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UNIVERSITÄTSMEDIZIN BERLIN

DZHK
DEUTSCHES ZENTRUM FÜR
HERZ-KREISLAUF-FORSCHUNG E.V.

Gender equality and gender dimension in academic research - how to define excellence

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Direktorin, Institut de la Médecine de Genre
Charité

The Gender Dimension in the Horizon2020 Work Programme:

- "the gender dimension is explicitly integrated into several topics across all the sections of the Work Programme" (…)
- "a topic is considered gender relevant when it and/ or its findings affect individuals of groups of persons. In these cases, gender issues should be integrated at various stages of the action and when relevant, specific studies can be included".
- Integrating a gender dimension means paying attention to sex differences and gender effects in the content of research; different relevance for different fields of sciences;

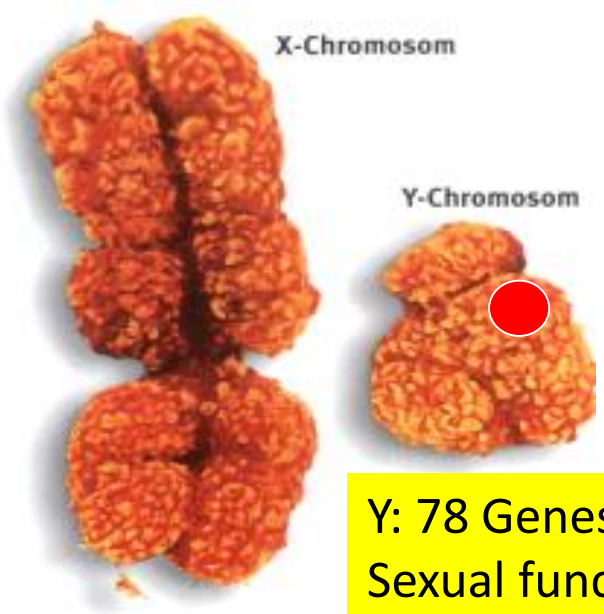
EUROPEAN Gender Medicine

Topics today

- Are Sex and Gender(S&G) important topics in academic medicine?
- Gender in medical education
- How to organize gender medicine
- Are gender equality and gender dimension in research related?
- What is excellent (gender) research?

Sex and Gender (S&G) are related in medicine

Sex – biological facts,
Genes and Hormones



Y: 78 Genes
Sexual function

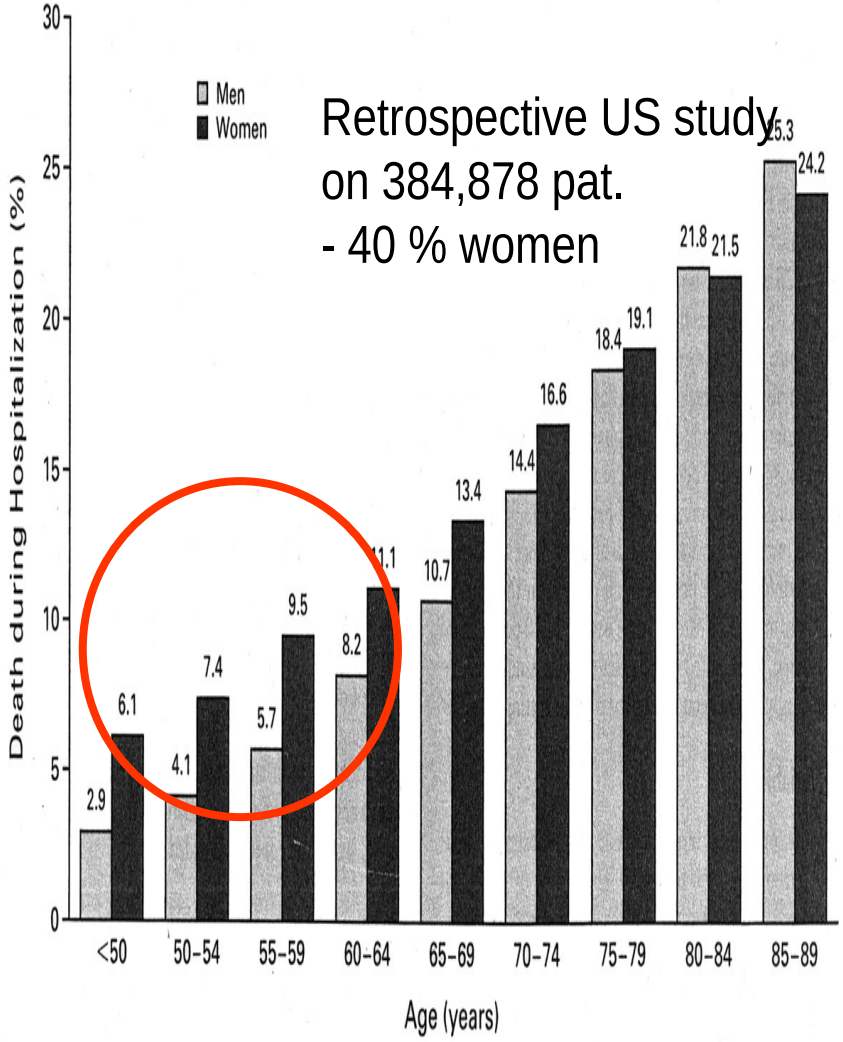
X: ca 1500 Genes
Heart-, Brain-, Immune function

Biological sex affects behaviour

Environment leads to epigenetic chromatin modifications

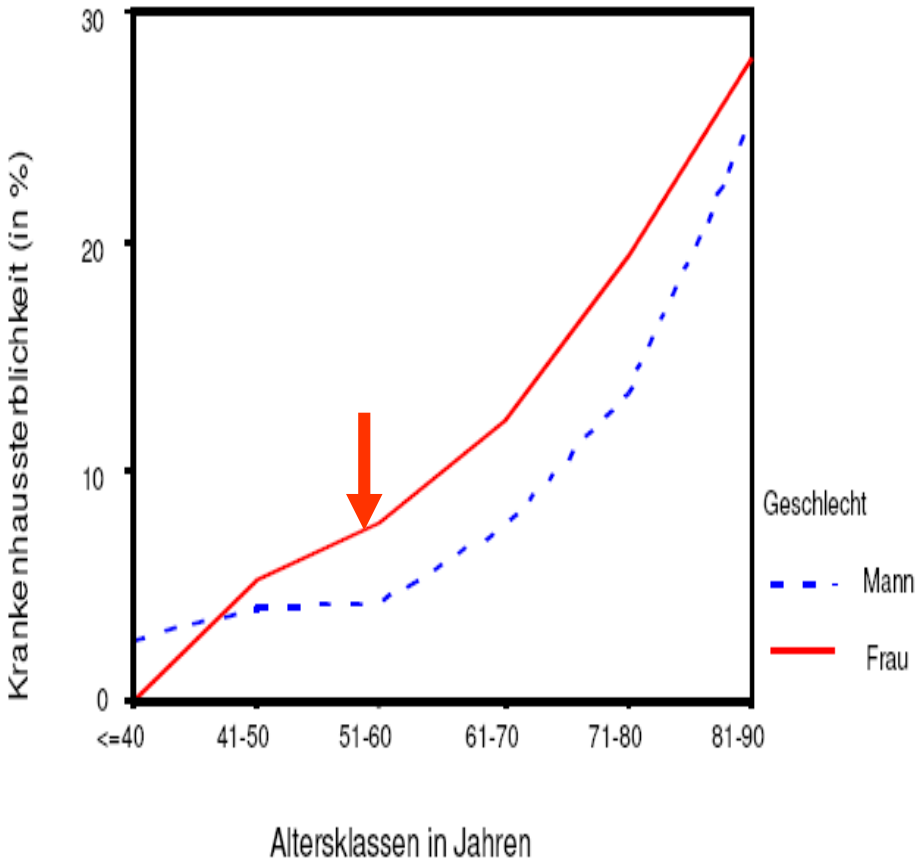
Gender –
Socio-cultural facts

S&G differences in cardiovascular disease - Higher early mortality in women with MI



NEJM 1999

Mortality after MI 2005 in Berlin, 5000 patients



Problem: Women with MI arrive later in hospital than men

Country	Condition	Intervall : Onset of symptoms - medical contact	Intervall: medical contact – hospital admission	Hospital admission-intervention	
France, all	STEMI	M 200 / W 245			Donataccio, 2015
Fr, Brittany	STEMI	M 209 / W 235			Leurent, 2014
Spain	STEMI	M 240 / W 307			deMiguel, 2013
NL	STEMI	<65 y: 150 / W 165		Men=women	Otten, 2013
DE	Stemi	154 / W 189			Ladwig , 2009
SW	STEMI	169 / W 190		Von 51/ 80 auf 43 / 48 nach intervention	Naegele 2011, rad 2012
US	STEMI	150 / W 195			
Australia	STEMI	161 / W 217			

Acute coronary syndromes: S&G differences in presentation

Häufige auslösende Ursachen der Angina pectoris: schweres Essen, Erschöpfung, Kälte, Rauchen

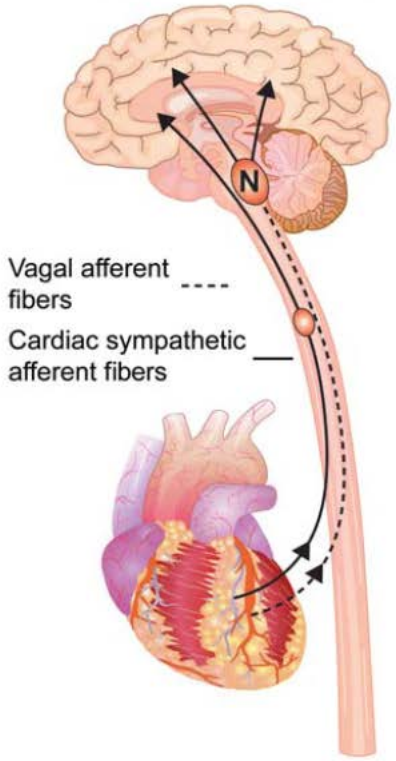
Charakteristische Schmerz-ausstrahlung bei Angina pector


ODD SYMPTOMS: For Kastan, diagnosis and treatment would prove difficult

Heart disease is the **No. 1 killer of women,** yet American research shows that only one in four women realize it is a greater th reat than cancer • A woman has a **50% chance of dying** from her first heart event, compared with a 30% chance f a man • Of those who survive their first he art attack, **38% of women will die within a year,** vs. 25% of men • **46% of women are disabled** by heart failure after a heart attack, compared with 22% of men

Why is there no research on mechanisms for S&G differences?

Anatomical and functional components of cardiac pain generation



Cortex	Perception emotion reporting
Brain stem, area postrema dorsal vagal complex	Modulation by Endorphins, Vegetative components
Afferent nerves: vagal and sympathetic	
Neurotransmitters, Receptors	Signal generation

Figure 1 Anatomical and functional components of cardiac pain generation.

Problem : High rate of normal angiographies in women with chest pain

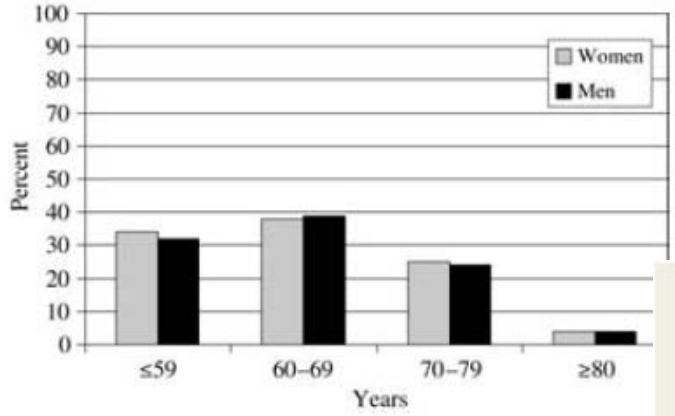


Figure 1 Proportion of patients undergoing first-time tic coronary angiography according to age (years) and

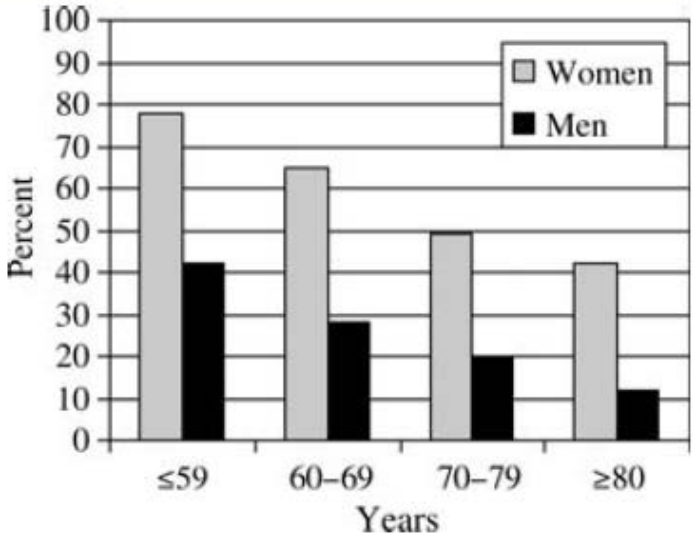
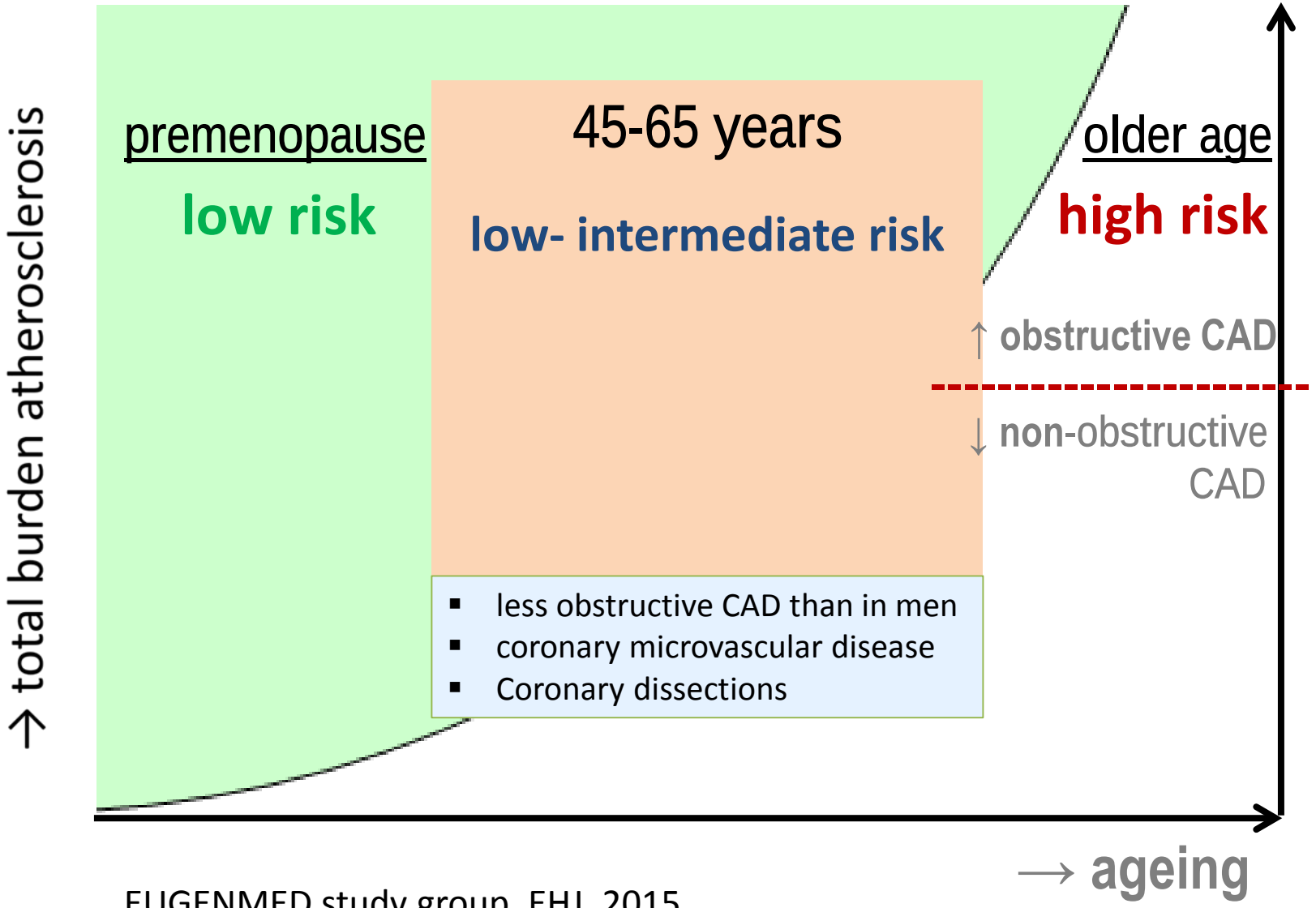


Figure 3 Proportion of patients with normal findings at coronary angiography according to age group and sex.

Johnston et al, EHJ 2011

Specific features of middle aged women

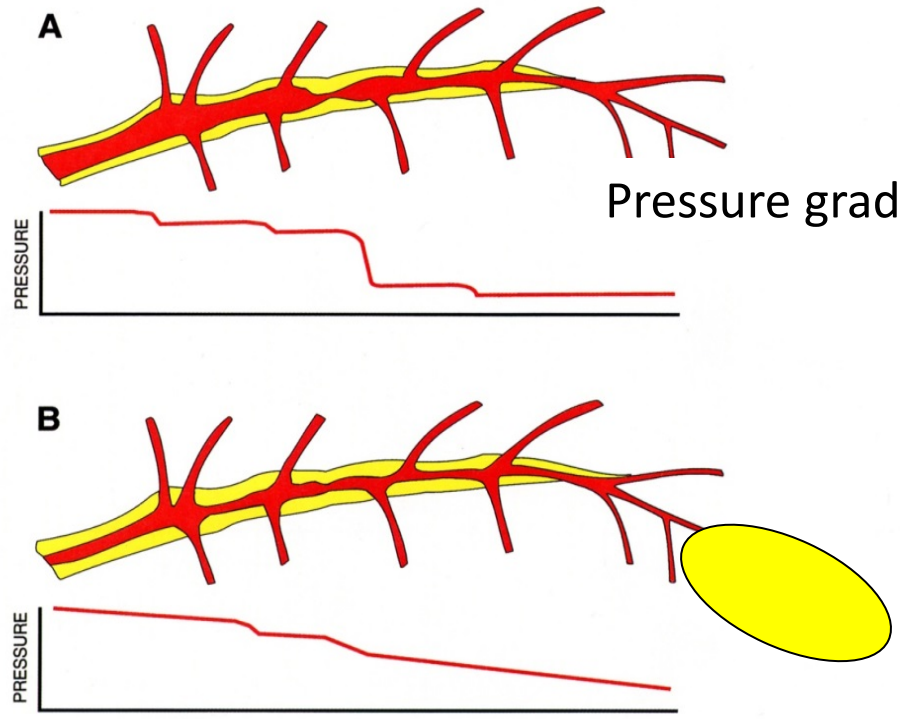


EUGENMED study group, EHJ, 2015

Differences in vascular pathophysiology in women and men

More frequent in men:
localized stenoses

More frequent in women:
non- obstructive CAD (NobCAD)
Wall thickening, microembolism, spasms, endo-thelial dysfunction

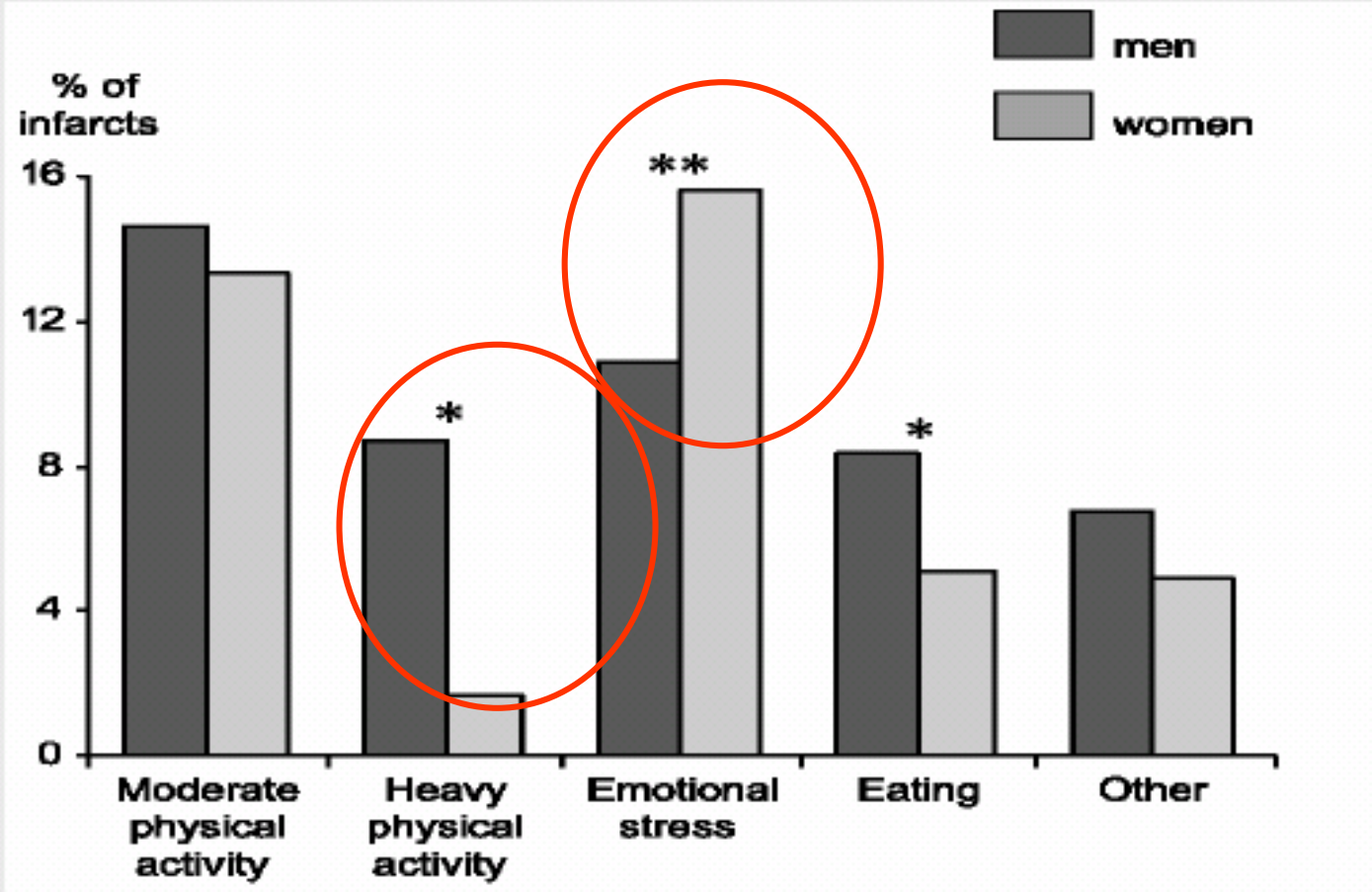


Mering G, Circ 2004; Bugiardini R, Merz NB JAMA 2005

Women may be different

Spasmen in in the big vessels are freqeunt in women.

Emotional Stress – physical activity as inducers of MI in women and men



Metaanalyse (17 Studien) Čulić et al., Int J Cardiol (2005)

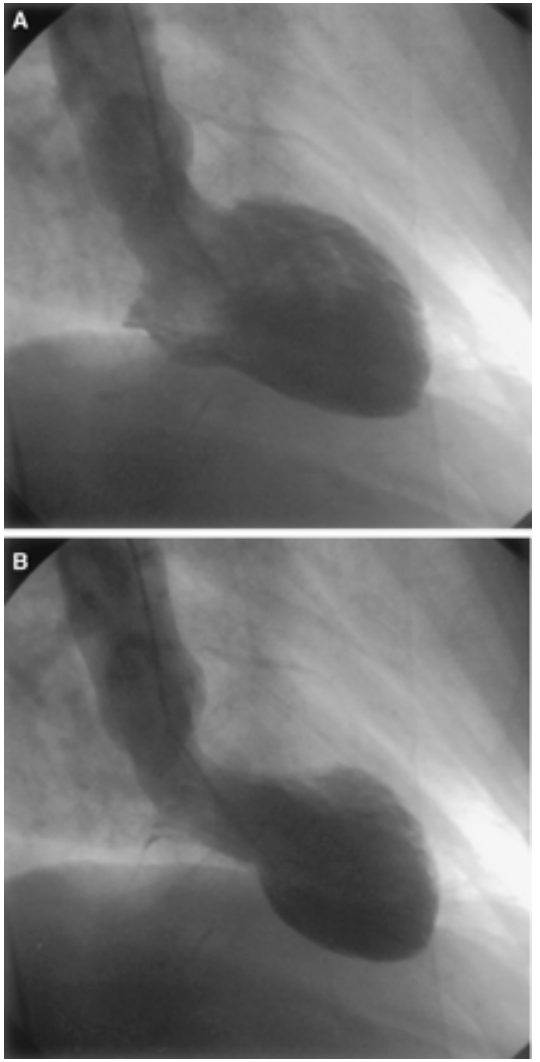
Stress induced cardiomyopathy: Tako tsubo, occurs in > 90 % in women

Mimics myocardial infarction
But normal coronary arteries
Severe disease
Triggered by massive psychological stress

Was believed to be extremly rare – German registry with more than 300 pts in 2 years

Now starting: Berlin Heart and Soul study – BEHERS – to identify

- Mechanisms and
- Novel treatment approaches in Tako tsubo



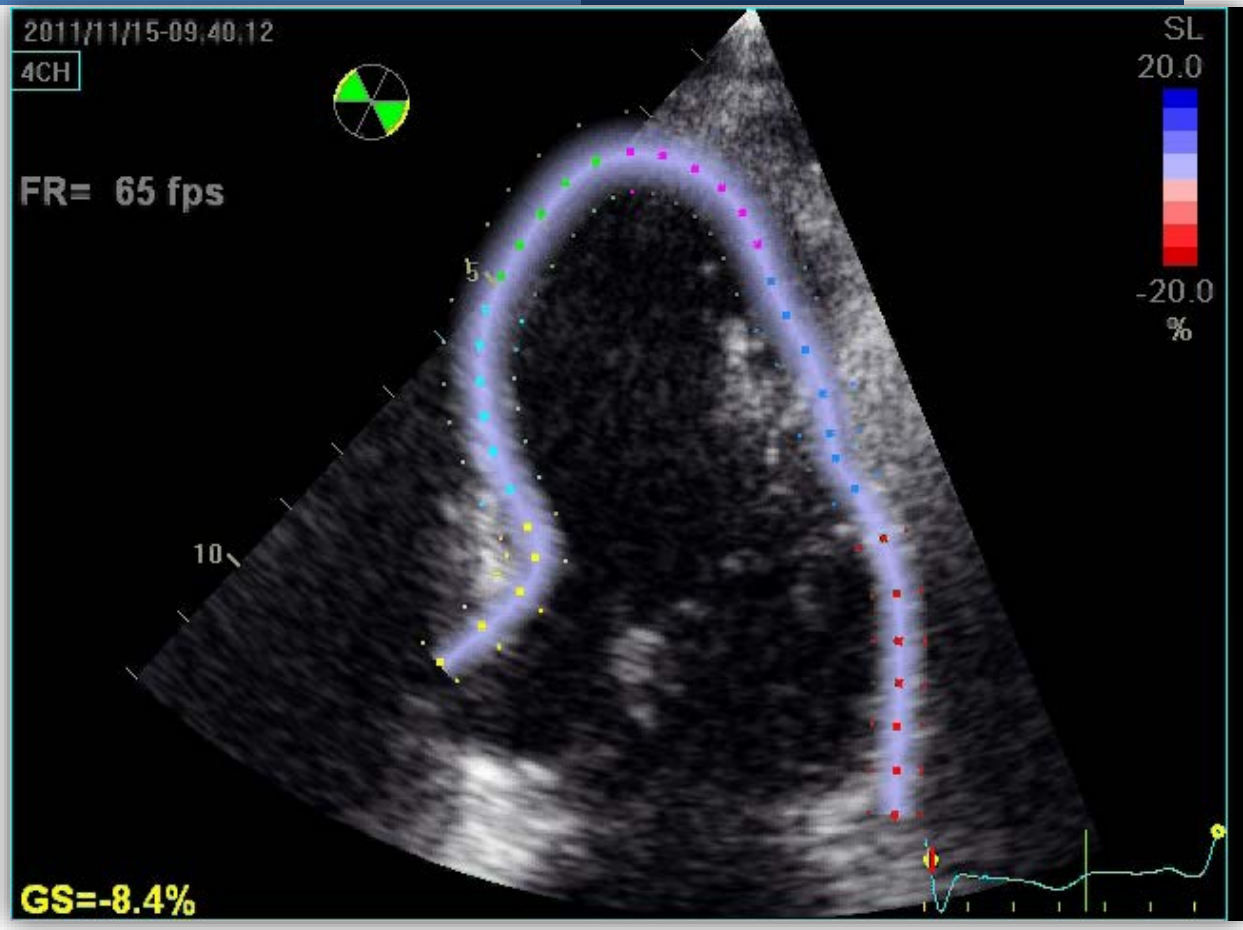
Sharkey, Circulation 2005

Tako-Tsubo – 70 – 90 % women

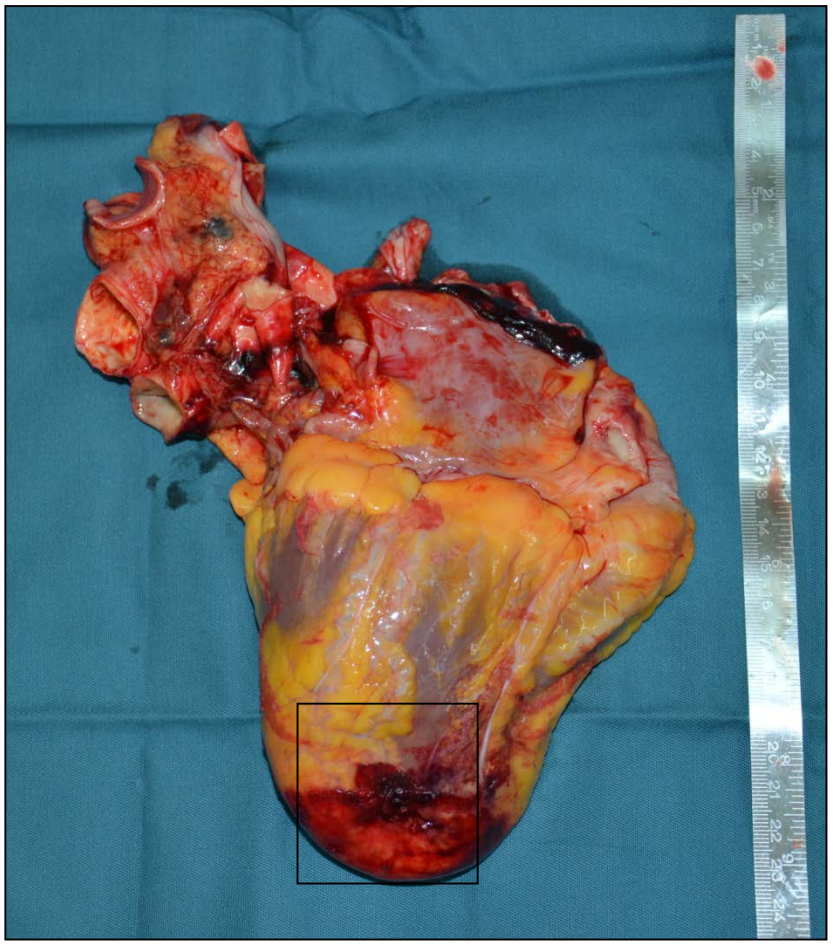
8 % of acute coronary syndromes in women

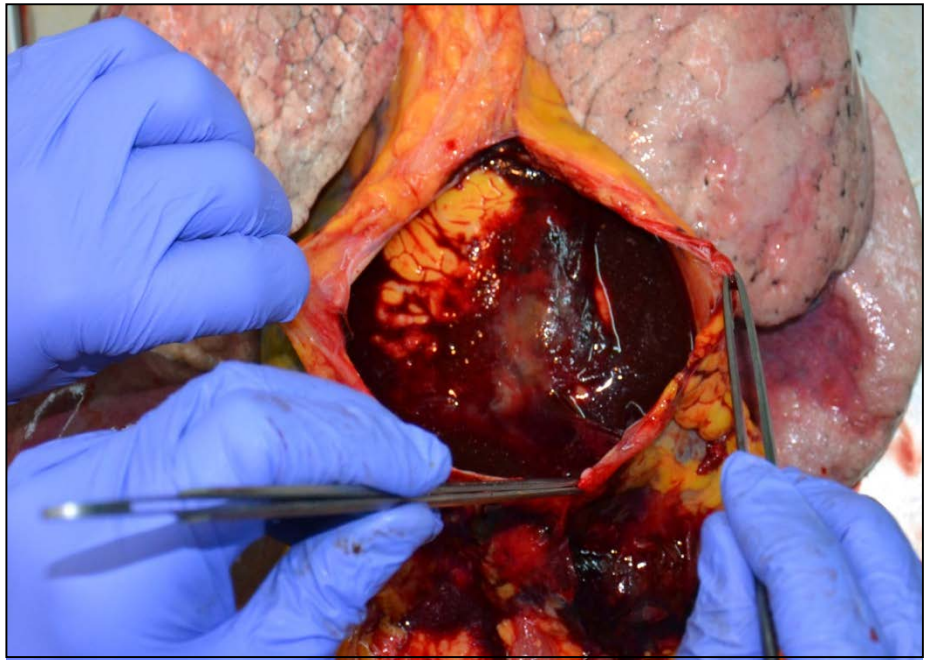
Mechanisms:
Sex specific activation of ß AR
Decrease in estrogens
Defect in microcirculation?

BEHRS study at Charité/GIM



Rare complication: Cardiac rupture

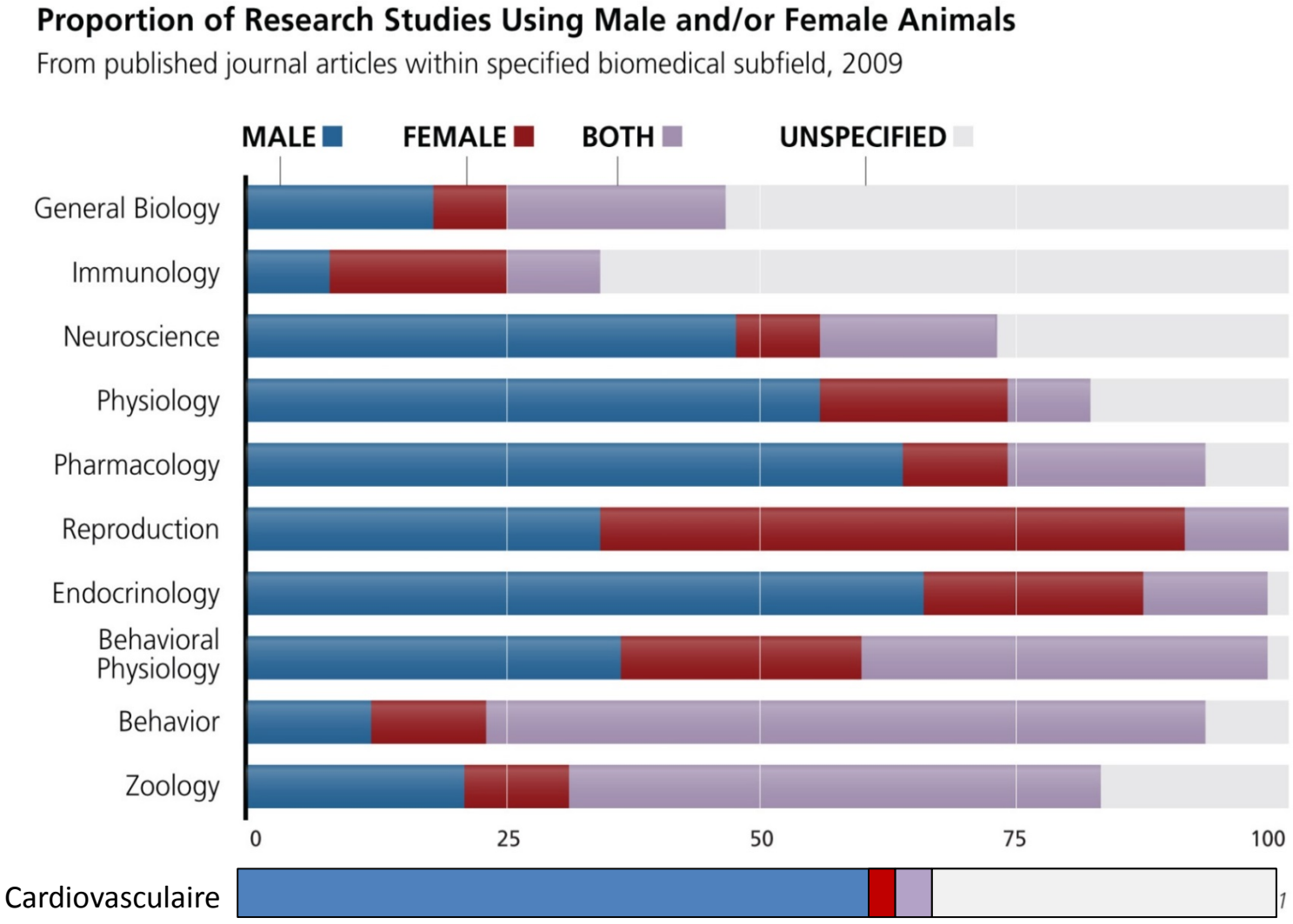




Extreme manifestation of women – typic heart disease

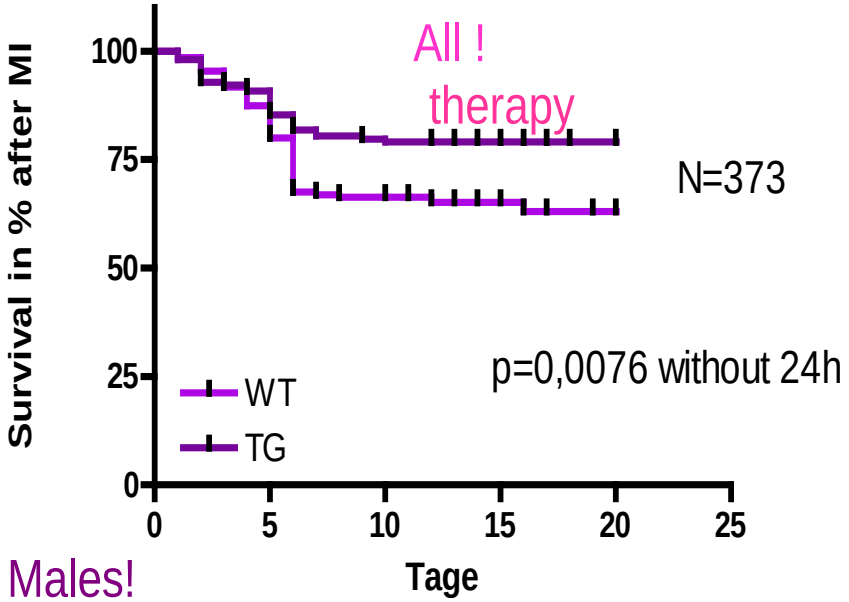
- Highly understudied, mortality 8 % (
- animal model: male rat

Basic research – mainly male animals



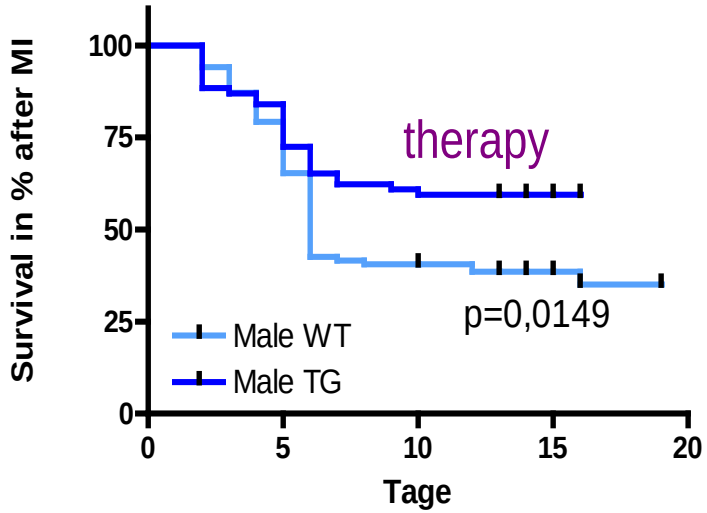
Nature , Zucker, 2010; VRZ, 2015

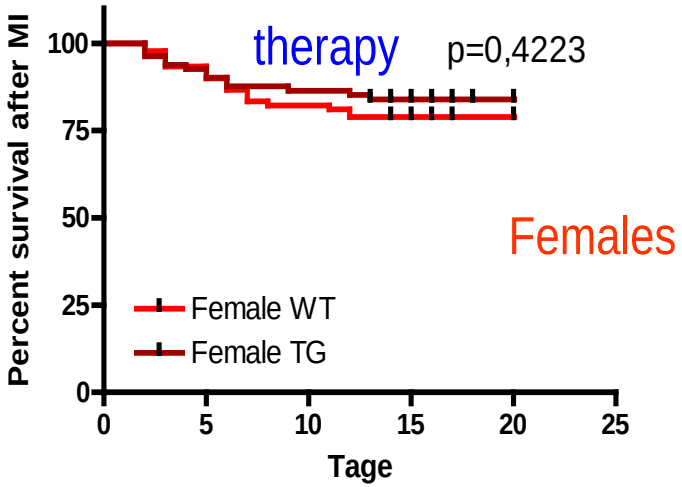
Drug development should be done in male and female mice - example: survival after MI!



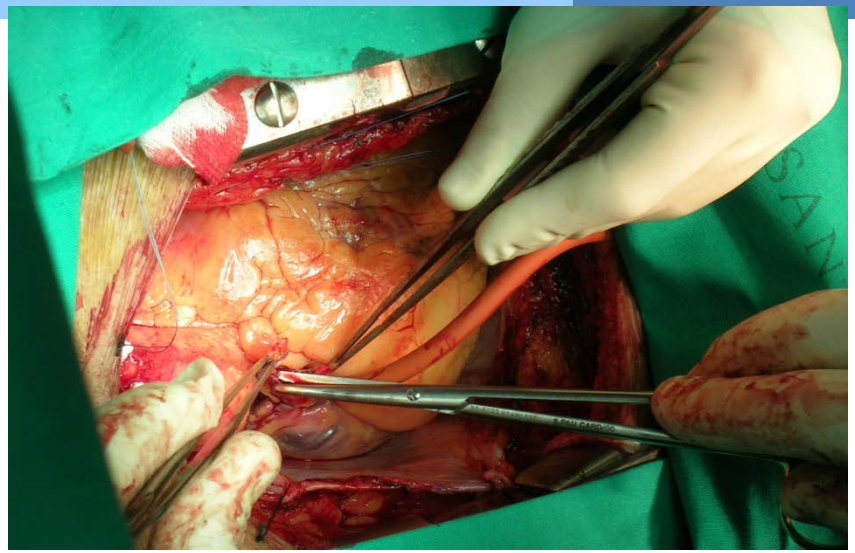
Males!

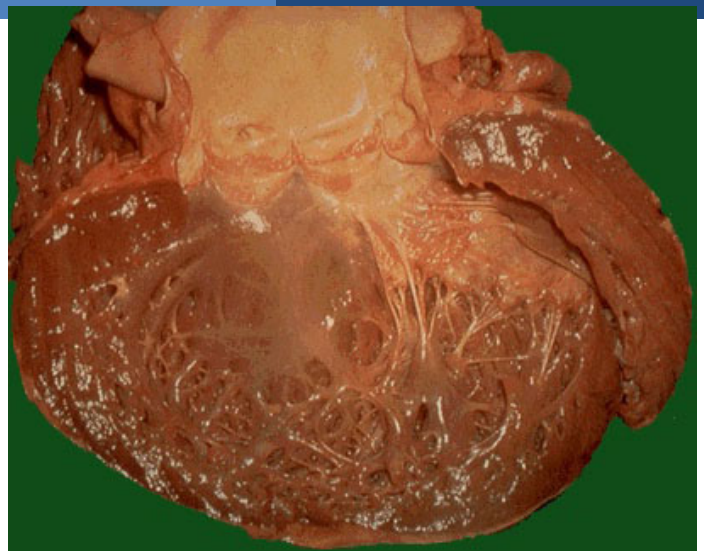
Improvement is seen in the whole cohort and in males, not in females.

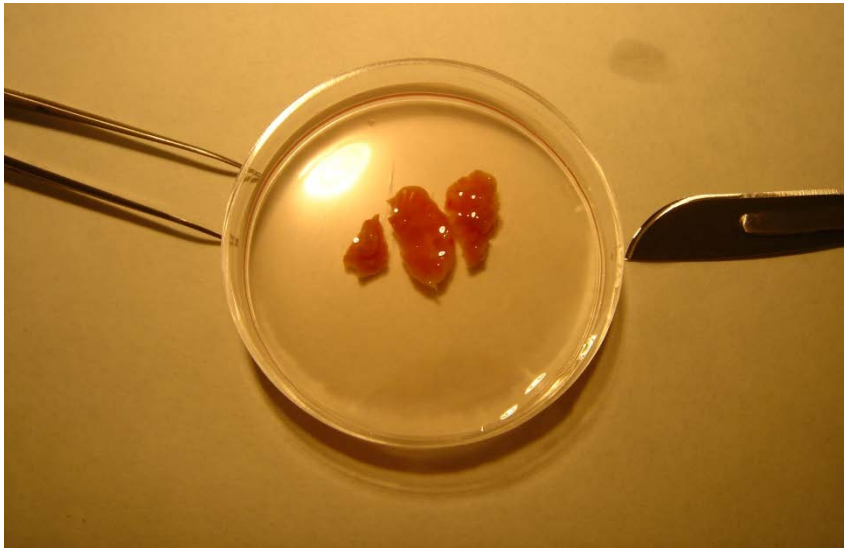


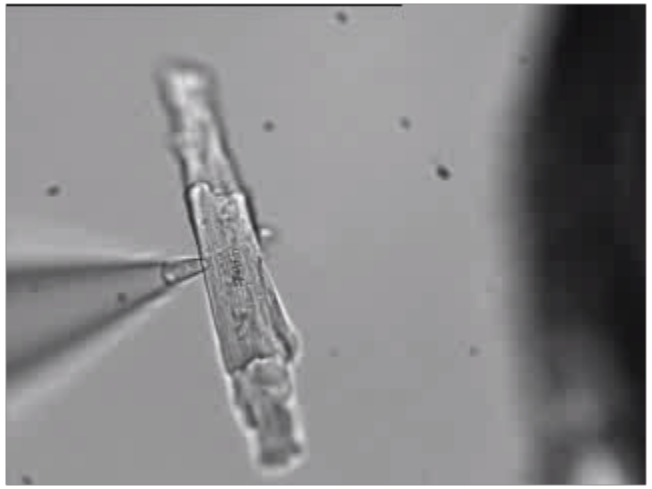


Human ventricular myocytes







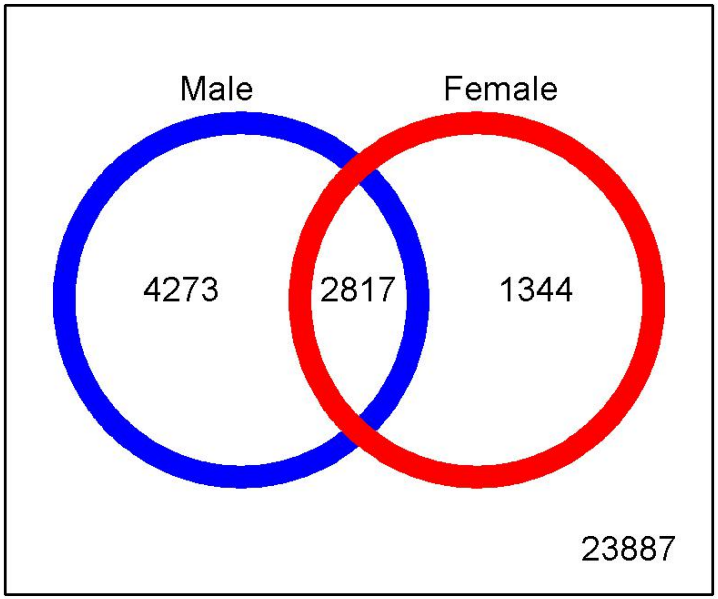


Patch-clamp

Cristina E. Molina, Barcelona, Spain

Sex differences in mechanistic pathways Of heart failure - dilated cardiomyopathy

- **Gene expression in LV samples of end-stage non-ischaemic DCM patients**

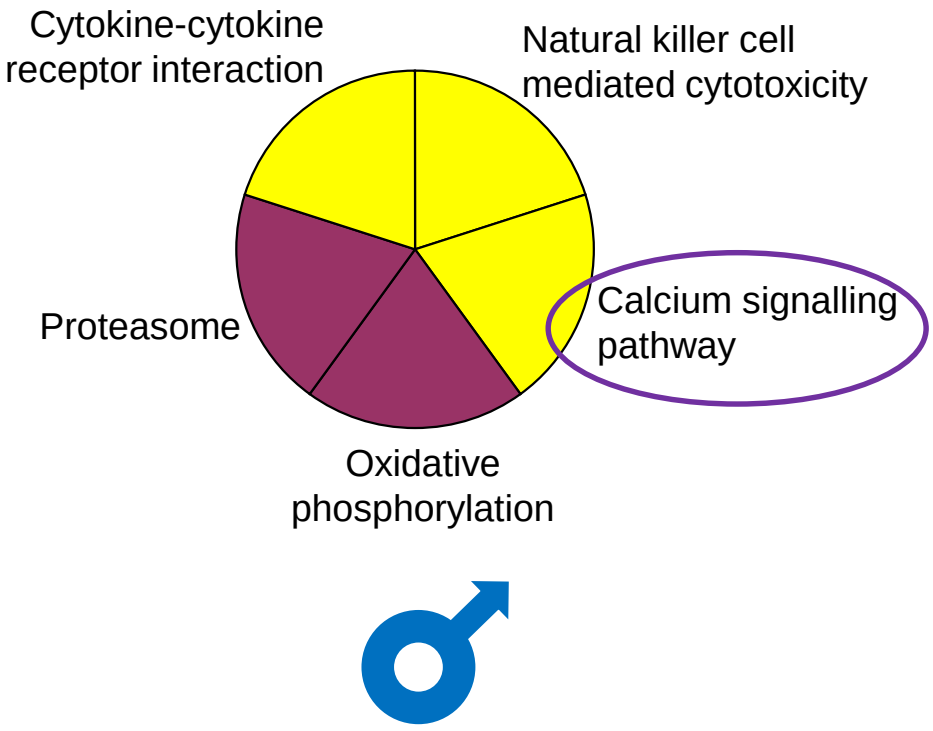


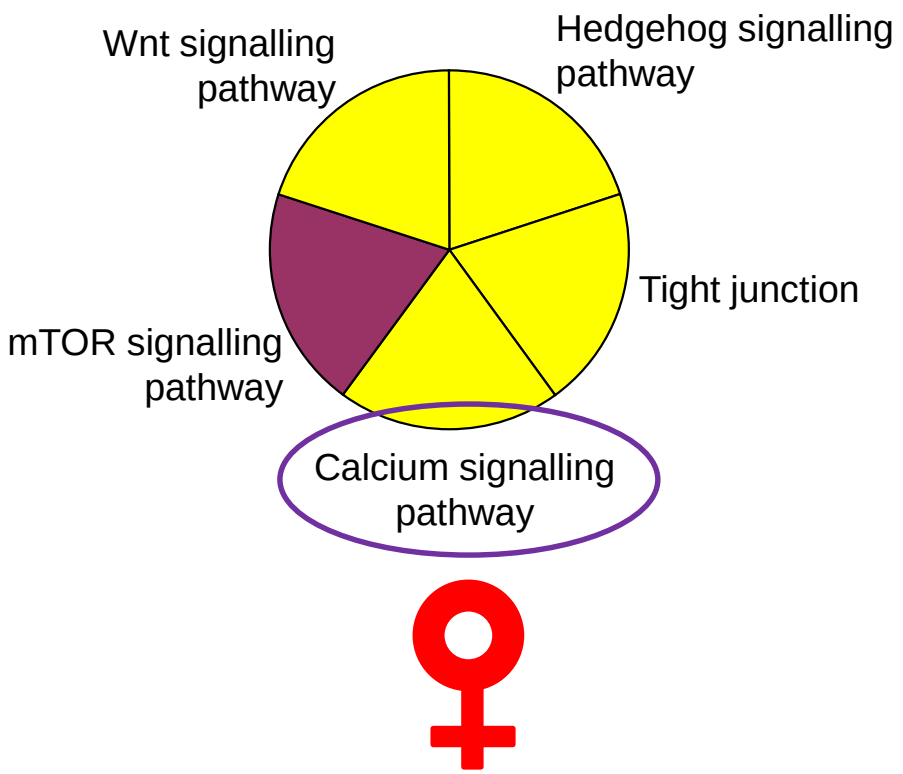
False discovery rate (FDR)-adjusted $P < 0.01$

Karagigas *et al.*, *unpublished*

Sex differences in molecular pathways for heart failure - drug targets

Yellow indicates induction and purple repression





Kyoto Encyclopedia of Genes and Genomes; 1000 permutations; adjusted $P < 0.05$

Consequences on unbalanced research:

Data from 48 cohort studies for novel drugs

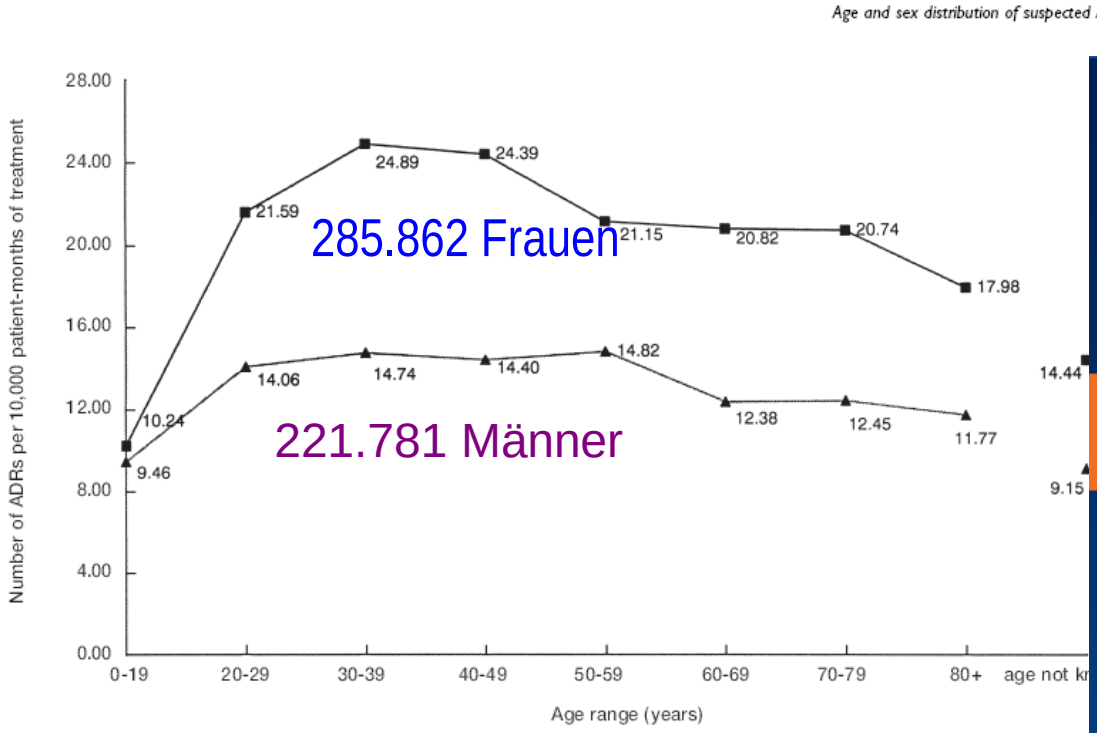


Figure 1 Age and sex specific incidence rates of suspected adverse drug reactions (ADRs) ■ female, ▲ male.

Martin RM, Br J Clin Pharmacol; 46: 505-511

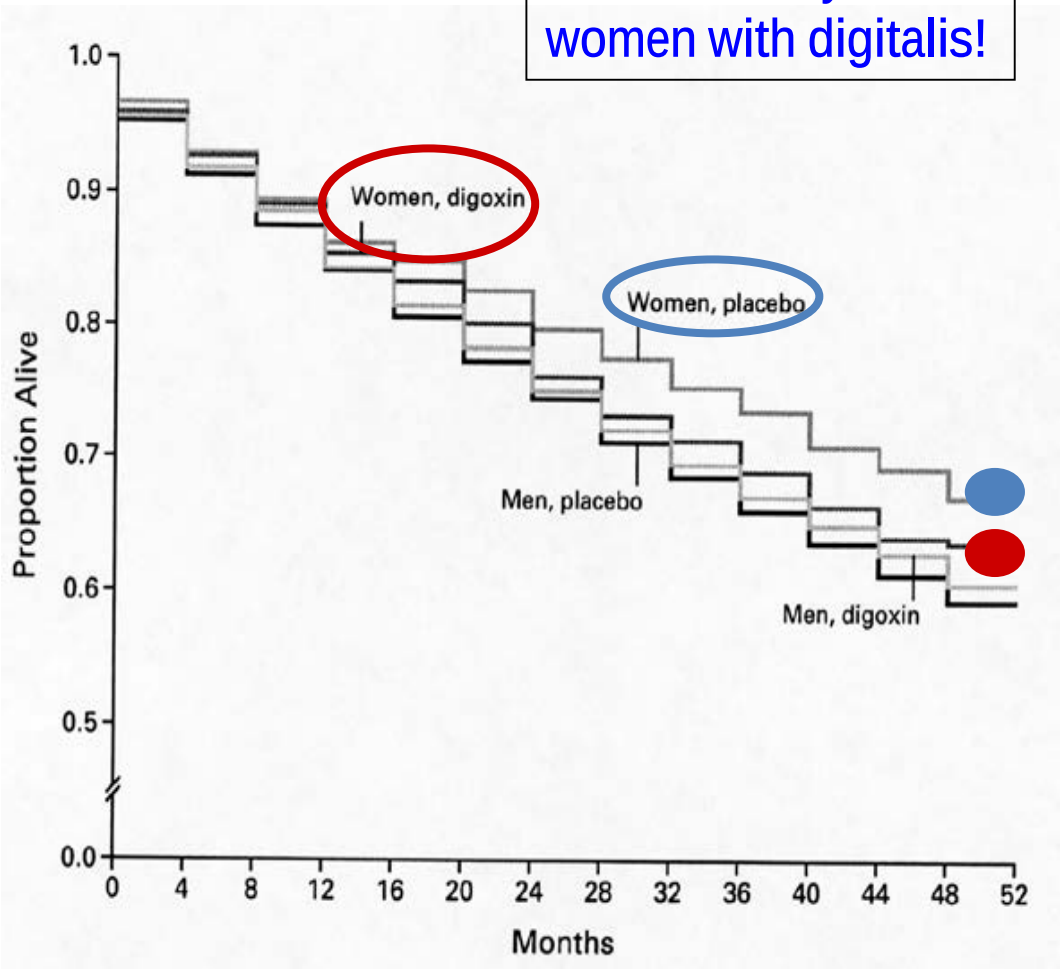
Drugs in heart failure

Sex differences in the effects of digitalis

1997: Digitalis-Study – Improvement of morbidity in HF by digitalis, no effect on mortality : inclusion in guidelines

2002: First sex-specific analysis

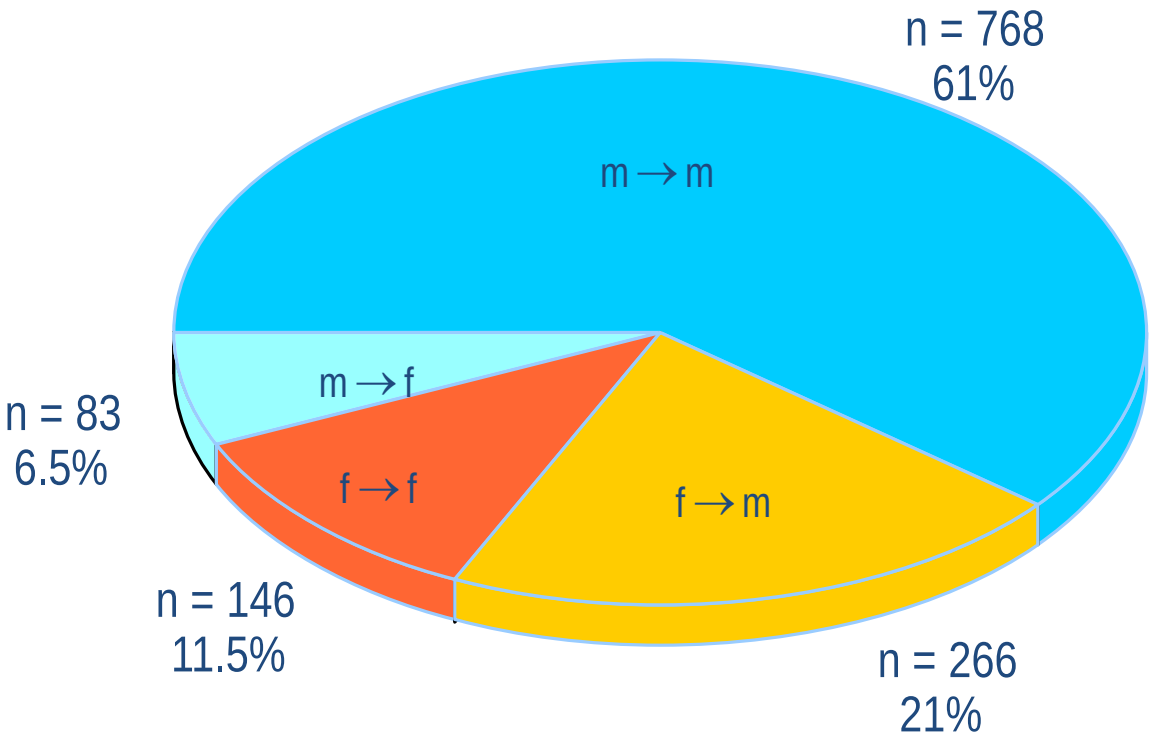
Over-mortality in women with digitalis!



Rathore et al, NEJM 347:1403, 2002

Heart transplantation – Deutsches Herzzentrum Berlin

n = 1263



Males receive 82 % of organs

Same in kidney transplant

Who does gender research?

- Gender congress, September 2015 in Berlin, BMBF
- Congress of International Society of Gender Medicine
- 300 participants

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Internationaler Kongress für Geschlechterforschung in der Medizin
22.-23.09.2015, Berlin

www.genderkongress.com

Das Vorhaben wird mit Mitteln des Bundesministeriums für Bildung und Forschung unter dem Förderkennzeichen 01FP1450 gefördert.

GEFÖRDERT VOM

Bundesministerium für Bildung und Forschung

PROGRAMM

Dienstag, 22. September 2015

Begrüssung:
Vera Regitz-Zagrosek, Charité,
Ministerialrätin Christina Hadulla-Kuhlmann,
BMBF,

Hauptreferat - Wie unterscheiden sich Frauen und Männer in der Herzchirurgie: Roland Hetzer

Spektrum der Gendermedizin weltweit:
Miyuki Katai, Karen Sliwa-Haenle, Janine A. Clayton, Alan White, Martina Kloepfer

Schlaganfall und Hypertonie:
Louise McCullough, Mia van E
Sandberg, Jane Reckelhoff

Innere Medizin, Reproduktionsmedizin:
Eva Gerdts, Eva Bossano-Prescott, Bettina Pfleiderer, Manfred Hecking, Birke Schneider,

Genetische und epigenetische Mechanismen:
Christine Disteche, Jeanette Erdmann, Nina H. Uhlenhaut, Arthur Arnold, Geert de Vries, Claudine Junien

Mainly women

Mittwoch, 23. September 2015

Grundlagen – Sex in Zellen und Organellen
Renee Ventura-Clapier, Valter Malorni, Junko Kurokawa, Gregor Majdic, Elke Dworatzek, Maria Barcena

Gender in der klinischen Praxis:
Noel Bairey Merz, Susanne Hoffmann, Duska Dragun, Verena Stangl, , Renata Cifkova, Ursula Müller-Werdan, DeLisa Fairweather,

Geschlechterunterschiede bei Public Health:
Ingeborg Jahn, Ineke Klinge, Floris Barnhoorn, Antonio Daponte, Renate Schnabel, Gabriele Bolte

cht und Gewalt
eale, Dov Feldberg

Gendermedizin in der Lehre
Giovannella Baggio, Margarethe Hochleitner, Sabine Ludwig

Sex und Gender in der Therapie
Flavia Franconi, Karen Nieber, Daniela Fliegner;

...und mehr: Symposien, Freie Vorträge, moderierte Poster,
Treffen/Lunch mit den ExpertInnen.

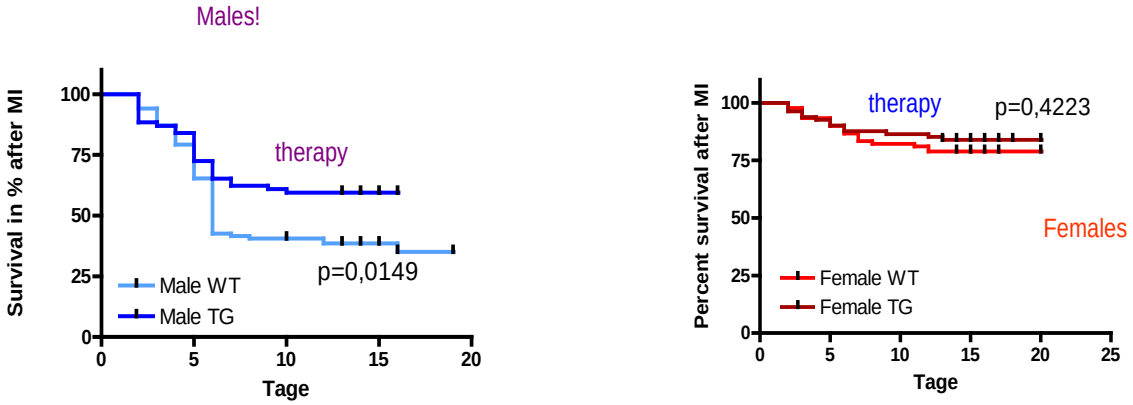
Where does the money go?

Founding Members of German Centre for Cardiovascular Research (DZHK)

- DZHK unifies the 7 most excellent Cardiovascular Research Centres in Germany – 42 Mill funding/year

What is excellent?

- Detecting novel molecular mechanims?
- Describing sex differences in animal models or human heart?

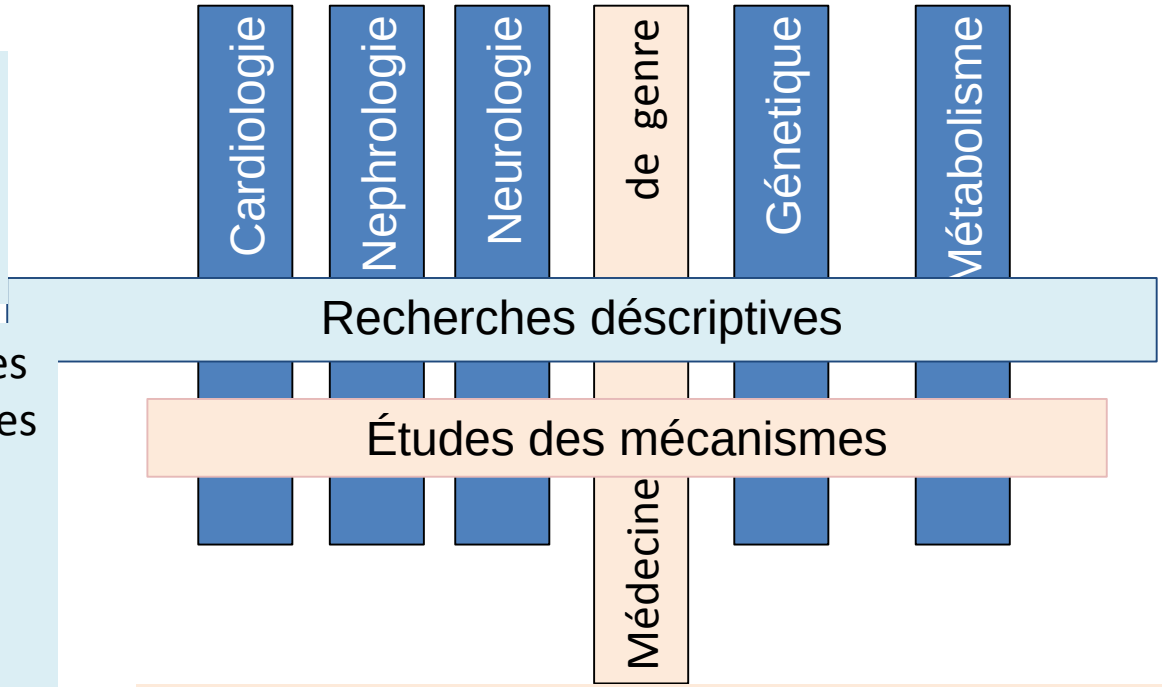


- Who defines excellence?

Comment organizer les études en médecine de genre?

Sexe et genre s'appliquent sur toutes les disciplines médicales de manière transversale

Les études sexe/genre simples et sans hypotheses – nombres hommes femmes,….. - n'aident souvent pas pour faire avancer les sciences



Excellence:
Hypotheses
Études des mécanismes
Voies de formation
Perspectives professionnelles pour les jeunes

La médecine de genre doit être une discipline propre!

Académie Francaise, Dec 2015

How to implement gender research - models

- **NIH: will** require all grant applicants “to report their plans for the balance of male and female cells and animals in preclinical studies in all future applications, unless sex-specific inclusion is unwarranted, based on rigorously defined exceptions [1]”.
- **CIHR** “expects that all research applicants will integrate sex and gender into their research designs when appropriate…. There is no simple "recipe" for integrating sex and gender in health research …..”
- Horizon2020: mentions in some calls, that S&G should be analysed

However:

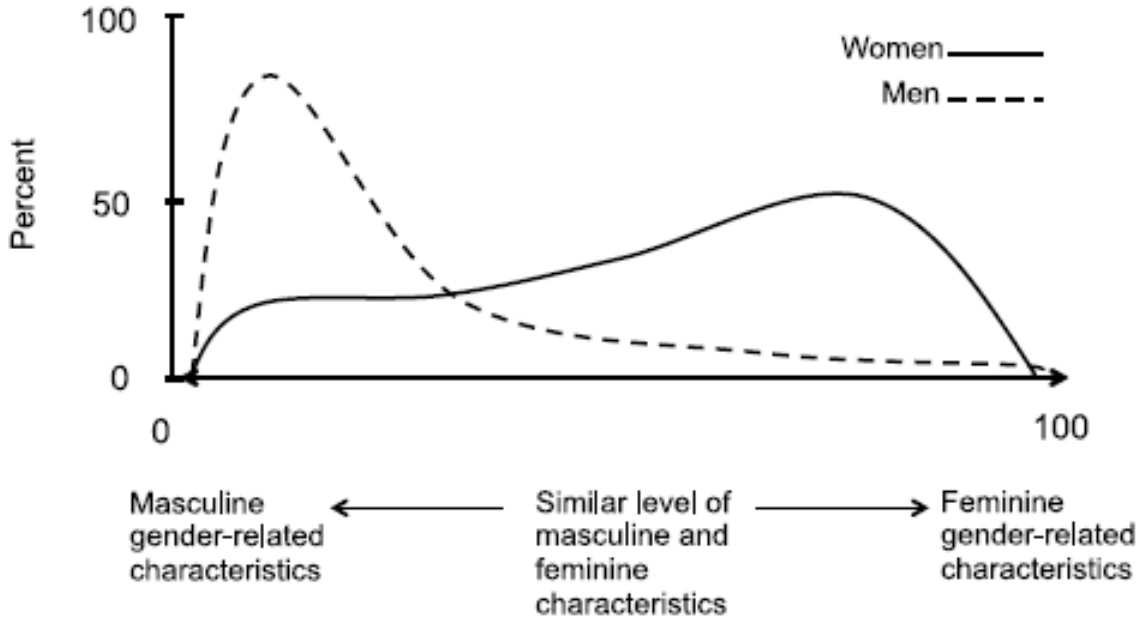
Not all applicants may have S&G expertise

Training centers needed

Truely focused studies on mechanisms of S&G are not included here

Example for mechanistic studies: developing a concept for gender

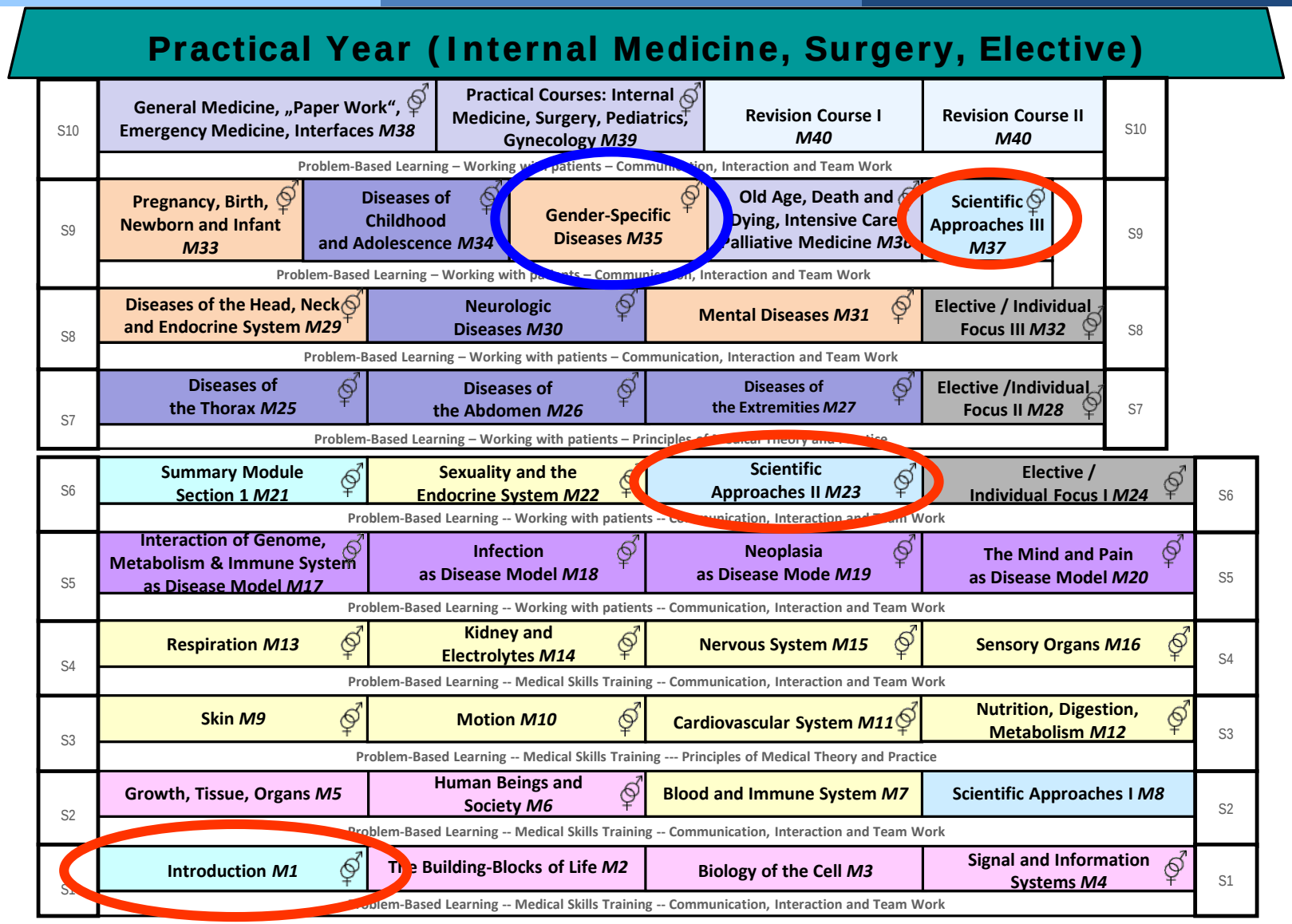
Gender distribution in men and women with premature acute coronary syndrome.



Sex als and Gender are associated with cardiovascular risik faktors

L Pilote, Psychosomatic medicine 2015

Modular Medical Curriculum at Charité: Integration of gender and sex aspects



Herzlich Willkommen auf unserer interaktiven, web-basierten Plattform eGENDER!

eGendermedizin

Nutzen Sie den vom Institut für Geschlechterforschung in der Medizin (GIM) - Charité-Universitätsmedizin Berlin entwickelten eLearning Kurs "eGendermedizin" für ihre persönliche Weiterbildung unabhängig von Zeit und Ort. Ziel des Kurses ist es, die aus Grundlagen- und klinischer Forschung systematisch erarbeiteten Kenntnisse zu Geschlechterunterschieden in der Medizin für die Praxis nutzbar zu machen.

Die Beachtung von Geschlechterunterschieden als ein Qualitätsmerkmal in der Medizin ist zunehmend anerkannt. Die sozialkulturelle Dimension "Geschlecht", im Englischen "Gender" integriert Einflüsse des Lebensstils, der Umgebung, von Stressfaktoren und genetischen Variabeln und ist nicht leicht durch andere Parameter zu ersetzen.

Zusammen mit international anerkannten Expertinnen der Gendermedizin hat die Autorin interessante und höchst relevante Inhalte aus den großen Fachdisziplinen der Inneren Medizin zusammengetragen und didaktisch aufgearbeitet.

Lernen lebt auch vom Dialog mit interessierten Kolleginnen und Kollegen. Daher bieten wir Ihnen über unsere "Kommunikationstools" Möglichkeiten zur Diskussion und online Zusammenarbeit. Wir wünschen uns, dass sich über die inhaltliche Arbeit eine aktive Fachgesellschaft Gendermedizin entwickelt mit dem Ziel die Gesundheitsversorgung für Frauen UND für Männer weiter zu verbessern.

Welcome to this interactive, web based eLearning platform eGENDER!

eGender Medicine

Use the eLearning course eGender Medicine for your personal education in Gender Medicine. You are independent of place and time. The Institute of Gender in Medicine (GIM) - Charité University Medicine Berlin developed this advanced training course based on systematic analysis of gender differences in basic and clinical research. Doctors should be able to integrate these concepts into clinical medicine and use the sex perspective for assessment in their daily practice.

Awareness of gender differences is nowadays accepted as a quality parameter in medicine. The term "gender" integrates behavioural, life style, environmental and stress factors as well as genetic variables and is not easy to replace by other parameters.

The author reviewed and worked up most interesting material of major medical disciplines based on the European curriculum of "Gender Medicine" provided by internationally renowned experts of Gender Medicine.

Social contacts to other students and experts are intended to being intensified with the possibility to use "communicative tools" like forum, chat and WIKI. This is exactly what we desire to support an active "gender medicine community"! "Gender Medicine" is a new and challenging research field of medicine that aims to assure an improved health care for both women and men around the world.

GEFÖRDERT VOM
Bundesministerium für Bildung und Forschung

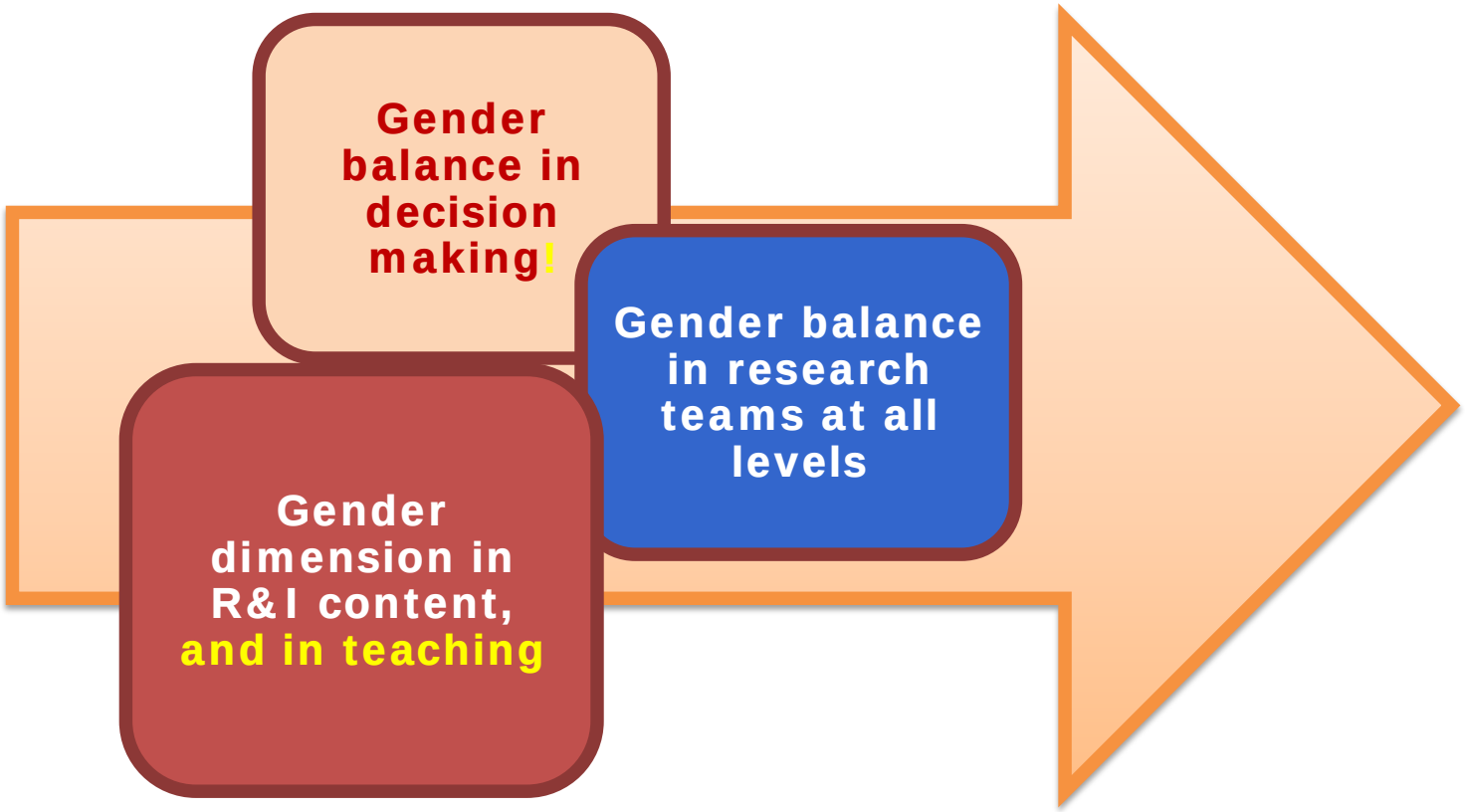
eLearning Kurs deutsch

eLearning course english

EUROPEAN Gender Medicine

How to organize research?

Horizon 2020 Gender Equality provisions



Danksagung

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Med Fakultät Innsbruck
Margrethe Hochleitner

Frau Margarethe Ammon

DFG Deutsche Forschungsgemeinschaft
DZHK DEUTSCHES ZENTRUM FÜR HERZ-KREISLAUF-FORSCHUNG E.V.
Bundesministerium für Bildung und Forschung
BAYER