From Basic Science to Global Health – Why Do We Need Gender Medicine

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History of Gender Medicine

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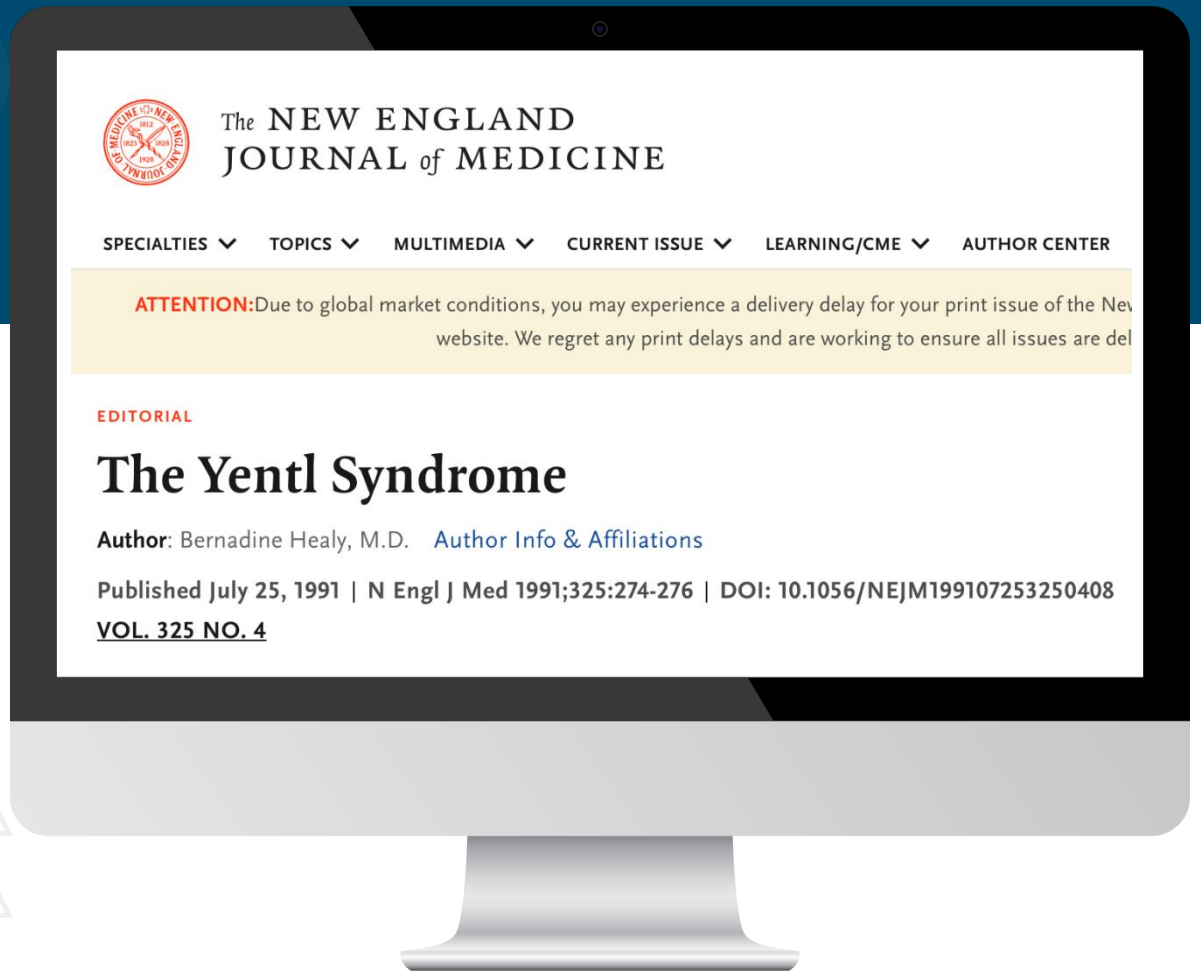
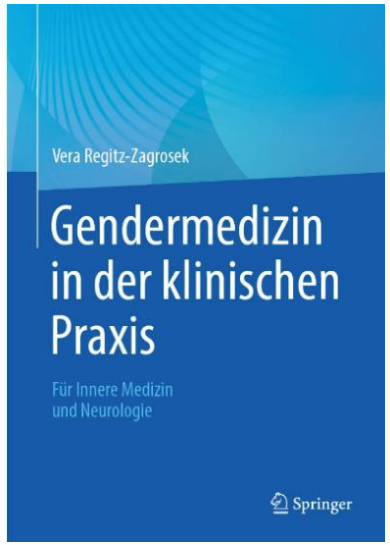


History of Gender Medicine



What is Sex- and Gender-sensitive Medicine?

1

Health and disease are affected by sex and gender

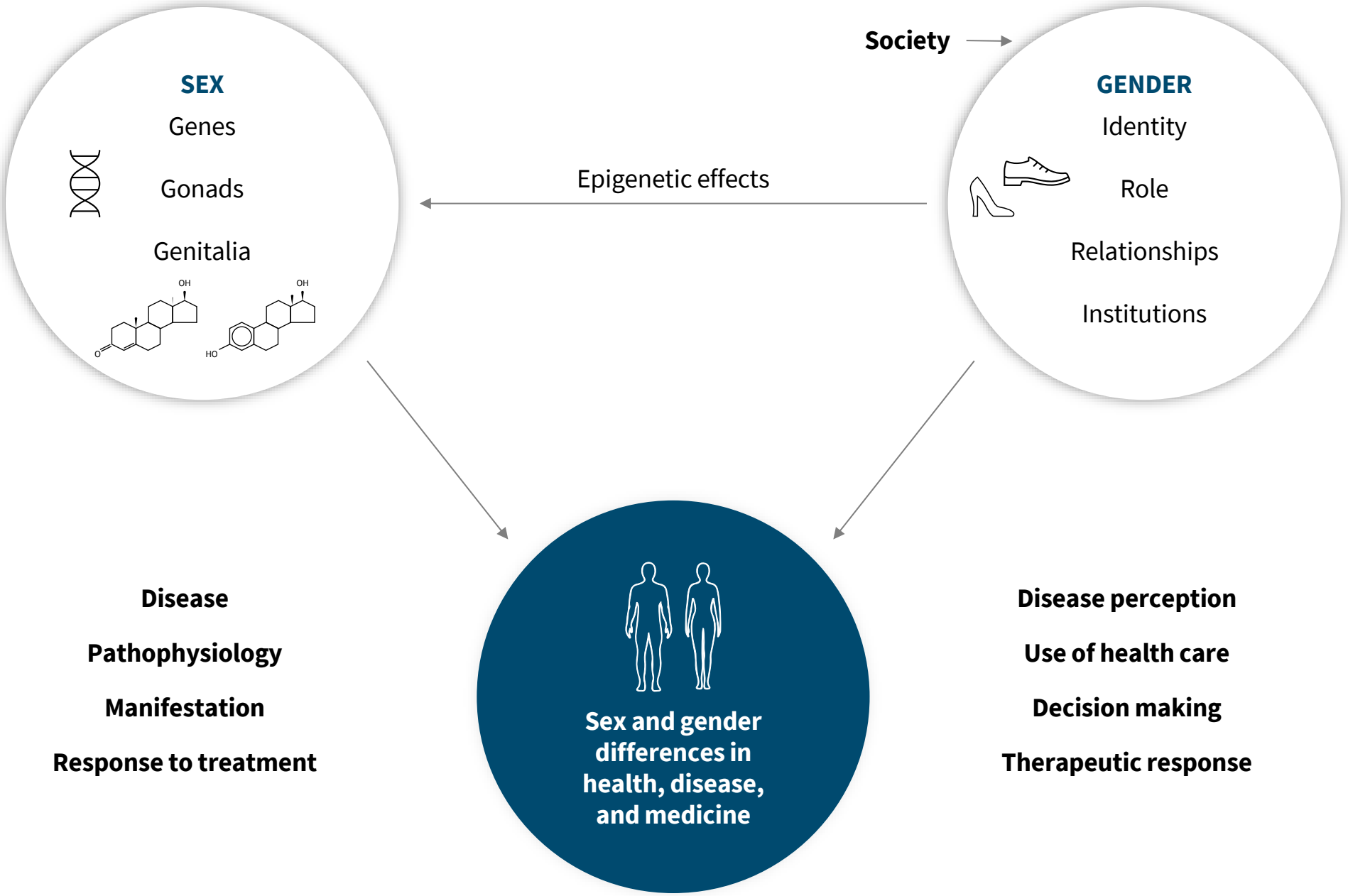
2

Both biological and sociocultural aspects need to be considered

3

Gendered aspects of the patient-doctor relationship are taken into account

The interaction of sex and gender



Modified from Mauvais-Jarvis et al., Lancet 2020

Examples


Depression


Osteoporosis


Exercise


Life Expectancy


Medication

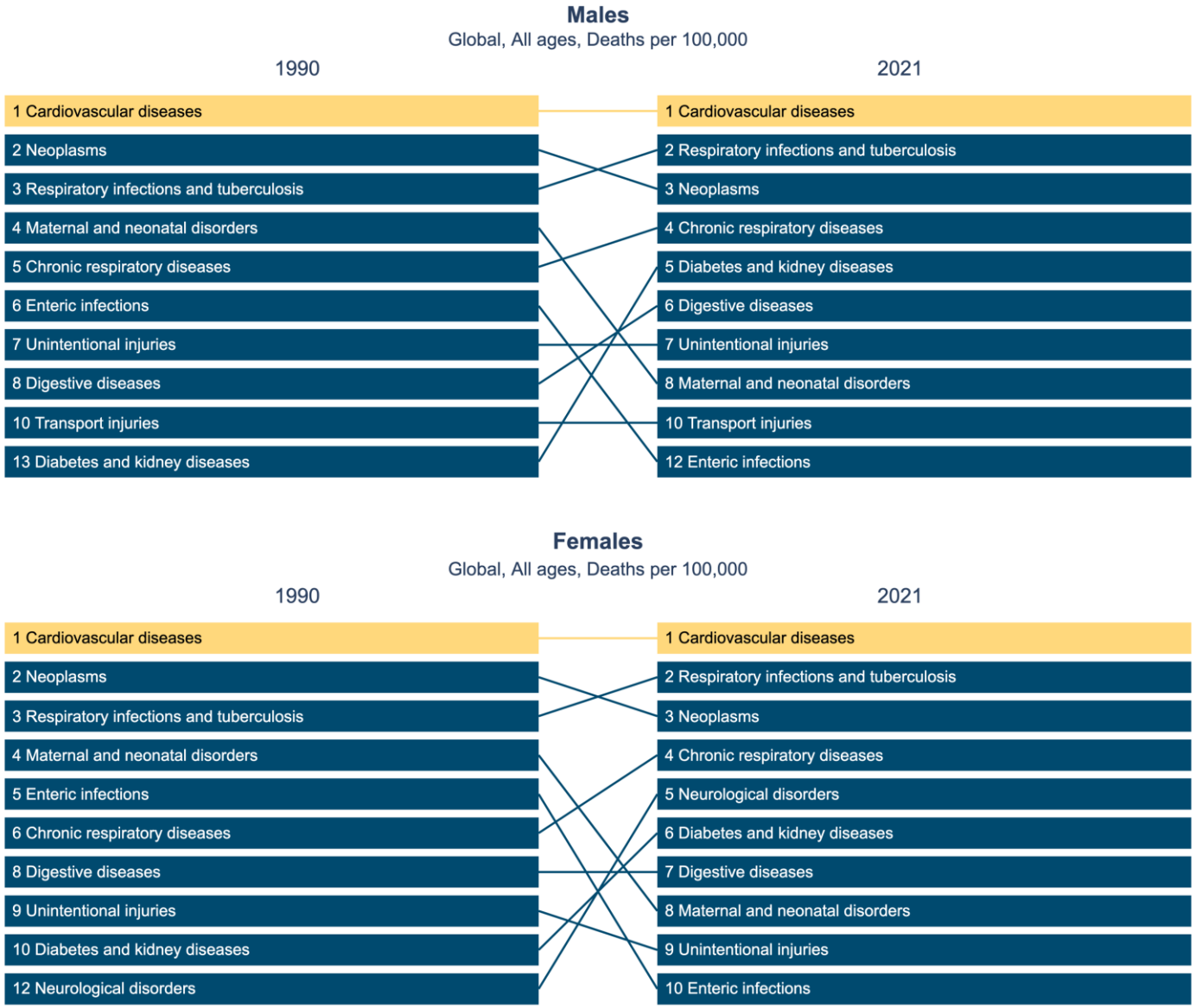

Immune system


Cancer


Pain

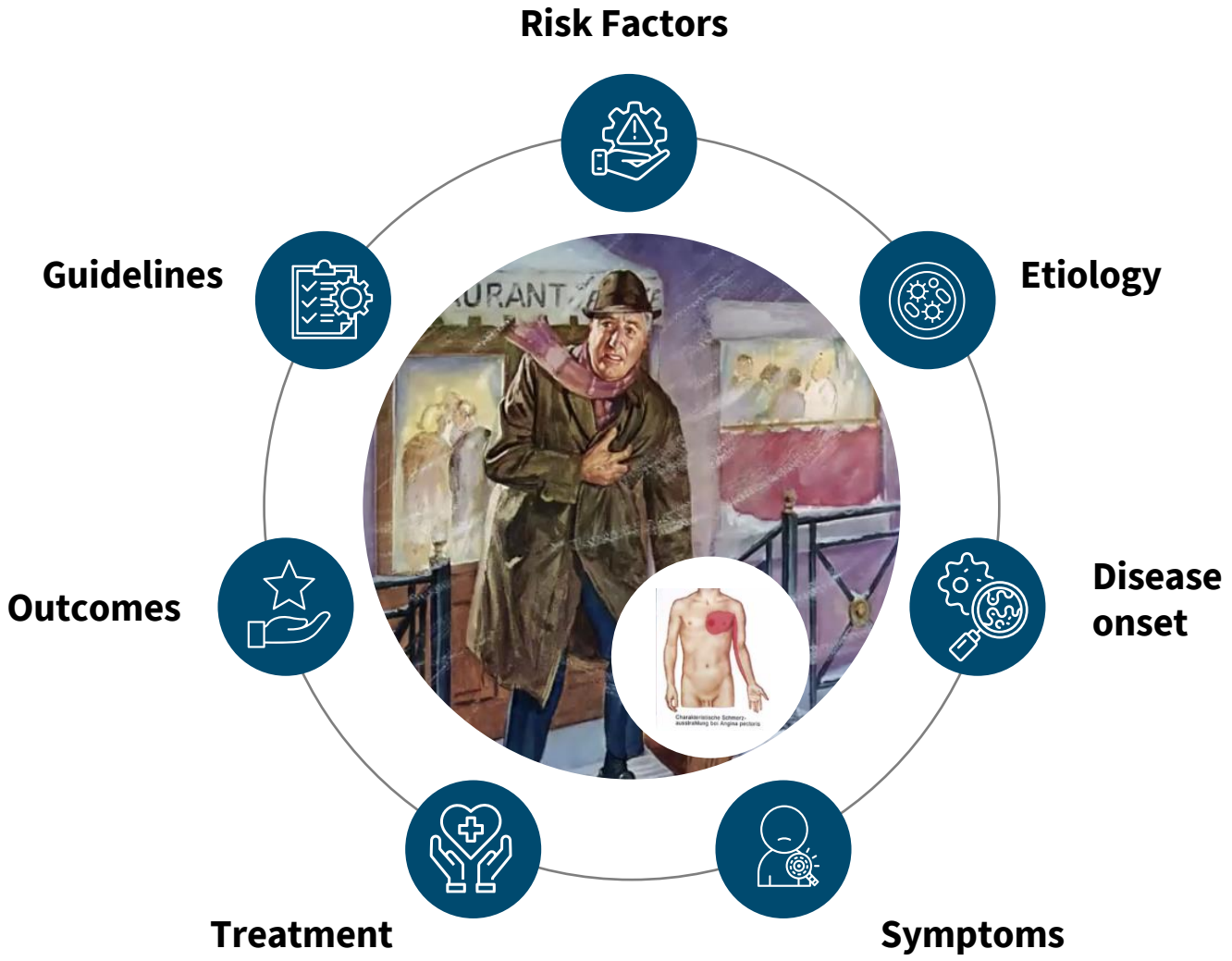

COVID

Global mortality men and women



Data Source: Institute for Health Metrics and Evaluation, GBD2021, University of Washington

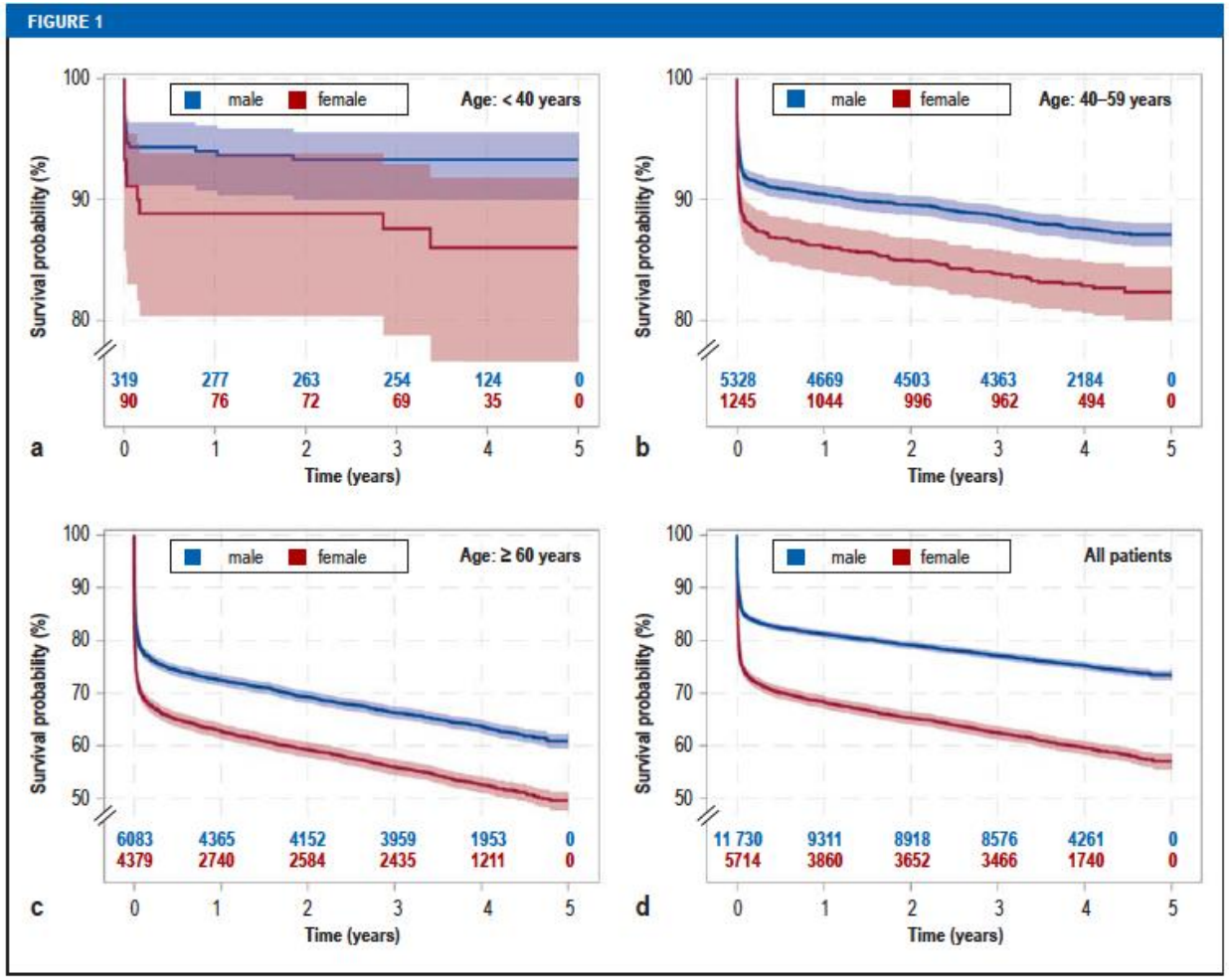
Biological AND sociocultural aspects at play



Stereotypes

Heart Attack as one better known but highly illustrative example

Survival after first STEMI



Kaplan–Meier estimates for overall survival after first STEMI, stratified by sex and age
a) Age < 40 years; b) 40–59 years; c) ≥ 60 years; d) all patients
STEMI, ST-elevation myocardial infarction

Dtsch Arztebl Int 2022; 119: 285–92. DOI: 10.3238/arztebl.m2022.0161

Differences in traditional cardiovascular risk factors

- Hypertension  **Different trajectories** **3x vs 2x**
- Diabetes  **Higher in women** **5x vs 2x**
- Lipids  **Changes in women**
- Tobacco  **Higher in women**
- Obesity  **Higher in women**
- No exercise  **Reduced fitness in women, less benefit in men**

Specific risk factors in women

Autoimmune disease

Prevalence

Inflammation

Immunity

Breast cancer therapy

Chemotherapy

Radiation

Pregnancy

Gestational HTN, DM

Preeclampsia

Eclampsia

Peripartum cardiomyopathy

Acute coronary syndrome

Stress Cardiomyopathy

Spontaneous Coronary Artery Dissection

Vasospasm

Microvascular Disease

Hormones

PCOS

Endometriosis

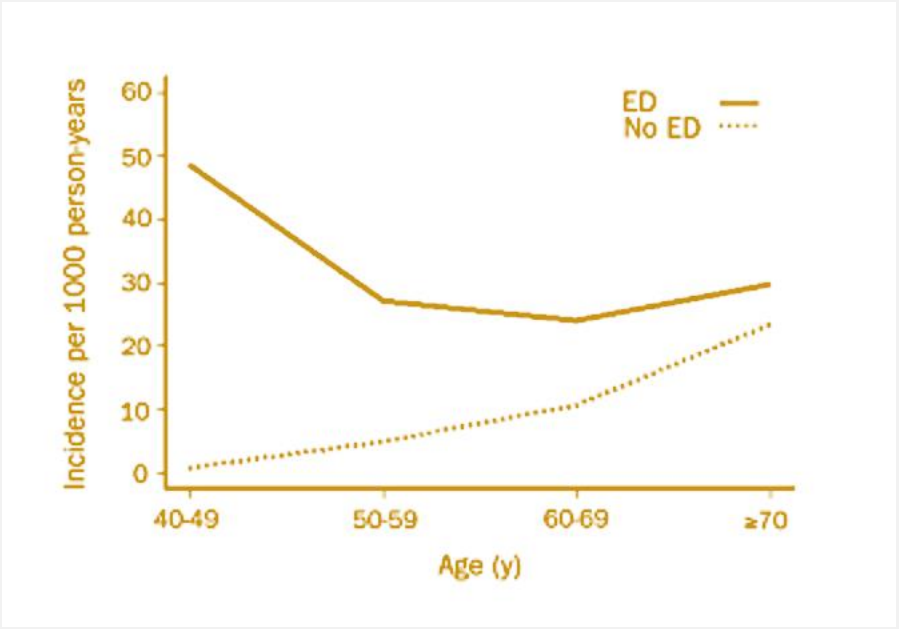
Hormone Replacement Therapy

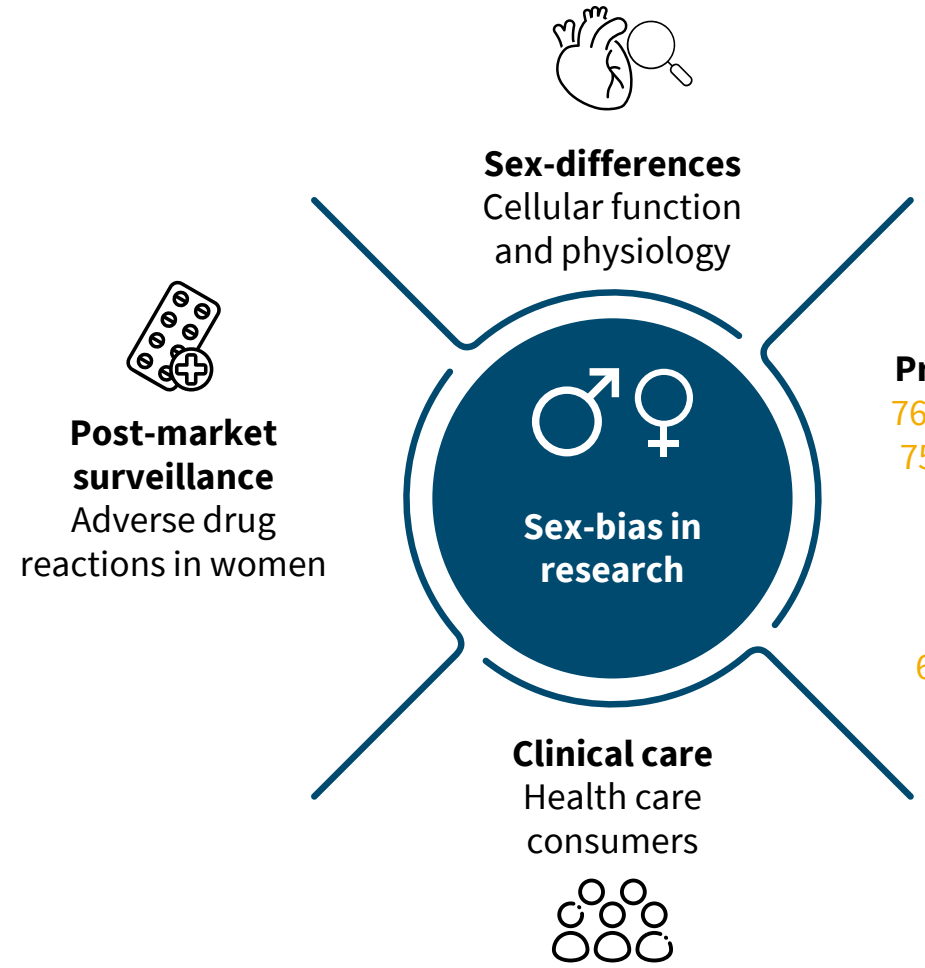
Menopausal Symptoms

Less traditional risk to consider in men

Erectile dysfunction

- Complication of CVD with common traditional risk factors and pathophysiology
- Independently predicts CVD




Sex-differences
Cellular function and physiology
Pre-clinical studies
76% male cell-based
75% animal studies
Phase I and II
67% male human studies
Clinical care
Health care consumers
Post-market surveillance
Adverse drug reactions in women
Sex-bias in research

Treatment – are recommendations personalized enough?

Absorption

Distribution

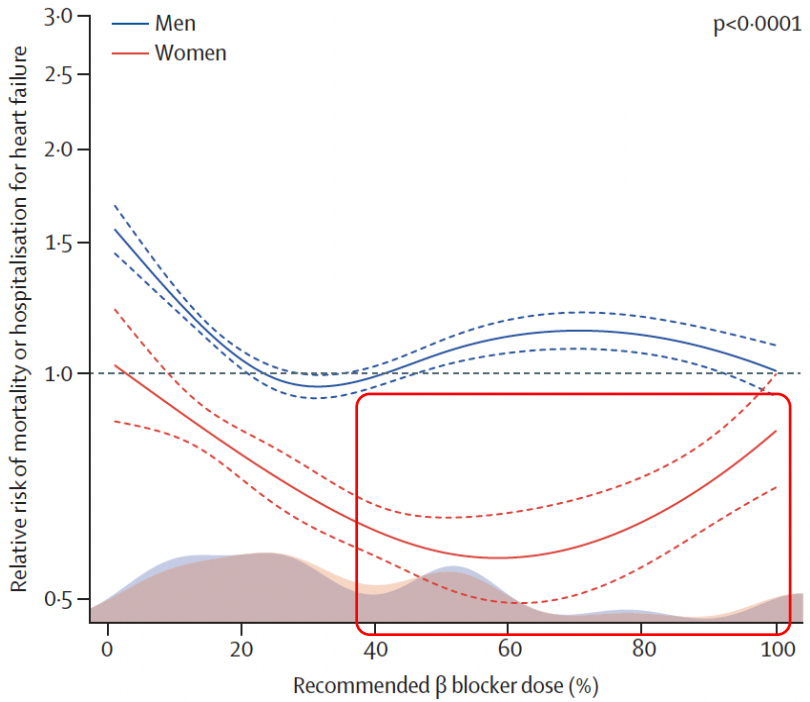
Metabolismus

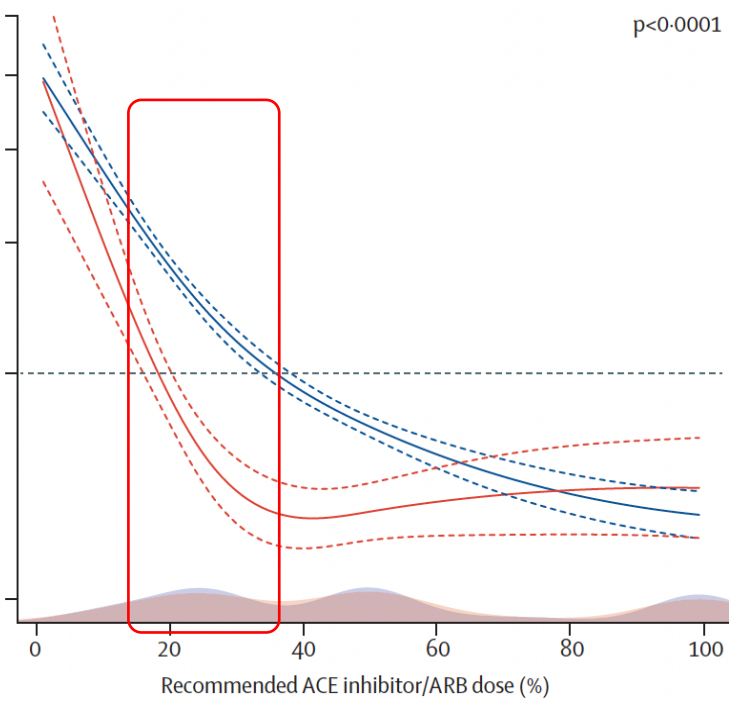
Elimination

Parameter	Physiologic Differences	Pharmacokinetic Impact
ABSORPTION		
• **Intestinal Transit Times**	>	Slower Intestinal Transit in Women
• **Transdermal Absorption**	>	↑Transdermal Absorption in Women
DISTRIBUTION		
• **Total Body Water**	> >	↑ Total Body Water in Pregnant Women & Men
• **Women Greater Adipose Tissue**	> >	↑ Adiposity in Women
• **Plasma proteins modulated by Estrogen**	> >	↑ Free Concentrations in Women (modulated by estrogen)
METABOLISM		
• **Organ Blood Flow**	> >	↓ Hepatic Blood Flow in Women
• **Cardiac Output**	> >	↑ Cardiac Output/ Rate of Distribution in Men vs Women
• **Body Fat**	> >	↑ Body Burden of Lipid Soluble Drugs in Women
ELIMINATION		
• **Renal Excretion**	> >	↑ Glomerular Filtration Rate, Tubular Secretion & Resorption in Men
• **Liver Metabolism**		↑ Renal Blood Flow in Pregnancy by 50%
	>	↓ Liver Enzyme Activity in presence of Estrogen: metabolism varies through pregnancy, menstrual cycle, use of contraceptives, after menopause in women

Treatment – are recommendations personalized enough?

- Post-hoc analyses from prospective Heart Failure medication study (11 countries, 1308 men, 402 women, LVEF <40% HFrEF
- Women had lowest risk of death or hospitalization at ½ of GDMT doses





Treatment – are recommendations personalized enough?

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 DECEMBER 26, 2019 VOL. 381 NO. 26

Efficacy and Safety of Low-Dose Colchicine after Myocardial Infarction

Table 1. Characteristics of the Patients.*

Characteristic	Colchicine (N=2366)	Placebo (N=2379)
Age — yr	60.6±10.7	60.5±10.6
Female sex — no. (%)	472 (19.9)	437 (18.4)

Table S3. Primary Efficacy Composite Endpoint in Prespecified Subgroups†.

Subgroup	Colchicine	Placebo	Hazard ratio (95% CI)
	no. of patients with event/total no. of patients (%)		
Sex‡			
Male	94/1894 (5.0%)	135/1942 (7.0%)	0.70 (0.54; 0.91)
Female	37/472 (7.8%)	35/437 (8.0%)	0.99 (0.63; 1.58)

Although the inclusion of 4745 patients was sufficient for the trial to show a significant benefit with regard to the primary composite efficacy end point, a larger trial could have allowed a better assessment of individual end points and subgroups

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 FEBRUARY 13, 2025 VOL. 392 NO. 7

Colchicine in Acute Myocardial Infarction

Table 1. Demographic and Clinical Characteristics at Baseline.*

Characteristic	Colchicine (N=3528)	Placebo (N=3534)
Demographic characteristics		
Mean age — yr	60.6±10.3	60.7±10.3
Age >75 yr — no. (%)	301 (8.5)	270 (7.6)
Female sex — no. (%)	725 (20.5)	713 (20.2)

Figure 2. Forest Plot of the Primary Outcome According to Prespecified Subgroups.

Subgroup	Colchicine	Placebo	Hazard Ratio for Death from Cardiovascular Causes, Myocardial Infarction, Stroke, or Revascularization (95% CI)
	no. of events/total no. of patients (%)		
Sex			
Female	72/725 (9.9)	64/713 (9.0)	1.12 (0.80–1.57)
Male	250/2803 (8.9)	263/2821 (9.3)	0.95 (0.80–1.13)

Our trial has limitations. Women and members of diverse racial and ethnic groups were underrepresented in the trial relative to the incidence of cardiovascular disease in these groups

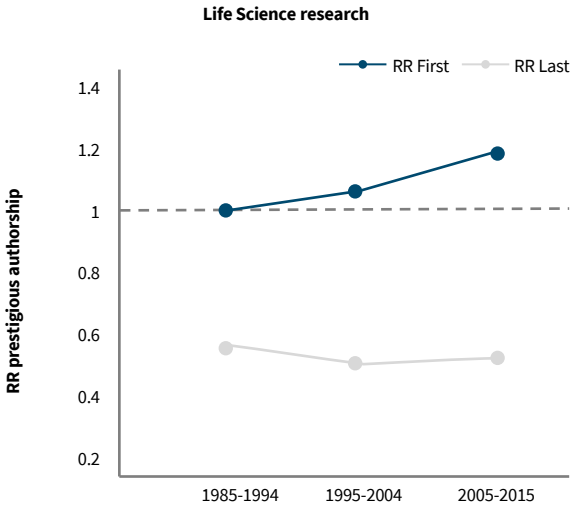
Treatment – Are recommendations personalized enough?

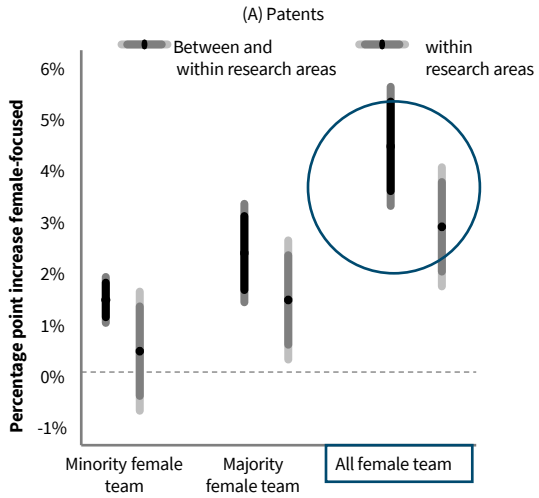
Medical Therapy for HFrEF	Name	Trial (% Women, Number Women)	
Beta blockers	Carvedilol	COPERNICUS[22] (20%, 469)	19-23% women
		US Carvedilol Study[21] (23%, 256)	
	Metoprolol succinate	MERIT-HF[24] (23%, 898)	
	Bisoprolol	CIBIS II[23] (19%, 515)	
ACEI	Captopril, enalapril, ramipril, trandolapril, zofenopril	Meta-analysis[17] (19%, 2373)	19-23% women
	Captopril, enalapril, lisinopril, quinapril, ramipril	Meta-analysis[16] (23%, 1587)	
ARB	Valsartan	Val-HeFT[19] (20%, 1003)	20-31% women
	Losartan	ELITE II[42] (31%, 966)	
	Candesartan	CHARM—low EF[18] (26%, 1188)	
Aldosterone antagonist or MRA	Eplerenone	EPHESUS[27] (29%, 1918)	22-29% women
		EMPHASIS-HF[26] (22%, 610)	
	Spironolactone	RALES[25] (27%, 446)	

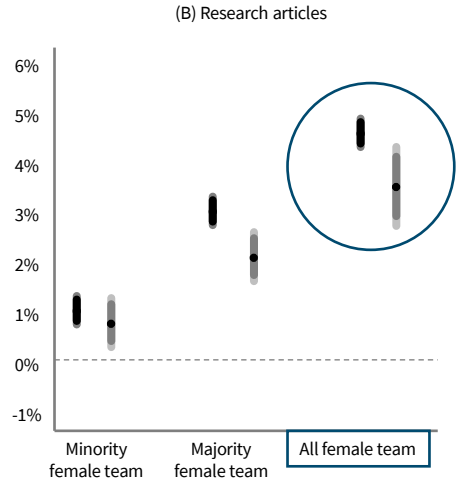
Health Equity Requires a Diverse Workforce - Research

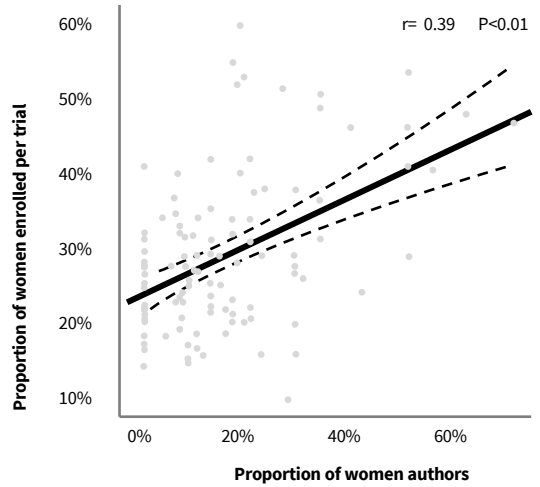
Women are underrepresented in life science research…

… to the disadvantage of women's health

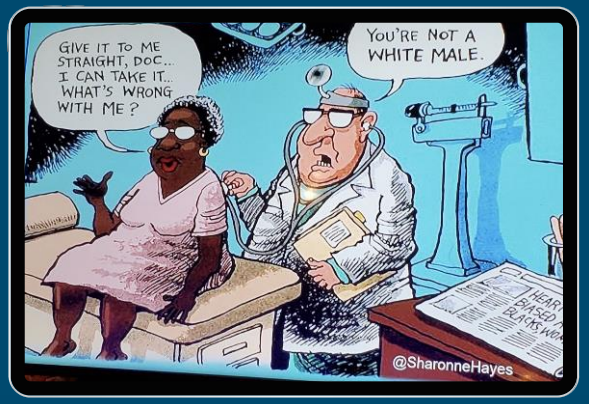


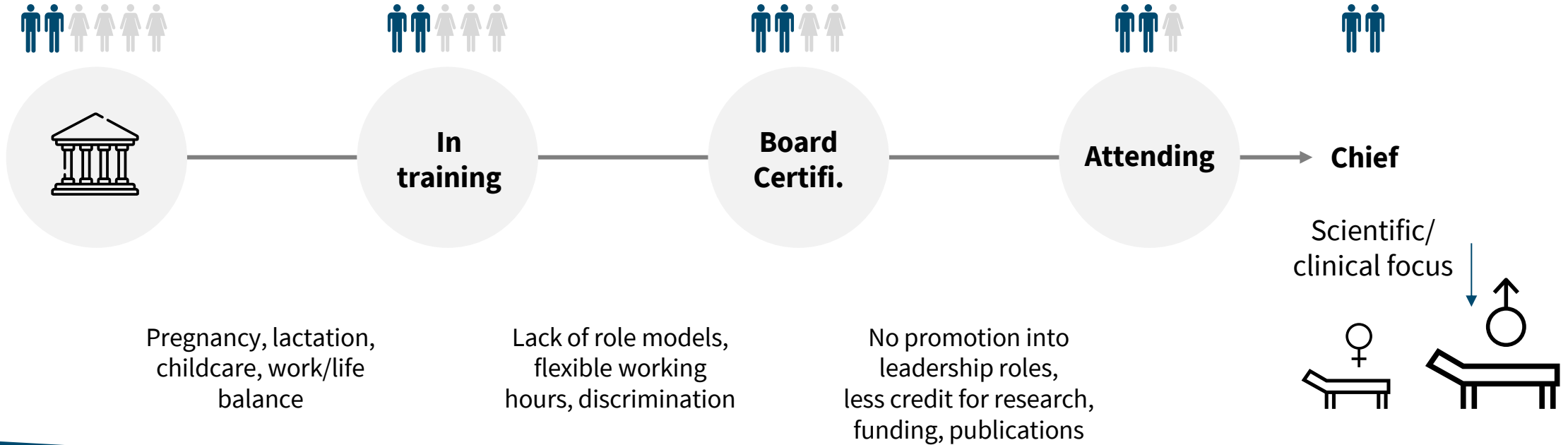




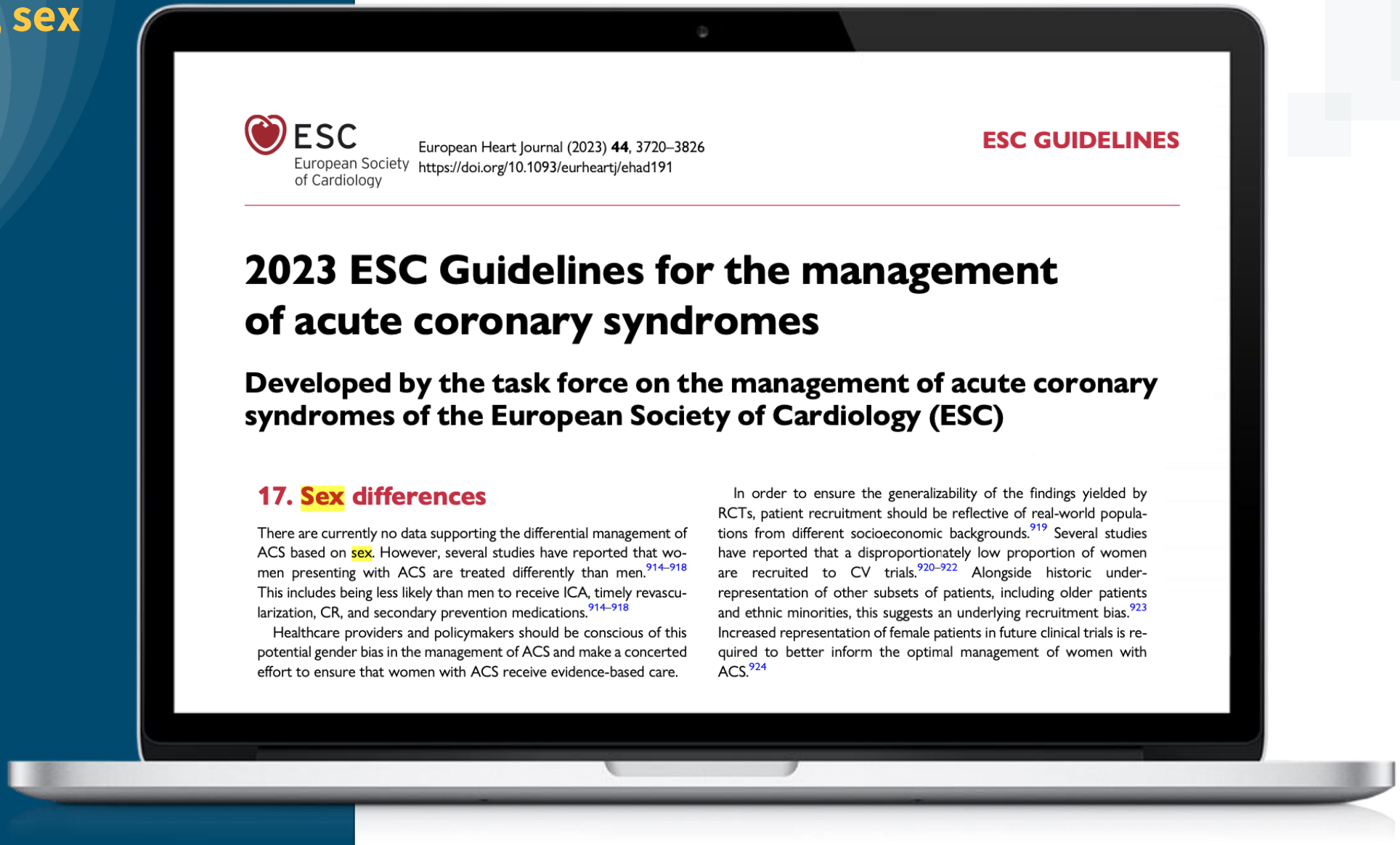


Health Equity Needs a Diverse Workforce - Hospitals





Guidelines – Search terms
women, gender, sex



ESC European Society of Cardiology
European Heart Journal (2023) **44**, 3720–3826
https://doi.org/10.1093/eurheartj/ehad191

ESC GUIDELINES

2023 ESC Guidelines for the management of acute coronary syndromes

Developed by the task force on the management of acute coronary syndromes of the European Society of Cardiology (ESC)

17. Sex differences

There are currently no data supporting the differential management of ACS based on sex. However, several studies have reported that women presenting with ACS are treated differently than men.[914–918] This includes being less likely than men to receive ICA, timely revascularization, CR, and secondary prevention medications.[914–918]

Healthcare providers and policymakers should be conscious of this potential gender bias in the management of ACS and make a concerted effort to ensure that women with ACS receive evidence-based care.

In order to ensure the generalizability of the findings yielded by RCTs, patient recruitment should be reflective of real-world populations from different socioeconomic backgrounds.[919] Several studies have reported that a disproportionately low proportion of women are recruited to CV trials.[920–922] Alongside historic underrepresentation of other subsets of patients, including older patients and ethnic minorities, this suggests an underlying recruitment bias.[923] Increased representation of female patients in future clinical trials is required to better inform the optimal management of women with ACS.[924]

Gender Data Gap

Data Gap becomes Health Gap

Science
Male body as prototype hinders sex- and gender-specific knowledge creation

Increased adverse events with drug treatment in women

Burden
Gender differences are insufficiently considered when evaluating disease burden

Menopause not separately listed in Global Burden of Disease Database

Care delivery
Gender differences in access to and availability of optimal health care

Gender-dependent health insurance payments

Investment
Investments in health and disease not relative to prevalence

5-6x more publications on erectile dysfunction than premenstrual syndrome

Gender Health Gap

Women live longer, but spend 25% more time in debilitating health

Improving women's health could, for example, enable women to participate in the workforce more actively

There is a potential to boost the economy by $1 Trillion annually

International Perspective

Administration Priorities

MARCH 18, 2024

Executive Order on Advancing Women's Health Research and Innovation

The Economist

MAY 29TH 2024

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How medicine is (still) failing women

National development of the field

Government

Wissenschaftliche Grundlagen
zur gesundheitlichen Chancengleichheit

Wie können die gesundheitlichen Bedürfnisse von Frauen besser berücksichtigt werden?

Das Geschlecht hat einen wichtigen Einfluss auf die Gesundheit und die Gesundheitsversorgung. Je nach Geschlecht sind wir verschieden von Krankheiten betroffen, zeigen ein anderes Gesundheitsverhalten und werden im Gesundheitswesen unterschiedlich wahrgenommen und behandelt. Dies führt zu Ungleichheiten. Ein Bericht des Bundesrates zeigt: Die gesundheitlichen Bedürfnisse von Frauen werden zu wenig berücksichtigt. Massnahmen in verschiedenen Bereichen sind notwendig, um eine optimale Gesundheit für alle und einen gerechten Zugang zur Versorgung zu gewährleisten.

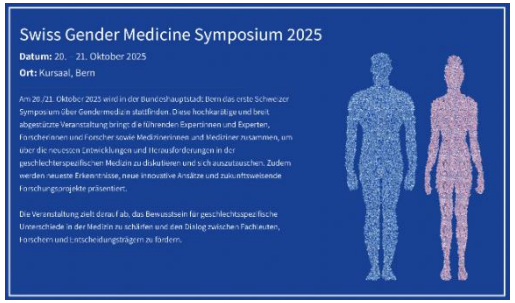
19 projects to foster multidisciplinary research in gender medicine and health (NRP 83)

National

gems Gender Education in Medicine for Switzerland

Gender and Medicine

A network of Swiss universities



Institutional

Universität Zürich[UZH]

30.01.2023 | Schweizer Premiere

Erster Lehrstuhl für Gendermedizin

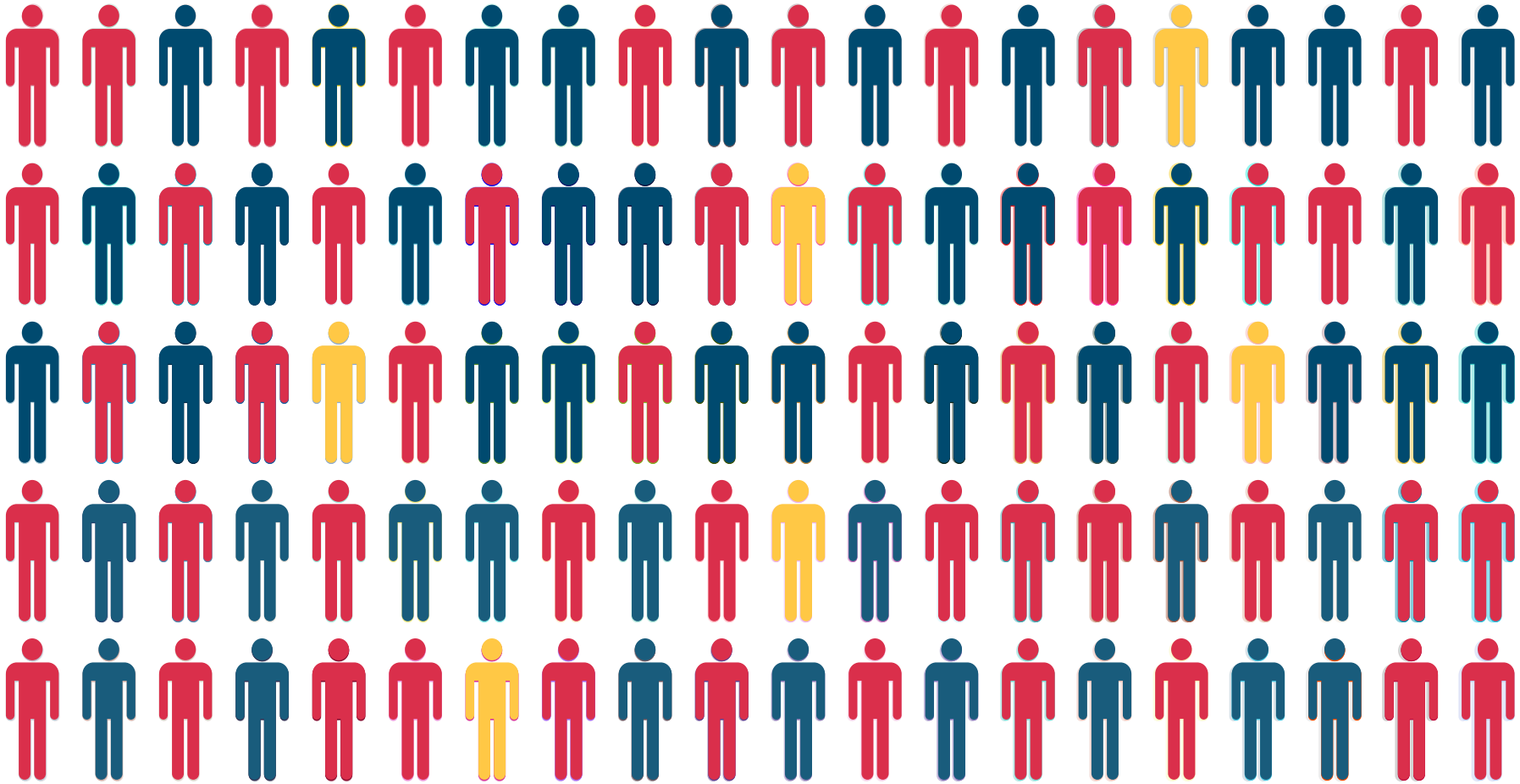
Die UZH fördert die Gendermedizin mit einem neuen Lehrstuhl. Die Berufungsverhandlungen laufen, der Lehrstuhl soll bis spätestens Anfang 2024 besetzt werden. Warum Gendermedizin wichtig ist, und wie die UZH sie auch in der Lehre verankern will, war Thema einer Informationsveranstaltung im Uniturm

USZ Universitäts Spital Zürich

Gendermedizin in der Kardiologie

Herz-Kreislauferkrankungen sind sehr häufig, allerdings gibt es teilweise bedeutende geschlechterspezifische Unterschiede hinsichtlich Diagnose, Pathophysiologie, Therapie, Krankheitsverlauf, Risikofaktoren etc. Dies erfordert eine entsprechende individuelle Betreuung, für die eine geschlechtersensible Betrachtungsweise förderlich ist.

Gender Medicine -> Personalized Medicine



Chair for Gender Medicine University of Zurich

Improved, equitable health care

Personalized Clinical Care

Targeted research efforts and identification of relevant knowledge gaps

Translation, Teaching, Policy

> Of all the forms of inequality, injustice in health care is the most shocking and inhumane
>
> – Dr. Martin Luther King jr.

Thank you!