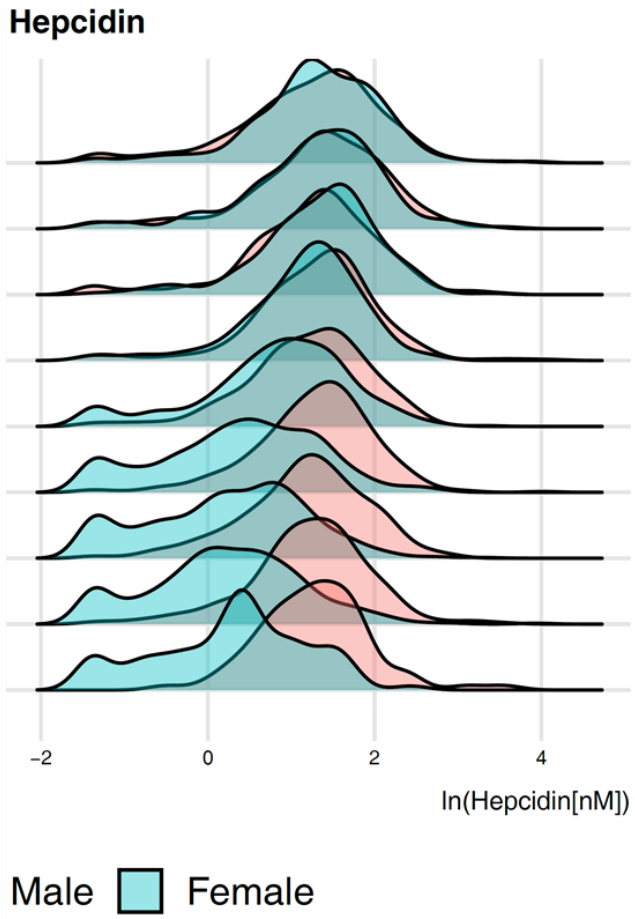




Time to shift from estrogen to iron hypothesis?





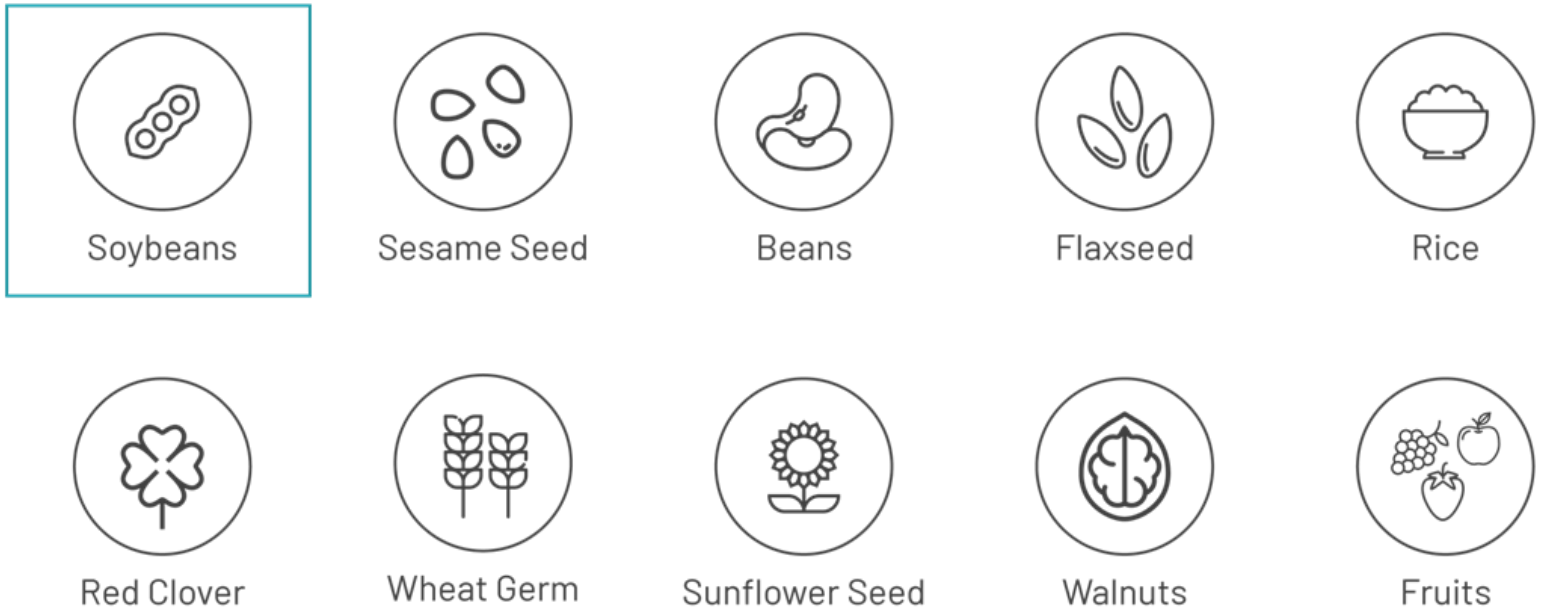


Estrogen Signaling

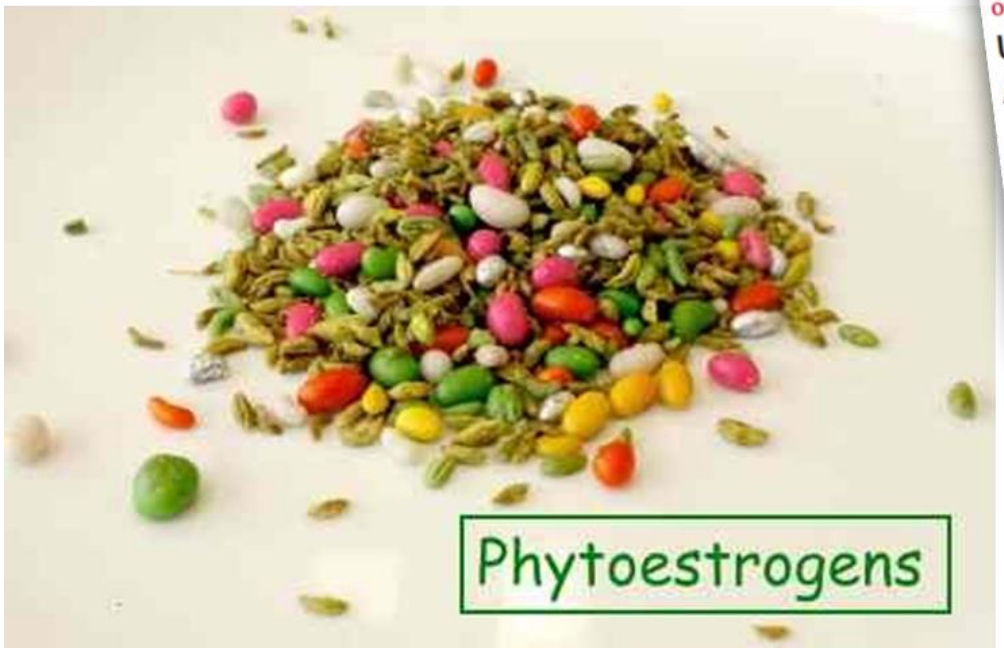
Arnold et al. 2005

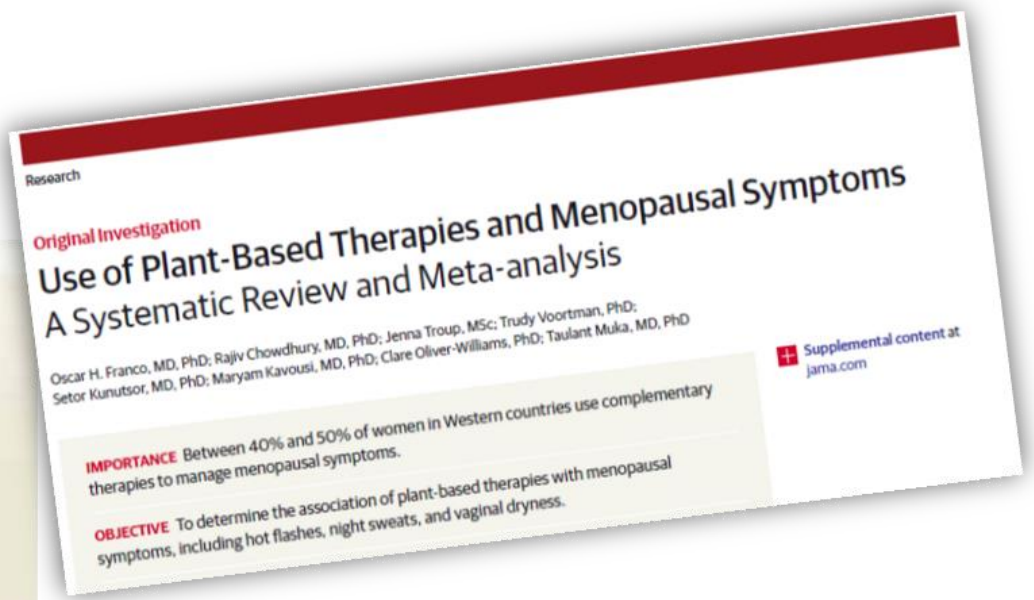
Alternative treatment

polyphenols that are structurally similar to endogenous estrogen and have weak estrogenic properties



Alternative treatment





Research

Original Investigation

Use of Plant-Based Therapies and Menopausal Symptoms
A Systematic Review and Meta-analysis

Oscar H. Franco, MD, PhD; Rajiv Chowdhury, MD, PhD; Jenna Troup, MSc; Trudy Voortman, PhD; Setor Kunutsor, MD, PhD; Maryam Kavousi, MD, PhD; Clare Oliver-Williams, PhD; Taulant Muka, MD, PhD

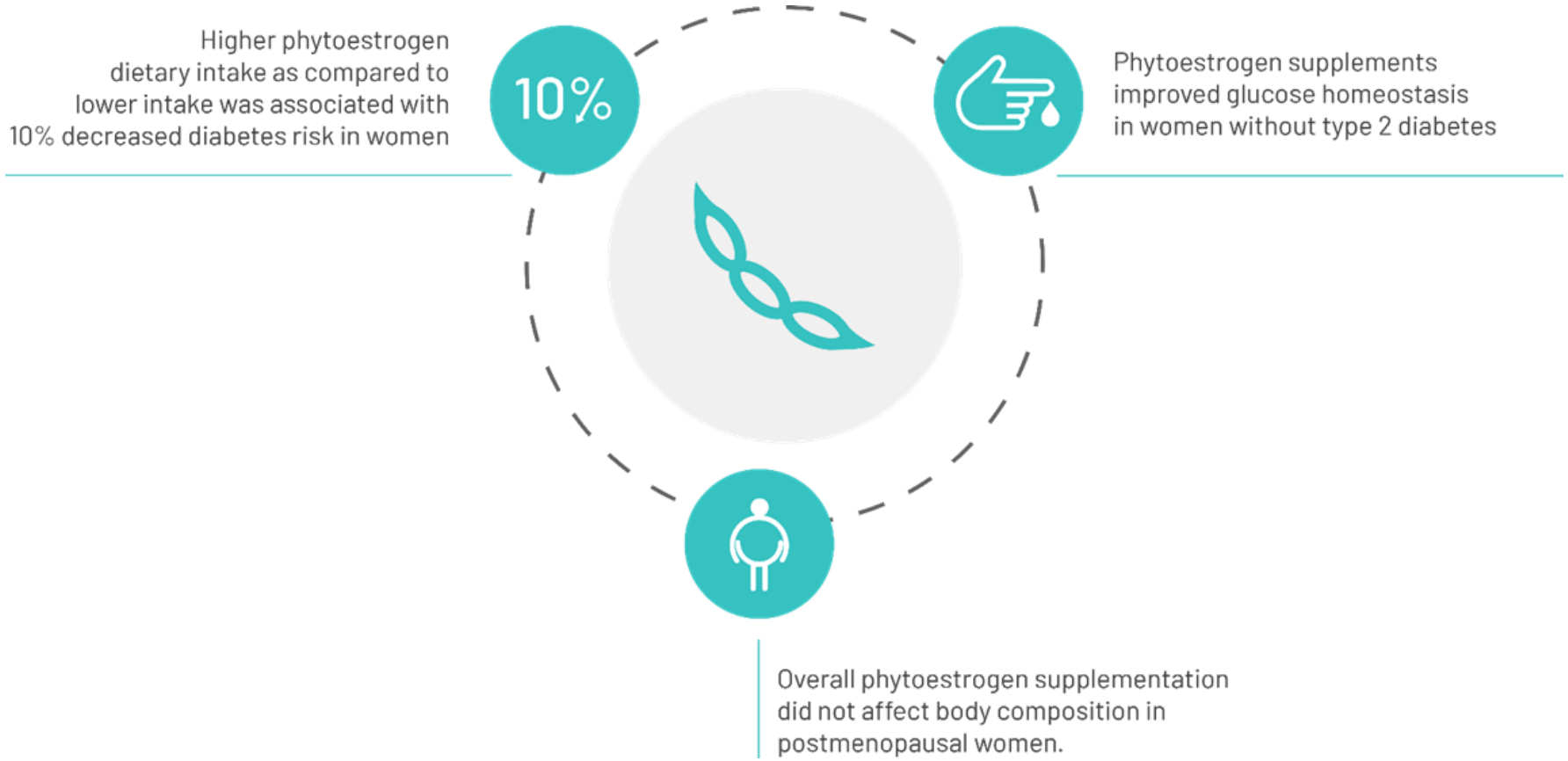
Supplemental content at jama.com

IMPORTANCE Between 40% and 50% of women in Western countries use complementary therapies to manage menopausal symptoms.

OBJECTIVE To determine the association of plant-based therapies with menopausal symptoms, including hot flashes, night sweats, and vaginal dryness.

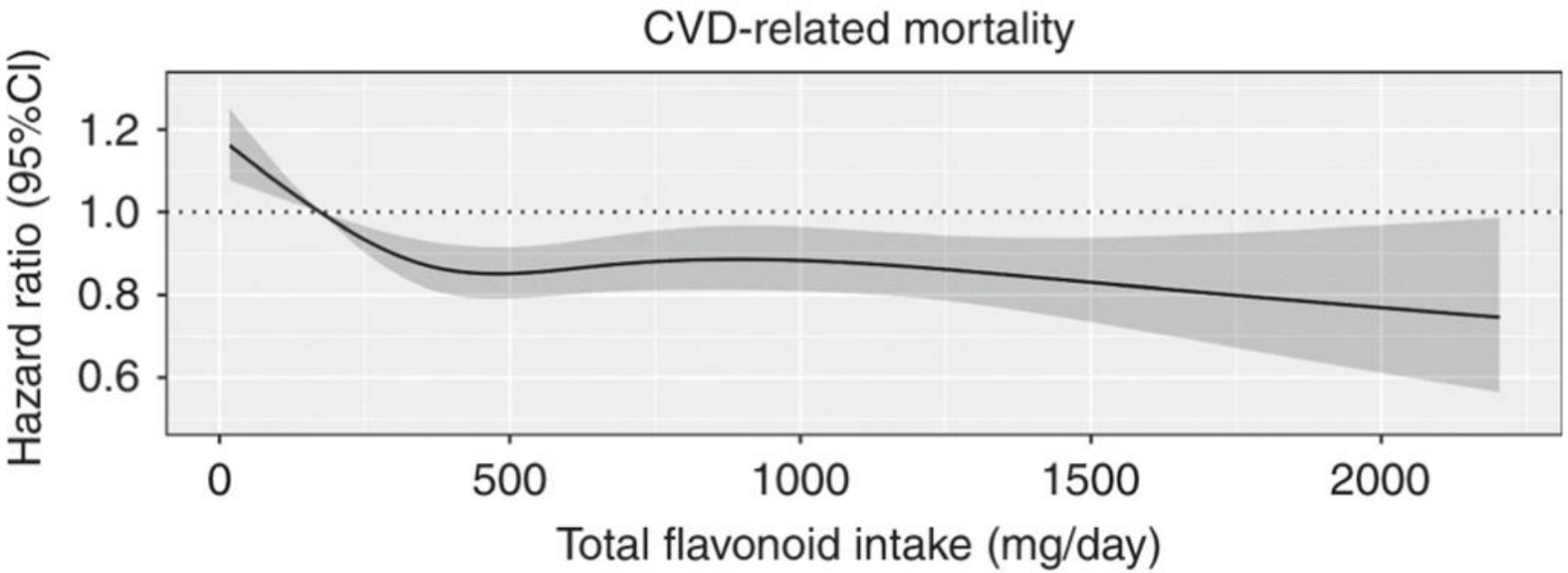
Muka et al. 2017 JAMA; Muka et al. Plos One

Phytoestrogens and risk of T2D in women



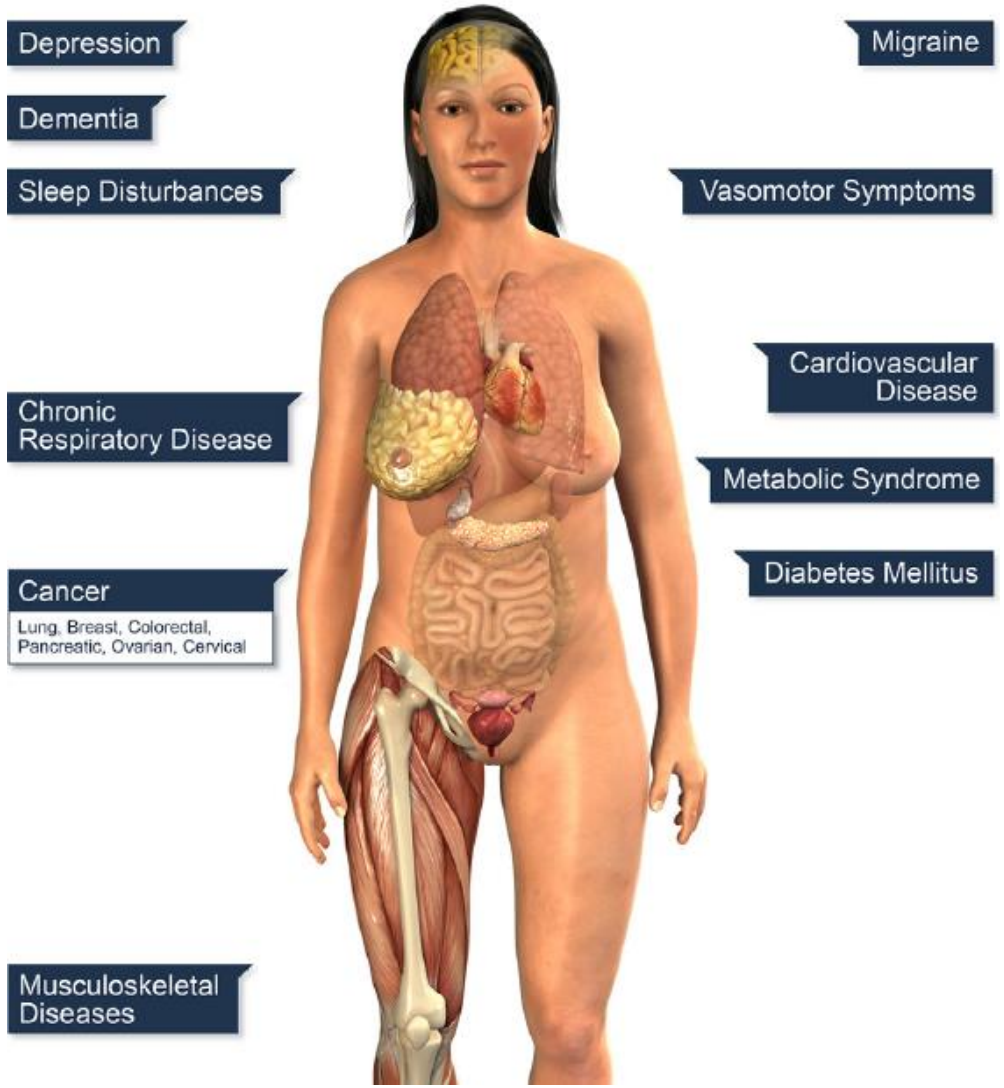
Glisic at al. 2018 Adv Nutr

Phytoestrogens, cardiovascular disease and all-cause mortality



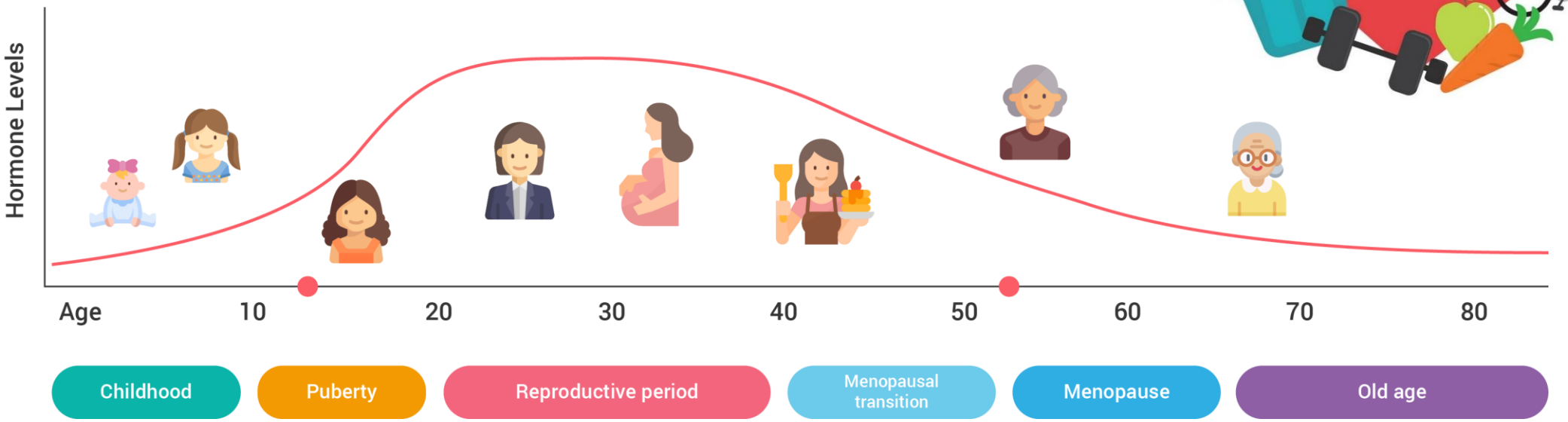
Bondonno NP et al. 2019

Major health issues for menopausal women



M. van Dijk et al. 2015 Maturitas

Women’s life cycle



Cardiometabolic Research Group

Thank you!