Material adicional

_____

Análisis de la disminución de la mortalidad por enfermedad coronaria en una población mediterránea: España 1988 - 2005

Gemma Flores-Mateo[a,b], María Grau[c], Martin O'Flaherty[d], Rafel Ramos[a,e], Roberto Elosua[c,f], Concepción Violan-Fors[a], Miquel Quesada[a,e], Ruth Martí[a,e], Joan Sala[g], Jaume Marrugat[c] y Simon Capewell[d,*]

[a]Institut d'Investigació en Atenció Primària Jordi Gol, Barcelona, España
[b]Ciber de Fisiopatología de la Obesidad y Nutrición, CIBEROBN, Instituto Salud Carlos III, Madrid, España
[c]Grupo de Epidemiología y Genética Cardiovascular, Programa de Investigación en Procesos Inflamatorios y Cardiovasculares, Institut Municipal d'Investigació Mèdica (IMIM), Barcelona, España
[d]Division of Public Health, University of Liverpool, Reino Unido
[e]Unitat de Suport a la Recerca de Girona, Institut d'Investigació en Atenció Primària Jordi Gol, Institut Català de la Salut, Barcelona, España
[f]Ciber de Epidemiología y Salud Pública, Instituto Salud Carlos III, Madrid, España
[g]Departamento de Cardiología, Hospital Universitari Dr. Josep Trueta, Girona, España

_____

Impact, a Validated, Comprehensive Coronary Heart Disease Model

Table 1

Main Data Sources for the Parameters Used in the Spain IMPACT Model

	1988	2005
Population statistics (number)	National Statistics Institute[1]	National Statistics Institute[1]
Deaths by age and sex (number)	National Statistics Institute[1]	National Statistics Institute[1]
CHD Mortality (rates)	National Statistics Institute[1] (ICD-9 codes 410-414, 429.2)	National Statistics Institute[1]
NUMBER OF PATIENTS ADMITTED YEARLY		
Myocardial infarction: ICD9: 410,411	Hospital Morbidity Survey[2]	Hospital Morbidity Survey[2]
Angina pectoris: ICD9: 413	Hospital Morbidity Survey[2]	Hospital Morbidity Survey[2]
Heart failure: ICD9: 425.4, 425.5, 425.9, 428.0, 428.1 and 428.9	Hospital Morbidity Survey[2]	Hospital Morbidity Survey[2]
Number of patients treated with		
CABG: ICD-9 36.1	Assume zero	Sociedad Española de Cirugía torácica y cardiovascular[3]
PTCA: ICD9 36.01-36.05	Assume zero	Sociedad Española de Cirugía torácica y cardiovascular[3]
Cardiopulmonary resuscitation in the community		
Numbers	IBERICA[4], REGICOR[5]	IBERICA[4], REGICOR[5]
Uptake	IBERICA[4], REGICOR[5]	IBERICA[4], REGICOR[5]
Acute myocardial infarction		
Hospital Resuscitation	REGICOR[5]	REGICOR[5], MASCARA[6]
Thrombolysis	REGICOR[5]	REGICOR[5], MASCARA[6]
Primary angioplasty	Assume zero	REGICOR[5], MASCARA[6]
Aspirin	REGICOR[5]	REGICOR[5], MASCARA[6]
Beta blockers	REGICOR[5]	REGICOR[5], MASCARA[6]
ACE inhibitors	Assume zero	REGICOR[5], MASCARA[6]
Primary CABG surgery	Assume zero	REGICOR[5], MASCARA[6]
Primary PTCA (angioplasty)	Assume zero	REGICOR[5], MASCARA[6]
Angina pectoris: unstable		
Prevalence	Hospital Morbidity Survey[2]	Hospital Morbidity Survey[2]

Platelet IIB/IIIA Inhibitors	Assume zero	MASCARA[6], EMMA*
Aspirin alone	Assume zero	MASCARA[6], EMMA*
Aspirin & Heparin	Assume zero	MASCARA[6], EMMA*
Primary CABG surgery	Assume zero	MASCARA[6], EMMA*
Primary PTCA (angioplasty)	Assume zero	MASCARA[6], EMMA*
Secondary prevention following AMI		
Aspirin	Assume zero	REGICOR[5], EMMA*
Beta blockers	Assume zero	REGICOR[5], EMMA*
ACE inhibitors	Assume zero	REGICOR[5], EMMA*
Statins	Assume zero	REGICOR[5], EMMA*
Warfarin	Assume zero	REGICOR[5], EMMA*
Rehabilitation	Assume zero	REGICOR[5], EMMA*
Secondary prevention following CABG or PTCA		
Aspirin	Assume zero	REGICOR[5], EMMA*
Beta blockers	Assume zero	REGICOR[5], EMMA*
ACE inhibitors	Assume zero	REGICOR[5], EMMA*
Statins	Assume zero	REGICOR[5], EMMA*
Warfarin / Acenocumarol	Assume zero	REGICOR[5], EMMA*
Rehabilitation	Assume zero	Assume zero
Congestive Heart Failure		
ACE inhibitors	Assume zero	EPISERVE Study[7]; The PRICE Study[8]
Beta blockers	Assume zero	EPISERVE Study[7]; The PRICE Study[8]
Spironolactone	Assume zero	EPISERVE Study[7]; The PRICE Study[8]
Aspirin	Assume zero	EPISERVE Study[7]; The PRICE Study[8]
Statins	Assume zero	EPISERVE Study[7]; The PRICE Study[8]
Treatment for chronic angina		
CABG surgery	Assume zero	REGICOR[5]

PTCA (angioplasty)	Assume zero	REGICOR[5]
Community angina pectoris: total		
Prevalence	PANES[9]	EMMA*
Aspirin	Assume zero	EMMA*
Statins	Assume zero	EMMA*
Community Chronic heart failure		
Prevalence	Rodríguez-Artalejo[10]	EMMA*
ACE inhibitors	Assume zero	EMMA*
Beta blockers	Assume zero	EMMA*
Spironolactone / Furosemida	Assume zero	EMMA*
Aspirin	Assume zero	EMMA*
Statins	Assume zero	EMMA*
Hypertension		
Prevalence	Banegas Banegas et al[11]	REGICOR[5]
Treated (%)	Banegas Banegas et al[11]	REGICOR[5]
Statins etc for primary prevention		
Hypercholesterolemia (%)	MONICA[12]	REGICOR[5]
Treated (%)	MONICA[12]	REGICOR[5]
POPULATION RISK FACTOR PREVALENCE		
Current smoking	National Health Survey[12]	National Health Survey[13]
Systolic blood pressure	CINDI Study[14]	Baena et al. 2006[15]
Cholesterol	MONICA[16]	REGICOR[5]
Physical activity	National Health Survey[12]	National Health Survey[13]
Obesity (BMI)	MONICA[16]	REGICOR[5]
Diabetes	National Health Survey[12]	National Health Survey[13]

ACE, angiotensin-converting enzyme; AMI, acute myocardial infarction; BMI, body mass index; CABG, coronary artery bypass grafts surgery; CHD, coronary heart disease; PTCA, percutaneous transluminal coronary angioplasty. * EMMA Estació de Monitoratge de les Malalties Ateroscleròtiques (Personal Communications)

Table 2

Clinical Efficacy of Interventions: Relative Risk Reductions Obtained From Meta-Analyses, and Randomised Controlled Trials*

Treatments	Relative Risk Reduction	Source paper: First author (year)
Acute myocardial infarction		
Thrombolysis	31%	Estess (2002)[17]
Aspirin	15%	Antithrombotic Trialists' Collaboration (2002)[18]
Primary angioplasty STEMI	27%	Keeley (2003)[19]
Primary PTCA Non-STEMI	28%	O'Donoghue (2008)[20]
Primary CABG surgery	39%	Yusuf (1994)[21]
Beta blockers	4%	Freemantle (1999)[22]
ACE inhibitors	7%	ACE Inhibitor Myocardial Infarction Collaborative Group (1998)[23]
Cardio-pulmonary resuscitation (CPR)		
Community CPR Spain	5%-15%**	Rea (2001)[24] Nichol (1999)[25]
Hospital CPR Spain	33% ***	Hospital Morbidity Survey[2]
Secondary Prevention in CHD Patients		
Aspirin	15%	Antithrombotic Trialists' Collaboration (2002)[18]
Beta blockers	23%	Freemantle (1999)[22]
ACE inhibitors	23%	Flather (2000)[26]
Statins	22%	Baigent (2005)[27]
Warfarin	15%	Lau (1992)[28]
Rehabilitation	27%	Taylor (2004)[29]
Chronic Angina		
CABG surgery years 0-5	39%	Yusuf (1994) [21]
CABG surgery years 6-10	17%	Yusuf (1994)[21]
Angioplasty in Chronic angina, with stents	8%	BASKET (2005)[30], Yusuf (1994)[21], Pocock (1995)[31], Folland (1997)[32]
Aspirin	15%	Antithrombotic Trialists' Collaboration (2002)[18]

Statins	22%	Baigent (2005)[27]
ACEI	17%	Al Mallah (2006)[33]
Unstable Angina		
Aspirin alone	15%	Antithrombotic Trialists' Collaboration (2002)[18]
Aspirin & Heparin	33%	Oler (1996)[34]
Platelet glycoprotein IIB/IIIA inhibitors	9%	Boersma(2002)[35]
Primary PTCA Non-STEMI	28%	O'Donoghue (2008)[20]
Primary CABG surgery	43%	Yusuf (1994)[21]
Heart failure in patients requiring hospitalisation		
ACE inhibitors	26%	Flather (2000)[26]
Beta blockers	35%	Shibata (2001)[36]
Spironolactone	30%	Pitt (1999)[37]
Aspirin	15%	Antithrombotic Trialists' Collaboration (2002)[18]
Statins	No effect	GISSI HF 2008[38], Kjekshus 2008 (CORONA)[39]
Heart failure in the community		
ACE inhibitors	20%	Flather (2000)[26]
Beta blockers	35%	Shibata (2001)[36]
Spironolactone	31%	Pitt (1999)[37]
Aspirin	15%	Antithrombotic Trialists' Collaboration (2002)[18]
Statins	No effect	GISSI HE (2008)[38], Kjekshus 2007 (CORONA)[39]
Hypertension treatment		
	13%	Law (2003)[40]
Statins for primary prevention		
	29%	Pignone (2000)[41]

ACE, angiotensin-converting enzyme; CABG, coronary artery bypass graft surgery; CHD, coronary heart disease; PTCA, percutaneous transluminal coronary angioplasty; STEMI, ST elevation myocardial infarction

* Relative Risk calculated as 1- Odds Ratio

** Rea (2001) 7265 out-of-hospital arrests attended. 15.3% survived to hospital discharge, consider as maximum value. Use Nichol (1999) 5% as SPAIN average.

*** Tunstall-Pedoe(1992) 12/12 survival in aged <65 >65 after in-hospital cardiopulmonary resuscitation for cardiac arrest is 16% and 8% in general wards, 31% and 16% in coronary care unit, etc. Assume better in SPAIN 2000, approximately 33% (consistent with NHDS discharge code for cardiopulmonary resuscitation in 0.74% in 2000, ie, 1/3 of 2% survive)

Table 3

Data Sources for Treatment Uptake Levels in SPAIN 2005: Medical and Surgical Treatments Included in the Model

Treatments	Treatment Uptake in 2005 (average)	Source (year)
Acute myocardial infarction		
Cardiopulmonary resuscitation		
In the Community	3% *	Giammaria et al[42]
In Hospital	100%	REGICOR[5]
Thrombolysis	30%	REGICOR[5], MASCARA[6]
Aspirin	78%	
Primary angioplasty	3%	
Primary CABG	1%	
Intravenous beta blockers	20%	
ACE inhibitors	13%	
Secondary prevention in CHD patients		
Aspirin	74%	REGICOR[5], MASCARA[6]
		REGICOR[5], MASCARA[6]
Beta blockers	40%	REGICOR[5], MASCARA[6]
ACE inhibitors	38%	REGICOR[5], MASCARA[6]
Statins	57%	REGICOR[5], MASCARA[6]
Warfarin	6%	REGICOR[5], MASCARA[6]
Rehabilitation	2%	REGICOR[5], MASCARA[6]
Chronic angina		
CABG surgery	100%	REGICOR[5]
Angioplasty	100%	REGICOR[5]
Aspirin in community	78%	EMMA†
Statins in community	69%	EMMA†
Unstable angina		
Aspirin & Heparin	67%	MASCARA[6], EMMA†
Aspirin alone	20%	MASCARA[6], EMMA†
Platelet glycoprotein IIB/IIIA	28%	MASCARA[6], EMMA†

inhibitors		
CABG surgery for UA	20%	MASCARA[6], EMMA†
Angioplasty for UA	30%	MASCARA[6], EMMA†
Heart failure including a hospital admission		
ACE inhibitors	48%	EPISERVE Study[7]; The PRICE study[8]
Beta blockers	28%	
Spironolactone	6%	
Aspirin	38%	
Heart failure in the community		
ACE inhibitors	30%	EMMA†
Beta blockers	27%	
Spironolactone	4%	
Aspirin	23%	
Hypertension treatment	43%	BANEGAS BANEGAS et al.[11]
Hyperlipidemia primary prevention		
Statins	9%	REGICOR[5]

ACE, angiotensin-converting enzyme; AMI, acute myocardial infarction; CABG, coronary artery bypass graft surgery; EMMA, Estació de Monitoratge de les Malalties Ateroscleròtiques, MASCARA MAnejo del Síndrome Coronario Agudo. Registro Actualizado, PTCA percutaneous transluminal coronary angioplasty, REGICOR Girona Heart Registry.

* Assume Italy average. Italy statistics suggest the incidence of sudden cardiac death ranges from 0.4 to 1.28 every 1000 inhabitants per year. Sudden cardiac death is responsible for about 10% of all deaths in Italy. Survival rates generally do not exceed 5% in out-of-hospital cardiac arrest. †Personal communication.

Table 4

Age-Specific Case Fatality Rates for Each Patient Group

GROUP	AMI	Post AMI	Unstable Angina	CABG surgery	Angioplasty	Heart Failure		Hypertension	Hypercholesterolemia
						Hospital	*Community*		
	30 day	**One year***	**One year***	**One year***	**One year***	**One year**	**One year**	**One year**	**One year**
Mean	0.084	0.051	0.065	0.020	0.016	0.251	0.033	0.010	0.006
Men									
25-34	0.01	0.009	0.016	0.003	0.003	0.068	0.010	0.000	0.000
35-44	0.01	0.009	0.024	0.003	0.003	0.097	0.014	0.001	0.001
45-54	0.02	0.034	0.034	0.007	0.007	0.138	0.021	0.002	0.002
55-64	0.05	0.034	0.056	0.012	0.012	0.190	0.029	0.006	0.006
65-74	0.10	0.056	0.070	0.023	0.025	0.283	0.042	0.014	0.014
75-84	0.16	0.111	0.091	0.042	0.042	0.337	0.051	0.035	0.035
85+	0.28	0.172	0.118	0.075	0.074	0.418	0.063	0.094	0.094
Women									
25-34	0.01	0.004	0.016	0.003	0.003	0.068	0.010	0.000	0.000
35-44	0.01	0.004	0.024	0.003	0.003	0.097	0.014	0.001	0.001
45-54	0.02	0.017	0.034	0.007	0.007	0.138	0.021	0.002	0.002
55-64	0.05	0.014	0.056	0.012	0.012	0.190	0.029	0.004	0.004
65-74	0.11	0.051	0.070	0.023	0.027	0.244	0.037	0.014	0.014
75-84	0.17	0.088	0.091	0.042	0.039	0.289	0.043	0.035	0.035
85+	0.27	0.134	0.118	0.075	0.061	0.368	0.055	0.094	0.094
Source	Medicare	Medicare	Van Domberg	Medicare	Medicare	Medicare	Medicare	US Census / Vital Statistics	

AMI, acute myocardial infarction; CABG, coronary artery bypass grafts surgery

*excluding heart failure patients (already considered in heart failure section)

Table 5

Specific Beta Coefficients for Major Risk Factors: Data sources, Values and Comments.

Estimated β coefficients from multiple regression analyses for the relationship between absolute changes in population mean risk factors and % changes in coronary heart disease mortality for men and women, stratified by age.

	Age groups (years)					
Cholesterol	25-44	45-54	55-64	65-74	75-84	85+
Men	**0.900**	**0.650**	**0.450**	**0.333**	**0.317**	**0.211**
Women	**0.734**	**0.530**	**0.367**	**0.272**	**0.258**	**0.172**
Men Lower 95% CI	0.782	0.564	0.391	0.289	0.275	0.172
Men Upper 95% CI	0.995	0.718	0.497	0.368	0.350	0.219
Women Lower 95% CI	0.474	0.342	0.237	0.175	0.167	0.104
Women Upper 95% CI	0.947	0.684	0.474	0.351	0.333	0.208

Source: Law Wald & Rudnicka meta-analysis[44]

*UNITS: % mortality change per 1 mmol/l (39mg/dl) change in total cholesterol

Strengths: includes US data, includes randomized clinical trials (consistent with observational data), adjusted for regression dilution bias, results stratified by sex and age, with 95% CIs

Limitations: some publication bias still possible

	Age groups (years)				
Body mass index (BMI)	<44	45-59	60-69	70-79	80+
Men*	**0.100**	**0.050**	**0.040**	**0.030**	**0.02**
Women*	**0.100**	**0.050**	**0.040**	**0.030**	**0.02**
Lower limits	0.08	.04	.03	.02	.015
Maximum values	1.110	1.090	1.050	1.040	1.03

Source: Whitlock et al[45], James et al. 2004[46]

*UNITS: % mortality change per 1 kg/m^2 change in BMI

Strengths: Mainly US cohorts, stratified by age, adjusted for regression dilution bias, consistent with James et al., 95% CIs available.

Limitations: may overestimate, because not adjusted for cholesterol, blood pressure, activity, or diabetes; observational data

	Age groups (years)					
Blood Pressure	25-44	45-54	55-64	65-74	75-84	84+
Men	**0.020**	**0.020**	**0.020**	**0.020**	**0.015**	**0.010**
Women	**0.020**	**0.020**	**0.020**	**0.020**	**0.015**	**0.010**
Min	0.002	0.002	0.002	0.002	0.034	0.034
Max	0.044	0.044	0.044	0.044	0.044	0.060

Source: Law & Wald meta-analysis 2003[44]

*UNITS: % mortality change per 1 mmHg diastolic blood pressure.

Strengths: includes US data, includes randomized clinical trials (consistent with observational data), cohorts adjusted for dilution bias, with 95% CIs.

Limitations: limited information on stratification by age and sex.

Table 6

Relative Risks Used in the Spain IMPACT Model for Diabetes and Physical Inactivity for Coronary Heart Disease Mortality. (Best, Minimum and Maximum Estimates taken from InterHeart)

	Both sexes		Men		Women	
	Young	**Old**	**≤55 years**	**>55 years**	**≤65 years**	**> 65 years**
Lifestyle factors						
Smoking	*3·33 (2·86-3·87)*	*2·44* (2·10-2·84)*	*3·33 (2·80-3·95)*	*2·52 (2·15-2·96)*	*4·49 (3·11-6·47)*	*2·14 (1·35-3·39)*
Fruit and vegetables	*0·69 (0·58-0·81)*	*0·72 (0·61-0·85)*	*0·72 (0·59-0.88)*	*0·77 (0·64-0·93)*	*0·62 (0·44-0·87)*	*0·55 (0·38-0·80)*
Exercise	*0·95 (0·79-1·14)*	*0·79 (0·66-0·94)*	*1·02 (0·83-1·25)*	*0·79 (0·66-0·96)*	*0·74 (0·49-1·10)*	*0·75 (0·46-1·22)*
Alcohol	*1·00 (0·85-1·17)*	*0·85 (0·73-1·00)*	*1·03 (0·87-1·23)*	*0·86 (0·73-1.01)*	*0·74 (0·41-1·31)*	*0·83 (0·49-1·42)*
Hypertension	*2·24 (1·93-2·60)*	*1·72 (1·52-1·95)*	*1·99 (1·66-2·39)*	*1·72 (1·49-1·98)*	*2·94 (2·25-3·85)*	*1·82 (1·39-2·38)*
Diabetes	*2·96 (2·40-3·64)*	*2·05* (1·71-2·45)*	*2·66 (2·04-3·46)*	*1·93 (1·58-2·37)*	*3·53 (2·49-5·01)*	*2·59 (1·78-3·78)*
Abdominal obesity	*1·79 (1·52-2·09)*	*1·50 (1·29-1·74)*	*1·83 (1·52-2·20)*	*1·54 (1·30-1·83)*	*1·58 (1·14-2·20)*	*1·22 (0·88-1·70)*
Psychosocial	*2·87 (2·19-3·77)*	*2·43 (1·86-3·18)*	*2·62 (1·91-3·60)*	*2·45 (1·82-3·29)*	*3·92 (2·26-6·79)*	*2·31 (1·22-4·39)*
High ApoB/ApoA1 ratio	*4·35 (3·49-5·42)*	*2·50* (2·05-3·05)*	*4·16 (3·19-5·42)*	*2·51 (2·00-3·15)*	*4·83 (3·19-7·32)*	*2·48 (1·60-3·83)*

Source: Yusuf InterHEART Study. Lancet 2004. *Table 5 Odds ratios for relative effect of risk factors (99% CI, NOT 95%)*[47]

Smoking, adverse lipid profile, hypertension, and diabetes had a greater relative effect on risk of acute myocardial infarction in younger than older individuals.

Table 7

Assumptions and Overlap Adjustments Used in the SPAIN IMPACT Model

Treatment category	Assumptions and overlap adjustments	Justification
Post-AMI patients	Assume 25% already counted as HF patients	Unal (2004)[48]
	Therefore assume residual case fatality halved, having transferred these HF patients to the HF group	Unal (2004)[48]
Post-CABG patients	Assume 2/3 had MI, already counted as Post AMI	Hospital Morbidity Survey[2]
Post-PTCA survivors	Assume 50% had prior AMI, already counted as Post AMI	Hospital Morbidity Survey[2]
	Assume 25% also had CABG, thus already counted as Post CABG	Hospital Morbidity Survey[2]
	Assume 25% had prior PTCA, i.e. repeats, already counted	Hospital Morbidity Survey[2]
Chronic angina treatment		
PTCA patients progressing to CABG surgery	Assume that 20% of PTCA go to CABG	
Efficacy of PTCA in angina	Assumed equivalent to CABG surgery for two vessel disease (maximum estimate), or equal to medical therapy (minimum estimate)	Sculpher (1994)[49] Folland (1997)[32] Yusuf (1994)[21]
Angina in the community	Start with the total patient numbers with angina in the community, based on Hospital Morbidity Survey prevalence Then deduct patients counted elsewhere: -Patients already treated for unstable angina in hospital, -50% of those receiving CABG for angina -50% of those receiving secondary prevention post AMI/post CABG/Post Angioplasty,	Capewell (2000)[50]
Heart failure in the community	Based on Morbidity Hospital Survey prevalence Assume 50% of heart failure is due to CHD Deduct patients treated for severe heart failure in the hospital (already counted)	Hospital Morbidity Survey[2]
Hypertension treatment: overlaps with other CHD patient groups	Total hypertensive patient numbers in community calculated, then deduct: -50% of post AMI patients -50% of community angina patients -50% of community heart failure patients	Hospital Morbidity Survey[2]
Fall in population blood pressure	Estimate the number of DPPs by hypertension treatment - Then subtract this from the total DPPs attributed to the secular fall in population BP	Capewell (1999)[51] Capewell (2000)[50]

AMI, acute myocardial infarction; CABG, coronary artery bypass graft surgery; CHD, coronary heart disease; DPPs, deaths prevented or postponed; HF, heart failure; PTCA, percutaneous transluminal coronary angioplasty.

EXAMPLE OF OVERLAP ESTIMATION

Heart failure in the community

Total prevalence in Spanish Population estimated as: **150 900**

(*Hospital Morbidity Survey[2]*)

Assume half have heart failure due to coronary heart disease: **75 450**

Subtract patients admitted to hospital with (more severe) heart failure: **9735**

(*EPISERVE Study[7]; The PRICE Study[8]*)

Total prevalence in Spanish Population of patients with heart failure,

after these adjustments, estimated as: **65 715**

REFERENCES

1. National Statistics Health. Health. Death Statistics according to cause of death [homepage on the internet]. Madrid; 2009 [updated 2009 April 6; cited 2009 Sept 18]. Available from: http://www.ine.es

2. Instituto de Salud Carlos III. [homepage on the Internet]. Madrid;2009. [cited 2009 Oct. 04]. Available from: http://193 146 50 130/raziel php

3. Sociedad Española de Cirugía Torácica y Cardiovascular. Registro Español de Actividad Cirugía Cardiovascular 2005. [homepage on the Internet] Madrid; 2007. [updated 2007 Jan 11; cited 2010 Des 13]. Available from: http://www.sectcv.es/

4. Alvarez-Leon EE, Elosua R, Zamora A, Aldasoro E, Galcera J, Vanaclocha H, et al. Recursos hospitalarios y letalidad por infarto de miocardio. Estudio IBERICA. Rev Esp Cardiol. 2004; 57:514-523.

5. Marrugat J, Elosua R, Covas MI, Fitó M, Schröder H. The REGICOR Study: A heart registry undertaken in Girona, Spain 1978-2008. Barcelona, 2008. [cited 2010 Des 13]. Available from: http://www.regicor.org

6. Ferreira-Gonzalez I, Permanyer-Miralda G, Marrugat J, Heras M, Cunat J, Civeira E, et al. Estudio MASCARA (Manejo del Sindrome Coronario Agudo. Registro Actualizado). Resultados generales. Rev Esp Cardiol. 2008;61:803-16.

7. Gonzalez-Juanatey JR, Alegria EE, Bertomeu MV, Conthe GP, de Santiago NA, Zsolt FI. Insuficiencia cardiaca en consultas ambulatorias: comorbilidades y actuaciones diagnóstico-terapéuticas por diferentes especialistas. Estudio EPISERVE. Rev Esp Cardiol. 2008;61:611-9.

8. Anguita SM, Crespo Leiro MG, de Teresa GE, Jimenez NM, Alonso-Pulpon L, Muniz GJ. Prevalencia de la insuficiencia cardiaca en la población general española mayor de 45 años. Estudio PRICE. Rev Esp Cardiol. 2008;61:1041-9.

9. Cosin J, Asin E, Marrugat J, Elosua R, Aros F, de los Reyes M, et al. Prevalence of angina pectoris in Spain. PANES Study group. Eur J Epidemiol. 1999;15:323-30.

10. Rodriguez-Artalejo F, Banegas B, Jr., Guallar-Castillon P. Epidemiología de la insuficiencia cardíaca. Rev Esp Cardiol. 2004;57:163-70.

11. Banegas BJ. Epidemiologia de la hipertension arterial en España. Situacion actual y prespectivas. Hipertension. 2005;22:353-62.

12. Encuestas Nacionales de Salud de España de años anteriores. [homepage on the Internet].Madrid, 1987. [cited 2009 Sept. 14]. Available from: http://www.msc.es/estadEstudios/estadisticas/encuestaNacional/añosAnteriores.htm

13. Encuestas Nacionales de Salud de España de años anteriores. Madrid; 2005. [cited 2009 Sept. 14]; Available from: http://www.msc. es/estadEstudios/estadisticas/encuestaNacional/aniosAnteriores.htm. 2005.

14. Countrywide Integrated Noncommunicable Diseases Intervention (CINDI) programme. 1999 [cited 2009 Sept. 14] Available from: http://www.wip.villa-bosch.de

15. Baena Diez JM, del Val Garcia JL, Tomas PJ, Martinez Martinez JL, Martin PR, Gonzalez T, et al. Epidemiología de las enfermedades cardiovasculares y factores de riesgo en atención primaria. Rev Esp Cardiol. 2005;58:367-73.

16. Tolonen H, Kuulasmaa K, Ruokokoski E, WHO MONICA Project. MONICA Population Survey Data Book. http://www.ktl fi/publications/monica/ [2005 [cited 2009 Sept. 25];

17. Estess JM, Topol EJ. Fibrinolytic treatment for elderly patients with acute myocardial infarction. Heart. 2002;87:308-11.

18. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. BMJ. 2002;324:71-86.

19. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. Lancet. 2003;361:13-20.

20. O'Donoghue M, Boden WE, Braunwald E, Cannon CP, Clayton TC, de Winter RJ, et al. Early invasive vs conservative treatment strategies in women and men with unstable angina and non-ST-segment elevation myocardial infarction: a meta-analysis. JAMA. 2008;300:71-80.

21. Yusuf S, Zucker D, Peduzzi P, Fisher LD, Takaro T, Kennedy JW, et al. Effect of coronary artery bypass graft surgery on survival: overview of 10-year results from randomised trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration. Lancet. 1994;344:563-70.

22. Freemantle N, Cleland J, Young P, Mason J, Harrison J. beta Blockade after myocardial infarction: systematic review and meta regression analysis. BMJ. 1999;318:1730-7.

23. Indications for ACE inhibitors in the early treatment of acute myocardial infarction: systematic overview of individual data from 100,000 patients in randomized trials. ACE Inhibitor Myocardial Infarction Collaborative Group. Circulation. 1998;97:2202-12.

24. Rea TD, Eisenberg MS, Culley LL, Becker L. Dispatcher-assisted cardiopulmonary resuscitation and survival in cardiac arrest. Circulation. 2001;104:2513-6.

25. Nichol MB, Venturini F, Sung JC. A critical evaluation of the methodology of the literature on medication compliance. Ann Pharmacother. 1999;33:531-40.

26. Flather MD, Yusuf S, Kober L, Pfeffer M, Hall A, Murray G, et al. Long-term ACE-inhibitor therapy in patients with heart failure or left-ventricular dysfunction: a systematic overview of data from individual patients. ACE-Inhibitor Myocardial Infarction Collaborative Group. Lancet. 2000;355:1575-81.

27. Baigent C, Keech A, Kearney PM, Blackwell L, Buck G, Pollicino C, et al. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. Lancet. 2005;366:1267-78.

28. Lau J, Antman EM, Jimenez-Silva J, Kupelnick B, Mosteller F, Chalmers TC. Cumulative meta-analysis of therapeutic trials for myocardial infarction. N Engl J Med. 1992;327:248-54.

29. Taylor RS, Brown A, Ebrahim S, Jolliffe J, Noorani H, Rees K et al. Exercise-based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomized controlled trials. Am J Med. 2004;116:682-92.

30. Kaiser C, Brunner-La Rocca HP, Buser PT, Bonetti PO, Osswald S, Linka A, et al. Incremental cost-effectiveness of drug-eluting stents compared with a third-generation bare-metal stent in a real-world setting: randomised Basel Stent Kosten Effektivitats Trial (BASKET). Lancet. 2005;366:921-9.

31. Pocock SJ, Henderson RA, Rickards AF, Hampton JR, King SB, III, Hamm CW, et al. Meta-analysis of randomised trials comparing coronary angioplasty with bypass surgery. Lancet. 1995;346:1184-9.

32. Folland ED, Hartigan PM, Parisi AF. Percutaneous transluminal coronary angioplasty versus medical therapy for stable angina pectoris: outcomes for patients with double-vessel versus single-vessel coronary artery disease in a Veterans Affairs Cooperative randomized trial. Veterans Affairs ACME InvestigatorS. J Am Coll Cardiol. 1997;29:1505-11.

33. Al-Mallah MH, Tleyjeh IM, Abdel-Latif AA, Weaver WD. Angiotensin-converting enzyme inhibitors in coronary artery disease and preserved left ventricular systolic function: a systematic review and meta-analysis of randomized controlled trials. J Am Coll Cardiol. 2006;47:1576-83.

34. Oler A, Whooley MA, Oler J, Grady D. Adding heparin to aspirin reduces the incidence of myocardial infarction and death in patients with unstable angina. A meta-analysis. JAMA. 1996;276:811-5.

35. Boersma E, Harrington RA, Moliterno DJ, White H, Theroux P, Van de WF, et al. Platelet glycoprotein IIb/IIIa inhibitors in acute coronary syndromes: a meta-analysis of all major randomised clinical trials. Lancet. 2002;359:189-98.

36. Shibata MC, Flather MD, Wang D. Systematic review of the impact of beta blockers on mortality and hospital admissions in heart failure. Eur J Heart Fail. 2001;3:351-7.

37. Pitt B, Zannad F, Remme WJ, Cody R, Castaigne A, Perez A, et al. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. Randomized Aldactone Evaluation Study Investigators. N Engl J Med. 1999;341:709-17.

38. Tavazzi L, Maggioni AP, Marchioli R, Barlera S, Franzosi MG, Latini R, et al. Effect of rosuvastatin in patients with chronic heart failure (the GISSI-HF trial): a randomised, double-blind, placebo-controlled trial. Lancet. 2008;372:1231-9.

39. Kjekshus J, Apetrei E, Barrios V, Bohm M, Cleland JG, Cornel JH, et al. Rosuvastatin in older patients with systolic heart failure. N Engl J Med. 2007;357:2248-61.

40. Law M, Wald N, Morris J. Lowering blood pressure to prevent myocardial infarction and stroke: a new preventive strategy. Health Technol Assess. 2003;7:1-94.

41. Pignone M, Phillips C, Mulrow C. Use of lipid lowering drugs for primary prevention of coronary heart disease: meta-analysis of randomised trials. BMJ. 2000;321:983-6.

42. Giammaria M, Ghiselli G, Manno E, Trinchero R. [Cardiac arrest management in outpatient clinics: integration between hospital emergency care and the 118 emergency system in the model of Turin ASL 3]. Ital Heart J Suppl. 2005;6:575-87.

43. van Domburg RT, van Miltenburg-van Zijl AJ, Veerhoek RJ, Simoons ML. Unstable angina: good long-term outcome after a complicated early course. J Am Coll Cardiol. 1998;31:1534-9.

44. Law MR, Wald NJ, Rudnicka AR. Quantifying effect of statins on low density lipoprotein cholesterol, ischaemic heart disease, and stroke: systematic review and meta-analysis. BMJ. 2003;326:1423.

45. Whitlock G, Lewington S, Mhurchu CN. Coronary heart disease and body mass index: a systematic review of the evidence from larger prospective cohort studies. Semin Vasc Med. 2002;2:369-81.

46. James W, Jackson-Leach R, Mhurchu CN. Overweight and obesity (high body mass indez). In Ezzati M, Lopez AD, Rodgers A, Murray CJL, editors. Comparative quantification of risk. Global and regional burden of disease attributable to selected major risk factors. Volume 1. Geneva: World Health Organization. 2004.

47. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet. 2004;364:937-52.

48. Unal B, Critchley JA, Capewell S. Explaining the decline in coronary heart disease mortality in England and Wales between 1981 and 2000. Circulation. 2004;109:1101-7.

49. Sculpher MJ, Seed P, Henderson RA, Buxton J, Pocock SJ, Parker J et al. Health service costs of coronary angioplasty and coronary artery bypass surgery: the Randomised Intervention Treatment of Angina (RITA) trial. Lancet. 1994;344:927-30.

50. Capewell S, Beaglehole R, Seddon M, McMurray J. Explanation for the decline in coronary heart disease mortality rates in Auckland, New Zealand, between 1982 and 1993. Circulation. 2000;102:1511-6.

51. Capewell S, Morrison CE, McMurray JJ. Contribution of modern cardiovascular treatment and risk factor changes to the decline in coronary heart disease mortality in Scotland between 1975 and 1994. Heart. 1999;81:380-6.