

Attenti alle differenze: sintomi, test diagnostici, malattia coronaria. Immaginazione o realtà

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QUANDO LA X NON E' UN PAREGGIO

S EX ROLES

Attività lavorativa;
socializzazione; aggressività

U NISEX ANALYSES

Attività fisica; DHEAS effetti positivi negli
uomini; estrogeni positivi per donne; parità

P OPULATION STUDIES

Abitudini voluttuarie

E NDOGENOUS ESTROGEN

Menopausa

R ISK FACTORS

Maggiori negli uomini; diabete equilibra il rischio

I NHERITANCE / GENES

Differenze genetiche legate ai cromosomi XX vs XY

O BESITY AND TESTOSTERONE

Maggiore obesità centrale e quindi sindrome
metabolica negli uomini

R ECONSTRUCTION

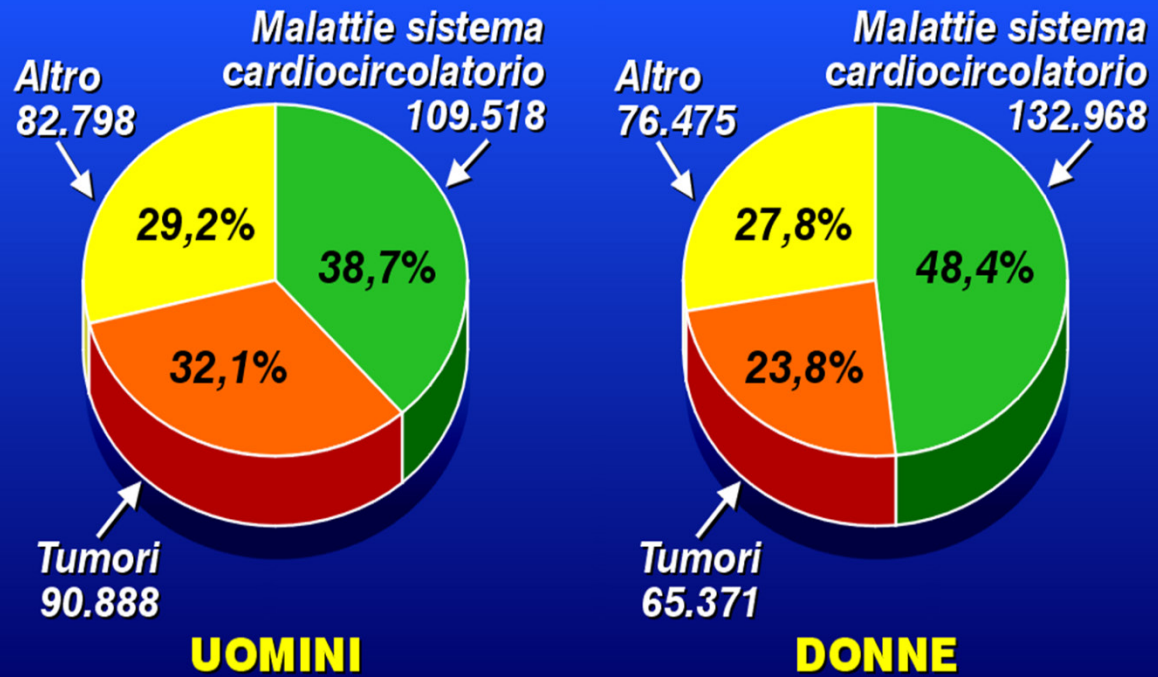
La medicina di genere studia le differenze sessuali, socio-culturali e comportamentali che influiscono sullo sviluppo, diagnosi e cura della malattia.

Sindrome di Yentl

L'articolo analizza i risultati di due studi effettuati nel Massachusset e nel Maryland su un gruppo di donne affette da coronaropatia. A differenza degli uomini le donne subivano più errori diagnostici, ricevevano meno cure e venivano sottoposte ad interventi chirurgici non risolutivi.

Mortalità per malattie cardiovascolari

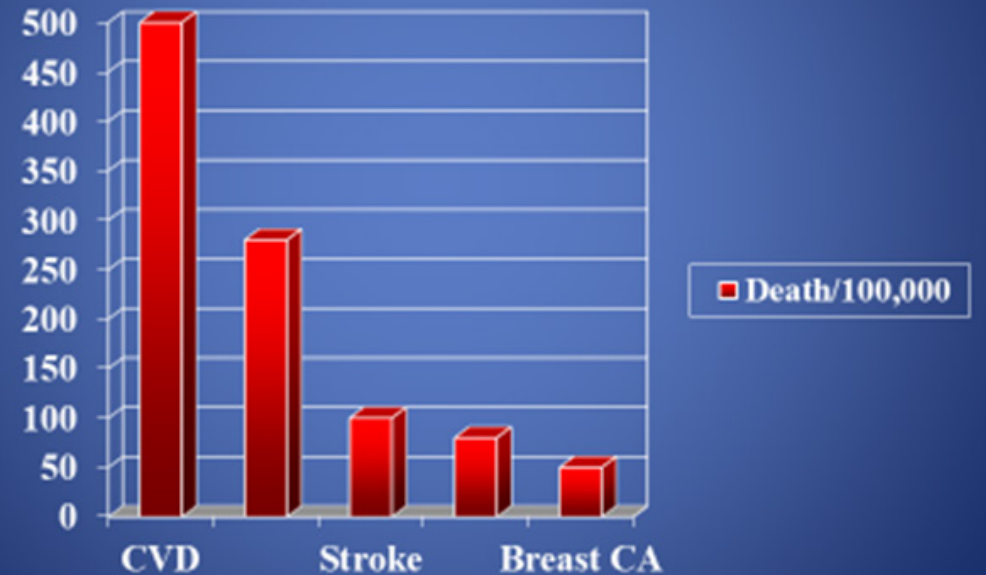
Principali cause di morte in Italia



Rapporti ISTISAN, 2001

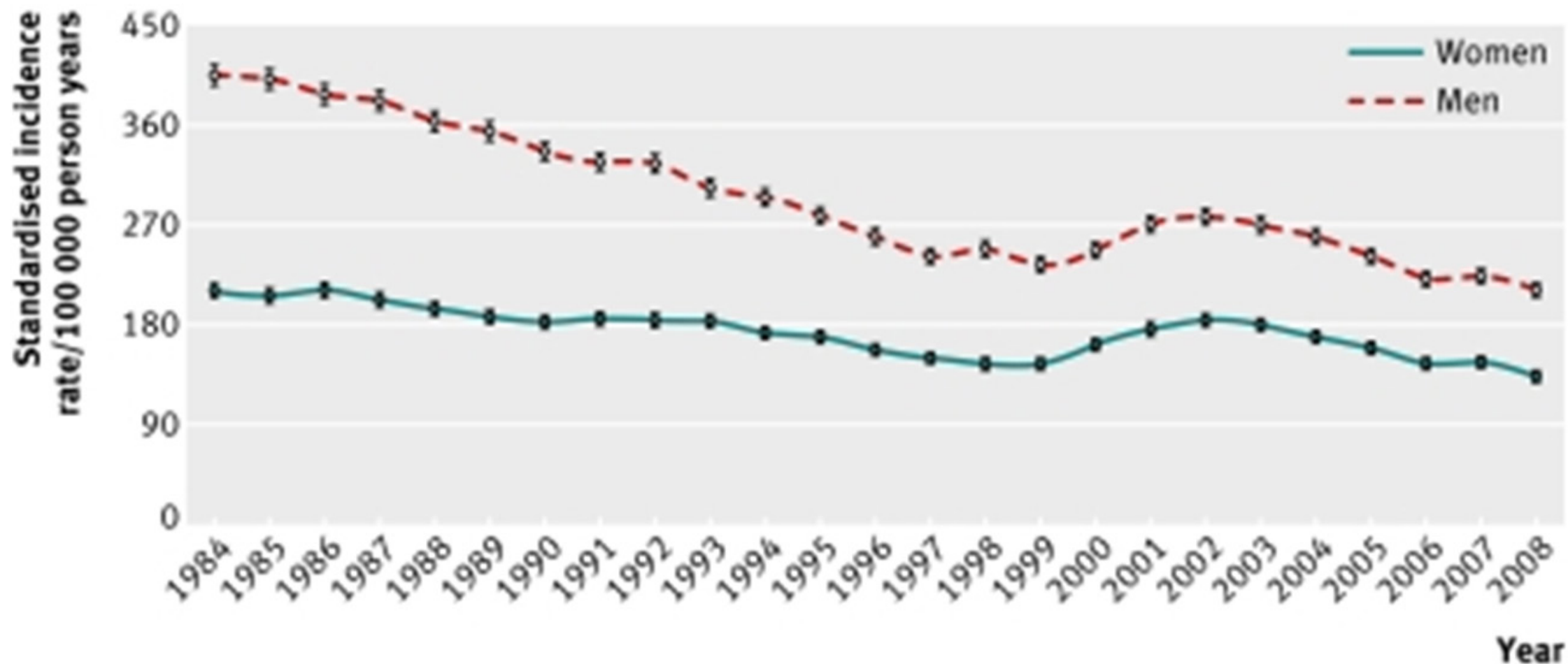
Campagna Nazionale di Prevenzione del Rischio Cardiovascolare Globale

CVD is the leading cause of death in women



AHA 2003

Mortalita a 1 anno post IMA



Transient increase in incidence starting around 2000 was presumably due to new diagnostic criteria for myocardial infarction^{41,46}

Men Are From Mars, Women Are From Venus



ANATOMIA e FISIOLOGIA

- **Compared to Men, Women have:**
 - **Lower LV mass**
 - **Greater contractility**
 - **Preserved mass with aging**
 - **Lower rate of apoptosis**
 - **Small coronary vessels**
 - **Lower blood pressure**
 - **Faster resting HR**
 - **Less catecholamine mediated vasoconstriction**

FISIOLOGIA

Qual é la differenza tra una donna con tensione premenstruale e un pitbull?
Il rosetto



- **Estrogen**
 - Receptors on cardiac cells
 - Estrogen affects hepatic gene expression
 - Improved lipids
 - Vascular effects: vasodilation
 - Stimulates immune system
 - Affects cytokine/inflammatory pathways
- **Testosterone**
 - Increases inflammation/cholesterol

Sintomi

Quando si ammala una donna

*Sto bene, sono solo
un po' stanca.*



Quando si ammala un uomo

*Ascoltatemi attentamente
miei cari. Queste potrebbero
essere le mie ultime parole...*



SINTOMI

Maschi

- Dolore toracico oppressivo, dolore simile a una coltellata
- Irradiazione al dorso, collo, braccia, mandibola
- Cambiamenti nel ritmo cardiaco
- Dispnea
- Bruciore, nausea, vomito, dolore epigastrico
- Sudorazione algida
- Vertigini

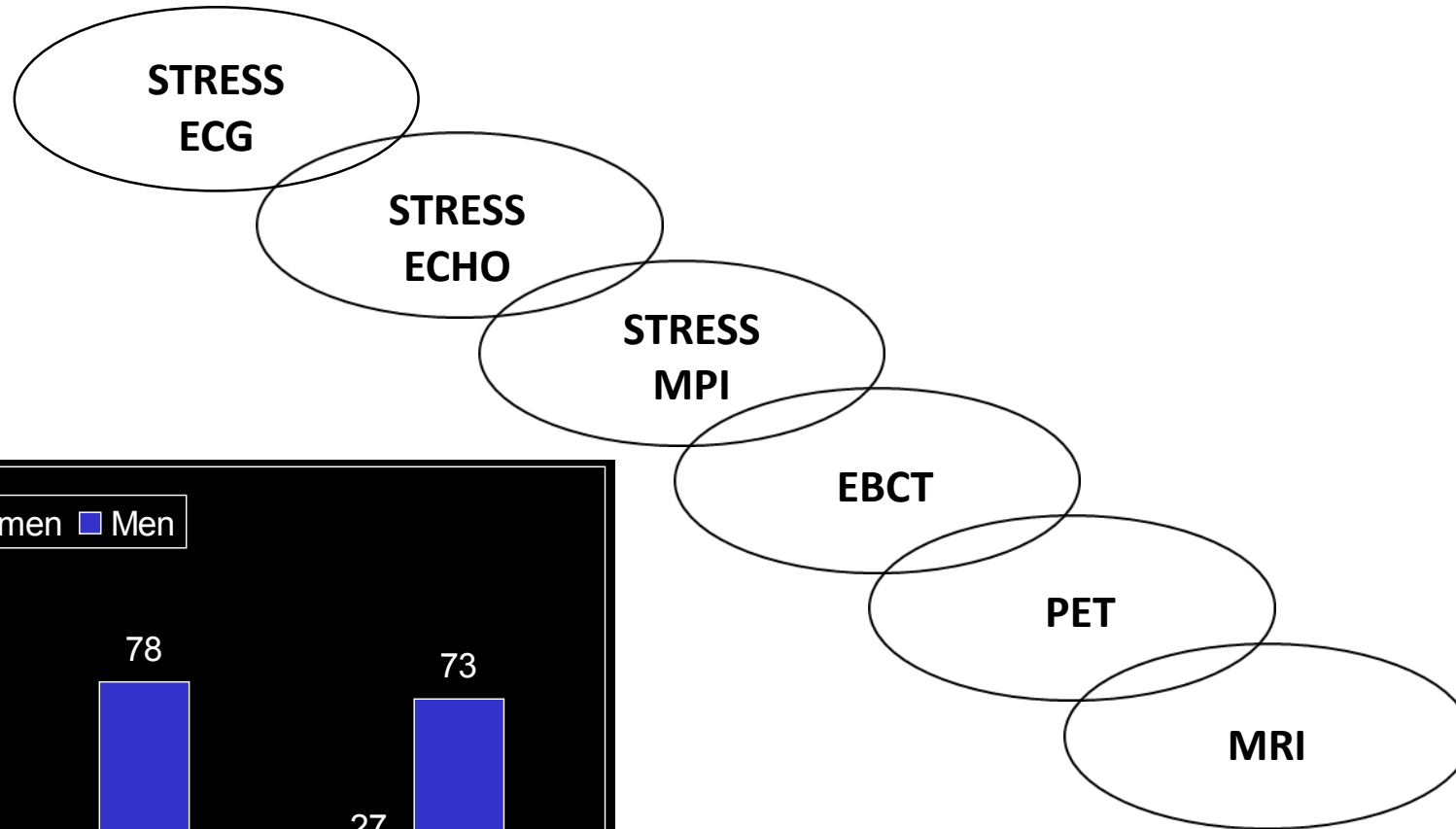
Femmine

- Sintomi più lievi, spesso senza dolore toracico
- Insorgenza improvvisa di debolezza, malessere generale
- Sensazione di fastidio al torace al dorso, al collo

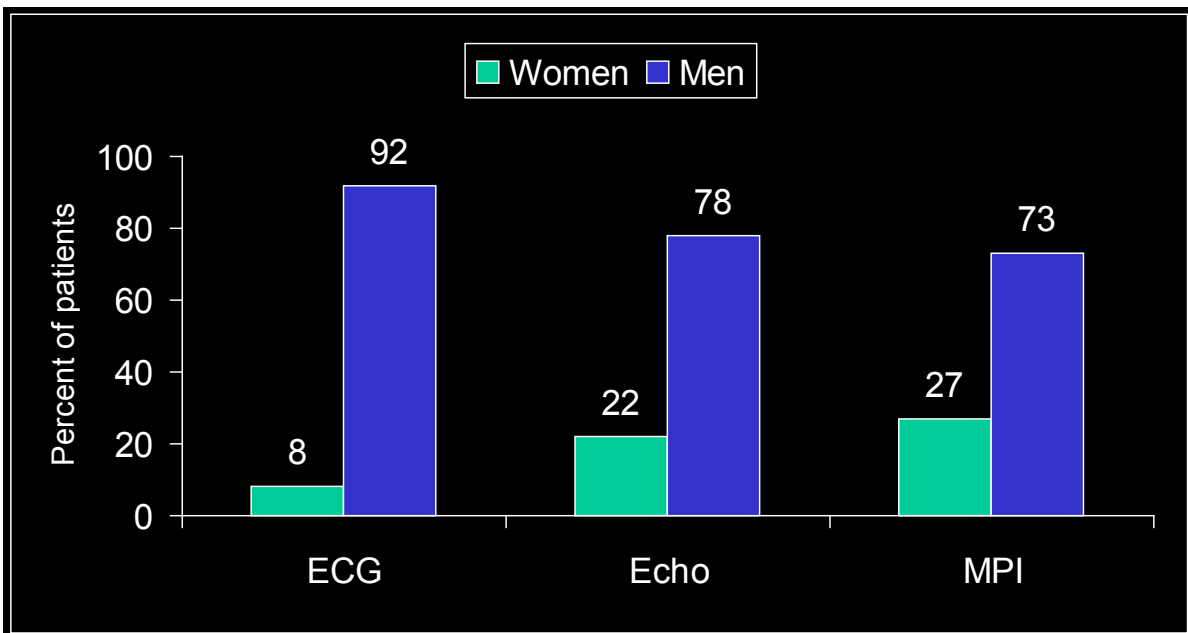
- Livello di inglese?
 - Ottimo
- Traduca "capire le donne"
- "Mission Impossible"
 - Assunto



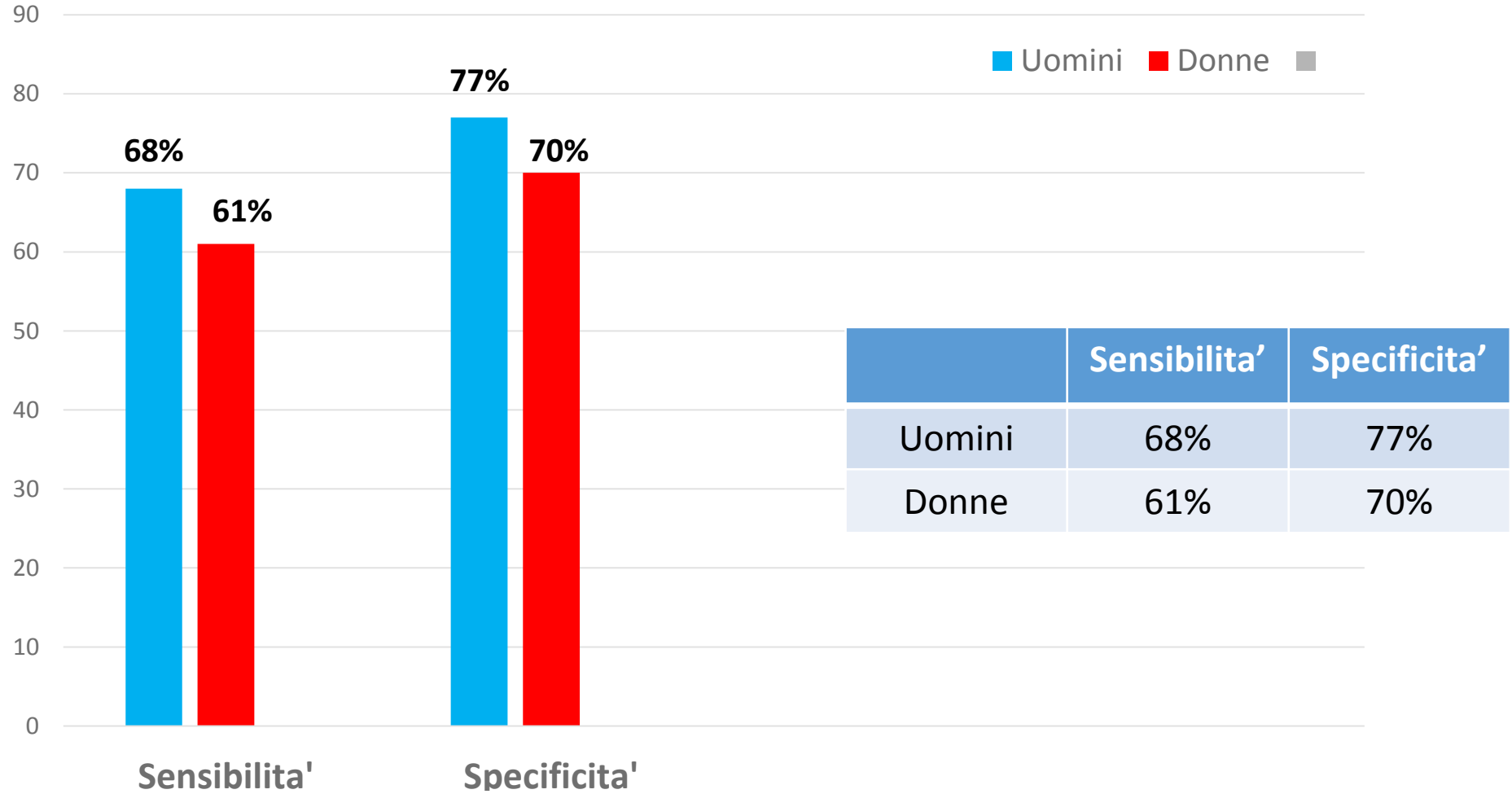
Dolore toracico -> cardiopatia ischemica?



Donne nei trials



Test Ergometrico





TEST ERGOMETRICO

Treadmill exercise testing

A low exercise capacity in symptomatic as well as in asymptomatic women is a strong predictor of five-year mortality.

Diagnostic accuracy of exercise testing in women can be further improved by assessment of the angina history, oestrogen status and the presence of major CHD risk factors.

FIGURA 2. Fotogrammi teleistolici da proiezioni parasternali di un normale ecocardiogramma da sforzo.



PLX = asse lungo; PSX = asse corto; AS = atri sinistru; VD = ventricolo destro; VS = ventricolo sinistro.
(Modificata da Di Iorio et al. The Echo Manual, 3rd ed.
Lippincott Williams and Wilkins, Philadelphia, 2001)

ECOSTRESS

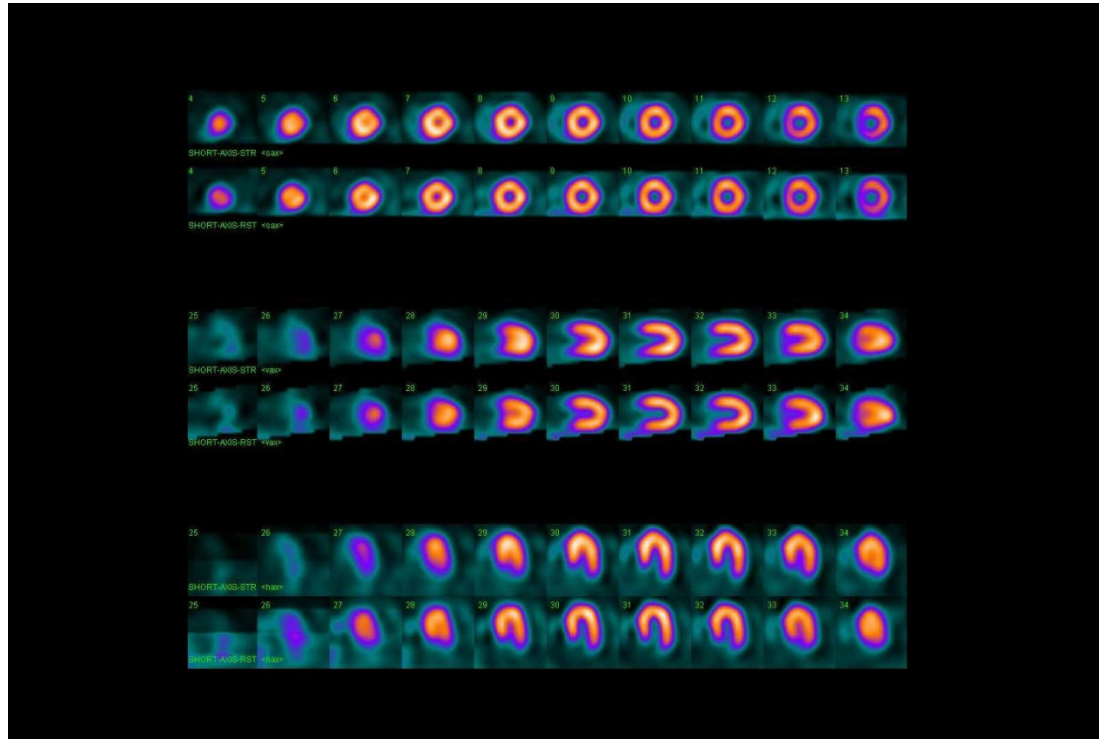
Stress echocardiography with exercise or dobutamine can be an important test to evaluate wall motion abnormalities and its clinical value is not different between the two genders.

Sensitivity 88%

Specificity 86%



SCINTIGRAFIA MIOCARDICA



The accuracy of myocardial perfusion imaging scans used to be less in women in the past due to smaller vessel size and breast attenuation

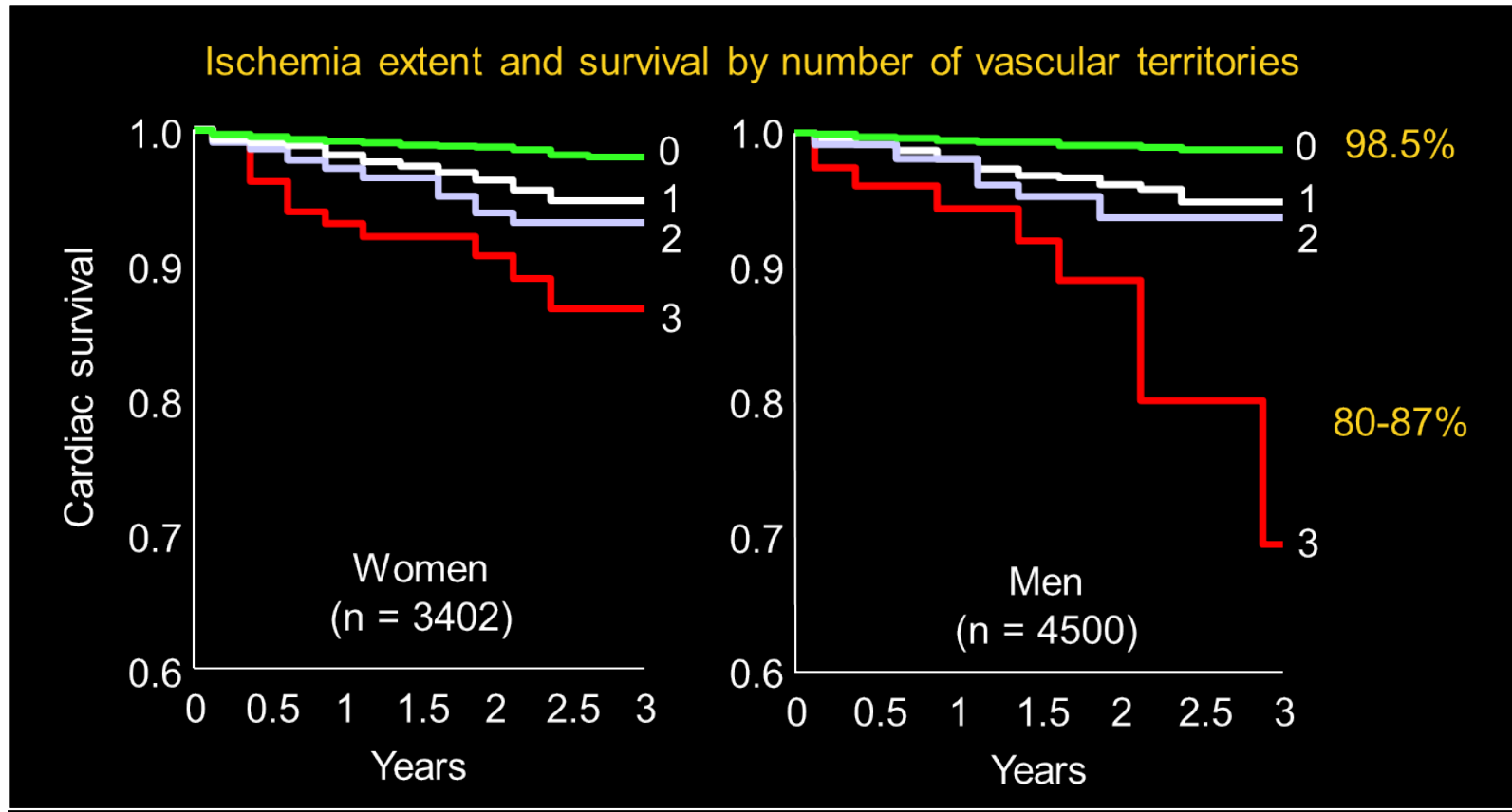
With more advanced SPECT imaging techniques performed with Technetium sestamibi the predictive value of the scans has improved dramatically.

It remains important, however, to include signs of chest pain, electrocardiographic abnormalities and a low functional capacity in the interpretation of the scans.

Sensitivity 84%

Specificity 94%

SCINTIGRAFIA MIOCARDICA





CORONARO-TC

Calcium scoring with EBTC or multi-slice CT is a very useful modality to rule out the presence of obstructive CHD, but the (cumulative) radiation exposure makes this technique less suitable in premenopausal women and for follow-up purposes.

In women >50 years of age who are at intermediate risk for CHD the absence of coronary calcium has a very high (99%) negative predictive value for obstructive coronary atherosclerosis.

In all age groups calcium scores are lower in women than in men

Coronarografia

Detailed Angiographic Analysis of Women With Suspected Ischemic Chest Pain (Pilot Phase Data from the NHLBI-Sponsored Women's Ischemia Syndrome Evaluation [WISE] Study Angiographic Core Laboratory)

Barry L. Sharaf, MD, Carl J. Pepine, MD, Richard A. Kerensky, MD, Steven E. Reis, MD, Nathaniel Reichel, MD, William J. Rogers, MD, George Sopko, MD, Sheryl F. Kelsey, PhD, Richard Holubkov, PhD, Marian Olson, MS, Nicholas J. Miele, BA, David O. Williams, MD, and C. Noel Bairey Merz, MD, for the WISE Study Group

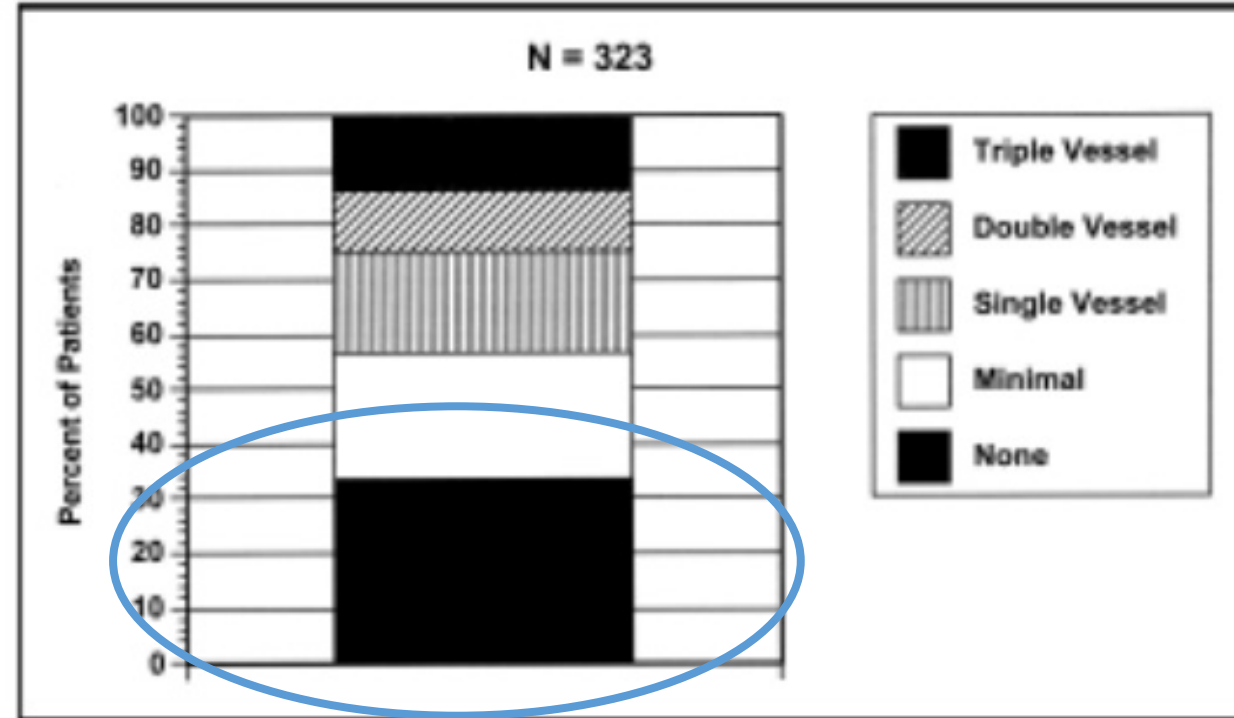


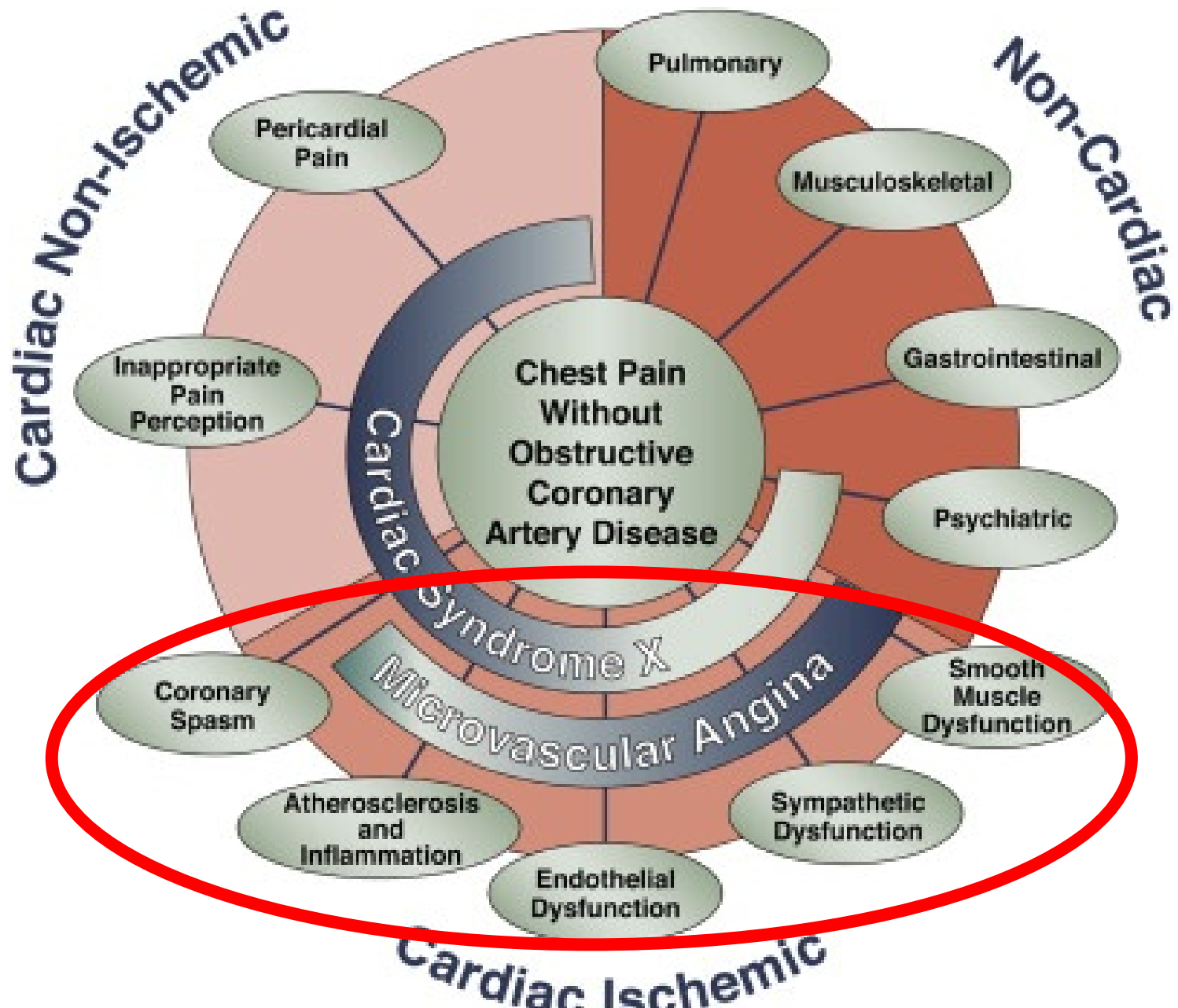
FIGURE 1. Extent of CAD in patients.

Chest pain syndromes are more common in women than in men and are less related to the presence of atherosclerosis in the large epicardial coronary arteries

Table. Prevalence of “Normal” and Nonobstructive Coronary Arteries in Women Compared With Men

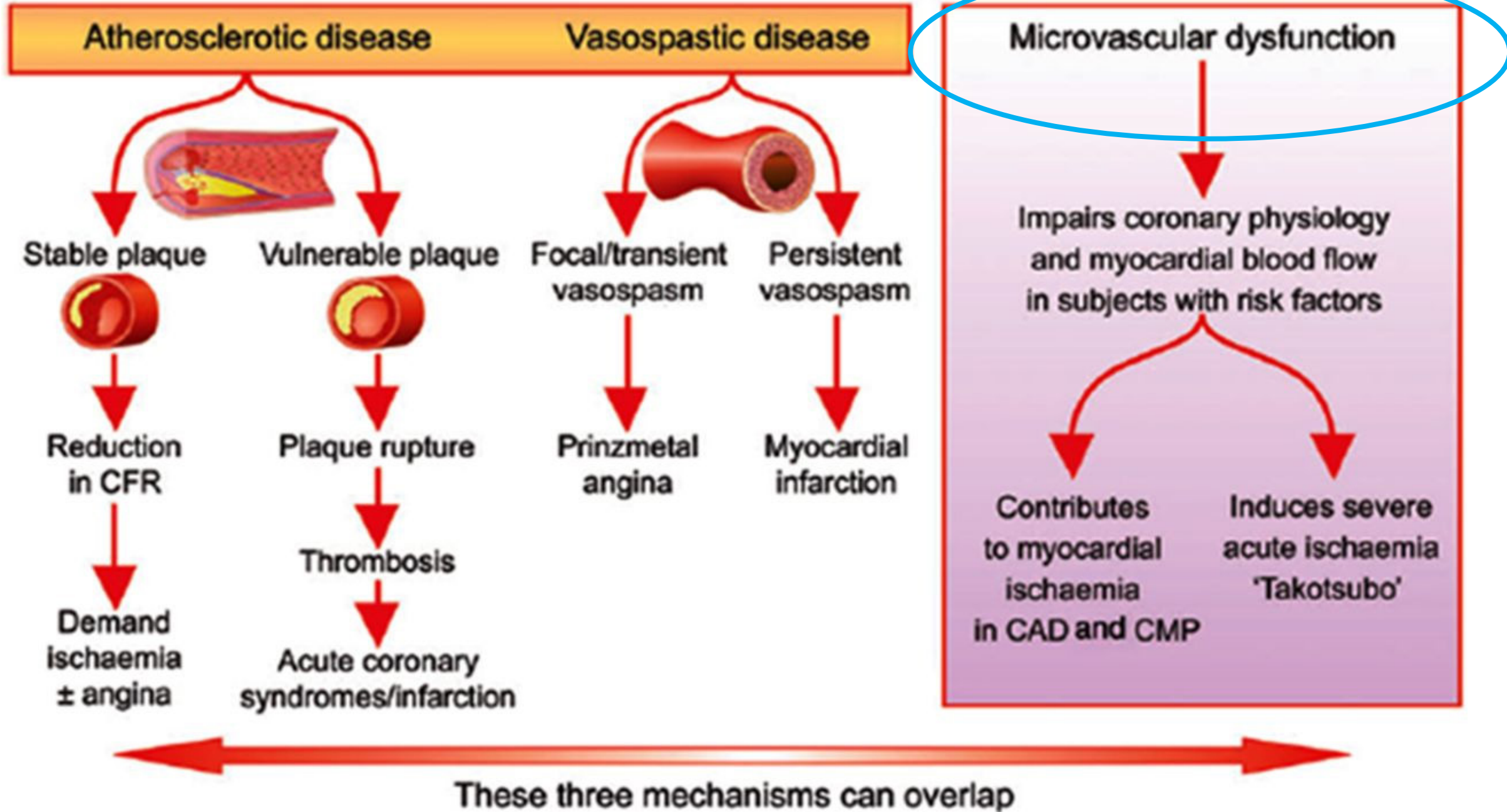
	No./Total (%)		P Value
	Women	Men	
Acute coronary syndrome			
GUSTO ²	343/1768 (19.4)	394/4638 (8.4)	<.001
TIMI 18 ³	95/555 (17)	99/1097 (9)	<.001
Unstable angina ²	252/826 (30.5)	220/1580 (13.9)	<.001
TIMI IIIa ⁶	30/113 (26.5)	27/278 (8.3)	<.001
MI without ST-segment elevation ²	41/450 (9.1)	55/1299 (4.2)	.001
MI with ST-segment elevation ²	50/492 (10.2)	119/1759 (6.8)	.02

Abbreviations: GUSTO, Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries; MI, myocardial infarction; TIMI, Thrombosis In Myocardial Infarction.



Epicardial coronary arteries

Coronary microcirculation



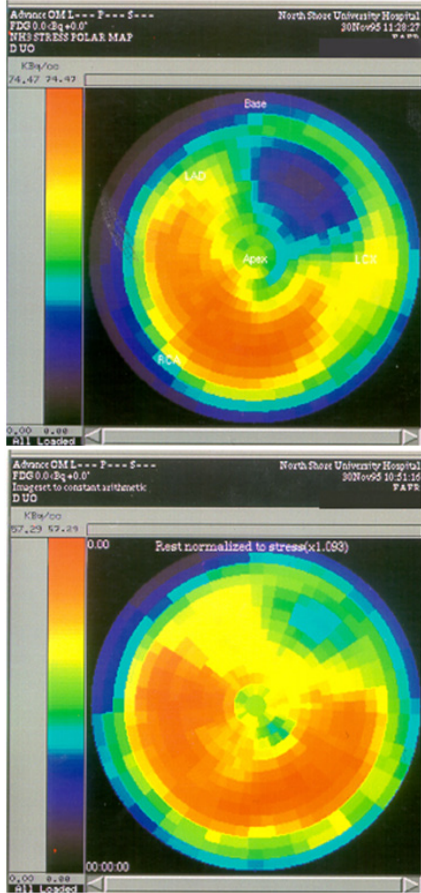
ANGINA MICROVASCOLARE

At **younger ages women** more often have ACS with angiographically 'normal' coronary arteries than men.

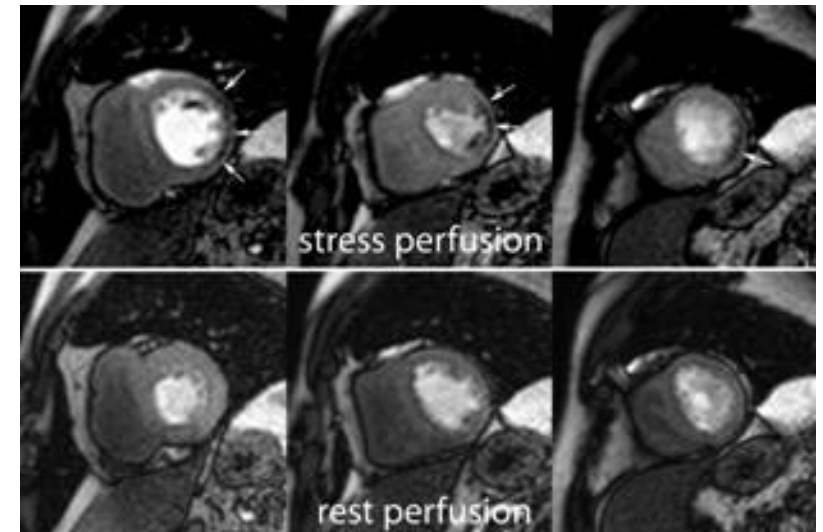
The **prognosis of this syndrome is less beneficial** than initially considered and often leads to recurrent hospitalisations and repeated coronary angiograms.

The underlying mechanisms of this so-called coronary microvascular dysfunction are diverse and may be related to **endothelial reactivity, low endogenous oestrogen levels, coagulation disorders, abnormal inflammatory reactions and its manifestation can have a substantial variability among individuals.**

Microvascular dysfunction and diffuse coronary atherosclerosis without obstructive lesions is more prevalent in women than in men and can be better visualised with positron emission tomography (PET**) and cardiovascular magnetic resonance (**CMR**) techniques.**



PET e CMR



The Yentl Syndrome is Alive and Well in 2011

Bairey Merz, EHJ 2011

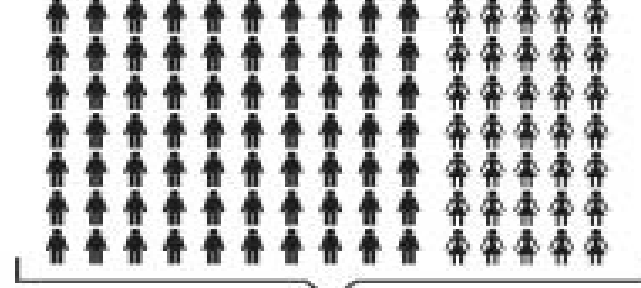
→
Men > women with
with recognized
angina/ACS

→
Men > women go to
coronary
angiography

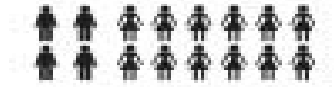
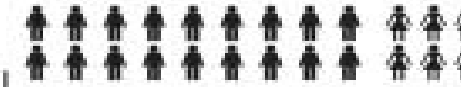
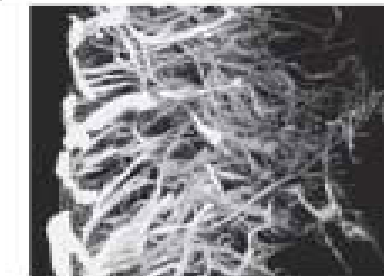
→
Men > women
receive
guidelines Rx

→
Women > men death

Angina/
ACS

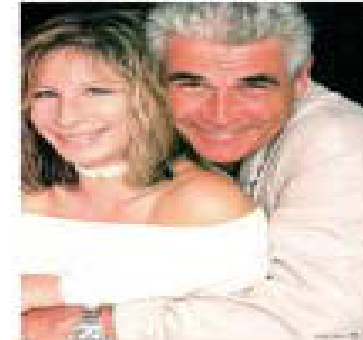
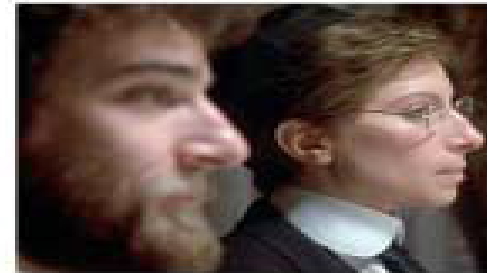


Coronary
Angiography



Obstructive CAD
Male-pattern

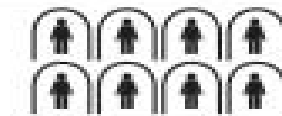
Microvascular CAD
Female-pattern



RX:
ASA,
BB,
ACE,
STATIN

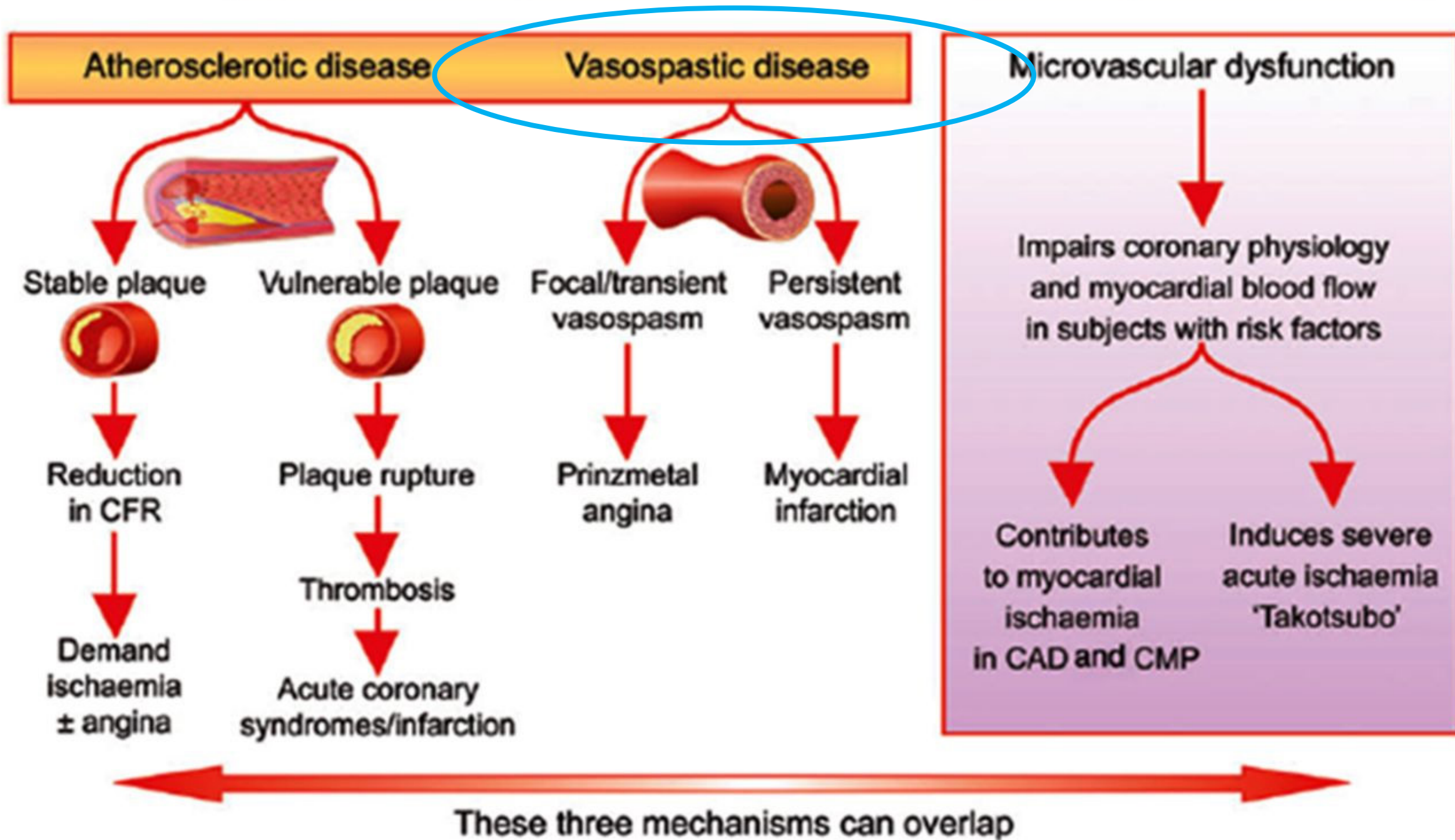


DEATH/MI
FOLLOWUP



Epicardial coronary arteries

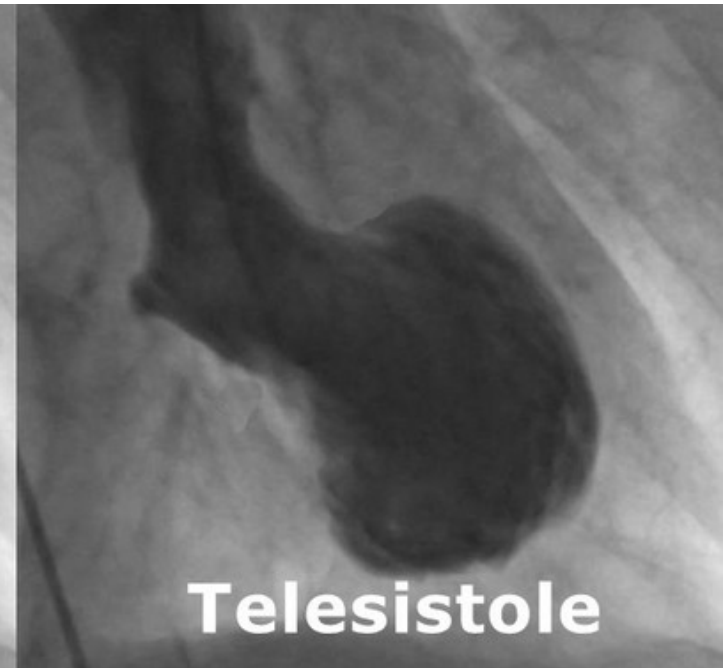
Coronary microcirculation



- < Sesso femminile più colpito
- < L'età più interessata tra i 58-77 anni
- < Disfunzione ventricolare sinistra transitoria
- < Alterazioni elettrocardiografiche che possono mimare l'infarto acuto
- < Minime alterazioni dei marcatori enzimatici di danno miocardico
- < Malattia coronarica non critica

TAKOTSUBO Apical Ballooning Syndrome

Cardiomiopatia da stress



Le catecolamine: ruolo non chiaro!

Ipotesi:

1. mediano lo spasmo delle coronarie epicardiche
2. mediano lo spasmo microvascolare
3. mediano un danno miocitario diretto

Un sovraccarico di catecolamine determina riduzione della vitalità dei miociti attraverso un sovraccarico di calcio.

- 3 Le catecolamine sono, inoltre, causa di produzione di radicali liberi dell'ossigeno.

Sono istologicamente correlate alla necrosi a bande di contrazione (evidente nella s.di takotsubo).

1

L'incremento del tono simpatico può causare vasocostrizione coronarica in soggetti privi di stenosi coronariche

MA

negli studi finora effettuati non c'è evidenza di spasmo coronarico alla coronarografia!

2

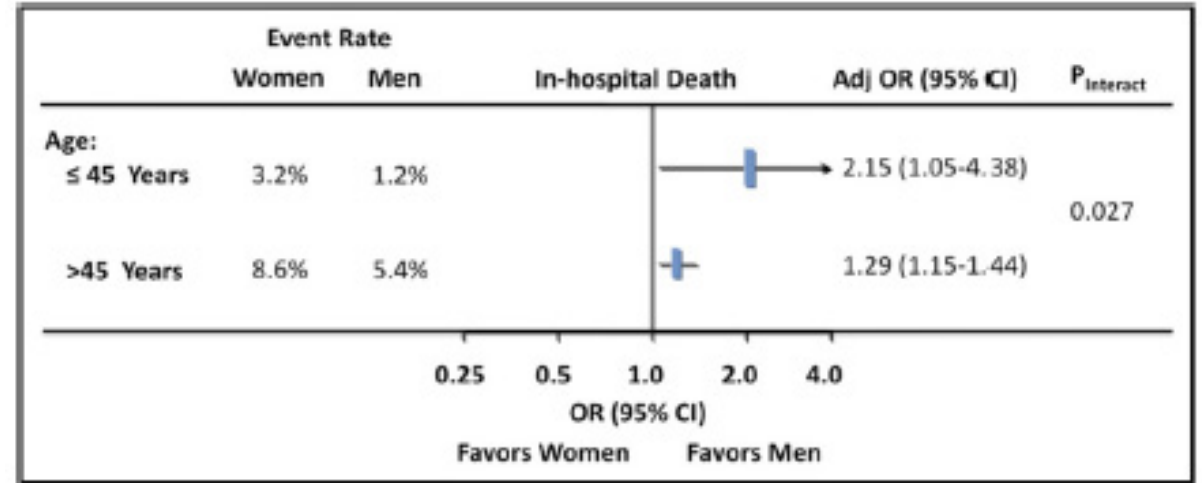
Un anomalo flusso coronarico microvascolare è stato recentemente individuato nei soggetti affetti da takotsubo

MA

non vi sono sufficienti evidenze per sostenere tale eziologia!

STEMI

At presentation in STEMI, both men and women have comparable symptoms of chest pain, but women tend to have more concomitant vaso-vegetative symptoms that can mask the chest pain, with less extensive ST-T elevations at admission especially at younger ages.



Age and Gender Differences in Quality of Care and Outcomes for Patients with ST-segment Elevation Myocardial Infarction
Sripal Bangalore

STEMI both genders have equal benefit of early percutaneous coronary interventions (PCI)

NSTEMI

The therapeutic strategies should be different between men and women. In the **FRISC II and RITA 3 trials, early invasive strategy of patients with unstable angina or non-STEMI ACS was proven to reduce mortality in men, but not in women.** A meta-analysis of eight combined non-STEMI trials has confirmed that an early conservative strategy in low-risk (biomarker-negative) women is better than an early invasive strategy, which is in line with the already updated ACC/AHA guidelines on non-STEMI in 2007.

NSTEMI

Furthermore, after PCI women have significantly **more bleeding complications,** especially when glycoprotein IIb/IIIa inhibitors are used

CABG

Mortality after coronary artery bypass surgery (CABG) is higher in women compared with men and this difference is more pronounced in the younger age groups, after adjustment for risk factors.



**Uomini – donne
1-9 % vs 4.6%**

Many factors influence this gender gap

- **comorbid conditions at older age**
- **smaller vessel size**
- **more urgent procedures in women**
- **presence of hypertensive heart disease**

RISCHIO DI MORTALITA' POST CABG

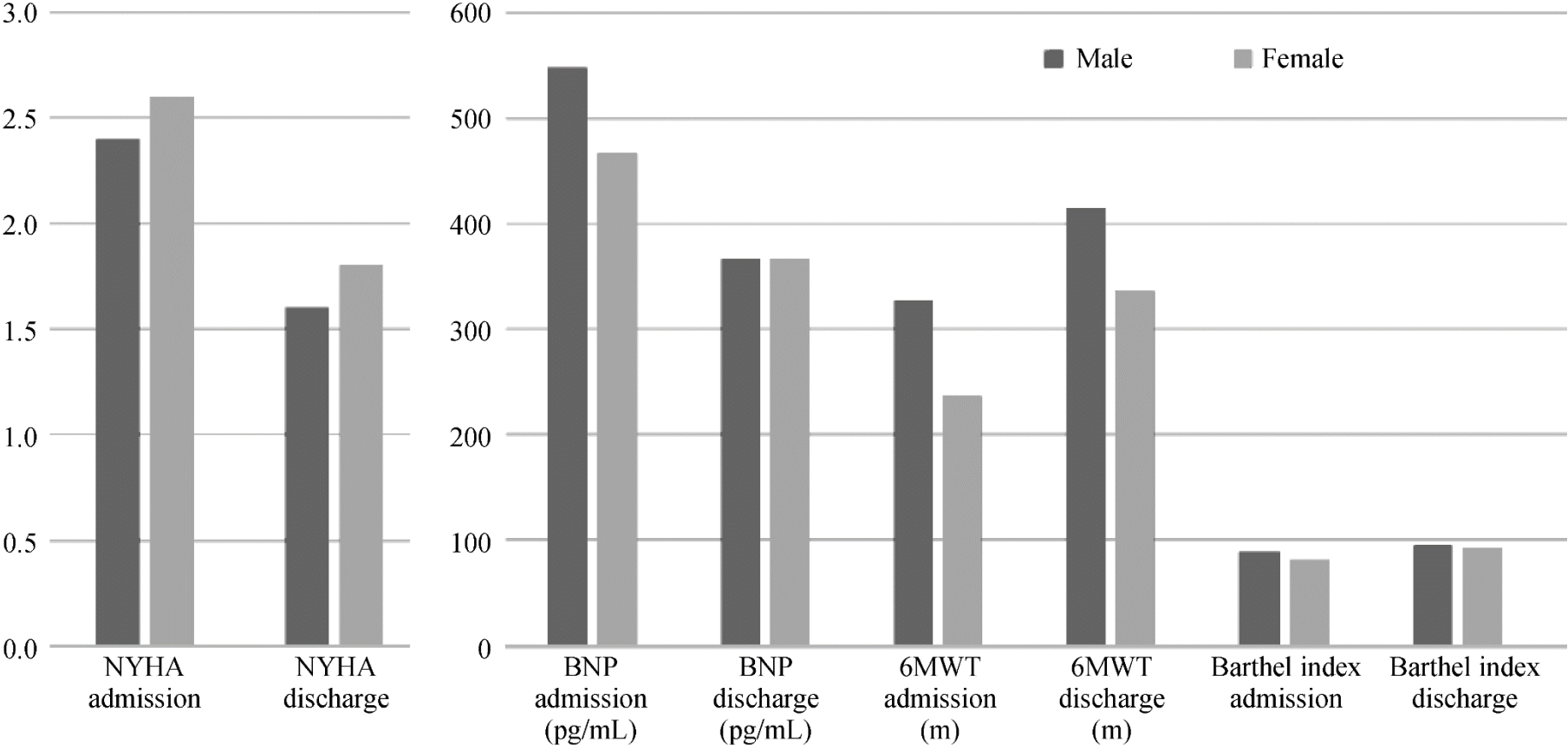
Author	n	Year	Mortality (Males vs Females)
Abramov	4823	2002	2.7% vs 1.8% ($p = 0.09$)
Aldea	1743	1999	1.5% vs 1.0% ($p = 0.33$)
Blankstein	15440	2005	4.24% vs 2.23% ($p < 0.0001$)
Carey	1335	1995	6.3% vs 3.1% ($p = 0.011$)
Christakis	7025	1995	3.5% vs 1.8% ($p < 0.0001$)
Doenst	1567	2006	7% vs 4% ($p = 0.026$)
Edwards	344913	1998	4.52% vs 2.61% ($p < 0.001$)
Hammar	3933	1997	3.0% vs 1.7% ($p < 0.01$)
Humphries	25212	2007	3.6% vs 2.0% ($p < 0.001$)
Koch	15597	2003	2.4% vs 1.4% ($p < 0.01$)
O'Connor	3055	1993	7.1% vs 3.3% ($p < 0.001$)
Ramstrom	220	1993	5.6% vs 2.4% ($p < 0.001$)
Vaccarino	15178	2002	5.3% vs 2.9% ($p < 0.001$)
Woods	5324	2003	3.16% vs 1.95% ($p = 0.007$)

The role of gender in coronary surgery

Justin D. Blasberg Gary S. Schwartz Sandhya K. Balaram

European Journal of Cardio-Thoracic Surgery, Volume 40, Issue 3, 1 September 2011

RIABILITAZIONE CARDIOVASCLARE



ACS

Factors influencing underutilization of evidence-based therapies in women[†]

Raffaele Bugiardini^{1*}, Andrew T. Yan², Raymond T. Yan², David Fitchett², Anatoly Langer², Olivia Manfrini¹, and Shaun G. Goodman², on behalf of the Canadian Acute Coronary Syndrome Registry I and II Investigators*

¹Dipartimento di Medicina Interna, Cardioangiologia, Epato-logia (Padiglione 11), University of Bologna, Via Massarenti 9, 40138 Bologna, Italy; and ²Terrence Donnelly Heart Centre, Division of Cardiology, St. Michael's Hospital, University of Toronto and the Canadian Heart Research Centre, Toronto, Ontario, Canada

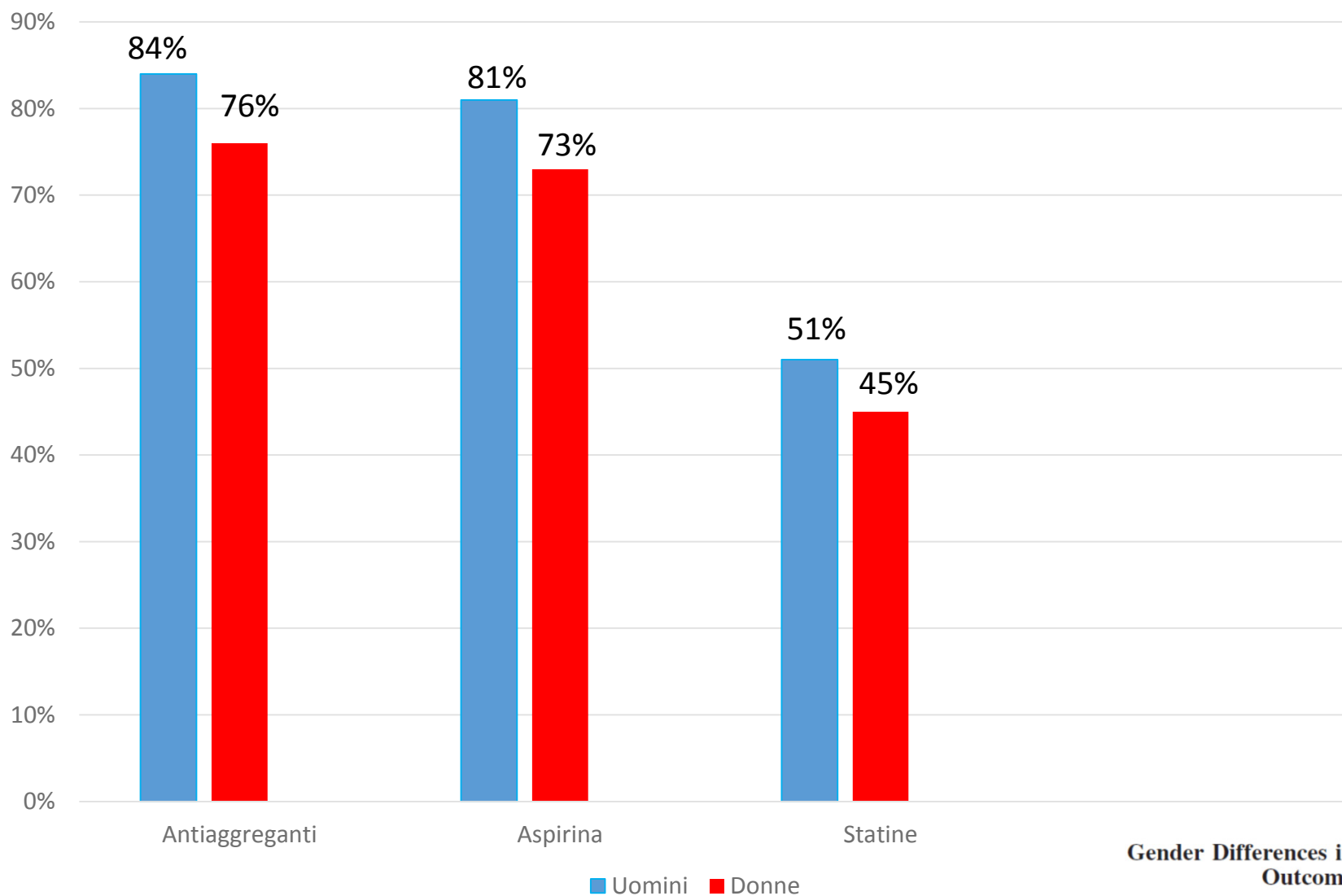
UOMINI

DONNE

	UOMINI	DONNE	
Medication at discharge, n (%)			
Anti-platelet agents	4146/4447 (93.23)	1924/2074 (92.77)	0.49
Beta-blockers	3528/4452 (79.24)	1575/2079 (75.75)	0.0015
Lipid-modifying agent	2912/4450 (65.44)	1172/2079 (56.37)	< 0.0001
ACE-inhibitors	2671/4452 (59.99)	1152/2075 (55.52)	0.0006
Procedures during hospitalization, n (%)			
Angiography	2218 (49.6)	874 (41.8)	< 0.0001
PCI	1026/4471 (23)	373/2087 (18)	< 0.0001
CABG	345/4471 (0.08)	93/2087(0.04)	< 0.0001
Outcomes at hospital discharge, n (%)			
Death	100/4471 (2.23)	70/2087 (3.35)	0.0078
Death/myocardial infarction	348/4471 (7.78)	176/2087 (8.43)	0.36
Outcomes at 1 year follow-up, n (%)			
Death	332/4138 (8.02)	203/1939 (10.47)	0.0017
Death/myocardial infarction	637/4059 (15.69)	331/1902 (17.40)	0.095



Trattamento angina stabile



IN SINTESI

Immaginazione

Realtà

Myths	Facts
Men are more likely to have heart disease	Heart disease is the #1 killer of men and women; 50,000 more women than men die of heart disease every year
Cancer is a bigger threat than heart disease	Nearly twice as many US women die from heart disease and stroke than from all cancers combined
Doctors are aware of women's risk for heart disease and act accordingly	Undertreatment and underdiagnosis of heart disease in women contributes to excess mortality in women

LE DONNE NON SONO PICCOLI UOMINI

Un recente studio ha dimostrato che le donne in sovrappeso vivono più a lungo dell'uomo che glielo fa notare.

Quello che le donne dicono alcolicesimo



DIFFERENZE

- ORMONALI
- GENETICHE
- VOLUTTUARIE
- PRESENTAZIONE CLINICA
- RISPOSTA ALLA TERAPIA
- OUTCOME



SOLUZIONI

- MAGGIORE RAPPRESENTANZA NEI TRIALS CLINICI**
- MAGGIORE ATTENZIONE DA PARTE DEL MEDICO A SINTOMI**
- OTTIMIZZAZIONE TEST DIAGNOSTICI NON INVASIVI**
- MAGGIORE «AGGRESSIVITA'» NEL TRATTAMENTO**
-**