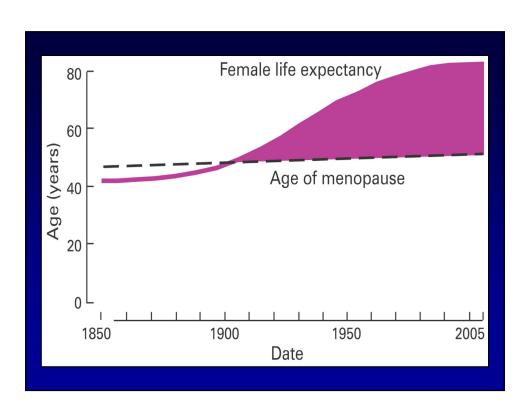
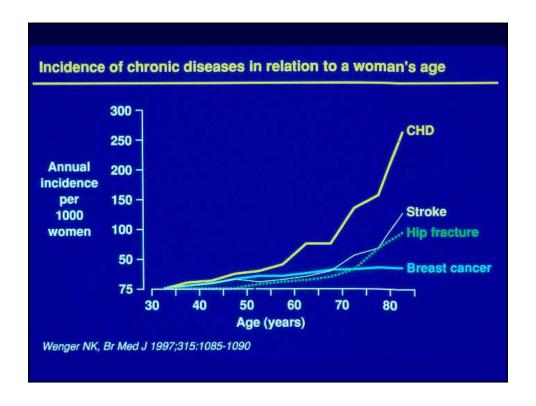
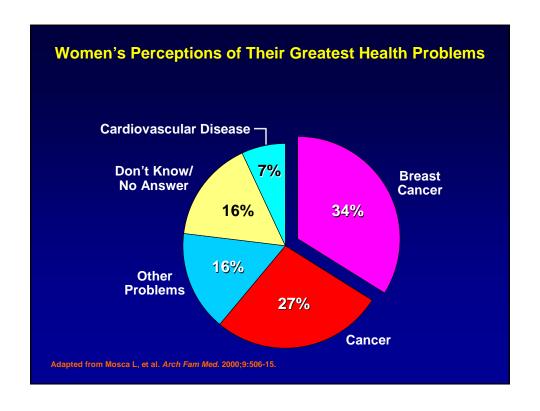
Gender issues in cardiovascular guidelines

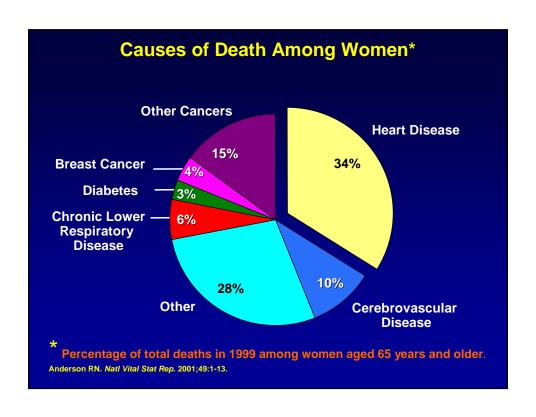
Peter Collins
Professor of Clinical Cardiology,
Royal Brompton Hospital & Imperial College
London, UK





 Many women and their physicians are unaware that cardiovascular disease (CVD) is the commonest cause of death in women.





Women Enrolled in Major Cardiovascular Trials

20%
14%
n) 0%
10%
17%
27%
ptopril) 26%

Clinical Practice Guidelines

- systematically developed statements to assist practitioners with decisions about appropriate health care for specific patients' circumstances
- Guidelines often assumed to be epitome of evidence-based medicine
- Guideline recommendations imply not only an evaluation of the evidence but also a value judgment based on personal or organizational preferences regarding the various risks and benefits of a medical intervention for a population

ACC/AHA Guidelines

- 20 years American College of Cardiology (ACC) and American Heart Association (AHA) have released clinical practice guidelines to provide recommendations on care of patients with cardiovascular disease.
- The ACC/AHA guidelines currently use a grading schema based on level of evidence and class of recommendation (available at http://www.acc org and http://www.aha.org).

Scientific Evidence Underlying the ACC/AHA Clinical Practice Guidelines

Pierluigi Tricoci; Joseph M. Allen; Judith M. Kramer; et al. *JAMA*. 2009;301(8):831-841

Context

 The joint cardiovascular practice guidelines of the American College of Cardiology (ACC) and the American Heart Association (AHA) have become important documents for guiding cardiology practice and establishing benchmarks for quality of care

Objective

 To describe the evolution of recommendations in ACC/AHA cardiovascular guidelines and the distribution of recommendations across classes of recommendations and levels of evidence

Data Sources and Study Selection

- Data from all ACC/AHA practice guidelines issued from 1984 to September 2008 were abstracted by personnel in the ACC Science and Quality Division
- Fifty-three guidelines on 22 topics
- Total of 7196 recommendations

Data Extraction

- Number of recommendations and the distribution of classes of recommendation (I, II, and III) and levels of evidence (A, B, and C) determined
- The subset of guidelines that were current as of September 2008 was evaluated to describe changes in recommendations between the first and current versions as well as patterns in levels of evidence used in the current versions

Classes	of	Recommendations

Classes of Recommendations	Definition
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.
Class Ila	Weight of evidence/opinion is in favour of usefulness/efficacy.
Class IIb	Usefulness/efficacy is less well established by evidence/opinion.
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective and in some cases may be harmful.

Levels of Evidence

Level of Evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of Evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of Evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

Results

- Guidelines with at least 1 revision or update by September 2008 - number of recommendations increased from 1330 to 1973 (48%) from the first to the current version - largest increase observed in use of class II recommendations
- 16 current guidelines reporting levels of evidence, only 314 recommendations of 2711 total are classified as level of evidence A (median, 11%)
- 1246 (median, 48%) are level of evidence C
- Level of evidence significantly varies across categories of guidelines (disease, intervention, or diagnostic) and across individual guidelines
- Recommendations with level of evidence A are mostly concentrated in class I, but only 245 of 1305 class I recommendations have level of evidence A (median, 19%)

Clinical Practice Guidelines published by AHA/ACC/ESC

Disease Guidelines

Atrial fibrillation

Heart failure

Perioperative evaluation

Stable angina

Unstable angina

Valvular heart disease

Change in recommendations and class in AHA guidelines

Table 1. Change in the Number of Recommendations and Distribution Across Classes of Recommendation Between First Guideline Version and Current Version^a

0.115 1 1/4 /	Cla	ssl	Clas	ss II	Cla	iss III
Guidelines by Year of Publication	No./Total (%)	Change, %	No./Total (%)	Change, %	No./Total (%)	Change, %
)isease guidelines Atrial fibrillation						
2001 ⁶	46/95 (48.4)		38/95 (40)		11/95 (11.6)	
2006 ⁷	41/111 (36.9)	-23.7	55/111 (49.5)	23.9	15/111 (13.5)	16.7
Heart failure 1995 ²⁶	73/127 (57.5)		33/127 (26)		21/127 (16.5)	
200528	66/129 (51.2)	-11.0	44/129 (34.1)	31.3	19/129 (14.7)	-10.9
Perioperative evaluation 1996 ³³	8/28 (28.6)		8/28 (28.6)		12/28 (42.9)	
200740	13/50 (26.0)	-9.3	27/50 (54.0)	88.8	10/50 (20.0)	-53.4
Stable angina 1999 ⁴⁸	67/162 (41.4)		62/162 (38.3)		33/162 (20.4)	
200247	78/235 (33.2)	-19.7	98/235 (41.7)	9.0	59/235 (25.1)	23.2
Unstable angina 2000 ⁴⁹	86/139 (61.9)		38/139 (27.3)		15/139 (10.8)	
200751	87/128 (62.8)	1.5	29/128 (27.5)	0.7	12/128 (9.7)	-10.2
Valvular heart disease 1998 ⁵³	152/321 (47.2)		114/321 (35.4)		55/321 (17.1)	
2008 ⁵⁶	156/320 (48.8)	3.3	124/320 (38.8)	9.5	40/320 (12.5)	-26.8
Change in No. of recommendations	+9		+84		+8	
Change in distribution across classes, median (IQR), %		-10.2 (-17.5 to -1.2)		16.7 (9.1 to 29.5)		-10.6 (-22.8 to 10.0

Change in recommendadtions and class in AHA guidelines

Table 1. Change in the Number of Recommendations and Distribution Across Classes of Recommendation Between First Guideline Version and Current Version^a

	Cla	iss I	Clas	ss II	Cla	ss III
Guidelines by Year of Publication	No./Total (%)	Change, %	No./Total (%)	Change, %	No./Total (%)	Change, %
Disease guidelines Atrial fibrillation				\wedge		
2001 ⁶	46/95 (48.4)		38/95 (40)	/ \	11/95 (11.6)	
20067	41/111 (36.9)	-23.7	55/111 (49.5)	23.9	15/111 (13.5)	16.7
Heart failure 1995 ²⁶	73/127 (57.5)		33/127 (26)		21/127 (16.5)	
2005 ²⁸	66/129 (51.2)	-11.0	44/129 (34.1)	31.3	19/129 (14.7)	-10.9
Perioperative evaluation 1996 ³⁸	8/28 (28.6)		8/28 (28.6)		12/28 (42.9)	
200740	13/50 (26.0)	-9.3	27/50 (54.0)	88.8	10/50 (20.0)	-53.4
Stable angina 1999 ⁴⁶	67/162 (41.4)		62/162 (38.3)	V	33/162 (20.4)	
200247	78/235 (33.2)	-19.7	98/235 (41.7)	9.0	59/235 (25.1)	23.2
Unstable angina 2000 ⁴⁹	86/139 (61.9)		38/139 (27.3)		15/139 (10.8)	
200751	87/128 (62.8)	1.5	29/128 (27.5)	0.7	12/128 (9.7)	-10.2
Valvular heart disease 1998 ⁵³	152/321 (47.2)		114/321 (35.4)		55/321 (17.1)	
2008 ⁵⁵	156/320 (48.8)	3.3	124/320 (38.8)	9.5	40/320 (12.5)	-26.8
Change in No. of recommendations	+9		+84		+8	
Change in distribution across classes, median (IQR), %		-10.2 (-17.5 to -1.2)		16.7 (9.1 to 29.5)		-10.6 (-22.8 to 10.0)

Interventional Guidelines

CABG

PCI

Pacemaker

Change in recommendadtions and class in AHA interventional guidelines

	Cla	ss	Clas	ss II	Cla	ass III
	No./Total (%)	Change, %	No./Total (%)	Change, %	No./Total (%)	Change, %
terventional guidelines	1101110101(70)	onango, /o	1100101011(70)	onango, /o	110210144 (70)	onango, 70
CABG						
1999 ¹⁰	26/56 (46.4)		19/56 (33.9)		11/56 (19.6)	
200411	39/56 (46.4)	0	34/56 (40.5)	19.3	11/56 (13.1)	-33.3
Pacemaker						
1984 ²⁹	27/87 (31.0)		29/87 (33.3)		31/87 (35.6)	
200814	38/122 (31.1)	0.4	50/122 (41.0)	23.0	34/122 (27.9)	-21.8
PCI						
1988 ³⁴	20/69 (29.0)		27/69 (39.1)		22/69 (31.9)	
2005 ³⁷	39/136 (28.7)	-1.1	69/136 (50.7)	29.7	28/136 (20.6)	-35.4
Change in No. of recommendations	+43		+78		+9	
Change in distribution across classes, median (IQR), %		0 (-0.6 to 0.2)		23.0 (21.2 to 26.4)		-33.3 (-34.4 to -27.

	Cla	ss	Clas	ss II	Cla	ass III
	No./Total (%)	Change, %	No./Total (%)	Change, %	No./Total (%)	Change, %
terventional guidelines CABG	(///	9•, /•				
1999 ¹⁰	26/56 (46.4)		19/56 (33.9)	\wedge	11/56 (19.6)	
200411	39/56 (46.4)	0	34/56 (40.5)	19.3	11/56 (13.1)	-33.3
Pacemaker 1984 ²⁰	27/87 (31.0)		29/87 (33.3)		31/87 (35.6)	
200814	38/122 (31.1)	0.4	50/122 (41.0)	23.0	34/122 (27.9)	-21.8
PCI 1988 ³⁴	20/69 (29.0)		27/69 (39.1)		22/69 (31.9)	
200537	39/136 (28.7)	-1.1	69/136 (50.7)	29.7	28/136 (20.6)	-35.4
Change in No. of recommendations	+43		+78	\cup	+9	
Change in distribution across classes, median (IQR), %		0 (-0.6 to 0.2)		23.0 (21.2 to 26.4)		-33.3 (-34.4 to -2

Diagnostic Guidelines

Echocardiography
Exercise testing
Radionuclide testing

Change in recommendadtions and class in AHA diagnostic guidelines

	Clas	ss I	Cla	ss II	Cla	ss III
	No./Total (%)	Change, %	No./Total (%)	Change, %	No./Total (%)	Change, %
Diagnostic guidelines Echocardiography			07/110/010		01/110/10 1	
199015	58/116 (50.0)		37/116 (31.9)		21/116 (18.1)	
200317	190/333 (57.1)	14.1	83/333 (24.9)	-21.9	60/333 (8.0)	-0.5
Exercise testing 1986 ²³	6/32 (18.8)		15/32 (46.9)		11/32 (34.4)	
2002 ²⁵	15/71 (21.1)	12.7	37/71 (52.1)	11.2	19/71 (26.8)	-22.2
Radionuclide imaging 1986 ⁴¹	14/98 (14.3)		78/98 (79.6)		6/98 (6.1)	
200343	36/84 (42.9)	200.0	43/84 (51.2)	-35.7	5/84 (6.0)	-2.8
Change in No. of recommendations	+163		+33		+46	
Change in distribution across classes, median (IQR), %		14.1 (13.4 to 107.1)		-21.9 (-28.8 to -5.4)		-2.8 (-12.5 to -1.7)
Summary of all guidelines Change in No. of recommendations	+215		+195		+63	
Change in distribution across classes, median (IQR), %		0.2 (–9.7 to 5.7)		15.3 (6.9 to 25.4)		-16.4 (-28.4 to -2.2)

Change in recommendadtions and class in AHA diagnostic guidelines

	Clas	ss I	Clas	ss II	Cla	ss III
	No./Total (%)	Change, %	No./Total (%)	Change, %	No./Total (%)	Change, %
Diagnostic guidelines Echocardiography	. ,		,	0,	, ,	0 ,
1990 ¹⁵	58/116 (50.0)	/ \	37/116 (31.9)		21/116 (18.1)	
200317	190/333 (57.1)	14.1	83/333 (24.9)	-21.9	60/333 (8.0)	-0.5
Exercise testing 1986 ²³	6/32 (18.8)		15/32 (46.9)		11/32 (34.4)	
200225	15/71 (21.1)	12.7	37/71 (52.1)	11.2	19/71 (26.8)	-22.2
Radionuclide imaging 1986 ⁴¹	14/98 (14.3)		78/98 (79.6)		6/98 (6.1)	
2003 ⁴³	36/84 (42.9)	200.0	43/84 (51.2)	-35.7	5/84 (6.0)	-2.8
Change in No. of recommendations	+163		+33		+46	
Change in distribution across classes, median (IQR), %		14.1 (13.4 to 107.1)		-21.9 (-28.8 to -5.4)		-2.8 (-12.5 to -1.7)
Summary of all guidelines Change in No. of recommendations	+215		+195		+63	
Change in distribution across classes, median (IQR), %		0.2 (-9.7 to 5.7)		15.3 (6.9 to 25.4)		-16.4 (-28.4 to -2.2)

CV Guidelines – general conclusions

- Most current articles called "guidelines" are actually expert consensus reports.
- Revisions of the American College of Cardiology (ACC)/American Heart Association (AHA) guidelines have shifted to more class II recommendations (conflicting evidence and/or divergence of opinion about the usefulness/efficacy of a procedure or treatment)
- 48% of the time, these recommendations are based on the lowest level of evidence (level C: expert opinion, case studies, or standards of care).

CV Guidelines - general

- This trend is especially disconcerting given the quantity of cardiovascular scientific literature published during the last decade
- Overreliance on expert opinion in guidelines is problematic
- All guideline committees begin with implicit biases and values, which affects the recommendations they make. However, bias may occur subconsciously and, therefore, go unrecognized
- Converting data into recommendations requires subjective judgments

CV Guidelines - general

Biases

- The most widely recognized bias is financial
- Guidelines often have become marketing tools for device and pharmaceutical manufacturers.
- While the ACC, AHA and ESC receive no industry funding for guideline development, they may receive industry support to disseminate guideline products such as pocket guides.

CV Guidelines - general

- ACC/AHA guidelines with at least 1 revision, the number of recommendations increased 48% from the first guideline to the most recent version
- Main messages tend to get lost in minutiae
- Guidelines are not patient-specific enough to be useful and rarely allow for individualization of care
- Most guidelines have a one-size-fits-all mentality and do not build flexibility or contextualization into the recommendations
- There are simply too many guidelines, often on the same topic

Women and Gender Issues in the ESC Clinical Practice Guidelines

Clinical Practice Guidelines published by AHA/ACC/ESC

Main Disease Topics

Atrial fibrillation

Heart failure

Perioperative evaluation

Stable angina

Unstable angina

Valvular heart disease

Atrial fibrillation (2001 revised 2006)

Women mentioned 7 times: prevalence, incidence and prognosis

- Among men, the age-adjusted prevalence has more than doubled over a generation, while the prevalence in women has remained constant
- Stroke risk greater in women
- amiodarone-associated bradycardia is more common in women than in men

No gender treatment differences discussed

Clinical Practice Guidelines published by ESC

Heart Failure - 2008 revised 1995, 1997, 2001, 2005

Women mentioned 6 times: epidemiology, and pregnancy

 Studies show that the accuracy of diagnosis of HF by clinical means alone is often inadequate, particularly in women, the elderly, and the obese

No gender treatment differences discussed

Perioperative evaluation

Women mentioned twice: ageing population and pulmonary disease

No gender management differences discussed

Clinical Practice Guidelines published by ESC

Stable Angina 2006

Women mentioned 67 times!

Discussed extensively

Focus on differences in diagnosis, presentation, investigation and treatment

- A considerable proportion of patients, especially women, who undergo coronary arteriography because of symptoms of chest paindo not have significant CAD'
- Also HRT discussed

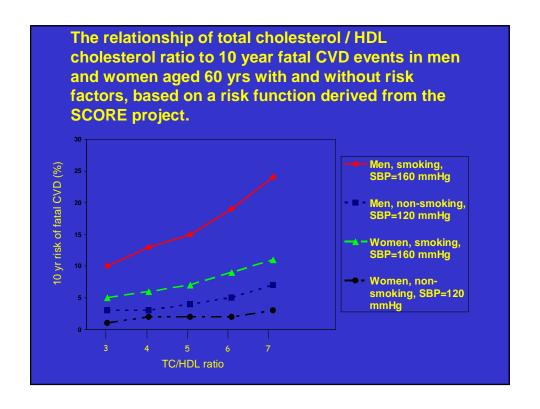
Women discussed as a special subgroup

CVD Prevention 2007

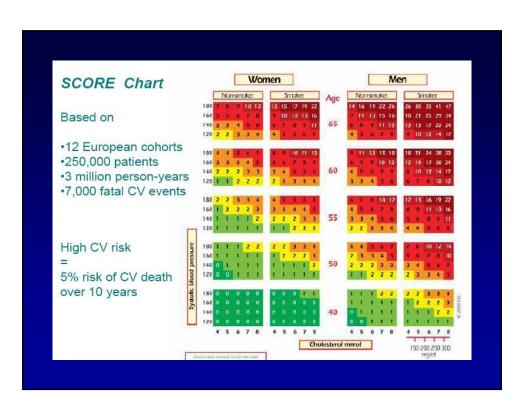
Women mentioned 60 times

Women discussed as a gender issue

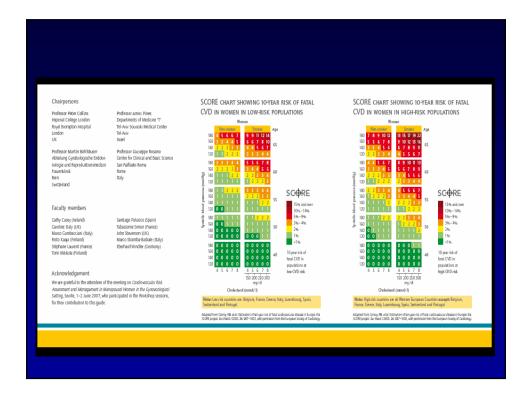
The benefits of statins in healthy asymptomatic women are unproven'



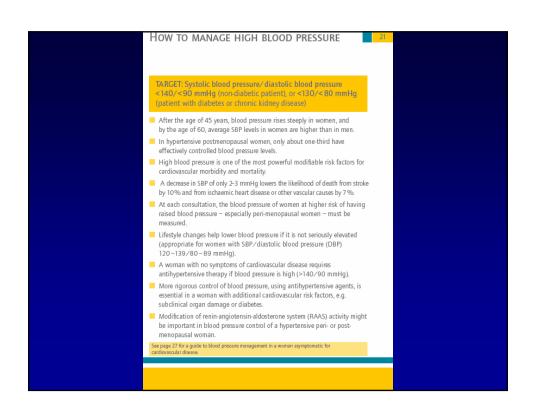
Cardiovascular Risk Assessment - Methodology





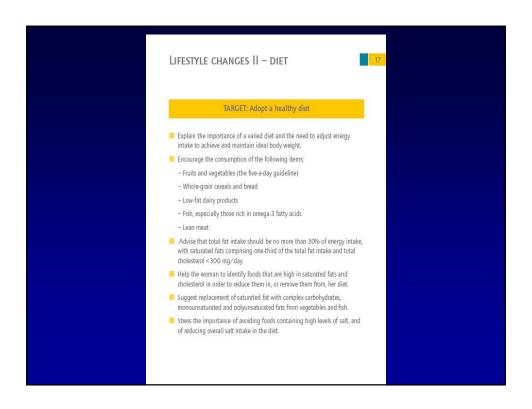






26	Accurate blood pressure measurement
	- HOW TO AVOID SOME TYPICAL PITFALLS
17	 Ensure that the woman has been comfortably seated for several minutes in a quiet room.
A.	Advise the woman to avoid caffeine, exercise and smoking for ≥30 minutes before measurement.
	Check that no tight clothing constricts the arm.
10	Rest the woman's arm on a table, preferably with the brachial artery level with the heart.
- 11	Use a standard cuff (12-13 x 35 cm); have larger and smaller cuffs available.
1	The bladder should encircle at least 80% of the arm (but not more than 100%).
A	 Check that any remaining air in the cuff is evacuated before putting it on the woman's arm.
	Inflate the cuff to >30 mmHg above the estimated SBP needed to occlude the pulse.
10	 Deflate slowly at a rate of 2-3 mmHg/second until regular tapping sounds are audible.
1)	Use Korotkoff sounds to identify SBP and DBP: first heard when the cuff pressure equals the SBP, and ceasing once the cuff has been deflated below the DBP.
	 Take at least two measurements at an interval of 1-2 minutes; additional measurements are required if the first two vary markedly.
10	 At the first examination, blood pressure should be checked in both arms to detect possible differences due to peripheral vascular disease.
	If values vary in different arms, use the higher one.

THE MENOPAUSE AND HORMONE REPLACEMENT THERAPY The initiation or continuation of hormone replacement therapy (HRT) should be decided according to the individual patient. Progestogen should be added to systemic oestrogen in all women with an intact uterus, to prevent endometrial hyperplasia and cancer. Some progestins have additional, specific, beneficial effects on blood pressure and plasma lipid and plasma glucose profiles, for example. In a woman aged 60 years, recently menopausal, with menopausal symptoms and without symptomatic cardiovascular disease, the initiation of HRT does not cause early harm, and possibly confers long-term cardiovascular benefit. If a woman is at increased global cardiovascular risk, HRT is safe to use in the younger woman with indications. HRT should not be initiated solely for the prevention of cardiovascular disease and should not be regarded as a substitute for antihypertensive treatment. A woman aged >60 years should be counselled on the potential benefits and risks of HRT in women in their age group.



Hypertension - 2007

Women mentioned 45 times!

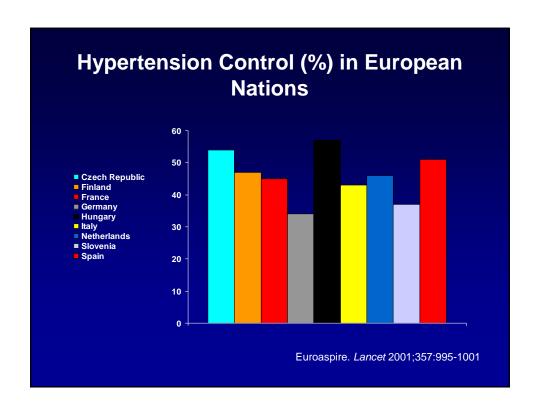
Discussed extensively

Treatment of HT as effective in men and women

Focus on treatment in women, pregnancy, preeclampsia

HRT and oral contraception discussed

Women discussed separately (7.7 Box18)



STEMI - 2008

Women mentioned 6 times (dose variation of drugs and metabolic syndrome)

No gender treatment differences discussed

Valvular Heart Disease

Women mentioned once
No treatment differences discussed

Clinical Practice Guidelines published by AHA/ACC/ESC

Interventional Guidelines

CABG

PCI

Pacemaker

CABG - 2004

Women mentioned 43 times (similar to stable angina guideline)

Discussed as a special group - extensive

Clinical Practice Guidelines published by ESC

<u>PCI</u>

Women mentioned twice

- Particular benefit in women for primary PCI
- Cardiogenic shock

Pacemaker

Women mentioned once

- Sleep apnoea!
- No discussion of gender differences

Evidence-Based Guidelines for Cardiovascular Disease Prevention in Women: 2007 Update

- Mosca, et al Circulation
- Very comprehensive but:
- Most recommendations IB or less (similar to other guidelines discussed)
- Again reinforcing a paucity of data

Conclusions

- Guideline statements are often not robustly evidence based
- Bias is prevalent
- Women and gender are often overlooked
- lack of clinical trial data
- There is much work to do there indeed is a need for action!