XI congresso nazionale

simeu

ROMA 24-26 MAGGIO 2018

La medicina di genere

Maria Pia Ruggieri

Direttore UOC PS e Breve Osservazione, AO San Giovanni Addolorata

- **MEDICINA TRADIZIONALE**:
impostazione **androcentrica** (salute femminile soli per aspetti specifici correlati alla riproduzione)

- **MEDICINA DI GENERE**:
approccio innovativo mirato a studiare l'impatto del genere e di tutte le variabili che lo caratterizzano (biologiche, ambientali, culturali e socioeconomiche) sulla fisiologia, sulla fisiopatologia e sulle caratteristiche cliniche delle malattie.

- 1991:
per la prima volta in letteratura la **"questione femminile"** (Healy, NEJM 1991)

The NEW ENGLAND JOURNAL of MEDICINE

The New England Journal of Medicine

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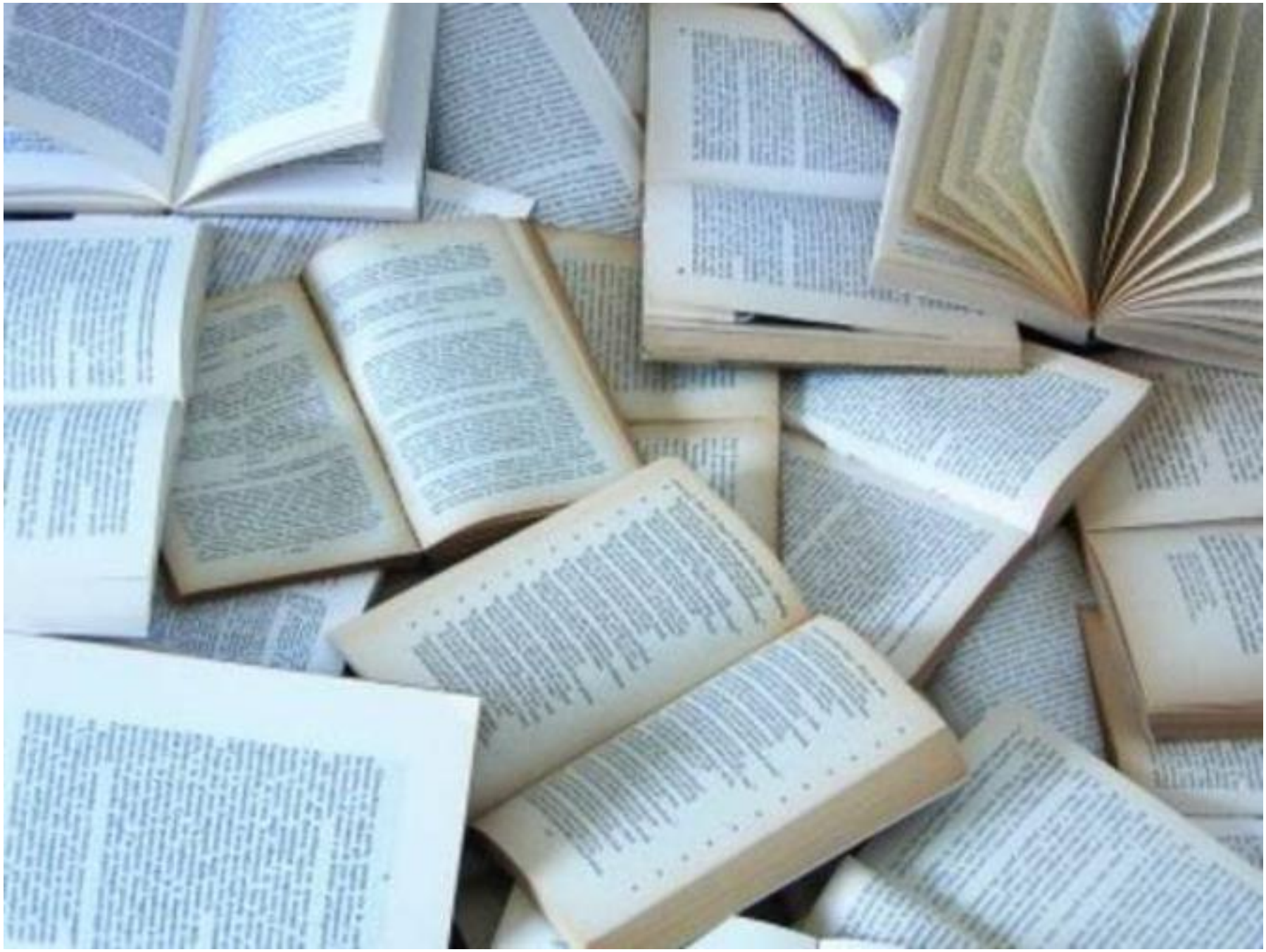
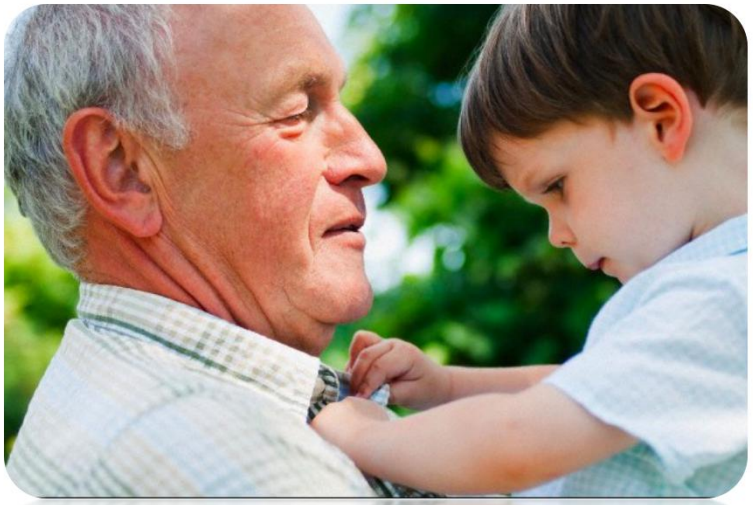
THE YENTL SYNDROME

YENTL, the 19th-century heroine of Isaac Bashevis Singer's short story,[1] had to disguise herself as a man to attend school and study the Talmud. Being "just like a man" has historically been a price women have had to pay for equality. Being different from men has meant being second-class and less than equal for most of recorded time and throughout most of the world. It may therefore be sad, but not surprising, that women have all too often been treated less than equally in social relations, political endeavors, business, education, research, and health care.



La Medicina di Genere

- Gli uomini e le donne, pur essendo soggetti alle medesime patologie, **presentano sintomi, progressione di malattie e risposta ai trattamenti molto diversi tra loro**.



- Da qui la necessità di porre attenzione allo studio del genere inserendo questa "nuova" dimensione della medicina in tutte le aree mediche.

- lo studio sulla salute della donna non è più circoscritto alle patologie esclusivamente femminili che colpiscono mammella, utero e ovaie, ma rientra nell'ambito della medicina genere-specifica ***(il bambino non è un piccolo adulto, la donna non è la copia dell'uomo e l'anziano ha caratteristiche ancora diverse)***

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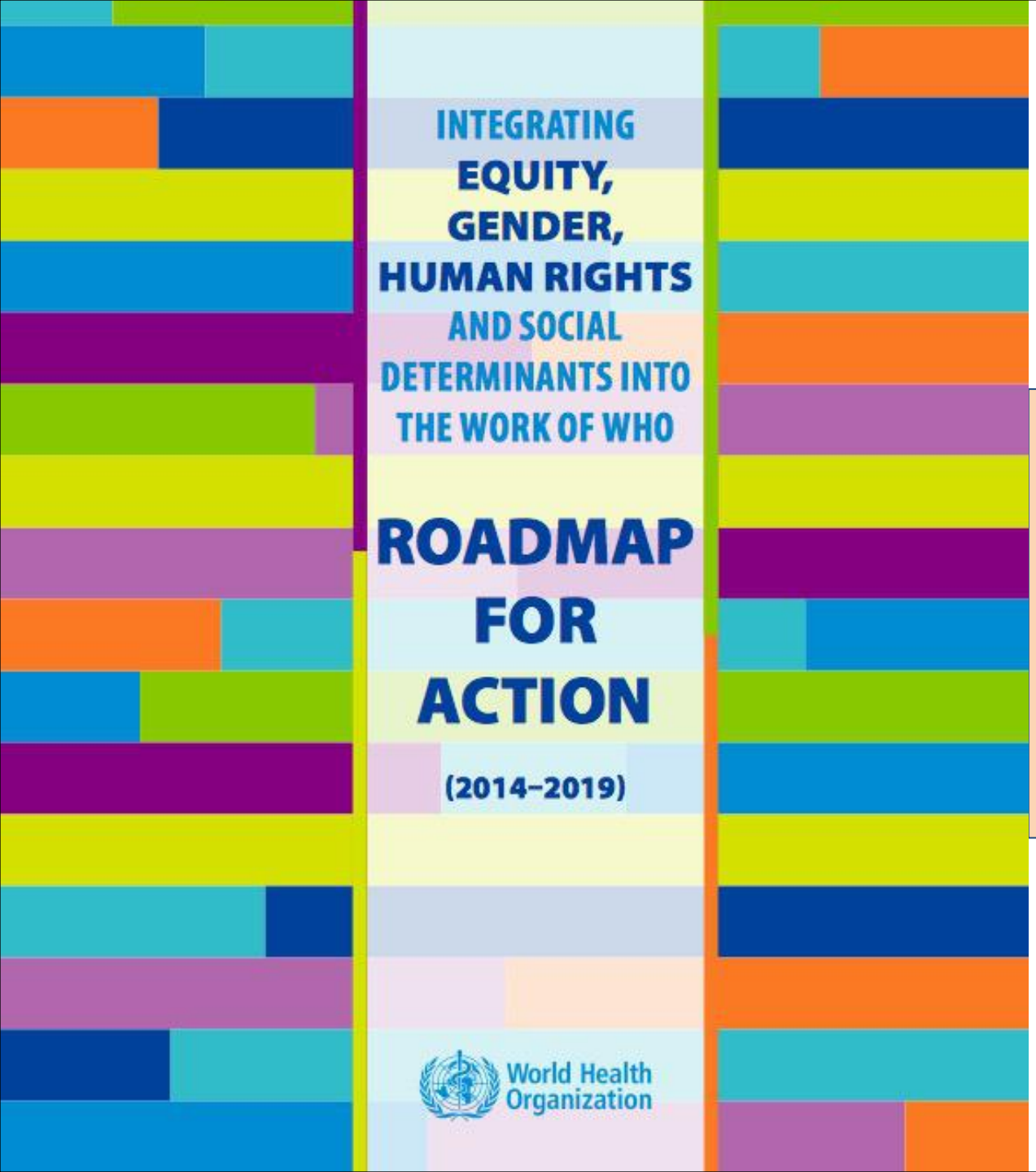

Politica della WHO:
il monitoraggio delle diseguaglianze e la revisione delle politiche sanitarie, dei programmi e dei piani delle singole Nazioni, finalizzati ad assicurare gli outcomes di salute nel mondo

Numerose Organizzazioni e Istituzioni dedicano all'argomento importanti Progetti di ricerca e finanziamenti

Attualmente, a livello sia nazionale sia internazionale, le pubblicazioni di studi clinici "Gender oriented" sono molteplici e di alto valore scientifico ma, nonostante le consolidate evidenze, **le linee guida disponibili nelle varie discipline ancora non inseriscono nei percorsi gestionali delle patologie il determinante "genere".**

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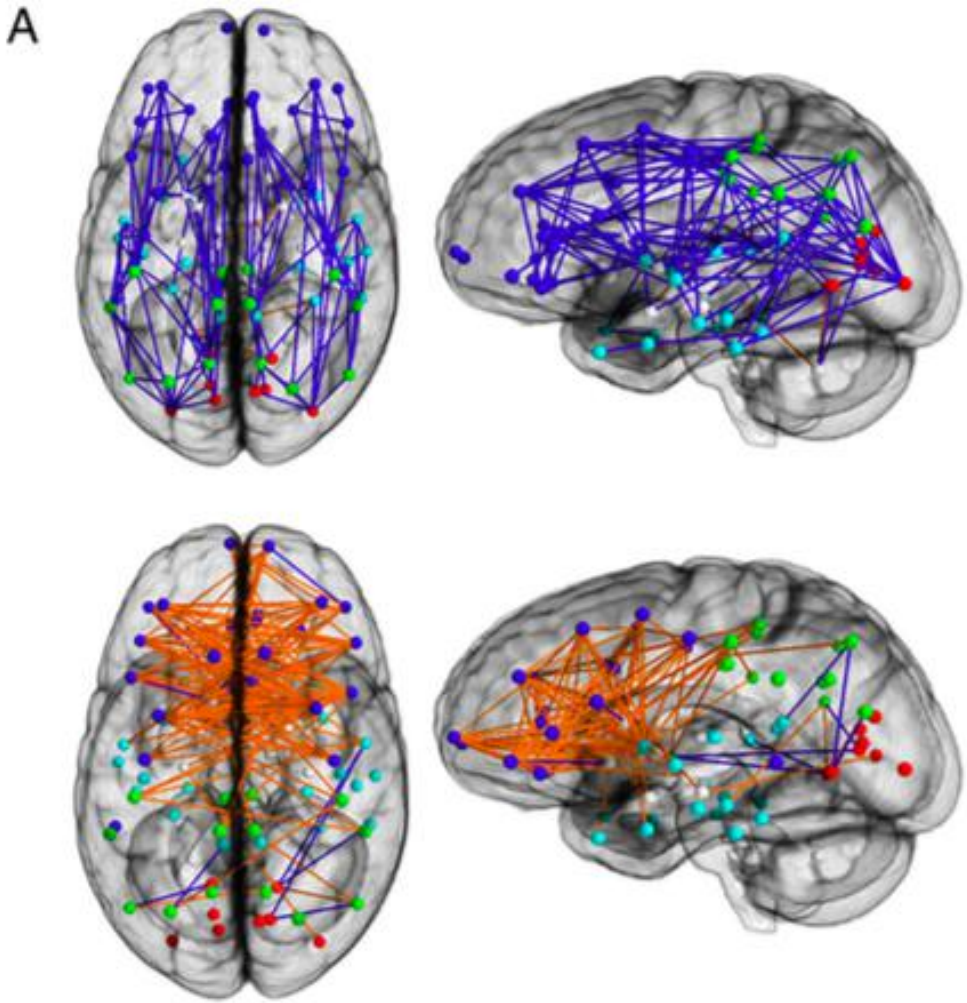
Alcune delle numerose prove...

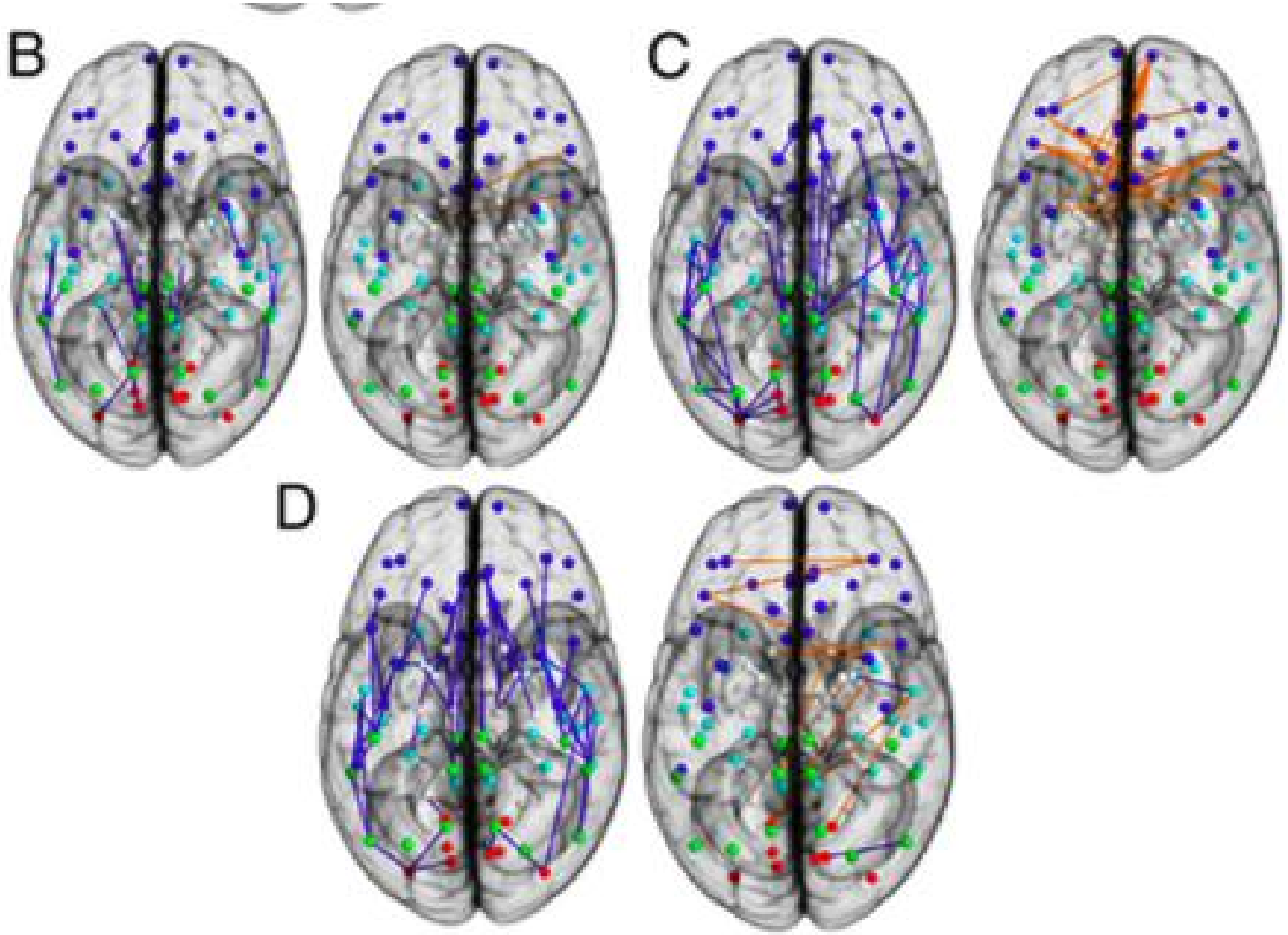
Sex differences in the structural connectome of the human brain

Madhura Ingalhalikar[a,1], Alex Smith[a,1], Drew Parker[a], Theodore D. Satterthwaite[b], Mark A. Elliott[c], Kosha Ruparel[b], Hakon Hakonarson[d], Raquel E. Gur[b], Ruben C. Gur[b], and Ragini Verma[a,2]



Università della Pennsylvania a Filadelfia

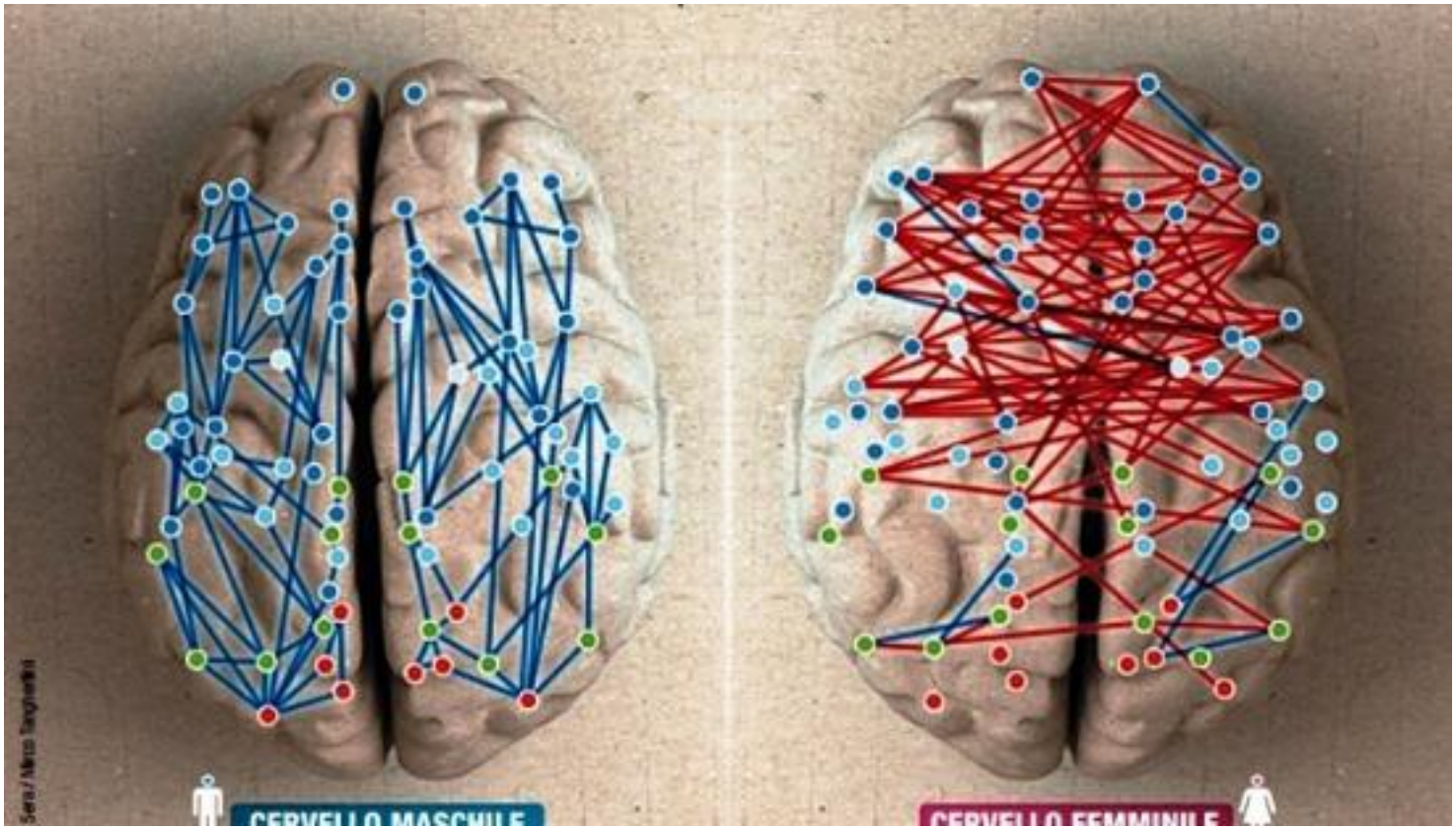
PNAS | January 14, 2014 | vol. 111 | no. 2 | 823–828



B: bambini

C: adolescenti

D: giovani adulti



I modelli di connettività del cervello **maschile** conferiscono ai maschi un sistema di coordinamento fra esperienze percettive e azione più efficiente, mentre i modelli di connettività dei cervelli **femminili** facilitano l'integrazione delle modalità di ragionamento analitico e sequenziale dell'emisfero sinistro con quelle spaziali e intuitive dell'emisfero destro.

Università della Pennsylvania a Filadelfia.“Proceedings of the National Academy of Sciences”, Ragini Verma et al

Differenze di sesso: geni

RESEARCH Open Access

Characterization of whole-genome autosomal differences of DNA methylation between men and women

1184 CpG sites differentially methylated between men and women, distributed across all autosomes;

the differentially methylated loci are enriched among imprinted genes;

some of the differentially methylated loci also exhibit differential gene expression between men and women.

XI congresso nazionale simeu ROMA 24-26 MAGGIO 2018

Singmann P et al Epigenetics and Chromatin. 2015;8:43

Gender-associated differences in plaque phenotype of patients undergoing carotid endarterectomy

Willem E. Hellings, MD,[a,b] Gerard Pasterkamp, MD, PhD,[b] Bart A. N. Verhoeven, MD, PhD,[a] Dominique P. V. De Kleijn, PhD,[b] Jean-Paul P. M. De Vries, MD, PhD,[c] Kees A. Seldenrijk, MD, PhD,[d] Theo van den Broek, MD,[b] and Frans L. Moll, MD, PhD,[a] *Utrecht and Nieuwegein, The Netherlands*

Table II. Comparison of carotid plaque histology between men and women

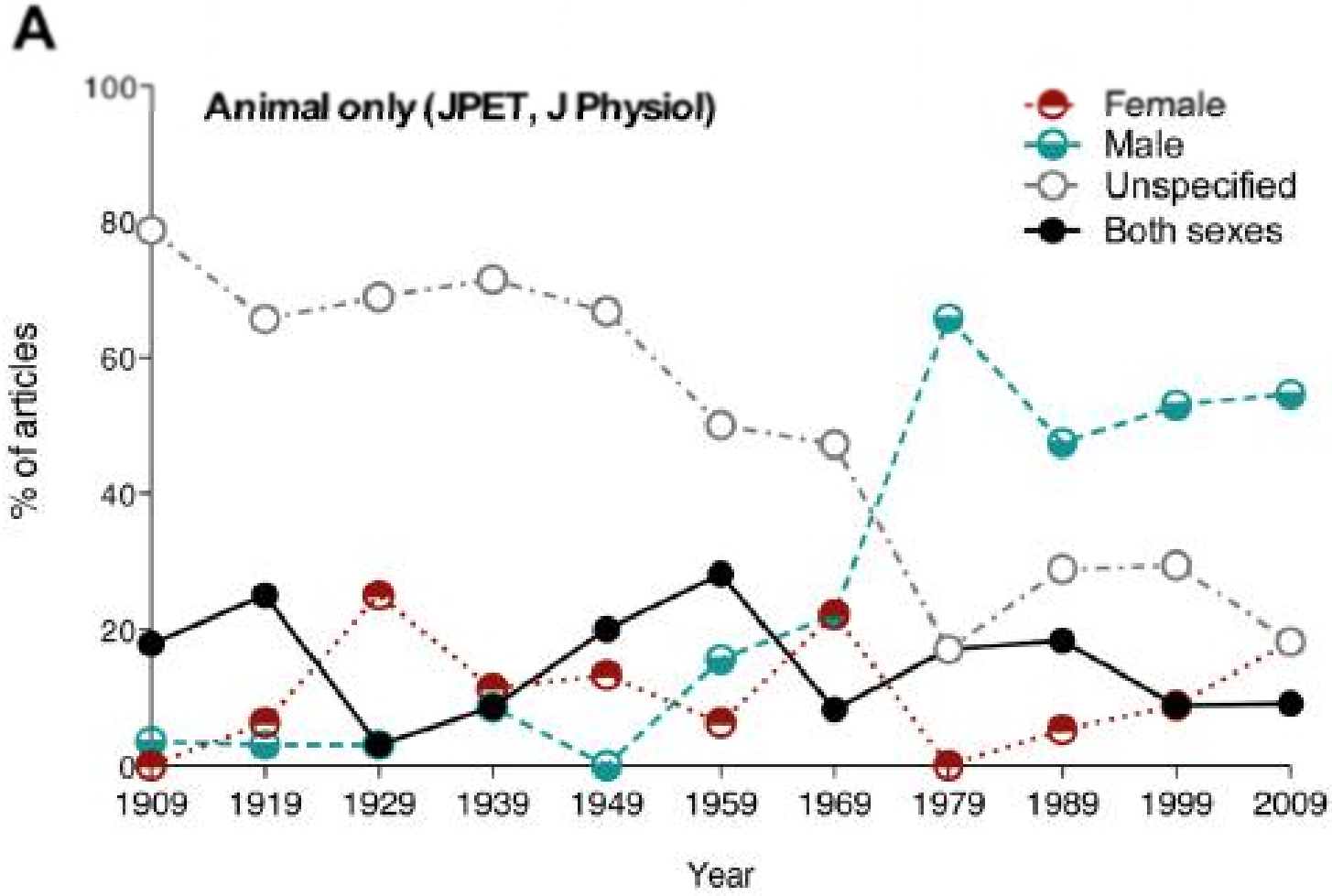
	Women (%)*	*Men* (%)*	P *(univariate)*	P *(multivariate)*[†]
Overall phenotype (semi-quantitative)			<.001[‡]	.006[‡]
Fibrous	40.7	24.4		
Fibroatheromatous	37.8	35.2		
Atheromatous	21.5	40.3		
Luminal thrombus			.26	.45
No	77.0	70.6		
Yes	23.0	29.4		
Macrophages (semi-quantitative)			.05[†]	.20
No	18	10.6		
Minor	31.6	33.2		
Moderate	36.8	35.2		
Heavy	13.5	21		
Macrophages (quantitative)			.12	.36
Median area %	0.26	0.39		
IQR	(0.08-0.95)	(0.07-1.30)		
SMC (semi-quantitative)			.001[‡]	.01[‡]
No	0.8	1.9		
Minor	20.3	32.9		
Moderate	41.4	41.9		
Heavy	37.6	24.2		
SMC (quantitative)			.03[‡]	.03[‡]
Median area %	2.27	1.62		
IQR	(0.86-4.35)	(0.47-3.58)		
Collagen (semi-quantitative)			.08	.39
No	0.0	0.3		
Minor	19.4	22.6		
Moderate	53.0	57.6		
Heavy	27.6	19.4		
Calcifications (semi-quantitative)			.41	.88
No	29.6	25.7		
Minor	15.6	24.8		
Moderate	28.9	31.1		
Heavy	25.9	18.4		

Carotid endarterectomy specimens of 450 consecutive patients (135 women, 315 men) were studied (75% sympt).
The main finding of this study is that women undergoing CEA have more stable plaques compared with men.
Plaques obtained from women contain less fat & macrophages and more smooth muscle cells.
This is accompanied by lower IL-8 content and lower MMP-8 activity.

Hellings WE et al. J Vasc Surg 2007;45:289-97.

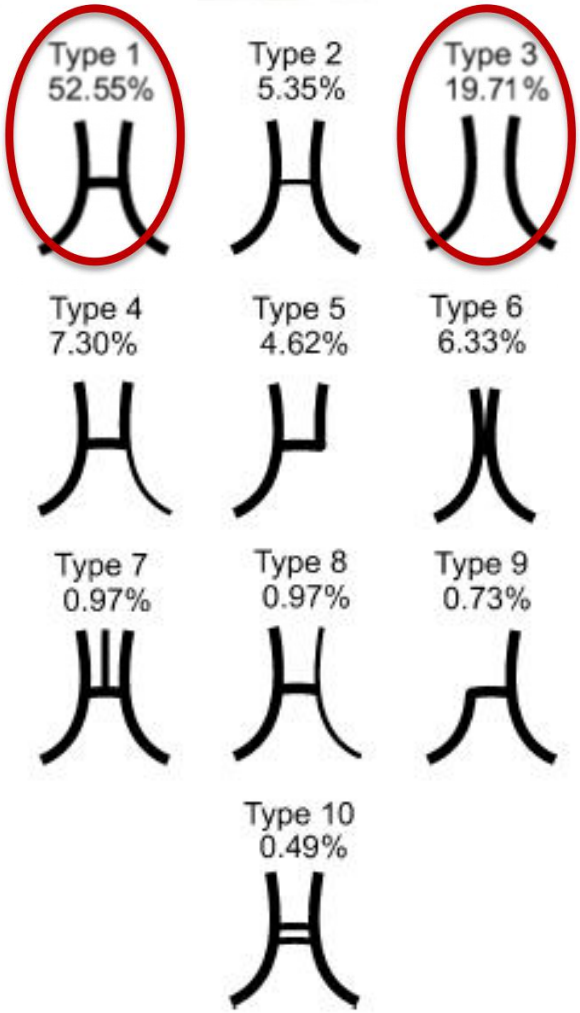
Males still dominate animal studies

Nature **465**, 690 (10 June 2010)



Beery AK et al. Neurosci Biobehav Rev. 2011;35(3):565

Differenze di sesso: anatomia



Type	Total ($n = 411$)	Female ($n = 215$)	Male ($n = 196$)	p value
1 (%)	216 (52.55)	99 (46.05)	117 (59.69)	<0.01
2 (%)	22 (5.35)	15 (6.98)	7 (3.57)	0.12
3 (%)	81 (19.71)	50 (23.26)	31 (15.88)	0.04
4 (%)	30 (7.30)	15 (6.98)	15 (7.65)	0.81
5 (%)	19 (4.62)	12 (5.58)	7 (3.57)	0.33
6 (%)	26 (6.33)	14 (6.51)	12 (6.12)	0.86
7 (%)	4 (0.97)	4 (1.86)	0 (0.00)	0.05
8 (%)	4 (0.97)	4 (1.86)	0 (0.00)	0.05
9 (%)	3 (0.73)	2 (0.93)	1 (0.51)	0.61
10 (%)	2 (0.49)	0 (0.00)	2 (1.02)	0.13
Unclassified	4 (0.97)	0 (0.00)	4 (2.04)	0.03

Krzyzewski RM et al. Surg Radiol Anatom. 2015;37:81:86

Differenze di sesso: fattori di rischio convenzionali

FA

le donne con AF non anticoagulate presentano un tasso annuale di eventi tromboembolici significativamente più elevato rispetto agli uomini (3.5% vs. 1.8%; 95% CI 1.3-1.9) *(Lip GYH et al. Europace. 2014 Jun 22)*

Ipertensione

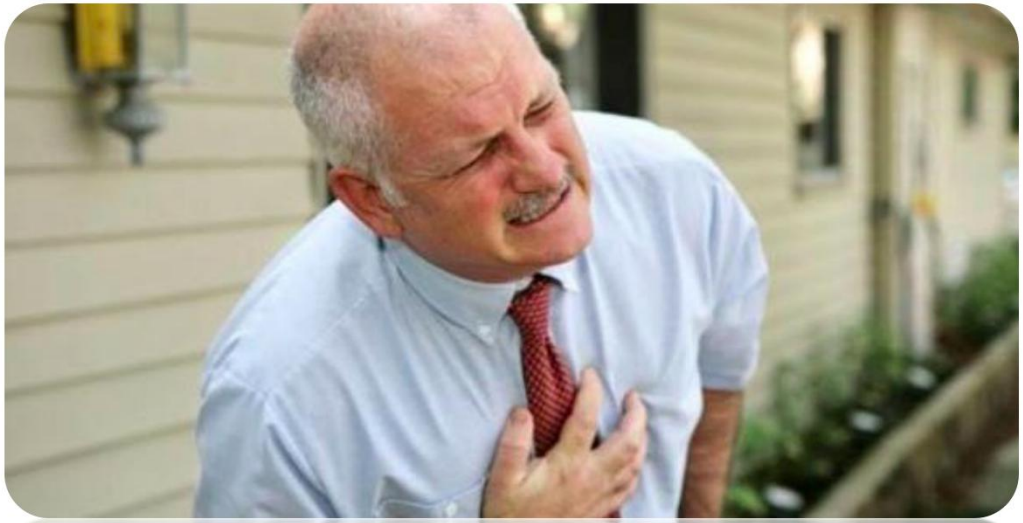
Higher prevalence at older age (65aa) *(Roger VL et al. Circulation 2012; 125:e2–e220).*

Higher association with strokes, LVH, and diastolic heart failure *(Gorgui J et al. Canadian Journal of Cardiology 2014; 30: 774 e782)*

Diabete

in significativo aumento nella donna parallelamente all'aumento di prevalenza di obesità e sovrappeso *(Diabetes Care 2005; 28:514–20)*

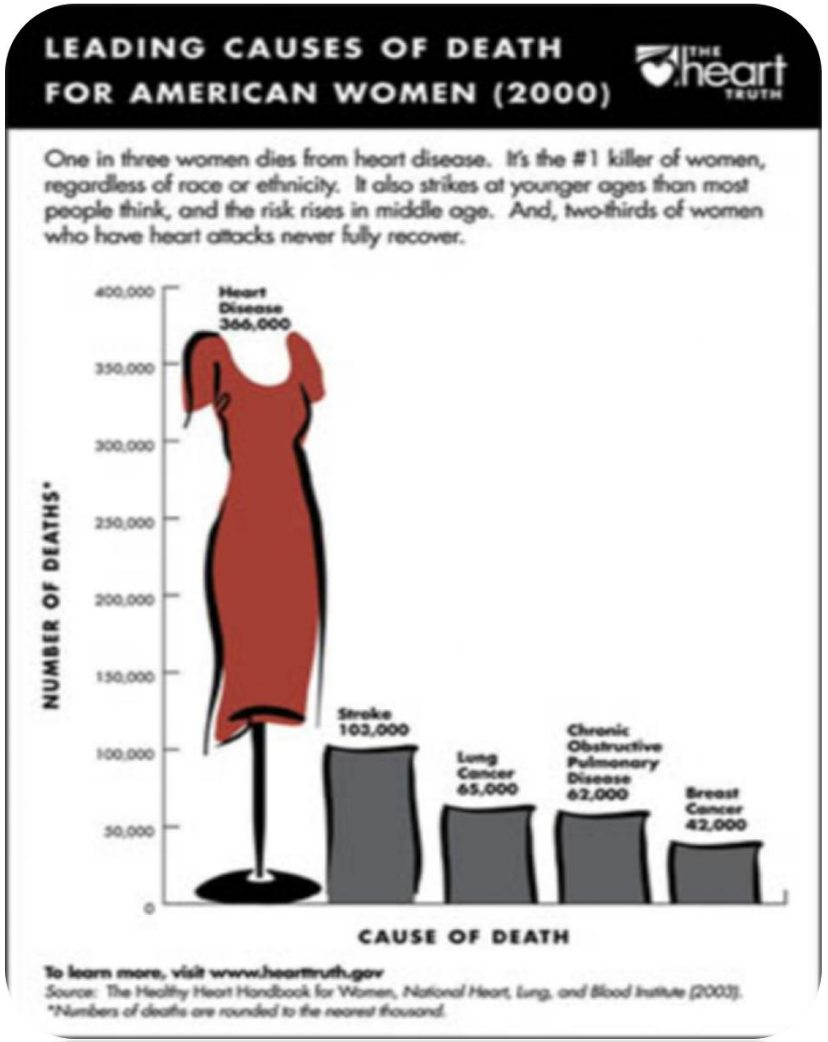
In urgenza?



Il MITO:
la coronaropatia è una patologia "maschile"

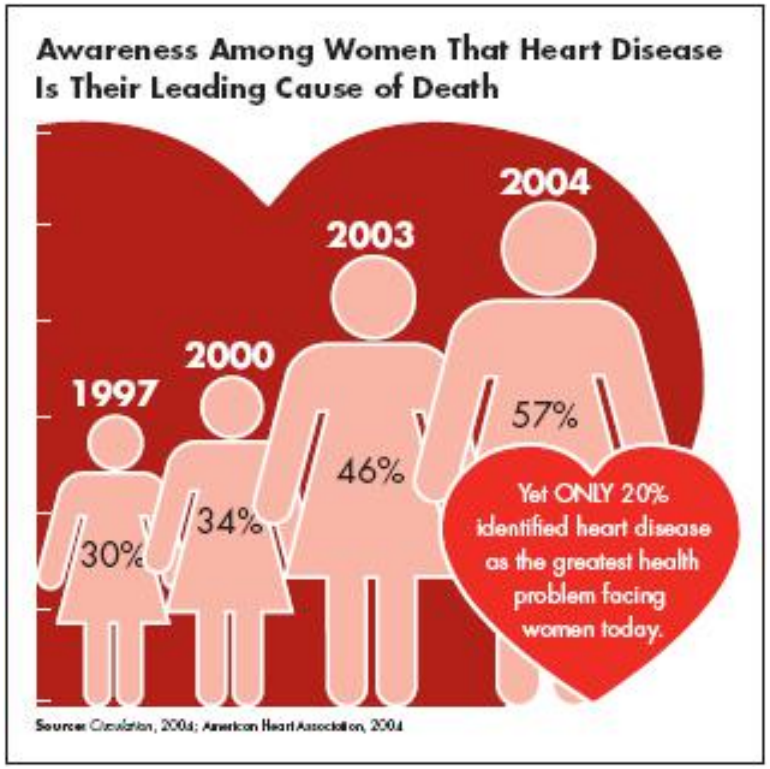
La realtà:

Heart Disease #1 killer of US women



www.hearttruth.gov

Who Knew?



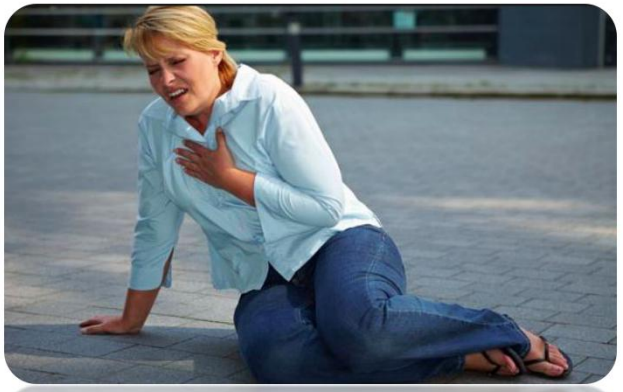
- 80% American women did not

AMWA Gallop Survey 1995

In Italia

- In Italia, la mortalità per malattie cardiovascolari (cardiache e cerebrali) è **del 48,4% nelle donne e del 38,7% negli uomini**
- La **prima causa di morte della donna in tutti i Paesi industrializzati è l'infarto del miocardio**
- L'ictus colpisce maggiormente la donna dell'uomo (+55%)
- Lo scompenso cardiaco ha caratteristiche diverse nella donna e colpisce nella terza età più donne che uomini

Cardiopatia ischemica nel genere "donna"



- aumenta con l'età;
- ha un ritardo di 10 anni rispetto all'uomo;
- in fase acuta, dopo 6 mesi dall'infarto e dopo 6 anni dalla rivascolarizzazione, ha mortalità maggiore;
- prevalenza di dolore atipico (con conseguente ritardo di accesso al PS);
- minor numero di CVG, stent, PTCA, BPAC;
- la terapia farmacologica alla dimissione è spesso meno completa;
- più ampia ipocinesia dell'area infartuata e maggiori aritmie;
- 90% di rottura di cuore come complicanza;
- la dissezione coronarica con conseguente SCA è più frequente nella donna giovane, spesso in epoca peripartum;
- la sindrome di Tako-Tsubo (tipica alterazione della cinetica ventricolare con acinesia medio-apicale con coronarie indenni ma rialzo degli enzimi di miocardio lisi) è tipica.

Risk Factors for Coronary Heart Disease

For both men and women

- Smoking
- Diabetes
- High Cholesterol (in particular high LDL and/or low HDL)
- High Blood Pressure
- Obesity
- Sedentary Lifestyle

For women only

- Menopause
- Birth Control Pills in Combination with Smoking

The New England
Journal of Medicine

VOLUME 341 JULY 22, 1999 NUMBER 4

SEX-BASED DIFFERENCES IN EARLY MORTALITY AFTER MYOCARDIAL INFARCTION

VIOLA VACCARINO, M.D., PH.D., LORI PARSONS, B.S., NATHAN R. EVERY, M.D., M.P.H., HAL V. BARRON, M.D., AND HARLAN M. KRUMHOLZ, M.D., FOR THE NATIONAL REGISTRY OF MYOCARDIAL INFARCTION 2 PARTICIPANTS*

Conclusioni Abbiamo riportato una significativa interazione tra il sesso e l'età rispetto alla mortalità a breve termine dopo infarto miocardico.
Il tasso di mortalità tra le donne di età inferiore ai 75 anni di età è stato doppio rispetto a quello tra gli uomini in quella fascia di età, mentre non abbiamo riscontrato differenze nella mortalità tra i pazienti più anziani.
L'età ha un effetto significativo sulla mortalità a breve termine dopo infarto miocardico e di determinare le ragioni di questo effetto. Abbiamo ipotizzato che più giovani sono i pazienti, più alto è il rischio di morte durante l'ospedalizzazione tra le donne rispetto agli uomini.

Mortalità intraospedaliera dopo IMA in differenti classi di età in U e D

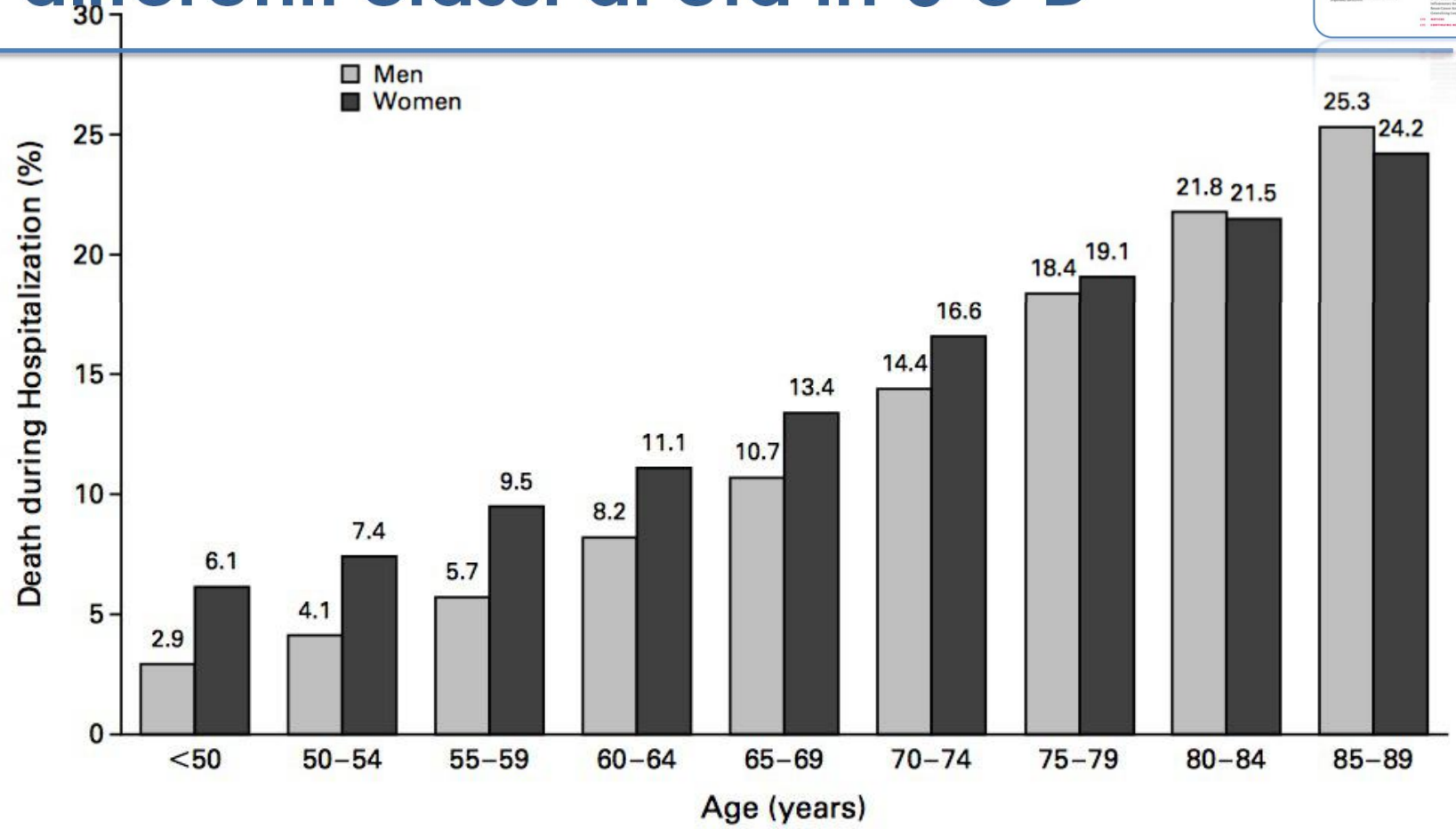
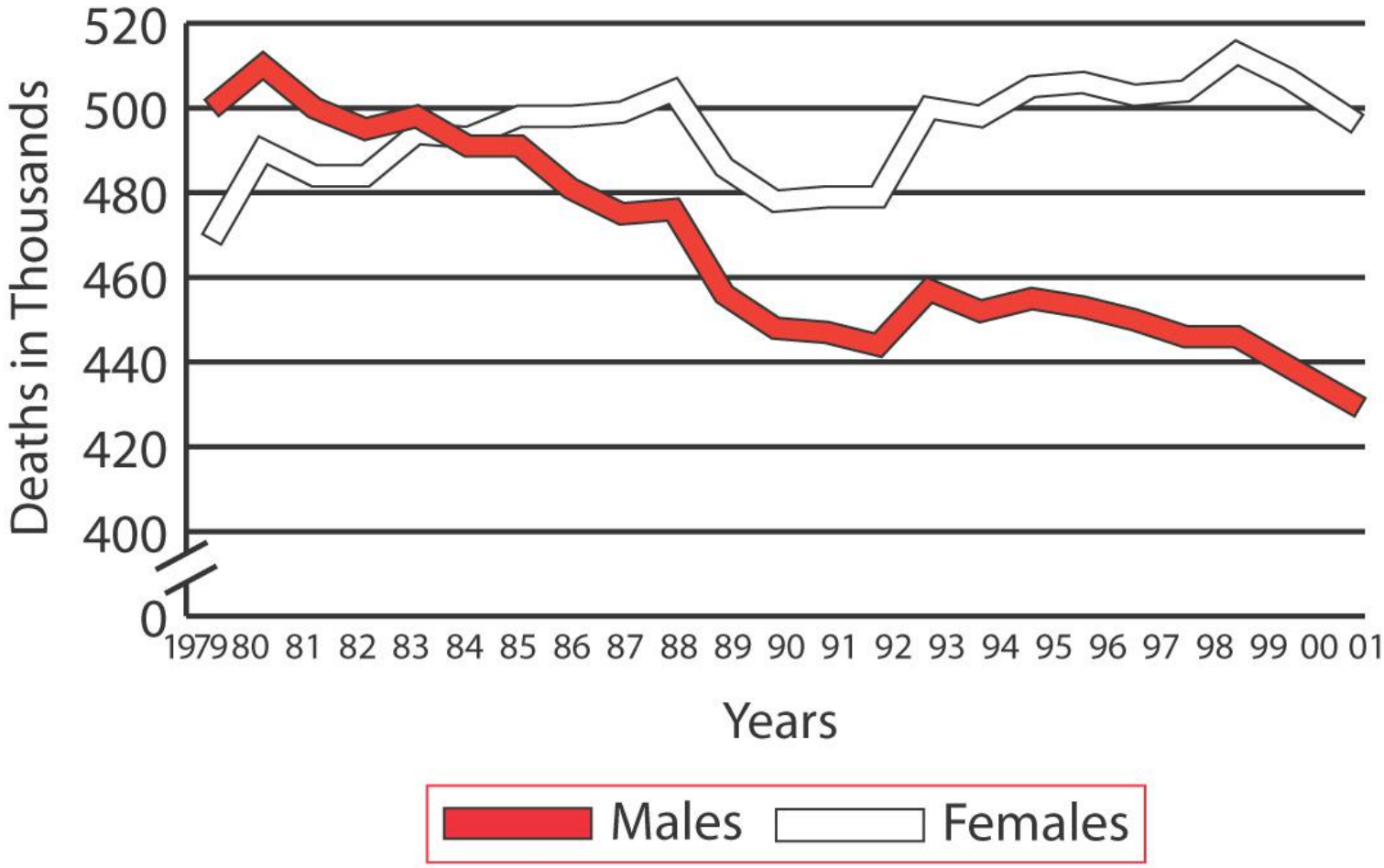


Figure 1. Rates of Death during Hospitalization for Myocardial Infarction among Women and Men, According to Age. The interaction between sex and age was significant ($P<0.001$).

Le donne, fino a 70 anni di età, hanno una maggiore mortalità rispetto ai coetanei maschi. Dopo i 75 anni, la tendenza si inverte

Cardiovascular Disease Deaths: Trends for Males and Females. United States: 1979-2001

Source: CDC/NCHS © AHA, 2004



The Three Paradoxes

1. Women have a higher prevalence of angina compared to men, yet have an overall lower prevalence of atherosclerosis and obstructive coronary artery disease

2. Symptomatic women undergoing coronary angiography have less extensive and severe CAD, despite being older with a greater risk factor burden, compared to men

3. Despite relatively less CAD, women have a more adverse prognosis compared to men

Bairey Merz, C. N. Women and Ischemic Heart Disease. JACC: Cardiovascular Imaging Vol 4, No 1, 2011.

Perhaps the most important risk factor for coronary heart disease is the misperception that coronary heart disease is a men's disease!

European Heart Journal (2011) 32, 1362–1368
doi:10.1093/eurheartj/ehr048

REVIEW

Red alert for women's heart: the urgent need for more research and knowledge on cardiovascular disease in women

Proceedings of the Workshop held in Brussels on Gender Differences in Cardiovascular disease, 29 September 2010

Angela H.E.M. Maas[1]*, Yvonne T. van der Schouw[2], Vera Regitz-Zagrosek[3], Eva Swahn[4], Yolande E. Appelman[5], Gerard Pasterkamp[6], Hugo ten Cate[7], Peter M. Nilsson[8], Menno V. Huisman[9], Hans C.G. Stam[10], Karin Eizema[10], and Marco Stramba-Badiale[11]

[1]Department of Cardiology, Isala Klinieken, Groot Wezenland 20, 8011JW, Zwolle, The Netherlands; [2]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands; [3]Center for Gender in Medicine and Cardiovascular Disease in Women and Cardiovascular Research Center Berlin, Berlin, Germany; [4]Department of Cardiology, University Linköping, Linköping, Sweden; [5]Department of Cardiology, VU Medical Center, Amsterdam, The Netherlands; [6]Department of Experimental Cardiology, University Medical Center Utrecht, Utrecht, The Netherlands; [7]Department of Internal Medicine and Biochemistry, University Maastricht, Maastricht, The Netherlands; [8]Department Clinical Sciences, Lund University Hospital, Malmö, Sweden; [9]Department of General Internal Medicine-Endocrinology, Leiden University Medical Center, Leiden, The Netherlands; [10]Netherlands Heart Foundation, The Hague, The Netherlands; and [11]Department of Rehabilitation Medicine, IRCCS Istituto Auxologico Italiano, Milan, Italy

Received 22 November 2010; revised 17 January 2011; accepted 2 February 2011; online publish-ahead-of-print 15 March 2011

A recent report of the EuroHeart project has shown that women are still underrepresented in many cardiovascular clinical trials, while important gender differences are present within most areas of heart disease. As the burden of cardiovascular disease is increasing in middle-aged women relative to men, a more profound understanding is needed of the fundamental biological differences that exist between men and women. In the current review, we aim to address the need for more explanatory sex-specific cardiovascular research to be able to adapt existing guidelines for a better heart health in women.

Keywords Atherosclerosis • Gender • Hormones • Risk factors • Women

Cardiovascular health needs more female-specific attention

The economic burden of cardiovascular disease (CVD) in Europe is progressively expanding with an increase in the incidence of obesity and diabetes, due to low adherence to a healthy lifestyle and poor control of CVD risk factors.[1] The risk of heart disease in women has been underestimated in the past due to the misperception that females are 'protected' against CVD.[2] Although clinical manifest CVD develops 7–10 years later in women than in men, it is the major cause of death in women older than 65 years of age (*Figure 1*). According to the latest World Health Organization (WHO) statistics the burden of CVD will increase further to 2030 and a large part of disability-adjusted life years (DALYs) will involve inhabitants of the Eastern and Central European Countries and in the developing countries such as Asia, Latin-America, and the Middle-East.[3] In *figure 2* world-wide DALYs in women >45 years are represented according to diseases and income level. Recent data from the National Health and Nutrition Examination Surveys (NHANES) have shown that over the past two decades the prevalence of myocardial infarctions has increased in midlife (35–54 years) women, while declining in similarly aged men.[4] Parallel with the rise in blood pressure and cholesterol levels after menopause there is almost a doubling in the prevalence of stroke among middle-aged women. As was demonstrated across Europe in the EUROASPIRE III survey,

* Corresponding author. Tel: +31 38 4242198, Fax: + 31 38 4243222, Email: amaas@diagram-zwolle.nl

Table 2 Gender differences in cardiovascular disease

Subject	Important aspects in women (relative to men)
Epidemiology	7–10 years later onset cardiovascular disease More DALYs lost to cardiovascular disease at older age
Atherosclerosis	Inflammation and oxidative stress Lower atheroma burden at younger ages (<65 years) Oestrogens involved in plaque composition/vascular function Vascular dysfunction and small vessel disease ACS with 'normal' or non-obstructive CAD More plaque erosions than plaque ruptures at ACS
Heart failure	Hypertension and diabetes main causes of heart failure Predominant heart failure with preserved LVEF Ageing women more LVH (men more fibrosis)
Thrombosis	Changes platelet activity, coagulation factors, fibrinolytic activity related to hormonestatus pre-/post-menopause, pregnancy, etc. Bleeding complications after interventions Increased risk thrombosis with AF
Risk factors	Hypertension Higher prevalence at older age Higher association with strokes, LVH, and diastolic heart failure Diabetes >50% higher CVD mortality Diffuse atherosclerosis, higher co-morbidity Independent risk factor for heart failure Lipids Low HDL and elevated TG more related to CVD Increase total cholesterol and LDL-C after menopause
Sex-related risk factors	Pregnancy-related hypertension and gestational diabetes Hormonal dysfunction pre-menopause/PCOS/POF Menopause
Life-style and psychosocial factors	Smoking <55 years higher risk ACS Obesity/physical inactivity Anxiety/stress Lower socio-economic status
Diagnosis	Differences in symptom presentation/communication More angina with less obstructive CAD Lower sensitivity and specificity non-invasive testing
Therapy	Gender differences effectivity/interaction/side effects

Table 1 Strategies to improve perspectives of cardiovascular disease in women

Governmental support to encourage more cardiovascular research in women
Public health efforts to increase awareness cardiovascular disease risk in women
Development educational programmes on gender differences cardiovascular diseases
Standardized registration of gender differences in cardiovascular care
More interaction among various medical disciplines involved in women's health
More gender-specific analysis and higher enrolment of women in clinical trials
Use of appropriate study designs and statistical tools to detect gender effects
Improve sensitivity and specificity for symptom evaluation of cardiovascular disease in women
Provide gender-specific data in all guidelines on cardiovascular disease
Implementation of gender-specific strategies in clinical practice

REVIEW

Red alert for women's heart: the urgent need for more research and knowledge on cardiovascular disease in women

Proceedings of the Workshop held in Brussels on Gender Differences in Cardiovascular disease, 29 September 2010

Cardiovascular health needs more female-specific attention

Europace (2015) 17, 24–31
doi:10.1093/europace/euu155

Sex-related differences in presentation, treatment, and outcome of patients with atrial fibrillation in Europe: a report from the Euro Observational Research Programme Pilot survey on Atrial Fibrillation

Table 3 Interventions performed/planned at enrolment

	Whole cohort	Females	Males	*P*-value
N	3119	1260	1859	
Interventions performed/planned at enrolment				
Electrical cardioversion (%)	22.8	18.9	25.5	<0.0001
Pharmacological conversion (%)	24.7	28.2	22.4	0.0002
Catheter ablation for AF[a] (%)	7.4	6.7	7.9	0.1905
Pacemaker implantation (%)	4.7	5.4	4.2	0.1017
ICD implantation (%)	1.1	0.6	1.4	0.0569
AF surgery (%)	0.4	0.3	0.4	>0.9999

AF, atrial fibrillation.
[a]Catheter ablation for AF includes any ablation for AF treatment.

	Whole cohort	Women	Men	*P*-value
OAC	80.8%	79.8%	81.5%	0.3646

Lip GYH et al. Europace 2015;17:24-31

Gender Differences in Human Sepsis

Jörg Schröder, MD; Volker Kahlke, MD; Karl-Hermann Staubach, MD; Peter Zabel, MD; Frank Stüber, MD

Conclusions: In this prospective study, gender differences were confirmed in human sepsis, with a significantly better prognosis for women, which may be related to increased levels of anti-inflammatory mediators. The hypothetical different ratio of proinflammatory and anti-inflammatory mediators may be important for further therapeutic interventions in sepsis.

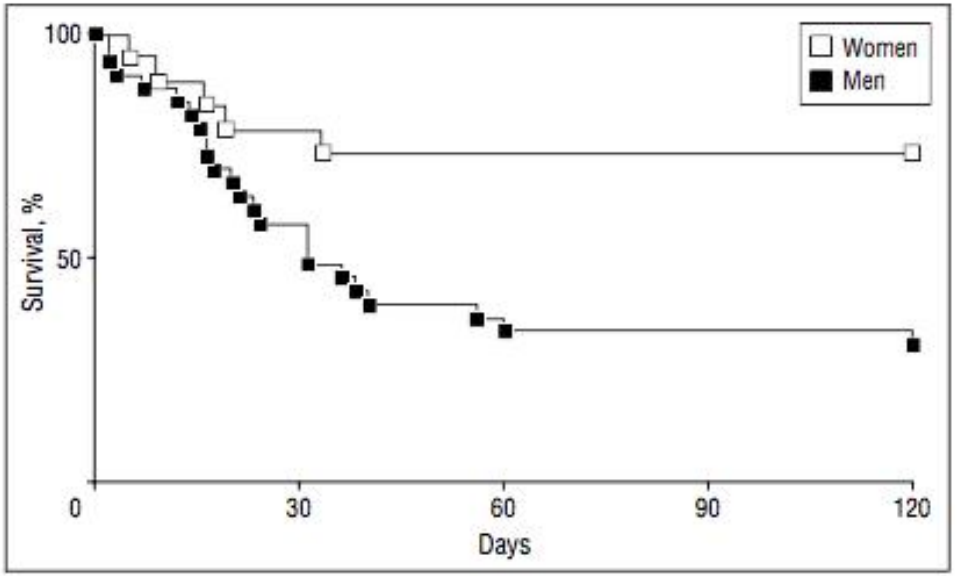
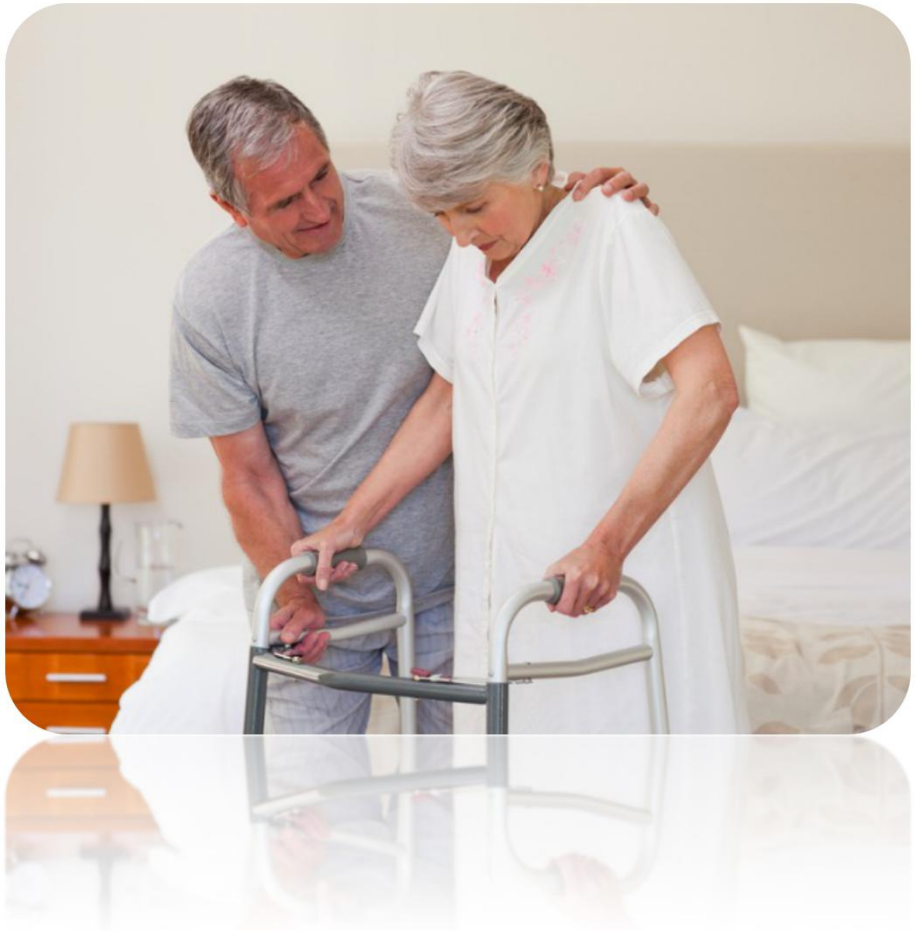


Figure 2. *Kaplan-Meier hospital survival analysis for female and male patients. Survival was significantly different between men and women with severe sepsis (P<.008 for hospital survival, log-rank test).*

ICTUS



European Journal of Internal Medicine 24 (2013) 167–171

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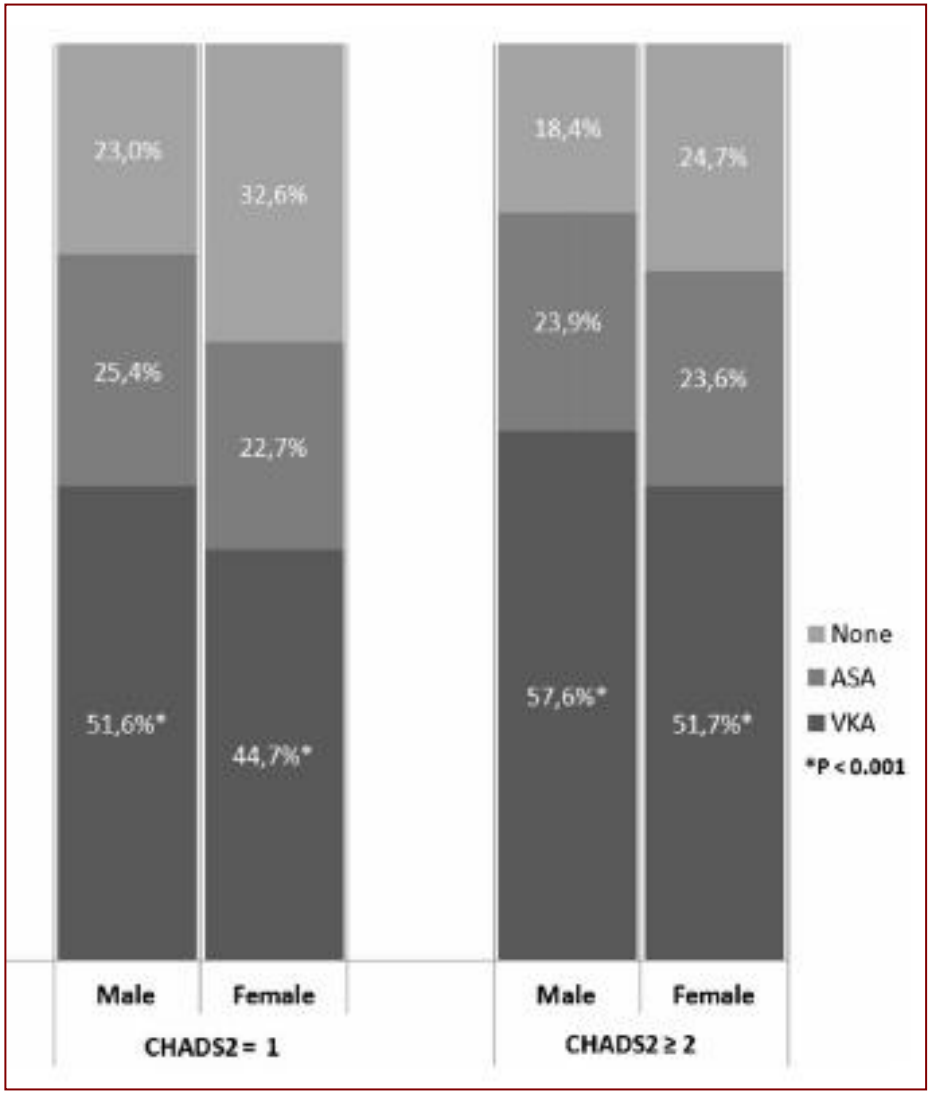
le donne sono più anziane all'esordio dell'ictus con gravità maggiore e hanno un esito funzionale peggiore rispetto agli uomini

Sex differences in stroke prevention in atrial fibrillation in French primary care. Results of the AFIGP (Atrial Fibrillation In General Practice) Database



Sabouret P et al. Clin Res Cardiol 2014;103:887-893

Comparison of stroke outcomes between male and female

il più alto rapporto mortalità per ictus è stato associato a 14 indicatori di diritti delle donne:

- differenze di genere nell'ottenere un lavoro
- differenza di genere nell'accesso al credito e apertura di un conto bancario
- esistenza della legislazione sulla violenza domestica
- disuguaglianze nel diritto alla proprietà

Items	n	mean ± SD	p
Can a married woman get a job in the same way as a married man?	No (n=18)	1 ± 0.2	0.003
	Yes (n=158)	0.9 ± 0.2	
Can a married woman choose where to live in the same way as a married man?	No (n=32)	1 ± 0.2	<0.001
	Yes (n=144)	0.9 ± 0.2	
Can a married woman be head of household or head of family in the same way as a married man?	No (n=34)	1 ± 0.2	0.044
	Yes (n=12)	0.9 ± 0.1	
Does the law prohibit discrimination by creditors on the basis of gender in access to credit?	No (n=131)	0.93 ± 0.2	0.002
	Yes (n=44)	0.85 ± 0.1	
Do protection orders for domestic violence exist?	No (n=51)	1 ± 0.2	<0.001
	Yes (n=125)	0.9 ± 0.2	
Is there domestic violence legislation?	No (n=46)	1 ± 0.2	0.033
	Yes (n=130)	0.9 ± 0.2	
Does domestic violence legislation cover emotional violence?	No (n=67)	1 ± 0.2	0.018
	Yes (n=125)	0.9 ± 0.2	
Are there civil remedies for sexual harassment in employment?	No (n=113)	0.94 ± 0.22	0.033
	Yes (n=63)	0.87 ± 0.13	
Do married men and married women have equal ownership rights to property?	No (n=17)	1.1 ± 0.2	0.001
	Yes (n=155)	0.9 ± 0.2	

Prevalenza dei fattori di rischio

Women are older at stroke onset[1-7]

and more likely to have:

- Atrial fibrillation[4,5,8,9]
- Hypertension[2,3,5,9]
- Dementia[2]
- Congestive heart failure[3]

1. Petrea RE et al. *Stroke* 2009;40;1032-1037
2. Kapral MK et al. *Stroke* 2005;36;809-814
3. Gargano JW et al. *Stroke* 2008;39;24-29
4. Reid JM et al. *Stroke* 2008;39;1090-1095
5. Di Carlo A et al. *Stroke* 2003;34;1114-1119

1. Appelros et al. *Stroke* 2009, 40:1082-1090
2. Eriksson M et al. *Stroke*. 2009;40:909-914
3. Niewada M et al. *Neuroepi*. 2005;24:123–128.
4. Silva GS et al. *Cerebrov Dis* 2010;30:470–475

Fattori di rischio propri del genere femminile

Oral contraceptive use

RR 2.75, 95% CI 2.24-33.8[1]

- combined hormonal contraception increased the risk of stroke 2.47-fold (95% CI 2.04–2.99)
- hormonal contraception is a very rare cause of ischaemic stroke and should be considered as such in clinical care

Pregnancy/peripartum period

Overall RR 2.4 (95% CI 1.6-3.6)[2]

- The rate of stroke is increased by **9 fold at the time of delivery** and **3 fold in the early postpartum period**, with an increase in the risk of both ischaemic and haemorrhagic stroke

1. Gillum LA et al. JAMA 2000;284;72-78
2. Kittner SJ, et al. N Engl J Med 1996;335:768-774.

Menopausa

The burden of risk factors for vascular dysfunction increases in women after the menopause, presumably owing to the **postmenopausal decrease in oestrogen,**
a hormone with vasoprotective properties

- Change in BMI, fat distribution, WC>80cm
- Inc LDL cholesterol
- Decreased HDL
- Increase TGs
- Blood pressure
- Glucose/insulin metabolism
- 4 fold increased risk CVD
- increased risk CHD

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Review article

Antiplatelet treatment in primary and secondary stroke prevention in women

Valeria Caso [a], Paola Santalucia [b,*], Monica Acciarresi [a], Francesca Romana Pezzella [c], Maurizio Paciaroni [a]

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Antiplatelet agents are claimed to be equally effective for both sexes in primary and secondary prevention of stroke, even though significantly fewer women have been studied in RCTs.

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aspirin has greater benefit in women for primary prevention of ischemic stroke without a significant increase of haemorrhage, while its **benefit in men is prevalent for primary prevention of MI, with a slight increase in the risk of haemorrhagic stroke**

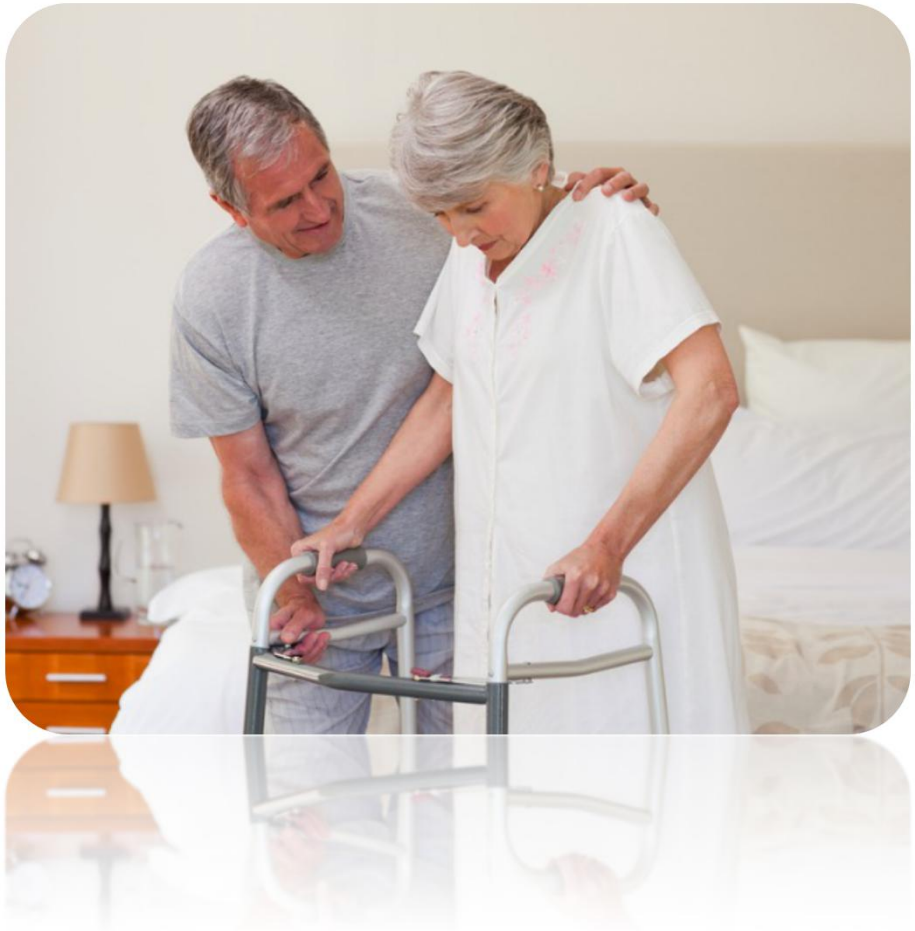
Nuovi Anticoagulanti Orali

- Dabigatran
- Rivoroxaban
- Apixaban
- Edoxaban

Nuovi Anticoagulanti Orali

	Ref.	Design	N° of patients	N° of women (%)	Mean or median age	Lenght of follow-up (median)	Risk factor
RE-LY (dabigatran 110mg or 150mg BID vs warfarin INR 2-3)	Connolly et al., 2009	RCT Double blind	18113	6599 (36.4%)	71.4 years	2 years	1 or more
ROCKET (rivaroxaban 20mg QD vs warfarin INR 2-3	Patel et al., 2011	RCT Double blind	14264	5663 (39.7%)	73 years	2 years	2 or more
AVERROES (apixaban 5mg BID vs ASA (81-324mg QD)	Connolly et al, 2011	RCT Double blind	5599	2319 (41%)	70 years	1 years	1 or more
ARISTOTLE (apixaban 5mg BID vs warfarin INR 2-3)	Granger et al., 2011	RCT Double blind	18201	6416 (35.2%)	70 yearS	1.8 years	1 or more
EDOXABAN (30 or 60mg QD vs warfarin INR 2-3)	Giugliano et al., 2013	RCT Double blind	21.105	8040 (38.1)	72 years	2.8 years	2 or more

FARMACOLOGIA di GENERE



Perché ridefinire le differenze farmacocinetiche e farmacodinamiche basate sul genere?

- ✓ Maggiori consumi di farmaci nelle donne
- ✓ Maggior frequenza di reazioni avverse
- ✓ Maggiori cambiamenti fisiologici
- ✓ Maggior frequenza di politerapia

Take Home Message

XI congresso nazionale
simeu
ROMA 24-26 MAGGIO 2018

Take home message

Quale link tra genere e personalizzazione delle cure?

Personalized medicine: use of biological information and aspects of patient-centered health care

Prevenzione:

fattori di rischio specifici

nuovi fattori di rischio emergenti convenzionali e non

Appropriatezza diagnostica-prescrittiva:

migliore conoscenza delle differenze nella fisiologia e fisiopatologia

Migliorare accesso e aderenza alle cure:

ruoli sociali (assenza di care-givers, essere nel ruolo di care-givers)

basso reddito

Ital J Gender-Specific Med 2015; 1: 3-5

Dalla medicina di genere alla medicina genere-specifica

Giovannella Baggio[1]

From gender medicine to gender-specific medicine

La Medicina di genere non è, quindi, una nuova specialità ma una necessaria e doverosa dimensione interdisciplinare della medicina, che vuole studiare l'influenza del sesso e del genere sulla fisiologia, fisiopatologia e patologia umana. All'inizio del terzo millennio sembra impossibile che sia ancora necessario colmare una lacuna così grande, eppure tutta la prassi medica ormai codificata da importanti linee guida è fondata su prove ottenute da grandi sperimentazioni condotte quasi esclusivamente su un solo sesso, quello maschile.

Academic Emergency Medicine
Official Journal of the Society for Academic Emergency Medicine

PRESENTATIONS

Future Directions in Sex- and Gender-specific Emergency Medicine

Marna R. Greenberg, DO, MPH, Basmah Safdar, MD, MSc, Esther K. Choo, MD, MPH, Alyson J. McGregor, MD, MA, Lance B. Becker, MD, and David C. Cone, MD

The 2014 *Academic Emergency Medicine* (AEM) consensus conference "Gender-Specific Research in Emergency Medicine: Investigate, Understand, and Translate How Gender Affects Patient Outcomes" convened a diverse group of stakeholders to target gaps in emergency medicine (EM) sex- and gender-specific research and identify research priorities. At the close of the conference, the executive committee sought feedback from group leaders and conference attendees about the next critical steps in EM sex- and gender-specific research, goals for their own future research, and anticipated barriers in pursuing this research. This article summarizes this feedback on the future directions in sex- and gender-specific research in emergency care and strategies to overcome barriers.

ACADEMIC EMERGENCY MEDICINE 2014;21:1339–1342

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GRAZIE PER L'ATTENZIONE!