Girona 16 de novembre de 2012

El control de la malaltia cardiovascular crònica en el sistema de salut

Prevenció primària: El control dels factors de risc

Rafel Ramos

- Prevalença i control dels factors de risc: Estudi DARIOS
- Reclassificació dels pacients de risc moderat
- Aspirina i prevenció primària

Prevalença, maneig i control de factors de risc cardiovascular a Espanya

El estudio DARIOS

Anàlisi de 11 estudis, 10 CCAA, 27 903 participants

Grau M. Estudio DARIOS . Rev Esp Cardiol. 2011;64:295–304

Prevalença dels factors de risc clàssics. Estudi DARIOS

	Smoker		High blood pressure		Dyslipidemia		Obesity		Type II diabetes mellitus	
	DARIOS	NHS 2006	DARIOS	NHS 2006	DARIOS*	NHS 2006	DARIOS	NHS 2006	DARIOS	NHS 2006
Men										
35-44 years	40%	41%	24%	10%	32%	14%	22%	15%	5%	1%
45-54 years	38%	41%	42%	20%	46%	21%	30%	21%	14%	1%
55-64 years	29%	31%	61%	38%	49%	29%	33%	21%	23%	6%
65-74 years	22%	21%	72%	44%	47%	31%	30%	26%	29%	14%
Women										
35-44 years	36%	34%	12%	8%	19%	7%	15%	12%	3%	2%
45-54 years	26%	31%	31%	18%	37%	17%	26%	16%	8%	4%
55-64 years	9%	13%	55%	35%	55%	31%	38%	24%	16%	9%
65-74 years	3%	5%	72%	56%	59%	37%	44%	29%	24%	16%

* Total cholesterol ≥250 mg/dL.

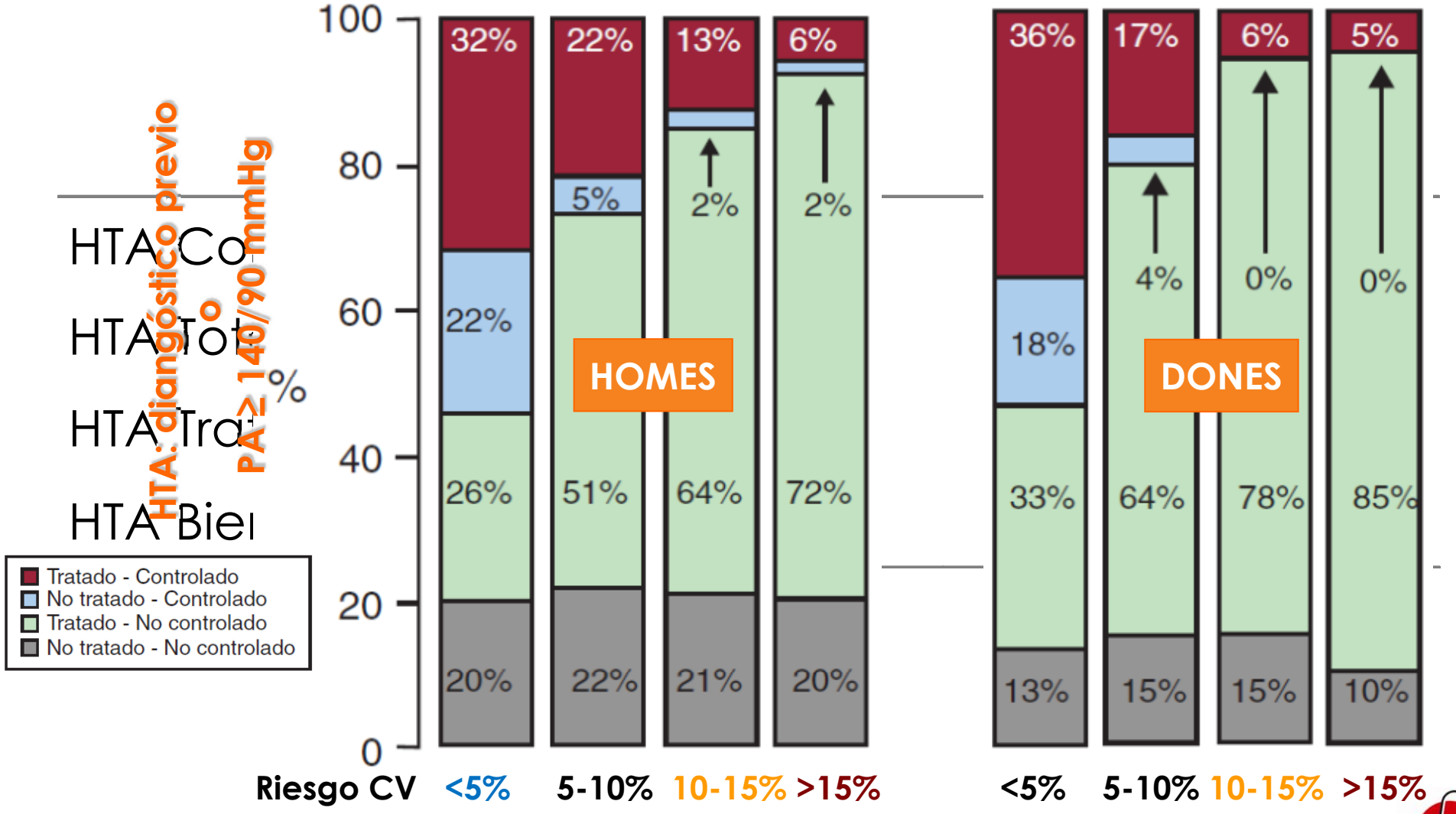
Grau M. Estudio DARIOS . Rev Esp Cardiol. 2011;64:295–304

Distribució dels pacients en funció del risc coronari. Estudi DARIOS

	Low, <5% (95% CI)	Moderate, 5%-9.9% (95% CI)	High, 10%-14.9% (95% CI)	Very high, ≥15% (95% CI)	Mean risk (95% CI)
Men					
	62 (58-66)	27 (24-30)	8 (7-9)	3 (3-4)	5.1 (4.7-5.5)
Women					
	86 (83-88)	12 (10-14)	2 (1-2)	0.3 (0.2-0.4)	2.8 (2.5-3)

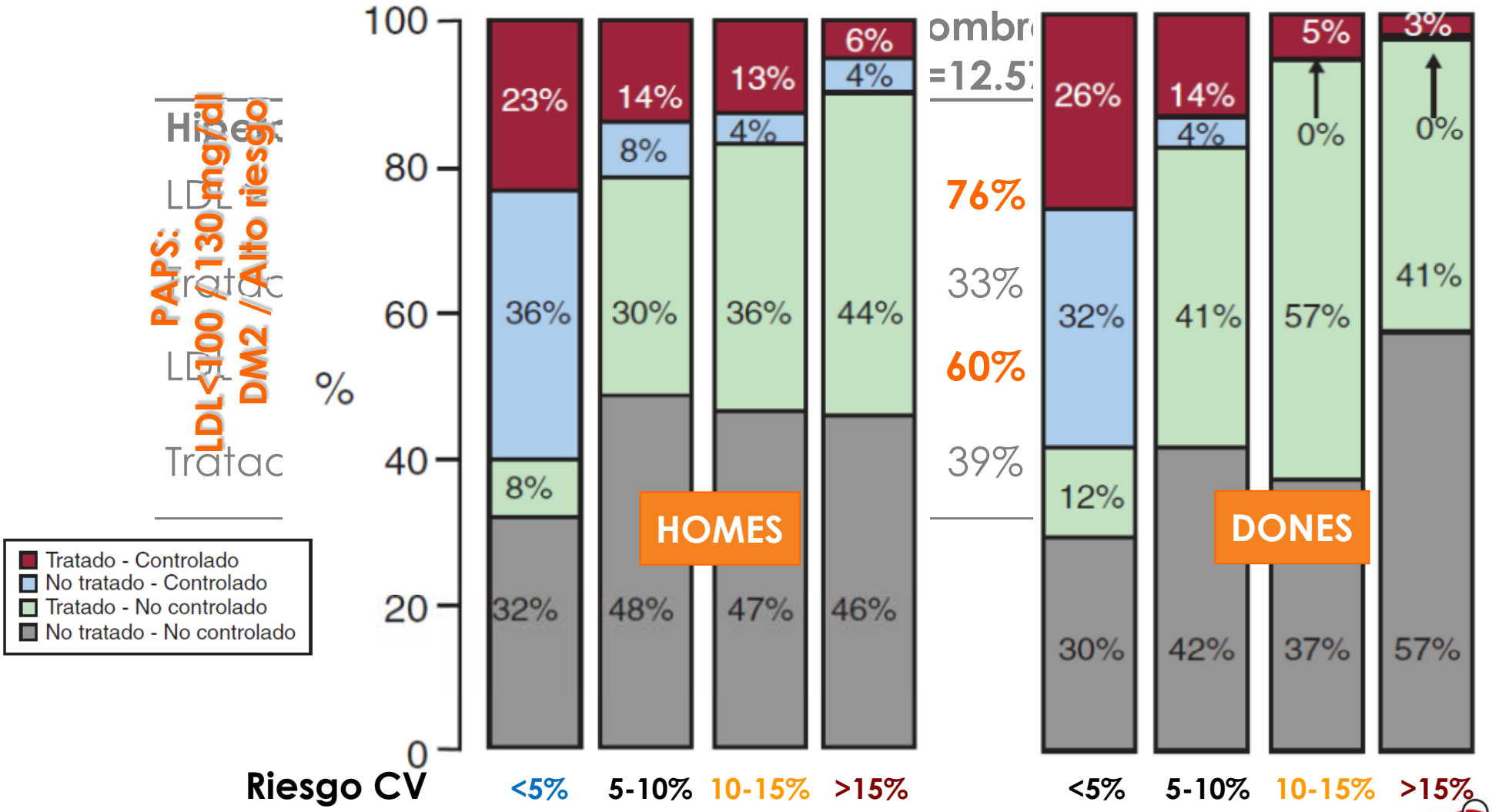
Grau M. Estudio DARIOS . Rev Esp Cardiol. 2011;64:295–304

Prevalença d'hipertensió arterial. Població de 35-74 anys. Estudi DARIOS



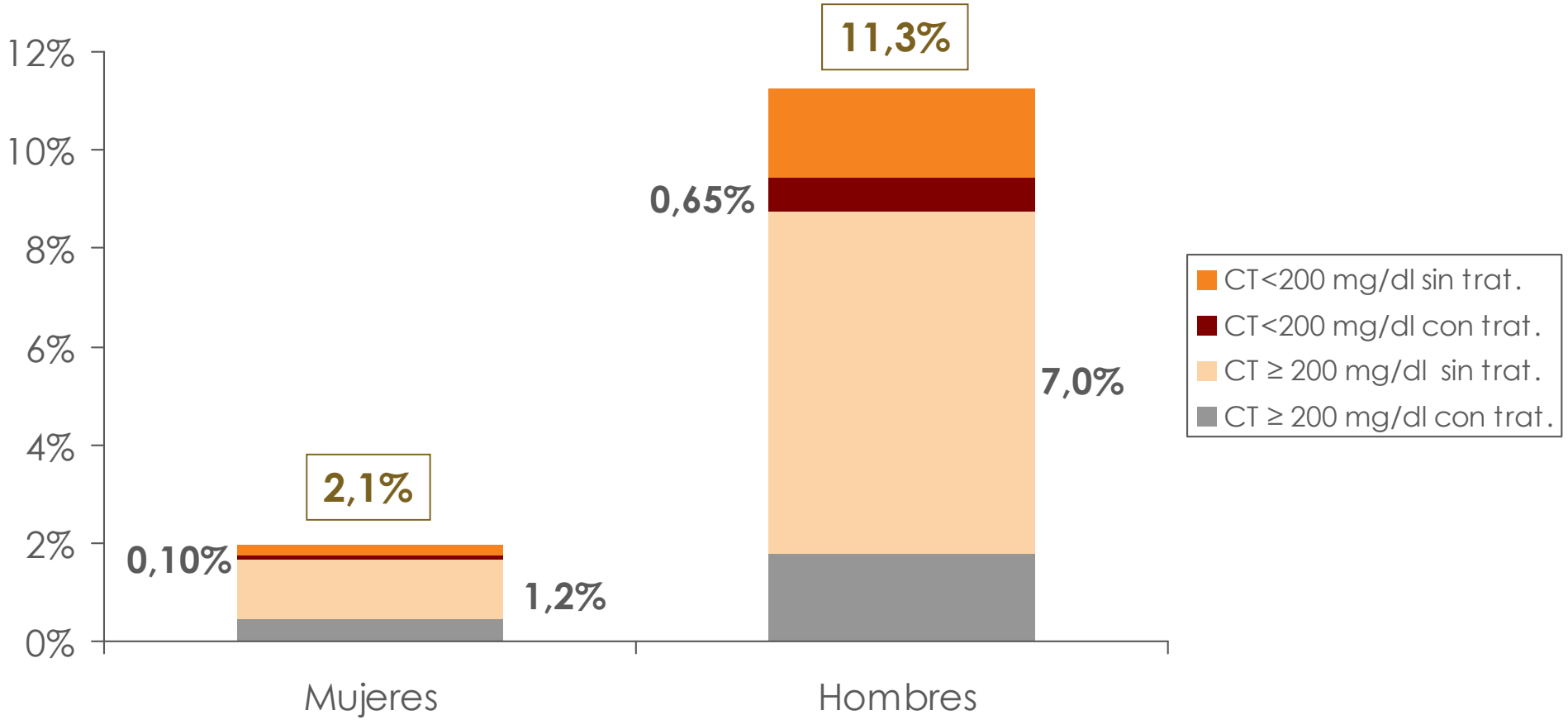
Grau M. Estudio DARIOS . Rev Esp Cardiol. 2011;64:295–304

Prevalença d'hipercolesterolemia. Població de 35-74 anys. Estudi DARIOS



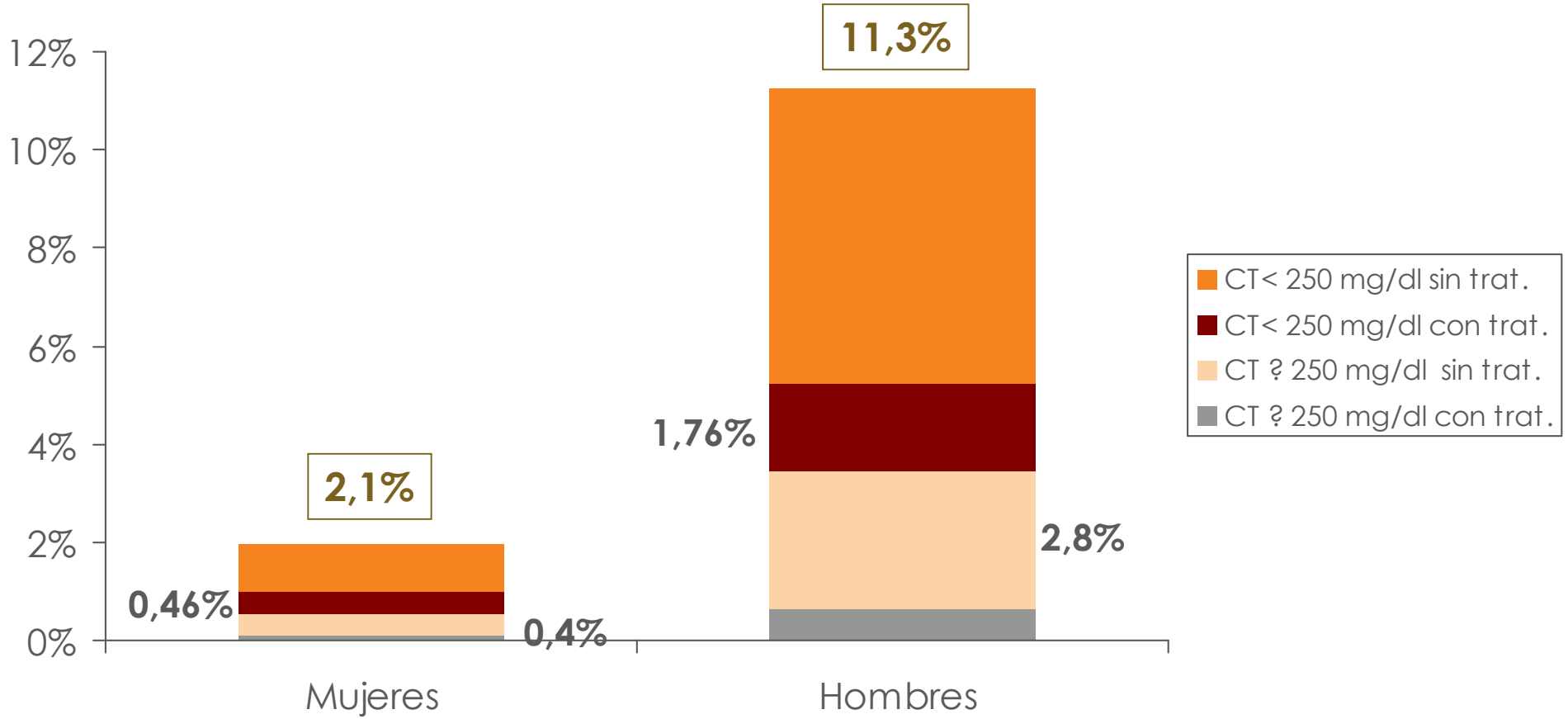
Grau M. Estudio DARIOS . Rev Esp Cardiol. 2011;64:295–304

Població amb risc ≥ 10% a 10 anys i tractamen segons CT < 200 mg/dl: 27.541 participants de 35-74 anys per sexe. Estudi DARIOS



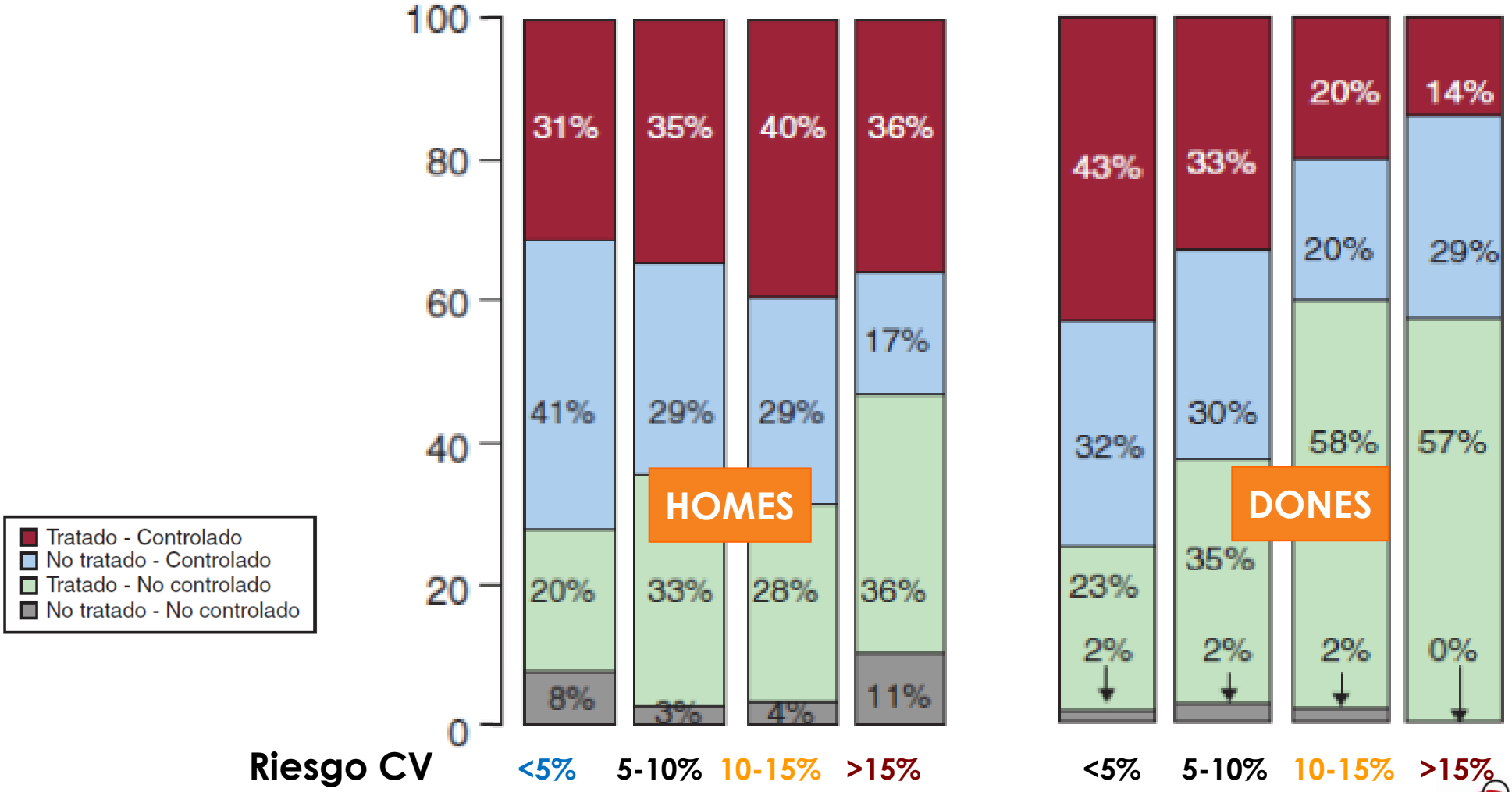
Grau M. Estudio DARIOS . Rev Esp Cardiol. 2011;64:295–304

Població amb risc ≥ 10% a 10 anys i tractamen segons CT < 250 mg/dl: 27.541 participants de 35-74 anys per sexe. Estudi DARIOS

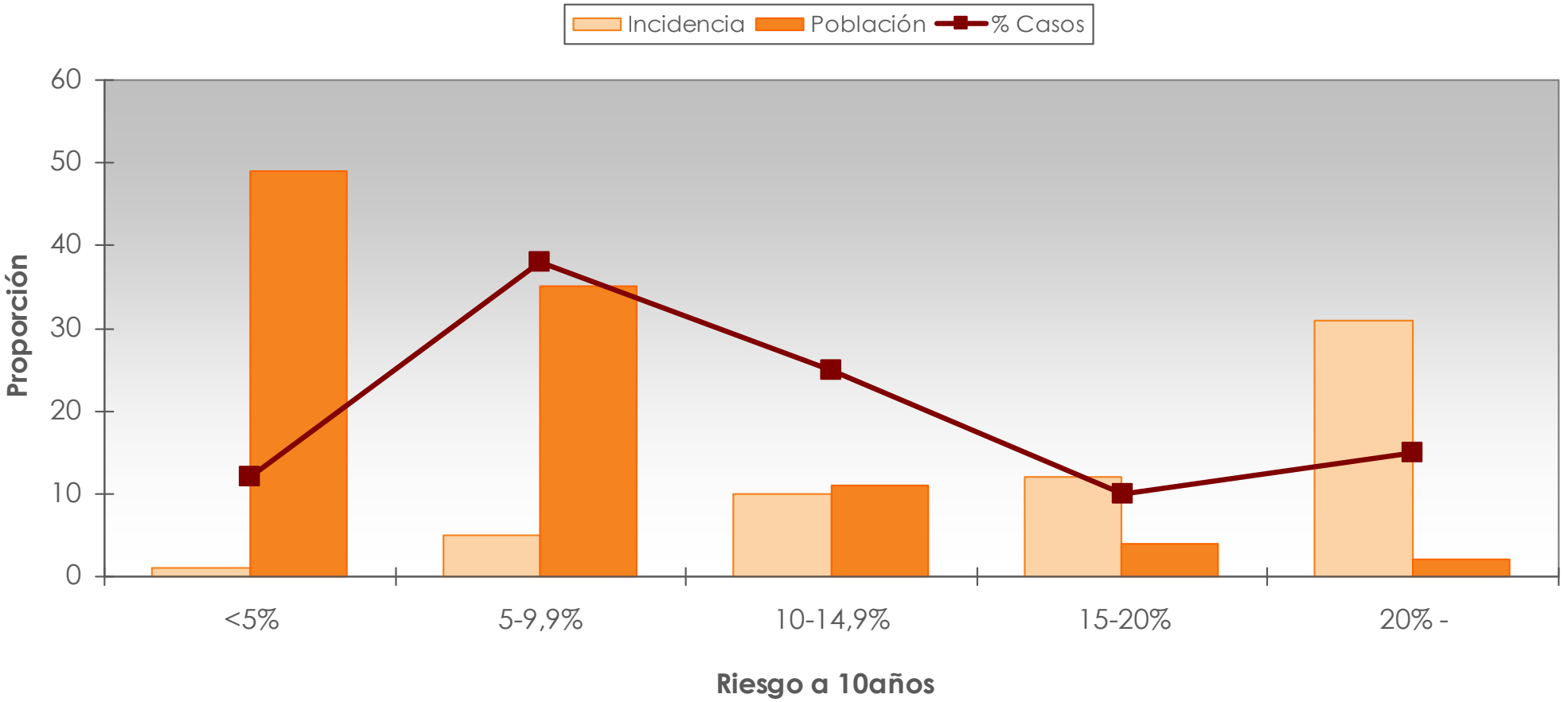


Grau M. Estudio DARIOS . Rev Esp Cardiol. 2011;64:295–304

Prevalença de diabetis. Població de 35-74 anys. Estudi DARIOS

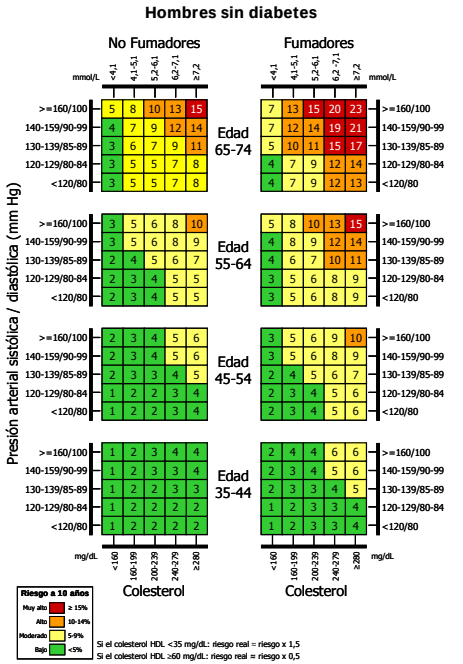


Risc coronari i incidència d'esdeveniments coronaris a 10 anys en l'estudi REGICOR (n=3200)

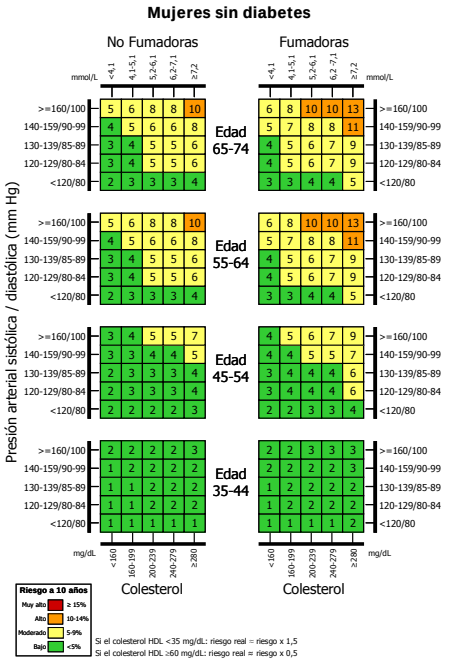


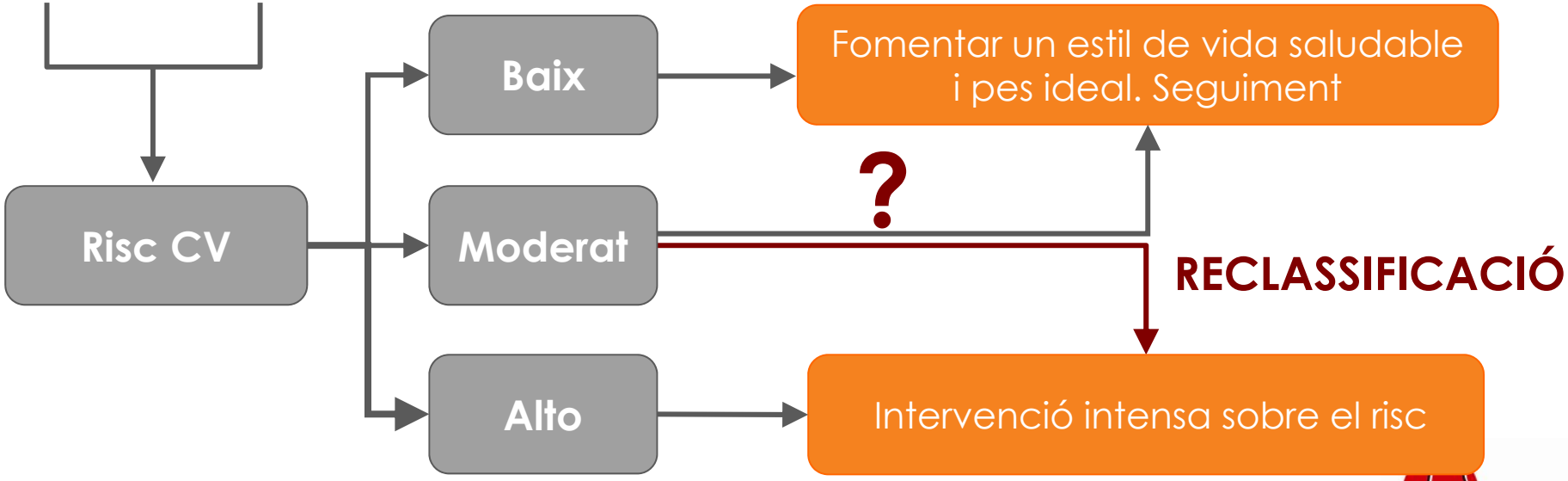
Marrugat J et al. Rev Esp Cardiol 2011; 64: 385-94

Hombres



Mujeres





Factors emergents: utilitat per a la reclassificació dels pacients de risc moderat

Posibles factores para la reclasificación de candidatos a prevención CV primaria

- Proteïna C reactiva -as > 1g/l, Lp(a) > 30 UI
- Història familiar de ECV precoç,
- Score Calç Coronari
- Gruix de la íntima mitja de la caròtida
- Índex turmell braç

Malaltia subclínica

- Perfil genètic advers (predisposició/càrrega genètica)

Yeboah J et al. JAMA. 2012;308(8):788-795
Lluís-Ganella C et al. Atherosclerosis. 2012;222:456-63.

Comparison of Novel Risk Markers for Improvement in Cardiovascular Risk Assessment in Intermediate-Risk Individuals

Marker	Univariable		Multivariable[b]	
	HR (95% CI)[c]	*P* Value	HR (95%CI)[c]	*P* Value
ABI	0.78 (0.66-0.93)	.005	0.79 (0.66-0.95)	.01
Brachial FMD	0.82 (0.66-1.03)	.09	0.93 (0.74-1.16)	.52
CAC[d]	2.72 (2.09-3.55)	<.001	2.60 (1.94-3.50)	<.001
Carotid IMT	1.33 (1.12-1.59)	.001	1.17 (0.95-1.45)	.13
Family history	2.39 (1.54-3.70)	<.001	2.18 (1.38-3.42)	.001
High-sensitivity CRP[d]	1.26 (1.01-1.57)	.05	1.28 (1.00-1.64)	.05

Yeboah J et al. JAMA. 2012;308(8):788-795

Net Reclassification Improvement (NRI) for Incident Cardiovascular Disease Events With Addition of Novel Risk Markers to the Framingham Risk Score in Intermediate-Risk

Variable	% Reclassified	Risk Category, No. of Events FRS Events (n = 123) FRS Nonevents (n = 1207) Low	Intermediate	High	% Net Correct Reclassification	NRI
FRS plus carotid IMT						.060
Events	3.3	0	119	4	3.3	
Nonevents	3.8	39	1161	7	2.7	
FRS plus CAC						.466
Events	36.6	16	78	29	10.6	
Nonevents	45.7	493	655	59	36.0	
FRS plus brachial FMD						.023
Events	2.4	3	120	0	−2.4	
Nonevents	5.6	62	1140	5	4.7	
FRS plus ABI						
Events	4.1	0	118	5	4.1	.068
Nonevents	4.6	44	1151	12	2.7	
FRS plus high-sensitivity CRP						.037
Events	1.6	0	121	2	1.6	
Nonevents	3.2	32	1168	7	2.1	
FRS plus family history						.040
Events	2.4	1	120	2	0.8	
Nonevents	4.9	49	1148	10	3.2	

Abbreviations: ABI, ankle-brachial index; CAC, coronary calcium score; CRP, C-reactive protein; FMD, flow-mediated dilation; FRS, Framingham Risk Score, IMT, intima-media thickness; MESA, Multi-Ethnic Study of Atherosclerosis.

Yeboah J et al. JAMA. 2012;308(8):788-795

Assessment of the value of a genetic risk score in improving the estimation of coronary risk

REGICOR

Coronary events	Classical risk factors	Classical risk factors + Genetic Score: Low risk	Intermediate-low risk	Intermediate-high risk	High risk
Cases					
	Low risk	24	6	0	0
	Intermediate-low risk	1	22	8	1
	Intermediate-high risk	0	4	10	5
	High risk	0	0	1	21
Non-cases					
	Low risk	1415	105	1	0
	Intermediate-low risk	115	339	64	9
	Intermediate-high risk	0	36	69	30
	High risk	0	5	20	40

Framingham

Coronary events	Classical risk factors	Classical risk factors + Genetic Score: Low risk	Intermediate-low risk	Intermediate-high risk	High risk
Cases					
	Low risk	60	11	0	0
	Intermediate-low risk	7	36	5	0
	Intermediate-high risk	0	4	30	9
	High risk	0	0	8	84
Non-cases					
	Low risk	2014	50	0	0
	Intermediate-low risk	57	444	49	1
	Intermediate-high risk	0	47	207	30
	High risk	0	0	34	350

		REGICOR		Framingham		Meta-analysis	
		All	Intermediate risk	All	Intermediate risk	All	Intermediate risk
NRI	Coronary event	12.17 [1.99;22.34]	24.76 [7.62;41.91]	2.56 [-2.89;8.01]	14.30 [3.08;25.51]	6.37 [-2.85;15.58]	17.44 [8.04;26.83]
IDI	Coronary event	1.62 [0.72;2.51]	0.54 [-0.38;1.46]	0.22 [0.03;0.42]	0.26 [-0.03;0.55]	0.85 [-0.52;2.21]	0.29 [0.01;0.56]

Lluís-Ganella C et al. Atherosclerosis. 2012 Jun;222(2):456-63..

Use of aspirin in primary prevention of cardiovascular disease and mortality

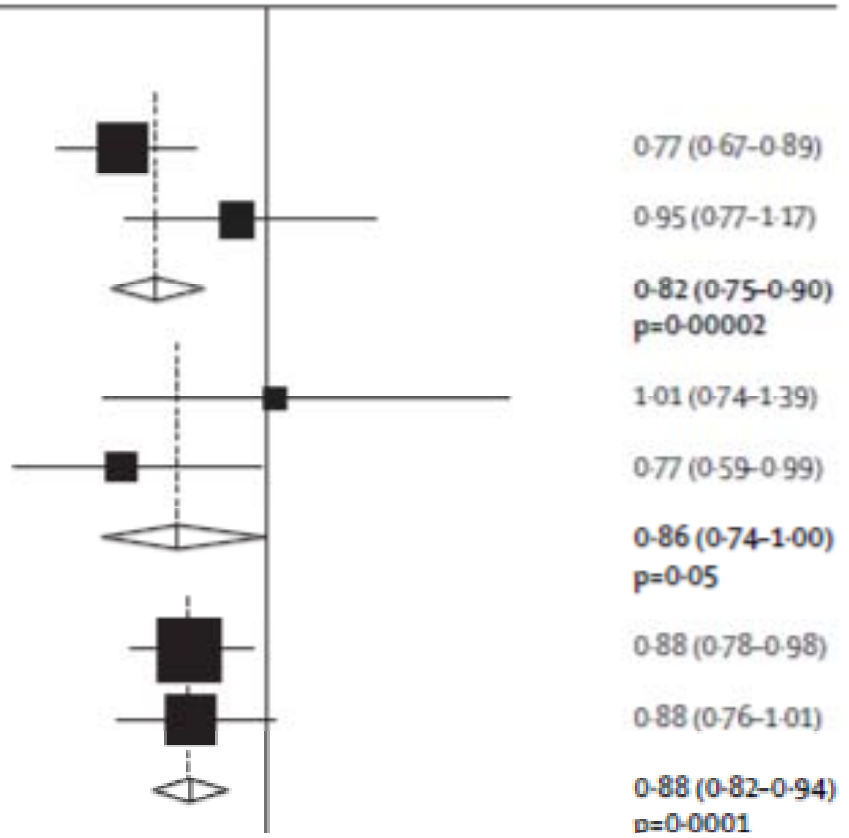
Aspirin for the Primary Prevention of Cardiovascular Events in Women and Men

	Infart de miocardi	Tots els Ictus	Ictus isquèmics	Sagnat greu
Homes	0.68 (0.54-0.86)	1.13 (0.96-1.33)	1.00 (0.72-1.41)	1.72 (1.35-2.20)
Dones	1.01 (0.84-1.21)	0.83 (0.70-0.97)	0.76 (0.63-0.93)	1.68 (1.13-2.52)

Berger JS et al. JAMA 2006; 295: 306-13

Selected outcomes in primary prevention trials of aspirin, by sex

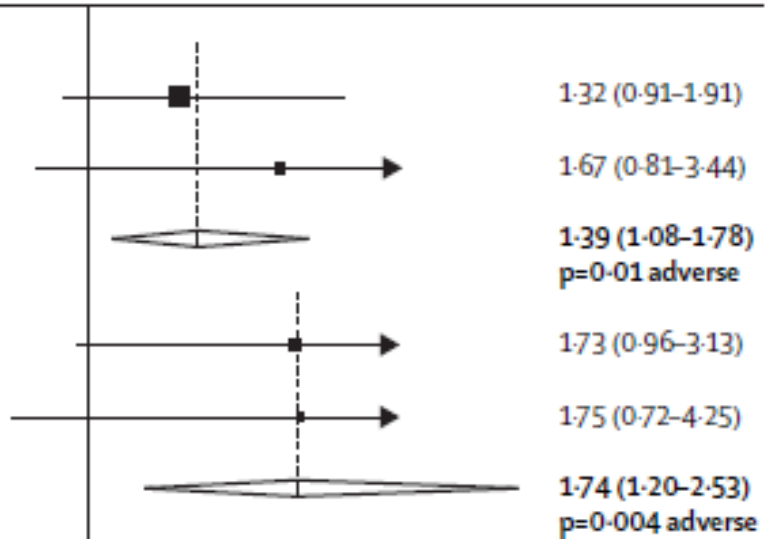
	Events (% per year)		Ratio (CI) of yearly event rates
	Allocated aspirin	Adjusted control	Aspirin:control
6 primary prevention trials			
Major coronary event (χ^2_1=4·7; p=0·03)			
Male	635 (0·57)	801 (0·72)	0·77 (0·67–0·89)
Female	299 (0·14)	314 (0·14)	0·95 (0·77–1·17)
Total	**934 (0·28)**	**1115 (0·34)**	**0·82 (0·75–0·90) p=0·00002**
Ischaemic stroke (χ^2_1=3·1; p=0·08)			
Male	141 (0·15)	138 (0·15)	1·01 (0·74–1·39)
Female	176 (0·09)	229 (0·11)	0·77 (0·59–0·99)
Total	**317 (0·11)**	**367 (0·12)**	**0·86 (0·74–1·00) p=0·05**
Serious vascular event* (χ^2_1=0·0; p=0·9)			
Male	1063 (0·95)	1193 (1·08)	0·88 (0·78–0·98)
Female	608 (0·28)	690 (0·32)	0·88 (0·76–1·01)
Total	**1671 (0·51)**	**1883 (0·57)**	**0·88 (0·82–0·94) p=0·0001**



Lancet 2009; 373: 1849–60

Stroke subtypes in primary and secondary prevention trials

		Events		Ratio (CI) of yearly event rates
		Allocated aspirin	Adjusted control	Aspirin:control
A	**Haemorrhagic stroke (χ^2_1=0·6; p=0·4)**			
	Primary	116	89	1·32 (0·91–1·91)
	Secondary	36	19	1·67 (0·81–3·44)
	Subtotal	**152**	**108**	**1·39 (1·08–1·78) p=0·01 adverse**
B	**Fatal haemorrhagic stroke (χ^2_1=0·0; p=1·0)**			
	Primary	52	30	1·73 (0·96–3·13)
	Secondary	24	12	1·75 (0·72–4·25)
	Subtotal	**76**	**42**	**1·74 (1·20–2·53) p=0·004 adverse**



Lancet 2009; 373: 1849–60

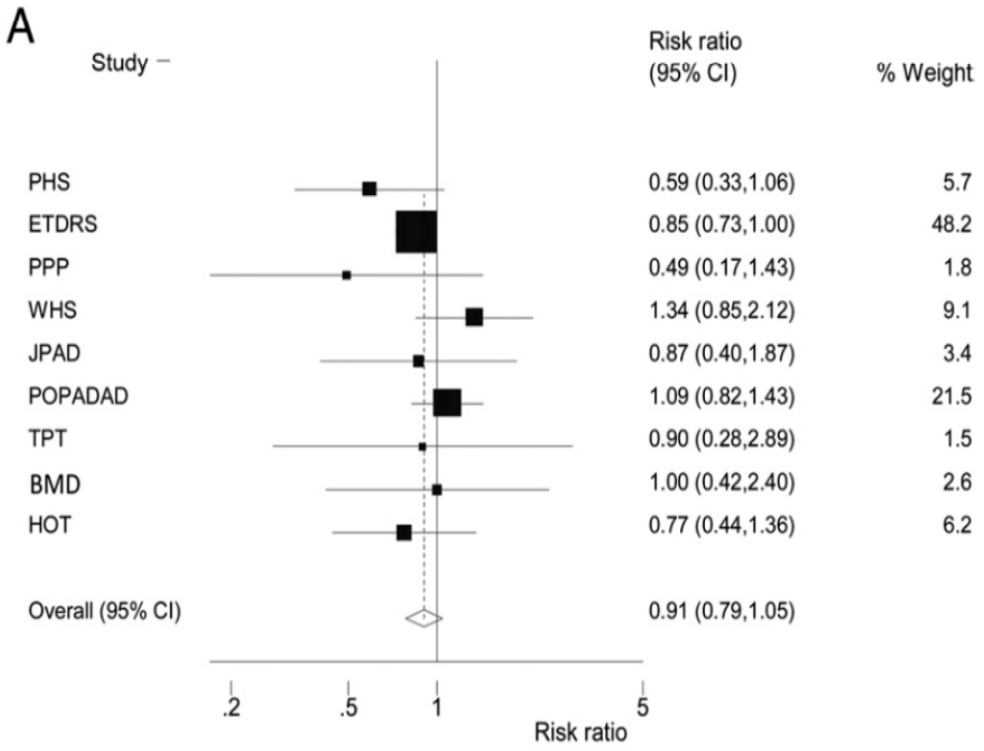
Major CV events
Relative risk reduction vs absolute risk reduction

	RRR	ARR
HIGH RISK PATIENTS*	22	25 per 1000 treated NNT 40
LOW RISK PATIENTS**	15	3 per 1000 treated NNT 333

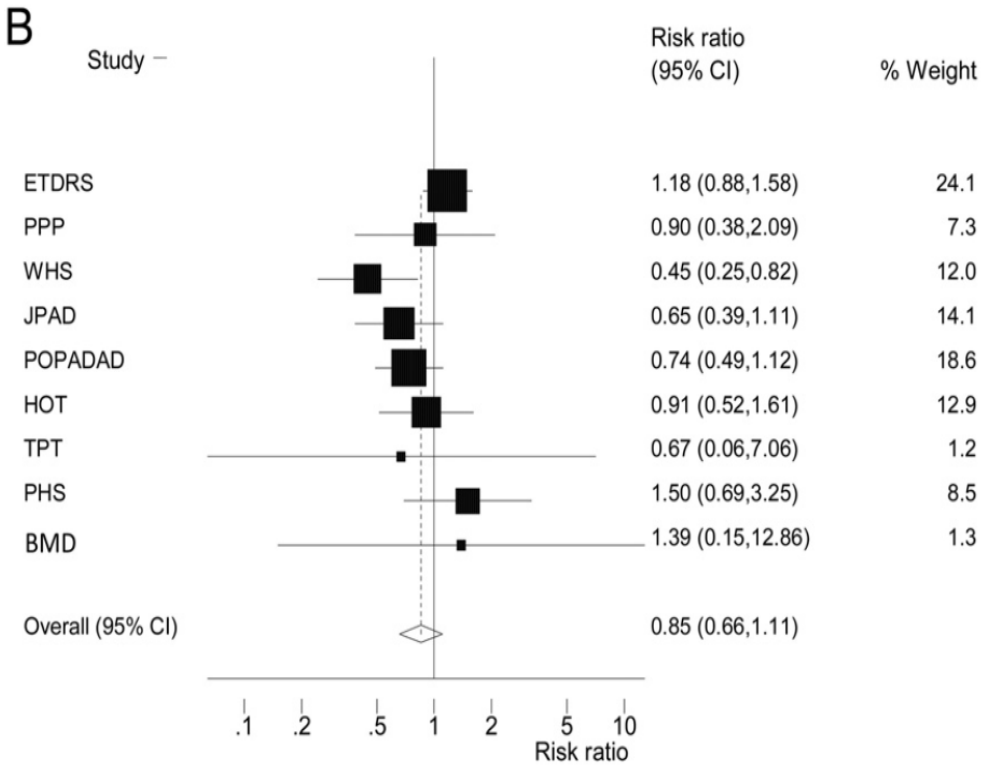
*Antithrombotic Trialists' Collaboration. BMJ 2002;324:71-86
** Meta-analysis of RCT. JAMA 2006;296

Aspirin for the Primary Prevention of Cardiovascular Events in patients with Diabetes

Coronary heart disease events



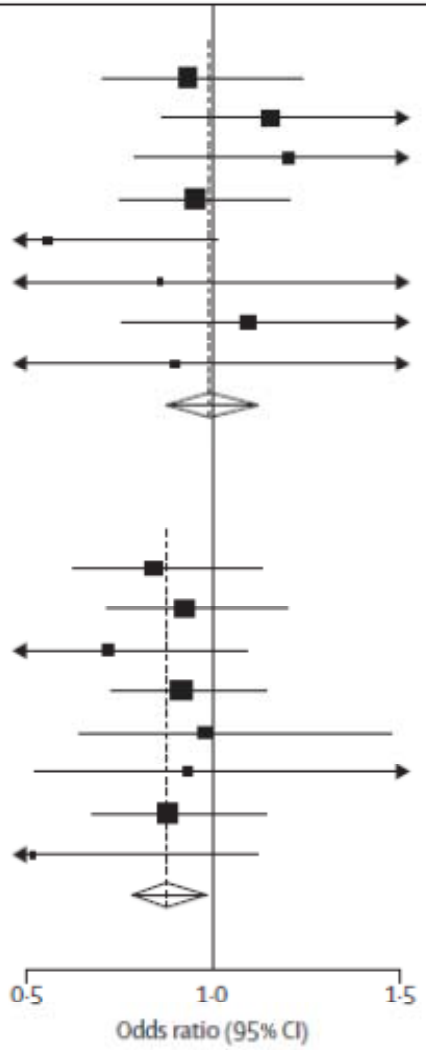
Stroke



Pignone et al. 2010; 25: 2878-86

Meta-analysis of the eff ect of aspirin on risk of vascular death and non-vascular death during 12 randomised trials of daily aspirin versus control in primary prevention of vascular events

	Events/participants		Odds ratio (95% CI)	p value
	Aspirin	Control		
Vascular death				
BDAT[15]	148/3429	79/1710	0·93 (0·70–1·23)	
TPT[16]	101/2545	88/2540	1·15 (0·86–1·54)	
POPADAD[17]	52/638	44/638	1·20 (0·79–1·82)	
HOT[20]	133/9399	140/9391	0·95 (0·75–1·20)	
PPP[19]	17/2226	31/2269	0·56 (0·31–1·01)	
JPAD[21]	11/1262	13/1277	0·85 (0·38–1·92)	
AAA[18]	61/1675	56/1675	1·09 (0·76–1·58)	
5 small trials[22–26]	19/843	21/839	0·90 (0·48–1·68)	
Total	**542/22017**	**472/20339**	**0·99 (0·87–1·12)**	0·50 (het) 0·88 (sig)
Deaths adjusted for randomisation ratio	542	551		
Non-vascular death				
BDAT[15]	122/3429	72/1710	0·84 (0·62–1·13)	
TPT[16]	115/2545	124/2540	0·92 (0·71–1·20)	
POPADAD[17]	42/638	57/638	0·72 (0·47–1·09)	
HOT[20]	151/9399	165/9391	0·91 (0·73–1·14)	
PPP[19]	45/2226	47/2269	0·98 (0·65–1·47)	
JPAD[21]	23/1262	25/1277	0·93 (0·52–1·65)	
AAA[18]	115/1675	130/1675	0·88 (0·68–1·14)	
5 small trials[22–26]	10/843	18/839	0·55 (0·25–1·19)	
Total	**623/22017**	**638/20339**	**0·88 (0·78–0·98)**	0·98 (het) 0·02 (sig)
Deaths adjusted for randomisation ratio	623	710		



***Lancet* 2012; 379: 1602–12**

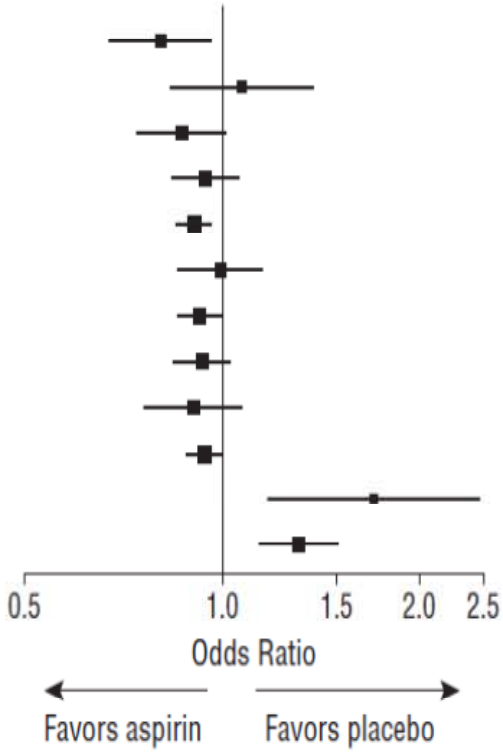
Pooled analysis of the effect of allocation to aspirin versus control on the risk of all incident cancer during trial follow-up in the six trials of low-dose aspirin in primary prevention of vascular disease, by years to notification

	Number of cancers		Odds ratio (95% CI)*	p*	Absolute reduction per 1000 patient-years (95% CI)†
	Aspirin	Control			
All patients					
<3 years	445	442	1·01 (0·88 to 1·15)	0·92	−0·06 (−1·15 to 1·04)
≥3 years	324	421	0·76 (0·66 to 0·88)	0·0003	3·13 (1·44 to 4·82)
Men					
<3 years	269	284	0·94 (0·80 to 1·12)	0·49	0·60 (−0·98 to 2·18)
≥3 years	192	245	0·77 (0·63 to 0·93)	0·008	3·09 (0·85 to 5·33)
Women					
<3 years	176	158	1·13 (0·91 to 1·40)	0·28	−0·83 (−2·38 to 0·72)
≥3 years	132	176	0·75 (0·59 to 0·94)	0·01	3·19 (0·61 to 5·77)
Age <60 years					
<3 years	115	141	0·83 (0·65 to1·07)	0·14	0·92 (−0·41 to 2·25)
≥3 years	105	149	0·72 (0·56 to 0·93)	0·01	2·74 (0·69 to 4·78)
Age ≥60 years					
<3 years	330	301	1·08 (0·92 to 1·27)	0·32	−0·75 (−2·46 to 0·96)
≥3 years	219	272	0·77 (0·65 to 0·93)	0·006	3·68 (1·03 to 6·33)
Non-smokers					
<3 years	317	320	0·99 (0·85 to 1·16)	0·95	0·01 (−1·20 to 1·22)
≥3 years	202	272	0·74 (0·61 to 0·89)	0·001	3·07 (1·18 to 4·97)
Smokers					
<3 years	128	122	1·05 (0·81 to 1·35)	0·72	−0·18 (−2·90 to 2·53)
≥3 years	122	149	0·79 (0·62 to 1·02)	0·07	3·34 (−0·20 to 6·88)

***Lancet* 2012; 379: 1602–12**

Effect of Aspirin in primary prevention on Vascular and Nonvascular Outcomes

Outcome	No. of studies	No. of cases/ participants, aspirin	No. of cases/ participants, placebo	Odds ratio (95% CI)	I^2 (95% CI)
Nonfatal MI	9	699/52145	841/50476	0.80 (0.67-0.96)	62.1% (21.7%-81.6%)
Fatal MI	9	329/52145	263/50476	1.06 (0.83-1.37)	37.4% (0.0%-71.2%)
Total CHD	9	1044/52145	1125/50476	0.86 (0.74-1.01)	64.8% (28.1%-82.7%)
Stroke	9	749/52145	755/50476	0.94 (0.84-1.06)	14.8% (0.0%-56.9%)
Total CVD events	9	2107/52145	2171/50476	0.90 (0.85-0.96)	0.0% (0.0%-55.4%)
CVD mortality	9	674/52145	611/50476	0.99 (0.85-1.15)	36.1% (0.0%-70.6%)
Non-CVD mortality	9	1276/52145	1311/50476	0.92 (0.85-1.00)	0.0% (0.0%-4.2%)
Cancer mortality	8	750/49919	762/48207	0.93 (0.84-1.03)	0.0% (0.0%-49.4%)
Noncancer, nonvascular mortality	8	481/49919	502/48207	0.90 (0.76-1.07)	32.1% (0.0%-69.9%)
All-cause mortality	9	1962/52145	1933/50476	0.94 (0.88-1.00)	0.0% (0.0%-0.0%)
Total bleeds	9	22297/50868	18415/49208	1.70 (1.17-2.46)	98.0% (97.3%-98.5%)
Nontrivial bleeds	9	5337/50868	4712/49208	1.31 (1.14-1.50)	65.7% (30.3%-83.1%)



***Arch int Med* 2012; 172: 209-216**

Conclusions/ elements per a la discussió

1. La proporció de persones amb bon control dels factors de CV a la població espanyola de 35 a 74 anys, és del 64% (homes amb DM) en el millor dels casos i del 34% en el pitjor (homes amb HTA). Amb els criteris del PAPPS, el control de la hipercolesterolèmia es situa al voltant del 50%.

2. La major part dels individus que patiran un esdeveniment coronari es situen en el grup de risc moderat (5-9%)

Conclusions/ elements per a la discussió

3. En els pacients amb risc moderat la mesura d'ITB i els antecedents familiars poden ser d'utilitat per a la reclassificació a un nivell superior de risc

4. L'ús d'AAS en la prevenció primària s'ha de basar en la estimació del risc cardiovascular i del risc de complicacions hemorràgiques

Moltes Gràcies

Manejo de la hipercolesterolemia
Objetivos en prevención primaria

	PAPS 2009	ATP III 2004	ESC 2011
Riesgo moderado	CT < 190 mg/dl LDL < 130 mg/dl	LDL<130 mg/dl	LDL<115 mg/dl
Riesgo alto	CT < 190 mg/dl LDL < 100 mg/dl	LDL <70 mg/dl	LDL<100 mg/dl
Ptes. diabéticos	CT < 190 mg/dl LDL < 100 mg/dl	LDL <100 mg/dl	LDL < 70 mg/dl o ↓ >50% del basal
Riesgo Alto	REGICOR ≥10%	REGICOR ≥10%	REGICOR ≥ 10%
Riesgo moderado	REGICOR 5-9,9%	REGICOR 5-9,9%	REGICOR 5-9,9%

NCEP, Adult Treatment Panel III update. Circulation 2004;110:227-239.
Maiques G et al PAPPS 2009. *Task Force Eur Heart J 2011. 32: 1769-1818*