La medicina di genere e le 4 P

Maria Lorenza Muiesan
Dipartimento di Scienze Cliniche e Sperimentali- UOC 2 Medicina
Università di Brescia & ASST Spedali Civili

Sex vs gender

Sex and gender are different constructs. According to the WHO

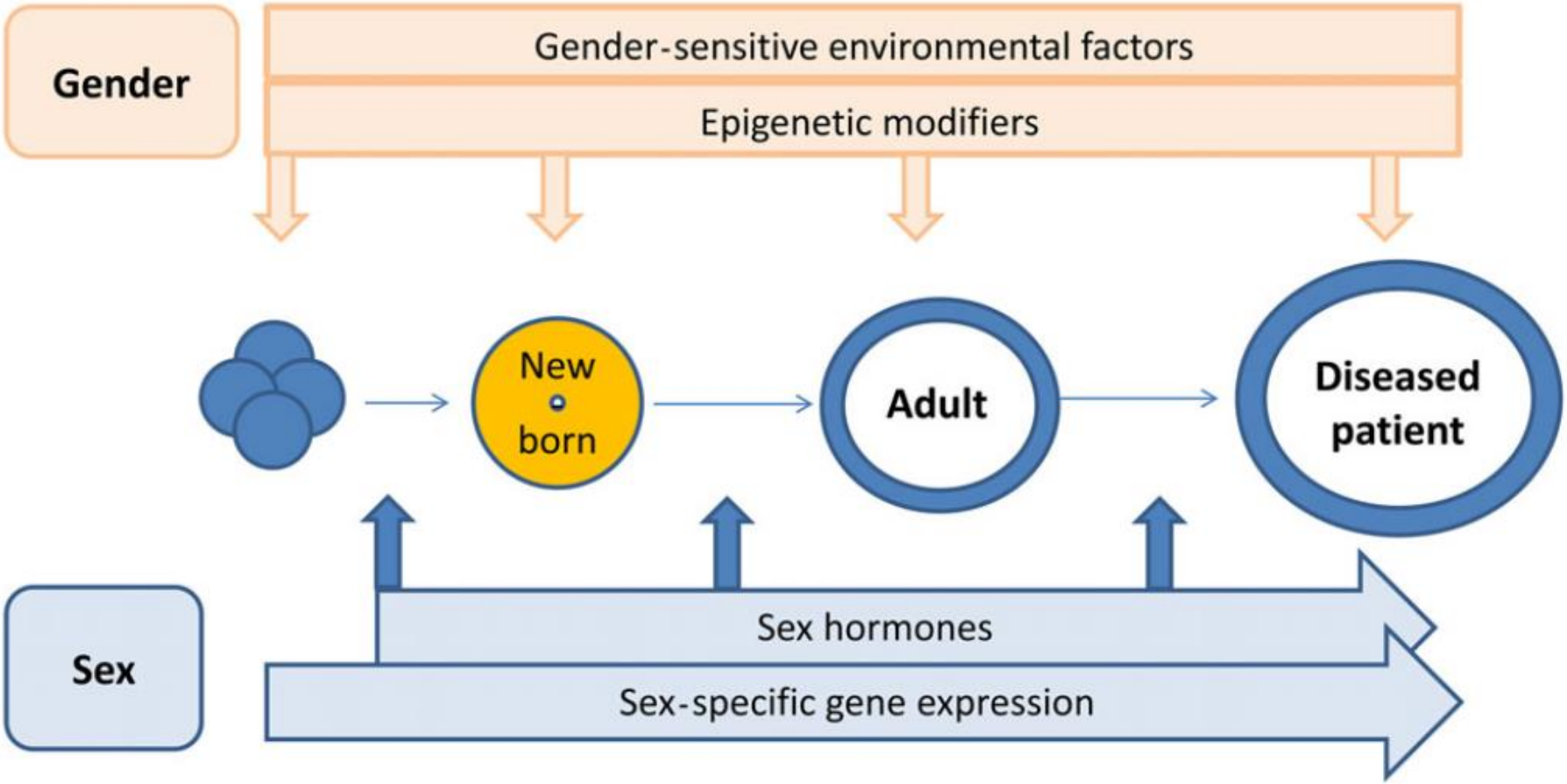
sex "set of biological characteristics that define humans as female or male";
primarily associated with physical and physiological features
(chromosomes, gene expression, hormone levels, and
reproductive/sexual anatomy)

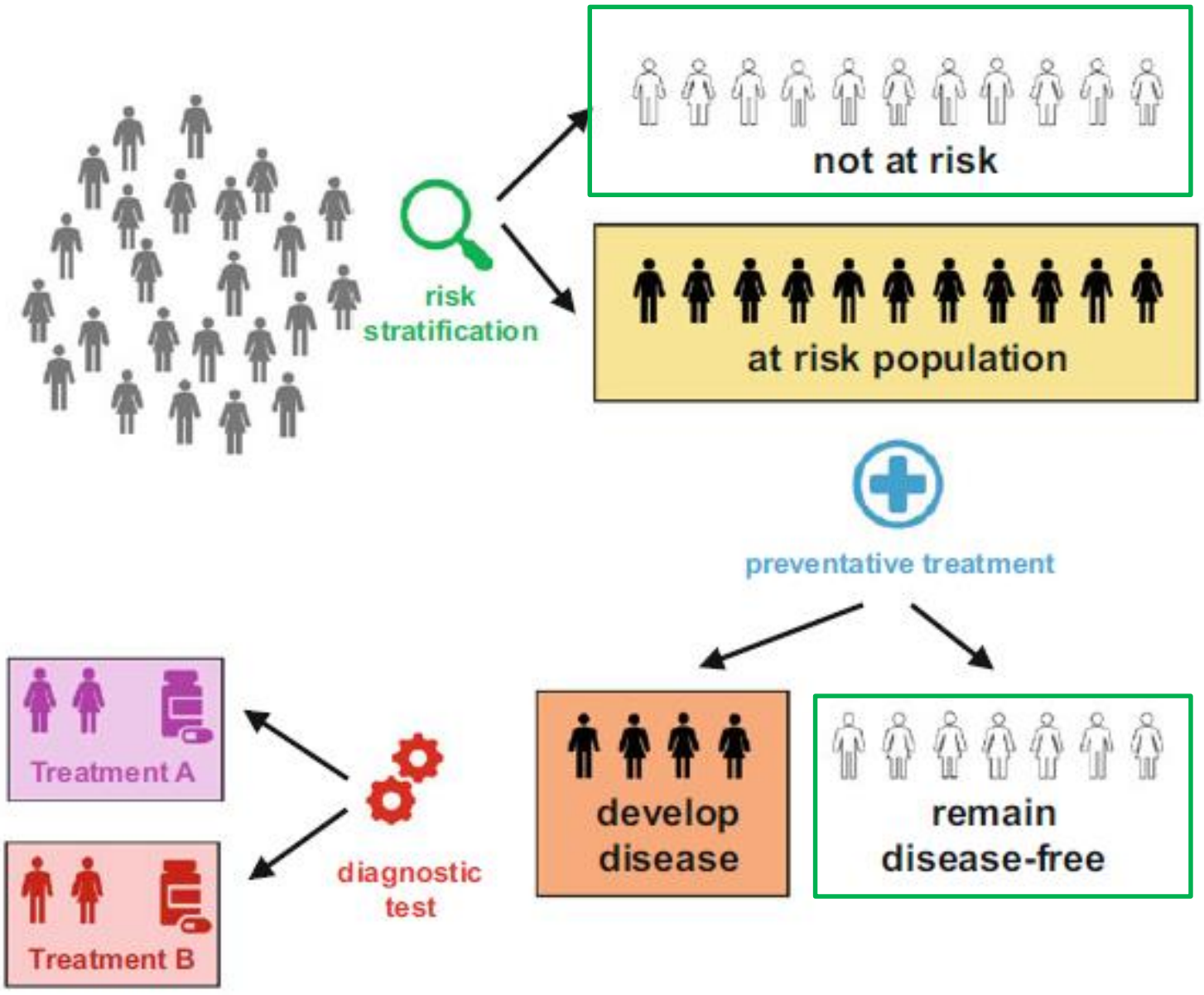
Gender "socially constructed roles, behaviors, activities, and attributes that a given
society considers appropriate for men and women"
influences the distribution of power and resources, including access to
healthcare.

http://www.who.int/reproductivehealth/topics/sexual_health/sh_definitions/en/.
http://www.who.int/gender-equity-rights/understanding/gender-definition/en/.

Complex interdependency of sex and gender in the human

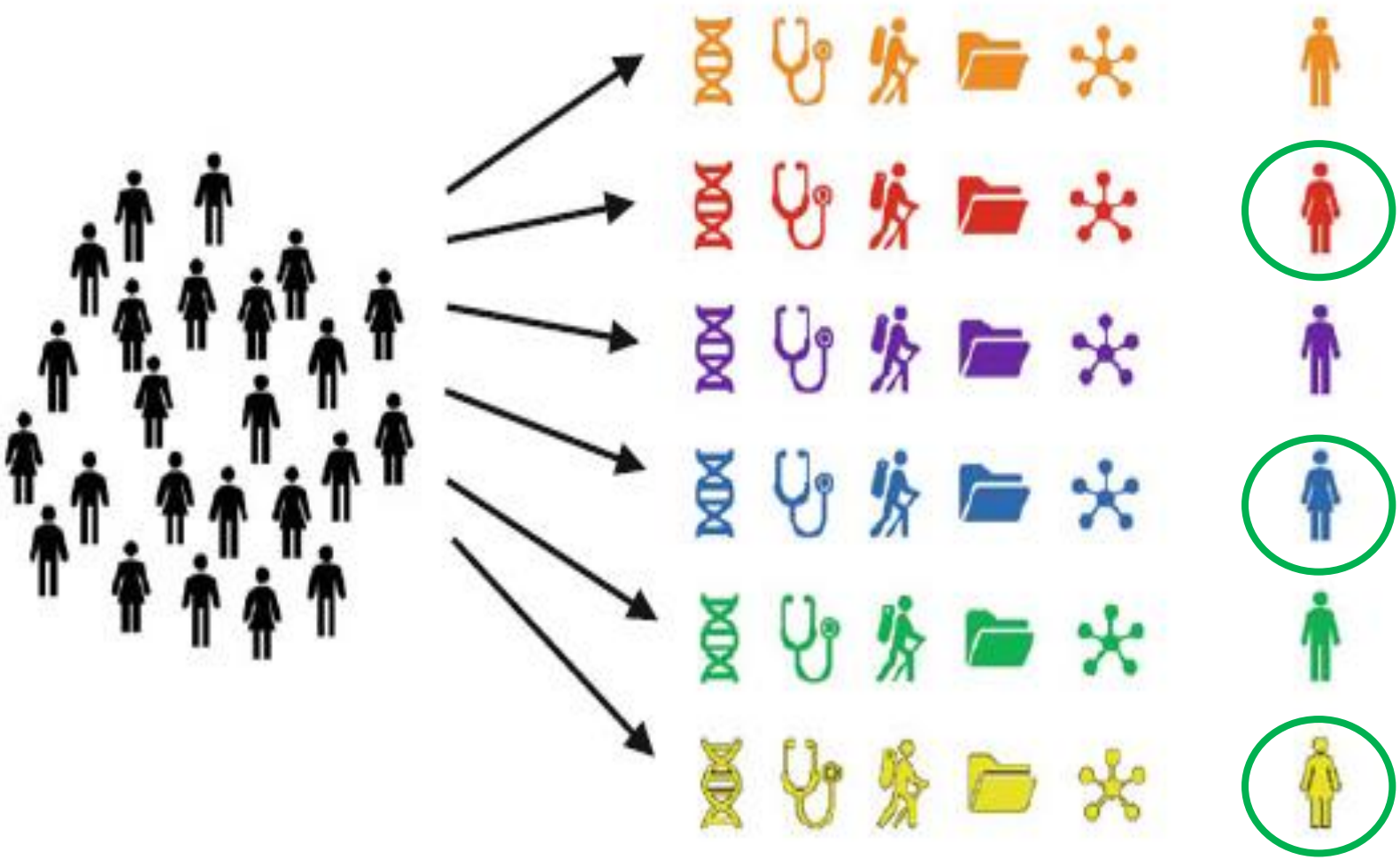
Sex and gender influence each other through complex interactions.
Both sex and gender are critical variables in preclinical and clinical research.





Traditional approach prevention & treatment

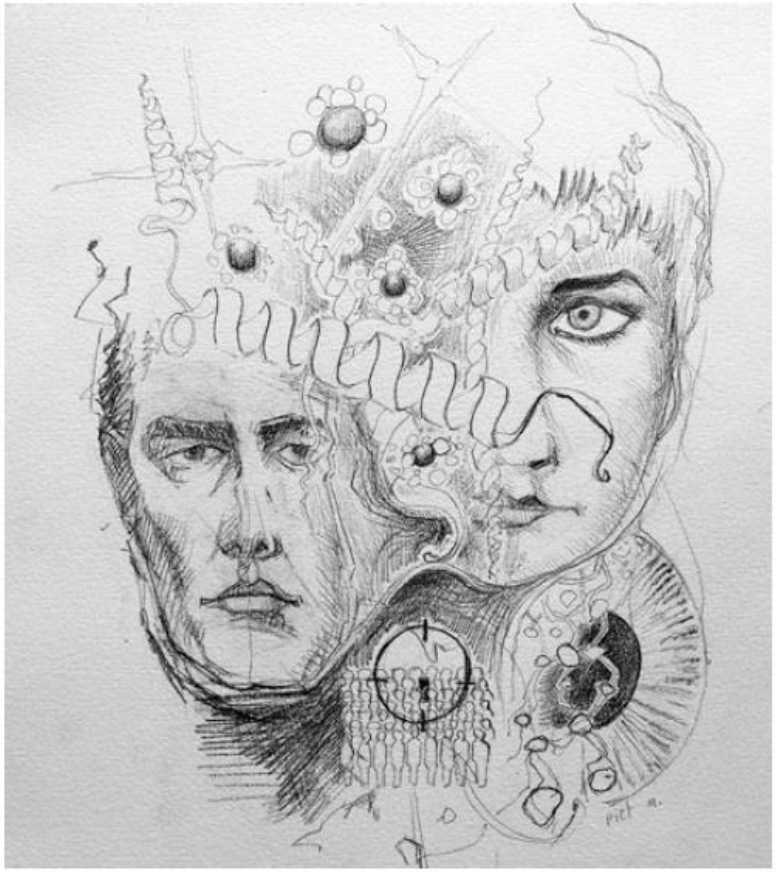
genetic/genomic
imaging and functional studies
individual lifestyle factor
medical records



personalised prevention and treatment

Medicina di genere e le 4 P

- Predittiva
- Preventiva
- Personalizzata
- Partecipativa

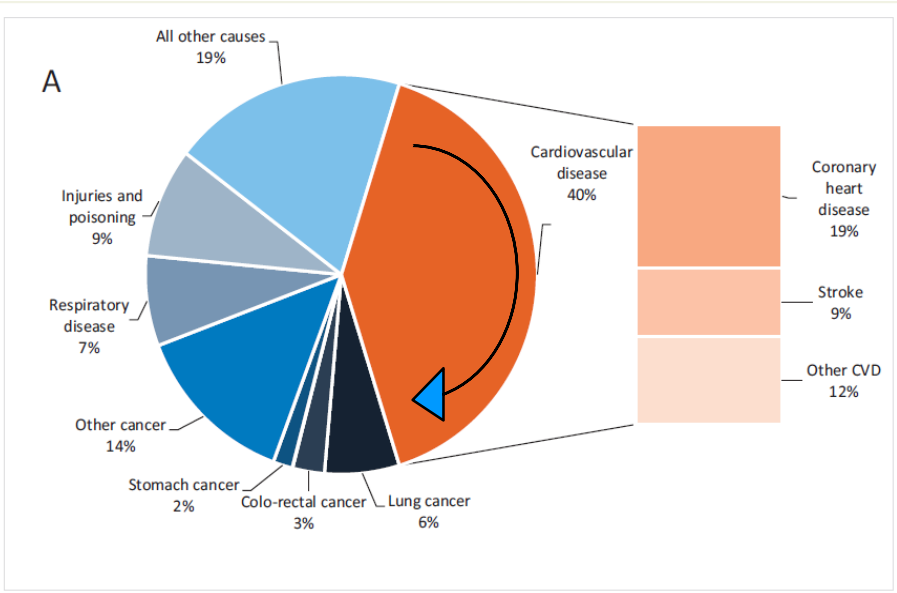


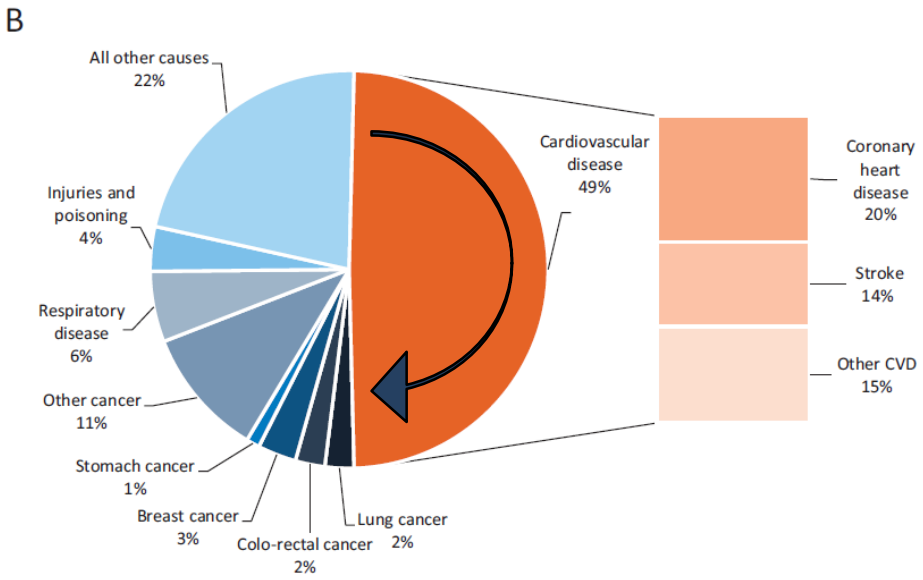
Precision medicine. Artwork by Piet Michiels, Leuven, Belgium

Cardiovascular disease (CVD) is the leading cause of mortality in Europe

MEN

WOMEN





•European Heart Journal 2017

Medicina di genere e le 4 P

- Predittiva
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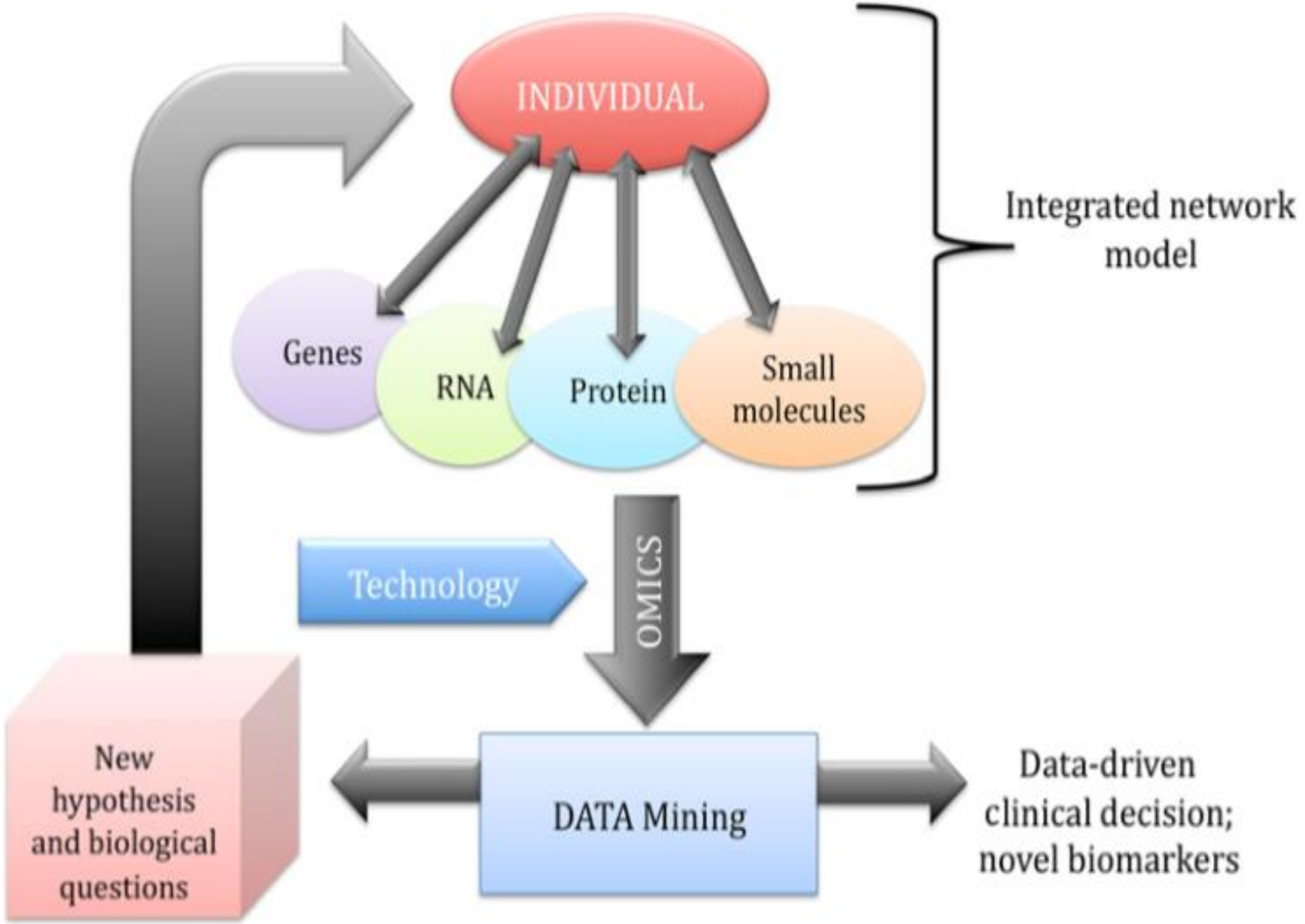
Punteggi di rischio CV

- Framingham RS
  - 20% malattia coronarica in assen
- Reynolds RS
  - + PCR + anamnesi f natura
- ASCVD athe ase
- PRO Ardiovascular Munster
- QRISK2

none of the most well-known ASCVD and CAD clinical risk prediction scores in the USA are highly accurate for both men and women

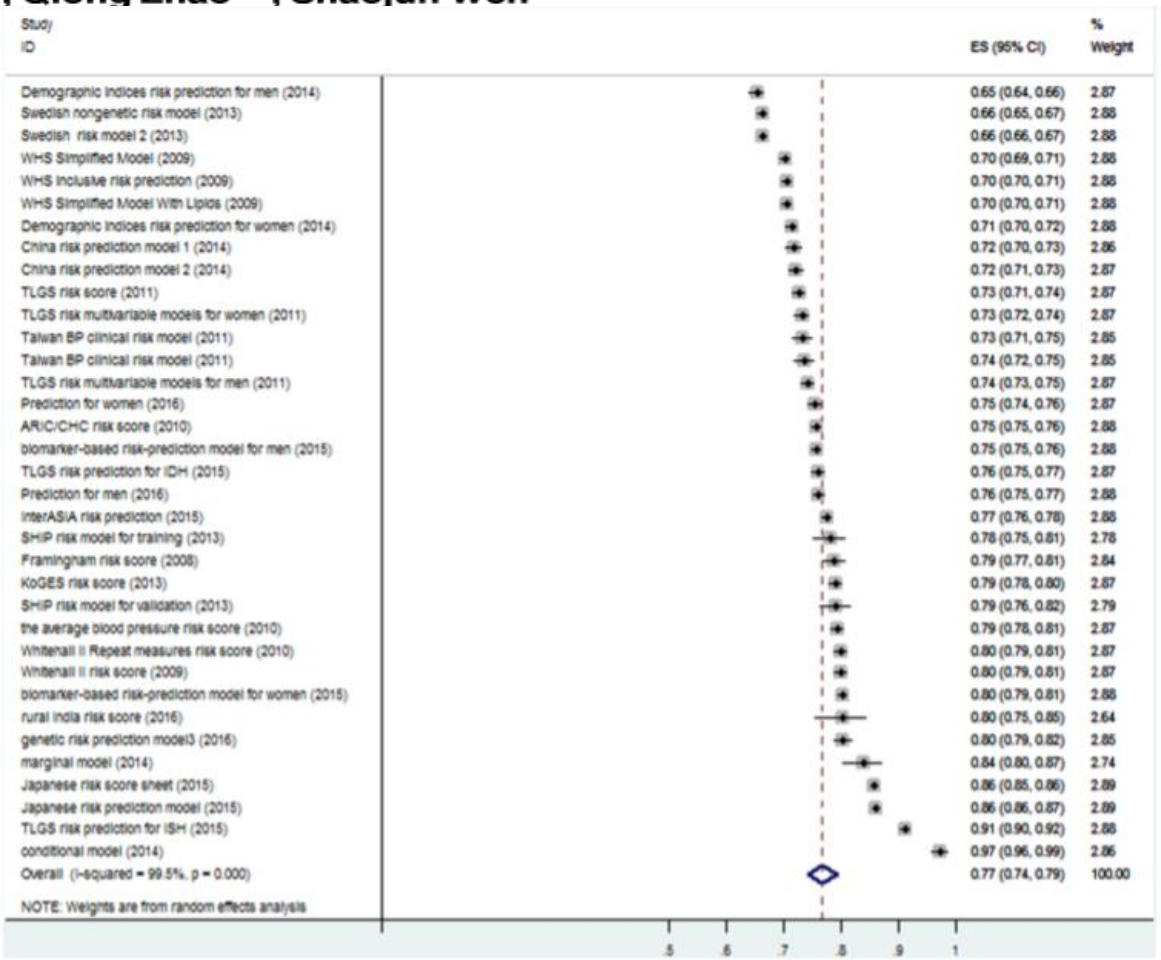

INDIVIDUAL
Genes
RNA
Protein
Small molecules
Integrated network model
Technology
OMICS
New hypothesis and biological questions
DATA Mining
Data-driven clinical decision; novel biomarkers

RESEARCH ARTICLE

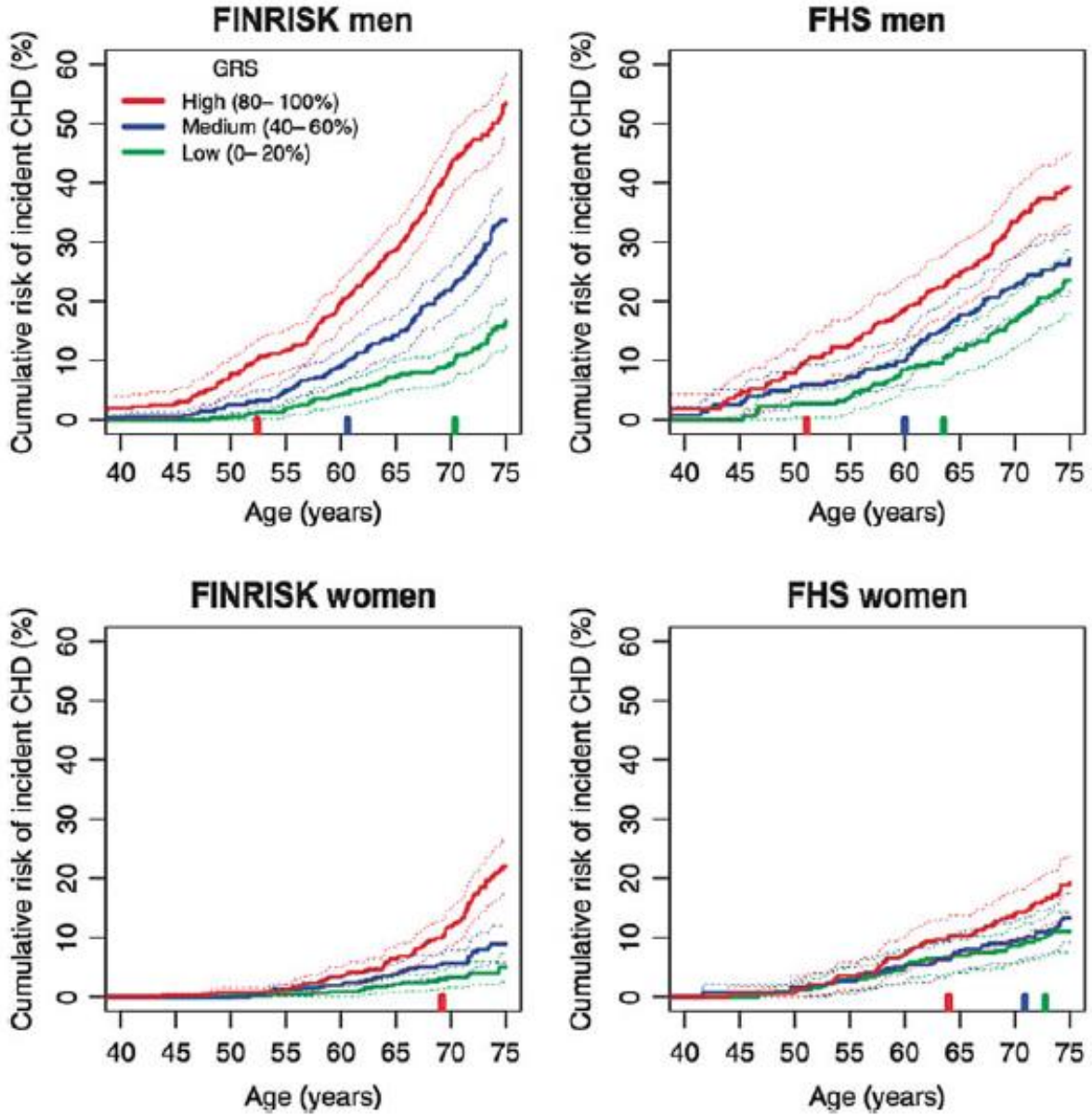
Recent development of risk-prediction models for incident hypertension: An updated systematic review

PLoS One. 2017;12(10): e0187240

Dongdong Sun[1,2☯‡], Jielin Liu[1,2☯‡], Lei Xiao[3], Ya Liu[1,2], Zuoguang Wang[1,2], Chuang Li[1,2], Yongxin Jin[1,2], Qiong Zhao[4]*, Shaojun Wen[1,2]*



Differences in the ability of the genomic risk score (GRS49k) to stratify men and women into high and low CAD risk groups



Sex and Ethnic Differences in 47 Candidate Proteomic Markers of Cardiovascular Disease

Sex differences in women compared to men.

Both AA and NHW			AA			NHW		
Higher	**Lower**	**No difference**	**Higher**	**Lower**	**No difference**	**Higher**	**Lower**	**No difference**
CRP	TIMP-1	VCAM	RAGE		P-selectin	Hsp27	P-selectin	RAGE
SAA	Lp-PLA_2 activity	IL-6	LDL size		Hsp27	MPO	Lp-PLA_2 mass	LDL size
ICAM	CT-proAVP	IL-18	ONN		MPO	NT-proBNP	OCN	ONN
ApoA-I		TNFRI	OCN		Lp-PLA_2 mass	MR-proANP		Factor VIII
ApoC-III		TNFRII	Factor VIII		NT-proBNP	CT-proET		vWF
ApoE		MCP-1	vWF		MR-proANP			
Lp(a)		E-selectin			CT-proET			
Leptin		MMP-2						
Adiponectin		MMP-9						
Resistin		TIMP-2						
MR-proADM		ApoB						
OPN		Ox-LDL						
Factor II		OPN						
Factor V								
Factor VII								
D-dimer								
ATIII								
Fibrinogen								

doi:10.1371/journal.pone.0009065.t006

ORIGINAL RESEARCH ARTICLE

April 2, 2019 Circulation. 2019;139:1698–1709

Placental Growth Factor as an Indicator of Maternal Cardiovascular Risk After Pregnancy

Women with low PlGF in midpregnancy have a greater aortic root diameter, left atrial diameter, and left ventricular mass and higher systolic blood pressure 6 and 9 years after pregnancy compared to women with higher PlGF, including women with uncomplicated pregnancies

Guidelines for the Prevention of Stroke in Women

A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association

Feb 2014 online

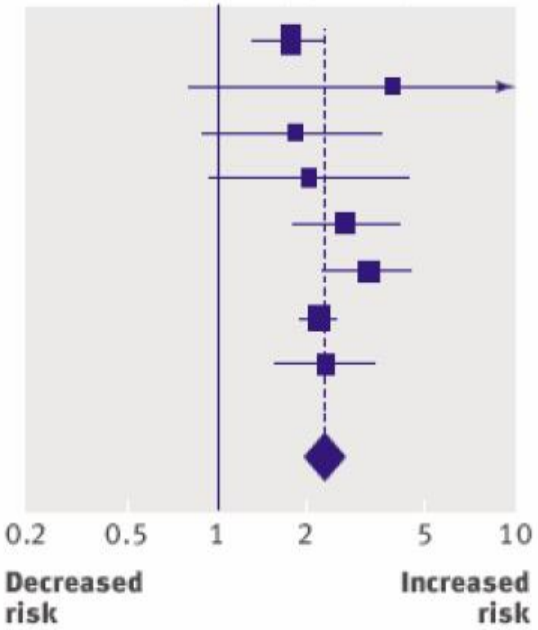
Risk Factor	Sex-Specific Risk Factors	Risk Factors That Are Stronger or More Prevalent in Women	Risk Factors With Similar Prevalence in Men and Women but Unknown Difference in Impact
Pregnancy	X		
Preeclampsia	X		
Gestational diabetes	X		
Oral contraceptive use	X		
Postmenopausal hormone use	X		
Changes in hormonal status	X		
Migraine with aura		X	
Atrial fibrillation		X	
Diabetes mellitus		X	
Hypertension		X	
Physical inactivity			X
Age			X
Prior cardiovascular disease			X
Obesity			X
Diet			X
Smoking			X
Metabolic syndrome			X
Depression		X	
Psychosocial stress		X	

Preeclampsia (PE) and risk of fatal/non-fatal IHD later in life:

Study	Ischaemic heart disease: Total No of cases/ women who had pre-eclampsia	Ischaemic heart disease: Total No of cases/ women who did not have pre-eclampsia	Relative risk (random) (95% CI)
Hannaford 1997[w8]	69/2371	216/14 831	1.65 (1.26 to 2.16)
Irgens 2001[w15]	27/24 155	325/602 117	3.61 (0.76 to 17.18)*
Smith 2001[w16]	12/22 781	31/106 509	1.70 (0.86 to 3.35)
Wilson 2003[w13]	26/1043	10/796	1.95 (0.90 to 4.22)
Kestenbaum 2003[w14]	35/20 552	64/92 902	2.55 (1.70 to 3.83)†
Funai 2005[w17]	41/1070	269/35 991	3.01 (2.18 to 4.33)
Ray 2005[w18]	228/36 982‡	1262/950 885	2.10 (1.82 to 2.42)
Wirkstrom 2005[w19]	176/12 533	2306/383 081	2.21 (1.56 to 3.31)†
Total (95% CI)	614/121 487	4483/2 187 112	2.16 (1.86 to 2.52)

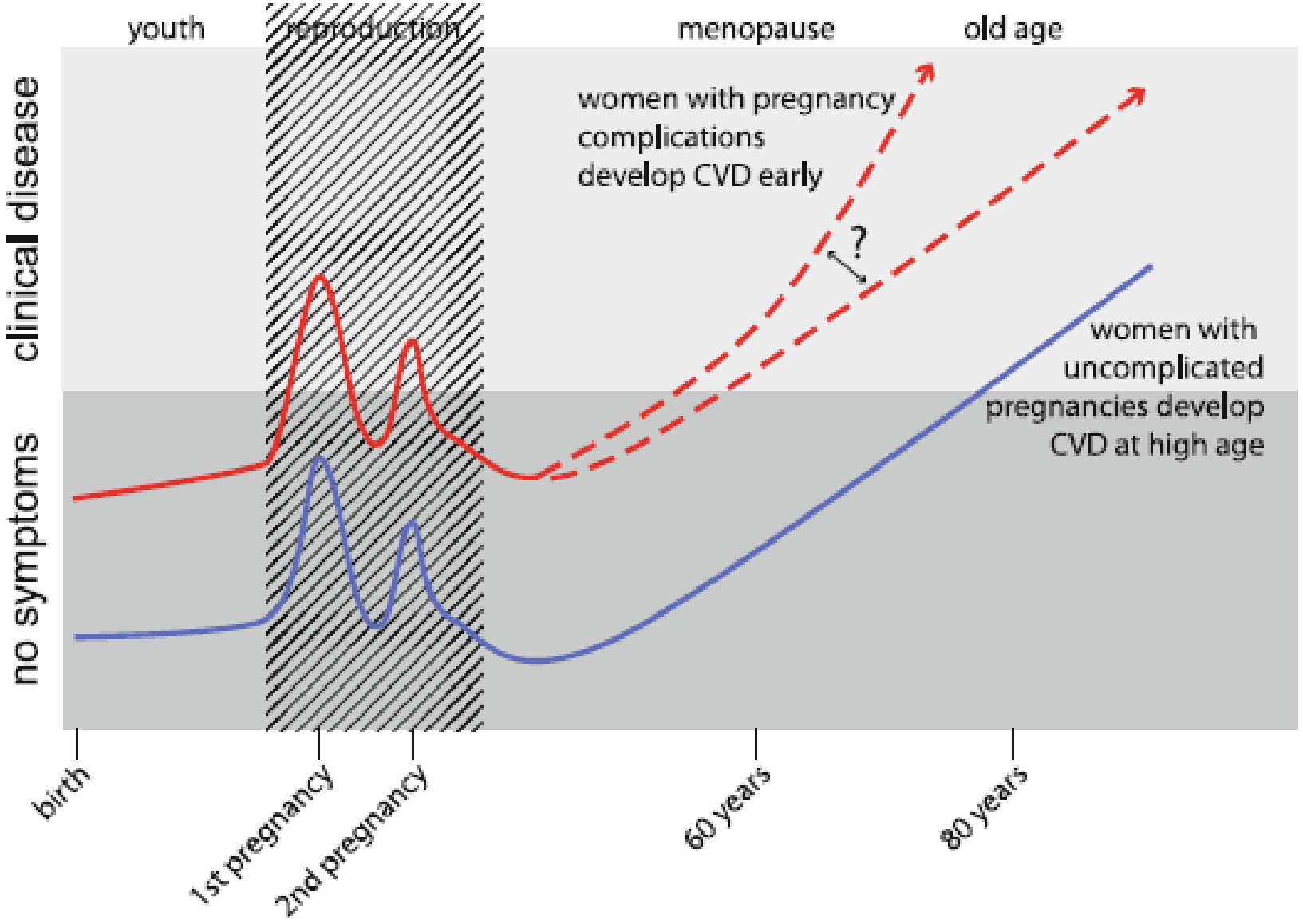
Test for heterogeneity: χ^2=9.60, df=7, P=0.21, I^2=27.1%

Test for overall effect: z=10.00, P=0.001



Bellamy, L. et al. BMJ 2007; 335:974

preeclampsia complica il 10 % delle gravidanze in USA



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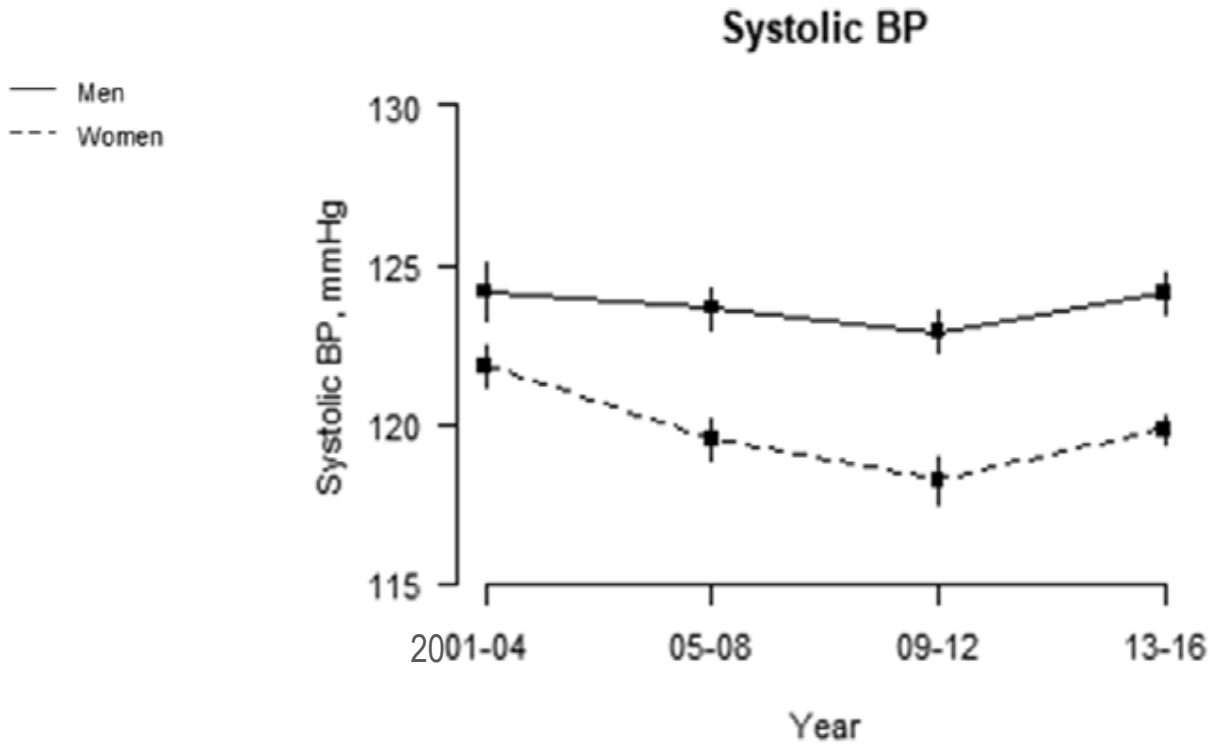
Sex Differences in Trends in CVD Risk Factors

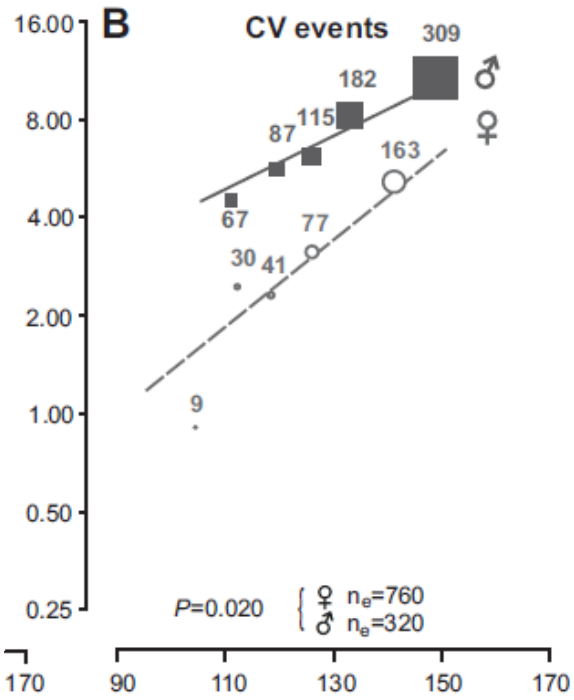
35 416 participants (51% women) National Health and Nutrition Examination Survey



Peters et al *Circulation.* 2019;139:1025–1035

Ambulatory Blood Pressure Monitoring in 9357 Subjects From 11 Populations Highlights Missed Opportunities for Cardiovascular Prevention in Women

9357 subjects (age, 52.8 yrs; 47% women)
Women compared with men were at lower risk (HR for CV events 0.62 p<0.001)
However, the relation of all events with 24-hour BP and with nighttime BP were steeper in women than in men



"…consequently, per a 1-SD (13.4 mmHg) decrease, the proportion of potentially preventable events was higher in women than in men for all cardiovascular events (35.9% vs 24.2%) in relation to 24-hour systolic BP…"

IDACO Investigators, Hypertension 2011

Sex Differences in Trends in CVD Risk Factors

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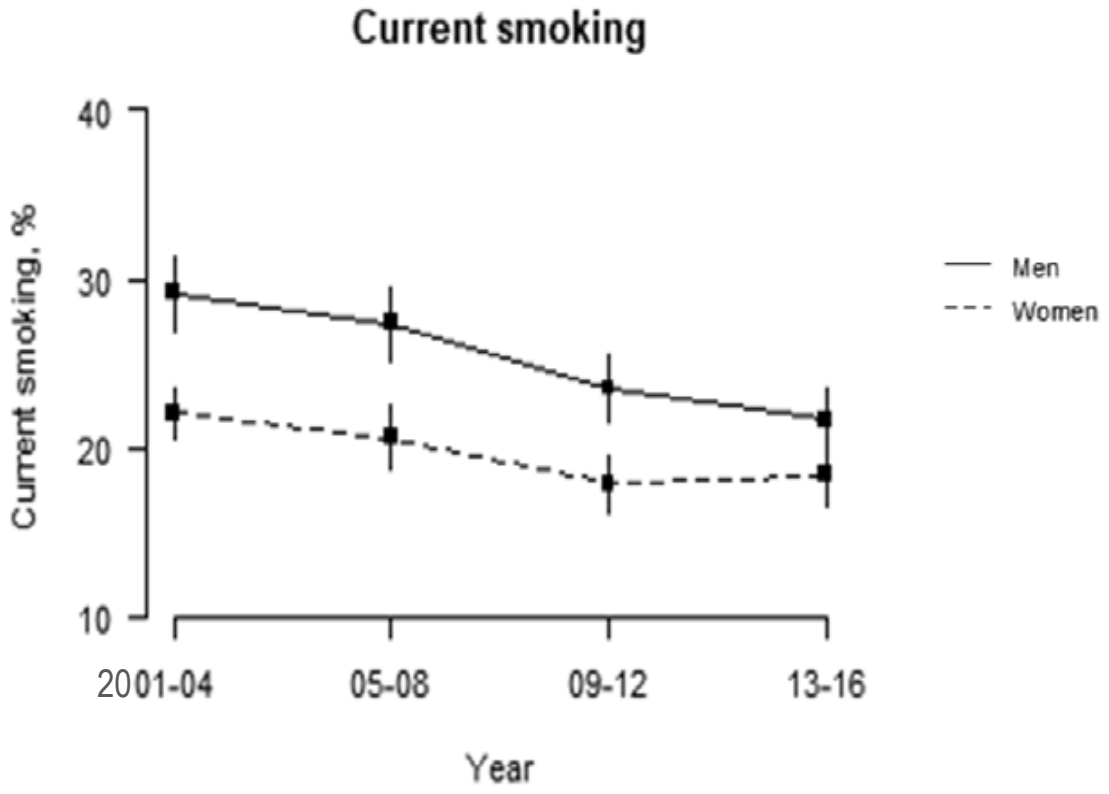
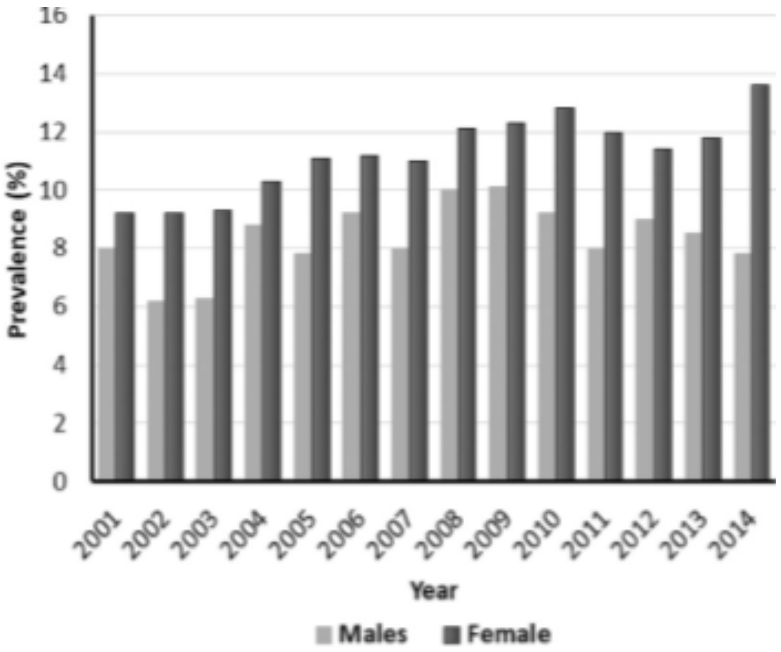
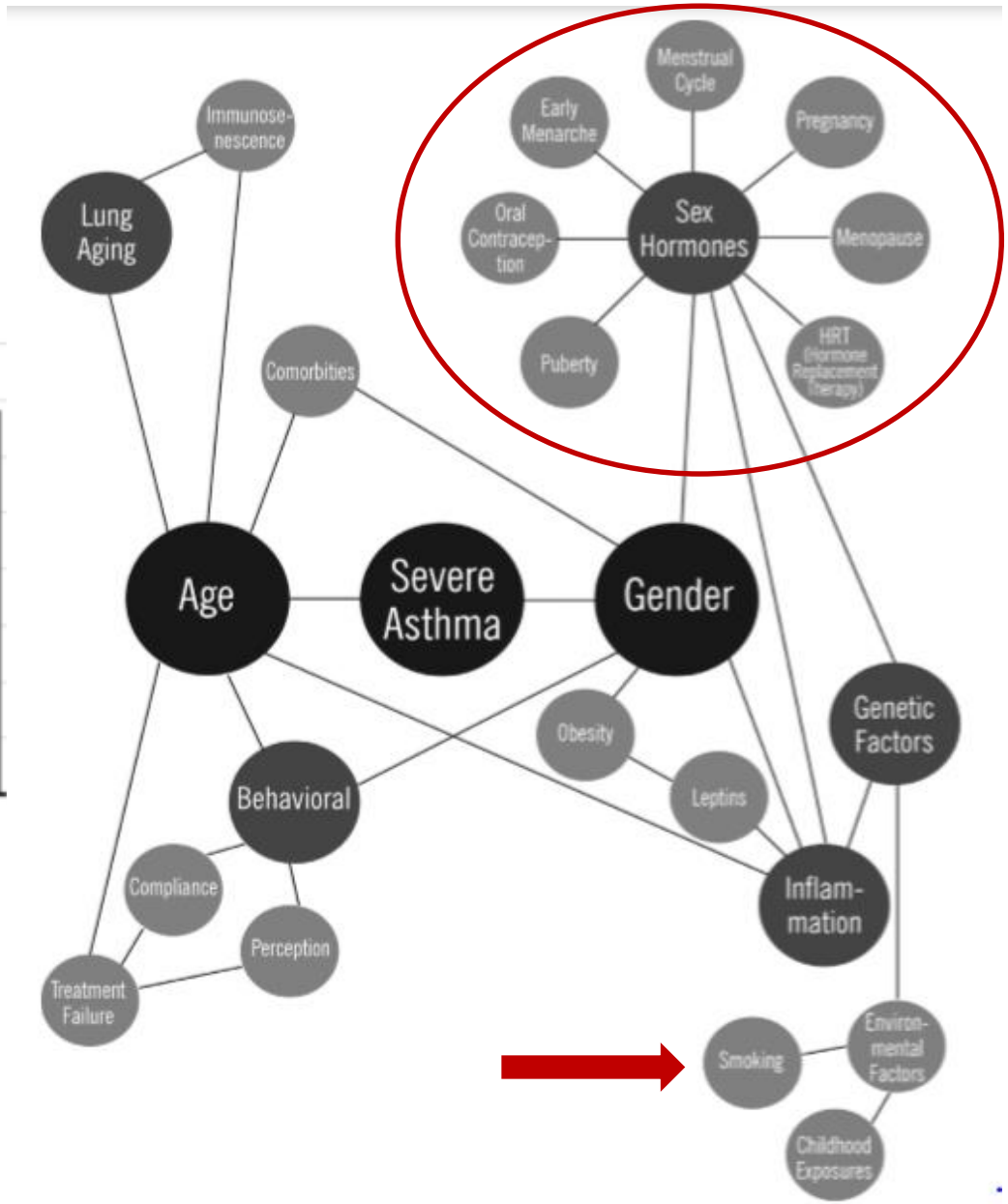


Peters et al *Circulation.* 2019;139:1025–1035

Gender and asthma





Gender and asthma

Female sex hormones and their receptors favour asthma development

Male sex hormones and their receptors have a protective effect

Gender and asthma

Female sex hormones and their receptors favour asthma development
Male sex hormones and their receptors have a protective effect

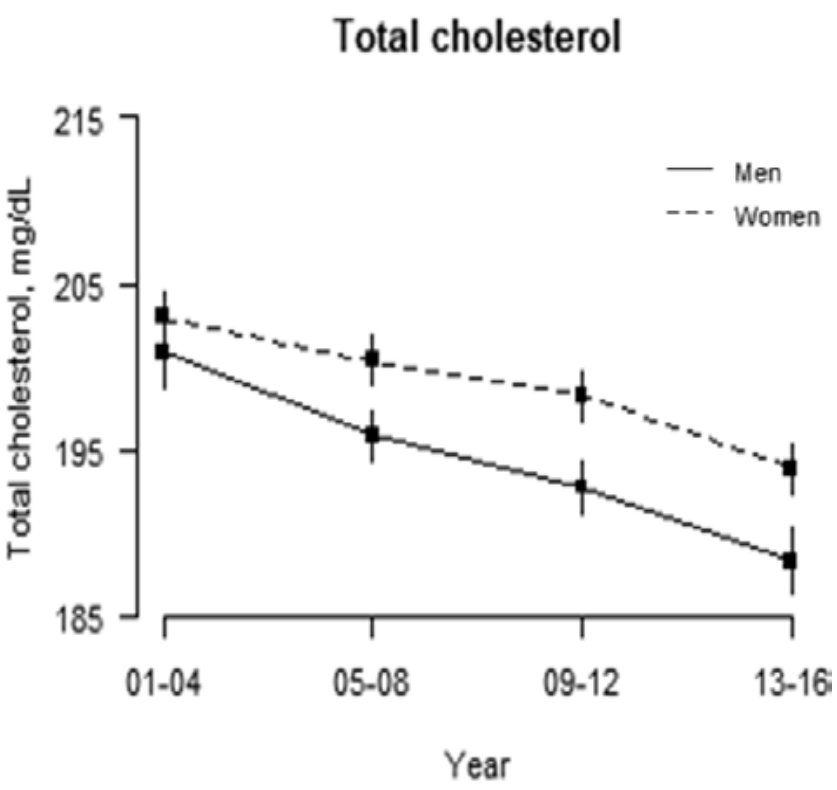
Female gender associated to pronounced asthma symptoms subject to menstruation, pregnancy, menopause

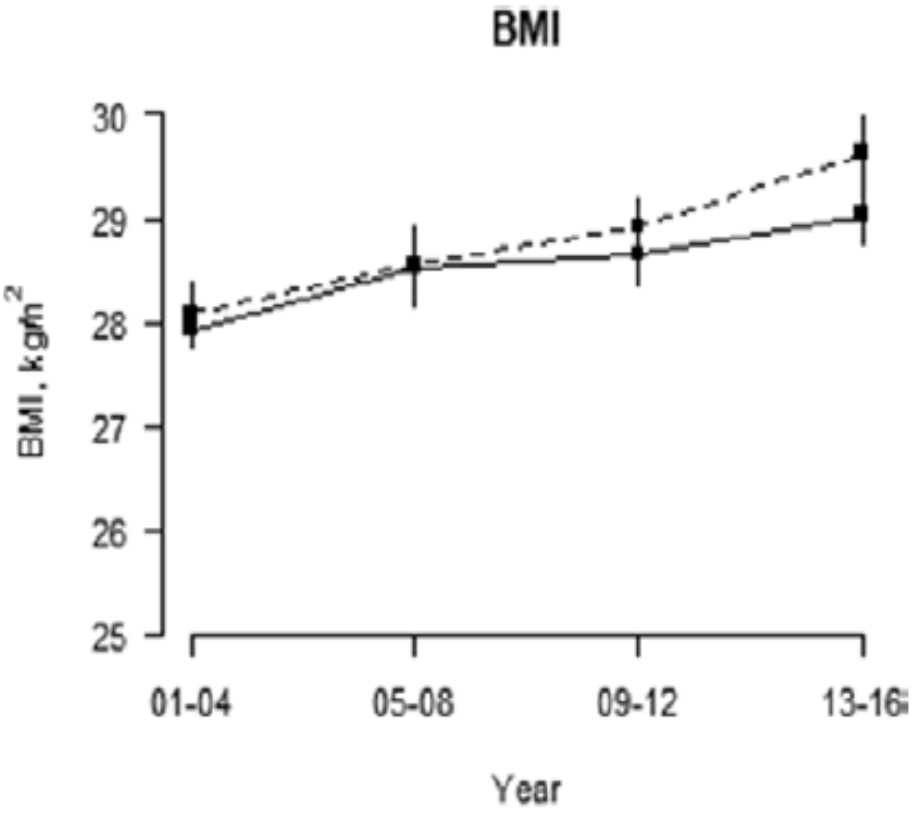
Perimenstrual asthma seems to be caused/affected by dynamic changes of oestrogen levels rather than by absolute levels

Higher susceptibility to cigarette smoke-, migraine-, and vocal cord dysfunction -related asthma or asthma-like symptoms

Lower asthma-related quality of life

Sex Differences in Trends in CVD Risk Factors





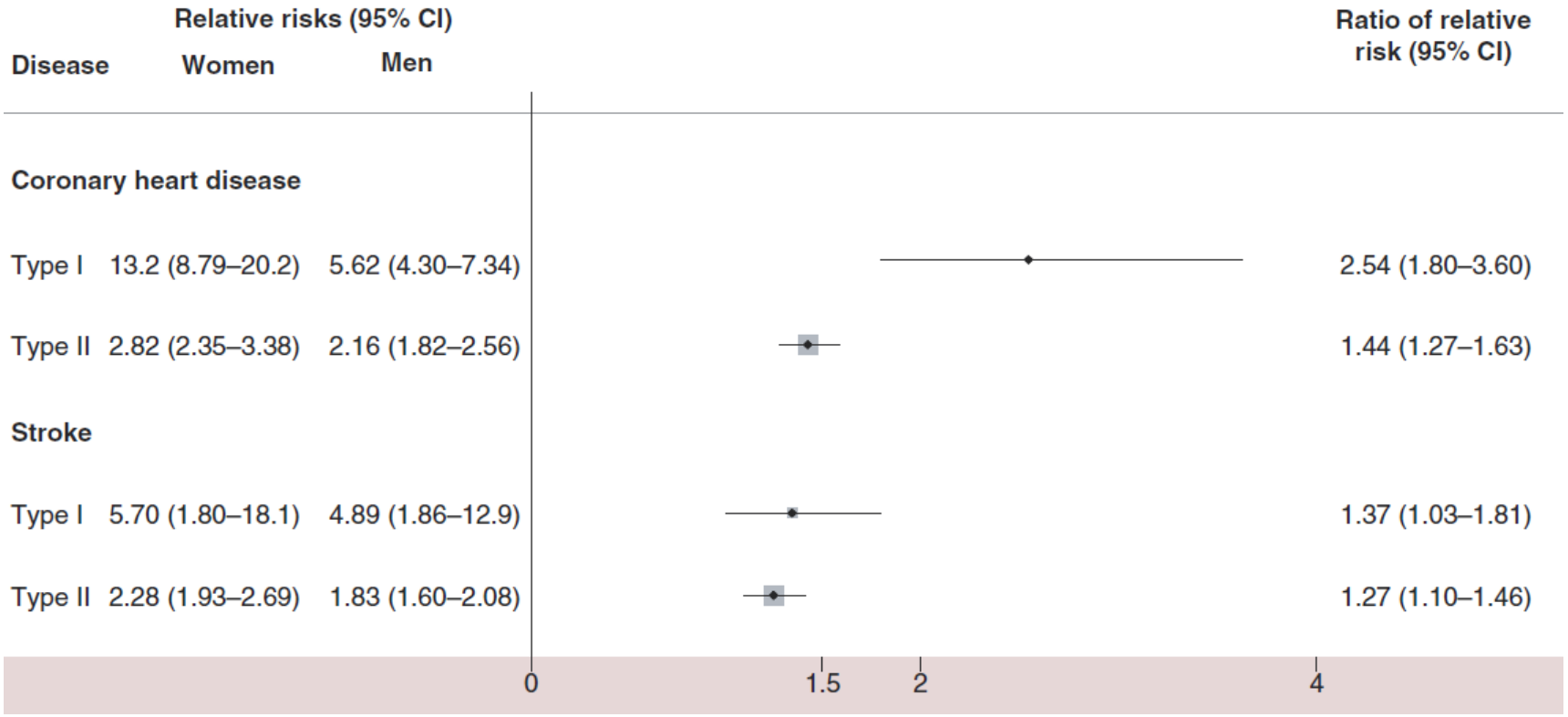
Peters et al *Circulation.* 2019;139:1025–1035

Males	Females
Increased fasting glucose	Increased insulin resistance
Diabetes develops at earlier age	Diabetes develops with higher BMI
–	Gestational diabetes
Increased overweight incidence	Increased obesity incidence
Abdominal obesity	Abdominal + peripheral obesity
Increased fatty liver	Unchanged incidence of fatty liver
Decreased androgens	Increased androgens
Increased erectile dysfunction	Increased polycystic ovary syndrome
Unchanged depression incidence	Increased depression incidence
–	Psychosocial risk factors
Increased neuropathy	Increased cardiovascular risk

+ HF

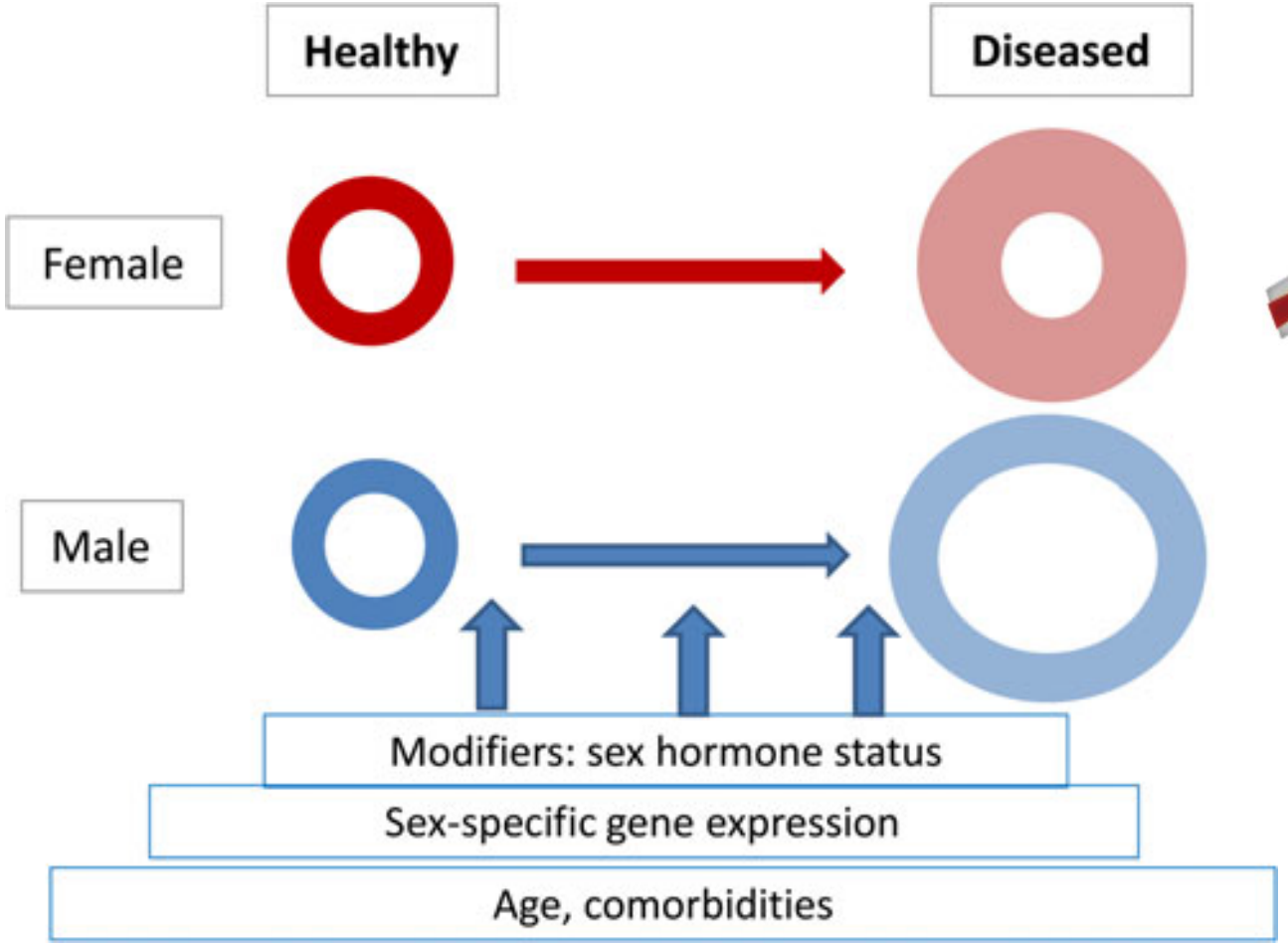
+ PAD

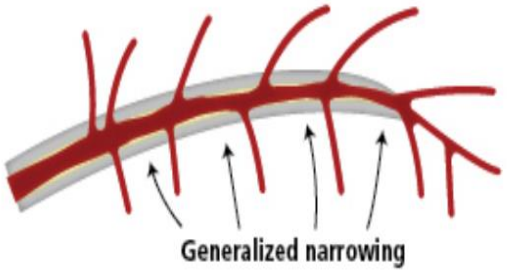
Diabetes and the Female Disadvantage

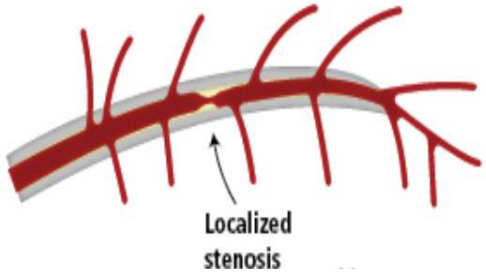


Peters SA et al Lancet. 2014 Jun 7;383(9933):1973-80.

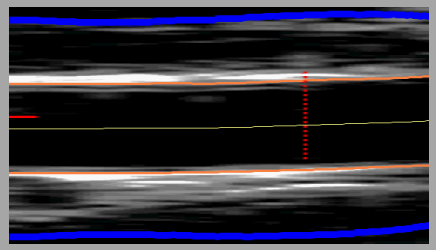
Cardiac remodelling in women and men



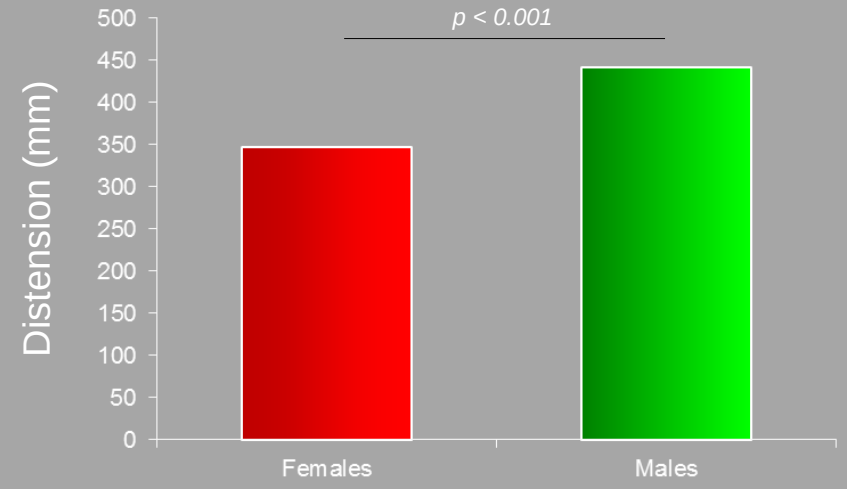


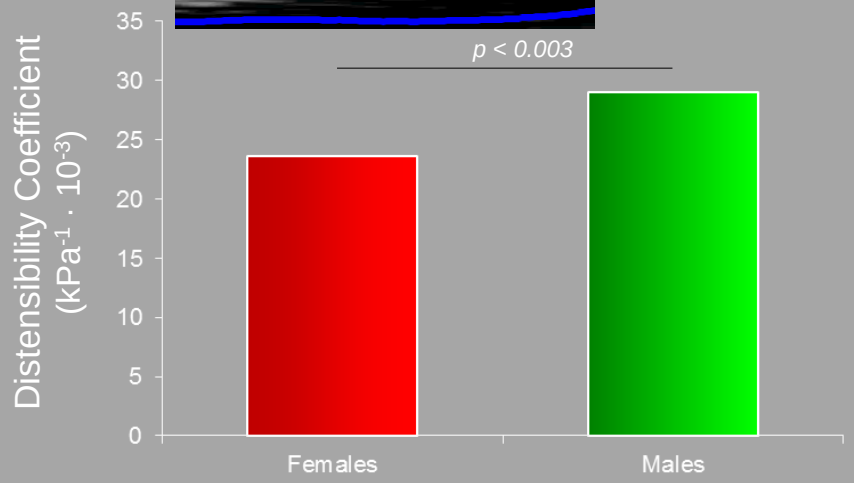


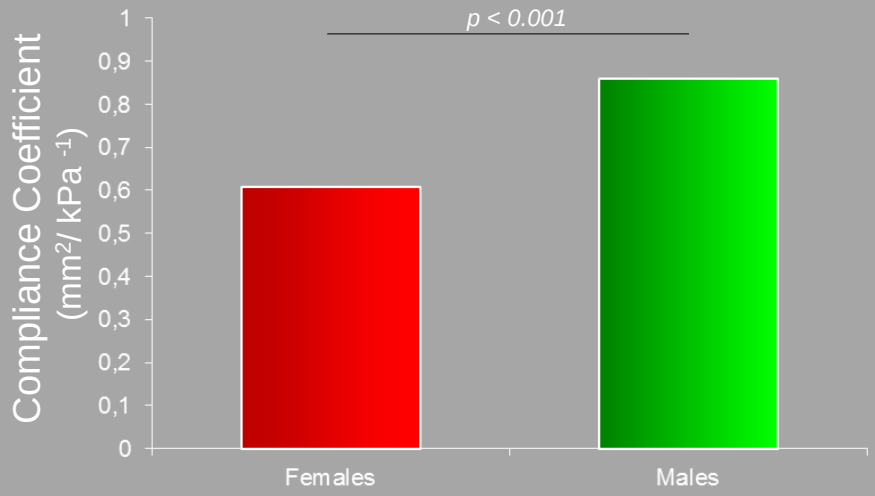
CAROTID ARTERIAL STIFFNESS PARAMETERS STUDIO VOBARNO

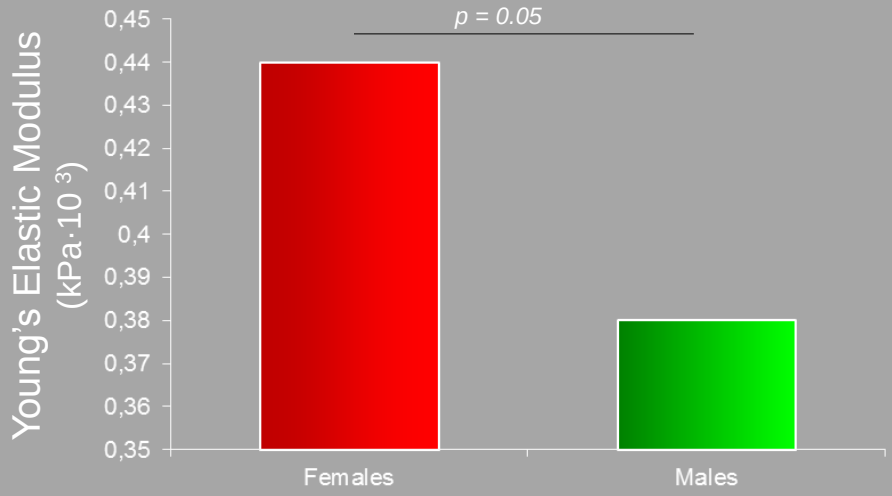


Artlab System
14 RF
Dist ± 1.7 µm







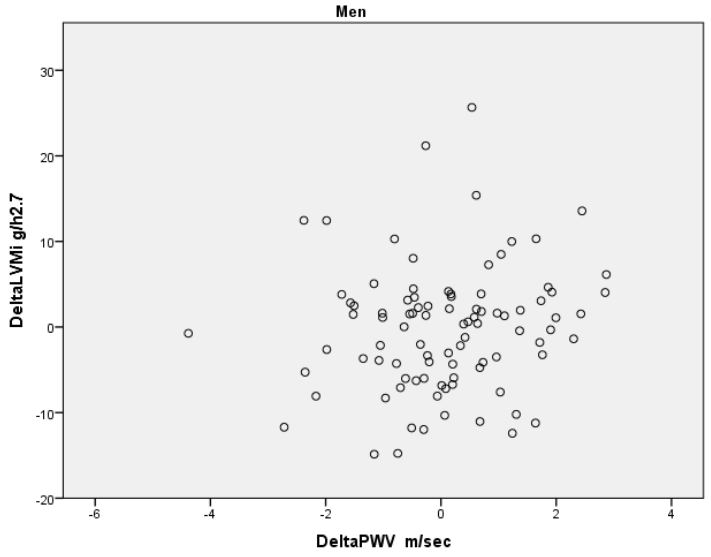


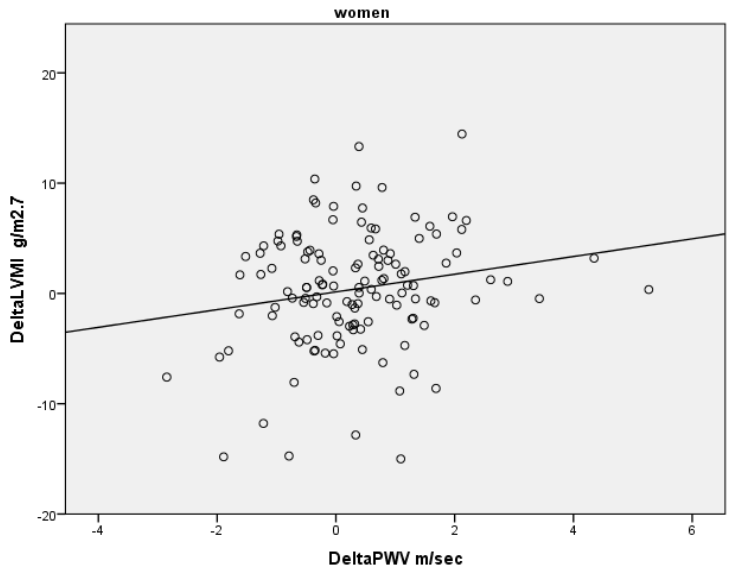
After adjustment for weight, height, MBP, glucose, creatinine, total cholesterol and tryglicerides.

Clinica Medica, Università di Brescia ed ASST Spedali Civili di Brescia

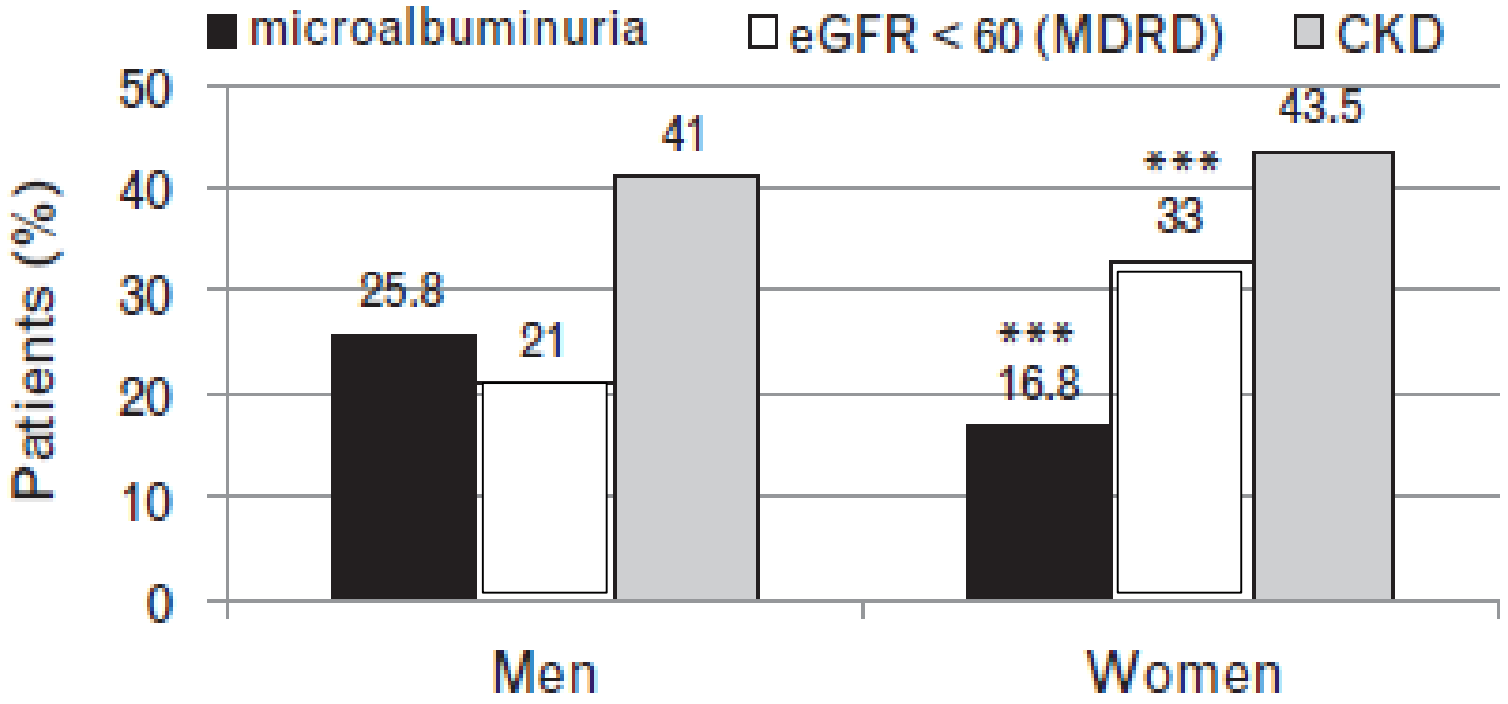
Sex differences in changes in left ventricular mass as related to aortic stiffness: the Vobarno Study

	MEN		WOMEN	
	Basal	Follow up	Basal	Follow up
LVMi g/h 2.7	38 ± 8	40 ± 9 **	33 ± 8	34 ± 8 **
PWV m/s	8.5 ± 1.4	8.6 ± 1.2	8.1 ± 1.6	8.5 ± 1.4**
Central aortic SBP mmHg	120 ± 14	124 ± 16 *	114 ± 16	120 ± 16 **





Sex differences in hypertension-related renal and cardiovascular diseases in Italy: the I-DEMAND study



Muiesan ML et al Journal of Hypertension 2012

Medicina di genere e le 4 P

- Predittiva
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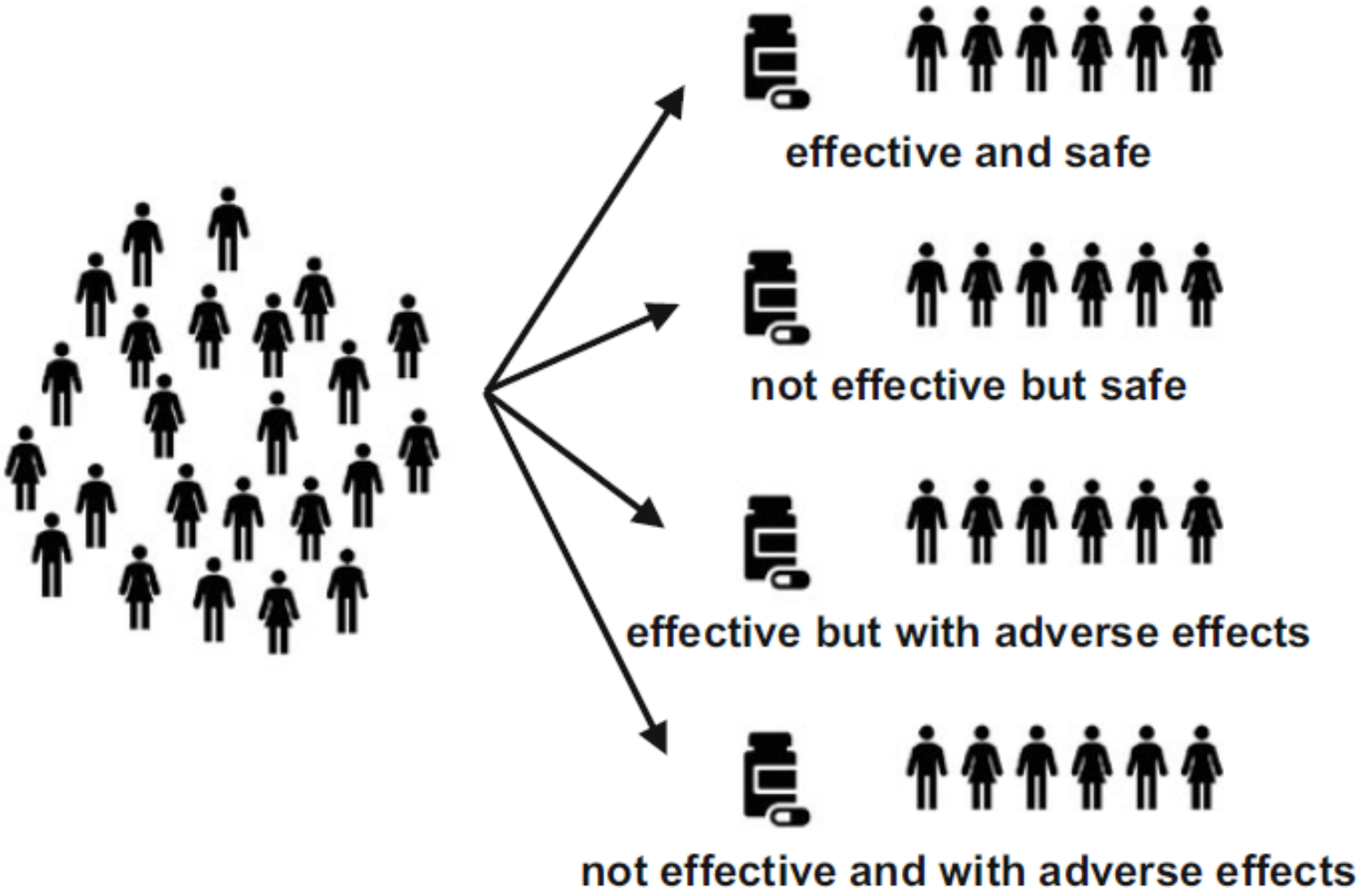
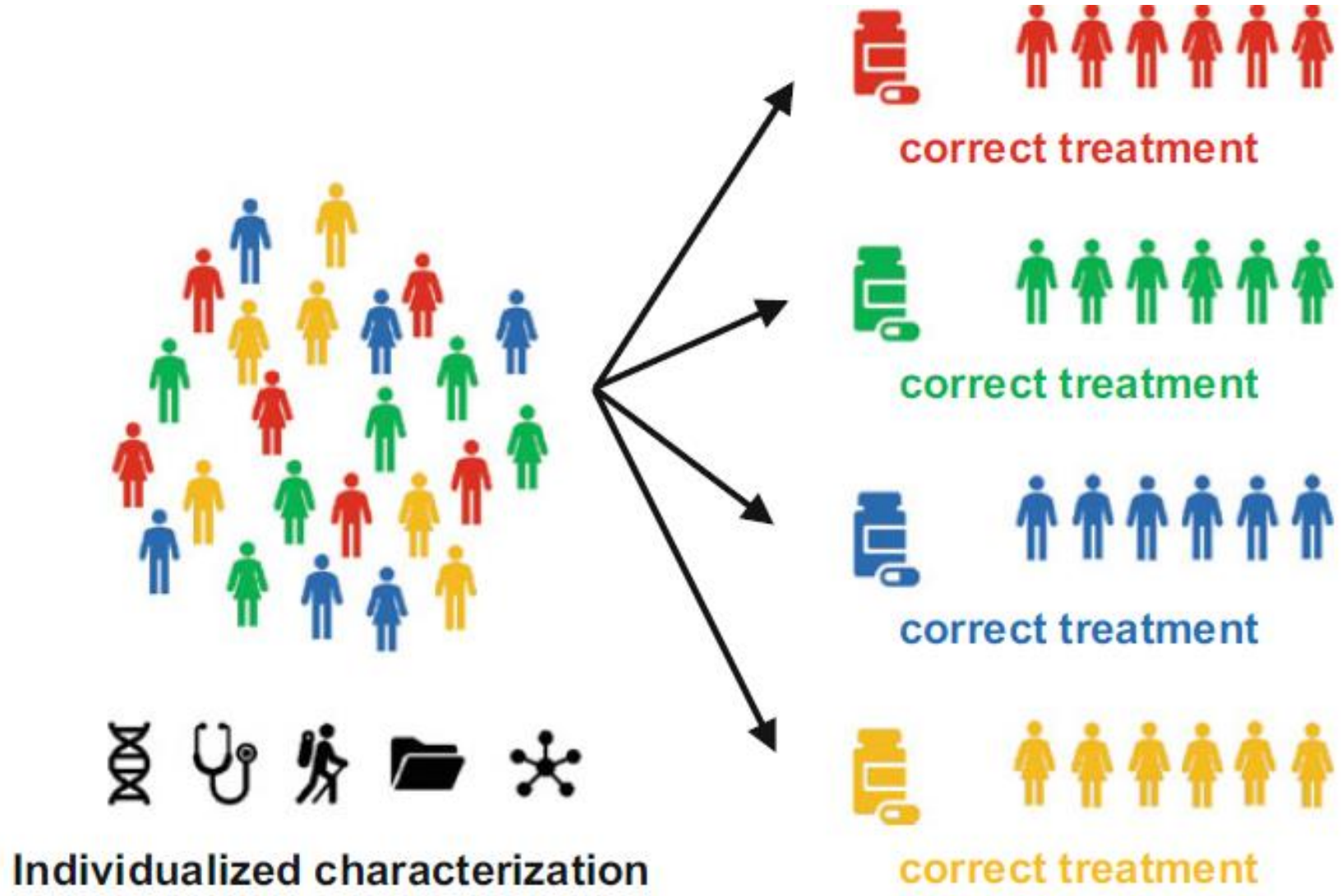
"the right treatment to the right patient at the right time."


effective and safe
not effective but safe
effective but with adverse effects
not effective and with adverse effects


correct treatment
correct treatment
correct treatment
correct treatment
Individualized characterization

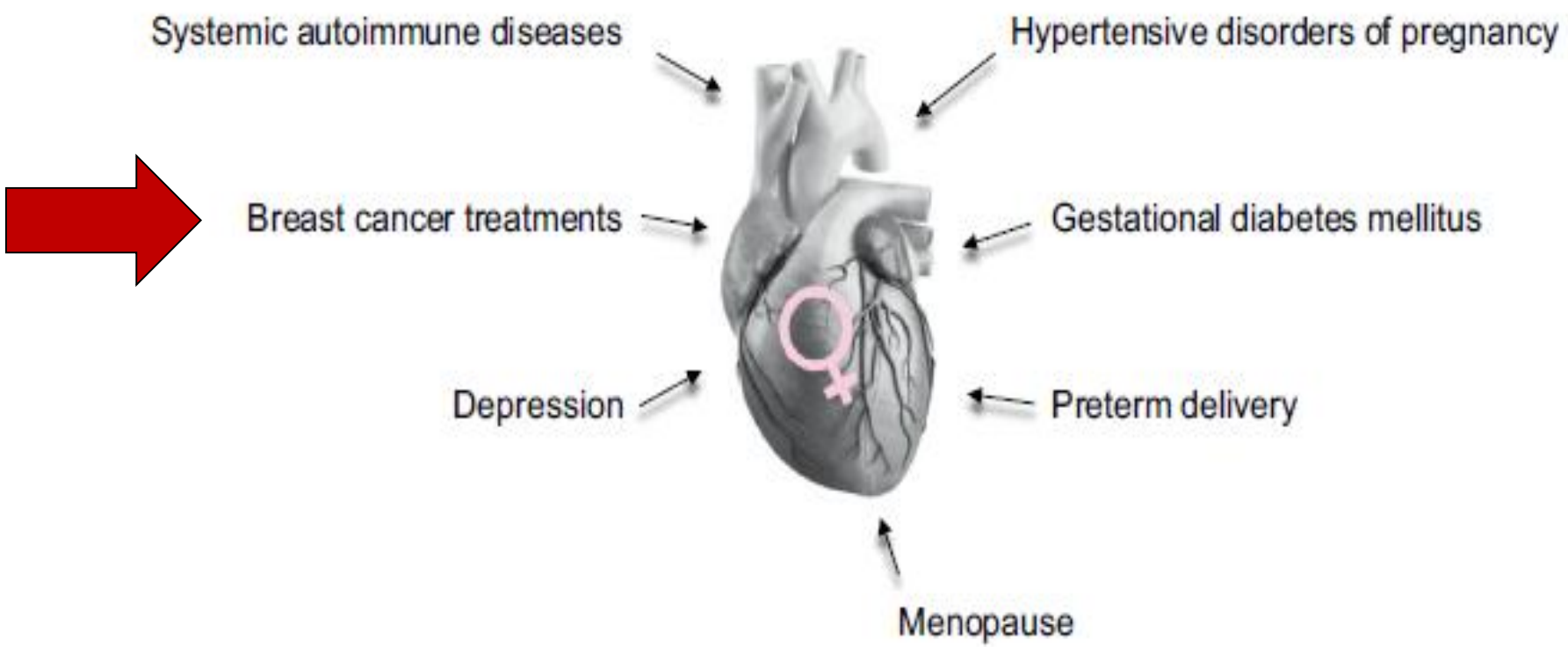
Precision medicine in breast & ovarian cancer

Universal testing for BRCA1 and BRCA2 mutations

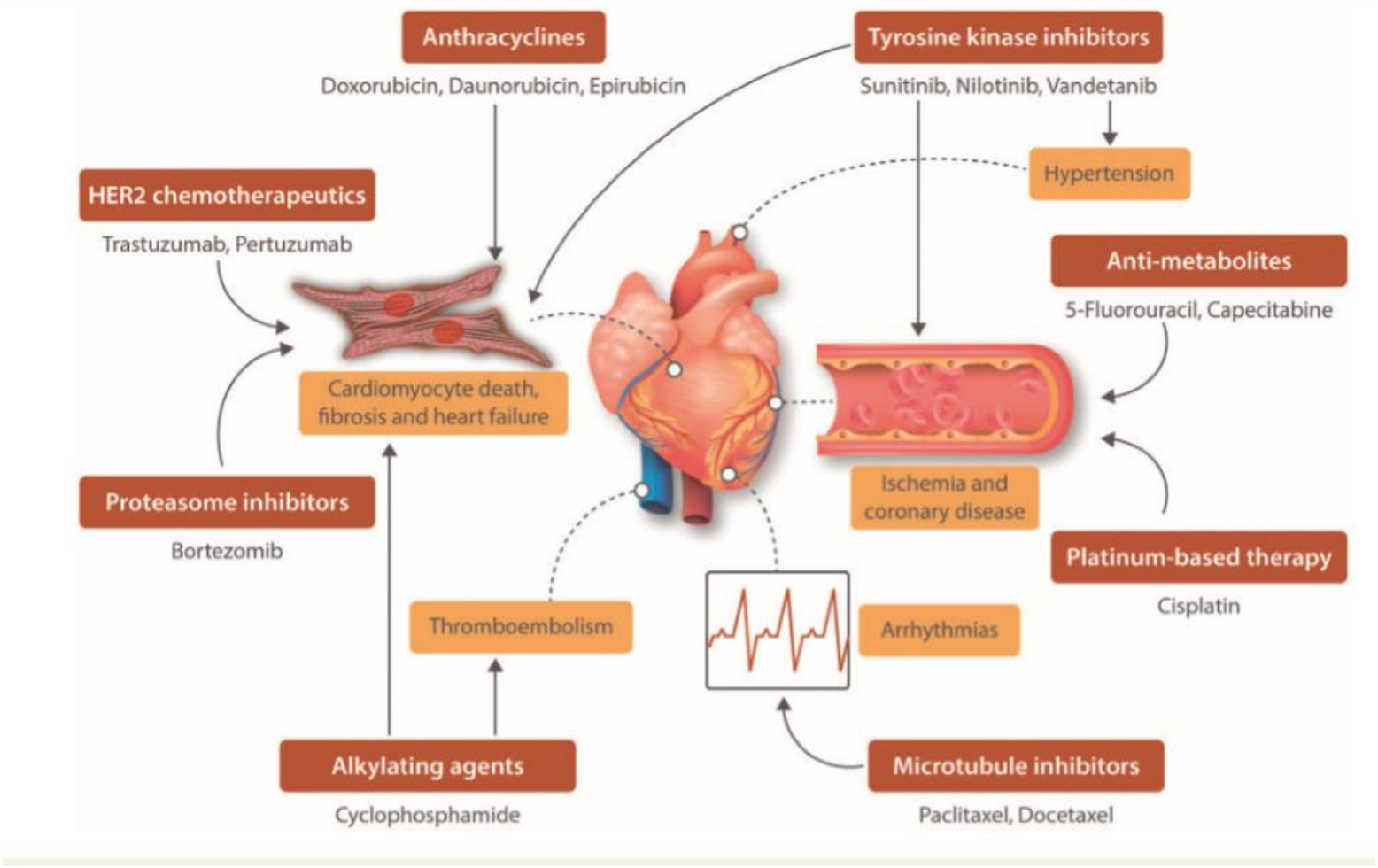
Accurate and inexpensive test which can be accessed online and the testing process is simple.
The risks associated with the mutations are known with accuracy and are substantial
Interpretation of a genetic test result is simple if restricted to known pathogenic mutations in BRCA1 and BRCA2
Effective means of prevention (preventive surgery), acceptable to high proportion of the women

However only 4% of breast cancer and 13% of ovarian cancers are due to BRCA1 and BRCA2 mutations and there is a very low uptake of testing to date when offered as a direct-to-consumer product.

Women-specific CVD risk factors

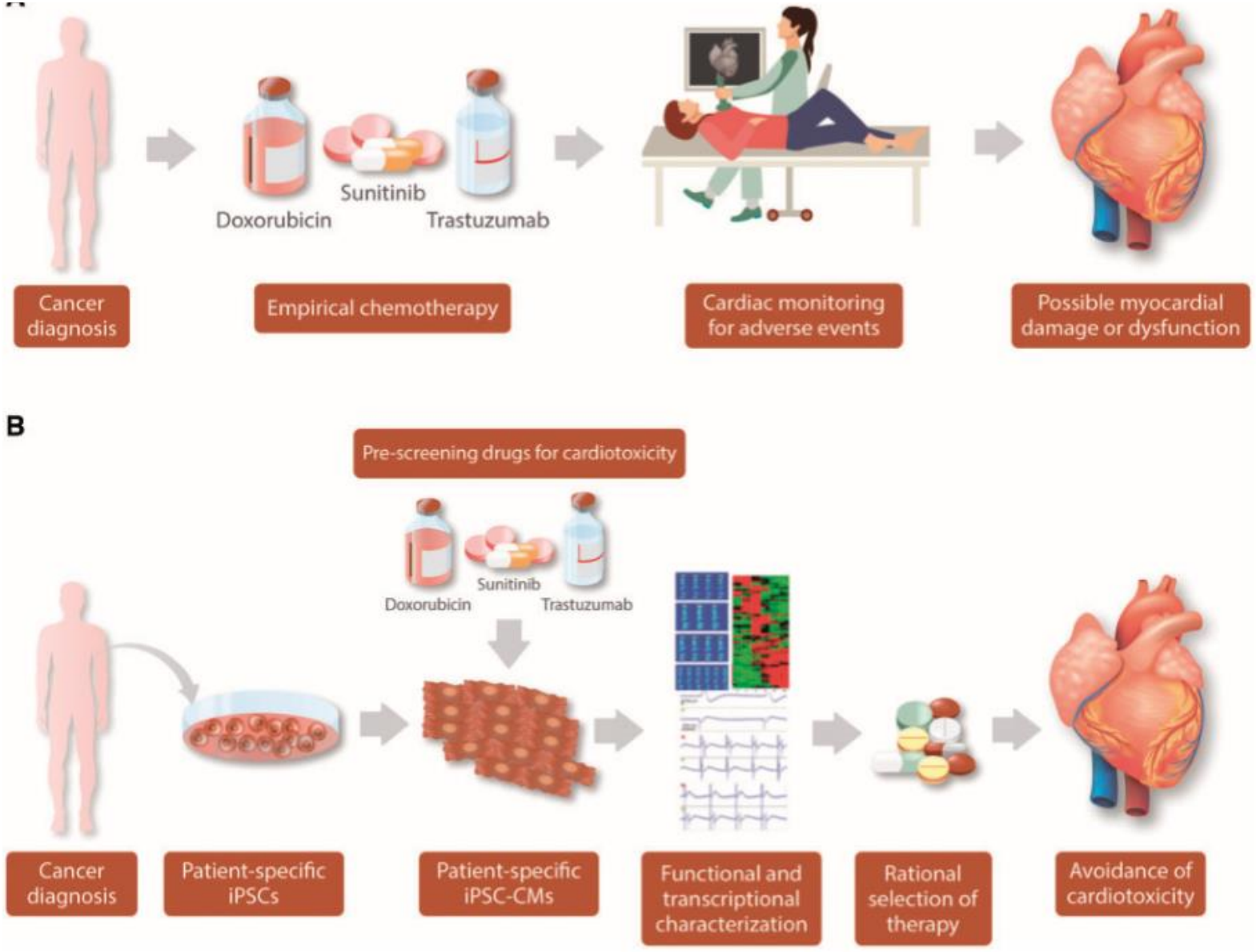


Human iPSCs for cardiotoxicity

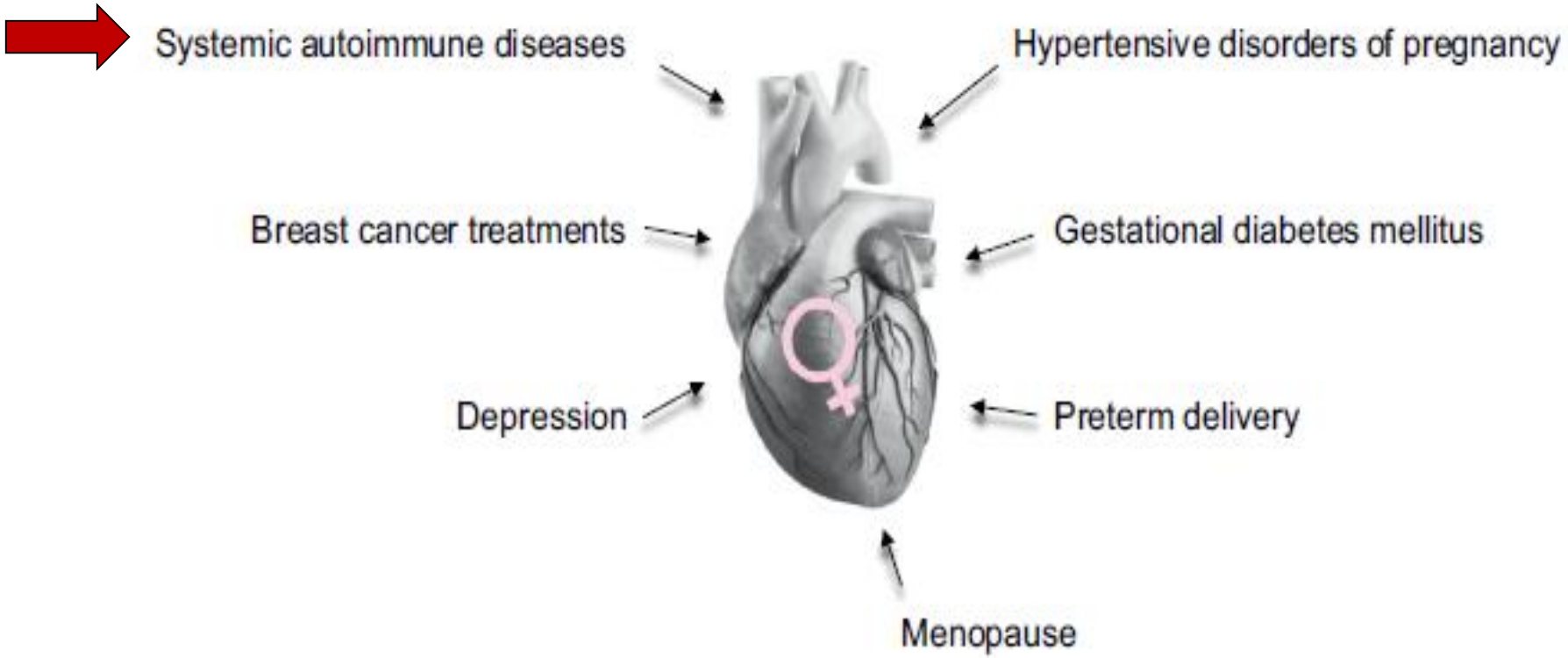


human induced pluripotent stem cell (iPSC) technology, researchers not only have the opportunity to model human diseases, but also to screen drugs for their efficacy and toxicity using human cell models

Human iPSCs for cardiotoxicity



Women-specific CVD risk factors



Sex & autoimmune diseases

Lupus Eritematoso sistemico

Hormones	Accelerated metabolic conversion of androgen precursors to E2 (aromatase activation) [38] E2 effects on immune function [3, 34]
Genetic factors	X-linked genes (FOXP3, TNF, TLR7) [5]
Epigenetic factors	X-linked miRNAs [22] Estrogen up-regulated miRNA (miR148a) [22] Estrogen down-regulated miRNA (miR146a, miR125a) [46]
Clinical phenotype	Incidence of Raynaud's phenomenon, alopecia, malar rash and arthralgia/arthritis higher in females than in males [47]

Artrite Reumatoide

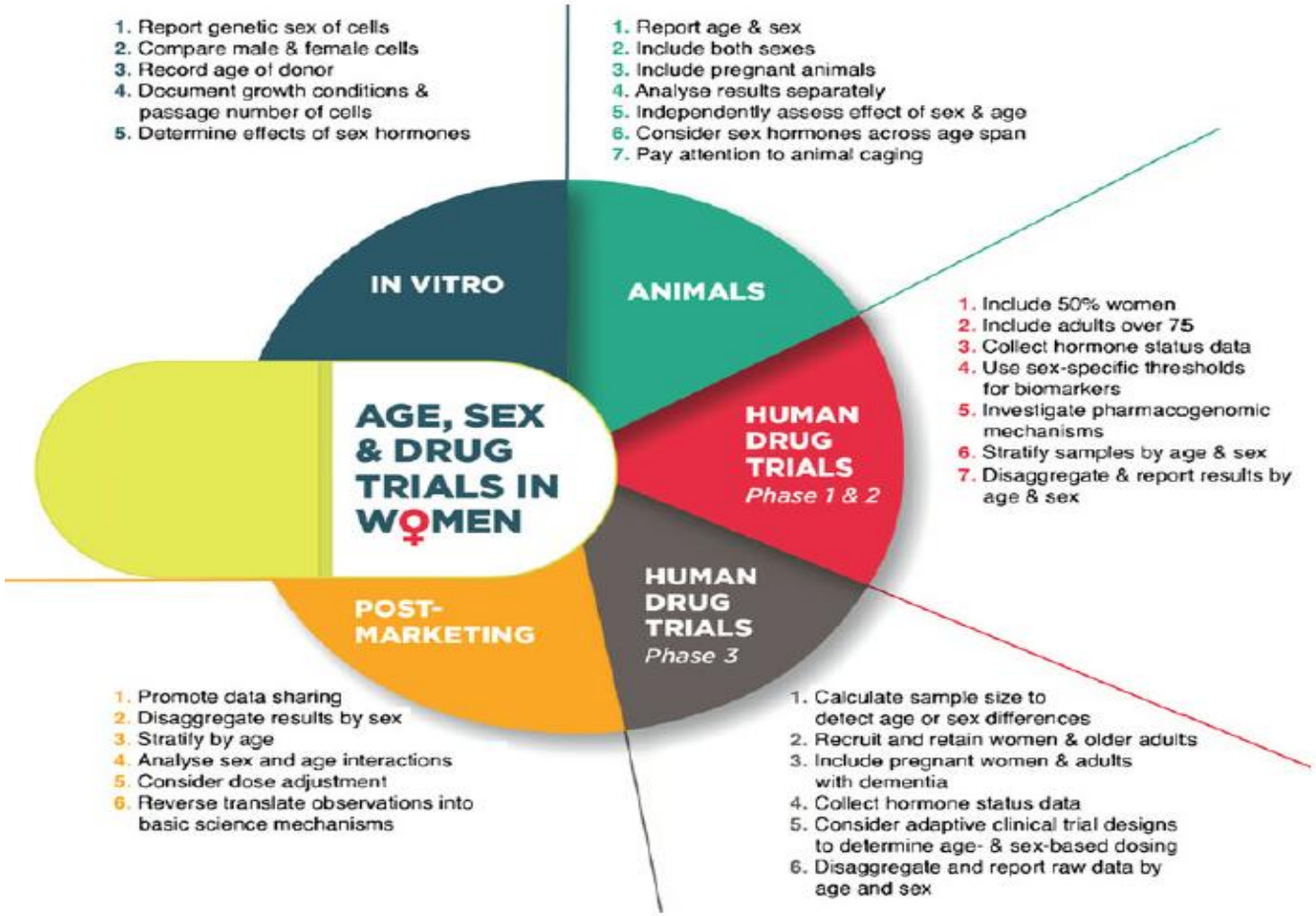
Hormones	Estrogen effects on immune function (both pro-inflammatory and anti-inflammatory effects, induction of Tregs) [50] Progesterone effects on immune function (anti-inflammatory effects, induction of Tregs) [50] Androgen effects on immune function (anti-inflammatory effects) [57] High aromatase activity in synovial fluid (↑ prevalence of synovial estrogens relative to androgens) [52]
Genetic factors	Single nucleotide polymorphisms of the CYB5A gene in RA females [61] Single nucleotide polymorphisms of the X-encoded genes *TIMP1* and *IL-9R* [62]
Clinical phenotype	Less severe course of illness and better response to therapy in males as compared to females [56, 58] Amelioration of RA in pregnant females [53]

Era della Medicina delle 4 P

- Predittiva
- Preventiva
- Personalizzata
- Partecipativa

Organization	Policy to: Fix the Numbers	Policy to: Fix the Institutions	Policy to: Fix the Knowledge	Policy to Integrate Gender Analysis into Research
Canadian Institutes of Health Research (CIHR)	Yes	Yes	Yes	In 2010, CIHR required all grant applicants to respond to mandatory questions about "whether their research designs include gender and sex." August 2015 released online training for Sex and Gender in Biomedical Research.
European Commission Directorate-General for Research and Innovation	Yes	Yes	Yes	Since 2003, the European Commission has supported "questioning systematically whether, and in what sense, sex and gender are relevant in the objectives and in the methodology of projects." In 2013, these policies were reaffirmed and expanded in Horizon 2020, the Commission's current funding framework. The Commission states, "Integrating gender/sex analysis in research and innovation (R&I) content helps improve the scientific quality and societal relevance of the produced knowledge, technology and/or innovation. In March 2015, the EC Gender Advisory Group published an advice paper on preparing grants that integrate the gender dimension into research.
US National Institutes of Health (NIH)	Yes	Yes	Yes	Guidelines for considering sex as a biological variable in research were released June 2015. Policy implemented January 1, 2016. (Notice Number: NOT-OD-15-102.) These guidelines are mainstreamed in "Enhancing Reproducibility through Rigor and Transparency" (Notice Number: NOT-OD-15-103.)

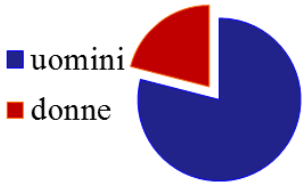
. Age and sex in drug development and testing for adults

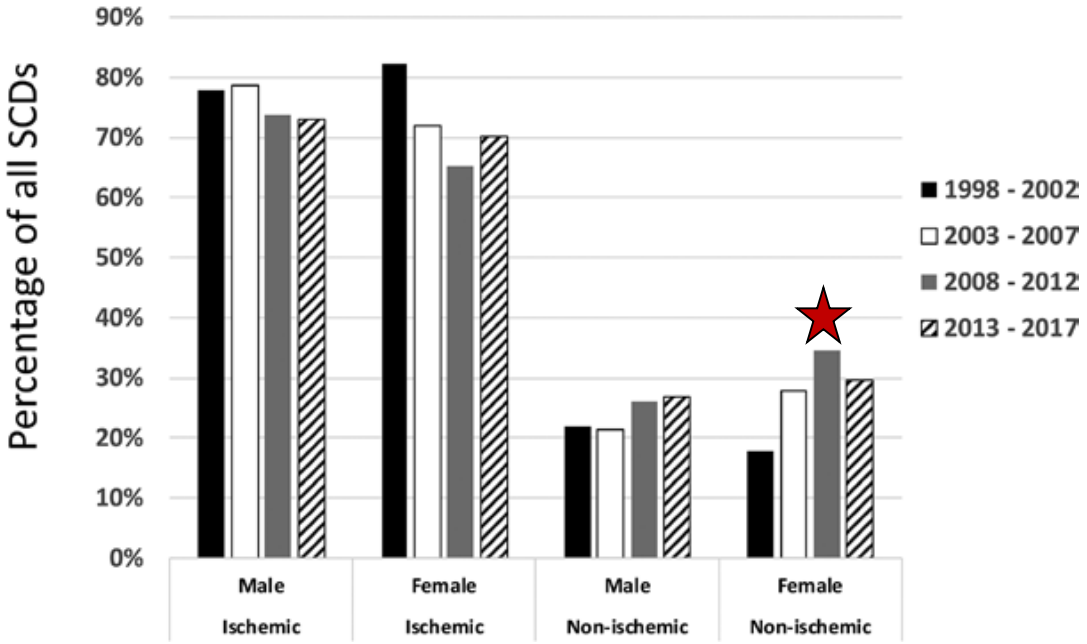


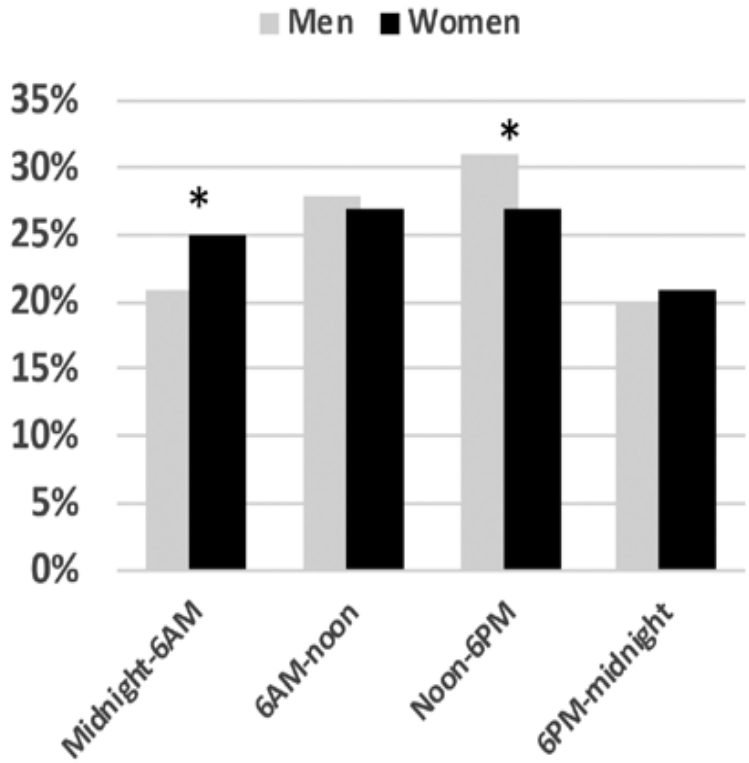
Tannenbaum C, Day D. Pharmacol Res. 2017; 121:83–93,

Sudden Cardiac Death in Women

The Fingesture population = 5869 autopsied subjects with SCD
(male n=4631, 78.9%; female n= 1238, 21.1%; mean age, 65±12 years)







Women : age ++; ECG-LVH ++ & myocardial fibrosis

Gender disparities in cardiopulmonary resuscitation delivery

- In public locations, 39% of females and 45% of males received bystander CPR ($P<0.01$),
- In private settings, 35% of females and 36% of males received BCPR (P=NS).
- Males had 23% increased odds of survival compared with females ($P<0.01$)

Blewer et al; Resuscitation Outcomes Consortium 2011-2015

Perceptions on Why Women Receive Less CPR Than Men

Women's bodies are sexualized

"I think that people are afraid to touch the breast region" –Male, age 39

"Bystanders, especially male bystanders, may be afraid to touch women especially in the chest area… anxious that their help my be unnecessary" –Female, age 48.

"Men are afraid of seeming like perverts" –Male, age 27.

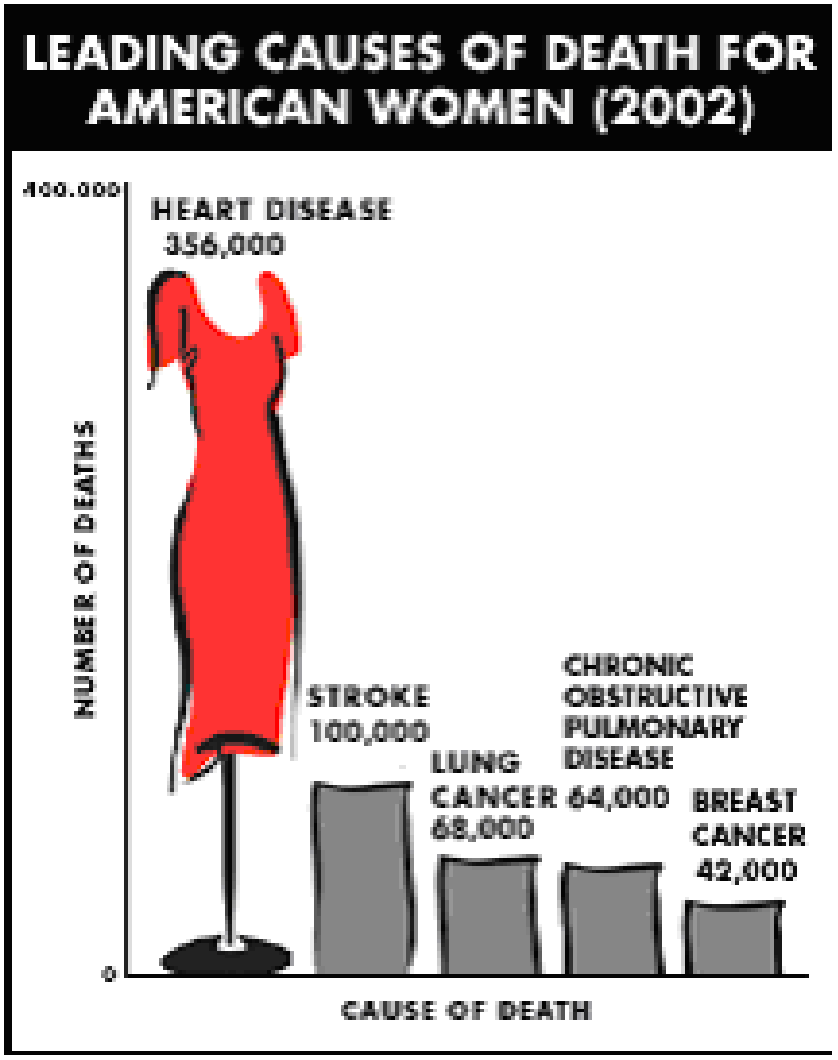
Women are perceived as physically weak or fragile and prone to injury

Women don't have cardiac arrest/cardiac disease /

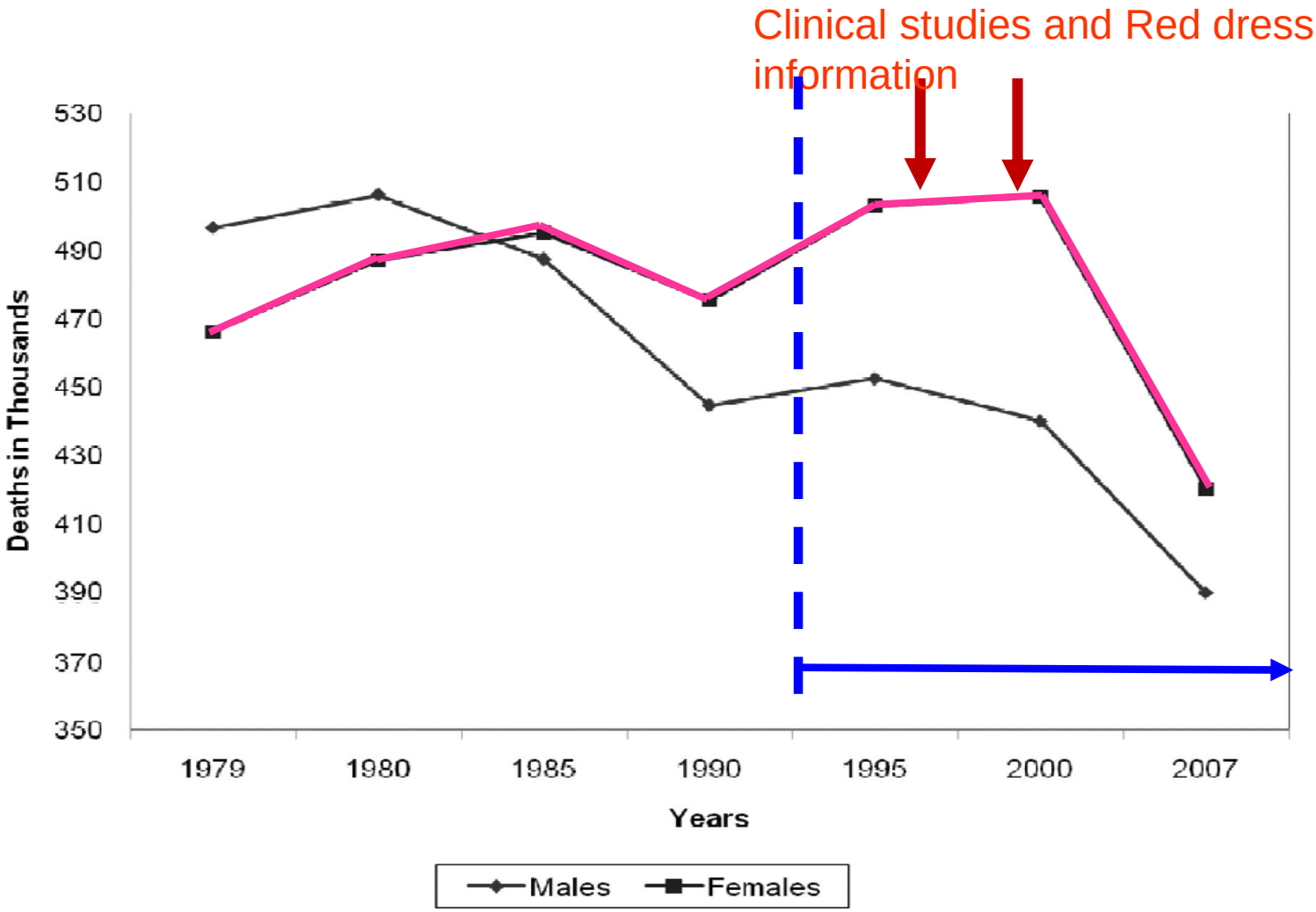
Women are emotional, overdramatic, faking

Perman S et al *Circulation.* 2019;139:1060–1068.

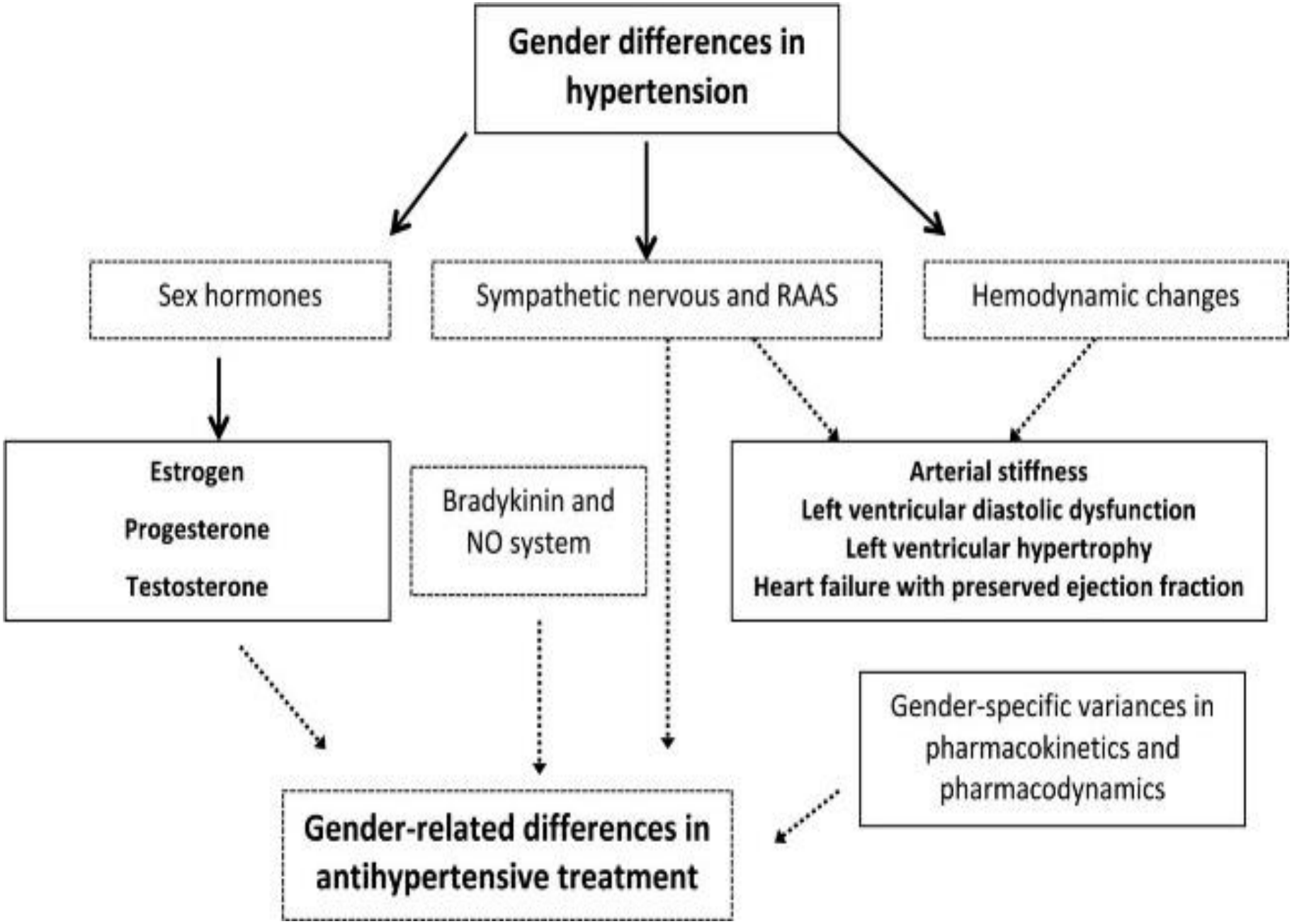

APRIL 28, 2003
www.time.com AOL Keyword: TIME
IRAQ: INSIDE THE OCCUPATION / THE SEARCH FOR SADDAM
TIME
WOMEN & HEART DISEASE
Is your biggest worry breast cancer? Think again. ONE OUT OF THREE women will die of heart disease. What you can do to protect yourself


LEADING CAUSES OF DEATH FOR AMERICAN WOMEN (2002)
400,000
0
NUMBER OF DEATHS
HEART DISEASE
356,000
STROKE
100,000
LUNG CANCER
68,000
CHRONIC OBSTRUCTIVE PULMONARY DISEASE
64,000
BREAST CANCER
42,000
CAUSE OF DEATH

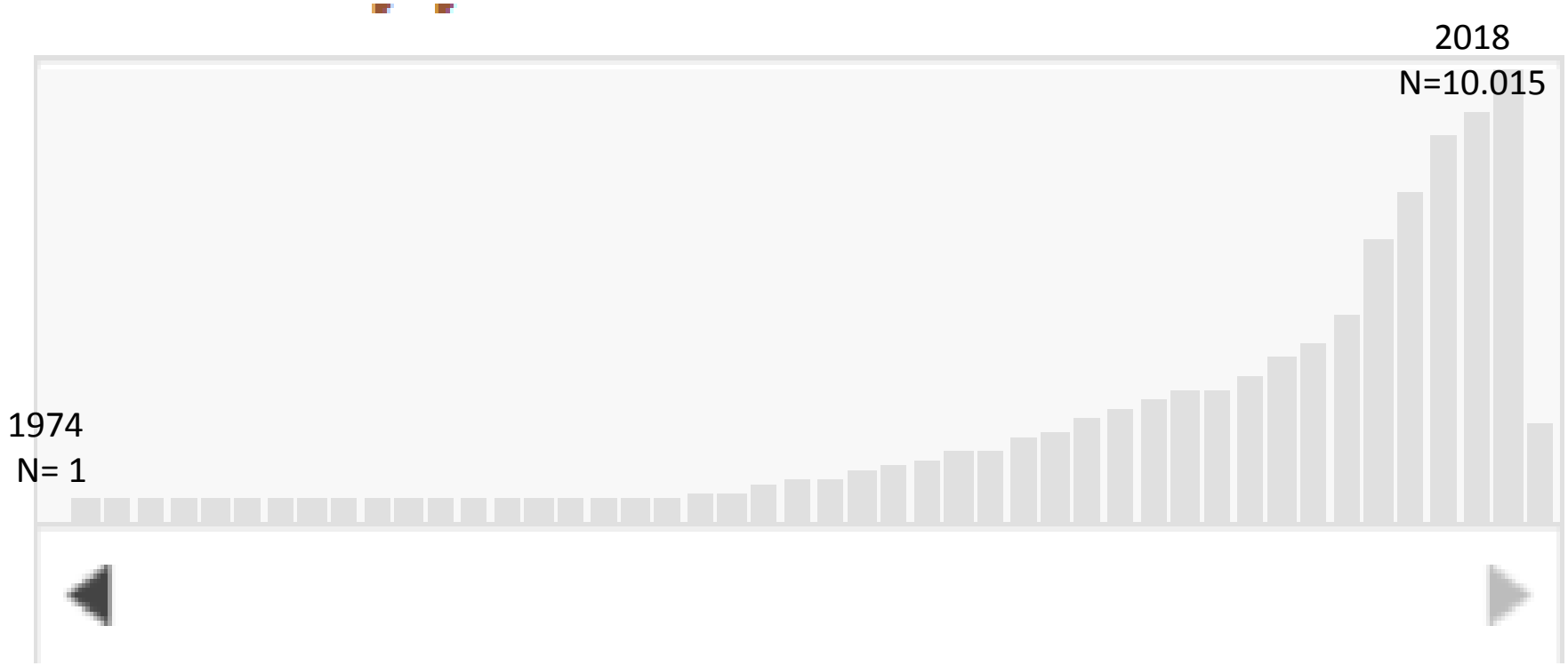
Trends in the total annual number of deaths caused by CV disease according to gender, United States, 1979 to 2007



Mosca L et al. Circulation 2011;124:2145-2154


Gender differences in hypertension
Sex hormones
Sympathetic nervous and RAAS
Hemodynamic changes
Estrogen
Progesterone
Testosterone
Bradykinin and NO system
Arterial stiffness
Left ventricular diastolic dysfunction
Left ventricular hypertrophy
Heart failure with preserved ejection fraction
Gender-specific variances in pharmacokinetics and pharmacodynamics
Gender-related differences in antihypertensive treatment

Publication trends of manuscripts including sex-gender issues in 9 different disciplines



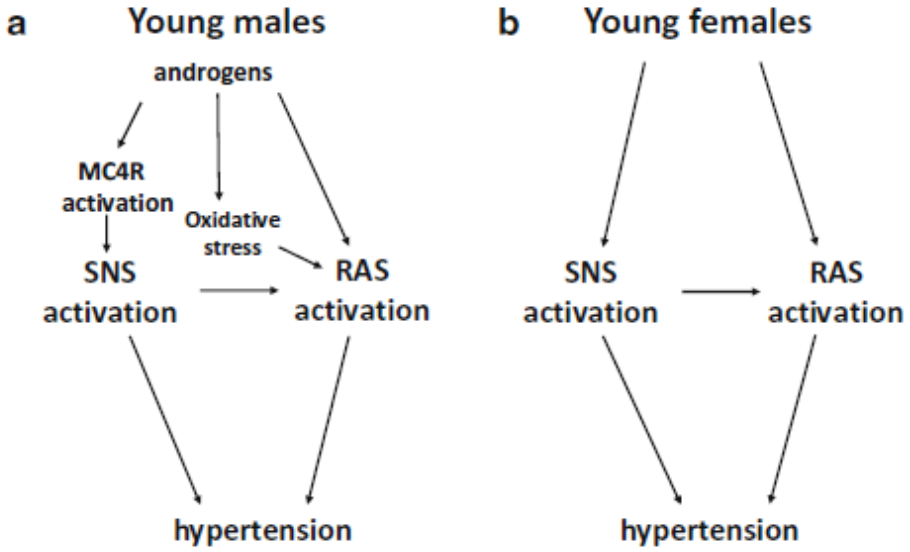


Fig. 9.1 Mechanisms responsible for hypertension in young male (**a**) and female (**b**) SHR. Abbreviations: *MC4R* melanocortin-4 receptor, *SNS* sympathetic nervous system, *RAS* renin-angiotensin system

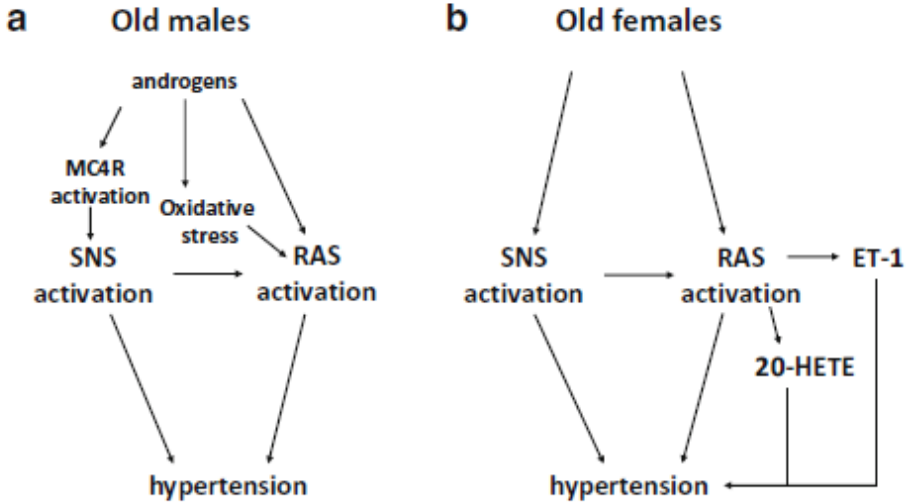
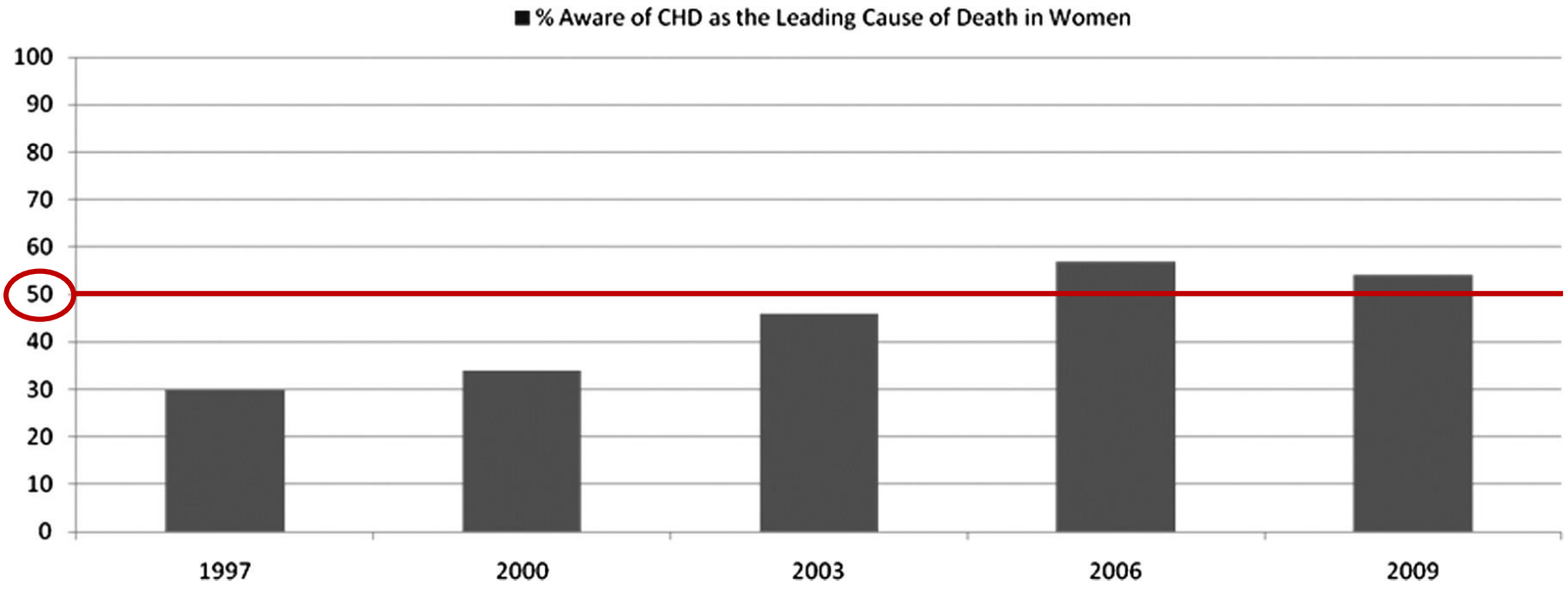


Fig. 9.2 Mechanisms responsible for hypertension in old male (**a**) and female (**b**) SHR. Abbreviations: *MC4R* melanocortin-4 receptor, *SNS* sympathetic nervous system, *RAS* renin-angiotensin system, *ET-1* endothelin

Trend in awareness
coronary artery disease is the leading cause of death in women



Mosca L et al. Circ Cardiovasc Qual Outcomes 2010;3:120-127

European Heart Journal (2016) **37**, 24–34
doi:10.1093/eurheartj/ehv598

CURRENT OPINION
Disease management

Gender in cardiovascular diseases: impact on clinical manifestations, management, and outcomes

In the vast majority of cardiovascular diseases (CVDs), there are well-described differences between women and men in epidemiology, pathophysiology, clinical manifestations, effects of therapy, and outcomes.

There is a lot of published knowledge on S&G differences, but the awareness is low. This may be due to the fact that existing knowledge is dispersed and not presented in a coherent manner.

Are there differences ?

- **Sex specific Risk factors**
- **Risk factors stronger in women**
- **Risk factors with similar prevalence but different impact**
- **Clinical presentation & Treatment**

Are there differences ?

- **Sex specific Risk factors**
- **Risk factors stronger in women**
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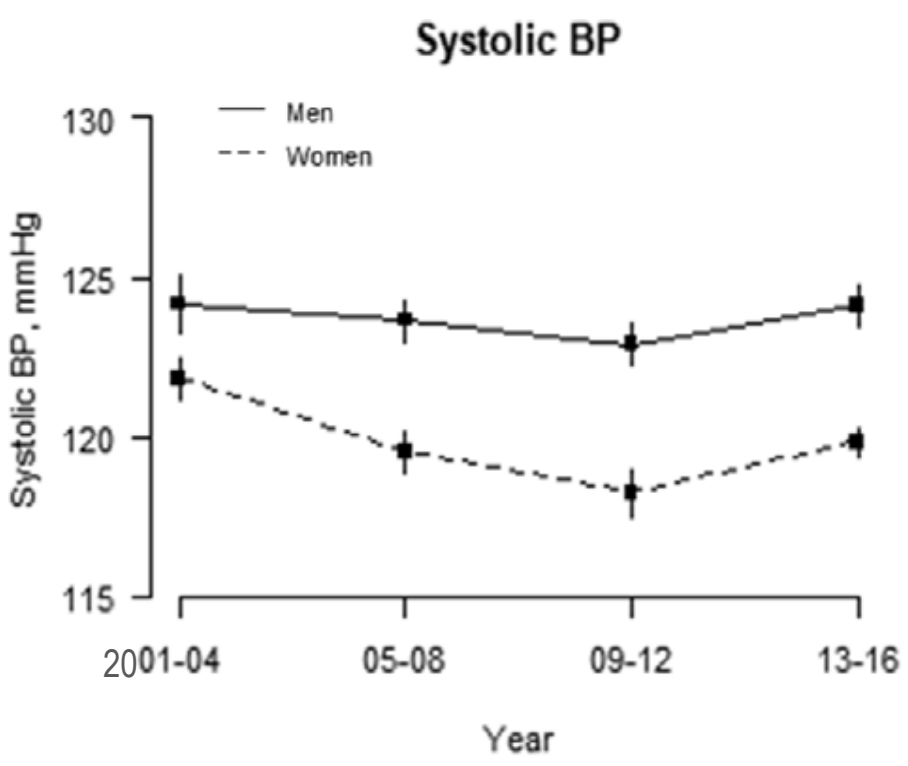
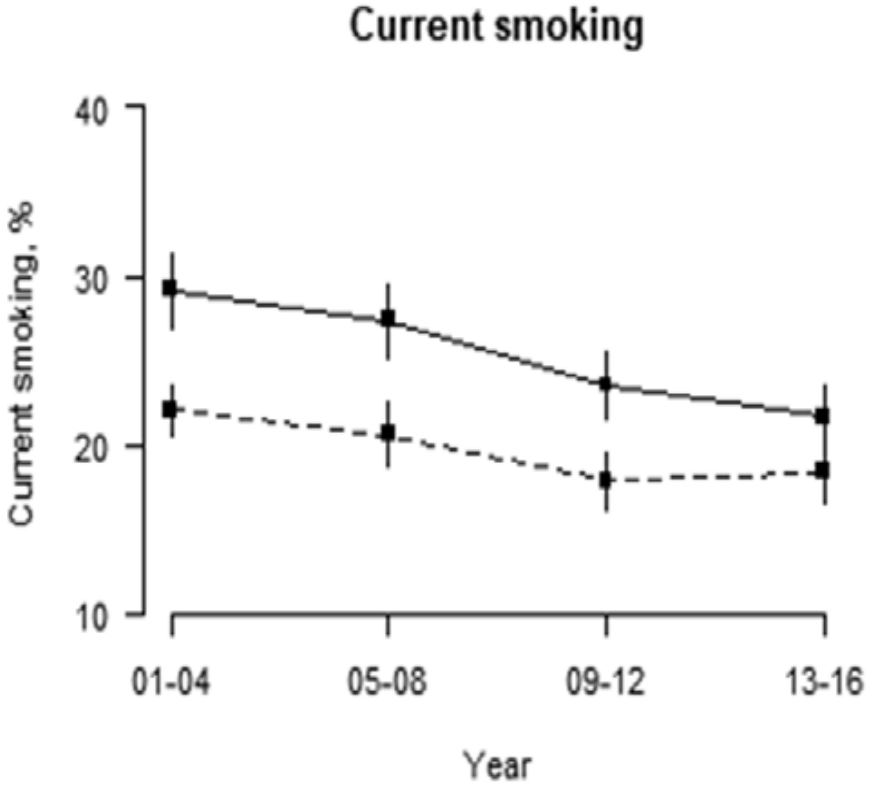
Sex Differences in Trends in CVD Risk Factors

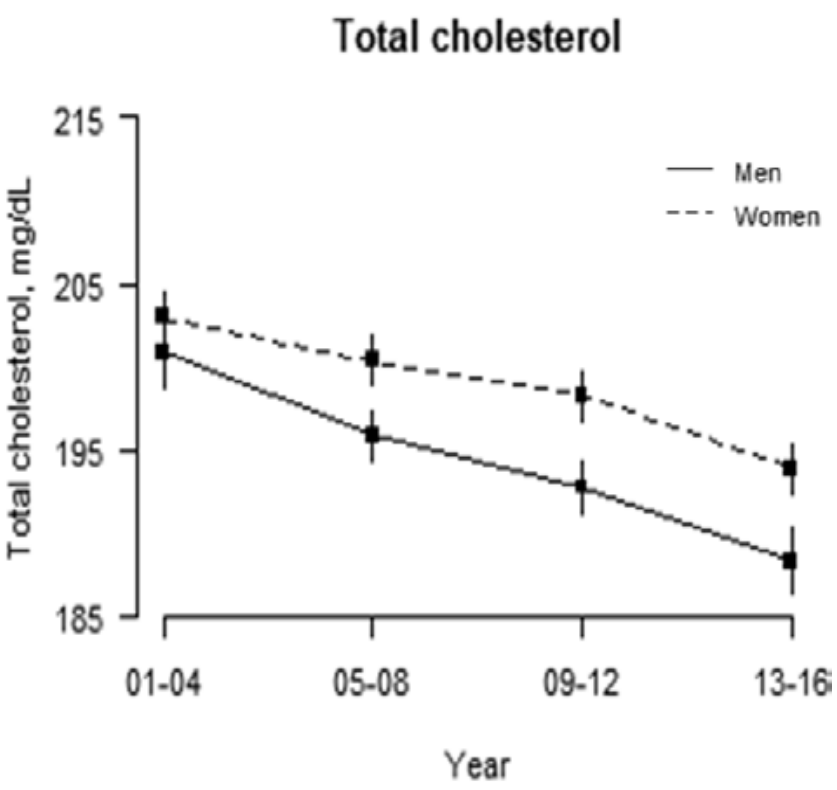
35 416 participants (51% women) National Health and Nutrition Examination Survey

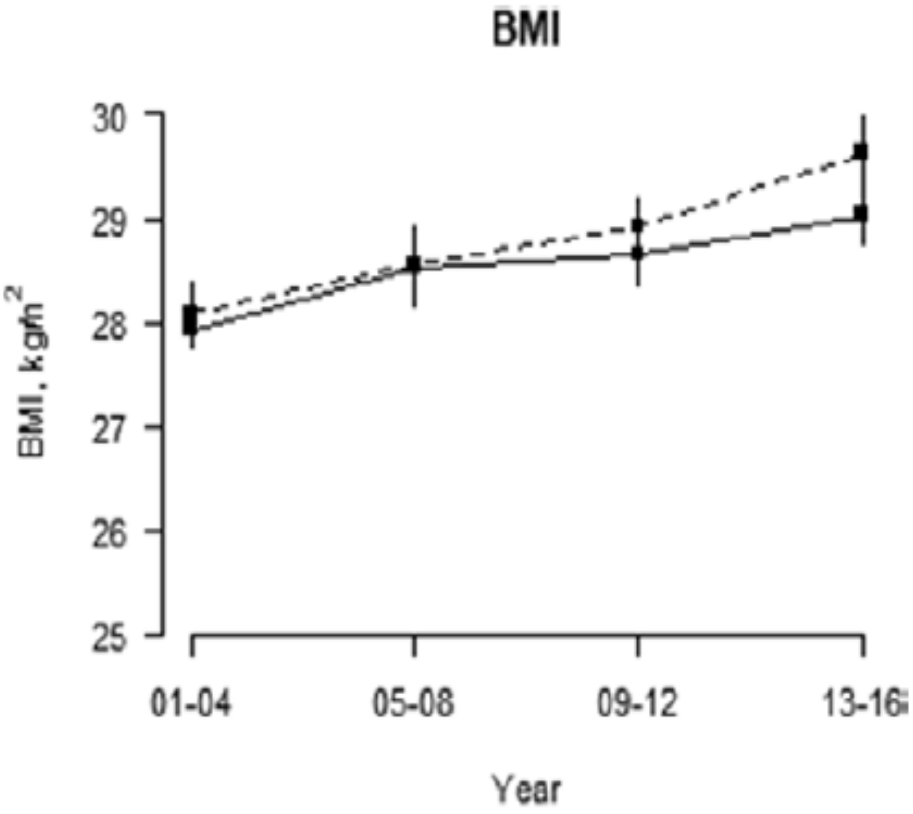




Peters et al *Circulation.* 2019;139:1025–1035

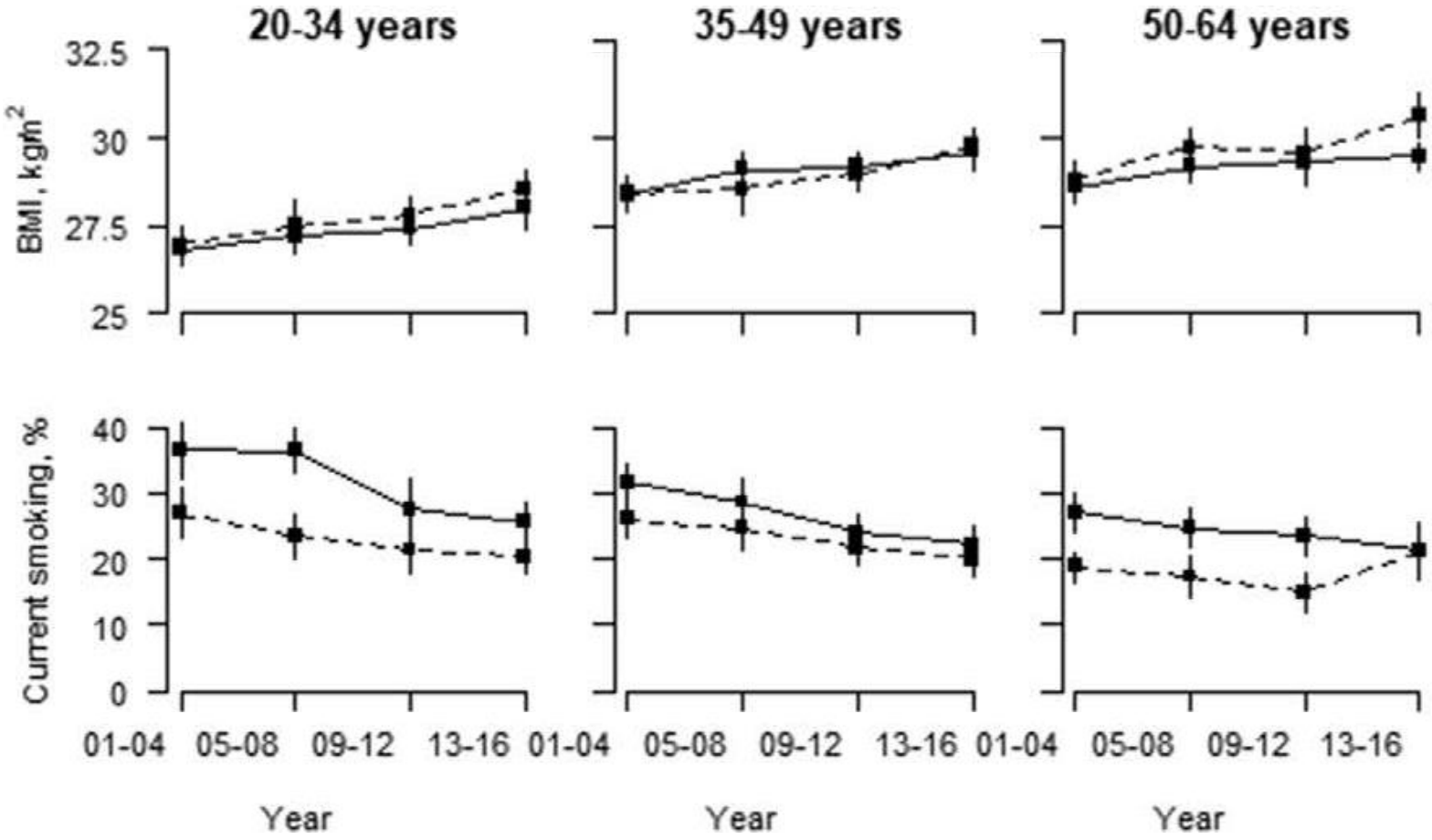
Sex Differences in Trends in CVD Risk Factors





Peters et al *Circulation.* 2019;139:1025–1035

Sex Differences in Trends in CVD Risk Factors

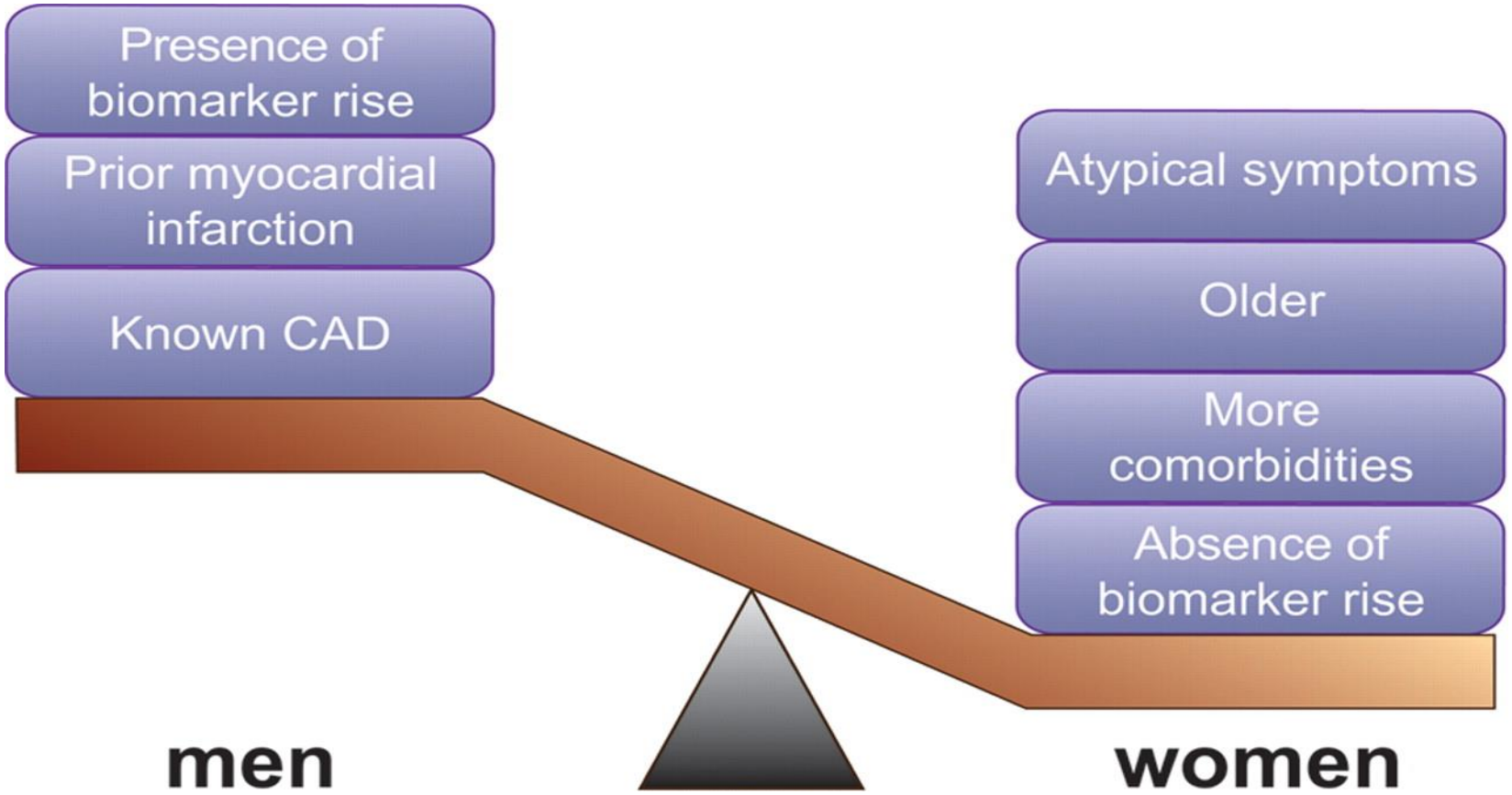


Peters et al *Circulation.* 2019;139:1025–1035

Are there differences ?

- **Sex specific Risk factors**
- **Risk factors stronger in W**
- **Risk factors with similar prevalence but different impact**
- **Clinical presentation & Treatment**

Coronary artery disease and heart failure diagnosis



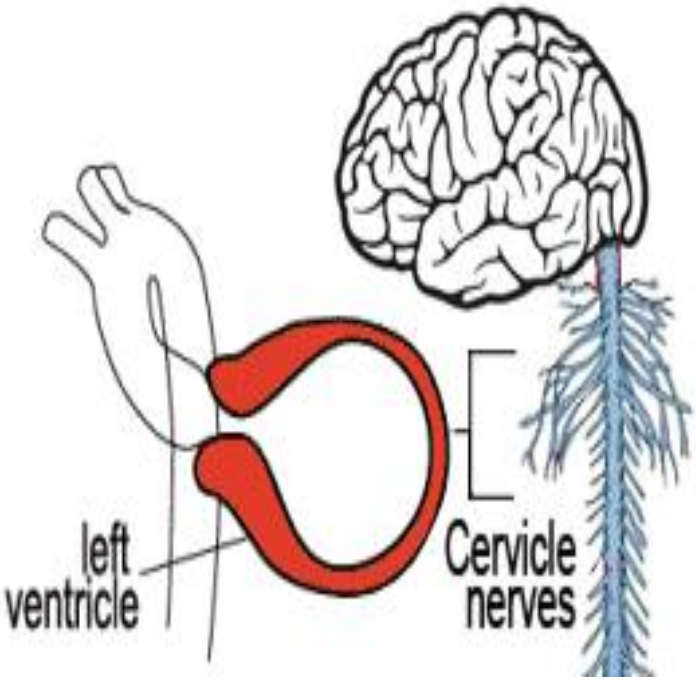
Möllmann H et al. Eur Heart J 2011;32:3070-3072

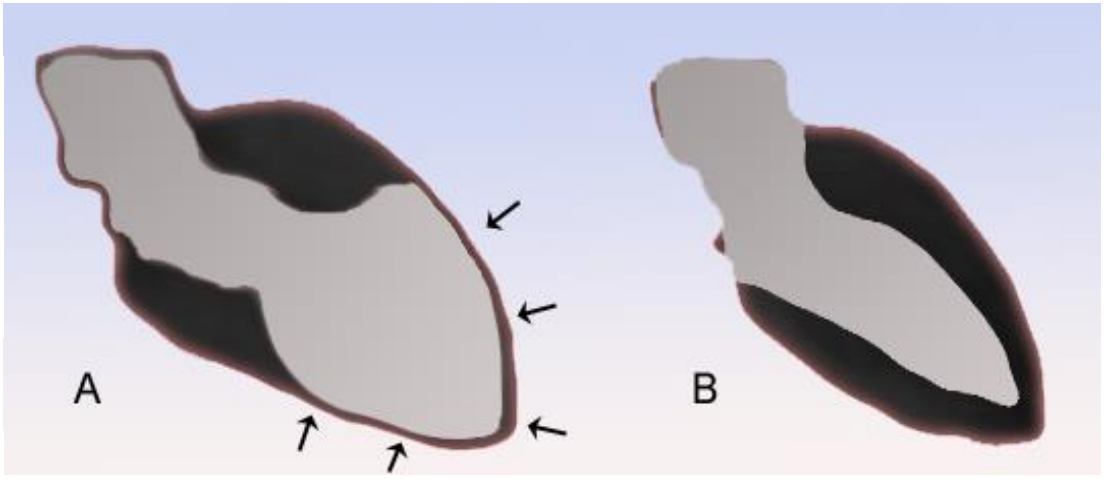
Sensitivity of diagnostic procedures

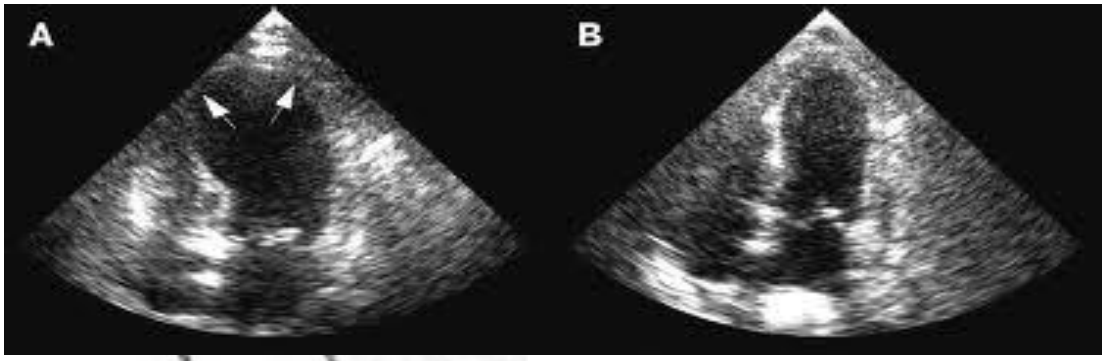
"We wanted to make the stress test as realistic as possible."

- Takotsubo cardiomyopathy:
- 70–90% women in most registries
- often preceded by acute massive psychological or physical stress.

8% of acute coronary syndrome in women
1% of acute coronary syndromes in men







Takotsubo: Japanese name of an octopus trap

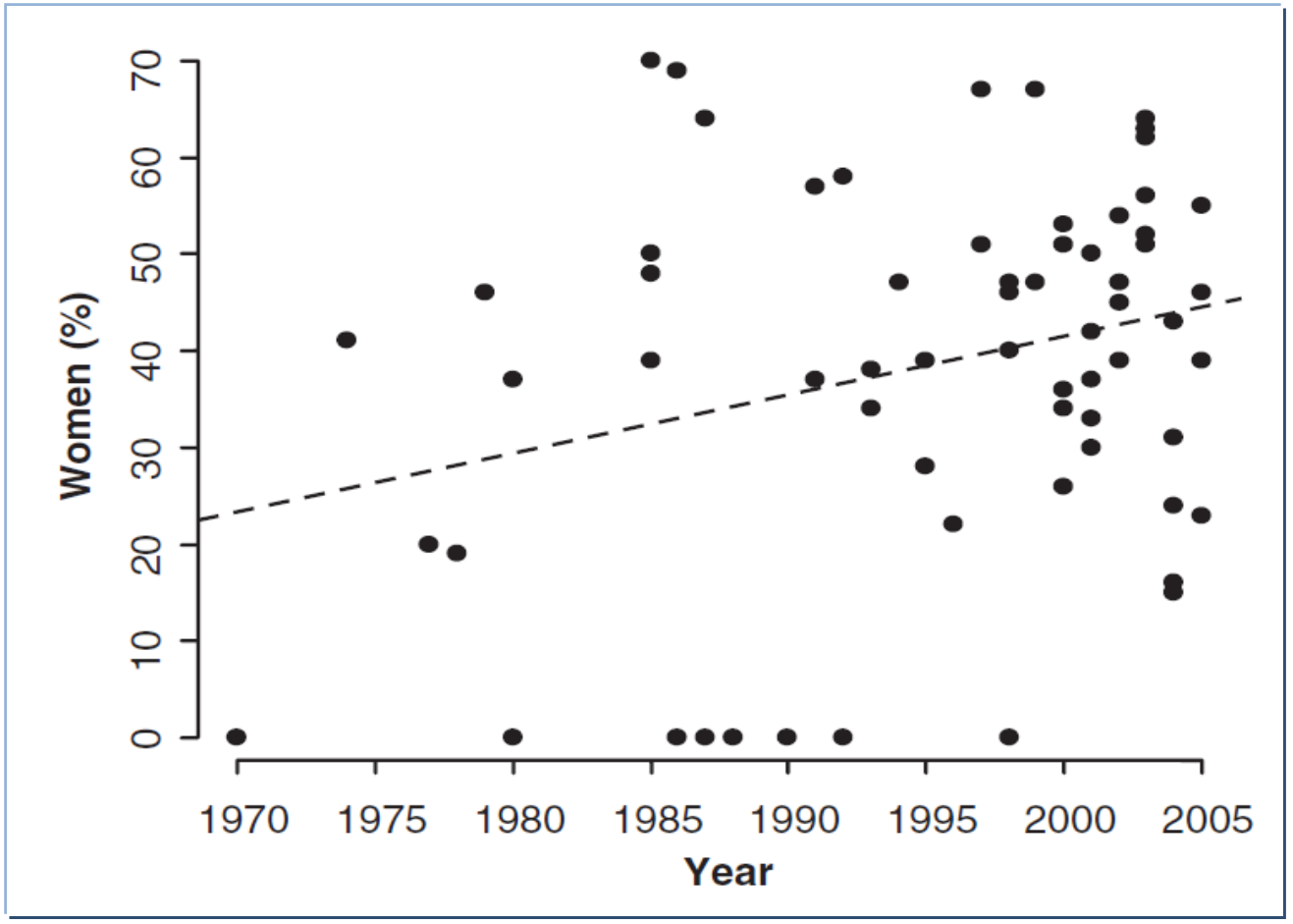
A BROKEN HEART
IS KNOWN MEDICALLY AS
TAKOTSUBO CARDIOMYOPATHY

Are there differences ?

- **Sex specific Risk factors**
- **Risk factors stronger in W**
- **Risk factors with similar prevalence but different impact**
- **Clinical presentation & Treatment**

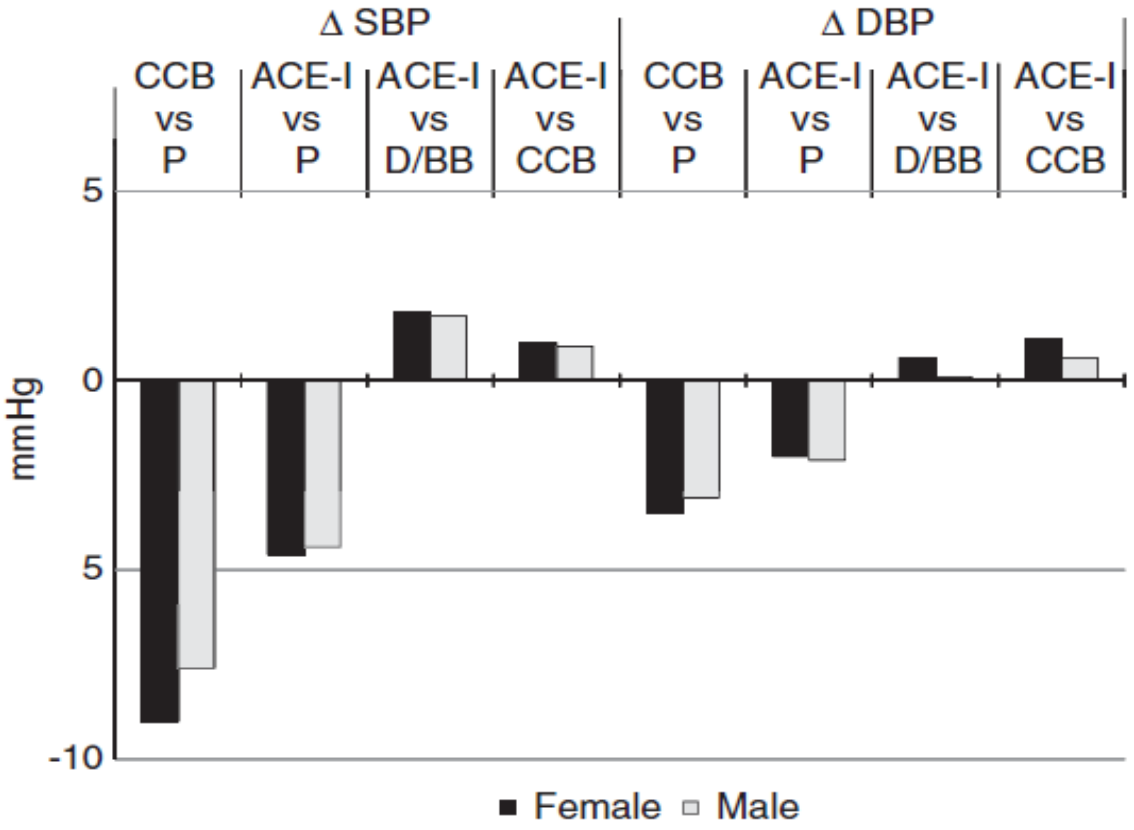
Treatment of mild to moderate hypertension

proportion of women included in the 67 studies according to the year of publication



JOURNAL OF WOMEN'S HEALTH 2009; 18 (7)

Do men and women respond differently to blood pressure-lowering treatment? Results of prospectively designed overviews of randomized trials



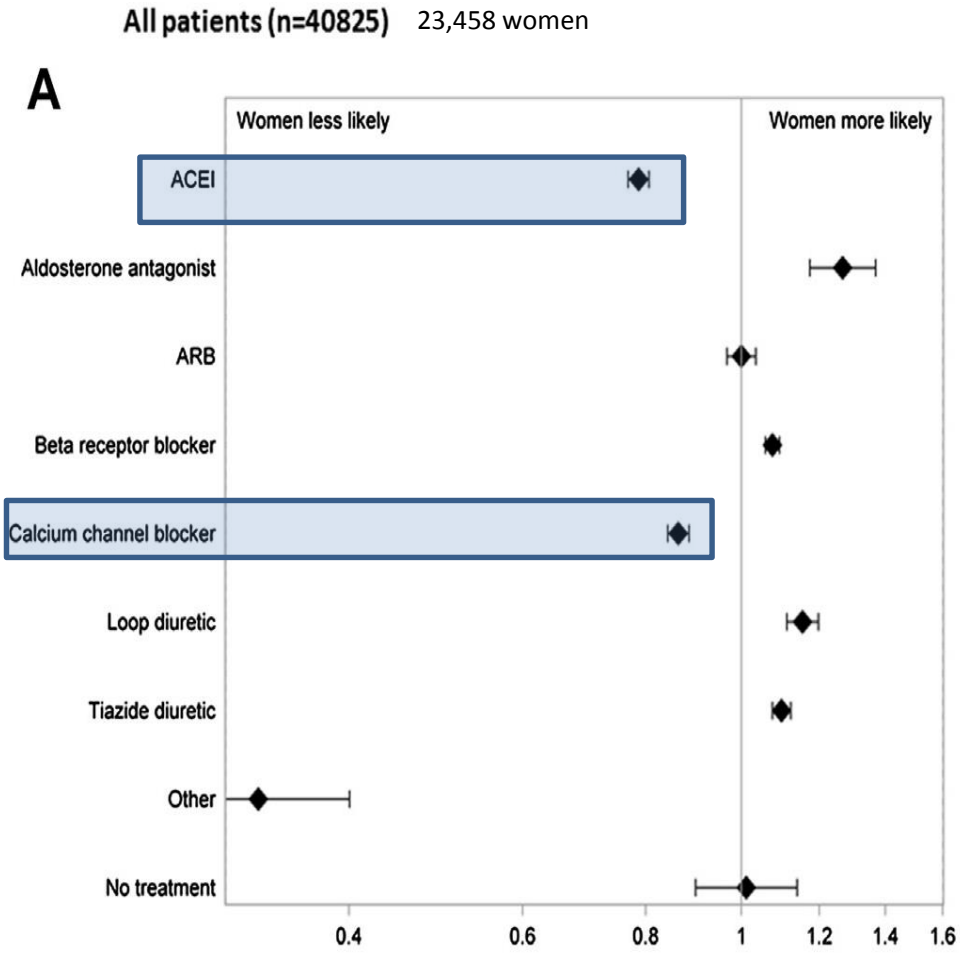
Turnbull F et al Eur Heart J. 2008 Nov;29(21):2669-80.

Gender differences in antihypertensive drug treatment: results from the SPCC Database

74,751 individuals > 30 years attending primary health care with the diagnosis of hypertension

- Men more often received treatment with ACEIs
- Women were more often than men treated with thiazide diuretics or beta-blockers.

Comorbidities	Women, n (%)	Men, n (%)	
Diabetes mellitus	4437 (18.9)	4561 (26.3)	*
Ischemic heart disease	3615 (15.4)	3629 (20.8)	*
Cerebrovascular disease	2263 (9.6)	2147 (12.4)	*
Heart failure	1612 (6.9)	1238 (7.1)	
Atrial fibrillation/ flutter	1666 (7.1)	1685 (9.7)	*
Asthma	896 (3.8)	564 (3.2)	*



C. Ljungman et al. Journal of the American Society of Hypertension 8(12) (2014) 882–890

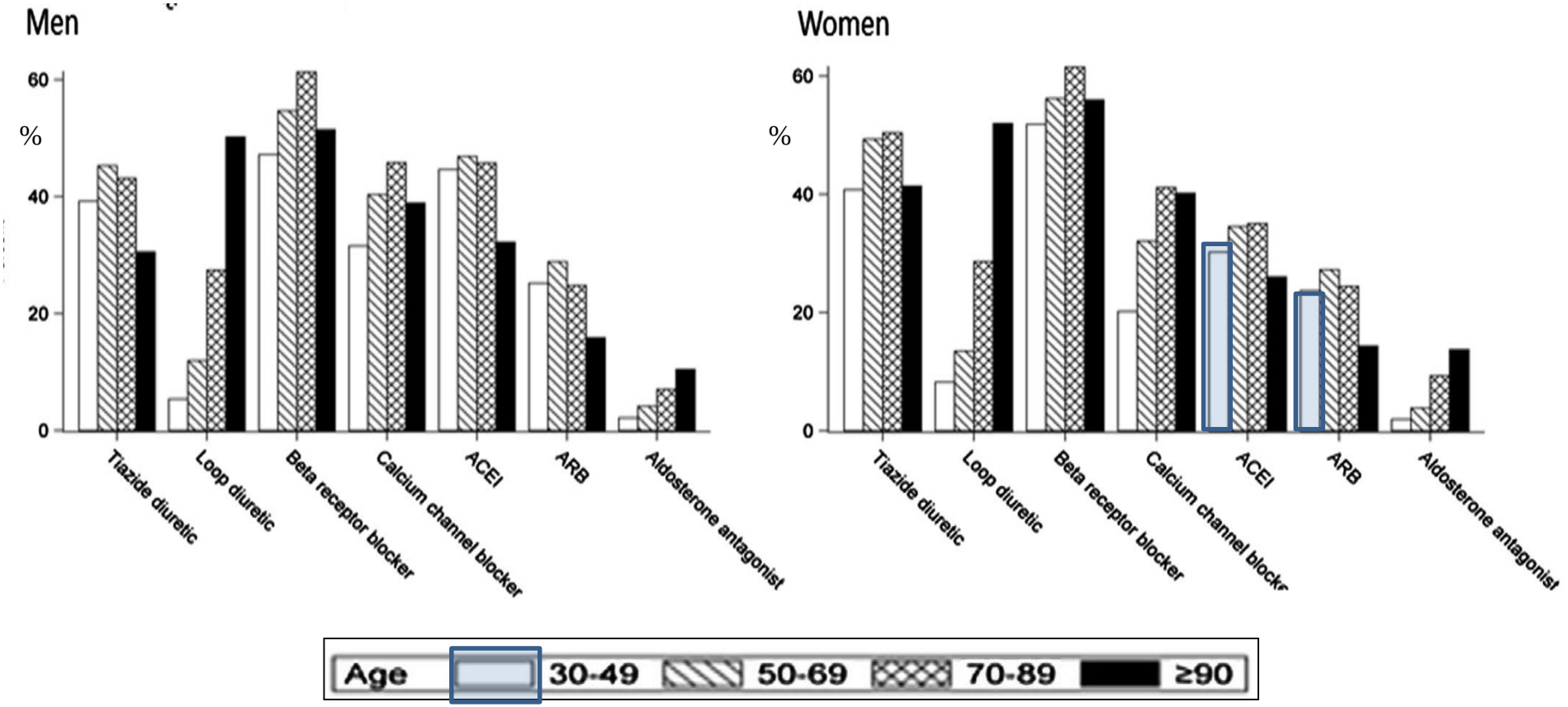
Treatment in women in child bearing age

- *« In women with child-bearing potential, ACE inhibitors and angiotensin receptor blockers should be avoided, due to possible teratogenic effects. This is the case also for aliskiren, a direct renin inhibitor, although there has not been a single case report of exposure to aliskiren in pregnancy.»*

In women with child-bearing potential RAS blockers are not recommended and should be avoided.	III	C

ESH and ESC Guidelines 2013

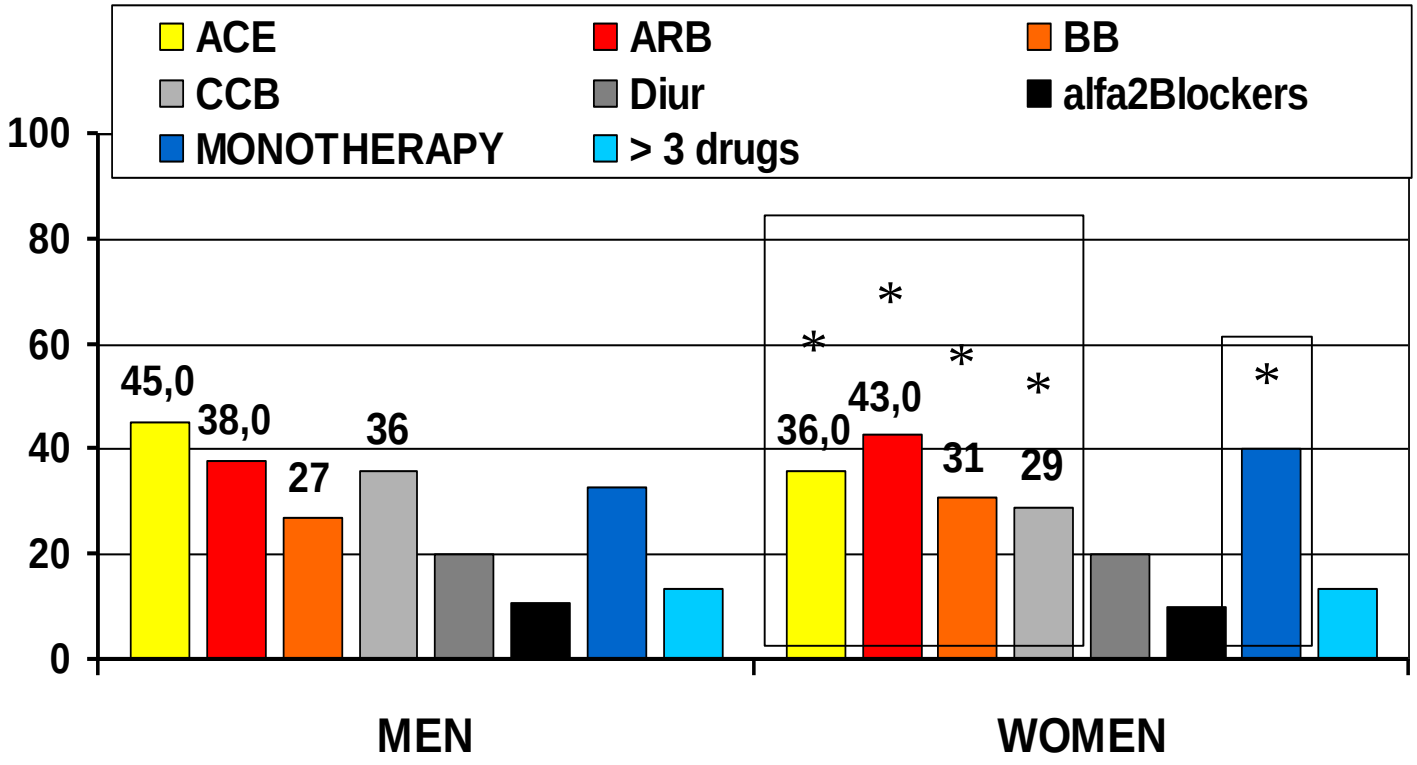
Gender differences in antihypertensive drug treatment: results from the SPCC Database



C. Ljungman et al. Journal of the American Society of Hypertension 8(12) (2014) 882–890

Sex differences in hypertension-related renal and cardiovascular diseases in Italy: the I-DEMAND study

3,558 study patients with renal data available, 1643 women, mean age 61 ± 12 years, 38 % diabetes mellitus

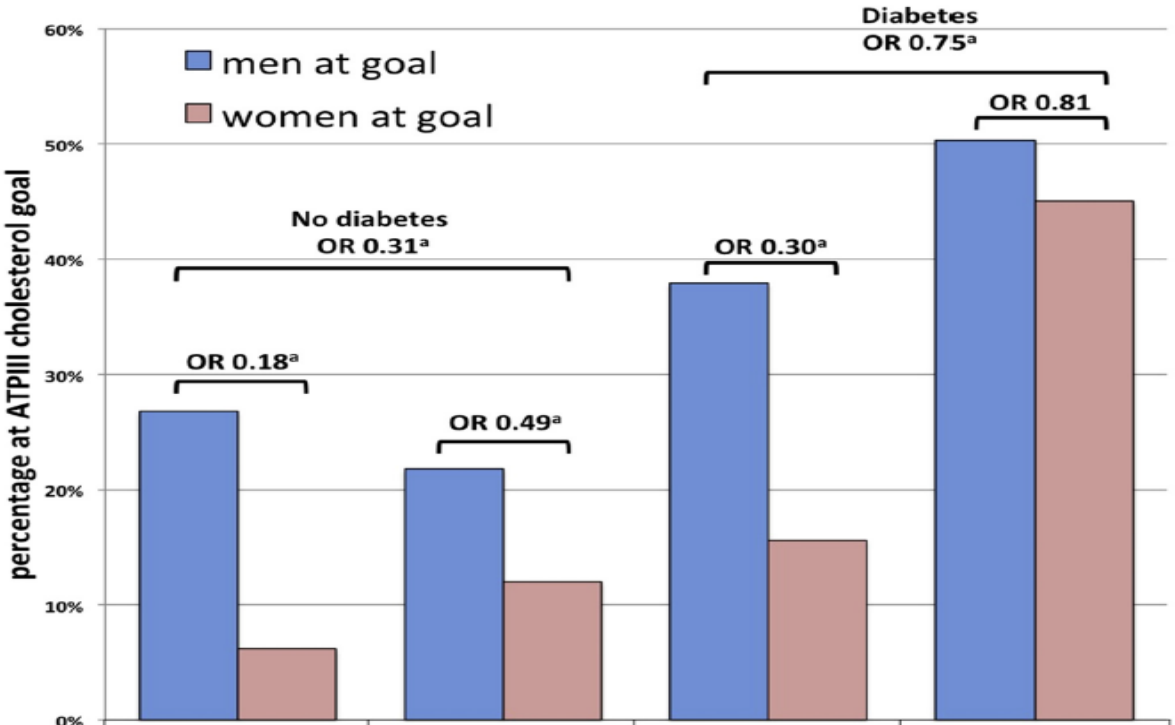


Muiesan ML et al J Hypertens 2012

Goal attainment by ASCVD and diabetes status in high-risk patients

Schoen M et al Am J Cardiol 2016;117:48e53

Statin treatment
Men 39%
Women 48%



	no ASCVD nor diabetes	ASCVD, no diabetes	ASCVD and diabetes	Diabetes, no ASCVD
Men at goal	88 (27)	31 (22)	39 (38)	154 (50)
Women at goal	5 (6)	13 (12)	15 (16)	222 (45)
OR (95% CI)	**0.18 (0.46-0.07)**	**0.49 (0.24-0.99)**	**0.30 (0.15-0.60)**	0.81 (0.61-1.08)
Men statins	103 (31)	89 (62.7)	70 (68)	137 (45)
Women statins	27 (33)	57 (52.8)	60 (63)	214 (43)
OR (95% CI)	1.1 (0.7-1.8)	0.67 (0.40-1.1)	0.79 (0.44-1.4)	0.95 (0.71-1.3)
Total patients	409	250	199	799

European Journal of Preventive Cardiology

EUROPEAN SOCIETY OF CARDIOLOGY®

Original scientific paper

European Journal of Preventive Cardiology
2016, Vol. 23(17) 1831–1838

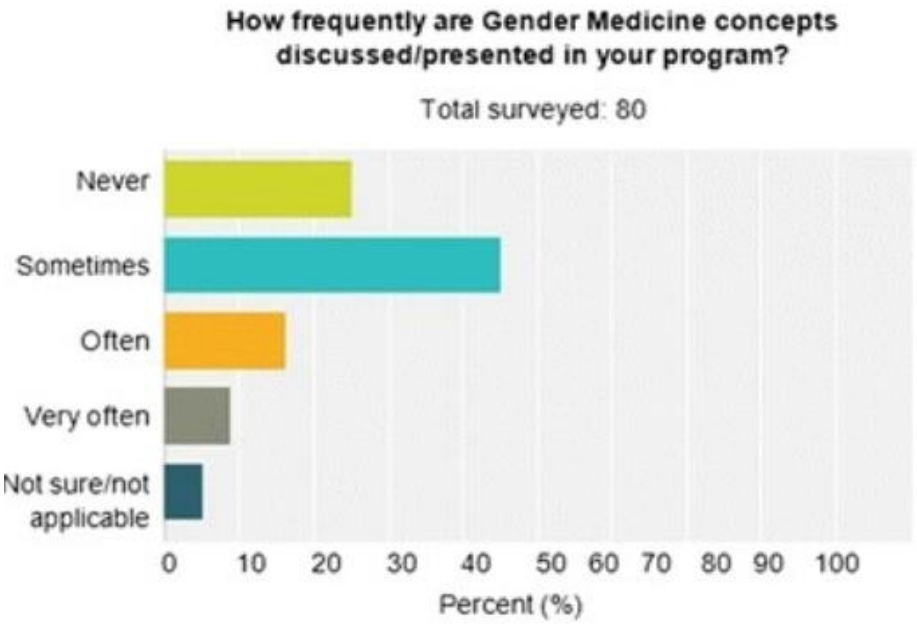
DOI: 10.1177/2047487316648476
ejpc.sagepub.com

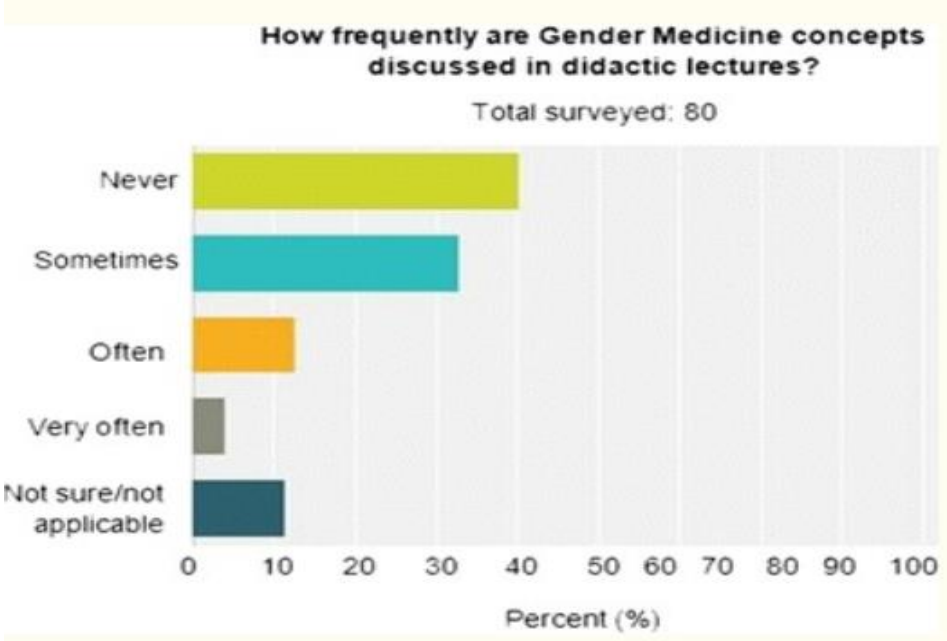
SAGE

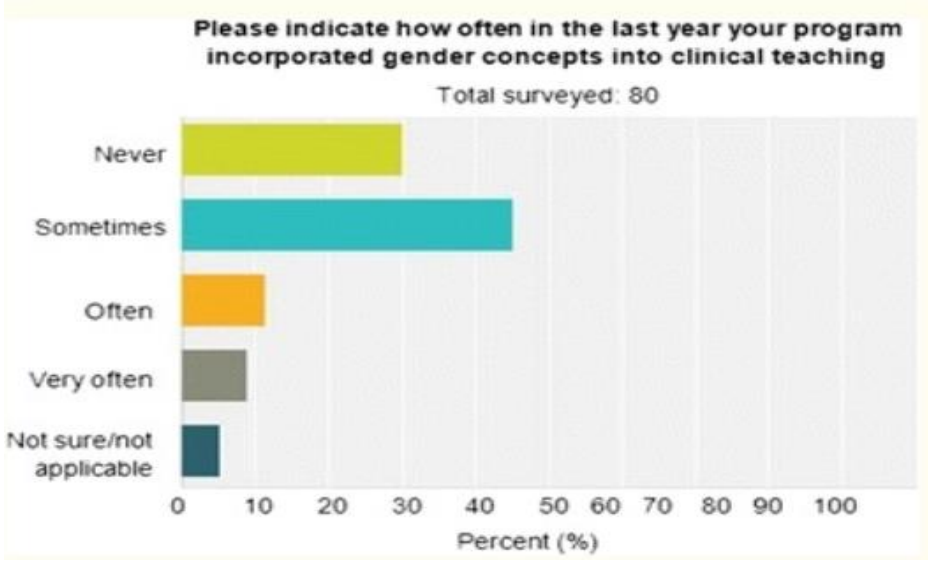
Primary prevention of cardiovascular disease: More patient gender-based differences in risk evaluation among male general practitioners

Raphaëlle Delpech[1], Virginie Ringa[2], Hector Falcoff[3,4] and Laurent Rigal[1,2]

Conclusion: Even before the onset of cardiovascular disease, women patients receive less satisfactory preventative management than men do, and these differences are even more marked when the physician is a man. More attention to the influence of gender stereotypes is needed in medical training in order to combat the inequalities that they cause.







65 % felt that gender medicine concepts are important
60 % agreed that gender medicine curriculum should be implemented and taught in their clinical program

Dhawan et al Biol Sex Differ. 2016; 7(Suppl 1): 37.

Research fields in Gender Medicine

Basic research for differences in

pathophysiological bases of diseases with sex specific outcome

Cell have sex too ie collagen synthesis different in fibroblasts in response to estrogens and testosterone

Clinical studies for differences in

clinical manifestations, clinical presentation, outcomes

Pharmacology for differences in

drug resorption, distribution, drug metabolism, and excretion

Epidemiology, Health care and prevention research

prospective studies, including a broad spectrum of gender-relevant risk factors

women are much more aware of risk factors and much easier to be convinced for preventive measures

Usage of antihypertensive drugs in M & W

Table 1
The prevalence of usage of different antihypertensive groups in women and men in the large studies.

Reference	Sample size	Women/men (%)	Study type	Main findings
Gu et al. [5]	5410 hypertensive patients	52/48	Cross-sectional study	W ++ diuretics and ARBs
Ljungman et al. [8]	40,825 hypertensive patients	57/43	Cross-sectional study	W ++ diuretics and BB
Van der Niepen et al. [11]	11,562 hypertensive patients	49/51	Cross-sectional study	W ++ diuretics e CCB
Turnbull et al. [31]	190,617 hypertensive subjects	46/54	Meta-analysis	No difference
Wallentin et al. [32]	292,428 hypertensive individuals	53/47	Cross-sectional study	W ++ diuretics, ARBs , BB

ACEI – angiotensin-convertin enzyme inhibitor, ARB - angiotensin II-receptor blocker, BB – beta-blocker, CCB - calcium channel blocker.