



Material adicional

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

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Impact, a Validated, Comprehensive Coronary Heart Disease Model

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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
<i>Unstable Angina</i>		
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
<i>Heart failure in patients requiring hospitalisation</i>		
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
<i>Heart failure in the community</i>		
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
<i>Hypertension treatment</i>		
	13%	Law (2003) ⁴⁰
<i>Statins for primary prevention</i>		
	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	CABG	Angioplasty	Heart Failure		Hypertension	Hypercholesterolemia
			Angina	surgery		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-analysis⁴⁴

*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 al⁴⁵, James et al. 2004⁴⁶

*UNITS: % mortality change per 1 kg/m² 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)					
<i>Blood Pressure</i>	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 2003⁴⁴

*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
<i>Lifestyle factors</i>						
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**

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