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Regione Lombardia

5° Workshop: La salute della differenza

L'evoluzione del Sistema Socio Sanitario Lombardo a promozione della salute della donna

Malattie cerebrovascolari e differenze di genere

Anna Bersano
Fondazione IRCCS Istituto Neurologico C.Besta

Castellanza 30 novembre 2016

Stroke &women

Stroke in women is a recognised public health issue wordwide because of several aspects:

- Since women have longer life expectancies they have higher stroke prevalence
- Women have different risk factors and different heritability
- Women have a worse outcome and higher mortality due to the oldest age, comorbidities and different access to stroke care and prevention
- Stroke in women has a different societal (elderly women are more likely to live alone and socially isolated)

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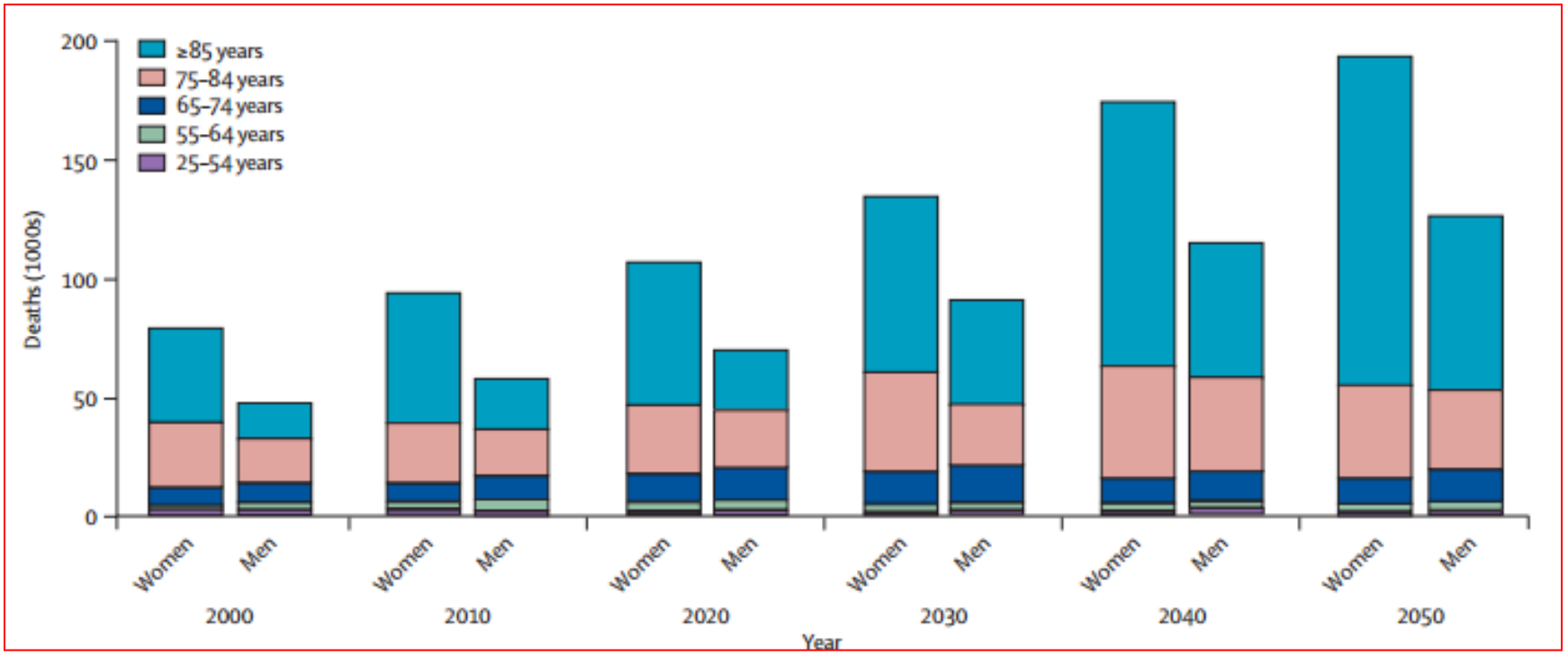
Projected number of deaths from stroke among whites 2000-2050



Need of addressing the specific biological, epidemiological clinical causes and features of stroke in women

Reeves et al Lancet Neurol 2008

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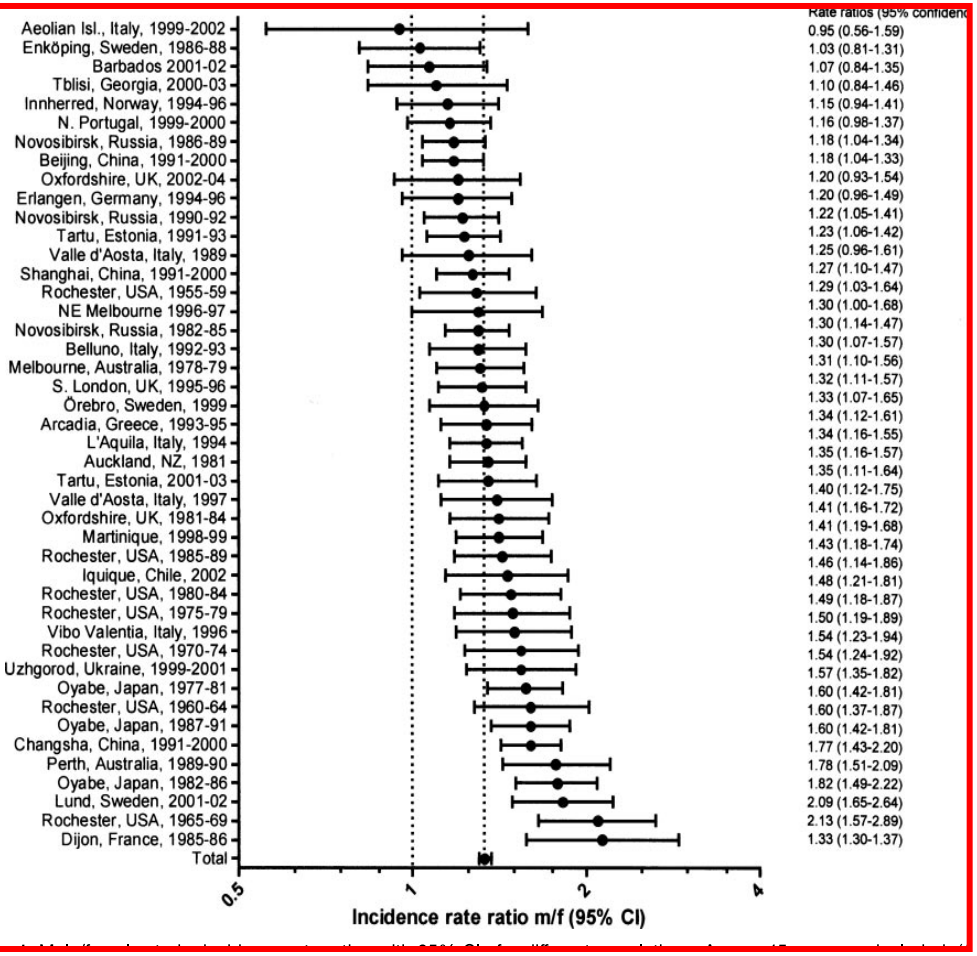
Go Red for Women

Sex Differences in Stroke Epidemiology
A Systematic Review

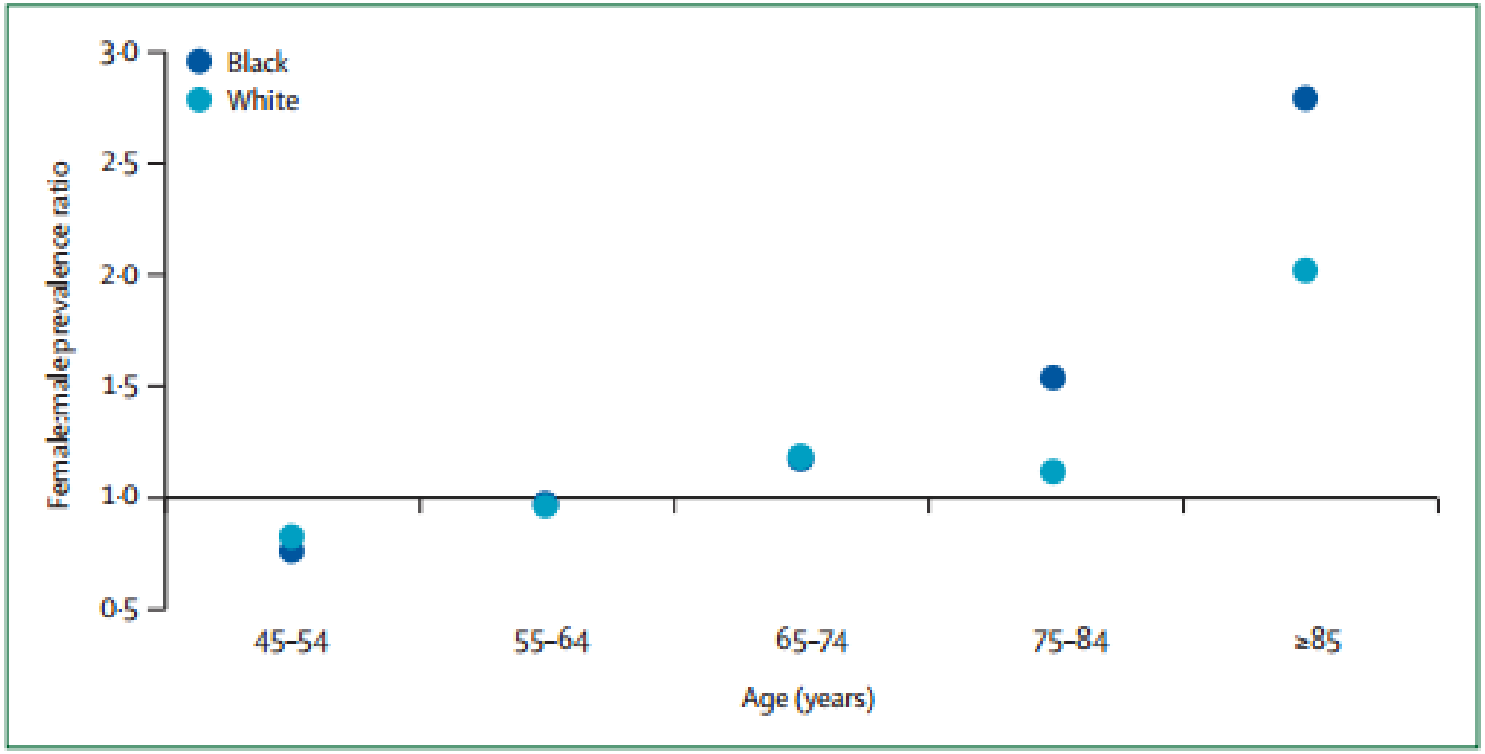
Peter Appelros, MD, PhD; Birgitta Stegmayr, PhD; Andreas Terént, MD, PhD



- 98 articles that contained relevant sex-specific information, including 59 incidence studies.
- The pooled age-adjusted rate ratio was 1.33 (95% CI, 1.30 to 1.37), meaning that stroke is 33% more incident in males than in females.

Stroke 2009

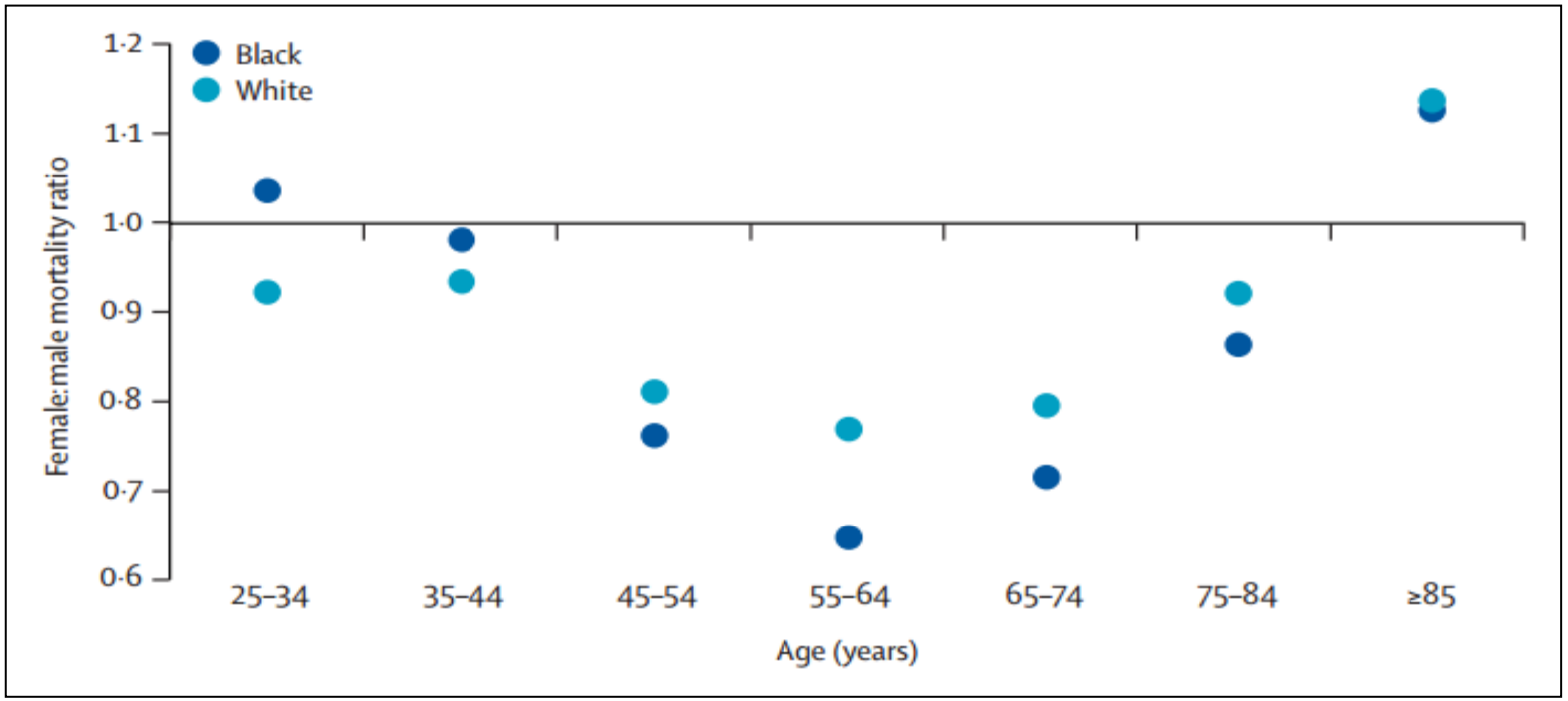
Epidemiology: Female:male prevalence ratio



Fewer women than men have prevalent stroke at youg age; over 75 years there are almost three time more blackand two time white women that men with stroke

Reeves et al Lancet Neurol 2008

Epidemiology: Female:male mortality ratio



Reeves et al Lancet Neurol 2008

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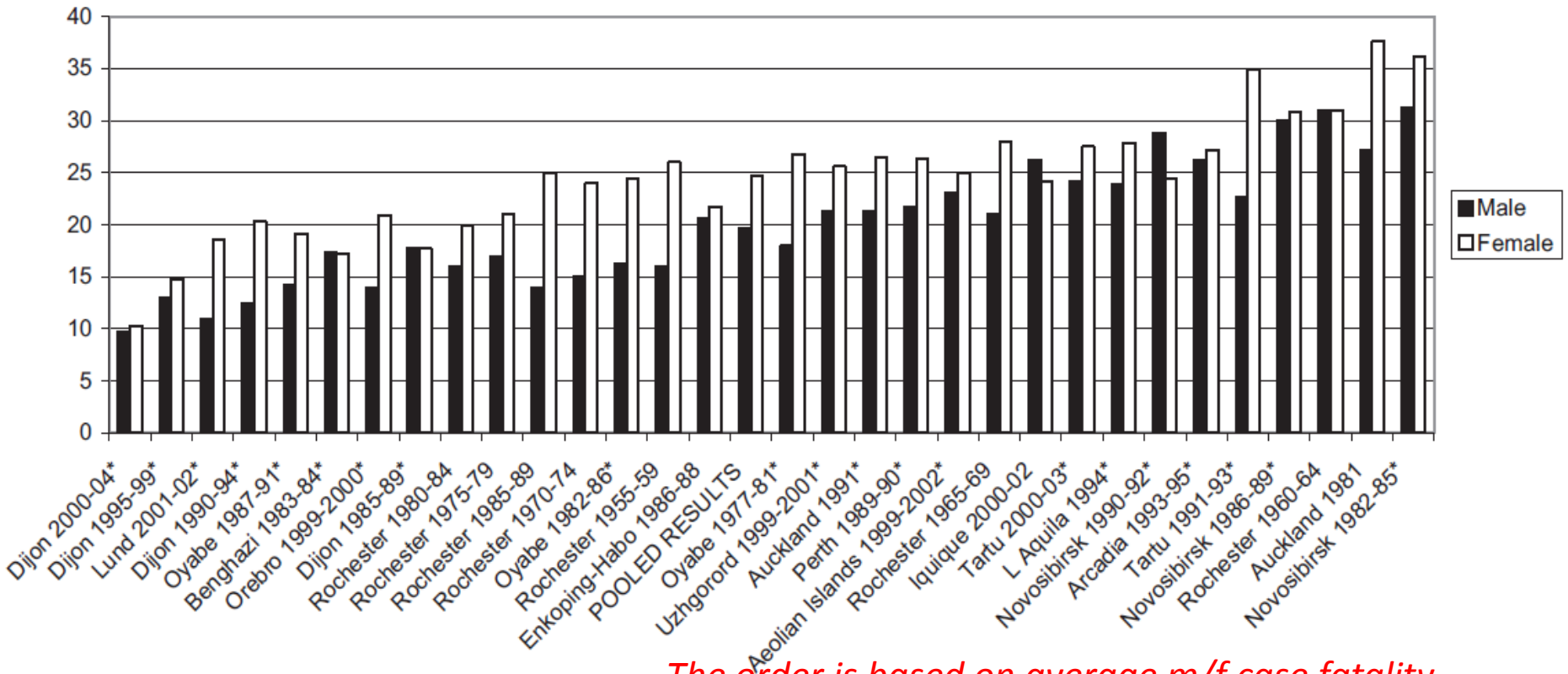

The order is based on average m/f case fatality.

In almost all studies reviewed here, women have higher 1-month case fatality than men.

Stroke 2009

Biological origin of sex differences in stroke

- Hormones
- Genetics
- Anatomics
- Drug methabolisms
- Cerebrovascular risk factors

Hormones

- The most common biological explanation for sex differences in stroke is related to sex steroid hormones, in particular estrogens
- Female rodents after MCA occlusion have smaller stroke volumes than males, whereas in ovariectomised females stroke volume is similar to males (after oestrogen replacementare similar to intact females)

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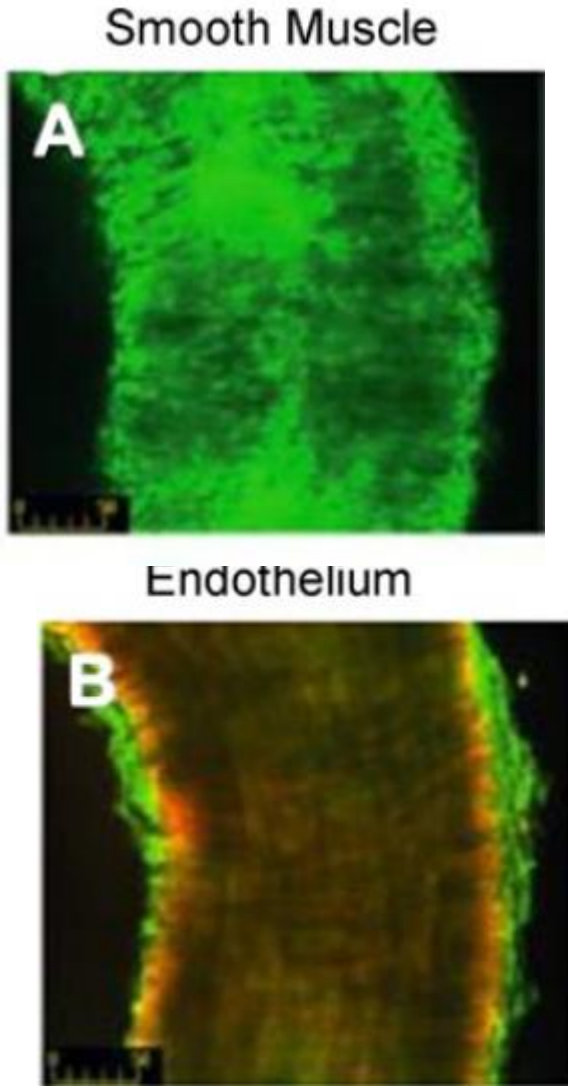
HIGHLIGHTED TOPIC | *Regulation of the Cerebral Circulation*

Influence of sex steroid hormones on cerebrovascular function

Diana N. Krause,[1] Sue P. Duckles,[1] and Dale A. Pelligrino[2]



Vasculature but mostly cerebral blood vessel are target for Estrogen
Estrogen acts on endothelium promoting dilation and blow flow; exerts antiinflammatory effects and reduces formation of ats plaque

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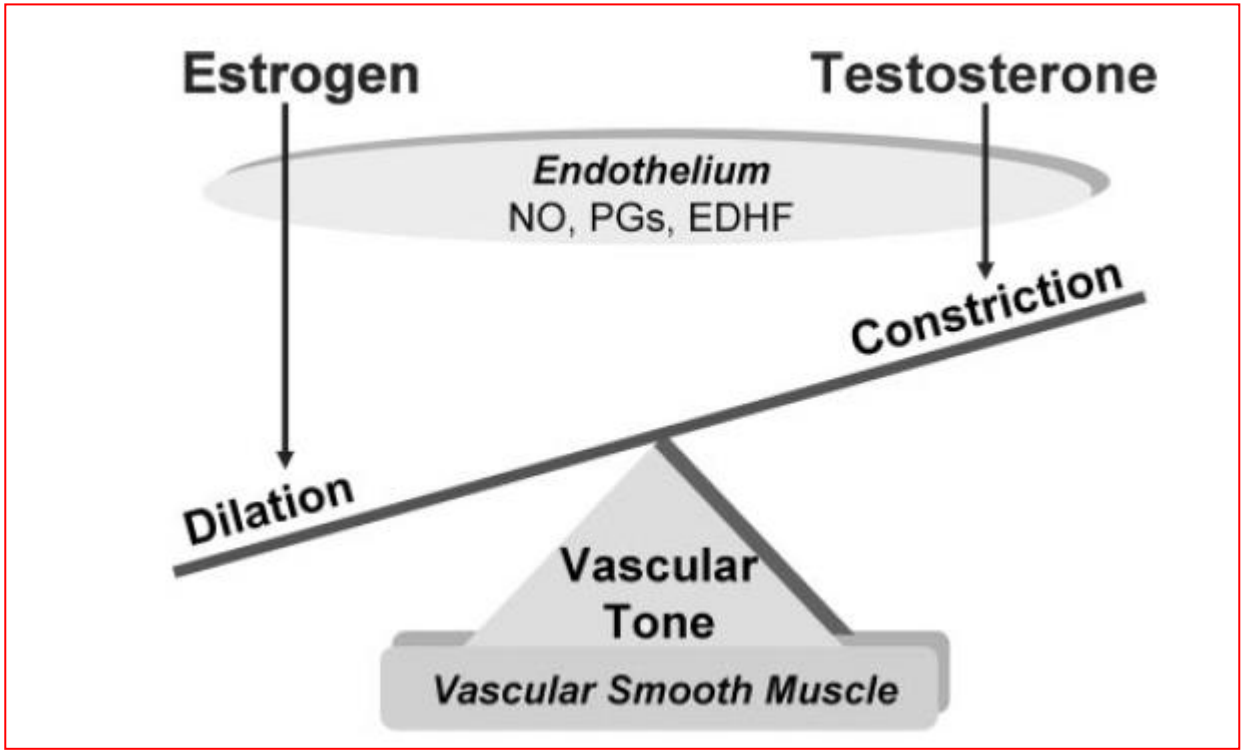

After chronic exposure, estrogen decrease vascular tone of cerebral arteries by NO, prostanoids and Endothelial Derived Hyperpolarizing factor

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HIGHLIGHTED TOPIC | *Regulation of the Cerebral Circulation*

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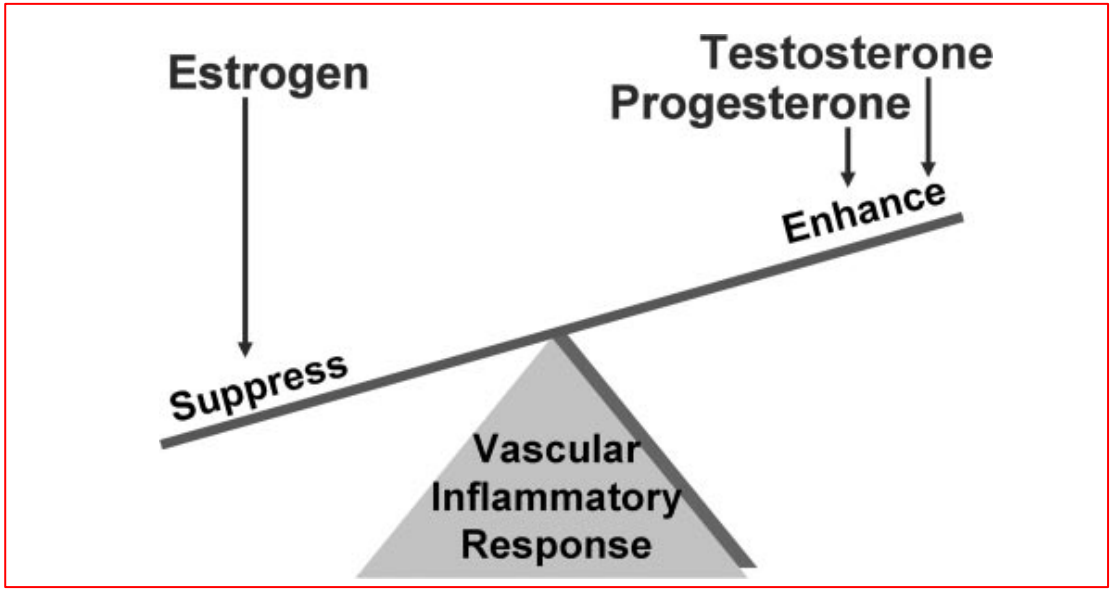

Chronic estrogen therapy suppresses leucocyte adhesion and induction of vascular inflammatory mediators such as iNOS and COX2 in cerebral blood vessels

Hormone Replacement

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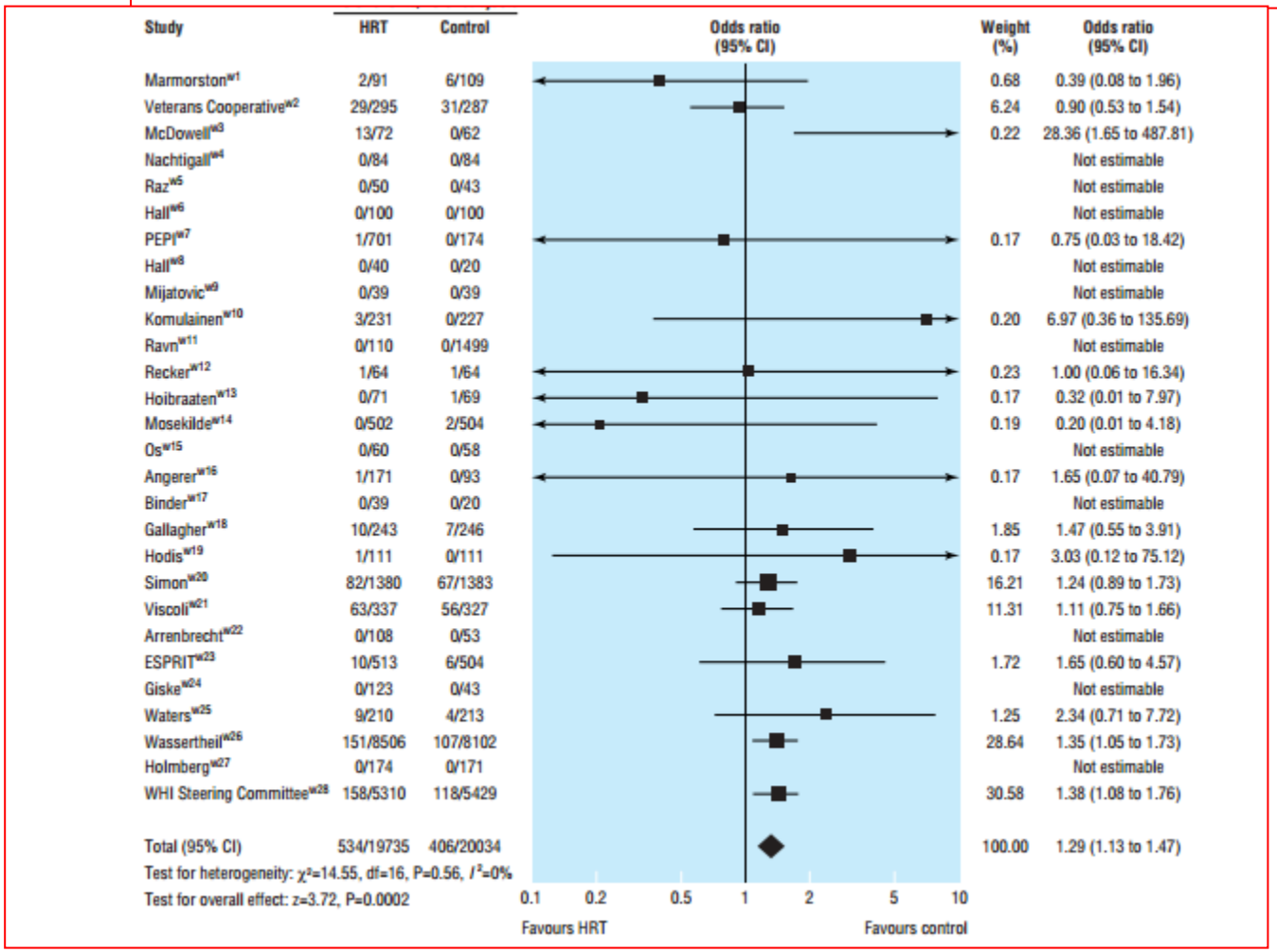
Association between hormone replacement therapy and subsequent stroke: a meta-analysis

Philip M W Bath, Laura J Gray

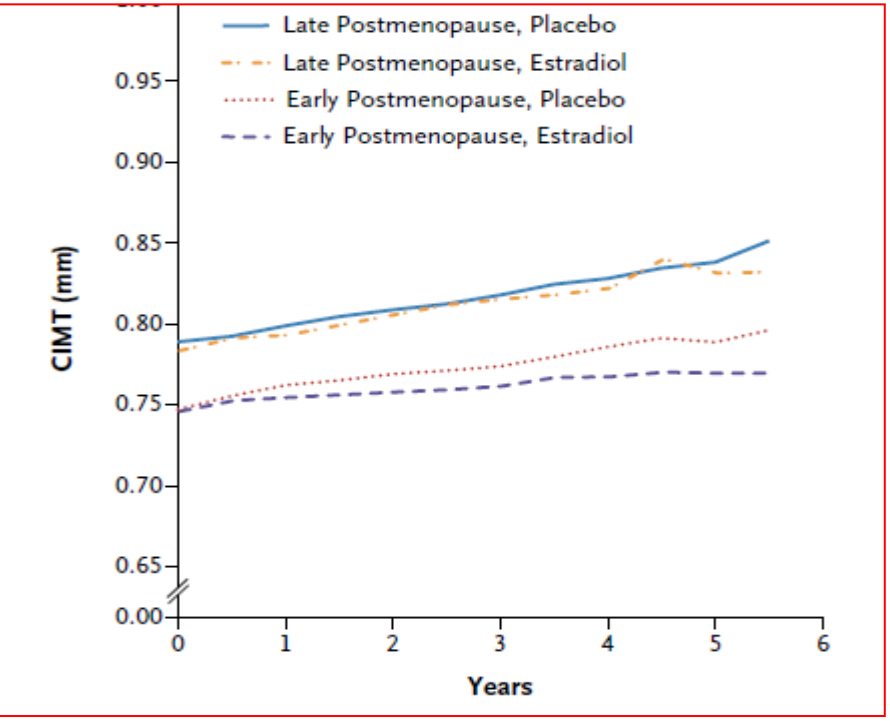


Bath et al BMJ 2005

Hormone Replacement

Vascular Effects of Early versus Late Postmenopausal Treatment with Estradiol

Howard N. Hodis, M.D., Wendy J. Mack, Ph.D., Victor W. Henderson, M.D., Donna Shoupe, M.D., Matthew J. Budoff, M.D., Juliana Hwang-Levine, Pharm.D. Yanjie Li, M.D., Mei Feng, M.D., Laurie Dustin, M.S., Naoko Kono, M.P.H., Frank Z. Stanczyk, Ph.D., Robert H. Selzer, M.S., and Stanley P. Azen, Ph.D., for the ELITE Research Group*



643 healthy postmenopausal women stratified according to time since menopause

Oral estradiol was associated with less progression of suclinical atherosclerosis when therapy was initiated within 6 years after menopause

NEJM 2016; 13:1221-31

Genes

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RESEARCH Open Access

CrossMark

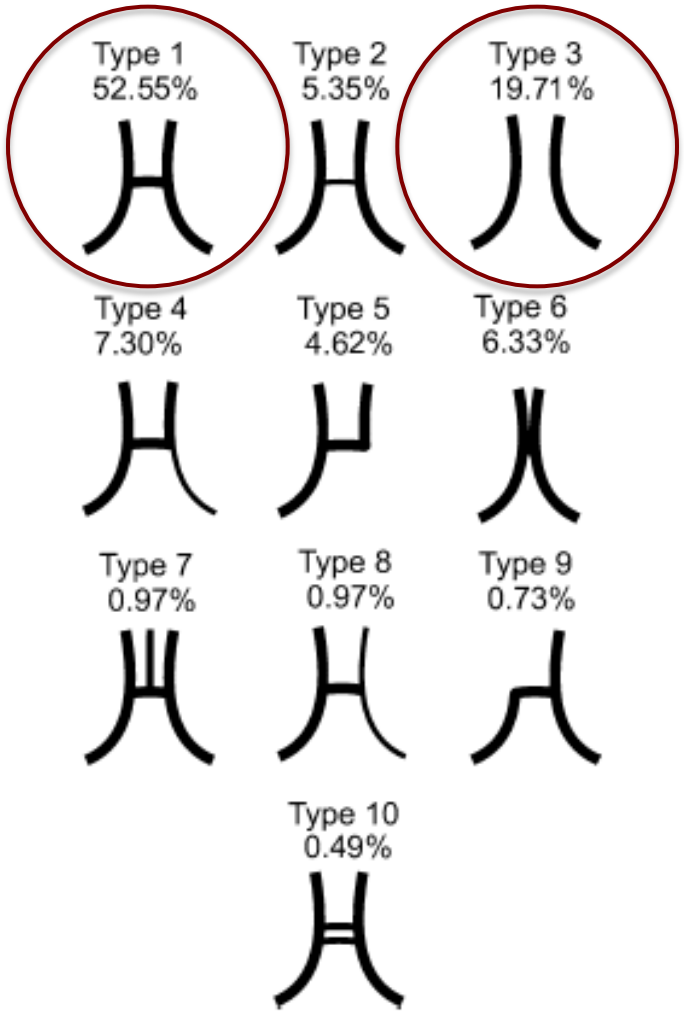
Characterization of whole-genome autosomal differences of DNA methylation between men and women

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

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

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

Anatomic differences



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

Giovannella Baggio*, Alberto Corsini, Annarosa Floreani, Sandro Giannini and Vittorina Zagonel

Gender medicine: a task for the third millennium

Mechanism	Gender-specific differences
General differences	
Lean/fat mass ratio	Lower lean/fat mass ratio in female
Distribution volume	Increased volume for lipophilic drugs in women
Drug binding	Smaller and fluctuating distribution volume in females
	Increased volume for hydrophilic drugs in males
	Hormonal influences on drug binding
Gastrointestinal differences	Longer gastric emptying time in women due to slower motility
	Higher pH
Metabolic differences (phase I)	
CYP	CYP1A2, CYP2E1, CYP2D6 all have higher activity in men
	CYP3A4 higher activity in females (maybe rate limiting step is P-glycoprotei
Metabolic differences (phase II)	Not enough information available
Excretion differences	Females generally have lower GFR, mostly due to body size
	Active secretion might be reduced in females

Clin Chem Lab Med 2013; 51(4): 713–727

Common Cerebrovascular Risk factors

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- **Age**

✓ Women with stroke are older at onset (about 4 yrs)

- **AF**

✓ Women were more likely to have AF

✓ Women with atrial fibrillation are at higher risk of stroke (3.5% vs. 1.8%; 95% CI 1.3-1.9), but they are less like to receive anticoagulation and ablation procedures compared to men

✓ Compared to men women are less likely to undergo cardiac monitoring, enzyme measurement, recovery in coronary care unit, coronary angiography, and revascularization

Common Cerebrovascular Risk factors

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Hypertension

- ✓ is more prominent in women
- ✓ higher association with strokes, LVH, and diastolic heart failure

Dyslipidemia

With the menopause transition low density lipoprotein (LDL) cholesterol increases in women However, in a meta-analysis of observational cohort studies of 86,000 women high level of total and LDL-cholesterol strongly predicted CHD in women

Diabetes

Type 2 diabetes has greater effects in women. It is a potent coronary risk factor in women, increasing their risk of developing or dying from CHD by three- to seven-fold, as compared with a two- to three-fold risk increase in men.

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The gender gap in stroke: a meta-analysis

Giralt D, Domingues-Montanari S, Mendioroz M, Ortega L, Maisterra O, Perea-Gainza M, Delgado P, Rosell A, Montaner J. The gender gap in stroke: a meta-analysis.
Acta Neurol Scand: 2012: 125: 83–90.

D. Giralt, S. Domingues-Montanari, M. Mendioroz, L. Ortega, O. Maisterra, M. Perea-Gainza, P. Delgado, A. Rosell, J. Montaner

45 studies for 673.935 patients

			Women		Men					
Variables	Number of studies	I^2% (IQ)	Event	Total	Event	Total	OR (95% CI)	*P*-value	OR removing large studies	*P*-value
Risk factors										
Alcohol *†	6	98 (97–99)	11,545	17,755	14,254	19,013	0.29 (0.16–0.51)	<0.001	–	
Cigarette smoking *†	27	97 (67–97)	40,369	250,913	57,132	227,879	0.51 (0.44–0.59)	<0.001	0.49 (0.4–0.61)	<0.001
Hyperlipidemia *†	19	84 (76–89)	76,623	224,690	75,462	201,926	0.9 (0.82–0.99)	0.033	0.9 (0.8–1.02)	0.09
Hypertension*†	33	93 (90–95)	214,728	309,163	187,858	288,504	1.15 (1.07–1.24)	<0.001	1.1 (1.07–1.13)	<0.001
Diabetes *†	36	80 (67–88)	82,657	314,521	81,428	293,084	0.88 (0.84–0.93)	<0.001	0.89 (0.8–0.98)	0.02
Atrial fibrillation *†	29	83 (77–88)	55,954	287,669	40,556	269,374	1.31 (1.24–1.4)	<0.001	1.31 (1.21–1.43)	<0.001
Myocardial infarction *†	11	95 (92–96)	50,412	216,671	60,025	193,904	0.76 (0.62–0.94)	0.013	0.76 (0.55–1.05)	0.99
Peripheral vascular disease†	8	94 (91–96)	2,202	33,967	2,245	32,806	0.76 (0.53–1.08)	0.121	–	
Stroke subtype and severity										
Transient cerebral ischemia†	6	74 (42–89)	2,513	9,881	2,052	9,455	1.1 (0.92–1.33)	0.305	–	
PACI†	7	74 (45–88)	2,265	6,116	2,302	6,514	1.03 (0.91–1.16)	0.671	–	
TACI†	7	81 (61–90)	3,447	14,119	3,171	15,777	1.16 (0.98–1.37)	0.084	–	
POCI*†	7	63 (16–84)	924	6,012	1,206	6,514	0.76 (0.66–0.87)	<0.001	–	
LACI†	11	54 (10–77)	3,612	16,101	4,551	18,423	0.96 (0.87–1.05)	0.363	–	
Cardioembolic *†	12	67 (39–82)	1,017	3,855	908	4,218	1.32 (1.08–1.62)	0.007	–	
Atherothrombotic *†	8	74 (48–87)	793	2,715	1,079	3,061	0.68 (0.51–0.91)	0.008	–	
Diagnosis tests										
Cranial MRI†	5	79 (49–91)	11,560	16,058	12,924	17,344	0.83 (0.67–1.03)	0.091	–	
Angiography†	6	68 (23–86)	996	6,165	1,117	6,123	0.85 (0.68–1.07)	0.159	–	
Ecocardiography†	7	78 (53–89)	3,492	7,680	3,772	7,802	0.86 (0.72–1.03)	0.109	–	
Carotid imaging†	3	75 (16–92)	1,816	2,499	2,063	2,688	0.76 (0.57–1.02)	0.068	–	
Holter†	2	81 (19–96)	459	2,838	497	3,210	1.01 (0.71–1.44)	0.952	–	
Lipids test†	4	91 (81–96)	2,735	6,982	2,949	6,685	0.91 (0.69–1.19)	0.488	–	
Acute-phase treatments and secondary prevention										
Antiplatelets *†	15	62 (33–78)	31,558	45,458	32,621	45,599	0.89 (0.84–0.94)	<0.001	–	
Warfarin *	6	40 (0–85)	1,972	8,654	2,101	8,141	0.93 (0.79–1.09)	0.373	–	
ACE Inhibitors	2	20 (–)	1,340	5,298	1,605	4,817	0.78 (0.34–1.81)	0.563	–	
Statins *†	6	74 (41–89)	3,759	10,030	4,191	9,095	0.71 (0.6–0.84)	<0.001	–	
tPA*	7	45 (0–77)	9,573	232,889	10,596	213,772	0.8 (0.73–0.87)	<0.001	0.76 (0.65–0.87)	<0.001

ACE, angiotensin converting enzyme.

Acta Neurol Scand 2011

Specific risk factors

Pregnancy

Pregnancy results in hemhostatic changes (increasing of clotting factors ab decreasing in anticoagulants and fibrinolytic activity). Risk of stroke 34 vs 11/100.000 deliveries

Oral anticonception (OAC)

OAC use is associated with up to 2-3 fold increase the risk of stroke

Additional factors such as age >35 yrs, migraine, hypertension, trombophilia and smoking increase the risk up to 20-30 times

Sex difference: atherosclerotic plaque

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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*

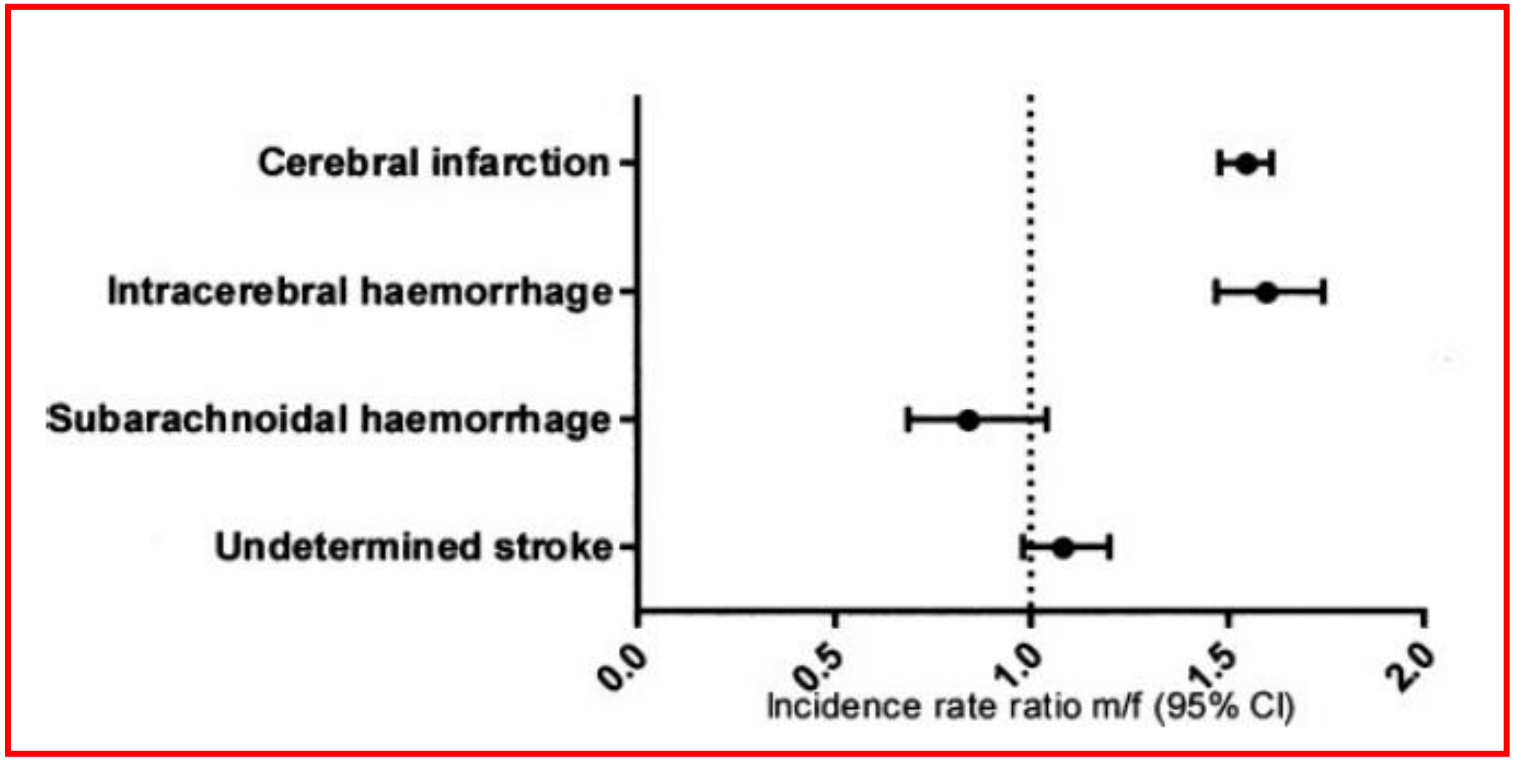
Table II. Comparison of carotid plaque histology between men and women

	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 pts(135 women, 315 men) (75% sympt).
- 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.

Sex differences in clinical presentation



Women are older when they get their first stroke, and SAH and cardioembolic strokes are proportionally more common among women

Stroke 2009

Sex differences in clinical presentation

- Women tend to have anterior circulation ischemia, whereas men are believed to have higher incidences of posterior circulation syndromes
- Labiche et al have reported that females at stroke onset were more likely to present with ‘‘non-traditional’’ stroke symptoms compared with men (pain and reduced level of consciousness)
- Females tended to have higher NIHSS at admission

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Acute Stroke Symptoms: Do Differences Exist between Sexes?

Monica Acciarresi, MD, Pierpaolo De Luca, MD, Valeria Caso, MD, PhD, Giancarlo Agnelli, MD, Cataldo D'Amore, MD, Andrea Alberti, MD, Michele Venti, MD, PhD, and Maurizio Paciaroni, MD

1883 patients, 1072 men (56.9%) and 811 women (43.1%)

	Total		Male		Female		
Type of stroke	n	%	n	%	n	%	*P* value
Total number of patients	1883		1072	56.9	811	43.1	
Age							
Mean ± SD			70.14 ± 12.61		75.40 ± 12.90		<.0001
Median			72		78		
Ischemic stroke/TIA	1626	86.4	921	85.9	705	86.9	.5
Hemorrhagic stroke	257	13.6	151	14.1	106	13.1	.5
Relapse	242	12.9	137	12.8	105	12.9	.9
TACI*	219	11.6	90	10.3	129	19.2	<.0001
PACI*	626	33.2	343	39.1	283	42.2	.22
LACI*	419	22.3	267	30.4	152	22.7	.001
POCI*	283	15.0	177	20.2	106	15.8	.029
Arteriosclerosis	430	22.8	269	25.1	161	19.8	.008
Cardiac embolism	470	25.0	219	20.4	251	30.9	<.0001
Small vessel disease	371	19.7	230	21.4	141	17.4	.03
Undetermined cause	427	22.7	245	22.8	182	22.4	.86
Others cause	163	8.7	95	8.9	68	8.4	.74
Thrombolysis i.a. or i.v.	156	8.3	99	9.2	57	7.0	.09

Journal of Stroke and Cerebrovascular Diseases 2014

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Racial and Gender Differences in Stroke Severity, Outcomes, and Treatment in Patients with Acute Ischemic Stroke

Amelia K. Boehme, MSPH,*† James E. Siegler, MD,‡ Michael T. Mullen, MD,§
Karen C. Albright, DO, MPH,*||¶ Michael J. Lyerly, MD,†
Dominique J. Monlezun, BS,‡ Erica M. Jones, BS,‡ Rikki Tanner, MPH,*
Nicole R. Gonzales, MD,# T. Mark Beasley, PhD,** James C. Grotta, MD,#
Sean I. Savitz, MD,# and Sheryl Martin-Schild, MD, PhD‡

4925 pts with AIS

	Women (N = 2372)	Men (N = 2605)	*P* value	Black (N = 1942)	White (N = 2983)	*P* value
Age, median (range)	68 (15-100)	63 (26-100)	<.0001	62 (25-100)	67 (13-100)	<.0001
Medical history, %						
Atrial fibrillation	430 (18.2%)	345 (13.3%)	<.0001	197 (10.2%)	573 (19.2%)	<.0001
Diabetes	802 (33.9%)	788 (30.3%)	.0059	686 (35.5%)	888 (29.8%)	<.0001
Hypertension	1847 (78.1%)	1863 (71.6%)	<.0001	1579 (81.6%)	2089 (70.2%)	<.0001
Hyperlipidemia	604 (29.5%)	674 (31.3%)	.2688	398 (27.4%)	873 (31.8%)	.0030
Congestive heart failure	248 (11.7%)	218 (9.6%)	.0256	195 (12.5%)	268 (9.6%)	.0027
NIHSS on admission, median (range)	8 (0-40)	6 (0-40)	<.0001	7 (0-40)	7 (0-40)	.4270
Stroke etiology, %			.0001			<.0001
Cardioembolic	783 (33.4%)	795 (30.9%)		547 (28.6%)	1018 (34.6%)	
Large vessel	477 (20.3%)	669 (26.0%)		436 (22.8%)	697 (23.7%)	
Small vessel	364 (15.5%)	412 (16%)		378 (19.7%)	387 (13.1%)	
Cryptogenic	82 (3.5%)	82 (3.1%)		89 (4.5%)	69 (2.3%)	
Other	638 (27.2%)	612 (23.8%)		466 (24.3%)	775 (26.3%)	
tPA use, %	679 (33.2%)	706 (32.5%)	.6745	434 (29.9%)	949 (34.6%)	.0019
Arrived within 3 h, %	1000 (48.9%)	1062 (49%)	.9441	659 (45.4%)	1399 (51%)	.0005

Journal of Stroke and Cerebrovascular Diseases 2014

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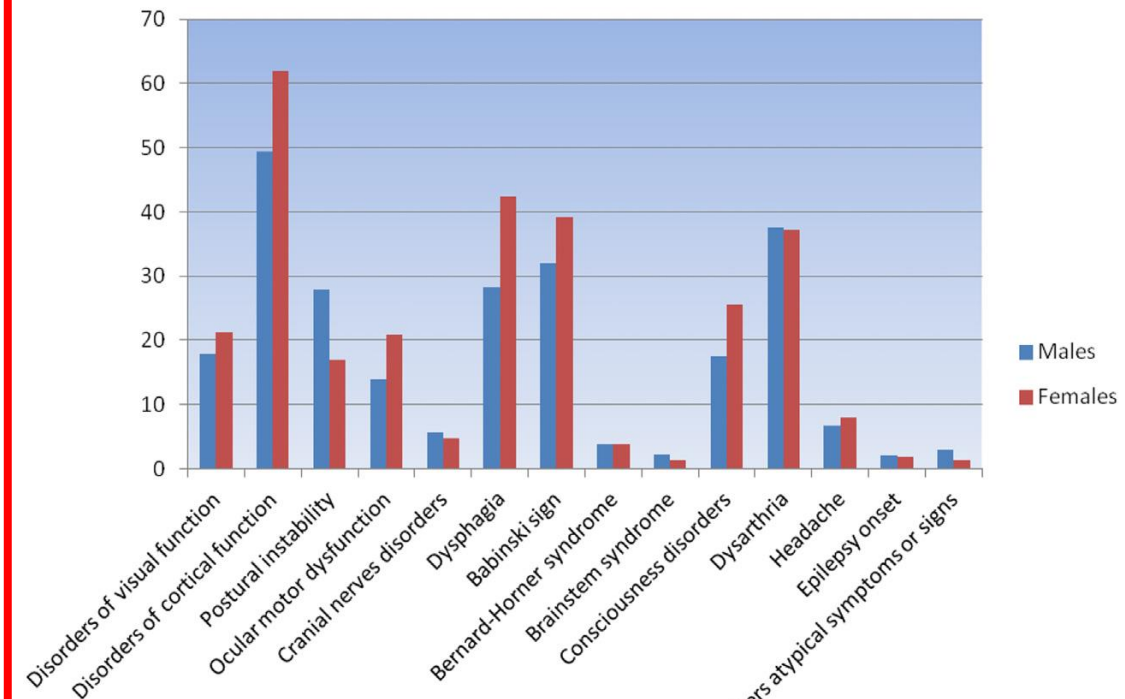
Acute Stroke Symptoms: Do Differences Exist between Sexes?

Monica Acciarresi, MD, Pierpaolo De Luca, MD, Valeria Caso, MD, PhD,
Giancarlo Agnelli, MD, Cataldo D'Amore, MD, Andrea Alberti, MD,
Michele Venti, MD, PhD, and Maurizio Paciaroni, MD



Journal of Stroke and Cerebrovascular Diseases 2014

Why stroke is more severe in women ?

- Biological phenomenon in which females response to brain ischemia and ischemic risk is different
- Older age (women develop stroke about 5 years later than men)
- Cardioembolic stroke
- Disparity in providing healthcare facilities between men and women

Giralt D et al. Acta Neurol Scand 2011

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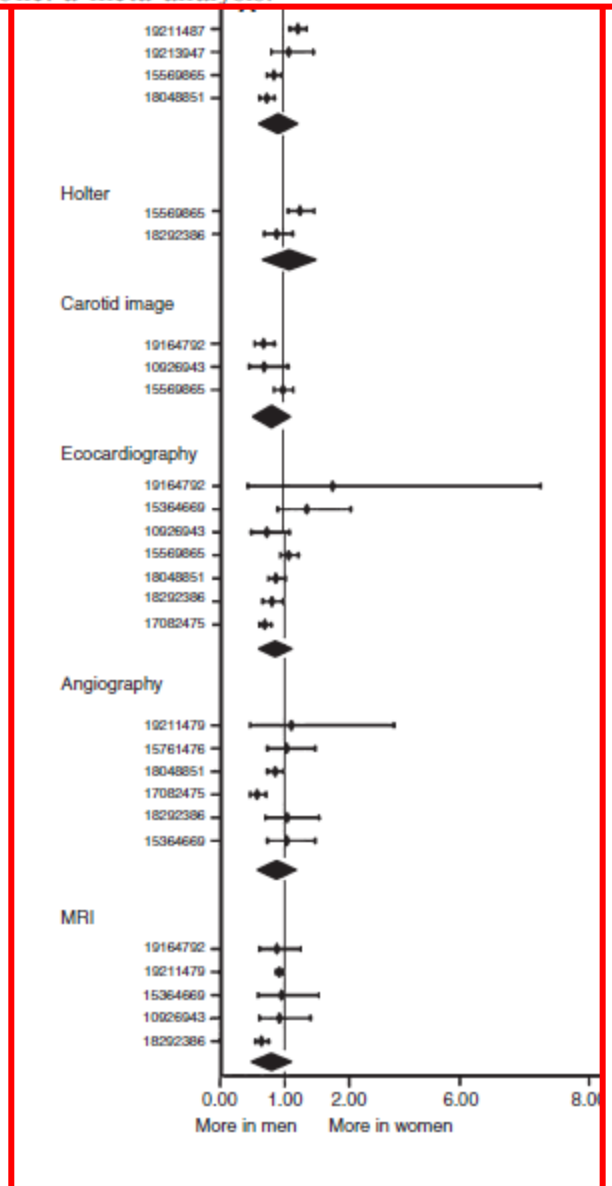
The gender gap in stroke: a meta-analysis

Giralt D, Domingues-Montanari S, Mendioroz M, Ortega L, Maisterra O, Perea-Gainza M, Delgado P, Rosell A, Montaner J. The gender gap in stroke: a meta-analysis.

D. Giralt, S. Domingues-Montanari, M. Mendioroz, L. Ortega, O. Maisterra



Comprehensive meta-analysis including 45 articles, representing a total of 673,935 patients

Giralt D et al. Acta Neurol Scand 2011

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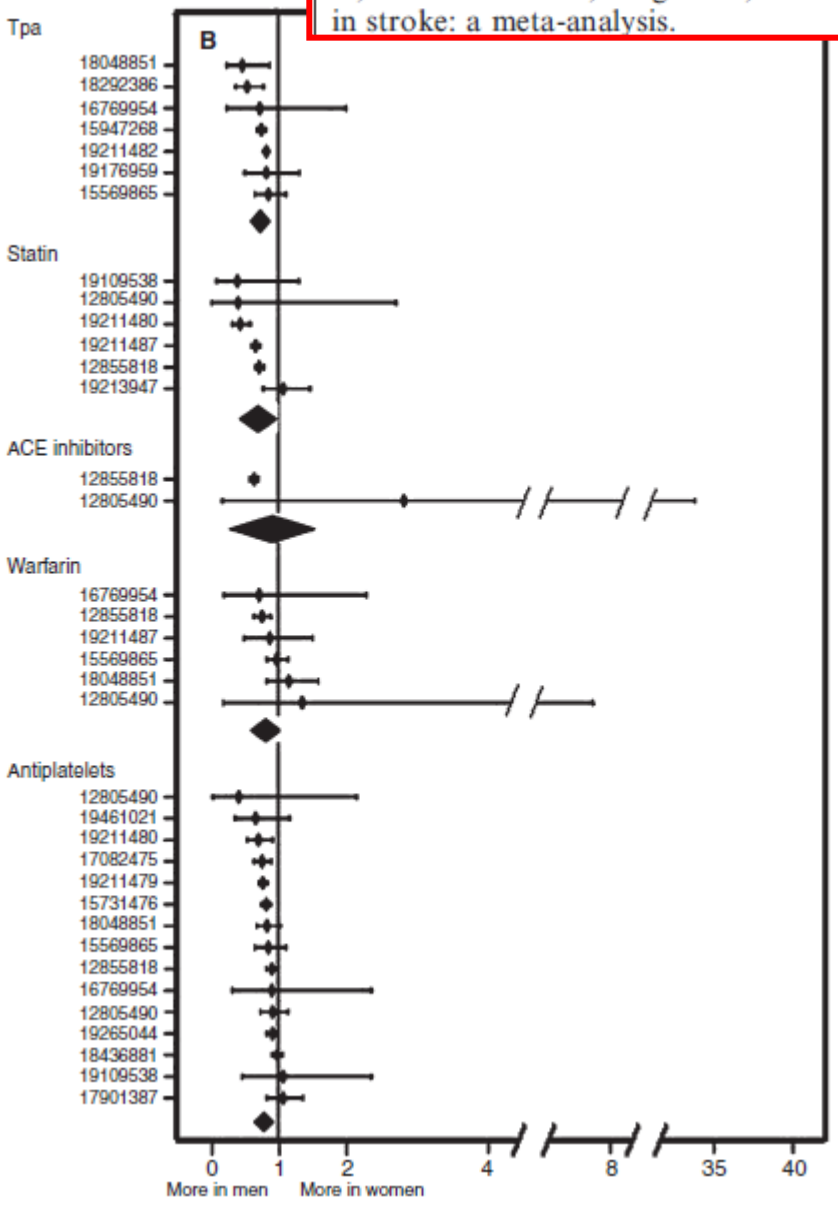

- Women suffered more cardioembolic strokes,
- Women were less likely to receive stroke-related treatments, such as antiplatelets ($P < 0.001$), statins ($P < 0.001$), and tPA ($P < 0.001$) than men.

Giralt D et al. Acta Neurol Scand 2011

Onset-to-door

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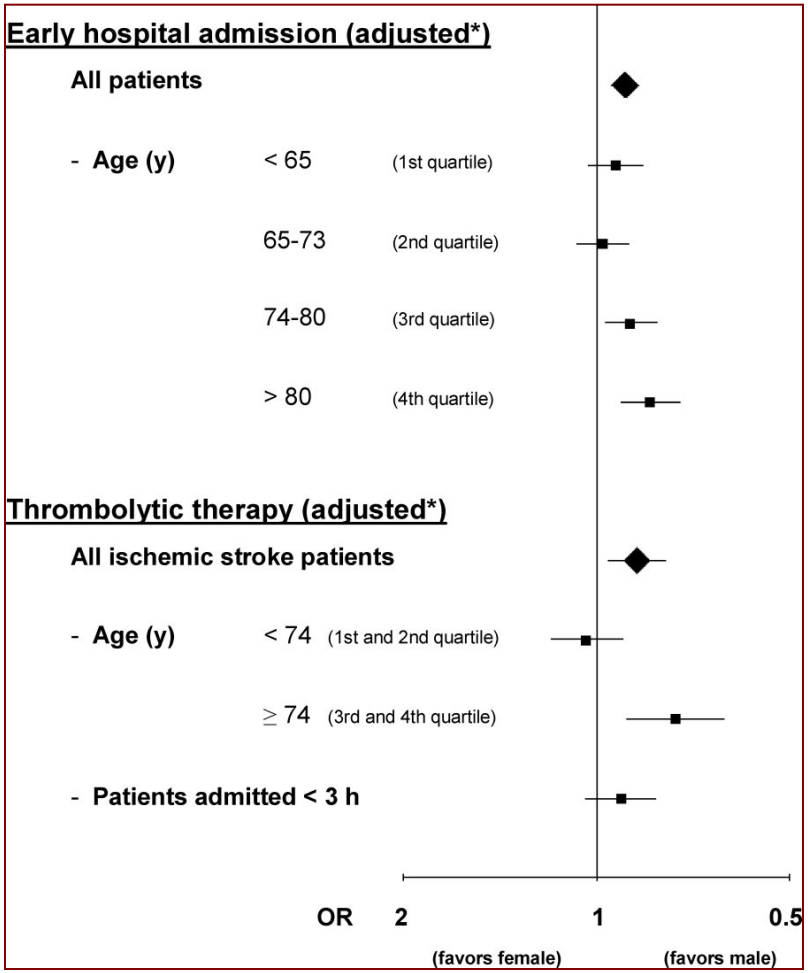
After multivariate adjustment, women were found to have a 10% smaller chance of being admitted <3 hours of symptom onset than men (odds ratio [OR]=0.902, 95% CI=0.860 to 0.945, P<0.001).

After adjustment in the multivariate model, the chance of a female stroke patient being treated with thrombolysis was 13% lower than that of a male patient (OR=0.867, 95% CI=0.782 to 0.960, P<0.006).

Elderly female patients had a 25% smaller chance of receiving thrombolytic treatment (OR=0.753, 95% CI=0.634 to 0.895, P<0.001).

	Women (n=26 319)	Men (n=27 095)
Age, mean±SD, y	75.3±12.3	69.1±11.9



Foerch C et al. Stroke. 2007

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

- Dataset of the Euro Observational Research Programme on Atrial Fibrillation (EORP-AF) Pilot survey (n= 3119) examined sex-related differences in presentation, treatment, and outcome of patients with AF in Europe
- Female subjects were older (P= 0.0001), with a greater proportion aged ≥75 years, with more heart failure and hypertension
- CHA2DS2-VASc score ≥2 was found in 94.7% of females and 74.6% of males (P , 0.0001)

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

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

	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

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

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Research Correspondence

Enrollment of Women in National Heart, Lung, and Blood Institute-Funded Cardiovascular Randomized Controlled Trials Fails to Meet Current Federal Mandates for Inclusion

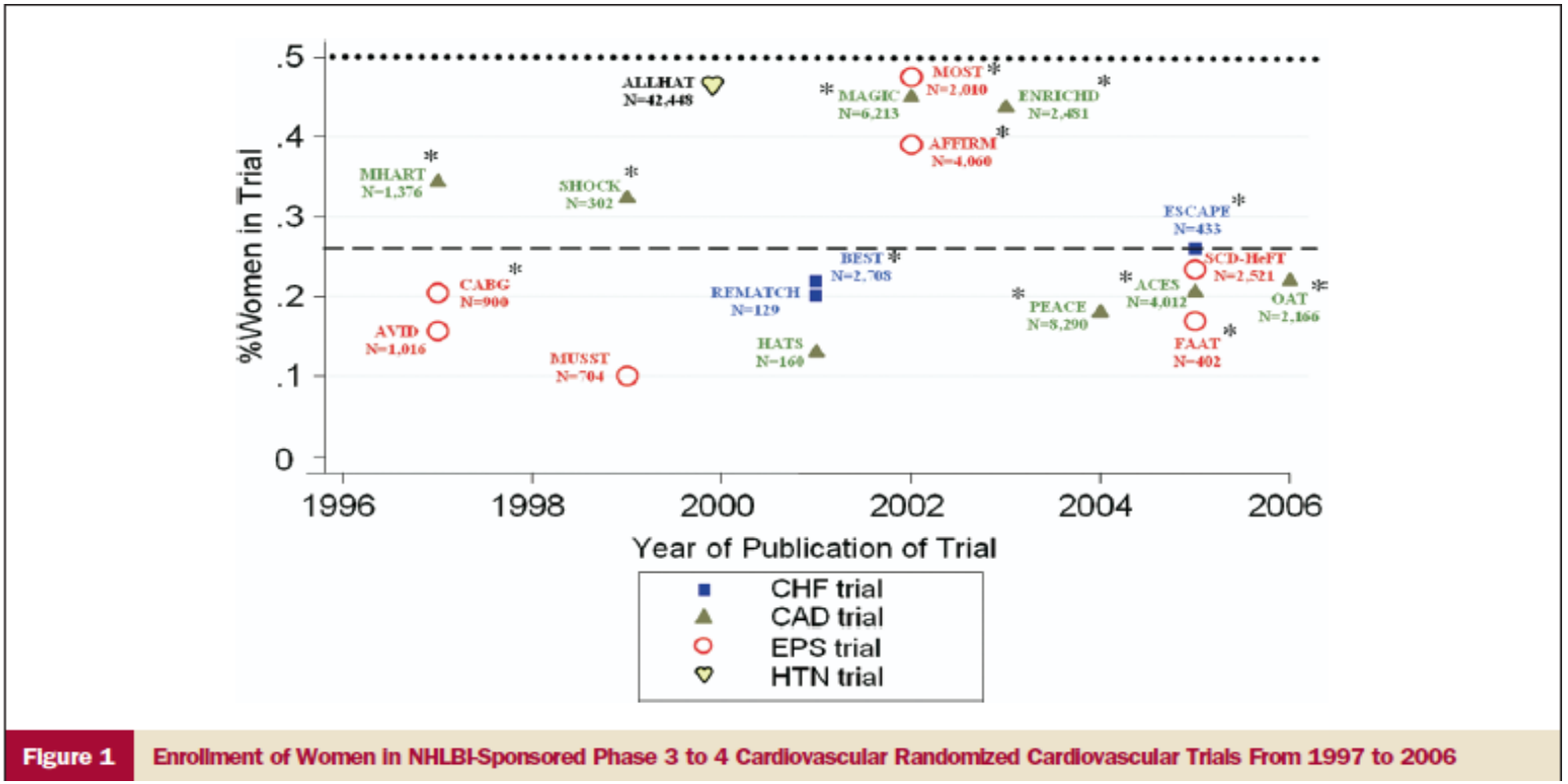

Figure 1 Enrollment of Women in NHLBI-Sponsored Phase 3 to 4 Cardiovascular Randomized Cardiovascular Trials From 1997 to 2006

Average women enrollment=27%

** Subgroup analysis based on gender*

Kim ESH et al. J Am Coll Cardiol. 2008;52(8):672.

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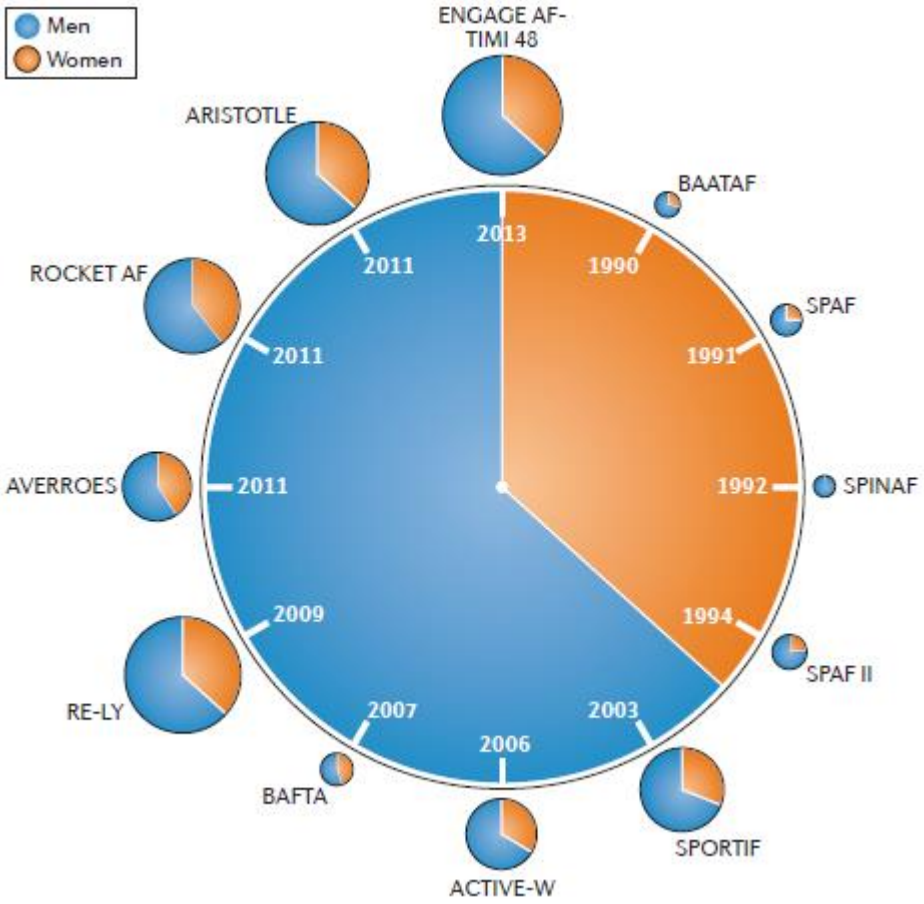
Atrial fibrillation in women: treatment

Darae Ko[1], Faisal Rahman[1]*, Maria A. P. Martins[2,3]*, Elaine M. Hylek[1], Patrick T. Ellinor[4], Renate B. Schnabel[5,6], Emelia J. Benjamin[3,7,8] and Ingrid E. Christophersen[4,9]*



Nature Reviews Cardiology 2016

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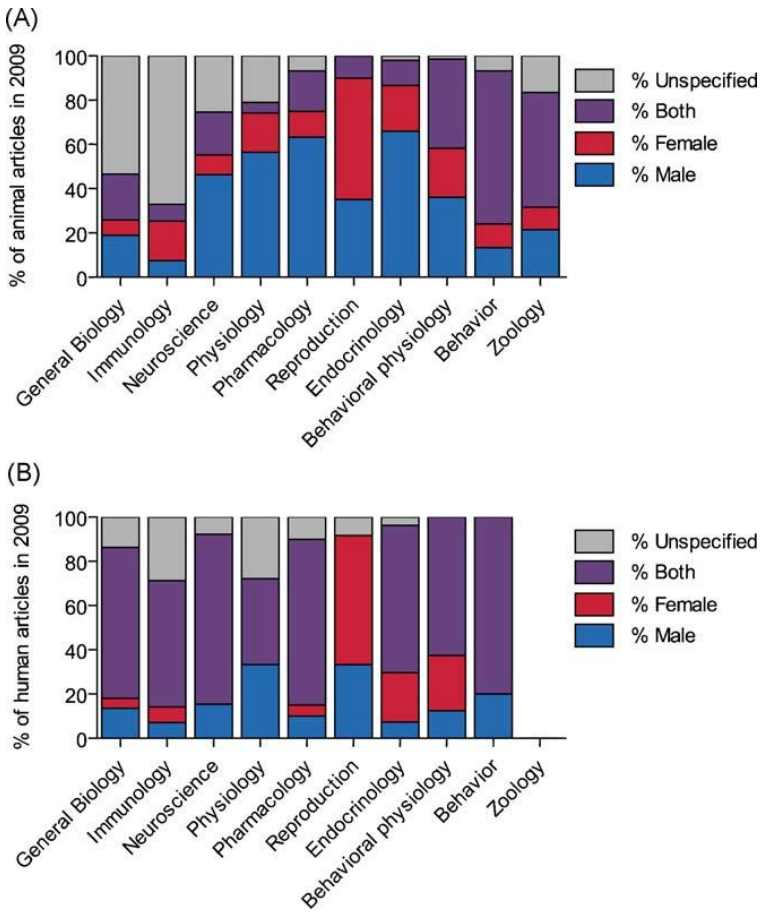
Sex bias in neuroscience and biomedical research

Annaliese K. Beery[a], Irving Zucker[b,c,*]

Single sex studies still predominate the research literature



Neuroscience and Biobehavioral Reviews 2011

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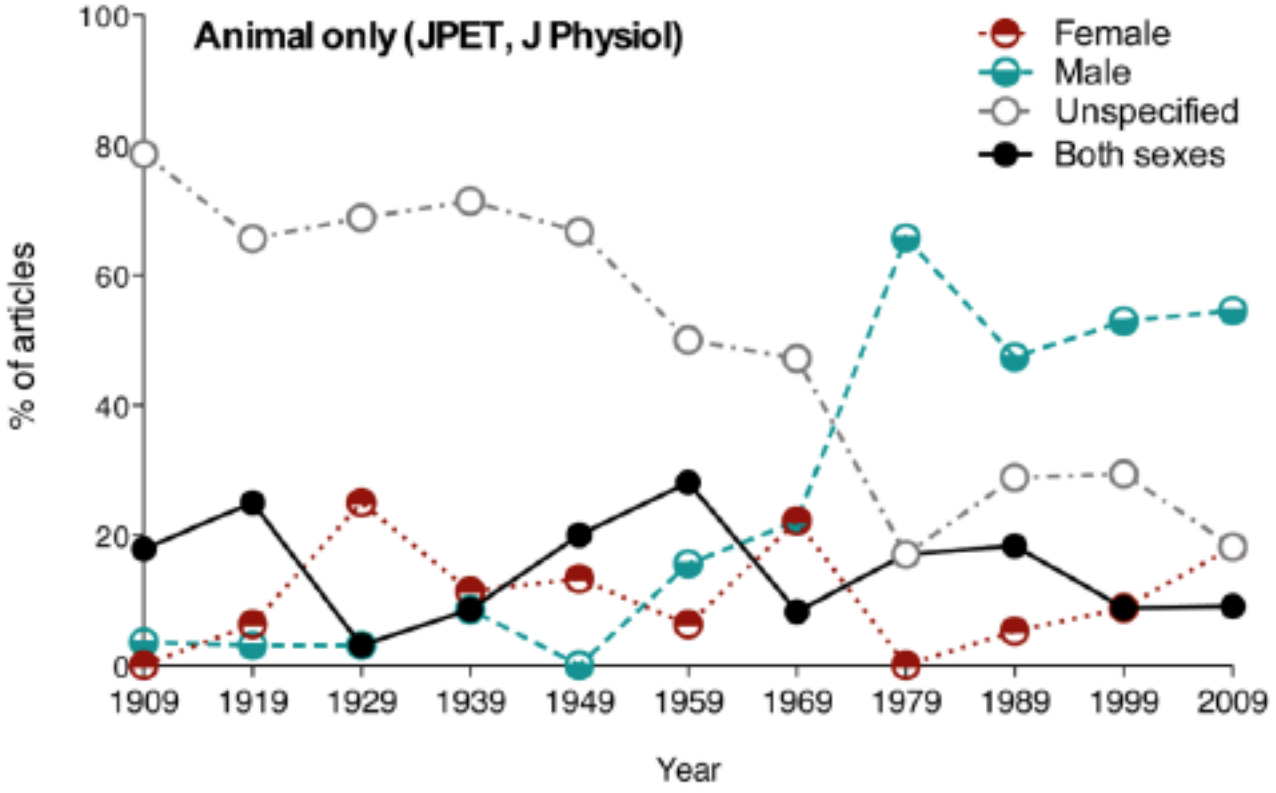
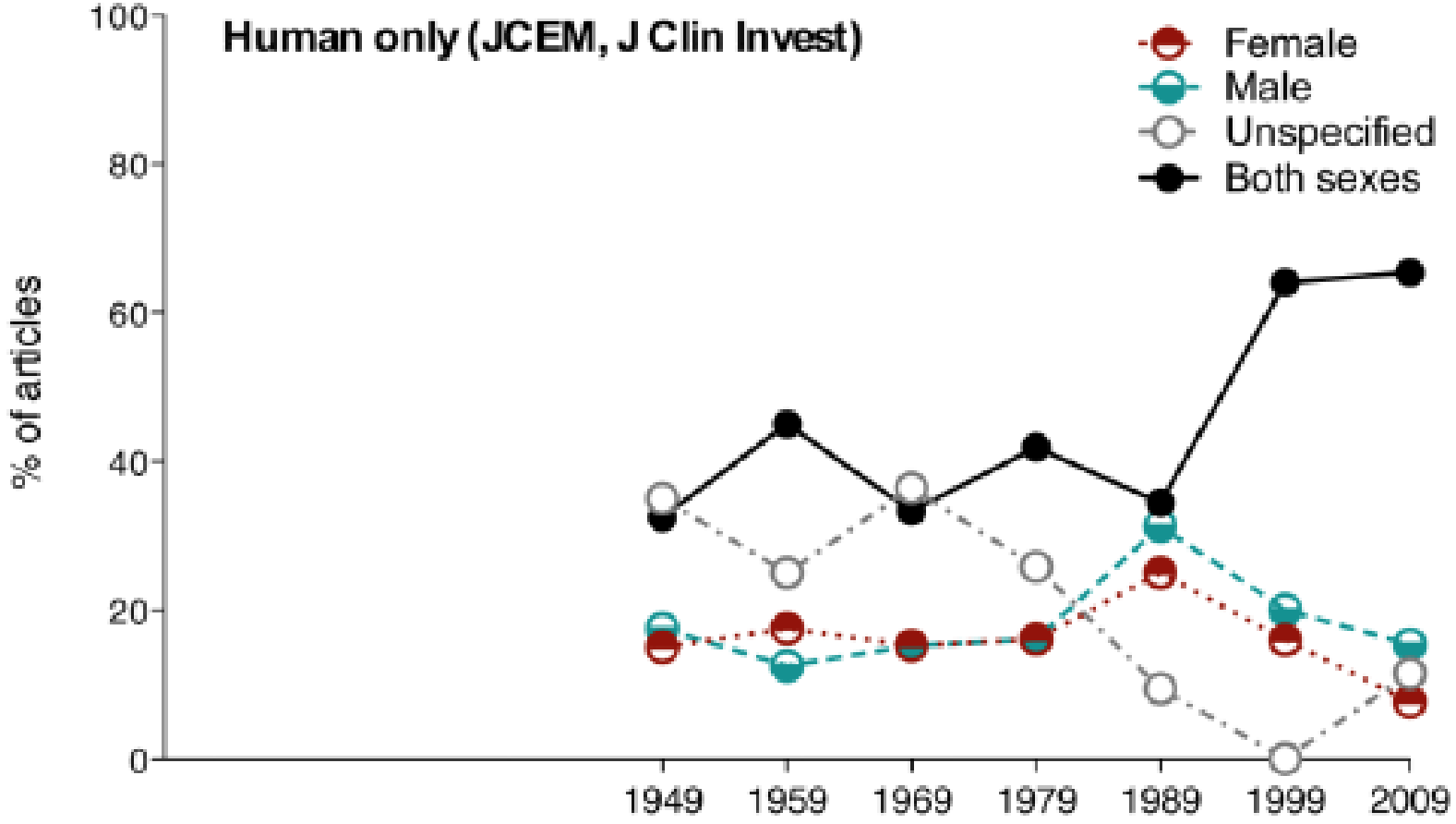
Males still dominate animal studies



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

..and human studies



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

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Review Article

Sex and Gender Differences in Central Nervous System-Related Disorders

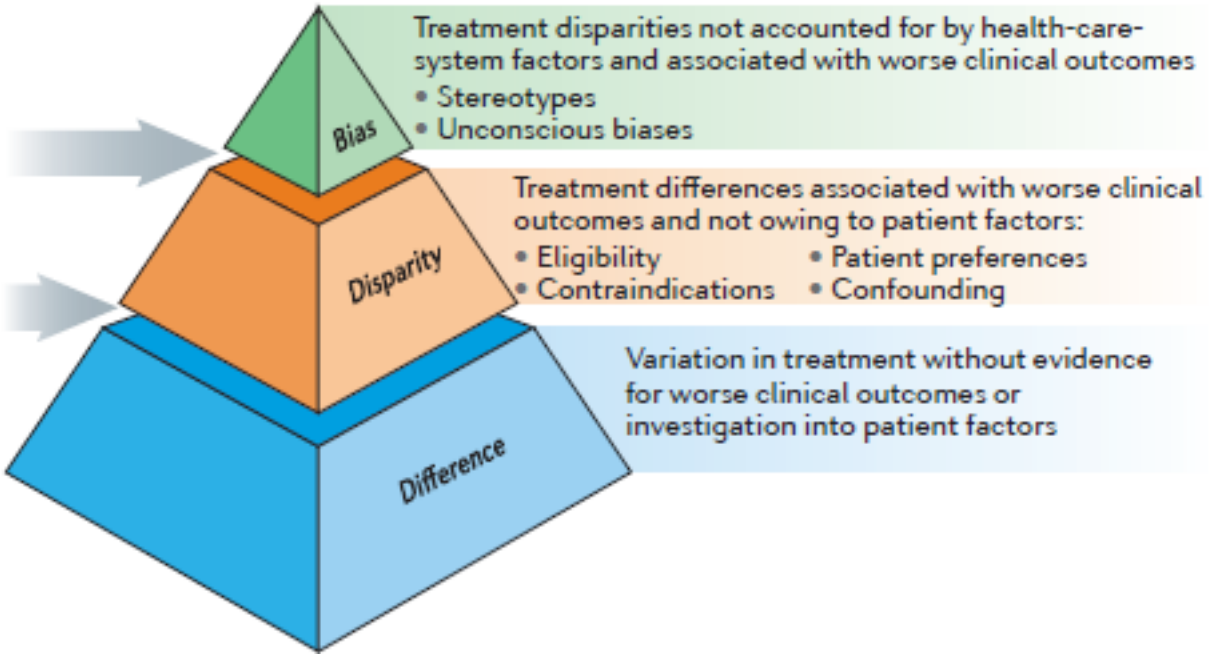
Emanuela Zagni,[1] Lucia Simoni,[2] and Delia Colombo[1]

Recommendations are

- the inclusion of both sexes in basic CNS science and RCT;
- the exploration of sex difference as a part of the standard preclinical evaluation of therapeutics;
- the implementation of research examining sex-specific risk factors
- the definition and use of relevant sex-specific outcome measures and therapeutic strategies.

Neuroscience Journal 2016

Overcoming bias, disparity and differences..



Future directions : Gender Medicine

Gender-specific medicine aims at:

- understanding how different clinical signs, diagnostic procedures and therapeutic needs are in men and women
- developing sex tailored diagnostic and therapeutic approach
- establishing a close cooperation between research centres, universities and public institution to promote a ‘new style of doing research’ and to improve public awarness of women’s health

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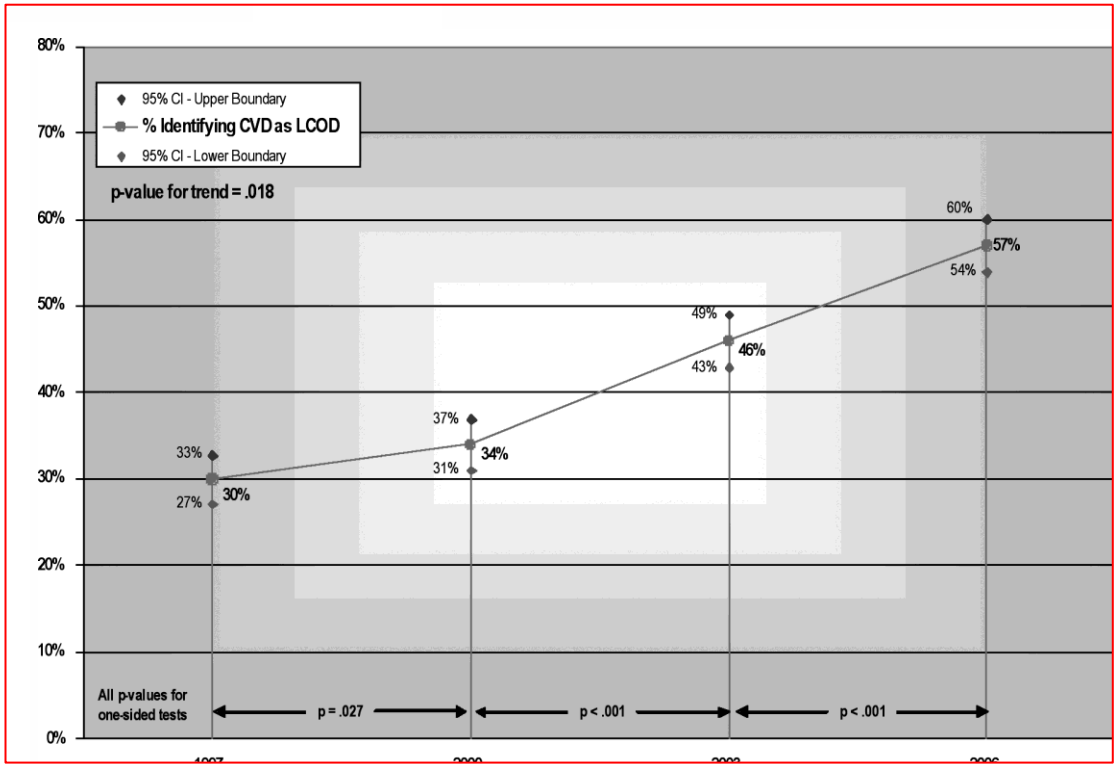
Nine-Year Trends and Racial and Ethnic Disparities in Women's Awareness of Heart Disease and Stroke: An American Heart Association National Study

ALLISON H. CHRISTIAN, Ed.D.,[1] WAYNE ROSAMOND, Ph.D.,[2]
ANTHONY R. WHITE, Ph.D.,[3] and LORI MOSCA, M.D., M.P.H., Ph.D.[1]

1,005 women (71% white, non-Hispanic, 12% black, non-Hispanic, 12% Hispanic, and 6% other ethnicities).



Trends in CVD as perceived leading cause of death

J of Women's Health 2007

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Special Report

National Study of Physician Awareness and Adherence to Cardiovascular Disease Prevention Guidelines

TABLE 8. Physician's Agreement With Statements About CVD Prevention and Guidelines*

	Physician Specialty		
	PCP (A) (n=300)	OBGyn (B) (n=100)	CARD (C) (n=100)
More women than men die each year of CVD.	8.3[C]	13.0	17.0
I am willing to seek additional training that will allow me to better engage in preventive health treatments for CVD in women.	28.0[B]	43.0[A,C]	25.0[B]

A striking finding in our study was a very low level of recognition (8% PCPs, 13% OBGyns, and 17% CARDs) that heart disease kills more women every year than men. According to AHA statistics, nearly 500 000 women die of CVD each year, exceeding the number of men. These physician data underscore the need for awareness campaigns about women and heart disease among healthcare providers, especially because awareness of risk is a critical first step in taking action to reduce it.

Mosca L et al. Circulation. 2005;111:499

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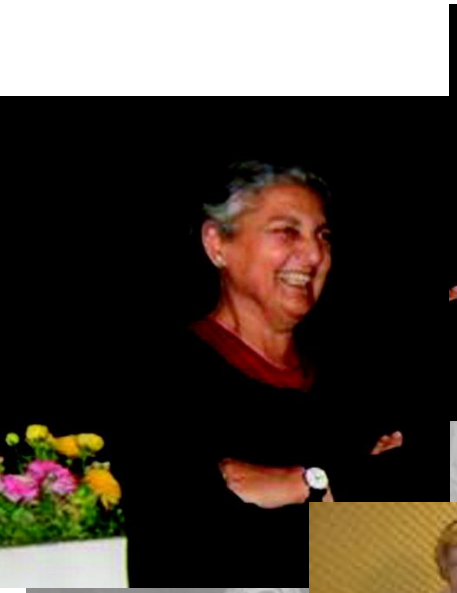
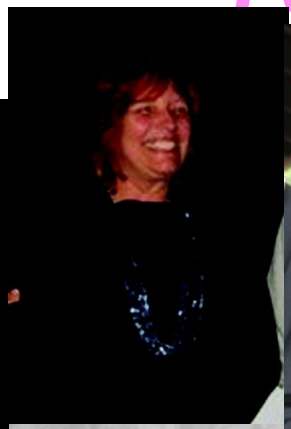
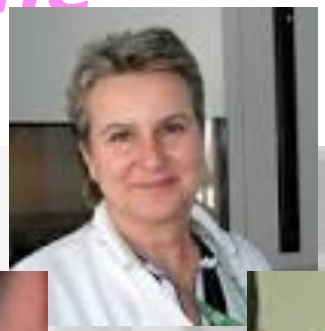
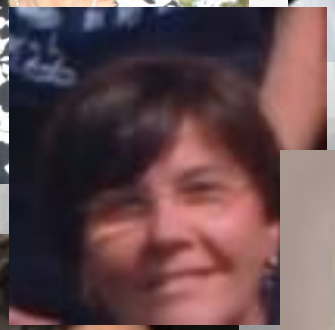
Grazie a tutti per l'attenzione











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