

The concerted effort to include sex and gender in (bio)medical research

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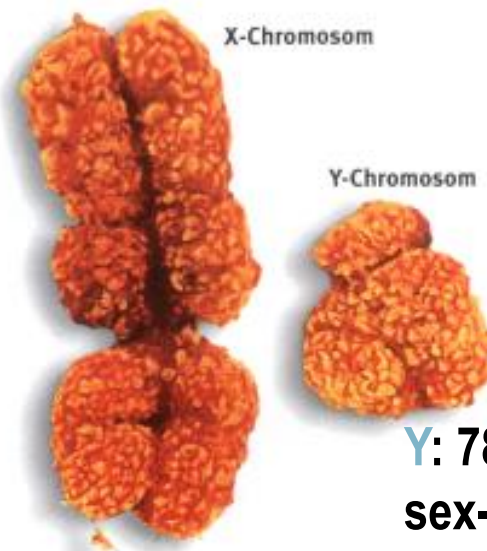
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Agenda

- What are sex and gender differences and how do they interact with health
- How a focus on sex and gender can change our research practice
- A concerted effort

Terminology: Sex and Gender

Sex – biological factors,
genes und hormones

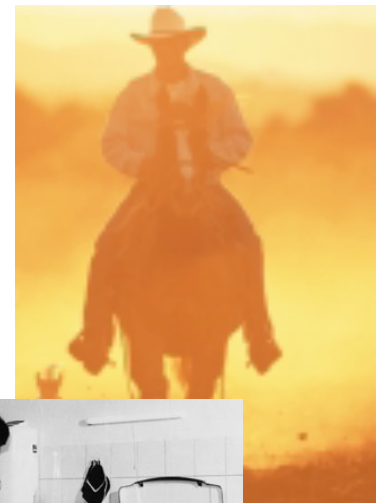


Y: 78 genes,
sex-specific

X: 1669 genes
heart, brain, immune function

Sex hormones

Gender – sociocultural aspects, gender
roles and stereotypes, subjective gender
perception

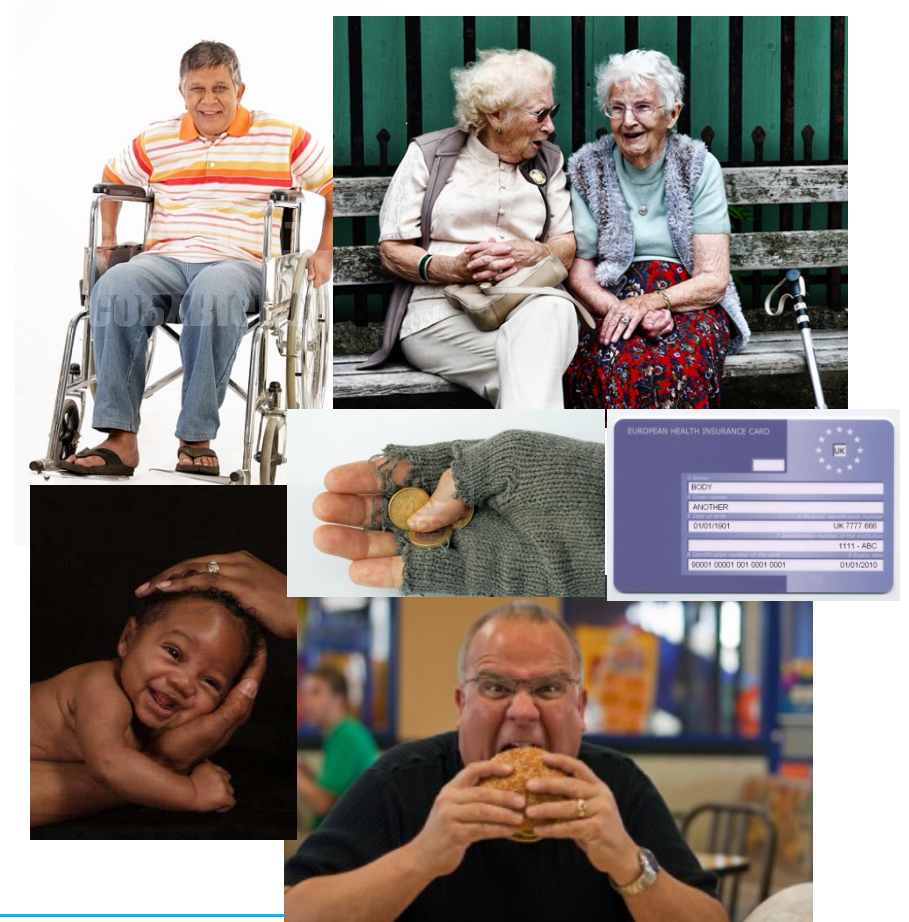


Personalization of medicine

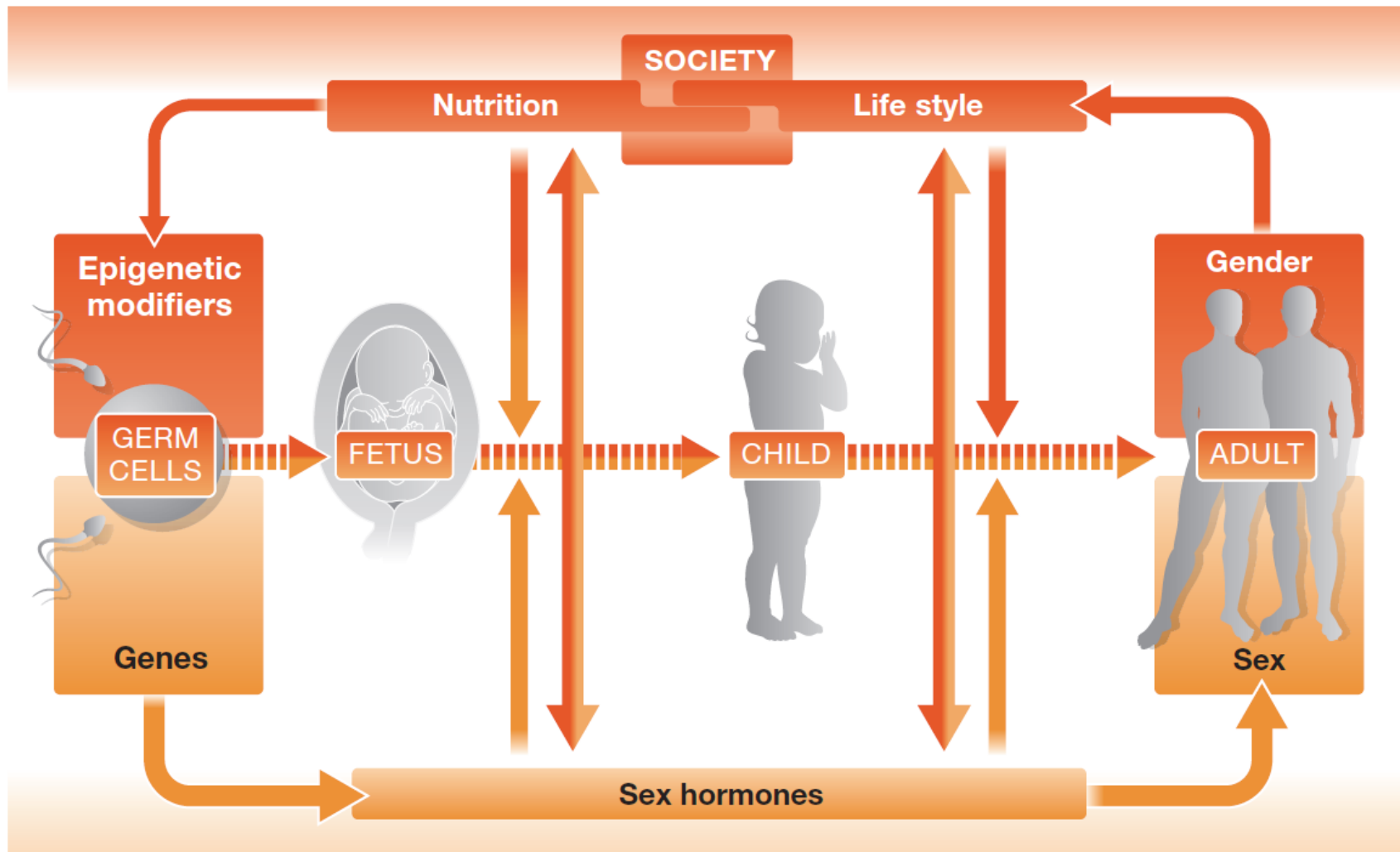
Biological personalization

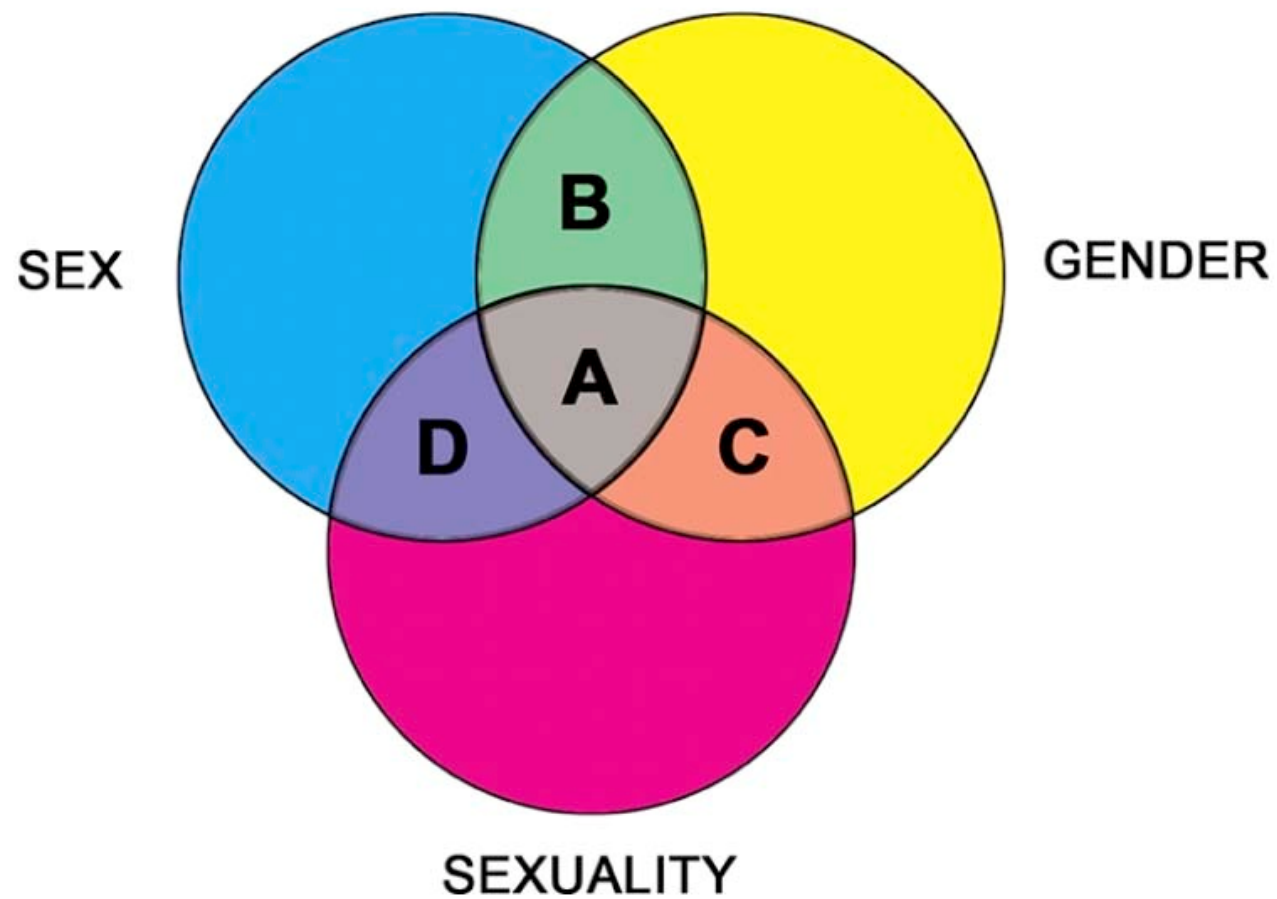


Social personalization

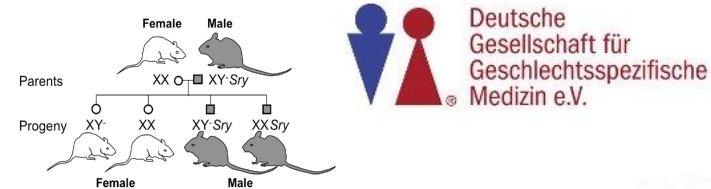


Interaction of sex and gender





Where are we coming from? A very brief history of sex and gender-sensitive medicine



Deutsche Gesellschaft für Geschlechtsspezifische Medizin e.V.



NIH Revitalization Act



1993

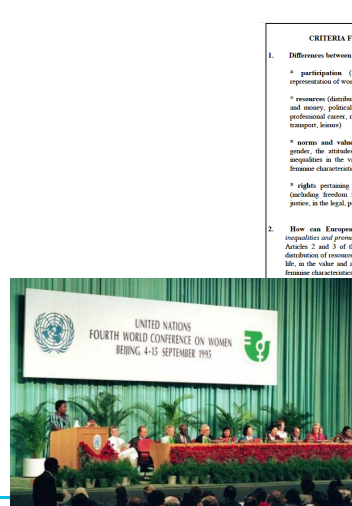
'90

2002/2003

2007

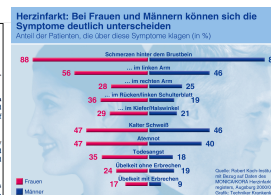
2008

2009



CRITERIA FOR GENDER IMPACT ASSESSMENT:

- Differences between women and men in the policy field, such as:
 - * participation (sex-composition of the target/population group(s), representation of women and men in decision-making positions)
 - * resources (distribution of critical resources such as time, space, information and money, political and economic power, education and training, job and professional career, new technologies, health care services, housing, means of transport, leisure)
 - * access and values which influence gender roles, division of labour by gender, the attitudes and behaviour of women and men respectively, and inequalities in the value attached to men and women or to masculine and feminine characteristics
 - * rights pertaining to direct or indirect sex-discrimination, human rights (including freedom from sexual violence and degradation), and access to justice, in the legal, political or socio-economic environment
- How can European policies contribute to the elimination of existing inequalities and promote equality between women and men (in compliance with Articles 2 and 3 of the Treaty of Amsterdam), in particular cases, as the distribution of resources, benefits, risks and responsibilities in private and public life, in the value and situation accorded to male and female, to masculine and feminine characteristics, behaviour and priorities?



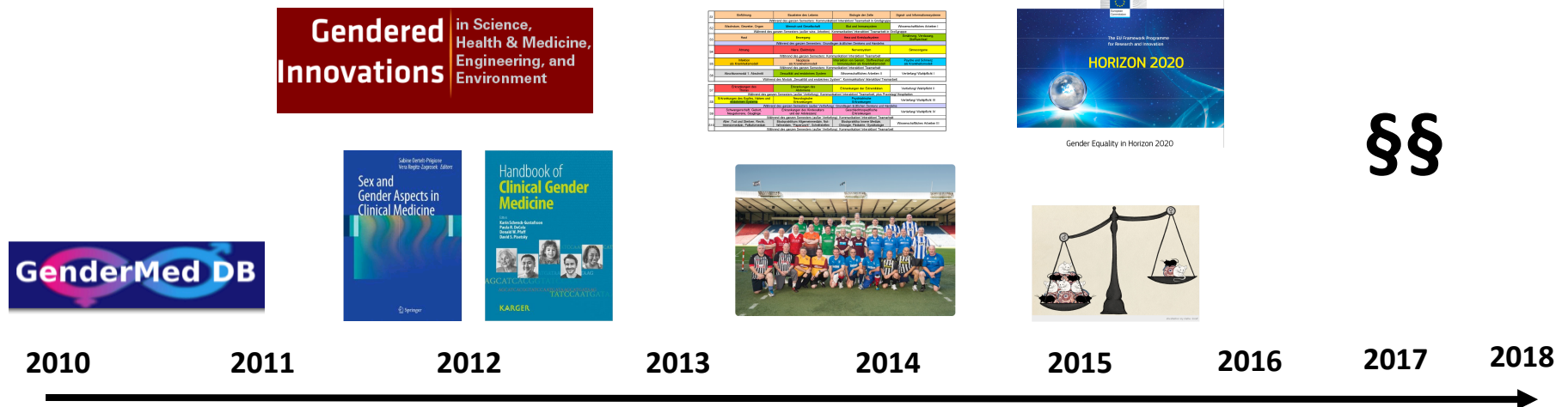
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Gender Inequality Index and related indicators

INDICATOR DATA										
1990-2000	Year	Country	Gender Inequality Index (GII)	Gender Development Index (GDI)	Gender Parity Index (GPI)	Population with access to basic services (in %)		Gender inequality in basic services (in %)		Total fertility rate (TFR)
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Radboudumc



Sex differences

- Genetics
- Hormones
- Epigenetics
- -> metabolism
- -> pharmacokinetics (drug toxicity)
- -> inflammation

Gender differences

- Gender roles
- Gender identity
- Gender relations
- Institutionalized gender

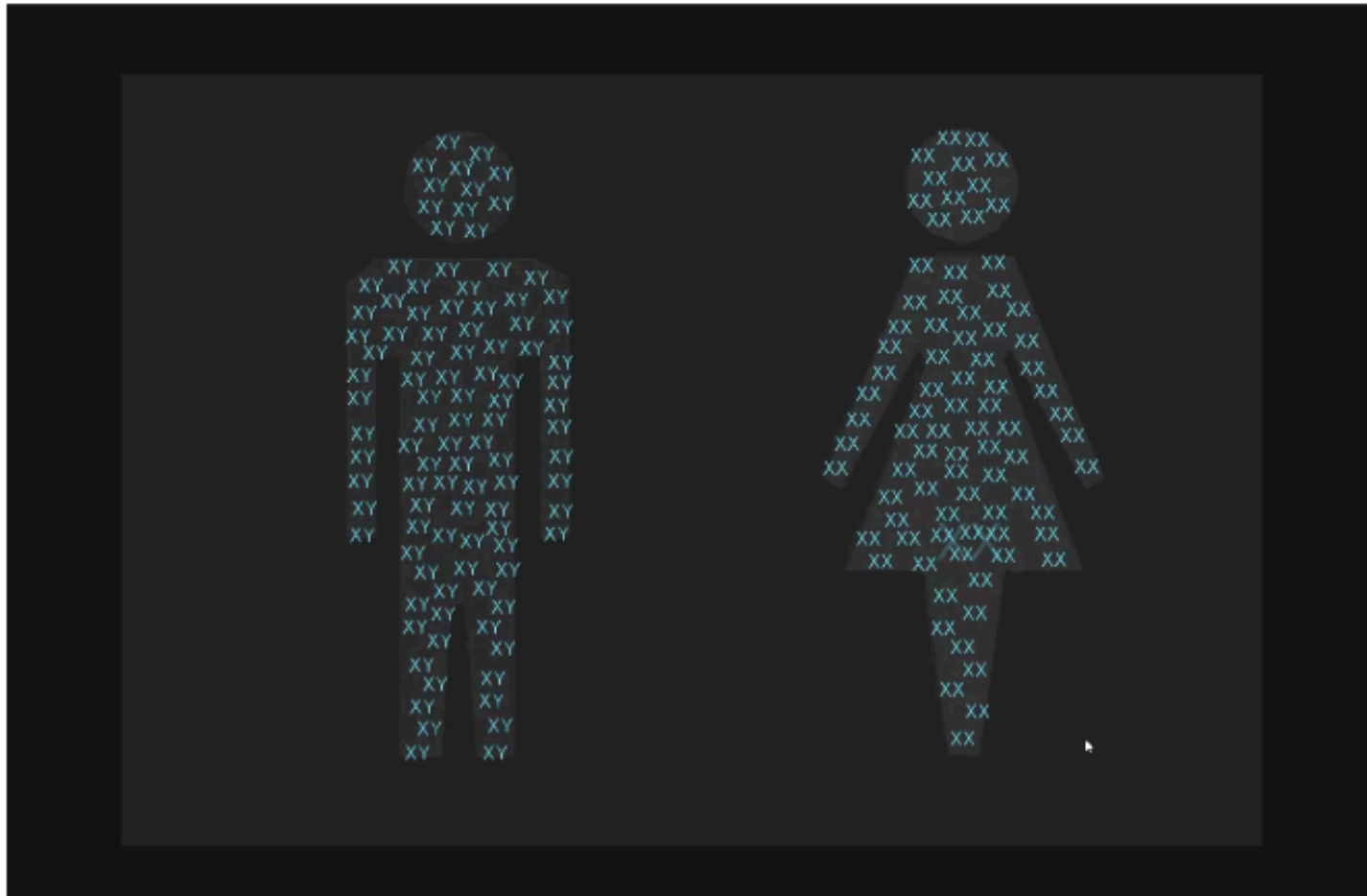
- -> disease perception

- -> access to healthcare

- -> therapeutic choices

- -> medical communication

Every cell has a sex



Hormones

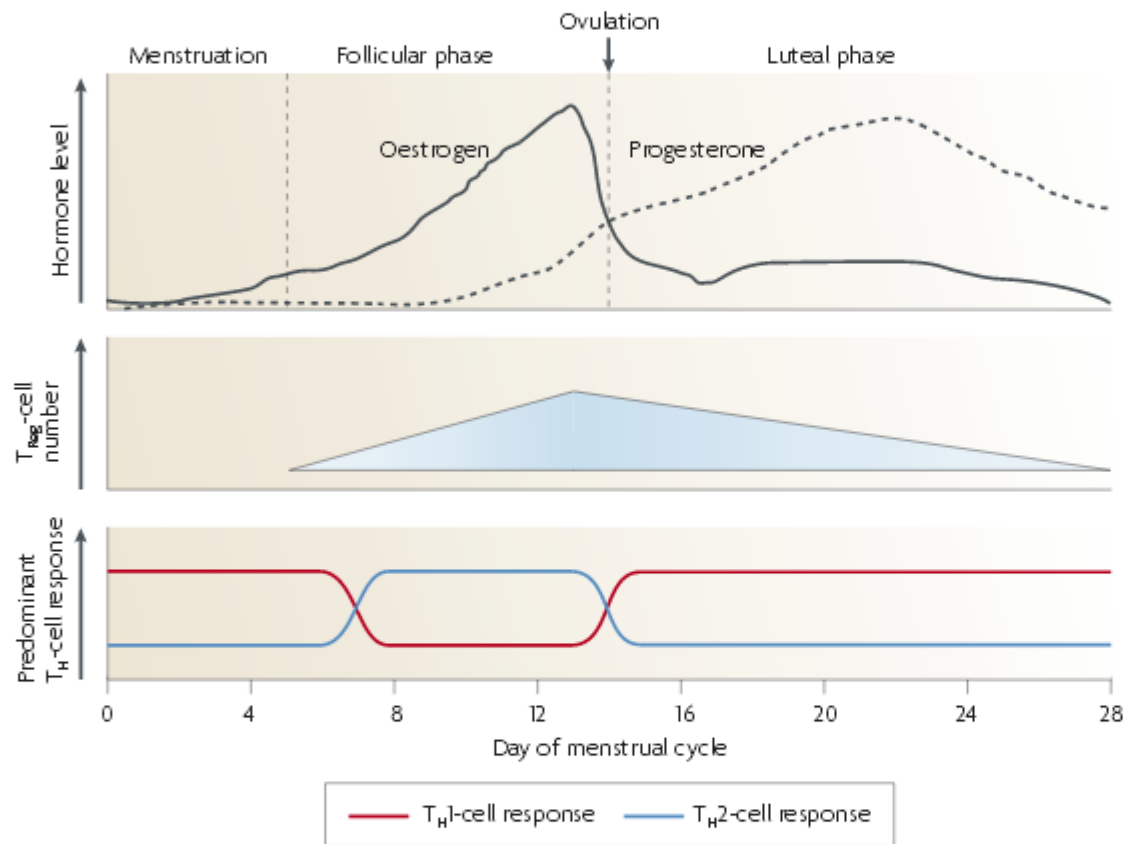
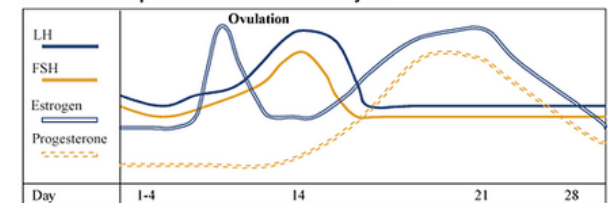


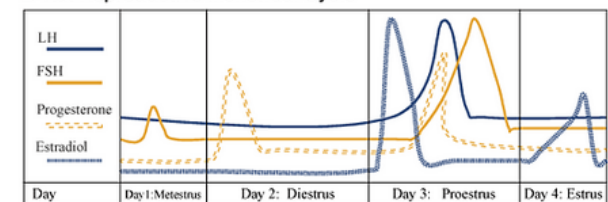
Figure 3 | Oestrogen and progesterone effects on T-cell responses during the menstrual cycle. Variations in oestrogen and progesterone levels during the different phases of the menstrual cycle influence T helper 1 (T_H1)-, T_H2 - and T regulatory (T_{Reg})-cell populations. The upper panel illustrates fluctuations in the levels of oestrogen and progesterone during the different phases of the 28-day menstrual cycle. In the middle and lower panels, the corresponding changes in the size of the T_{Reg} -cell population and the T_H -cell bias, respectively, are shown.



A Human Reproductive Menstrual Cycle

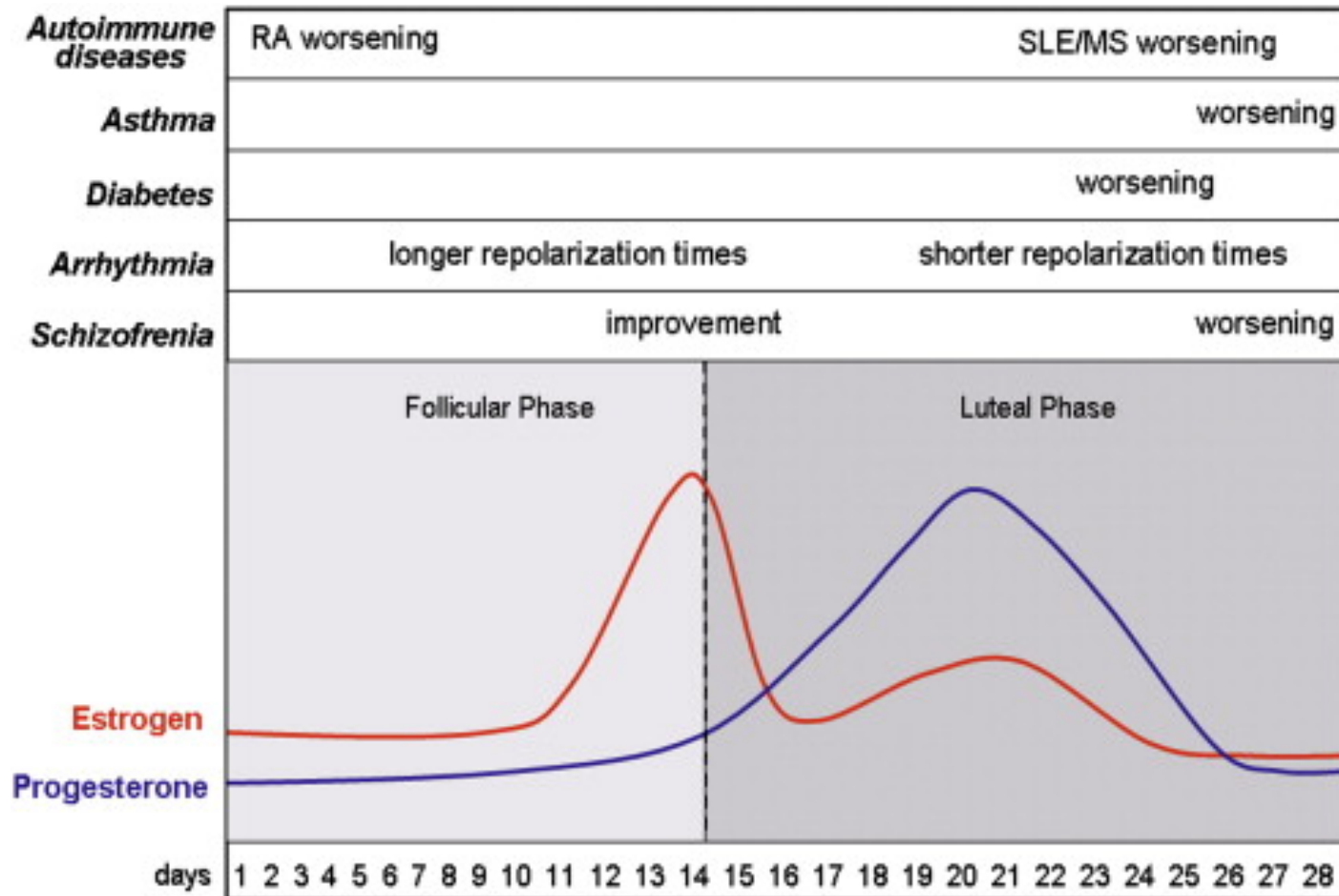


B Rat Reproductive Menstrual Cycle



Fish EN, Nature Rev Immunology, 2008
Emanuele MA, Wezeman F, Emanuele NV,
NIAAA Publications, 2003

Hormonal changes and disease



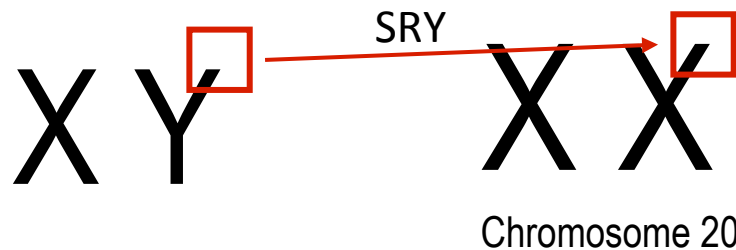
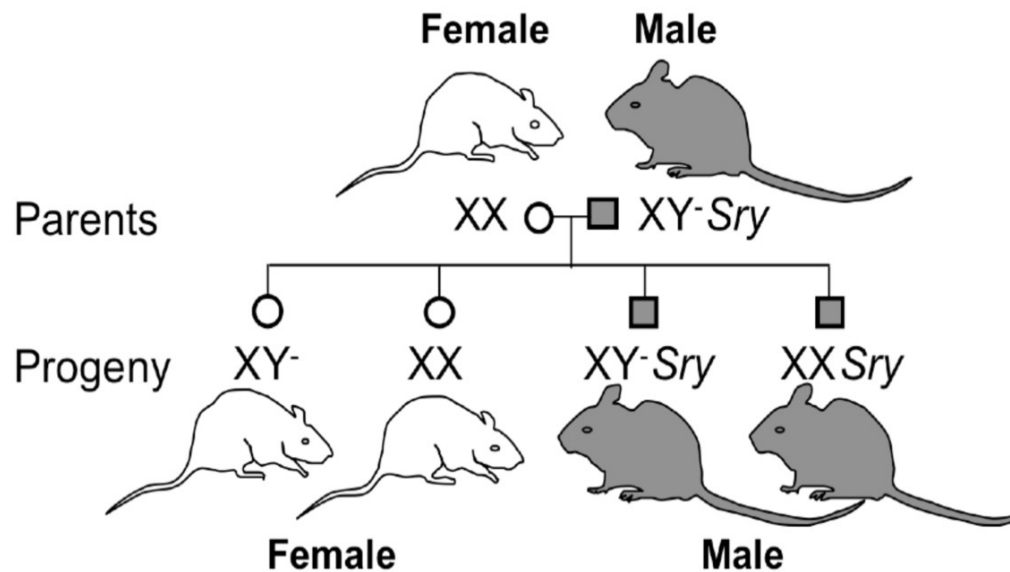
Pharmacokinetics and drug toxicity

TABLE 1. PRESCRIPTION DRUGS WITHDRAWN FROM UNITED STATES MARKET, JANUARY 1, 1997–DECEMBER 31, 2000

<i>Drug</i>	<i>Type of drug</i>	<i>Date approved</i>	<i>Date withdrawn</i>	<i>Primary health risk</i>
Pondimin (fenfluramine hydrochloride)	Appetite suppressant	6/14/1973	9/15/1997	Valvular heart disease
Redux (dexfenfluramine hydrochloride)	Appetite suppressant	4/29/1996	9/15/1997	Valvular heart disease
Seldane (terfenadine)	Antihistamine	5/8/1985	2/27/1998	Torsades de pointes
Posicor (mibefradil dihydrochloride)	Cardiovascular	6/20/1997	6/8/1998	Bradycardia in elderly and adverse drug interaction
Hismanal (astemizole)	Antihistamine	12/19/1988	6/18/1999	Torsades de pointes
Rezulin (troglitazone)	Diabetic	1/29/1997	3/21/2000	Liver failure
Propulsid (cisapride monohydrate)	Gastrointestinal	7/29/1993	7/14/2000	Torsades de pointes
Lotronex (alosetron hydrochloride)	Gastrointestinal	2/9/2000	11/28/2000	Ischemic colitis
Raxar (grepafloxacin hydrochloride)	Antibiotic	11/6/1997	11/1/1999	Torsades de pointes
Durac (bromfenac sodium)	Analgesic and anesthetic	7/15/1997	6/22/1998	Liver failure

The need for new considerations in our research practice...

The separation of genes and hormones



Four Core Genotypes

	XX	XY-Sry		
	●	■		
	●	●	■	■
genotype	XX	XY-	XXSry	XY-Sry
abbreviation	XXF	XYF	XXM	XYM
gonads	ovaries	ovaries	testes	testes
Y chrom	-	+	-	+
X chrom	two	one	two	one
X imprint	M+P	M	M+P	M

2 x 2 Comparisons

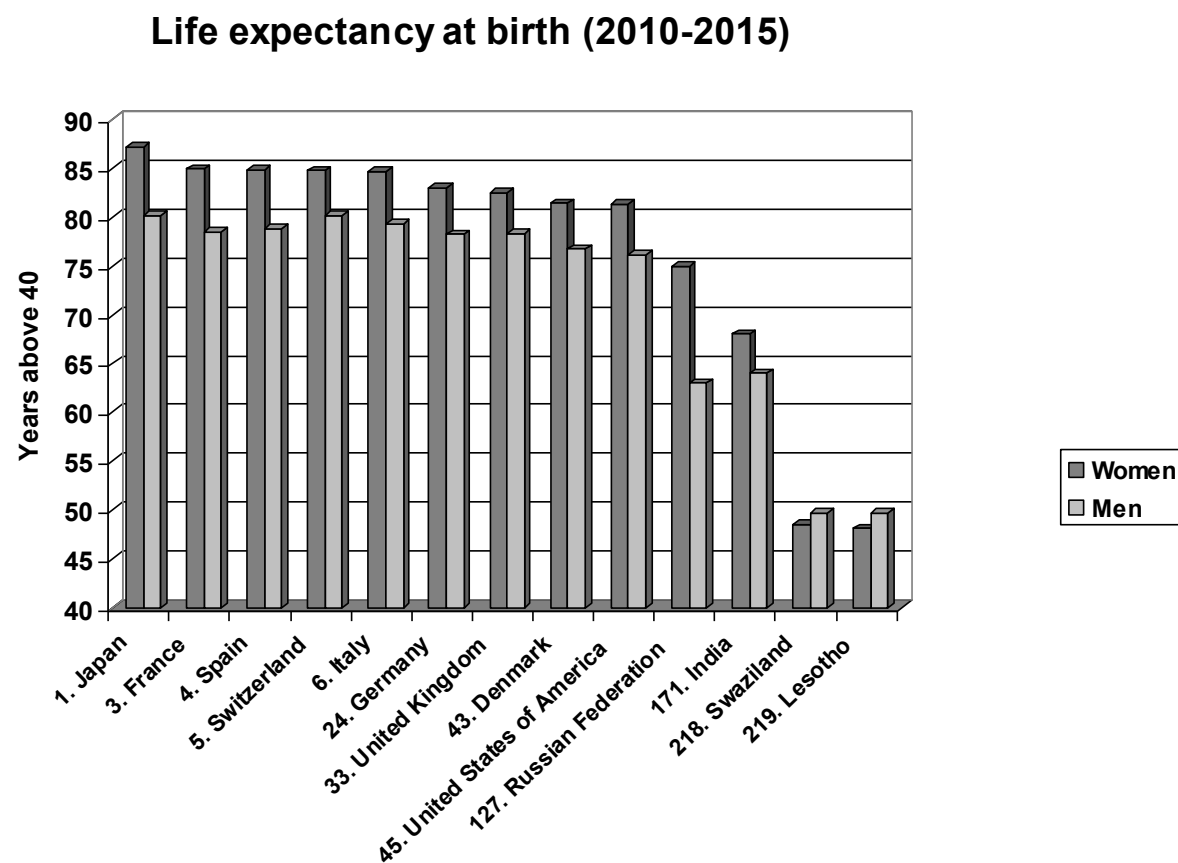
sex chromosome effect

XXF XYF

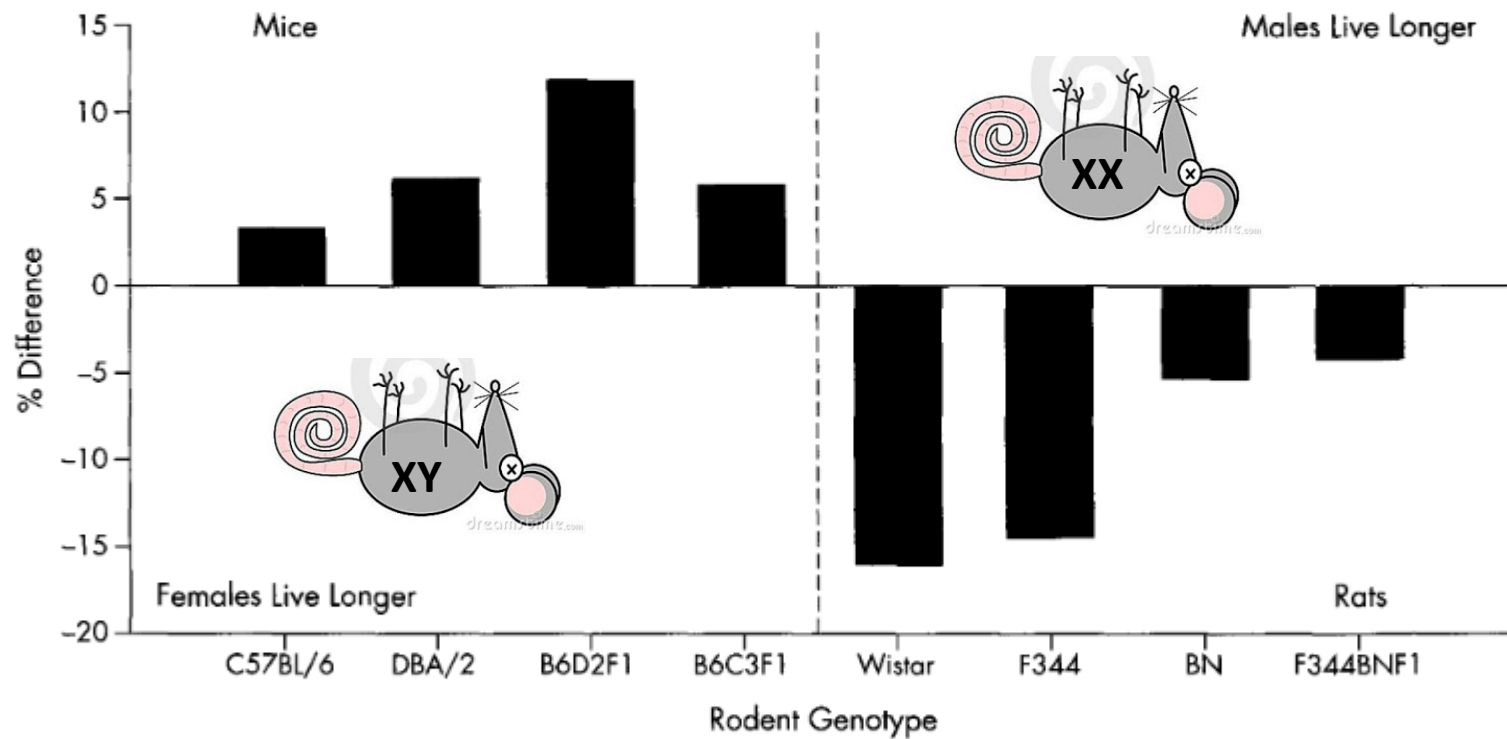
XXM XYM

sex effect

Human life expectancy



Mouse life expectancy



Impact of the examiner's sex on lab animal behavior

We found that exposure of mice and rats to male but not female experimenters produces pain inhibition. Male-related stimuli induced a robust physiological stress response that results in stress-induced analgesia. This effect could be replicated with T-shirts worn by men, bedding material from gonadally intact and unfamiliar male mammals, and presentation of compounds secreted from the human axilla.

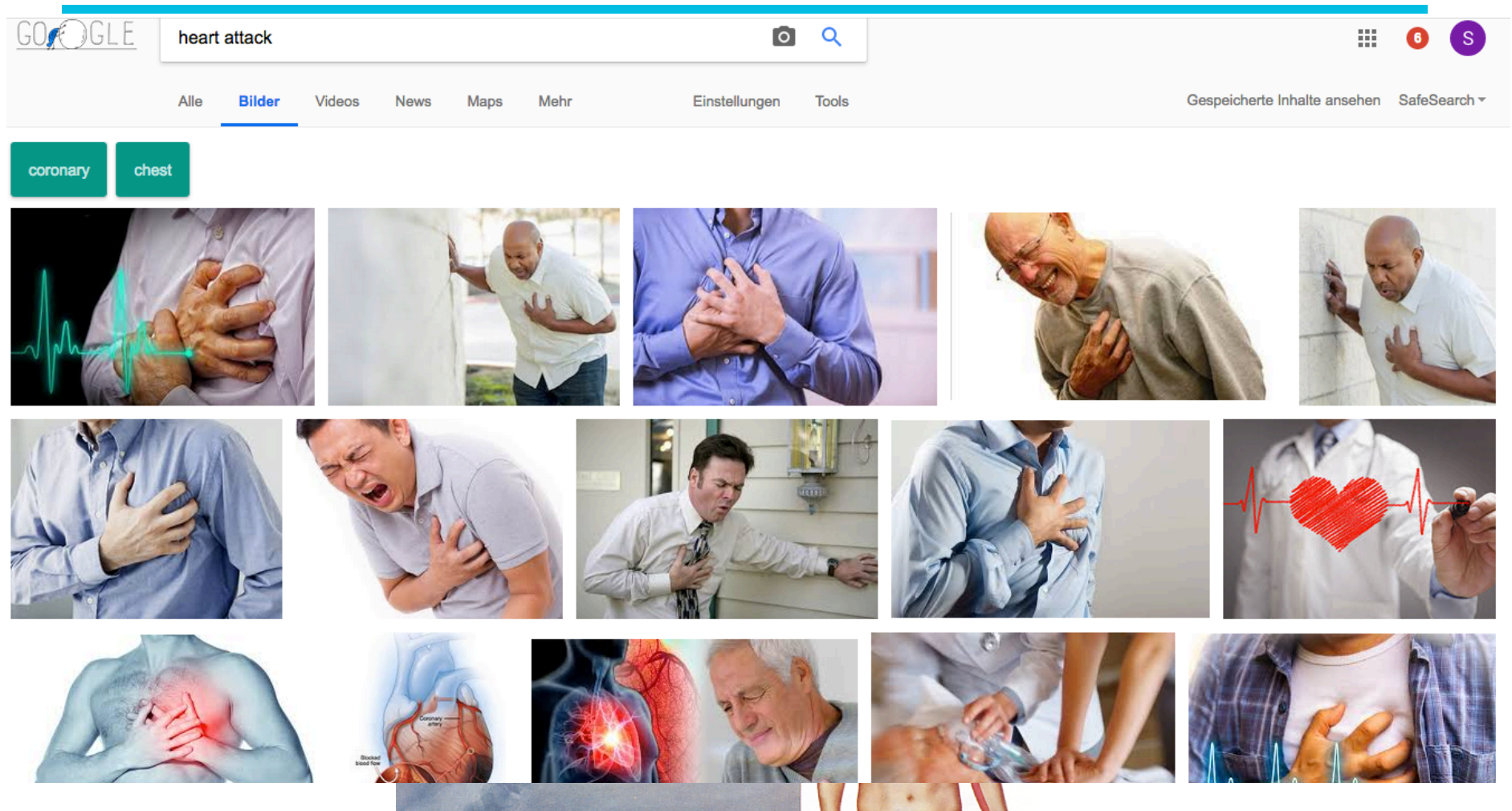
Experimenter sex can thus affect apparent baseline responses in behavioral testing.

Gender Index – a potentially different impact of sex and gender on recurrence of cardiovascular disease

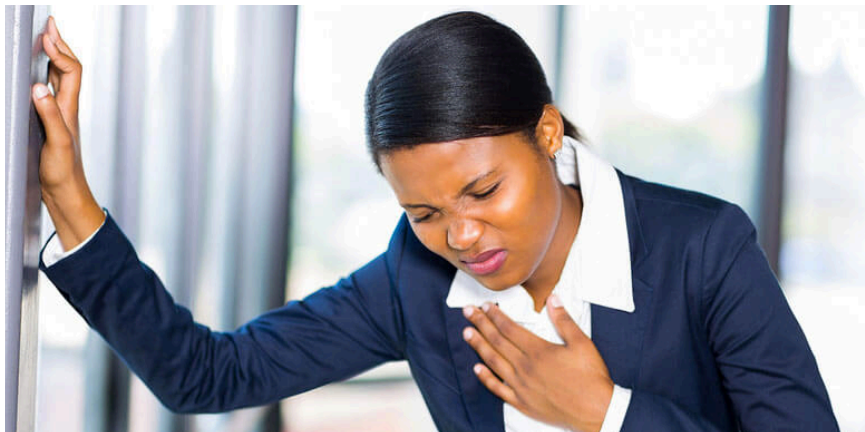
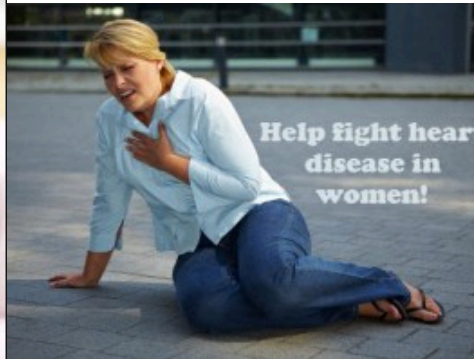
- (1) primary earner in the household,
- (2) personal income,
- (3) numbers of hours per week spent doing housework,
- (4) status of primary person responsible for doing housework,
- (5) level of stress at home,
- (6) Bem Sex Role Inventory masculinity score, and
- (7) Bem Sex Role Inventory femininity score.

The gender-related score represents the probability (between 0% and 100%) for each patient to be a “woman”. The lower the reported score, the more the patient reported characteristics traditionally ascribed to men and the higher the score, the more the patient reported characteristics ascribed to being a woman. Intermediate scores represent patients with an equivalent level of characteristics traditionally ascribed to women and men.

A concerted effort...



Of the first 100 Google images about „heart attack“ 4 are women....



 **American Heart Association®**
life is why™

Common Heart Attack Warning Signs



- 1 Pain or discomfort in chest
- 2 Lightheadedness, nausea, or vomiting
- 3 Jaw, neck or back pain
- 4 Discomfort or pain in arm or shoulder
- 5 Shortness of breath

The story of the “female” heart attack – a concerted effort

Increased death rates in young women

Reduced awareness in physician

Reduced awareness in women

Investigation of symptoms

Campaigns: Go Red for Women

Women’s sections within Cardiological Societies

FDA Office on Women’s Health

NIH mandates inclusion of information about sex

Inclusion in teaching

Barbra Streisand and Laura Bush

Problem identification

Science to identify causes -
provider

Science to identify causes -
population

Science to identify causes -
clinical

Awareness raising general
public

Parallel organization

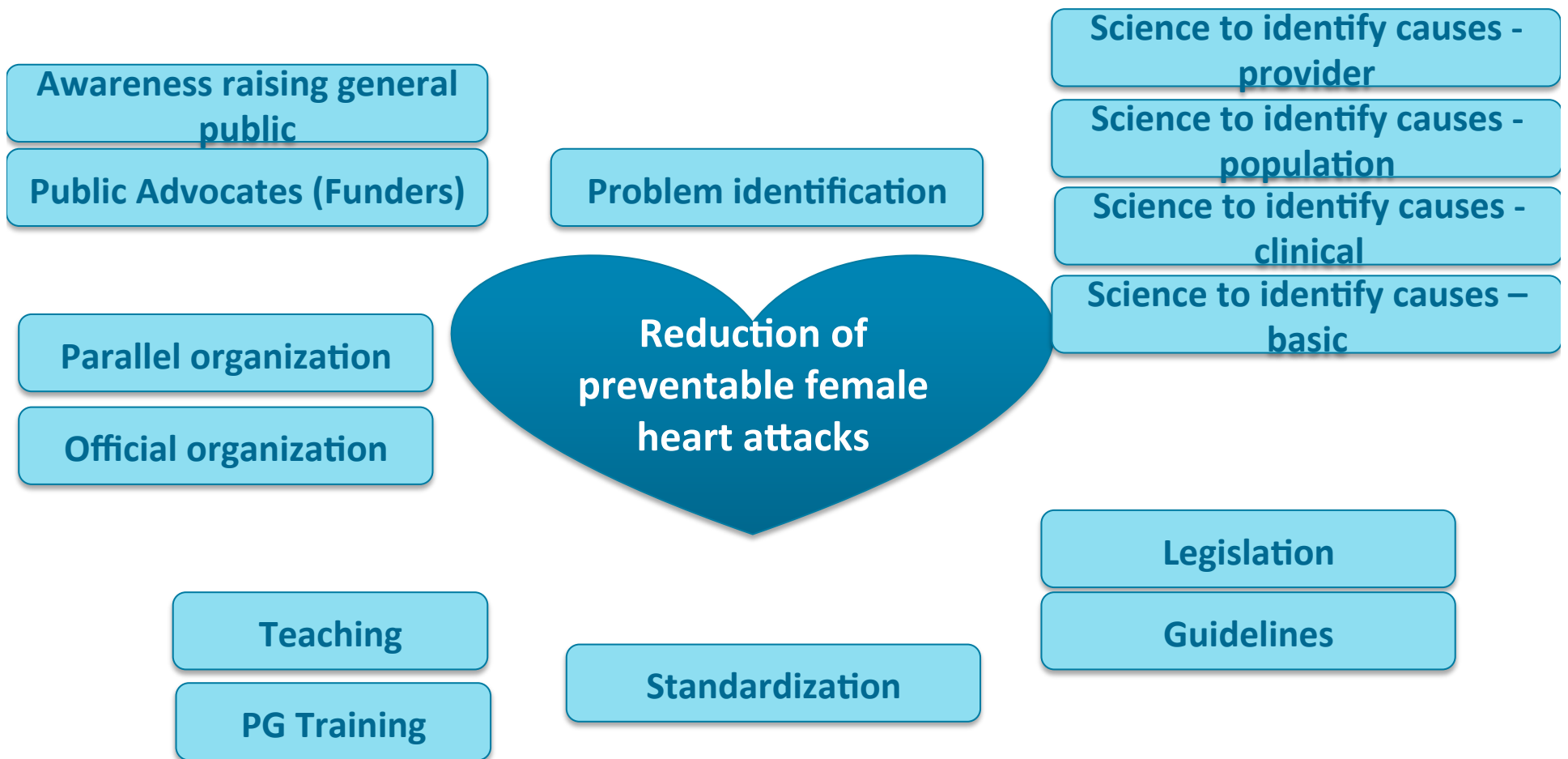
Official organization

Inclusion by funding bodies

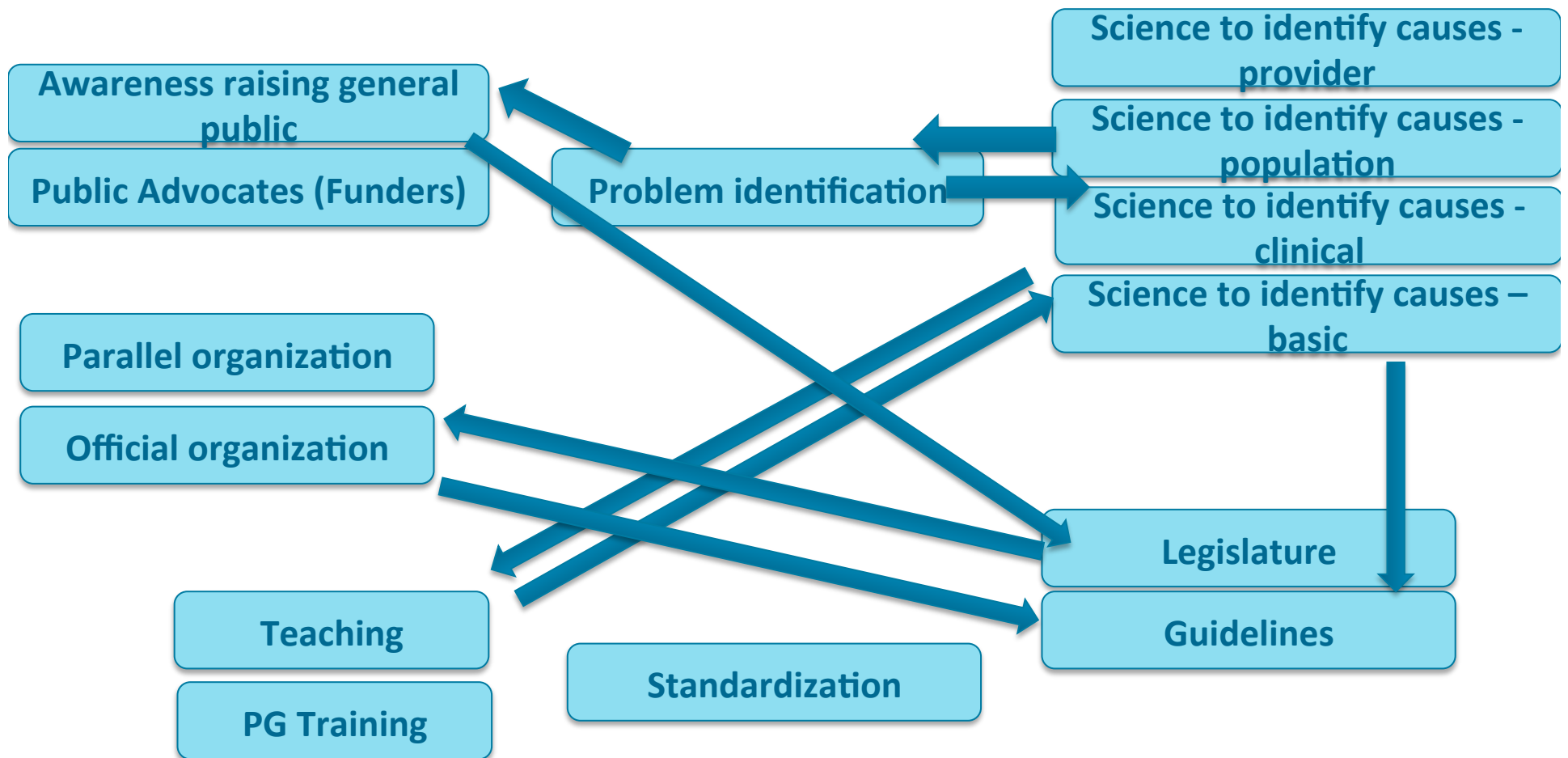
Teaching

Public Advocates (Funders)

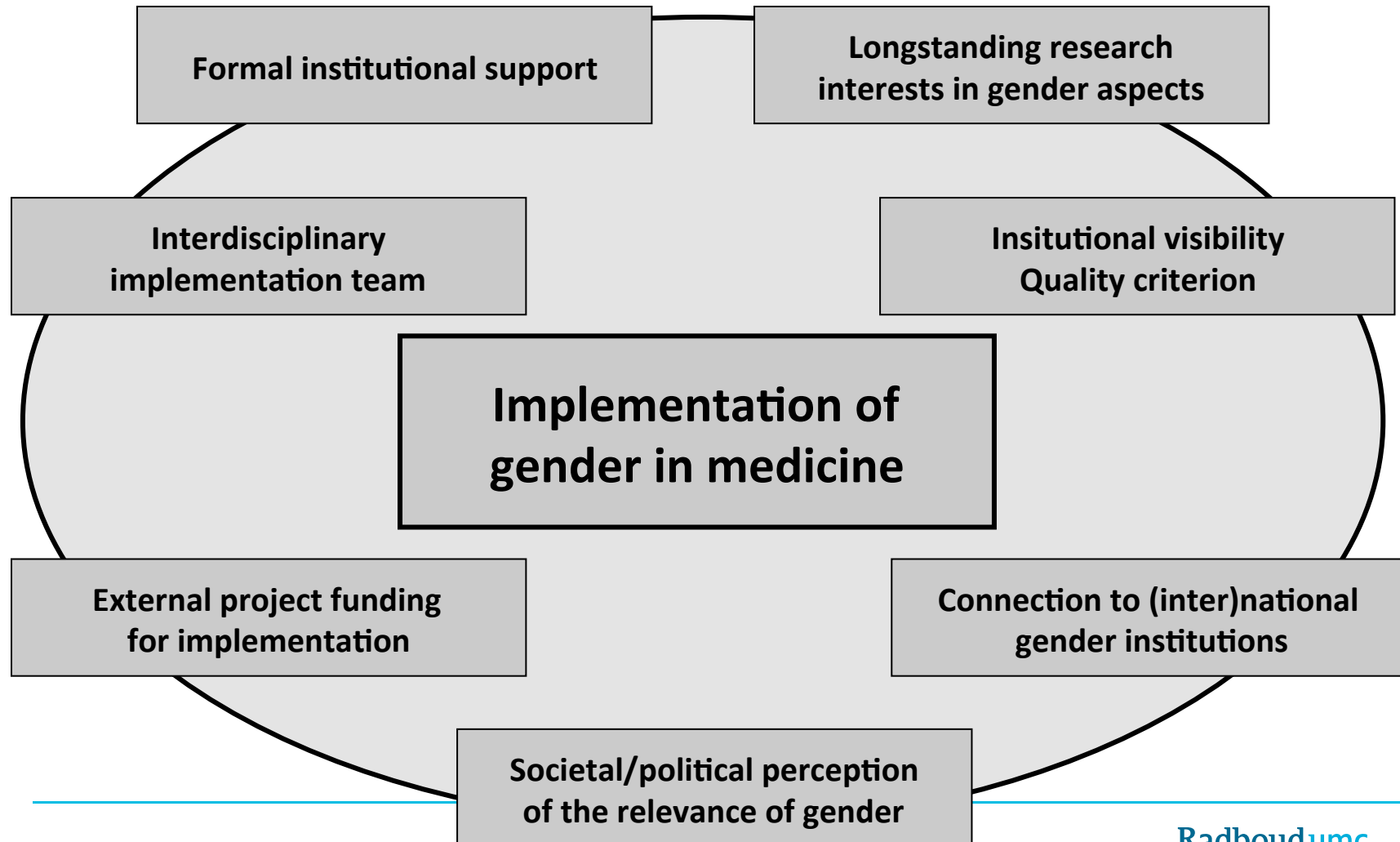
Which elements were necessary?



Which elements were necessary?



Implementation needs for sex and gender-sensitive research and practice



The road ahead....

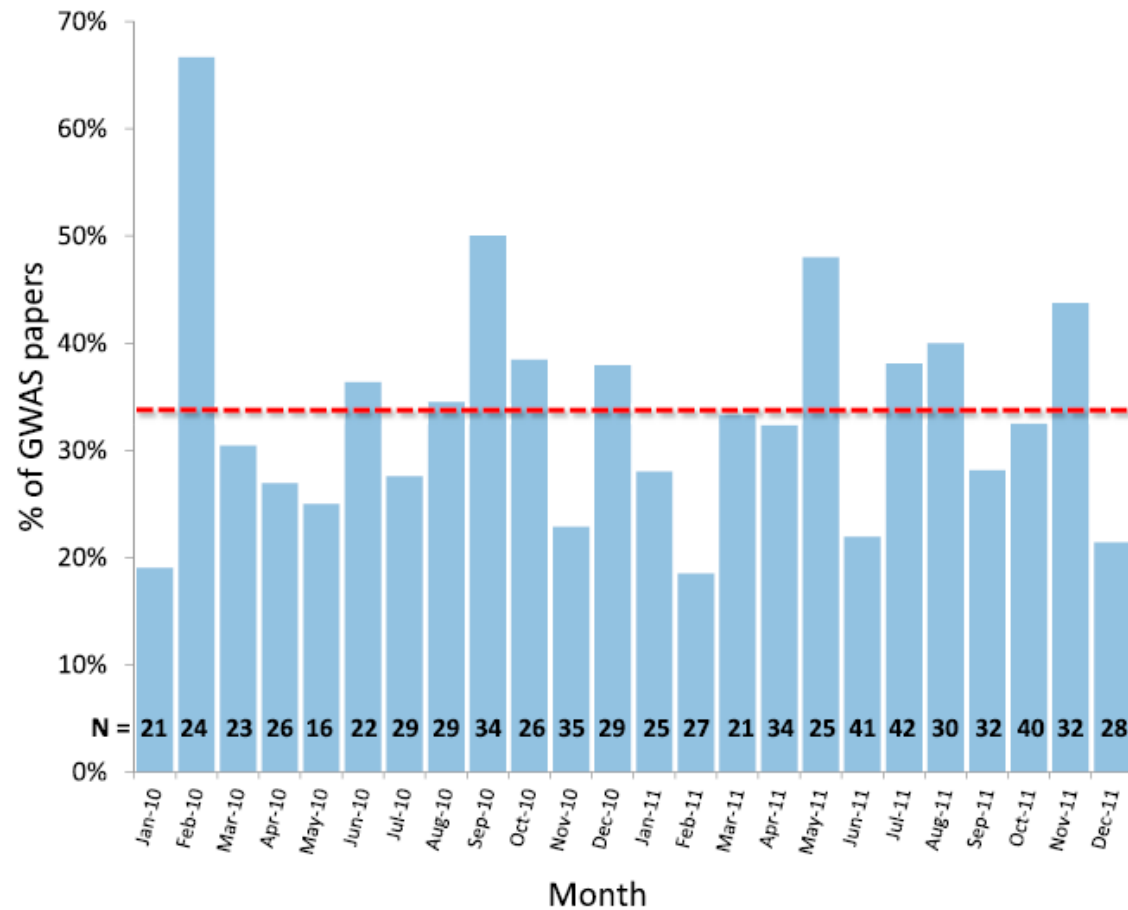
- Sex and gender-sensitive medicine is in a transition phase
- From personal to systemic
- Structural roles and elements will come to the forefront

How can each stakeholder in their capacity support this process?

Thank you for your attention!

For question, comments, remarks....
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GWAS Studies



Principles of implementation research

„the systematic study of how designated strategies are an evidence-based public health specific settings“ (CDC,

„the exchange, and ethical –within a complex set of and users- to accelerate research for Canadians effective services and public care system“ (Canadian

- Health care systems perspective
- Evidence-based (PH)
- Specific settings (intersectional, culturally-aware and socioeconomically informed perspective)
- Ethically sound
- Stakeholder inclusive