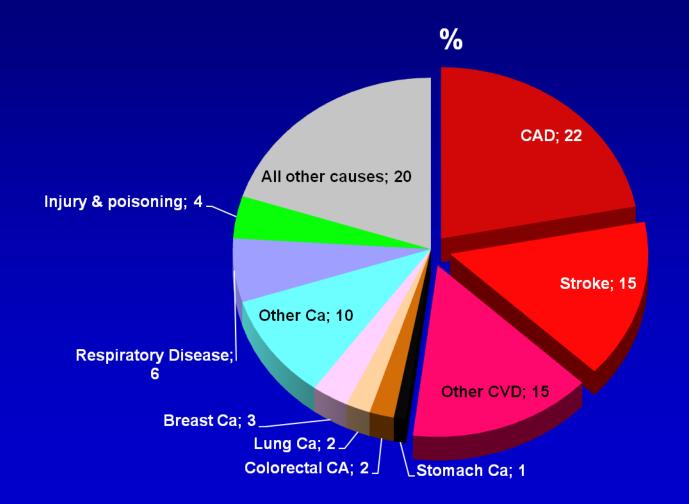
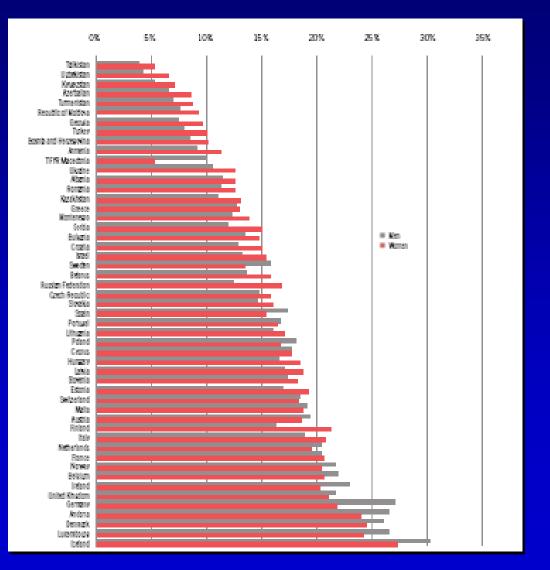
Dyslipidemia in women: Who should be treated and how ?

Lale Tokgozoglu, MD, FACC, FESC Professor of Cardiology *Hacettepe University Faculty of Medicine Ankara, Turkey.*

Cause of Death in Women: European Cardiovascular Statistics 2012



Prevalance of hypercholesterolemia above 6.2 mmol/l (240 mg/dl) by gender in Europe



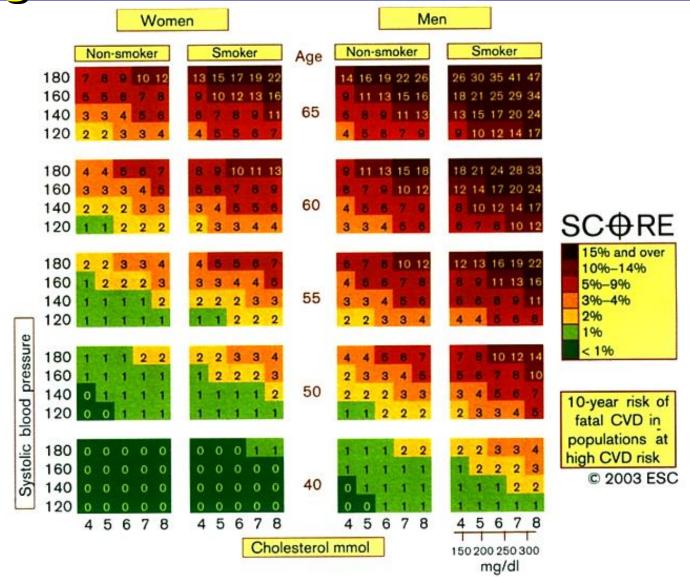
Ranking and Magnitude of Risk Differs in Two Genders: 21 y FU Copenhagen City Heart Study (n=12077, women 6478)

Ranking by relative risk (RR)

Me	n	RR	%
1	Diabetes	1.69	4
2	Hypertension	1.46	48
3	Smoking	1.41	71
4	Physical inactivity	1.28	20
5	No daily alcohol intake	1.24	56
6	Hypercholesterolemia	1.22	47
7	Obesity	1.20	57
8	Low or middle income	1.14	78
9	Hypertrigliseridemia	1.06	40
10 <i>Jr H</i>	School education ≤ 10 years eart J 2002: 23:620	1.01	84

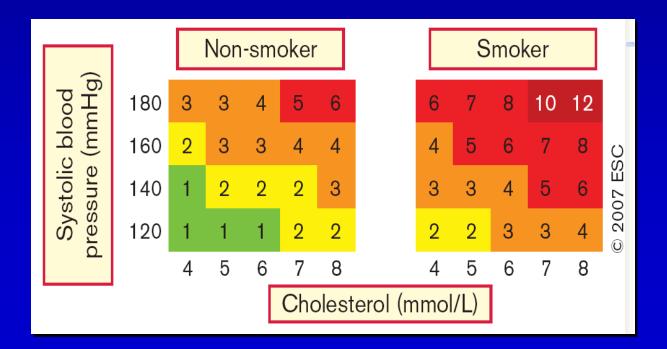
Wo	men	RR	%
1	Diabetes	2.74	2
2	Smoking	2.02	58
3	Hypertension	1.42	40
4	Physical inactivity	1.36	19
5	Hypertriglyceridemia	1.33	19
6	Hypercholesterolemia	1.23	57
7	Obesity	1.19	39
8	School education ≤ 10 years	1.28	89
9	Low or middle income	1.22	82
10	No daily alcohol intake	0.99	88

Principles of risk estimation and management are same for both sexes

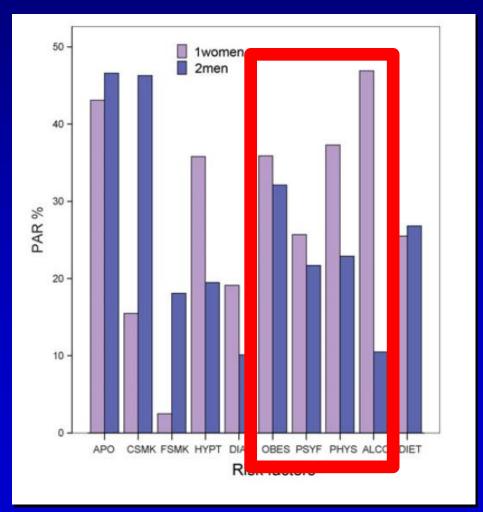


A low absolute risk in a younger women may conceal a high relative risk:

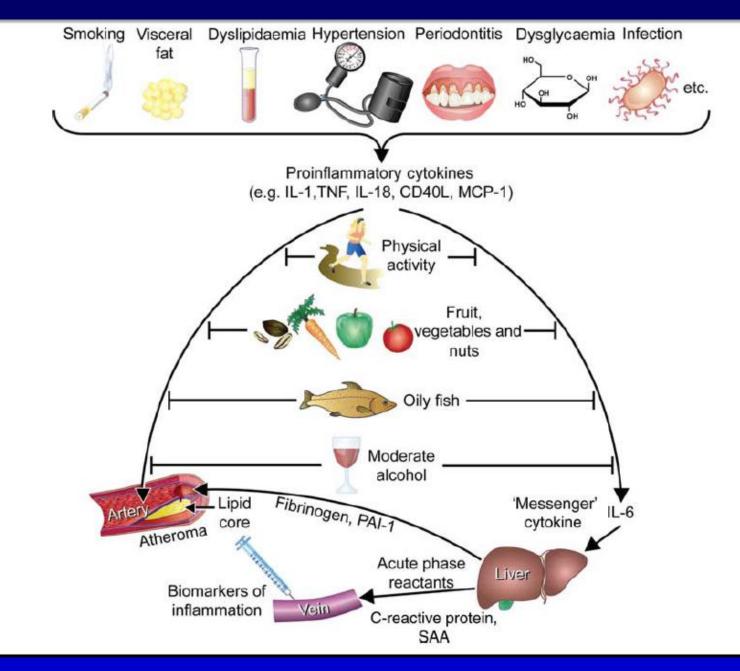
- Extrapolate to older age
- Use relative risk chart
- Lifestyle advice to prevent risk



INTERHEART: The PAR for Lifestyle Factors Significantly Higher in Women



Eur Heart J 2008; 29:932



Eur Heart J 2010;31:777

Canadian Dyslipidemia Guidelines

Target lipid le	vels			
	Primary targets			
Risk level	Initiate treatment if:	LDL-C	Alternate	
High	Consider treatment	<2 mmol/L or	apoB <0.80 g/L	
CAD, PVD,	in all patients	≥50% ↓ LDL-C	Class I, level A	
atherosclerosis	*	Class I, level A		
Most patients				
with diabetes				
FRS ≥20%				
RRS ≥20%				
Moderate	LDL-C >3.5 mmol/L	<2 mmol/L or	apoB <0.80 g/L	
FRS 10%-19%	TC/HDL-C >5.0	≥50% ↓ LDL-C	Class IIa, level A	
	hs-CRP >2 mg/L	Class IIa, level A		
	Men >50 years			
	Women >60 years			
	Family history and			
	hs-CRP modulates			
	risk (RRS)			
Low	LDL-C ≥5.0 mmol/L	≥50% ↓ LDL-C		
FRS <10%		Class IIa, level /	Α	

Can J Cardiol 2009;25(10): 567-579.

ESC/EAS Dyslipidemia Guideline: Intervention strategies as a function of total CV risk and LDL-C level

Total CV risk		LDL-C levels									
(SCORE) %	<70 mg/dL <1.8 mmol/L	70 to <100 mg/dL 1.8 to <2.5 mmol/L	100 to <155 mg/dL 2.5 to <4.0 mmol/L	155 to <190 mg/dL 4.0 to <4.9 mmol/L	>190 mg/dL >4.9 mmol/L						
<	No lipid intervention	No lipid intervention	Lifestyle intervention	Lifestyle intervention	Lifestyle intervention, consider drug if uncontrolled						
Class ^a /Level ^b	I/C	I/C	I/C	I/C	IIa/A						
≥l to <5	Lifestyle intervention	Lifestyle intervention	Lifestyle intervention, consider drug if uncontrolled	Lifestyle intervention, consider drug if uncontrolled	Lifestyle intervention, consider drug if uncontrolled						
Class*/Level ^b	I/C	I/C	IIa/A	Ila/A	I/A						
>5 to <10, or high risk	Lifestyle intervention, consider drug*	Lifestyle intervention, consider drug*	Lifestyle intervention and immediate drug intervention	Lifestyle intervention and immediate drug intervention	Lifestyle intervention and immediate drug intervention						
Class ^a /Level ^b	IIa/A	Ila/A	IIa/A	I/A	I/A						
≥10 or very high risk	Lifestyle intervention, consider drug*	Lifestyle intervention and immediate drug intervention									
Class ^a /Level ^b	lla/A	IIa/A	I/A	I/A	I/A						

Atherosclerosis 2011:217S;S1–S44

ESC/EAS Dyslipidemia Guidelines 2011

Recommendations	Class ^a	Level ^b
In patients at VERY HIGH CV risk (established CVD, type 2 diabetes, type I diabetes with target organ damage, moderate to severe CKD or a SCORE level ≥10%) the LDL-C goal is <1.8 mmol/L (less than ~70 mg/dL) and/or ≥50% LDL-C reduction when target level cannot be reached.		A
In patients at HIGH CV risk (markedly elevated single risk factors, a SCORE level ≥5 to <10%) an LDL-C goal <2.5 mmol/L (less than ~100 mg/dL) should be considered.	lla	A
In subjects at MODERATE risk (SCORE level >I to ≤5%) an LDL-C goal <3.0 mmol/L (less than ~115 mg/dL) should be considered.	lla	С

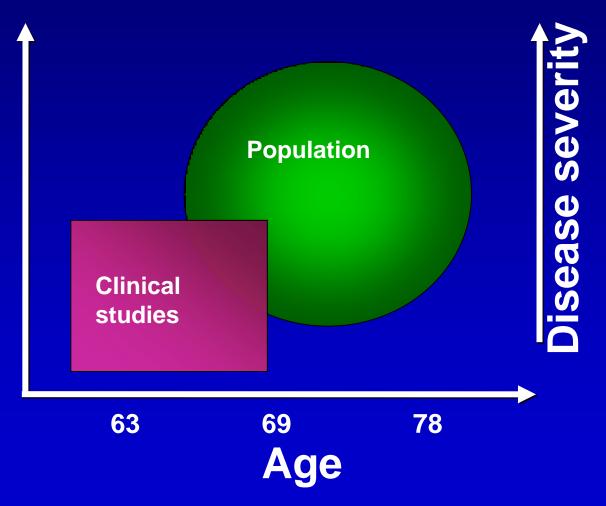
Same medications used, Response to Therapy in Women is Different

- Lower body weight
- Higher propotion of fat
- Different endogenous hormone levels
- Differences in enzyme activities involved in drug metabolism
- Lower GFR

Are statins just as beneficial in women ?

Women are underrepresented in trials



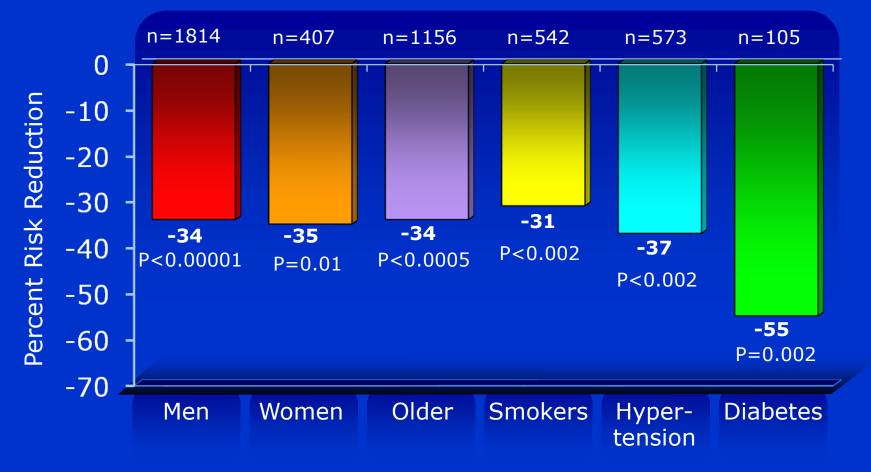


CTT: Effects on major vascular events per 1-0 mmol/L reduction in LDL cholesterol

	Events (% per a	annum)	RR (CI) per reduction		Heterogeneity/ trend test
	Statin/more	Control/less			
Previous vascular disea	se				
CHD	8395 (4·5%)	10123 (5-6%)		0.79 (0.76-0.82)	χ²=2·28
Non-CHD vascular	674 (3·1%)	802 (3.7%)		0.81 (0.71-0.92)	(p=0·3)
None	1904 (1.4%)	2425 (1.8%)		0.75 (0.69-0.82)	(p=0.5)
Diabetes					
Type 1 diabetes	145 (4·5%)	- ()		- 0·77 (0·58-1·01)	χ ² =0·41
Type 2 diabetes		2920 (5.1%)		0.80 (0.74-0.86)	(p=0.8)
No diabetes	8272 (3-2%)	10163 (4.0%)		0.78 (0.75-0.81)	4
Sex					1.445
Male		10725 (4.4%)		0.77 (0.74-0.80)	$\chi_{1}^{2} = 4.13$
Female	2261 (2.5%)	2625 (2.9%)	+ ∎	0.83 (0.76-0.90)	(p=0·04)
Age (years)	(05) (0.00)	(D. (m))	<u></u>	0.70 (0.75, 0.05)	
≤65	- 1 - 1	7455 (3.6%)		0.78 (0.75-0.82)	χ ² ≓0.70
>65 to ≤75	4032 (3.7%)	4908 (4.6%)		0.78 (0.74-0.83)	(p=0·4)
>75	885 (4·8%)	987 (5·4%)		0.84 (0.73-0.97)	
Treated hypertension	6176 (3.7%)	7350 (4·5%)	<u>i</u>	0.80 (0.76-0.84)	χ²=2·67
Yes				0.76 (0.72-0.80)	(p=0·1)
No	4543 (2.7%)	5707 (3.5%)	- T	0.76 (0.72-0.80)	(p=0.1)
Systolic blood pressure <140	(mm Hg) 5470 (3·2%)	6500 (3-8%)	i i i i i i i i i i i i i i i i i i i	0-80 (0-77-0-85)	
<140 ≥140 to <160	3145 (3.0%)	4049 (3·9%)		0.75 (0.70-0.80)	$\chi_{1}^{2}=1.19$
≥160	2067 (3.6%)	2473 (4·5%)	_	0.79 (0.73-0.85)	(p=0·3)
Diastolic blood pressure		24/3(45%)	T	075(075-0-05)	
<80	4558 (3·5%)	5306 (4.2%)		0.81 (0.76-0.85)	
≥80 to <90	3670 (3.0%)			0.77 (0.73-0.82)	χ ² _f =2·01
≥90	2452 (3.0%)	3128 (3.9%)		0.77 (0.72-0.82)	(p=0·2)
Body-mass index (kg/n			7		
<25	3030 (3.0%)	3688 (37%)	- é -	0.79 (0.74-0.84)	
≥25 to <30	5033 (3-3%)	6125 (4.1%)		0.78 (0.74-0.82)	$\chi_{1}^{2}=0.10$
≥30	2732 (3.3%)	3331 (4.1%)	- 	0.78 (0.73-0.84)	(p=0-8)
HDL cholesterol (mmol	/L)		Ţ		
≤1.0	5032 (4.0%)	6165 (5.0%)	.	0.78 (0.75-0.82)	v2-0.15
>10to≤1-3	3656 (3.1%)	4452 (3.9%)	-	0.77 (0.73-0.82)	χ ² =0·15 (p=0·7)
>13	2199 (2·4%)	2633 (2.9%)		0.80 (0.74-0.87)	(p=0.7)
Smoking status					
Current smokers	2268 (3.6%)	2896 (47%)	<u> </u>	0.78 (0.73-0.84)	χ ² =0.02
Non-smokers	8703 (3.1%)	10 452 (3.9%)	0.78 (0.75-0.82)	(p=0-9)
Estimated GFR (mL/mi			T		
<60	2712 (4.1%)	3354 (5·1%)	- 	0.77 (0.72-0.83)	-1.0.02
≥60 to < 90	6161 (3-2%)	7540 (4.0%)		0.78 (0.75-0.82)	$\chi_1^2 = 0.02$
≥90	1315 (2.5%)	1571 (3.0%)		0.77 (0.69-0.85)	(p=0·9)
Total	10973 (3-2%)	13350 (4.0%)	Φ	0.78 (0.76-0.80)	
- 99% or			1	+	
- -		0.5	0.75	1 1.25	
<>> 95% CI		•	6 <i>6 1</i> 1 <i>1</i> 1	<u> </u>	
			Statin/more better	Control/less better	

Lancet 2010; 376: 1670

Secondary Prevention: Coronary Events were reduced to same extent in both genders in 4S



4S Group. Lancet 1994;334:1383–1389.

HPS:

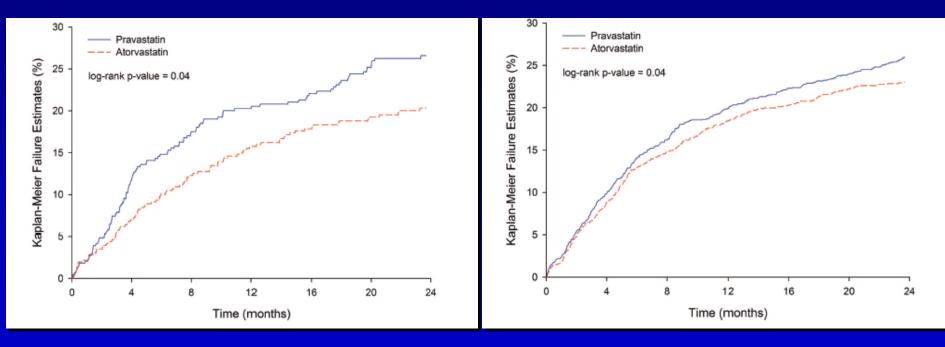
Statin reduces vascular deaths 17 % in men, 19 % in women with DM or CVD

Presenting feature	Simvastatin -allocated	Placebo -allocated	Death rate rat (95% CI)	tio Heterogeneity p-value
Gender Male Female	653/ 7727 (8.5%) 128/ 2542 (5.0%)	780/ 7727 (10.1%) 157/ 2540 (6.2%) —		p=0.9
Age (years) <65 ≥65 to <70 ≥70	223/ 4903 (4.5%) 219/ 2447 (8.9%) 339/ 2919 (11.6%)	273/ 4936 (5.5%) 256/ 2444 (10.5%) 408/ 2887 (14.1%)		p=0.9
LDL cholesterol (mr <3.0 ≥3.0 to <3.5 ≥3.5	nol/L) 241/ 3389 (7.1%) 180/ 2549 (7.1%) 360/ 4331 (8.3%)	285/ 3404 (8.4%) 225/ 2514 (8.9%) 427/ 4349 (9.8%)		p=0.8
Total cholesterol (m <5.0 ≥5.0 to <6.0 ≥6.0	mol/L) 145/2030 (7.1%) 271/3942 (6.9%) 365/4297 (8.5%)	170/ 2042 (8.3%) 346/ 3941 (8.8%) 421/ 4284 (9.8%)		p=0.6
ALL PATIENTS	781/10269 (7.6%)	937/10267 (9.1%)	0.8	33 (0.75 - 0.91) p<0.0001
				cebo better

How about statin use in ACS? Benefit of Intensive Statin Therapy in Women Results From PROVE IT-TIMI 22

Women





Circ Cardiovasc Qual Outcomes. 2011;4:328

Should statins be used for primary prevention in women ?

Meta-analysis of Drug Treatment Studies in Primary Prevention in Women: No change in total and CV mortality

	Diana	N		ention,		
	Placel	bo, No.	N	lo.		P Value for
	Events	At Risk	Events	At Risk	RR (95% CI)	Heterogeneity
		Tot	al Mortal	ity		
Colestipol	21	583	20	601	0.92 (0.51-1.69)	
ACAPS	5	227	0	218	0.09 (0.01-1.70)	
AFCAPS/TEXCAPS	1.53 (0.62-3.81)					
ALLHAT	NR†	2540	NR†	2511	0.98 (0.83-1.17)	
Total and summary	UC	3848	UC	3829	0.95 (0.62-1.46)	.98
		CH	D Mortal	ity		
Colestipol	9	583	10	601	1.08 (0.44-2.63)	
ACAPS	1	227	0	218	0.35 (0.01-8.47)	
AFCAPS/TEXCAPS	0	498	1	499	2.99 (0.12-73.3)	
Total and summary	10	1308	11	1318	1.07 (0.47-2.40)	.87
		No	onfatal M	11		
ACAPS	3	227	1	218	0.35 (0.04-3.31)	
AFCAPS/TEXCAPS	6	498	4	499	0.69 (0.21-2.28)	
Total and summary	9	725	5	717	0.61 (0.22-1.68)	.70
		Reva	sculariza	tion		
AFCAPS/TEXCAPS	8	498	7	499	0.87 (0.33-2.31)	
		C	ID Event	s		
AFCAPS/TEXCAPS	13	498	7	499	0.55 (0.22-1.34)	
ALLHAT	NR†	2540	NR†	2511	1.02 (0.81-1.28)	
ASCOT-LLA	17	963	19	979	1.10 (0.57-2.12)	
HPS	168	902	130	914	0.76 (0.62-0.94)	
Total and summary	UC	4903	UC	4903	0.87 (0.69-1.09)	.17

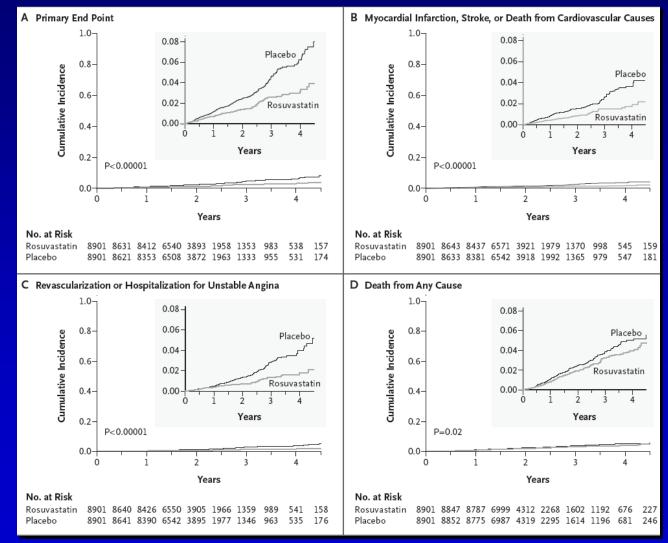
JAMA. 2004;291:224<u>3-2252</u>

Why was no benefit shown for women ?

- Underrepresentation of women in trials
- NNT to prevent one event high since risk is lower in women
- Small number of events
- Relatively young women included
- Follow up times 2.6 years
- Focusing on a lack of statistical significance is misleading

JUPITER:

Statins in Primary Prevention reduce CV events significantly



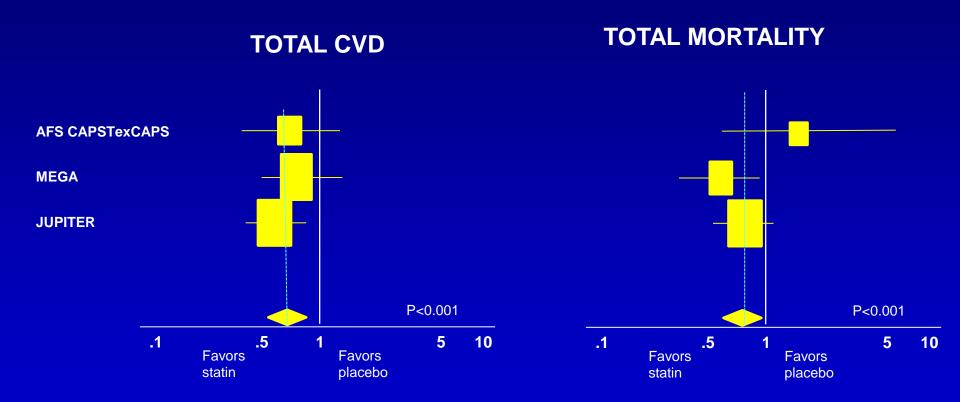
N Engl J Med 2008;359:2195

JUPITER: Effects on CV outcome in subgroups show similiar risk reduction in both genders

Subgroup	No. of Patients	Hazard Ratio (95% CI)	P Value for Interaction
Sex			0.80
Male	11,001		
Female	6,801		
Age			0.32
≤65 yr	8,541		
>65 yr	9,261		
Smoker			0.63
Yes	2,820		
No	14,975		
Race or ethnic group			0.57
White	12,683		
Nonwhite	5,117		
Geographic region			0.51
United States or Canada	6,041		
Other	11,761		
Hypertension			0.53
Yes	10,208		
No	7,586		
Family history of CHD			0.07
Yes	2,045		
No	15,684		
BMI			0.70
<25.0	4,073		
25.0-29.9	7,009		
≥30.0	6,675		
Metabolic syndrome			0.14
Yes	7,375		
No	10,296		
Framingham risk score			0.99
≤10%	8,882	+	
>10%	8,895	- # - ·	
ATP-III risk factor			0.43
0	6,375		
≥1	11,399		
Time of event			0.56
≤24 mo	17,802		
>24 mo	7,765		
All participants	17,802		
	-	0.25 0.50 1.00 2.00	4.00
		Rosuvastatin Placebo Better Better	-

N Engl J Med 2008;359:2195-207.

Meta-analysis of Primary Prevention Trials in Women: 1/3 reduction in CV events

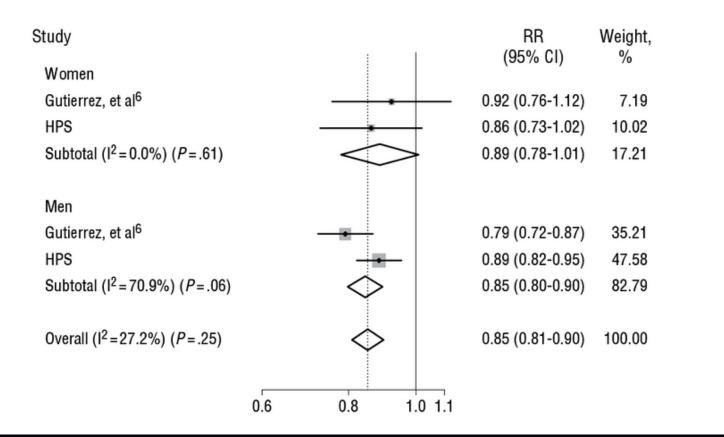


Circulation 2010; 121: 1069

All cause mortality and stroke not decreased for women on statin: A sex based meta-analysis

	Stat	ins	Con	itrol						
Study or Subgroup	Events	Total	Events	Total	Weight, %	Risk Ratio (95% CI)		Risk Ratio	(95% CI)	
1.1.1 Women										
FLORIDA study	1	41	1	51	0.0	1.24 (0.08-19.29)	-			→
Fluvastatin on CE	0	69	1	71	0.0	0.34 (0.01-8.27)	-			→
CCAIT study	4	30	4	32	0.1	1.07 (0.29-3.89)				-
PLAC-I study	5	44	12	48	0.3	0.45 (0.17-1.19)	-			
MIRACL study	3	546	12	528	0.3	0.24 (0.07-0.85)	*			
ASCOT-LLA	19	979	17	963	0.4	1.10 (0.57-2.10)				
CARE study	33	286	63	290	1.6	0.53 (0.36-0.78)				
Four S study	59	407	91	420	2.3	0.67 (0.50-0.90)		I		
SPARCL study	134	938	174	970	4.3	0.80 (0.65-0.98)				
PROSPER study	186	1495	194	1505	4.9	0.97 (0.80-1.16)			_	
LIPID study	207	756	250	760	6.3	0.83 (0.71-0.97)		-=-		
Subtotal (95% CI)		5591		5638	20.6	0.81 (0.74-0.89)		•		
Total No. of Events	651		819							
Heterogeneity: $\chi^2_{10} = 15.95$ Test for overall effect: $z = 4$		7%								
1.1.2 Men										
Fluvastatin on CE	3	118	9	107	0.2	0.30 (0.08-1.09)	-	-8	-	
MIRACL study	10	992	13	1020	0.3	0.79 (0.35-1.80)				
FLORIDA study	14	214	16	234	0.4	0.96 (0.48-1.91)				
CCAIT study	11	135	16	134	0.4	0.68 (0.33-1.42)		ı		
PLAC-I study	50	162	69	154	1.8	0.69 (0.52-0.92)				
ASCOT-LLA	81	4189	137	4174	3.5	0.59 (0.45-0.77)		_ - -		
PROSPER study	222	1396	279	1408	7.1	0.80 (0.68-0.94)				
CARE study	274	1799	341	1788	8.7	0.80 (0.69-0.92)		-8		
SPARCL study	254	1427	341	1396	8.8	0.73 (0.63-0.84)		-=-		
Four S study	372	1814	531	1803	13.5	0.70 (0.62-0.78)		-=-		
LIPID study	1266	3756	1364	3742	34.7	0.92 (0.87-0.98)				
Subtotal (95% CI)		16002		15960	79.4	0.82 (0.78-0.85)		*		
Total No. of Events	2557		3116							
Heterogeneity: $\chi_{10}^2 = 35.15$	5 (P<.001); I ² =	72%								
Test for overall effect: $z = 8$	8.90 (<i>P</i> < .001)									
Subtotal (95% CI)		21593		21598	100	0.81 (0.78-0.85)		*		
Total No. of Events	3208		3935							
Heterogeneity: $\chi_{21}^2 = 51.21$	I (P<.001); I ² =	59%								
Test for overall effect: z = 9	9.98 (<i>P</i> < .001)									
Test for subgroup difference	ces: χ ₁ ² =0.04 (P	=.84); I ² =0%								
							0.20	0.5 1	2	5
								Favors Statins	Favors Control	-
									ravois control	

ARCH INTERN MED 2012: 172 ;914



Cochrane 2013 Analysis: Mortality and morbidity with statins in primary prevention: All cause mortality and CV events reduced

Study or subgroup	Statin Therapy Group	Usual Care or Placebo	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H,Fixed,95% CI		M-H,Fixed,95% CI
ACAPS 1994	0/460	6/459	·+	0.4 %	0.08 [0.00, 1.36]
Adult Japanese MEGA Study	125/3866	172/3966	+	11.6 %	0.75 [0.59, 0.93]
CAIUS 1996	3/151	2/154	·	0.1 %	1.53 [0.26, 9.03]
CARDS 2008	80/1429	124/1412	+	8.5 %	0.64 [0.49, 0.84]
CERDIA 2004	2/103	12/79	·	0.9 %	0.13 [0.03, 0.55]
HYRIM 2007	11/142	15/143		1.0 %	0.74 [0.35, 1.55]
MRC/BHF Heart Protection	276/2006	367/1976	-	25.3 %	0.74 [0.64, 0.85]
PREVEND IT 2004	22/433	25/431		1.7 %	0.88 [0.50, 1.53]
WOSCOPS	584/3302	732/3293		50.2 %	0.80 [0.72, 0.88]
Total (95% CI)	11892	11913	•	100.0 %	0.75 [0.70, 0.81]
Total events: 1103 (Statin Therapy Heterogeneity: Chi ² = 11.63, df = 1		or Placebo)			
Test for overall effect: Z = 7.66 (P					
Test for subgroup differences: Not					
			0.1 0.2 0.5 1 2 5 10	0	
			Favours treatment Favours contro	i i i i i i i i i i i i i i i i i i i	

Are statins effective in primary prevention in both genders ?



Overall the populations sampled within this review were white,male and middle aged. Therefore, caution needs to be taken regarding generalisability to women who are at lower risk of CVD events.

Widespread use of statins in people at below a 1% annual all-cause mortality risk is not supported by the existing evidence

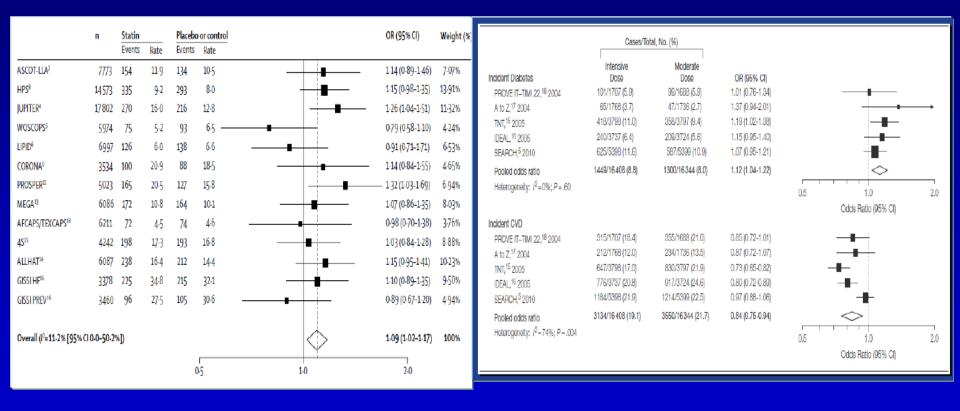
- Fourteen randomised control trials (16 trial arms; 34,272 participants) were included.
- All-cause mortality was reduced by statins (RR 0.83, 95% CI
- 0.73 to 0.95) as was combined fatal and non-fatal CVD endpoints (RR 0.70, 95% CI 0.61 to 0.79). Benefits were also seen in the reduction of revascularisation rates (RR 0.66, 95% CI 0.53 to 0.83).

Meta-Analysis of Statin Effects in Women Versus Men in Primary Prevention: Mortality and events reduced in all risk levels

Group by	_	Subgroup within study	Statistics for each study		L	Odds ratio and 95% Cl			
Risk 3 Way			Odds ratio	Lower limit	Upper limit	p-Value			
HGH	ALLHAT-LLT	WOMEN	0.94	0.79	1.13	0.5253	-	·	1
HIGH	ATOZ	WOMEN	0.91	0.66	1.24	0.5508		-	
HIGH	AURORA	WOMEN	1.01	0.77	1.32	0.9549		-	
HIGH	CORONA	WOMEN	0.85	0.65	1.10	0.2130		8	
HIGH	HPS	WOMEN	0.78	0.67	0.91	0.0015			
HIGH	PROSPER	WOMEN	0.96	0.77	1.19	0.7117		.	
HIGH	SEARCH	WOMEN	0.85	0.68	1.05	0.1284			
HIGH			0.88	0.81	0.95	0.0014	\diamond		
LOW	AF-TEXCAPS	WOMEN	0.53	0.21	1.34	0.1807		-	
LOW	GREACE	WOMEN	0.42	0.21	0.84	0.0141			
LOW	MEGA	WOMEN	0.74	0.45	1.23	0.2481		-	
LOW			0.59	0.41	0.87	0.0066	$\langle \rangle$		
MEDIUM	4S	WOMEN	1.12	0.64	1.97	0.6866		⊷ I I	
MEDIUM	ASCOT-LLA	WOMEN	1.10	0.57	2.13	0.7745		⊷– I	
MEDIUM	CARE	WOMEN	0.50	0.33	0.76	0.0009	_		
MEDIUM	GISSI-P	WOMEN	1.07	0.59	1.96	0.8191		<u> </u>	
MEDIUM	JUPITER	WOMEN	0.54	0.37	0.81	0.0025	_ _		
MEDIUM	LIPID	WOMEN	0.81	0.62	1.07	0.1374			
MEDIUM	PROVENT	WOMEN	0.69	0.51	0.94	0.0176			
MEDIUM	TNT	WOMEN	0.80	0.66	0.96	0.0192			
MEDIUM			0.75	0.64	0.89	0.0011	\diamond		
Overall			0.84	0.79	0.91	0.0000			
						0.1	0.2 0.5 1	2 5	10
							Favors Active	Favors Control	
							Pavors Active	Pavors Control	

Other issues to be considered in primary prevention: **Diabetes risk** Cost

Statins diabetes and CV risk



Lancet 2010;375:735 JAMA 2011;305:2556

Statins and diabetes

- The risk of developing diabetes is 1 in every 255 patients treated
- Higher dose of statins, elderly, patients with hypertension, multiple risk factors and metabolic syndrome
- HbA1c over 6 %

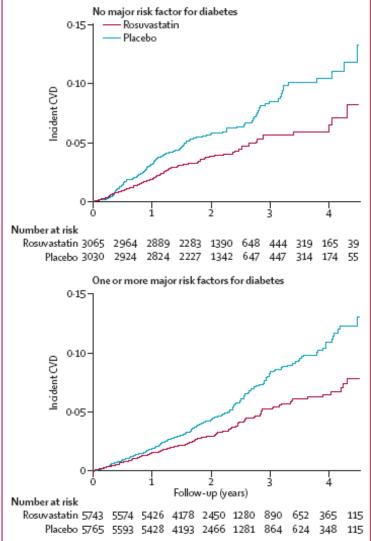
Statin Use and Risk of Diabetes Mellitus in Postmenopausal Women in the WHI Study

Table 5. Risk of Diabetes Mellitus (DM) by Statin Use at Baseline and 3-Year Follow-up in 125575 Participants

Description	Statin Use Only at Baseline	Statin Use Only at 3-y Follow-up	Statin Use at Baseline and 3-y Follow-up	Never Use
Participants, No.	1531	9571	7076	107 397
Incident DM cases, No.	98	644	442	4294
Cumulative incidence rate, %	6.40	6.73	6.25	4.00
Unadjusted HR (95% CI) ^a	1.75 (1.43-2.14)	1.81 (1.67-1.97)	1.82 (1.65-2.00)	1 [Reference]
Adjusted HR (95% CI)				
Age and race/ethnicity ^b	1.65 (1.35-2.01)	1.79 (1.65-1.95)	1.81 (1.64-2.00)	1 [Reference]
Multivariate ^c	1.49 (1.19-1.86)	1.65 (1.51-1.81)	1.56 (1.41-1.74)	1 [Reference]
Propensity score ^d	1.49 (1.20-1.85)	1.63 (1.49-1.78)	1.43 (1.28-1.58)	1 [Reference]
Multivariate, including propensity score ^e	1.44 (1.15-1.80)	1.60 (1.47-1.75)	1.47 (1.32-1.64)	1 [Reference]

Arch Intern Med. 2012;172(2):144-152.

Cardiovascular benefits exceeded the diabetes risks of statin therapy in primary prevention: an analysis from the JUPITER trial



DM risk limited to subjects with high BMI,HbA1C ,MS or obesity

Lancet 2012; 380: 565

Statins in primary prevention: Cost effectiveness analysis

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Cite this as: BMJ 2011;342:d1672 doi:10.1136/bmj.d1672 ABSTRACT

Objective To assess the cost-effectiveness of low dose statins for primary prevention of vascular disease, incorporating current prices, non-adherence (reduced clinical efficacy while maintaining healthcare costs), and the results of the recently published JUPITER trial. Design Cost-effectiveness analysis using a Markov model. Sensitivity analyses and Monte Carlo simulation evaluated the robustness of the results.

Setting Primary care in The Netherlands.

Participants Hypothetical populations of men and women aged 45 to 75 years without a history of vascular disease at different levels of risk for vascular disease (myocardial infarction and stroke) over 10 years.

Interventions Low dose statin treatment daily versus no treatment for 10 years.

Main outcome measures Number of fatal and nonfatal vascular events prevented, quality-adjusted life-years (QALYs), costs, and incremental cost-effectiveness ratios over 10 years.

Results Over a 10-year period, statin treatment cost \in 35000 (£30000, \$49000) per QALY gained for men aged 55 years with a 10-year vascular risk of 10%. The incremental cost-effectiveness ratio improved as risk for vascular disease increased. The cost per QALY ranged from approximately \in 5000 to \in 125000 when the 10-year vascular risk for men aged 55 years was varied from 25% to 5%. The incremental cost-effectiveness ratio slightly decreased with age after the level of vascular risk was specified. Results were sensitive to the costs of statin treatment, statin effectiveness, non-adherence, disutility of taking medication daily, and the time horizon of the model.

Conclusions In daily practice, statin treatment seemed not to be cost-effective for primary prevention in populations at low risk of vascular disease, despite low costs of generic drug pills. Adherence to statin treatment needs to be improved to enhance the cost-effectiveness of the use of statins for primary prevention.

Use of statins in low risk women



CV benefits

What other parameter can help us decide ?

- Family history
- CRP levels, biomarkers
- Imaging

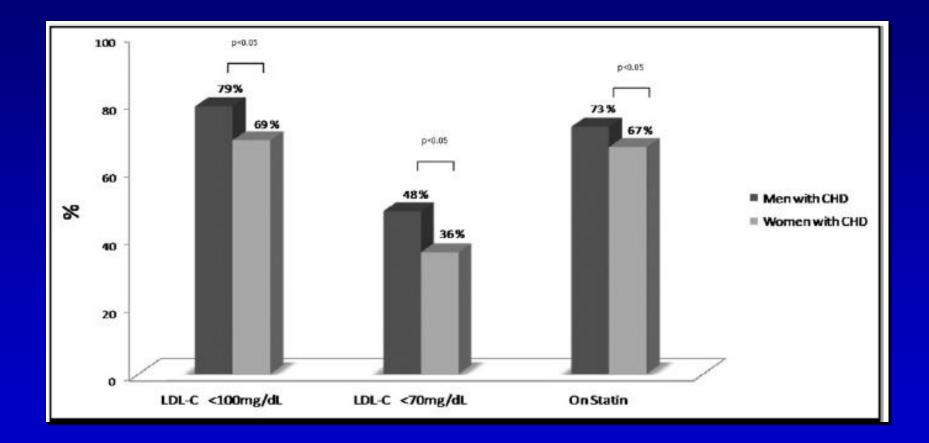
Problems in real life: Lack of recognition Less agressive treatment

Gender disparities in the assessment and management of cardiovascular risk in primary care: the AUSHEART Study

	Men (N=2325) n (%)	Women (N = 2968) n (%)	Age-adjusted relative risk	P-value			
Blood pressure-lowering therapy							
Low (<10%)	76 (38)	356 (45)	1.13 (0.93-1.36)	0.22			
Moderate (10–15%)	112 (51)	132 (60)	1.15 (0.97-1.37)	0.11			
High (>15%)	665 (69)	793 (67)	0.96 (0.90-1.02)	0.19			
Established CVD	681 (80)	506 (77)	0.95 (0.90-1.00)	0.05			
Statin therapy							
Low (<10%)	51 (25)	234 (29)	1.09 (0.84–1.41)	0.51			
Moderate (10–15%)	67 (30)	67 (31)	0.99 (0.74-1.31)	0.92			
High (>15%)	430 (44)	532 (45)	1.02 (0.92-1.13)	0.66			
Established CVD	648 (76)	437 (67)	0.87 (0.81-0.93)	< 0.001			
Antiplatelet therapy							
Low (<10%)	34 (17)	135 (17)	0.92 (0.65-1.31)	0.65			
Moderate (10–15%)	43 (20)	54 (25)	1.12 (0.78-1.63)	0.53			
High (>15%)	353 (37)	407 (35)	0.91 (0.81-1.02)	0.09			
Established CVD	637 (75)	436 (67)	0.88 (0.82-0.94)	< 0.001			
Combination therapy ^a							
Low (<10%)	12 (6)	47 (6)	0.86 (0.46-1.59)	0.63			
Moderate (10–15%)	20 (9)	21 (9)	0.95 (0.52-1.73)	0.86			
High (>15%)	191 (19)	218 (18)	0.92 (0.77-1.10)	0.36			
Established CVD	483 (56)	297 (44)	0.78 (0.70-0.87)	< 0.001			

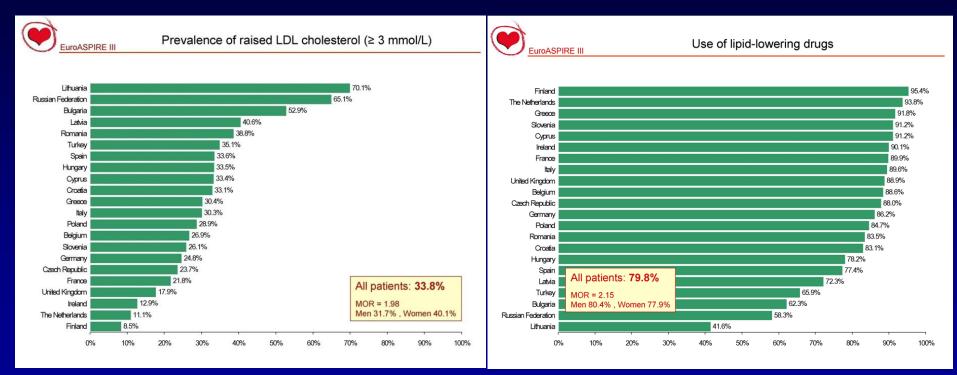
European Journal of Cardiovascular Prevention & Rehabilitation 2011 18: 498

Effect of Gender on Cholesterol Control and Statin Use for Secondary Prevention Among Hospitalized Patients With Coronary Heart Disease

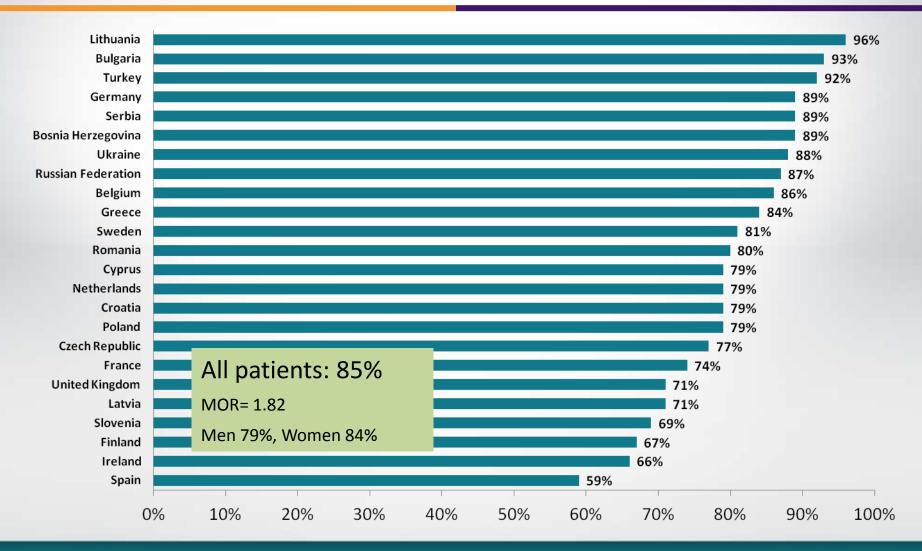


Am J Cardiol 2012;110:1613–1618

LDL Control and Statin Use: EUROASPIRE III



Euroaspire IV LDL cholesterol ≥1.8 mmol/L



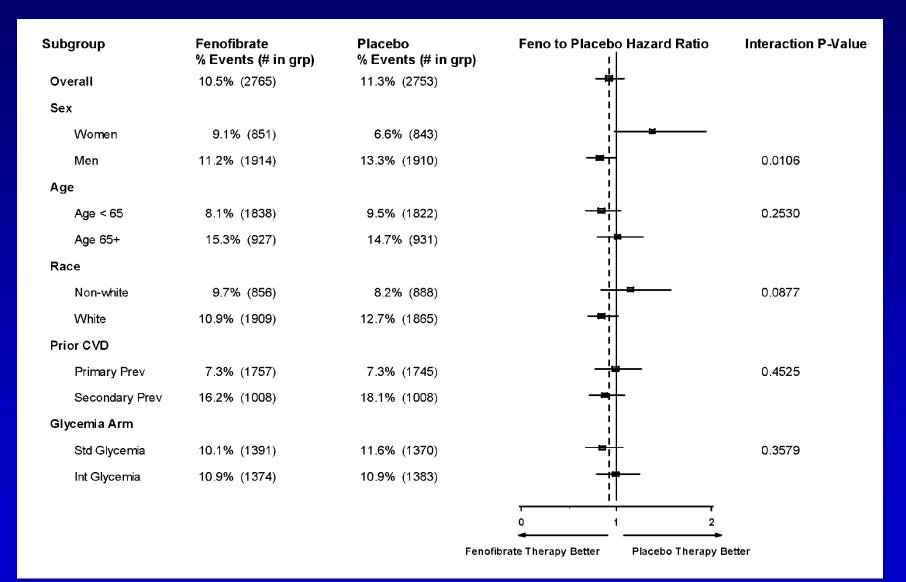
How do we treat dyslipidemia in women today ?

- Lifestyle modification is extremely important
- For secondary prevention, statins are recommended as same indications and targets in men
- Statins are recommended for high risk primary prevention
- LLT should not be given before, during pregnancy and at breastfeeding
- For low risk primary prevention each patient should be evaluated individually

ESC/EAS Dyslipidemia Guidelines 2011: Recommendations for diabetics

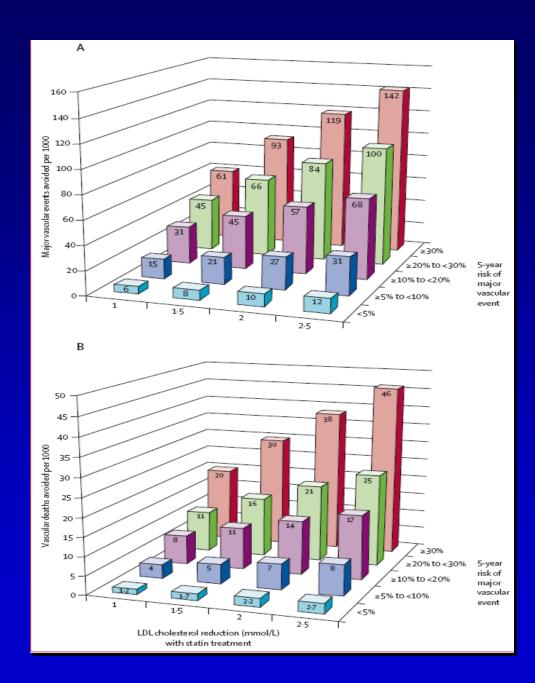
Recommendations	Class ^a	Level⁵	Ref ^c
In all patients with type I diabetes and in the presence of microalbuminuria and renal disease, LDL-C lowering (at least 30%) with statins as the first choice (eventually drug combination) is recommended irrespective of the basal LDL-C concentration.	I	C	
In patients with type 2 diabetes and CVD or CKD, and in those without CVD who are over the age of 40 years with one or more other CVD risk factors or markers of target organ damage, the recommended goal for LDL-C is <1.8 mmol/L (less than ~70 mg/dL) and the secondary goal for non- HDL-C is <2.6 mmol/L (100 mg/dL) and for apo B is <80 mg/dL.	I	B	15, 16
In all people with type 2 diabetes LDL-C <2.5 mmol/L (less than ~100 mg/dL) is the primary target. Non-HDL-C <3.3 mmol/L (130 mg/dL) and apo B <100 mg/dL are the secondary targets.	I	B	15, 16

Accord Lipid Trial Primary Outcomes



N Engl J Med 2010;362:1563

CTT Analysis shows LDL reduction beneficial even in low risk



Lancet 2012

JUPITER Analysis Shows Intermediate Risk Patients Benefit From Statin

Risk category	Event rate per 100-person years, rosuvastatin 20 mg	Event rate per 100-person years, placebo	Hazard ratio (95% CI)
Framingham 10- year risk			
<5% (n=2791)	0.22	0.34	0.64 (0.23-1.81)
5%-10% (n=6091)	0.50	0.92	0.55 (0.36-0.84)
11%-20% (n=7340)	0.95	1.84	0.51 (0.39-0.68)
>20% (n=1555)	1.72)	2.41	0.70 (0.45-0.90)

Circulation, 2010; Aug 24; epub.