

Contribution of trends in survival and coronary event rates to changes in coronary heart disease mortality: 10-year results from 37 WHO MONICA Project populations

Hugh Tunstall-Pedoe, Kari Kuulasmaa, Markku Mähönen, Hanna Tolonen, Esa Ruokokoski, Philippe Amouyel, for the WHO MONICA (monitoring trends and determinants in cardiovascular disease) Project*

Summary

Background The WHO MONICA (monitoring trends and determinants in cardiovascular disease) Project monitored, from the early 1980s, trends over 10 years in coronary heart disease (CHD) across 37 populations in 21 countries. We aimed to validate trends in mortality, partitioning responsibility between changing coronary-event rates and changing survival.

Methods Registers identified non-fatal definite myocardial infarction and definite, possible, or unclassifiable coronary deaths in men and women aged 35–64 years, followed up for 28 days in or out of hospital. We calculated rates from population denominators to estimate trends in age-standardised rates and case fatality (percentage of 28-day fatalities=[100–survival percentage]).

Findings During 371 population-years, 166 000 events were registered. Official CHD mortality rates, based on death certification, fell (annual changes: men –4.0% [range –10.8 to 3.2]; women –4.0% [–12.7 to 3.0]). By MONICA criteria, CHD mortality rates were higher, but fell less (–2.7% [–8.0 to 4.2] and –2.1% [–8.5 to 4.1]). Changes in non-fatal rates were smaller (–2.1%, [–6.9 to 2.8] and –0.8% [–9.8 to 6.8]). MONICA coronary-event rates (fatal and non-fatal combined) fell more (–2.1% [–6.5 to 2.8] and –1.4% [–6.7 to 2.8]) than case fatality (–0.6% [–4.2 to 3.1] and –0.8% [–4.8 to 2.9]). Contribution to changing CHD mortality varied, but in populations in which mortality decreased, coronary-event rates contributed two thirds and case fatality one third.

Interpretation Over the decade studied, the 37 populations in the WHO MONICA Project showed substantial contributions from changes in survival, but the major determinant of decline in CHD mortality is whatever drives changing coronary-event rates.

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Introduction

The WHO MONICA (monitoring trends and determinants in cardiovascular disease) Project was designed to answer key questions arising from the 1978 Bethesda Conference on the Decline in Coronary Heart Disease Mortality.¹ The continuing relevance of these questions was highlighted by results from the ARIC study.² Are reported declines in coronary heart disease (CHD) mortality genuine? If they are, how much is attributable to improved survival rather than to declining coronary-event rates? Consequential hypotheses arise from the latter question about inter-relations of changes in coronary-event rates, survival (or case fatality), risk factors, and coronary care.

The WHO MONICA Project set out to measure, within defined populations over 10 years, trends in rates of events from CHD and their case fatality, trends in risk factors, and trends in acute coronary care.^{3–5} The protocol, developed between 1979 and 1982, identified six possible associations: between risk factors and incidence; medical care and case fatality; incidence and case fatality; medical care and incidence; risk factors and case fatality; and medical care and risk factors. The first two relations, between trends in risk factors and incidence (or event rates) and between trends in coronary care and case fatality, were the basis of the two major null hypotheses of the study, reflecting the continuing concerns of those involved in health promotion versus those involved in coronary care (WHO MONICA Project protocol available at: URL: www.ktl.fi/publications/monica/manual/part1/i-1.htm URN: NBN:fi-fe 19981147).

This report covers the first definitive 10-year results from 37 populations in 21 countries across four continents. It addresses the original Bethesda questions. The results of standardised measurement of trends are compared with the routine mortality statistics. We estimate the contribution to trends in validated CHD mortality of changing survival compared with changing coronary-event rates.

Methods

Registration of events

MONICA populations and registration procedures have been described with full specification of diagnostic criteria (for relevant section of MONICA Manual see URL: www.ktl.fi/publications/monica/manual/part4/iv-1.htm URN: NBN:fi-fe 19981154).⁵ Standard coding and criteria were applied throughout, with internal and external quality control, to validate all suspected coronary events in individuals aged 35–64 years of defined populations. MONICA coronary events were made up of specified non-fatal events—survival to 28 days from onset—and fatal events—CHD deaths occurring before or

*Participating centres listed at end of paper

Cardiovascular Epidemiology Unit (MONICA Quality Control Centre for Event Registration), University of Dundee, Ninewells Hospital and Medical School, Dundee DD1 9SY, UK (Prof H Tunstall-Pedoe MD); **Department of Epidemiology and Health Promotion (MONICA Data Centre), National Public Health Institute, KTL, Helsinki, Finland** (K Kuulasmaa PhD, M Mähönen MD, H Tolonen MSc, E Ruokokoski MSc); **INSERM U508, Pasteur Institute, Lille, France** (Prof P Amouyel MD)

Correspondence to: Prof Hugh Tunstall-Pedoe (e-mail: h.tunstallpedoe@dundee.ac.uk)

Country	Population	Abbreviation	Registration		Mean population aged 35–64 years (1000s)	Data quality scores	
			Years	n		Coronary events	Demographic
Australia	Newcastle	AUS-NEW	1985–1993	9	148	1.6	1.6
	Perth	AUS-PER	1984–1993	10	381	1.1	1.0
Belgium	Charleroi	BEL-CHA	1983–1992	10	77	0.5	2.0
	Ghent	BEL-GHE	1983–1992	10	85	0.8	2.0
Canada	Halifax County	CAN-HAL	1984–1993	10	108	1.8	2.0
China	Beijing	CHN-BEI	1984–1993	10	283	1.2	1.0
Czech Republic	Czech Republic	CZE-CZE	1984–1993	10	238	1.8	1.0
Denmark	Glostrup	DEN-GLO	1982–1991	10	133	0.8	2.0
Finland	Kuopio Province	FIN-KUO	1983–1992	10	96	1.8	2.0
	North Karelia	FIN-NKA	1983–1992	10	65	1.8	2.0
France	Turku/Loimaa	FIN-TUL	1983–1992	10	78	1.8	2.0
	Lille	FRA-LIL	1985–1994	10	339	1.2	2.0
Germany	Strasbourg	FRA-STR	1985–1993	9	333	1.7	1.0
	Toulouse	FRA-TOU	1985–1993	9	321	0.9	2.0
	Augsburg	GER-AUG	1985–1994	10	215	1.3	2.0
	Bremen	GER-BRE	1985–1992	8	217	1.4	0.5
Iceland	East Germany	GER-EGE	1985–1993	9	246	1.1	0.0
	Iceland	ICE-ICE	1981–1994	14	75	1.8	1.7
Italy	Area Brianza	ITA-BRI	1985–1994	10	343	1.7	2.0
	Friuli	ITA-FRI	1984–1993	10	376	1.7	2.0
Lithuania	Kaunas	LTU-KAU	1983–1992	10	146	1.7	1.0
New Zealand	Auckland	NEZ-AUC	1983–1991	9	289	1.5	2.0
Poland	Tarnobrzeg Voivodship	POL-TAR	1984–1993	10	197	0.9	1.0
	Warsaw	POL-WAR	1984–1994	11	202	1.4	2.0
Russia	Moscow-Control	RUS-MOC	1985–1993	9	85	0.9	1.0
	Moscow-Intervention	RUS-MOI	1985–1993	9	230	0.9	1.0
	Novosibirsk-Control	RUS-NOC	1984–1992	9	175	0.9	1.0
	Novosibirsk-Intervention	RUS-NOI	1984–1993	10	54	1.1	1.0
Spain	Catalonia	SPA-CAT	1985–1994	10	389	1.5	2.0
Sweden	Gothenburg	SWE-GOT	1984–1994	11	153	1.4	2.0
	Northern Sweden	SWE-NSW	1985–1995	11	194	1.9	2.0
Switzerland	Ticino	SWI-TIC	1985–1993	9	114	1.1	2.0
	Vaud/Fribourg	SWI-VAF	1985–1993	9	292	0.9	2.0
UK	Belfast	UNK-BEL	1983–1993	11	158	1.9	1.0
	Glasgow	UNK-GLA	1985–1994	10	130	1.9	2.0
USA	Stanford	USA-STA	1980–1992	13	99	1.6	1.0
Yugoslavia	Novi Sad	YUG-NOS	1984–1995	12	113	1.9	1.0

*See text explanation of scores and scoring.

Table 1: Populations studied, years of coronary-event registration, mean population size, and summary scores of data quality*

after admission or discharge from hospital but within 28 days of onset.^{5,6} MONICA definition 1 for coronary events was used in the main analysis. It included non-fatal events satisfying the criteria for definite myocardial infarction, and fatal events classified as definite, possible, and unclassifiable coronary deaths, the latter comprising mainly sudden deaths with no available diagnostic information. MONICA definition 1 therefore excluded “possible” non-fatal events.^{5,7} Previous angina or infarction were recorded, but first and recurrent events were not distinguished, except in secondary analyses.⁵

Contemporaneous routine death certificates that listed CHD as the underlying cause of death were enumerated for comparison with validated MONICA fatal events, and calculation of official CHD mortality rates.

Statistical procedures

Event rates for age-group 35–64 years were standardised directly by 5-year groups to the World Standard Population.⁸ We used the relation between the Poisson and χ^2 distributions to derive 95% CIs for weighted sums of Poisson parameters.⁹ The annual numbers of events within age-groups was assumed to follow a Poisson distribution with allowance for overdispersion.^{10,11} We calculated trends from the age-standardised annual rates (r_t) with the log-linear model, where log denotes the natural logarithm, t the year, and e_t the error term of the regression model:

$$\log r_t = a + bt + e_t.$$

The estimate $100b$ is the rate of change of the event rate expressed in this paper as average annual percentage change. For small changes, it is about $100[\exp(b) - 1]$, the estimated change during a year.

Case fatality (percentage of events becoming fatal by 28 days from onset) was standardised to the distribution of MONICA events (weighting age 35–44 years by 1, 45–54 years by 3, and

55–64 years by 7, divided by 11), with elimination of empty cells by amalgamation when necessary. The 95% CIs were calculated from the SE of the weighted sum of binomial variables with use of the normal approximation. We calculated trends from annual age-standardised case fatality by log-linear regression, with the assumption that the annual case fatality within age-groups follows the binomial distribution, and with allowance for additional deviation from the regression line, as for trends in event rates. Percentage change in case fatality is expressed as the relative change from 100%, so, for example, a change from 50% to 49% is 2%, for reasons listed.

We calculated correlation coefficients without consideration of SEs of the variables, and probably underestimated them.¹²

MONICA CHD mortality (fatal event) rate M , coronary-event rate C , and case fatality F are related by $M = C \times F$. With the assumption of constant rates of change, where M' indicates the average annual change in MONICA mortality rate (and similarly for C' and F'), then by calculus: $M'/M = (C'/C) + (F'/F)$.

Change in MONICA CHD mortality rates is therefore the sum of change in coronary-event rates plus change in case fatality, all expressed as average annual percentage change. This calculation allows partitioning of the relative contribution to the percentage change in mortality rates of percentage change in coronary-event rates and percentage change in case fatality, specifically where the latter is reported as relative rather than absolute percentage change. (In practice, in any given population, the accuracy of this theoretical equation will depend on the precision of the separately estimated trends. The accuracy may be influenced by the effects of age-standardisation of rates and of possible non-linearity in trends on linear estimates).

Sensitivity analyses

We did the main analyses on all the populations with equal weighting, and all the years accepted for each population. Trends in coronary events qualifying for MONICA definition 1

Population	Official CHD deaths*	Numbers of events in MONICA			Case fatality (%) (SE)	Official CHD mortality rate per 100 000*	Mean (SE) rates per 100 000 in MONICA		
		Fatal†	Non-fatal‡	Coronary§			CHD mortality	Non-fatal‡	Coronary events§
AUS-NEW	1233	1296 (24%)	1917	3213	40.6 (1.7)	181 (5)	191 (5)	288 (7)	479 (9)
AUS-PER	2292	2483 (11%)	4366	6849	36.8 (1.2)	131 (3)	142 (3)	247 (4)	389 (5)
BEL-CHA	587	991 (46%)	1005	1996	50.1 (2.2)	139 (6)	237 (8)	250 (8)	487 (11)
BEL-GHE	431	728 (46%)	818	1546	47.4 (2.5)	94 (5)	161 (6)	185 (7)	346 (9)
CAN-HAL	814	901 (10%)	1544	2445	37.5 (2.0)	176 (6)	194 (7)	328 (8)	523 (11)
CHN-BEI	653	683 (9%)	484	1167	58.8 (2.9)	46 (2)	48 (2)	33 (2)	81 (2)
CZE-CZE	3105	3105 (10%)	2842	5947	52.8 (1.3)	266 (5)	266 (5)	249 (5)	515 (7)
DEN-GLO	1171	1697 (27%)	1564	3261	52.5 (1.7)	187 (5)	271 (7)	246 (6)	517 (9)
FIN-KUO	1490	1542 (2%)	1855	3397	45.7 (1.7)	313 (8)	324 (8)	394 (9)	718 (12)
FIN-NKA	1280	1309 (2%)	1419	2728	48.1 (1.9)	389 (11)	398 (1)	437 (12)	835 (16)
FIN-TUL	949	986 (1%)	1042	2028	48.5 (2.2)	255 (8)	265 (8)	284 (9)	549 (12)
FRA-LIL	1433	2792 (46%)	2031	4823	58.7 (1.4)	89 (2)	172 (3)	126 (3)	298 (4)
FRA-STR	1180	2076 (45%)	2230	4306	49.0 (1.5)	80 (2)	141 (3)	152 (3)	292 (4)
FRA-TOU	751	1294 (40%)	1983	3277	40.0 (1.7)	53 (2)	91 (3)	142 (3)	233 (4)
GER-AUG	1438	1734 (32%)	1425	3159	55.1 (1.8)	130 (3)	157 (4)	129 (3)	286 (5)
GER-BRE	1182	1542 (36%)	1594	3136	49.6 (1.8)	137 (4)	178 (5)	183 (5)	361 (6)
GER-EGE	1539	1930 (16%)	1952	3882	50.0 (1.6)	149 (4)	186 (4)	184 (4)	370 (6)
ICE-ICE	901	919 (5%)	1578	2497	36.9 (1.9)	175 (6)	178 (6)	308 (8)	486 (10)
ITA-BRI	1789	1948 (24%)	2902	4850	40.7 (1.4)	103 (2)	112 (3)	167 (3)	279 (4)
ITA-FRI	1964	2223 (20%)	2746	4969	45.1 (1.4)	99 (2)	112 (2)	141 (3)	253 (4)
LTU-KAU	1940	1678 (11%)	1439	3117	54.8 (1.8)	313 (7)	271 (7)	228 (6)	498 (9)
NEZ-AUC	2575	2649 (5%)	2740	5389	49.5 (1.4)	207 (4)	213 (4)	221 (4)	434 (6)
POL-TAR	1968	3711 (41%)	799	4510	82.7 (1.1)	202 (5)	378 (6)	83 (3)	461 (7)
POL-WAR	1878	3505 (42%)	2382	5887	59.9 (1.3)	187 (4)	347 (6)	238 (5)	586 (8)
RUS-MOC	1160	1005 (12%)	663	1668	60.7 (2.4)	330 (10)	285 (9)	192 (8)	477 (12)
RUS-MOI	2914	2507 (11%)	1565	4072	62.5 (1.5)	326 (6)	280 (6)	173 (4)	453 (7)
RUS-NOC	1834	1876 (0%)	1292	3168	59.9 (1.8)	271 (6)	276 (6)	188 (5)	464 (8)
RUS-NOI	970	653 (4%)	451	1104	60.1 (3.0)	410 (13)	279 (1)	189 (9)	468 (14)
SPA-CAT	1259	1505 (41%)	2650	4155	36.7 (1.5)	63 (2)	76 (2)	135 (3)	210 (3)
SWE-GOT	1309	1376 (10%)	1757	3133	43.6 (1.8)	151 (4)	159 (4)	205 (5)	363 (7)
SWE-NSW	2002	2081 (4%)	3614	5695	36.1 (1.3)	178 (4)	185 (4)	324 (5)	509 (7)
SWI-TIC	467	474 (36%)	987	1461	33.5 (2.5)	94 (4)	95 (4)	195 (6)	290 (8)
SWI-VAF	1064	1091 (38%)	1831	2922	38.4 (1.8)	84 (3)	86 (3)	144 (3)	231 (4)
UNK-BEL	2488	2476 (12%)	3594	6070	41.0 (1.3)	280 (6)	279 (6)	416 (7)	695 (9)
UNK-GLA	2394	2627 (8%)	2823	5450	48.2 (1.3)	332 (7)	365 (7)	412 (8)	777 (11)
USA-STA	955	1182 (9%)	1333	2515	47.9 (2.0)	163 (5)	201 (6)	230 (6)	431 (9)
YUG-NOS	1293	1428 (3%)	1370	2798	51.9 (1.9)	195 (5)	215 (6)	208 (6)	422 (8)
Mean	1477	1730 (20%)	1854	3584	49.0	189	211	223	434
SD	672	808 (16%)	905	1510	9.9	98	89	93	160

*Based on death-certificate enumeration. †Percentage unclassifiable deaths without diagnostic information. ‡Definite myocardial-infarction rate. §WHO MONICA definition 1. ¶Data missing for 1 year.

Table 2: Number of events, age-standardised 28-day case fatality, and mean (SE) annual event rates per 100 000 during registration in men

were estimated by log linear regression. We then did sensitivity analyses on the findings to find out whether they were robust.

Results

Availability and quality of data

37 populations provided data for this report on men and women aged 35–64 years. Table 1 lists the populations, years of registration, and population sizes. Most populations provided data for 10 years (range 8–14), and all provided data for 1985–91. Table 1 shows centrally generated quality scores for the coronary-event and demographic data from which event rates and trends were calculated. In the WHO MONICA Project a full score is 2.0 and 0 denotes at least one serious problem with the data, but not that they are necessarily invalid. Full reports on data quality are available (coronary events URL: www.ktl.fi/publications/monica/coreqa/coreqa.htm URN: NBN:fi-fe 19991072; for demographic data URL: www.ktl.fi/publications/monica/demoqa/demoqa.htm URN: NBN:fi-fe 19991073).

Coronary-event rates and case fatality

During 371 population-years of observation, 166 000 coronary events were registered that met criteria for MONICA definition 1. 35 populations provided data on men and women, and two on men only. We analysed data for men (table 2) and women (table 3) separately and show by population first the numbers of events registered in different categories and then the mean annual event rates derived from them. Numbers of events shown are: the total

of certified (official) CHD deaths; the number of MONICA fatal events registered; the percentage of these in the unclassifiable MONICA category; numbers of MONICA non-fatal and of coronary events (fatal plus non-fatal). The mean case fatality is followed by the mean (SE) annual event rates for the different event categories averaged over the years of registration, all rates sharing the same population denominators.

The mean number of events registered by population was 3584 (range 1104–6849) in men and 951 (398–2143) in women. Mean MONICA coronary-event rates and case fatality, with 95% CIs, are ranked by population in descending order for each sex (figure 1). Subsequent descriptions of average annual percentage changes in rates are against a background of different mean rates.

North Karelia (Finland) had the highest 10-year mean coronary-event rate in men, and Beijing (China) the lowest. In women the highest rate was in Glasgow (UK) and the lowest in Catalonia (Spain). Coronary-event rates in women were, on average, 24% of those in men, but the sex ratio varied between populations.

Tarnobrzeg Voivodship (Poland), a rural community with limited potential for diagnostic confirmation of non-fatal events, had the highest case fatality in the two sexes, whereas Ticino (Switzerland) had the lowest case fatality in men, and Halifax (Canada) the lowest in women. Unlike coronary-event rates, the range of case fatality was similar in the two sexes, but the mean was higher in women, even after age standardisation (men 49.0%, women 53.8%).

Population	Official CHD deaths*	Numbers of events in MONICA			Case fatality (%) (SE)	Official CHD mortality rate per 100 000*	Mean (SE) rates per 100 000 in MONICA		
		Fatal†	Non-fatal‡	Coronary§			CHD mortality	Non-fatal‡	Coronary events§
AUS-NEW	401	445 (34%)	626	1071	40.9 (3.1)	57 (3)	63 (3)	90 (4)	153 (5)
AUS-PER	554	686 (15%)	921	1607	41.7 (2.5)	32 (1)	39 (2)	53 (2)	92 (2)
BEL-CHA	168	332 (52%)	224	556	59.3 (4.3)	35 (3)	70 (4)	48 (3)	118 (5)
BEL-GHE	126	231 (52%)	167	398	58.0 (5.1)	25 (2)	45 (3)	33 (3)	77 (4)
CAN-HAL	186	229 (10%)	449	678	33.6 (3.6)	38 (3)	47 (3)	92 (4)	139 (5)
CHN-BEI	350	350 (13%)	125	475	73.6 (4.3)	26 (1)	25 (1)	9 (1)	35 (2)
CZE-CZE	761	749 (13%)	586	1335	53.9 (2.8)	57 (2)	56 (2)	45 (2)	101 (3)
DEN-GLO	283	529 (39%)	380	909	58.0 (3.3)	44 (3)	82 (4)	58 (3)	140 (5)
FIN-KUO	248	258 (2%)	402	660	38.7 (4.2)	46 (3)	48 (3)	76 (4)	124 (5)
FIN-NKA	216	214 (2%)	315	529	41.3 (4.6)	59 (4)	59 (4)	86 (5)	145 (6)
FIN-TUL	205	212 (2%)	221	433	48.9 (5.3)	44 (3)	46 (3)	48 (3)	94 (5)
FRA-LIL	290	816 (55%)	361	1177	69.5 (2.8)	16 (1)	44 (2)	19 (1)	64 (2)
FRA-STR	271	583 (52%)	446	1029	57.1 (3.2)	17 (1)	36 (2)	27 (1)	64 (2)
FRA-TOU	137	333 (57%)	228	561	59.8 (4.2)	9 (1)	22 (1)	15 (1)	36 (2)
GER-AUG	385	496 (34%)	268	764	64.6 (3.6)	32 (2)	41 (2)	22 (1)	63 (2)
GER-BRE	263	429 (45%)	379	808	52.0 (3.6)	26 (2)	42 (2)	38 (2)	81 (3)
GER-EGE	454	632 (18%)	351	983	62.8 (3.2)	36 (2)	50 (2)	28 (2)	78 (2)
ICE-ICE	178	182 (7%)	336	518	34.1 (4.3)	34 (3)	34 (3)	64 (4)	99 (4)
ITA-BRI	341	424 (35%)	382	806	52.5 (3.7)	18 (1)	22 (1)	20 (1)	42 (1)
ITA-FRI	479	528 (27%)	526	1054	49.9 (3.2)	21 (1)	24 (1)	24 (1)	47 (1)
LTU-KAU	498	367 (25%)	302	669	53.7 (4.1)	60 (3)	44 (2)	36 (2)	80 (3)
NEZ-AUC	723	745 (6%)	699	1444	51.4 (2.6)	57 (2)	59 (2)	55 (2)	115 (3)
POL-TAR	366	1087 (62%)	138	1225	88.4 (1.9)	33 (2)	98 (3)	13 (1)	110 (3)
POL-WAR	572	1075 (40%)	729	1804	59.2 (2.3)	48 (2)	91 (3)	62 (2)	153 (4)
RUS-MOC	389	315 (17%)	202	517	60.2 (5.0)	67 (3)	55 (3)	36 (3)	92 (4)
RUS-MOI	986	793 (15%)	369	1162	66.5 (3.1)	76 (2)	61 (2)	29 (2)	90 (3)
RUS-NOC	691	717 (1%)	359	1076	66.5 (3.0)	72 (3)	74 (3)	37 (2)	111 (3)
RUS-NOI	361	296 (4%)	130	426	70.6 (4.5)	113 (6)	91 (5)	39 (3)	130 (6)
SPA-CAT	240	336 (44%)	396	732	45.5 (3.7)	11 (1)	16 (1)	19 (1)	35 (1)
SWE-GOT	315	358 (9%)	412	770	45.4 (3.7)	34 (2)	39 (2)	45 (2)	84 (3)
SWE-NSW	401	458 (3%)	872	1330	34.4 (2.7)	35 (2)	41 (2)	78 (3)	119 (3)
UNK-BEL	833	842 (18%)	1117	1959	41.5 (2.3)	79 (3)	79 (3)	108 (3)	188 (4)
UNK-GLA	942	1018 (11%)	1125	2143	46.4 (2.2)	114 (4)	123 (4)	142 (4)	265 (6)
USA-STA	347	488 (14%)	417	905	53.7 (3.3)	51 (3)	72 (3)	62 (3)	134 (4)
YUG-NOS	321	381 (5%)	376	757	49.9 (3.6)	43 (2)	51 (3)	51 (3)	101 (4)
Mean	408	512 (24%)	438	951	53.8	45	54	49	103
SD	225	254 (19%)	257	445	12.3	25	24	30	47

*Based on death-certificate enumeration. †Percentage unclassifiable deaths without diagnostic information. ‡Definite myocardial-infarction rate. §WHO MONICA definition 1. ¶Data missing for 1 year.

Table 3: Numbers of events, age-standardised 28-day case fatality, and mean (SE) annual event rates per 100 000 during registration in women

Mortality rates estimated according to MONICA criteria, which include unclassifiable deaths, were higher in almost all populations than the official rates based on routine death certification.⁵ Exceptions to this difference were found in the former Soviet Union. Populations varied substantially, however, in the proportion of unclassifiable deaths and in whether unclassifiable deaths came more from cases attributed originally to CHD or to other causes.

There was a high correlation across populations between the rates in men and women: official CHD mortality $r=0.87$, MONICA CHD mortality $r=0.80$, non-fatal events $r=0.91$, MONICA coronary events $r=0.84$, and case fatality $r=0.86$.

Trends in event rates and case fatality

The average (SE) annual percentage relative trends in different event rates and in case fatality are shown separately for men (table 4) and women (table 5). The population rankings of trends in MONICA coronary-event rates, and trends in case fatality, by sex, with 95% CIs, are shown in figure 2. CIs were generally wider for women than for men, which reflected the smaller numbers of events. Imprecision of estimates was also a consequence of non-linearity of trends.

There were correlations across populations between trends in rates in the two sexes: official CHD mortality $r=0.67$, MONICA CHD mortality $r=0.70$, non-fatal events $r=0.51$, MONICA coronary events $r=0.68$, case fatality $r=0.57$.

Most rates were falling. The decline in MONICA mortality rates was generally smaller in percentage terms

than that in official mortality rates, but greater than that in non-fatal event rates. The latter changed little on average in women. Trends for coronary-event rate were intermediate. Change in case fatality was smaller on average than change in mortality rates or in coronary-event rates.

Coronary-event rates in men decreased in 28 of 37 populations (unequivocally in 22) and increased in nine (two). Case fatality in men decreased in 25 (11) and increased in 12 (six). In women, coronary-event rates decreased in 22 (14) of 35 populations and increased in 13 (two). Case fatality decreased in 22 (eight) populations and increased in 13 (two).

The greatest fall in coronary-event rates in men occurred in three north European populations, the leader being North Karelia (Finland), which had the highest rates at the start. With the exception of Catalonia (Spain), male populations experiencing notable increase in rates were mainly eastern (central and eastern Europe and Asia). In women, the populations experiencing the greatest increases were also generally eastern, but the general pattern of increases and decreases seemed to be less geographically stereotyped. There was no significant trend in the coronary-event rate for the population with the highest rate in women. In Glasgow (UK), a non-significant tendency for non-fatal event rates to increase equalled a similar tendency for MONICA mortality rates and case fatality to decline.

For case fatality, trends in men were more consistent geographically than those in women. Lower than median

rankings for improvement in case fatality were seen in all 11 of the populations that historically belonged to the eastern bloc, joined only by the three Finnish populations, Lille (France), Augsburg (Germany), and Glostrup (Denmark; figure 2). Trends in women were less striking when viewed in isolation, but were compatible with those in men, in that seven of the 11 former eastern bloc populations had trend rankings lower than the median.

Associations between changes in rates

The first question from the Bethesda Conference, whether declining trends in CHD mortality were real,¹ is answered in tables 4 and 5. For both sexes there was reasonable agreement in most populations between trends in official CHD mortality rates—accepting death certification data at face value—and in MONICA CHD mortality rates, based on standardised MONICA registration of fatal events. In populations in which rates were declining, the percentage change in MONICA CHD mortality was generally smaller than that for official rates. Discrepancies of more than 5.0% between trends in official and MONICA CHD mortality rates occurred for men in Beijing (China) and Novosibirsk-Control (Russia). In women, added to these two populations were Lille (France), Friuli (Italy), Novosibirsk-Intervention (Russia), and Novi Sad (Yugoslavia). Discrepancies of more than 3.0% occurred for another four male and five female populations. For many of the remaining populations, differences were small, especially for those in which mortality rates were high and falling.

Trends in MONICA non-fatal event rates showed a moderately positive correlation with those in MONICA CHD mortality in men ($r=0.37$) and in women ($r=0.23$). Comparison, across populations for the 10-year period,

of the annual change in MONICA coronary-event rate and the mean 10-year rates (tables 2–5) showed a weak inverse relation in men ($r=-0.33$) that reflected a tendency for high rates to fall and for low rates to rise. There was no equivalent pattern in women ($r=-0.03$).

Determinants of change in MONICA CHD mortality rates

The second question from the Bethesda Conference was whether declining mortality rates from CHD were driven by changes in coronary-event rates or in case fatality.¹ Within a population the percentage change in the MONICA CHD mortality rate is theoretically equal to the sum of the percentage change in case fatality and the percentage change in coronary-event rates, although the actual goodness of fit will vary with the precision of the estimates. Small differences arise from the method of estimation. We ranked populations by percentage decline in MONICA CHD mortality rates (figure 3). Mortality decline was not plotted directly, but by its two components, change in case fatality and change in coronary-event rates. If these were both positive or both negative we presented cumulated results; where one was negative and the other positive, the difference between the two values represented the change in MONICA CHD mortality rates. There was greater consistency in the two trends for men than for women. The contribution to the change of MONICA CHD mortality rates is greater from change in coronary-event rates than from case fatality. Change in coronary-event rates seems to influence the trend more where mortality is decreasing than where it is increasing. With smaller numbers of events for analysis, results in women show greater inconsistency than those for men.

The relative contributions from change in coronary-event rates and change in case fatality, in the study as a whole, and in groups of populations defined by what

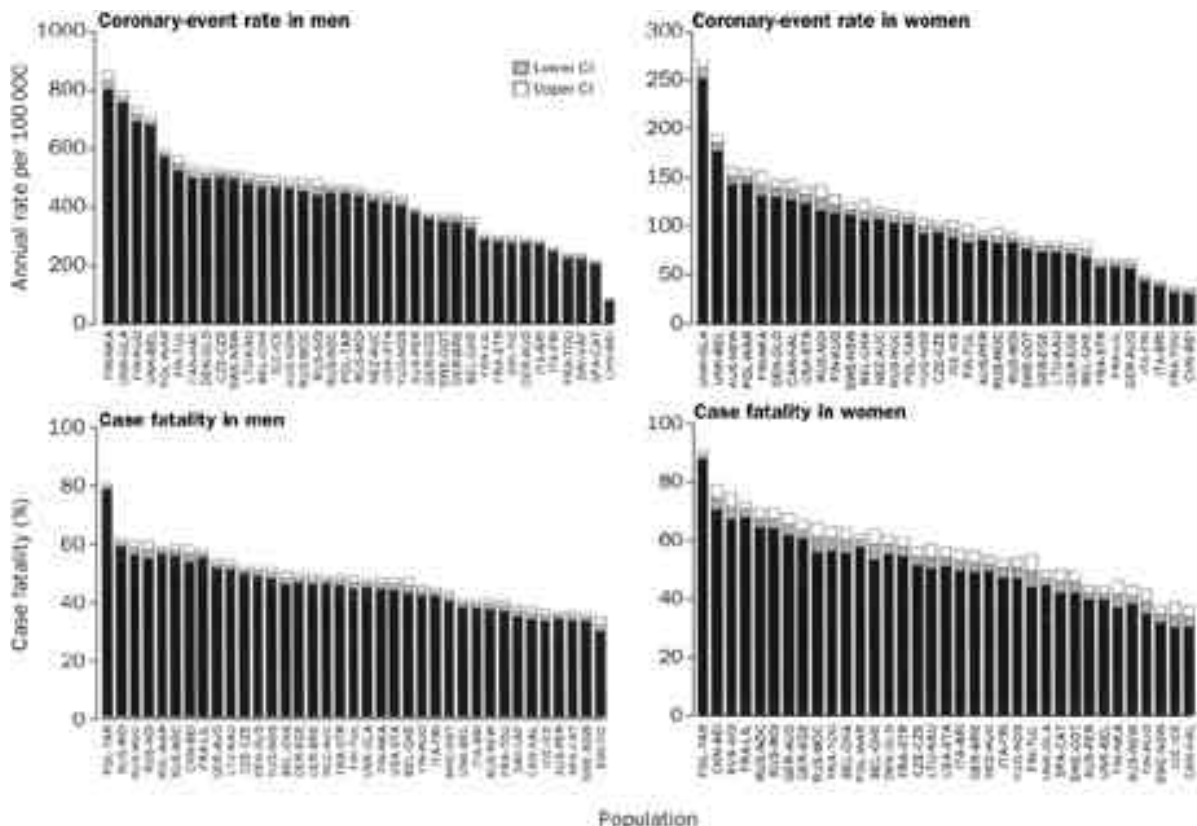


Figure 1: Population rankings of coronary event rates and case fatality by sex with 95% CIs

Population	Number of years	Official CHD mortality rate	MONICA CHD mortality rate	MONICA non-fatal event rate	MONICA coronary-event rate	MONICA 28-day case fatality
AUS-NEW	9	-7.4 (1.0)	-7.4 (1.2)	-3.5 (0.5)	-5.1 (0.6)	-2.2 (0.9)
AUS-PER	10	-5.4 (0.5)	-4.5 (0.5)	-2.3 (0.3)	-3.1 (0.3)	-1.5 (0.6)
BEL-CHA	10	-5.5 (1.0)	-1.5 (1.9)	2.0 (1.1)	0.3 (1.1)	-1.8 (1.1)
BEL-GHE	10	-6.2 (1.4)	-4.8 (0.9)	-1.8 (1.3)	-3.2 (0.9)	-1.6 (0.9)
CAN-HAL	10	-7.5 (1.5)	-6.3 (0.9)	-3.8 (1.1)	-4.7 (0.8)	-1.5 (0.9)
CHN-BEI	10	-2.1 (1.8)	3.4 (1.6)	0.6 (1.7)	2.3 (1.0)	1.1 (1.1)
CZE-CZE	10	-0.9 (1.1)	0.3 (0.9)	-1.2 (0.7)	-0.4 (0.6)	0.7 (0.4)
DEN-GLO	10	-4.7 (1.1)	-2.7 (1.1)	-5.7 (1.1)	-4.2 (0.8)	1.5 (0.8)
FIN-KUO	10	-5.5 (0.8)	-5.0 (0.8)	-6.9 (1.3)	-6.0 (0.7)	1.0 (0.9)
FIN-NKA	10	-6.8 (0.6)	-7.0 (0.5)	-6.1 (1.3)	-6.5 (0.7)	-0.5 (0.7)
FIN-TUL	10	-4.7 (1.3)	-4.5 (1.4)	-3.8 (1.0)	-4.2 (1.0)	-0.2 (0.8)
FRA-LIL	10	-3.3 (1.1)	-1.5 (1.0)	-0.6 (1.3)	-1.1 (0.9)	-0.3 (0.6)
FRA-TOU	9	-6.2 (1.0)	-5.7 (0.9)	-2.3 (0.7)	-3.9 (0.8)	-1.7 (0.6)
FRA-STR	9	-9.8 (0.8)	-6.2 (1.0)	0.6 (0.8)	-2.1 (0.8)	-3.8 (0.8)
GER-AUG	10	-3.7 (0.7)	-2.2 (0.7)	-4.4 (0.8)	-3.2 (0.4)	1.3 (0.6)
GER-BRE	8	-6.0 (1.0)	-4.2 (1.0)	-2.6 (1.5)	-3.4 (0.8)	-0.9 (0.8)
GER-EGE	9	1.4 (1.5)	0.9 (1.0)	-1.9 (1.2)	-0.5 (0.9)	1.7 (0.8)
ICE-ICE	14	-6.4 (1.0)	-6.4 (1.1)	-3.7 (0.7)	-4.7 (0.7)	-2.1 (0.6)
ITA-BRI	10	-3.5 (0.7)	-3.4 (0.5)	-1.5 (0.5)	-2.3 (0.2)	-0.8 (0.6)
ITA-FRI	10	-6.3 (0.9)	-2.9 (1.5)	0.8 (0.4)	-0.9 (0.7)	-2.0 (0.9)
LTU-KAU	10	0.9 (0.9)	2.0 (0.9)	0.2 (0.7)	1.2 (0.5)	1.0 (0.6)
NEZ-AUC	9	-5.0 (0.6)	-5.5 (0.9)	-4.7 (1.3)	-5.1 (0.8)	-0.6 (0.8)
POL-TAR	10	3.2 (1.7)	2.2 (1.0)	-4.1 (2.4)	1.1 (0.8)	1.2 (0.5)
POL-WAR	11	0.3 (0.8)	0.5 (1.1)	1.2 (1.2)	0.8 (1.1)	-0.4 (0.4)
RUS-MOC	9	2.2 (1.2)	2.0 (1.5)	-5.7 (1.7)	-1.0 (0.7)	3.0 (1.1)
RUS-MOI	9	3.1 (1.1)	2.8 (1.3)	-5.2 (1.6)	-0.1 (0.9)	3.1 (0.8)
RUS-NOC	9	-10.8 (4.6)	0.2 (1.9)	1.7 (2.9)	0.9 (1.6)	-0.1 (1.5)
RUS-NOI	10	2.9 (1.9)	4.2 (1.9)	0.9 (3.3)	2.8 (1.5)	1.4 (1.6)
SPA-CAT	10	-1.8 (1.3)	0.3 (1.2)	2.8 (1.3)	1.8 (1.0)	-1.7 (1.0)
SWE-GOT	11	-5.5 (0.7)	-3.8 (0.7)	-4.4 (0.9)	-4.2 (0.6)	0.3 (0.6)
SWE-NSW	11	-7.9 (1.2)	-8.0 (0.9)	-3.5 (0.7)	-5.1 (0.7)	-2.9 (0.6)
SWI-TIC	9	-5.6 (1.7)	-5.8 (1.7)	-1.1 (1.2)	-2.6 (1.2)	-4.2 (1.5)
SWI-VAF	9	-6.4 (1.6)	-6.8 (1.6)	-1.7 (0.8)	-3.6 (0.7)	-3.0 (1.4)
UNK-BEL	11	-6.1 (0.8)	-6.0 (0.6)	-3.6 (0.8)	-4.6 (0.6)	-1.5 (0.5)
UNK-GLA	10	-2.3 (0.8)	-2.6 (0.6)	-0.4 (1.3)	-1.4 (0.6)	-1.3 (0.9)
USA-STA	13	-5.5 (1.0)	-5.5 (0.9)	-3.1 (0.9)	-4.2 (0.8)	-1.6 (0.6)
YUG-NOS	12	-4.0 (1.1)	-0.4 (1.2)	1.3 (1.0)	0.4 (0.6)	-0.4 (0.9)
Mean (SD)	10	-4.0 (3.6)	-2.7 (3.5)	-2.1 (2.5)	-2.1 (2.5)	-0.6 (1.7)

Table 4: Trends in age-standardised event rates for men aged 35-64 years expressed as average (SE) annual relative percentage change

happened to their CHD mortality, are shown in figure 3 and summarised in table 6. The top third of populations in figure 3 have the greatest decline in CHD mortality. In this third there was a clear dominance of trends in coronary-event rates over trends in case fatality. Change in case fatality contributed about a third to the total change, and change in coronary-event rates the other two thirds. The lower two-thirds of the results are less consistent, but these ratios still seem to be roughly true for all populations that have any decline in CHD mortality, when taken together. In male populations, mainly eastern, in which mortality is rising, the increase in case fatality makes a larger contribution. In men, case fatality seemed to contribute 21% and coronary-event trend 79% of the averaged decline in CHD mortality, and in women 35% and 65%, when all populations were analysed together.

Sensitivity analyses

We reran the preceding analyses, testing for sensitivity of the results to the definitions, populations, years, and analytical models used.

For incidence versus event rates, MONICA recorded history of angina or myocardial infarction, but this information was missing for death outside hospital in many populations. MONICA coronary-event definition 1 includes first and recurrent events. There was a high correlation across populations between changes in event rates and changes in first event rates defined in different ways. MONICA definition 1 is a good proxy measure of incidence.

The analysis of trends uses a log-linear model. Data for each population were censored, with removal of the

first and last years, to exclude potential start-up or run-down effects in coronary-event registration. Results did not change greatly for most centres. Next, trends were compared in the first and second halves of each population registration period, with the assumption of a linear trend in each, meeting in the middle. Trends differed significantly between the two periods in a few populations, (which posed potential difficulties and benefits for MONICA hypothesis testing). Such differences were generally inconsistent between the sexes.

Data for case fatality and event rates were reworked with exclusion of unclassifiable deaths. The findings affected results for individual centres, with dilution of the overall conclusions without negation. Inclusion or exclusion of unclassifiable deaths had no consistent effect on the relation between trends in official and MONICA CHD mortality.

Mean annual trends in non-fatal events overall in men were -1.6% when possible non-fatal events were added to the non-fatal definites, diminishing the trend estimate of -2.1% by 0.5%, whereas in women the annual trend estimate of -0.8% was unchanged. However, we have previously reported that collection of data on possible non-fatal events was so restricted in some MONICA populations because it was not the definitive MONICA endpoint for non-fatal events, that a subset of MONICA populations would be needed for a formal comparison of trends in definitive and possible non-fatal events.⁶

Ten centres, with quality scores of less than 1.0 for coronary event or demographic data were excluded and the analyses rerun. Overall findings were not affected enough to suggest that centres with poor scores had

Population	Number of years	Official CHD mortality rate	MONICA CHD mortality rate	MONICA non-fatal event rate	MONICA coronary-event rate	MONICA 28-day case fatality
AUS-NEW	9	-9.4 (2.3)	-8.5 (2.3)	-3.4 (2.2)	-5.6 (1.5)	-3.0 (2.1)
AUS-PER	10	-6.6 (1.9)	-4.0 (1.1)	-0.8 (1.4)	-2.2 (0.8)	-2.3 (1.1)
BEL-CHA	10	-5.0 (2.7)	-0.8 (1.9)	3.8 (2.8)	1.1 (1.3)	-1.8 (1.5)
BEL-GHE	10	-8.9 (3.4)	-4.6 (3.5)	0.4 (2.1)	-3.0 (2.2)	-1.8 (1.8)
CAN-HAL	10	-4.0 (2.1)	-4.1 (1.8)	2.9 (1.1)	0.5 (0.8)	-4.6 (1.9)
CHN-BEI	10	-4.5 (1.6)	1.1 (1.4)	-5.1 (5.5)	-0.5 (1.4)	1.3 (1.3)
CZE-CZE	10	-0.3 (1.9)	1.2 (2.0)	3.3 (1.9)	2.1 (1.7)	-1.2 (0.9)
DEN-GLO	10	-4.0 (1.7)	0.1 (1.5)	-6.1 (1.5)	-2.5 (1.3)	2.5 (1.0)
FIN-KUO	10	-5.2 (1.5)	-4.1 (1.5)	-4.6 (1.6)	-4.5 (1.1)	1.0 (1.7)
FIN-NKA	10	-5.0 (2.6)	-5.1 (2.5)	-5.0 (1.2)	-5.1 (1.5)	-0.2 (2.0)
FIN-TUL	10	-7.5 (2.8)	-7.3 (2.1)	-1.5 (2.4)	-4.5 (1.6)	-1.9 (1.9)
FRA-LIL	10	-5.7 (2.3)	-0.7 (1.3)	-3.4 (1.4)	-1.6 (1.2)	0.8 (0.7)
FRA-STR	9	-7.6 (2.3)	-8.3 (2.4)	-4.1 (1.6)	-6.6 (1.7)	-2.3 (1.0)
FRA-TOU	9	-5.7 (4.1)	-4.4 (2.1)	2.3 (2.5)	-1.7 (1.5)	-3.6 (1.3)
GER-AUG	10	-1.1 (1.1)	0.9 (1.3)	1.0 (3.3)	0.9 (1.7)	-0.4 (0.9)
GER-BRE	8	-2.0 (3.4)	-1.9 (3.4)	3.4 (1.3)	0.7 (1.6)	-2.9 (2.2)
GER-EGE	9	0.8 (1.6)	0.0 (1.7)	6.8 (1.2)	2.5 (1.3)	-2.2 (0.9)
ICE-ICE	14	-3.4 (1.8)	-4.3 (1.5)	-3.5 (1.4)	-3.7 (1.3)	-1.0 (1.5)
ITA-BRI	10	-11.3 (1.9)	-8.2 (2.2)	1.4 (1.6)	-3.5 (1.2)	-4.8 (1.2)
ITA-FRI	10	-8.1 (1.7)	-2.6 (1.2)	1.0 (1.9)	-0.8 (1.4)	-2.0 (1.0)
LTU-KAU	10	0.8 (1.7)	1.7 (2.7)	3.9 (2.9)	2.7 (2.0)	-1.2 (1.6)
NEZ-AUC	9	-1.8 (1.7)	-3.2 (1.2)	-3.9 (2.5)	-3.5 (1.4)	0.6 (1.4)
POL-TAR	10	3.0 (1.5)	-0.8 (1.6)	5.4 (5.1)	-0.1 (1.2)	-0.7 (0.6)
POL-WAR	11	-2.2 (1.2)	-1.1 (0.9)	4.1 (1.5)	1.0 (0.4)	-2.1 (0.9)
RUS-MOC	9	-2.8 (2.1)	-4.6 (1.5)	-9.8 (2.5)	-6.7 (1.5)	1.5 (1.4)
RUS-MOI	9	0.1 (1.3)	-0.3 (1.9)	-7.2 (1.4)	-2.5 (1.4)	2.5 (0.8)
RUS-NOC	9	-12.7 (3.9)	2.7 (1.0)	1.5 (3.8)	2.3 (1.8)	0.3 (1.2)
RUS-NOI	10	-0.9 (2.5)	4.1 (2.6)	-5.1 (4.8)	1.4 (1.9)	2.9 (2.0)
SPA-CAT	10	0.5 (2.5)	3.3 (1.9)	0.8 (1.8)	2.0 (1.3)	1.5 (1.5)
SWE-GOT	11	-5.0 (2.0)	-2.7 (1.8)	-4.6 (1.4)	-3.7 (1.1)	1.2 (1.3)
SWE-NSW	11	-1.4 (1.9)	-2.0 (1.7)	-2.7 (0.9)	-2.4 (0.8)	0.4 (1.3)
UNK-BEL	11	-3.9 (1.5)	-3.9 (1.3)	-1.4 (1.2)	-2.4 (0.6)	-1.7 (1.2)
UNK-GLA	10	-2.3 (1.2)	-2.0 (1.5)	2.0 (1.4)	0.2 (0.8)	-2.1 (1.5)
USA-STA	13	-3.2 (1.8)	-3.1 (1.6)	-1.6 (1.2)	-2.4 (1.0)	-0.4 (0.9)
YUG-NOS	12	-3.2 (1.8)	4.1 (1.7)	1.6 (2.1)	2.8 (1.3)	0.5 (1.6)
Mean (SD)	10	-4.0 (3.6)	-2.1 (3.4)	-0.8 (4)	-1.4 (2.8)	-0.8 (2.0)

Table 5: Trends in age-standardised event rates for women aged 35–64 years expressed as average (SE) annual relative percentage change

biased the study's conclusions. This finding was also true when summary results were recalculated with weighting for data quality or precision.

Discussion

The WHO MONICA Project arose from recognition in 1978 that the reported decline in mortality from CHD in the USA was neither validated nor explained.¹ Collection of standard data, from many heterogeneous populations over 10 years, would facilitate general understanding. The protocol was, however, impracticable for less-developed countries without adequate diagnostic facilities or population denominators. It was also a challenge for more-developed countries, with some participants dropping out. MONICA populations with declining CHD mortality, are not representative of the whole world.^{4,13,14} In less-developed countries, CHD mortality is probably increasing.

Genuine and spurious influences on coronary-event registration^{5,15} can be seen through the imagery of weighing scales. The burden of coronary events is the sum of fatal and non-fatal events, each weighing down one side of the scales, but survival (100–case fatality percentage) is the way the balance tilts between them. The challenge is to discriminate real trends in event rates and survival from false ones—most difficult when trends are small. Clinicians inevitably focus on the impact of treatment on survival in cases reaching hospital, but they may ignore deaths outside hospital, and the difficulties of disease recognition, diagnosis, severity, and changing incidence. Measurement of trends in event rates necessitates defined and accurate population

denominators. The suspicion, recognition, and confirmation of non-fatal versus fatal events determine the tilt of the balance, but are subject to opposing influences. Diagnosis of non-fatal cases depends on the patient seeking appropriate help, leading to appropriate tests, in a clinical, mainly hospital, setting. Diagnosis of fatal cases is mainly that of death outside hospital, according to local medicolegal practices. New financial barriers to hospital treatment, plus pressures to misuse coronary diagnoses to conceal increasing drug-related or alcohol-related deaths, would lead to increases in apparent case fatality. Better identification of minor, otherwise silent infarction,¹⁶ better access to health care, more intensive use of sensitive tests, and rejection of doubtful deaths would lower it. These apparent trends would be spurious in being independent of the natural history of the disease. However, changes in lifestyle or early development might genuinely change the threshold for ventricular fibrillation, deflecting the balance between fatal and non-fatal events, independent of diagnosis or medical treatment.

We identified previously the high percentage of unclassifiable⁵ presumed coronary deaths in MONICA in which no diagnostic information was available for review. We also found higher case fatality in women than in men, characteristically in low incidence populations which suggested that non-fatal events in women were being less consistently recognised and detected. 10-year results suggest little change over the decade since then.

Data quality scores (table 1) were calculated centrally with explicit criteria for identified problems. These scores did not necessarily reflect factors that

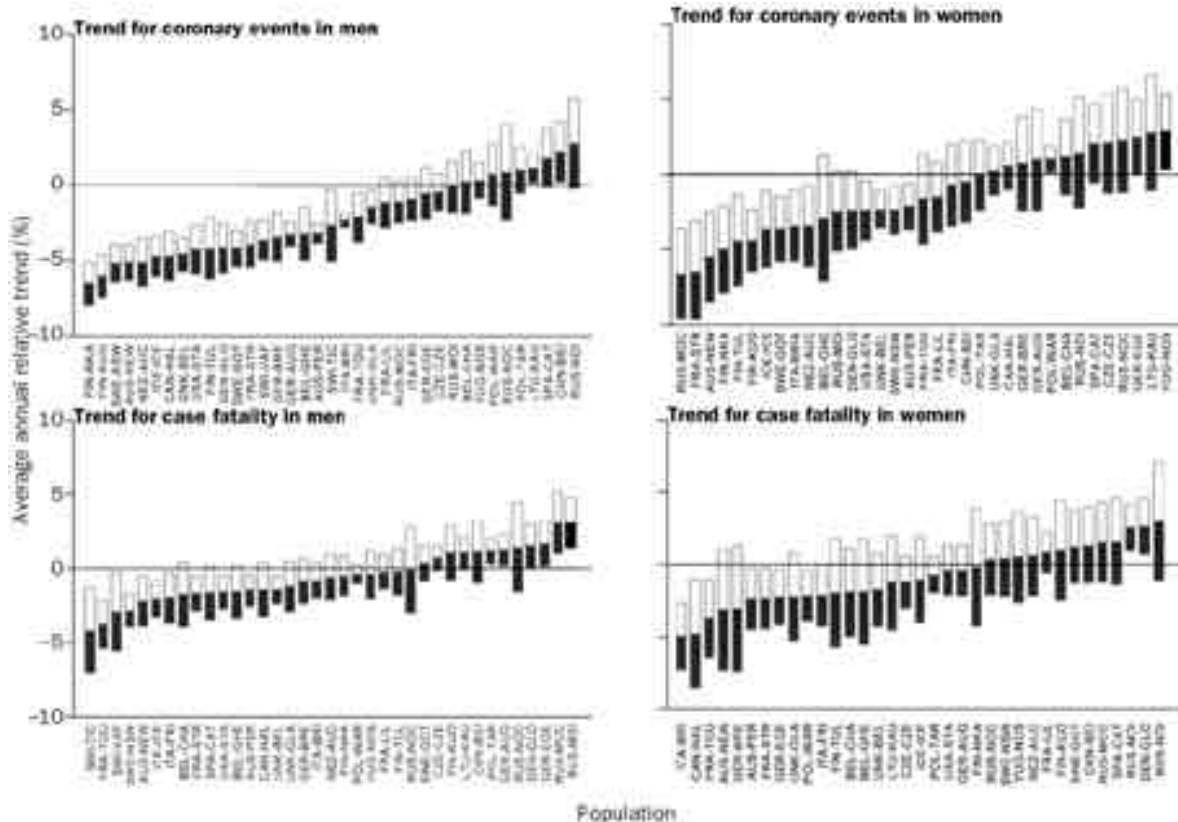


Figure 2: Population rankings, by sex, of trends in coronary-event rates and case fatality with 95% CIs

investigators could influence directly. They were determined by medical and medicolegal constraints on data quality and data acquisition, and the stability of the register environment, including funding. MONICA results correlate with quality scores for coronary events. In men, the scores for quality of coronary-event registration correlated positively with mean coronary-event rates ($r=0.39$); negatively with mean case fatality ($r=-0.36$); negatively with trends in coronary-event rates ($r=-0.38$); and negatively with trends in case fatality ($r=-0.20$). In women, correlations were in the same direction: $r=0.27$ with mean coronary-event rates; $r=-0.68$ with mean case fatality; and $r=-0.12$ and $r=-0.26$ with trends in coronary-event rates and case fatality, respectively.

Coronary-event registration necessitates continuing preoccupation with access, quality, and completeness of data coming from different parts of the local health-care system. Our concern with some components of our dataset has been diminished by the results of our sensitivity analyses. These show findings to be robust overall, with no major impact from changing the criteria for inclusion of data or populations.

An enduring controversy is whether the focus of coronary-event registration should be on incident cases, a term that raises complex issues, or on all events, including recurrences. Mortality statistics do not discriminate. In many, but not all MONICA populations, the medical history was unavailable for many coronary deaths, although the distinction could be made for hospital admissions, as was done by ARIC.² For these analyses we used coronary-event rates and found that they correlated highly with variously defined first-event rates.

Although said to be spurious when it began, the

decline in CHD mortality has been too large and too long-term to support this argument. There are no competing causes of death large enough to have absorbed a decline of anything up to 70% in CHD over 20–30 years. MONICA has corroborated reported mortality trends in many populations, even those in which the current MONICA findings suggest that the

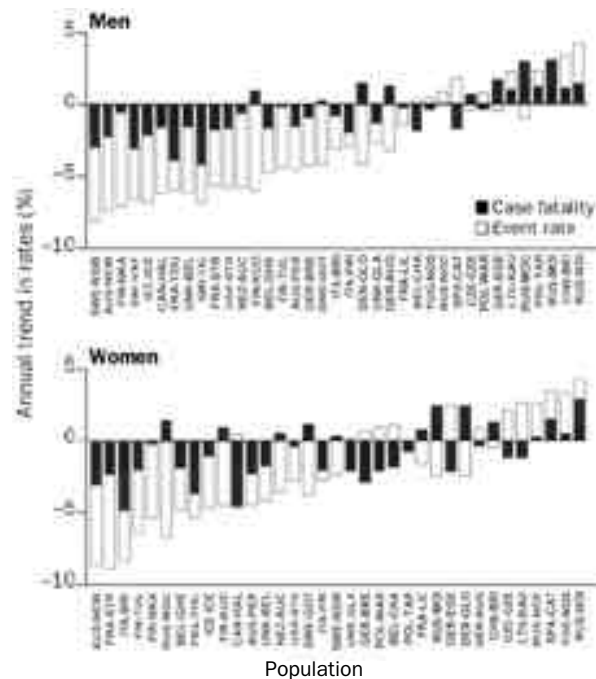


Figure 3: Population rankings, by sex, of trends in MONICA CHD mortality rate showing contribution of trends in coronary-event rate and in case fatality

Populations defined by trends in mortality rate	Number of populations	Mean trend in mortality rates (%)	Mean change in coronary-event rates (%)	Mean relative change in case fatality (%)
Third with greatest decline				
Men	12	-6.4	-4.3	-2.1
Women	12	-5.6	-3.9	-1.9
All populations with a decline				
Men	26	-4.6	-3.4	-1.2
Women	25	-3.7	-2.5	-1.2
All populations with an increase				
Men	11	1.7	0.8	1.0
Women	10	1.9	1.4	0.4
All populations				
Men	37	-2.7	-2.1	-0.6
Women	35	-2.1	-1.4	-0.8

Table 6: **Populations grouped by trends in MONICA CHD mortality rates to show contribution of change in case fatality and change in coronary-event rates**

official CHD mortality rates may be imperfect estimates of the true absolute rates. Study populations were carefully chosen at the outset, but the amount of diagnostic information on fatal cases is commonly inadequate. Validation of the diagnosis by the local MONICA investigators had to be done with the same, or less evidence, than that available to the certifying doctors. Unavailable evidence, or tests, cannot subsequently be created. Medicolegal precedents, local rules on confidentiality, and health-service organisation commonly precluded adequate audit of the certification of this major cause of premature and sudden death. Death certification has remained resistant to the transparency, quality control, and standardisation to which other medical conduct is now being subjected.

The percentage of unclassifiable deaths in tables 2 and 3 show these difficulties. The percentages were highest in Belgium, France, Germany, Poland, Spain, and Switzerland. A third or more of presumed coronary deaths among men were involved, and larger proportions in women. The case for inclusion of these deaths has been argued elsewhere.⁵ Unclassifiable deaths explain discrepancies in CHD death rates between populations with varying proportions of non-coronary, non-stroke, cardiovascular deaths, and are relevant to the southern European or French "paradox". Tables 2 and 3 explain why inclusion or exclusion of unclassifiable deaths had an inconsistent effect in the validation of trends in official CHD mortality. Populations differed in whether their unclassifiable deaths had originally been certified as attributable to CHD or to other causes. These percentages may reflect, to some extent, the diligence of local investigators in the searching of records of different causes of death, and in questioning the diagnosis. When starting registration, each centre had to identify locally, and then monitor, those causes of death that might conceal potentially misdiagnosed coronary deaths.³ The complex relations between unclassifiable deaths and the original death-certificate diagnoses in different populations were first analysed in our earlier cross-sectional paper.⁵

What drives changes in CHD mortality and by how much is a question that has remained topical ever since the Bethesda Conference on the Decline of CHD Mortality.¹ It has implications for strategies on primary and secondary prevention and medical care and for the two main hypotheses that we are testing. These hypotheses are that changes in survival rates are determined by changes in medical care, and that changes

in the incidence of CHD are driven by changes in known coronary risk factors. Greater complexity can be postulated, four other potential associations being listed in the MONICA protocol. The determinants of changes in CHD mortality have been investigated in four US populations in the ARIC study.² In these populations, CHD mortality and case fatality fell together, but overall incidence remained stable from 1987 to 1994.

The ARIC study was done at the same time as, and was associated with MONICA, although the age-groups and criteria differed. The ARIC 8-year results from four populations are not corroborated in our results. Even the five North American and Australasian MONICA populations, which have similarities in mortality trends, populations, and cultures, all disagreed with ARIC. All five had a decline in CHD mortality, especially in men, dominated by a fall in coronary-event rates, and associated with a highly significant fall in non-fatal event rates.

MONICA results are heterogeneous. No one population is typical. Some are dominated by change in case fatality. Populations (mainly eastern) in which CHD mortality is increasing differ from the remainder. However, the largest decreases or increases in mortality rates occur in populations in which coronary-event rates and case fatality are going in the same direction. In populations in which CHD mortality is declining, the contribution of change in coronary-event rates seems to be twice that of trends in case fatality. Contributions are partitioned two thirds to one third. That seems to be the best summary statement of what drives declining CHD mortality.

These results record the heterogeneity of experience of the WHO MONICA Project, and the limitations of previous generalisations, made from small numbers of populations that were similar to one another. After 20 years, the WHO MONICA Project has answered the original questions from the Bethesda conference on the validity of mortality trends, and on whether survival or coronary-event rates contribute more. The answers raise further questions. Why do results from MONICA and ARIC differ? Which component of declining mortality will be carried forward into subsequent decades? Is the preoccupation of the past 20 years with relating case fatality to medical treatment and coronary-event rates to lifestyle and risk factors still valid, or are some of the other potential relations listed in the MONICA protocol equally deserving of exploration? Why did case fatality rise in some MONICA populations? Can lifestyle influence case fatality? Can medical care influence coronary-event rates? Many of these questions await analysis by the WHO MONICA Project in the future.

The conclusion of these first definitive 10-year results is that, despite substantial contributions from changing survival, the main determinant of the decline in CHD mortality is whatever drives changing coronary-event rates.

Participating centres in the WHO MONICA Project

Australia—University of Western Australia, Nedlands: M S T Hobbs (principal investigator), K Jamrozik (coprincipal investigator), R W Parsons, C Spencer, P L Thompson; University of Newcastle, Newcastle: A Dobson (principal investigator), H Alexander, R Heller, P Colley.

Belgium—Ghent State University, Ghent: G De Backer (principal investigator), F van Onsem, S De Henaau, D De Bacquer; Free University of Brussels, Brussels: M Kornitzer (principal investigator), L Berghmans, M Lannoy, R Desqueve, L Bara, I Beriot, M Candeur, P de Smet.

Canada—Dalhousie University, Halifax, Nova Scotia: R D Gregor (principal investigator), H K Wolf (principal investigator), B R Mackenzie, P M Rautaharju, I R Bata.

China—Beijing Heart, Lung and Blood Vessel Research Institute, Beijing: Wu Zhaosu (principal investigator), Wu Yingkai (former principal investigator), Yao Chonghua, Hong Zhaoguang.

Czech Republic—Institute for Clinical and Experimental Medicine, Prague: Z Kodová (principal investigator), Z Piša, Z Hejl, P Vojtěšek, K Emrová, Z Cicha, L Berka, M Hoke, J Pikhartová, K Hrdlicková, E Wiesner.

Denmark—Centre of Preventive Medicine (The Glostrup Population Studies) Copenhagen University: M Schroll (principal investigator), M Kirchhoff, B Hansen, S Quitsau Lund, H Schnack, M Madsen.

Finland—National Public Health Institute, Helsinki: J Tuomilehto (principal investigator), P Puska (former principal investigator), M Arstila, P Immonen-Räihä, E Kaarsalo, M Ketonen, S Lehto, H Miettinen, H Mustaniemi, M Niemelä, P Palomäki, K Pyörälä, M Romo, V Salomaa, J Torppa, T Vuorenmaa.

France—National Institute of Health and Medical Research (INSERM U258) Paris: P Ducimetiere (country coordinator), J L Richard (former country coordinator), A Bingham, T Lang; National Institute of Health and Medical Research, Toulouse: J Ferrieres (principal investigator), J B Ruidavets, P Marqués-Vidal, J P Cambou (former principal investigator), P Rodier, C Saulet; Department of Epidemiology and Public Health, Faculty of Medicine, Strasbourg: D Arveiler (principal investigator), P Schaffer (principal investigator), A Facello, E Marine Barjoan, E Uettwiller, D Jacques, C Veron, V Meyer, M Veltan, B Haas, N Lamamy, A Wagner, F Pierau, V Goetz; Department of Epidemiology and Public Health, (INSERM U508), Pasteur Institute, Lille: P Amouyel (principal investigator), M Montaye-Faivre (principal investigator), J-L Salomez (former principal investigator), M-C Nuttens (former principal investigator), S Beauchant, C Graux, N Marecaux.

Germany—Bremen Institute for Prevention Research and Social Medicine, Bremen: E Greiser (principal investigator), B Herman (coprincipal investigator), G Stüdemann; GSF-Institute for Epidemiology, Neuherberg/Munich: U Keil (principal investigator), H Löwel, M Lewis, A Hörmann, J Gostomzyk, H D Bolte; Centre for Epidemiology and Health Research, Berlin: W Barth (principal investigator), L Heinemann (principal investigator), E Classen, D Quietzs, S Brasche, S Böthig, G Voigt.

Iceland—Heart Preventive Clinic, Reykjavik: N Sigfusson (principal investigator), II Gudmundsdottir, I Stefansdottir, Th Thorsteinsson, H Sigvaldason.

Italy—National Institute of Health, Rome: A Menotti (country coordinator), S Giampaoli, A Verdecchia; Institute of Cardiology, Regional Hospital, Udine: D Vanuzzo (principal investigator), G A Feruglio (former principal investigator), L Pilotto, G Zanata, M Scarpa, G B Cignacco, R Marini, M Spanghero, G Zilio; Research Centre for Chronic Degenerative Diseases, University of Milan at Monza: G C Cesana (principal investigator), M Ferrario (principal investigator), M T Gussoni, G De Vito, R Segà, F Valagussa.

Lithuania—Kaunas Medical Academy, Institute of Cardiology: J Bluzhas (principal investigator), V Grinius, R Grazuleviciene, D Rastenyte, D Rastenyte.

New Zealand—University of Auckland: R Beaglehole (principal investigator), R T Jackson, A W Stewart, W Bingley.

Poland—Institute of Public Health, Collegium Medicum, Jagiellonian University, Kraków: A Pajak (principal investigator), J Sznajd (former principal investigator), E Kawalec, R Toper-Madry, M Malczewska-Malec, B Idzior-Walu; Stefan Cardinal Wyszyński National Institute of Cardiology, Warsaw, Department of Cardiovascular Epidemiology and Prevention: S Rywik (principal investigator), G Broda (coprincipal investigator), M Polakowska, A Pytlak, H Wagrowska, P Kurjata, W Kupsc.

Russian Federation—National Research Centre for Preventive Medicine, Moscow: T Varlamova (principal investigator), V Naumova, M Ossokina, N Serdyuchenko, N Popova, E Bolshakova; Institute of Internal Medicine, Novosibirsk: Yu P Nikitin (principal investigator), S Malyutina, V Gafarov, G Simonova.

Spain—Institute of Health Studies, Department of Health and Social Security, Barcelona: S Sans (principal investigator), I Balaguer-Vintró (former principal investigator), A Puigdefàbregas, R Martínez, M Font, C Tirvio, G Paluzie.

Sweden—Östra Hospital Preventive Cardiology Unit, Göteborg: L Wilhelmsen (principal investigator), S Johansson, M Falkman, G Lappas; Department of Internal Medicine, Kalix Lasarett, Kalix: T Messner (principal investigator), F Huhtasaari (former principal investigator), V Lundberg, E Jägare Westerberg, B Wikström, S Boström; Umeå University Hospital, Department of Medicine: K Asplund (principal investigator), P O Wester (former principal investigator), B Stegmayr, M Peltonen.

Switzerland—University Institute of Social and Preventive Medicine, Lausanne: F Gutzwiller (principal investigator, Zürich), M Rickenbach, V Wietlisbach, F Barazzoni, F Paccaud;

UK—The Queen's University of Belfast, Northern Ireland: A E Evans (principal investigator), Z M Mathewson, E E McCrum, A Hall,

T Falconer, E L McIlmoyle; University of Dundee, Scotland: H Tunstall-Pedoe (principal investigator), C Brown, M Shewry, M-K Hannah; Royal Infirmary, Glasgow, Scotland: C Morrison (coprincipal investigator), G Watt (former coprincipal investigator), Wilma Leslie, B Fitzpatrick.

USA—Stanford Center for Research in Disease Prevention, Stanford University, California: S P Fortmann (principal investigator), A Varady.

Yugoslavia—Novi Sad Health Centre: M Planojevic (principal investigator), D Jakovljevic (former principal investigator), T Dapi, D Stojši, M Krco, Šolak

MONICA Management Centre—World Health Organization, Geneva: I Martin (responsible officer), I Gyrfas (former responsible officer), Z Pisa (former responsible officer), S R A Dodu (former responsible officer), S Böthig (former responsible officer), M J Watson, M Hill.

MONICA Data Centre—National Public Health Institute, Helsinki, Finland: K Kuulasmaa (responsible officer), J Tuomilehto (former responsible officer), M Mähönen, H Tolonen, E Ruokokoski, A-M Rajakangas.

MONICA Quality Control Centre for ECG Coding—Hungarian Institute of Cardiology, Budapest, Hungary: P Ofner (responsible officer), A Madai (former responsible officer).

MONICA Quality Control Centre for Event Registration—University of Dundee, Scotland: Hugh Tunstall-Pedoe (responsible officer), Kristin Barrett, Colin Brown.

MONICA Steering Committee—M Hobbs (chair), M Ferrario (publications coordinator), K Asplund, A Evans, H Tunstall-Pedoe (rapporteur), I Martin (MONICA Management Centre) K Kuulasmaa (MONICA Data Centre), A Shatchkute, (WHO, Copenhagen). Consultant: A Dobson, and previous steering committee members R Beaglehole, S P Fortmann, F Gutzwiller, U Keil, A Menotti, P Puska, SL Rywik, S Sans, and former chiefs of CVD/HQ, Geneva, V Zaitsev (WHO, Copenhagen) J Tuomilehto. Former consultants: M J Karvonen (Helsinki, Finland), R J Prineas (Minneapolis, USA), M Feinleib (Bethesda, USA), F H Epstein (Zürich, Switzerland), Z Pisa (Prague, Czech Republic), O D Williams (Birmingham, Alabama, USA).

Contributors

Hugh Tunstall-Pedoe drafted the study protocol and diagnostic criteria, was project rapporteur and head of the quality control centre for event registration, and led the drafting and writing of the manuscript. Kari Kuulasmaa heads the data centre, was responsible for all features of data handling and the statistical design, conduct, and reporting of the analyses, and drafted relevant sections of the manuscript. Markku Mahonen worked with each centre on the integrity and quality of their data and led the 10-year data quality assessment. Hanna Tolonen and Esa Ruokokoski worked on the database, on the extraction and analysis programs for the tables and figures, and on final checking. Philippe Amouyel contributed to data quality assessment and derivation of the coronary-event quality score. All the above contributed to the paper, which was also approved by the principal investigators.

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