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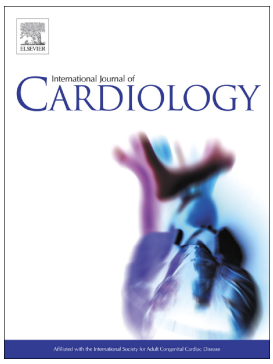

Explaining the decline in coronary heart disease mortality rates in Japan: Contributions of changes in risk factors and evidence-based treatments between 1980 and 2012

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PII: S0167-5273(18)34148-2
DOI: https://doi.org/10.1016/j.ijcard.2019.02.022
Reference: IJCA 27451

To appear in: *International Journal of Cardiology*

Received date: 28 June 2018
Revised date: 14 December 2018
Accepted date: 12 February 2019

Please cite this article as: S. Ogata, K. Nishimura, M. Guzman-Castillo, et al., Explaining the decline in coronary heart disease mortality rates in Japan: Contributions of changes in risk factors and evidence-based treatments between 1980 and 2012, International Journal of Cardiology, https://doi.org/10.1016/j.ijcard.2019.02.022

Title: Explaining the decline in coronary heart disease mortality rates in Japan: contributions of changes in risk factors and evidence-based treatments between 1980 and 2012

Short title: CHD mortality rate between 1980 and 2012 in Japan

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Acknowledgments and Sources of Funding

This research was supported by AMED under Grants Number JP17jk0110007h0003 and JP16ek0210018, by a grant-in-aid from the Ministry of Health, Labour and Welfare, Health and Labour Sciences research grants, Japan and Life-Style Related Diseases (H27–Junkankitou [Seishuu]–Ippan–009 and H29–Junkankitou [Seishuu]–Ippan–003), and by Intramural Research Fund of National Cerebral and Cardiovascular Center (27-4-3). We acknowledge Kei Matsumaru for proofreading the present manuscript by improving the sentences written in the English language.

Disclosures

No COI that should be reported.

Key words: population of Japan, risk factors, treatment, coronary heart disease, mortality

Abstract

Background

We aimed to quantify contributions of changes in risks and uptake of evidence-based treatment to coronary heart disease (CHD) mortality trends in Japan between 1980 and 2012.

Methods

We conducted a modelling study for the general population of Japan aged 35 to 84 years using the validated IMPACT model incorporating data sources like Vital Statistics. The main outcome was difference in the number of observed and expected CHD deaths in 2012.

Results

From 1980 to 2012, age-adjusted CHD mortality rates in Japan fell by 61%, resulting in 75,700 fewer CHD deaths in 2012 than if the age and sex-specific mortality rates had remained unchanged. Approximately 56% (95% uncertainty interval [UI]: 54–59%) of the CHD mortality decrease, corresponding to 42,300 (40,900–44,700) fewer CHD deaths, was attributable to medical and surgical treatments. Approximately 35% (28–41%) of the mortality fall corresponding to 26,300 (21,200–31,000) fewer CHD deaths, was attributable to risk factor changes in the population, 24% (20–29%) corresponding to 18,400 (15,100–21,900) fewer and 11% (8–14%) corresponding to 8,400 (60,500–10,600) fewer from decreased systolic blood pressure (8.87 mmHg) and smoking prevalence (14.0%). However, increased levels of cholesterol (0.28 mmol/L), body mass index (BMI) (0.68 kg/m^2), and diabetes prevalence (1.6%) attenuated the decrease in mortality by 2% (1–3%), 3% (2–3%), and 4% (1–6%), respectively.

Conclusions

Japan should continue their control policies for blood pressure and tobacco, and build a strategy to control BMI, diabetes, and cholesterol levels to prevent further CHD deaths.

Introduction

Japan has the lowest coronary heart disease (CHD) mortality rate in the world [1]. Death rates from acute myocardial infarction further declined in Japan from the 1980s to 2000s. Additionally, the relative decline in death rates from acute myocardial infarction was larger in Japan than in other Western populations [2–4]. The decline in age-adjusted CHD mortality in Japan has occurred in spite of recent increases in key risk factors including elevated levels of body mass index (BMI) and cholesterol [5–7]; however, that has occurred accompanied with a decrease of total cholesterol in other developed countries [7]. Due to this uniqueness related to CHD mortality and its trend in Japan, strategies preventing further CHD deaths in Japan could be different from other developed countries. Therefore, it is important to quantify contributions of changes in risk factor levels towards changes in CHD mortality rates to identify effective strategies for preventing further CHD deaths in Japan.

The IMPACT model was developed to explain the decline in CHD deaths by quantifying the contributions of temporal changes in exposure to risk factors and uptake of treatments. The model has been previously validated and used to help explain such falls in mortality in more than 20 countries [8–13]. However, to our knowledge, no studies have attempted to quantify the relative contributions of specific therapies and risk factors in Japan, which has a population with low risk of CHD mortality.

We, therefore, applied the IMPACT model to estimate the contribution of changes in risk factor levels and uptake of evidence-based treatment on trends in CHD deaths between 1980 and 2012 in Japan.

Methods

We implemented the previously validated, cell-based, IMPACT mortality model for the Japanese adult population [11]. The model was used to estimate the contributions of population-level risk factor changes and increases in the uptake of evidence-based treatments

on the CHD mortality decline in Japan between 1980 and 2012 for adults aged 35 to 84 years.

The IMPACT mortality model applies the relative risk reduction quantified in previous randomised controlled trials (RCT) and meta-analyses to estimate the mortality reduction attributable to A) temporal change in risk factor prevalence and B) net change over the period in the uptake of specific treatments in patients with each specific form of CHD.

The model includes all the major CHD risk factors: smoking, systolic blood pressure (SBP), total cholesterol, BMI, diabetes, and physical inactivity. It also includes the 16 evidence-based medical and surgical treatments that are widely used in nine different disease groups [11]. The present study was approved by the ethical committee of the National Cerebral and Cardiovascular Center in Suita, Japan (M27-104-2).

Data

We investigated all possible sources in Japan providing data to inform model parameters and selected the most up-to-date, representative datasets. We obtained mortality rates specific to age-sex groups for coronary heart disease from Vital Statistics in Japan (http://www.mhlw.go.jp/english/database/db-hw/vs01.html). Population estimates and CHD death counts ICD 9 (International classification of diseases, ninth revision codes 410-414, 429.2 for 1980 and ICD 10 I20-I25 for 2012) by ten-year age-bands and sex were also obtained from Vital Statistics in Japan.

Data on admissions and medical treatments came from the Japanese Registry of All Cardiac and Vascular Diseases (JROAD) registry of the Japanese Circulation Society [14], National Patient Survey of Ministry of Health, Labour and Welfare [15], and the All-Japan-Utstein Registry [16]. Data on trends in risk factors came from the National Survey on Circulatory Disorders in 1980 and the National Health and Nutrition Survey (NHNS) in 2012 [17]. More details on data sources are available in the Technical Appendix (see Appendix 5.3).

Diabetes prevalence in 1980 was defined as a casual blood sugar >200 mg/dl or treated

diabetes. However, we were unable to obtain diabetes prevalence in 2012 based on the same definition because casual blood sugar levels were not measured in 2012. Note that HbA1c levels were not measured in 1980. Therefore, we calculated the diabetes prevalence in 2012 as follows to use similar definitions between 1980 and 2012. First, we calculated the prevalence of diabetes based on HbA1c (≥6.5%) in 2012. Second, we calculated ratios of prevalence of diabetes based on casual blood sugar to that based on HbA1c in 2010. The ratios were 0.88 for men and 0.78 for women. Finally, the prevalence of diabetes calculated in the first step were multiplied by the ratio calculated in the second step. More details on this adjustment are provided in the Technical Appendix.

Observed and expected number of CHD deaths

Substantial changes in the coding of causes of death in Japan from ICD 9 to ICD 10 were introduced in 1995. Therefore, to estimate the true decline in the observed number of deaths from coronary heart disease in Japan for 1980-2012, official vital statics data needed to be adjusted. We estimated the number of deaths from coronary heart disease before 1995 by using a Poisson regression model, fitting the number of deaths from coronary heart disease as the outcome and years as the explanatory variable. A detailed explanation of these calculations is available in section 2.1 of the Technical Appendix.

The number of CHD deaths expected in 2012 was calculated by multiplying the age and sex-specific CHD mortality in 1980 by the relevant population counts for 2012, yielding the expected number of deaths in 2012 had age and sex-specific mortality rates remained unchanged since 1980. The difference between the number of expected and observed deaths represented the mortality fall, expressed as the total number of CHD deaths prevented or postponed (DPPs). This needed to be explained by the combined changes in risk factor levels and treatment uptake between 1980 and 2012. If the model did not fully explain all deaths prevented, we assumed any shortfalls would reflect unmeasured risk factors or imprecision in

the model parameters.

Mortality reductions attributable to treatment uptake

We specified relevant treatments for each of the nine mutually exclusive disease groups (see Technical Appendix). The first component of the IMPACT mortality model calculates the net benefit of treatments in 2012. Firstly, we calculated the estimated number of DPPs in 2012 by multiplying the 2012 age-sex- specific treatments uptake levels by the population counts for 2012 in that age-sex-stratum, by the one-year case fatality rate and by the relative reduction in the case fatality rate estimated to be due to the administered treatment.

Many effective treatments were not in use in 1980 in Japan. We therefore calculated the net benefit of treatments in 2012 as the difference between the number of untreated patients in 1980 and the number of patients treated in 2012 (i.e. using the 2012 uptake rates).
We specified nine mutually exclusive disease groups (see Technical Appendix). To avoid double counting of patients, we constructed distinct, non-overlapping CHD patient subgroups. The patient numbers in some groups, for instance angina in community and heart failure in community, were therefore adjusted for several conditions. For example, we adjusted the number of angina patients in community to account for the fact that Japan has a large prevalence of vasospastic angina, estimated to be at 40% of angina cases [18]. We also adjusted the number of heart failure patients in the community to allow for probable underestimation in the Patient Survey conducted by the Ministry of Health, Labour and Welfare, Japan. Details of these assumptions are presented in the Appendix, section 5.1.

Mortality reductions attributable to risk factor changes

We calculated the absolute change in each risk factor between 1980 and 2012 by using generalized linear models with normal distribution and identity link for the continuous risk factors (such as total blood cholesterol and BMI) and generalized linear models with a binomial

distribution and logit link function for categorical variables (for the details, please see Technical Appendix 2.1.). We then estimated the mortality benefits of an absolute change in each risk factor between 1980 and 2012 with a regression-based approach for factors measured on a continuous scale, using sex and age-specific independent regression coefficients of mortality benefit for a unit change in mean risk factor obtained from published multivariate analyses (Technical Appendix, table I). For binary variables (such as smoking), we used a population attributable risk fraction approach using sex and age-specific relative risks from the most recent meta-analyses and population cohort studies (Technical Appendix, Table J).

Recent reductions in CHD mortality obviously reflect the result of simultaneous changes in multiple risk factors. We therefore jointly estimated mortality benefits of changes in risk factors by using the cumulative risk reduction approach, rather than simple addition (Technical Appendix, section 1.3).

Sensitivity analysis

We calculated 95% uncertainty intervals (UI) around the model output by using the Monte Carlo simulation. This calculation involved replacing all fixed input parameters used in the model by appropriate probability distributions and by repeatedly recalculating the model output with values sampled from the defined input distributions. We used the Excel add-in Ersatz software (www.epigear.com) to do 1000 runs to determine the 95% UIs of the deaths prevented or postponed (2.5th and 97.5th percentile values corresponding to the lower and upper limits) (see Technical Appendix).

Results

The number of CHD deaths in 2012 observed and expected (based on an assumption that CHD age and sex-specific mortality rates in 1980 persisted through 2012) were 49,300 and 125,000 respectively. Thus, a total of 75,700 deaths were prevented or postponed (DPPs) (Table 1).

Of the 75,700 DPPs, approximately 42,300 ([UI]: 40,900–44,700) fewer CHD deaths were attributable to medical and surgical treatments representing some 56% (95% UI: 54% to 59%) of the total mortality fall (Table 2 and Supplemental Figure 1). Approximately 26,300 (21,200–31,000) fewer CHD deaths were attributable to risk factor changes in the population, representing some 35% (28% to 41%) (Table 2 and Supplemental Figure 1). The remaining 9% was attributed to changes in other unmeasured factors or model imprecision.

Medical and Surgical Treatments

Substantial contributions came from therapy for angina in the community (21.1% [20.5% to 21.8%]) of the total mortality decrease corresponding to 16,000 [15,500 to 16,500] fewer CHD deaths) and for heart failure in the hospital (7.2% [6.4% to 8.1%] of the total mortality decrease corresponding to 5,500 [4,800 to 6,100] fewer CHD deaths)(Table 3 and Supplemental Figure 1). ACE inhibitor and beta-blocker benefits across all diseases accounted for approximately 12% (corresponding to 9,100 fewer CHD deaths) and 13% (corresponding to 9,800 fewer CHD deaths) respectively of the total mortality fall. Both had been introduced after1980. For the details, please see Table 3.

Risk factor changes

We observed both favourable and un-favourable risk factor changes. The largest contribution from risk factor changes at population level was due to the 8.4 mmHg fall in SBP in people not on antihypertensive drugs; this generated approximately 18,400 (14,900 to 22,300) fewer deaths, representing 24.4% (19.7% to 29.4%) of the total mortality decrease (Table 2). In contrast, the additional benefits from the treatment of SBP were three-fold less, and approximately 7,200 (5,800 to 8,600) deaths averted corresponding to 9.5% (7.7% to 11.4%) of the total mortality decrease (Table 3). The second largest contribution came from the fall in population smoking rates, accounting for approximately 8,400 (5,900 to 10,600) deaths averted, corresponding to

11.1% (7.8% to 14.0%) of the total fall. Increased leisure time physical activity accounted for approximately 5,700 (4,500 to 6,700) deaths prevented or postponed corresponding to 7.5% (5.9% to 8.9%) of the total mortality decrease.

The gains from decreases in SBP, smoking, and physical activity, were partly cancelled out by increases in cholesterol, BMI, and diabetes. Diabetes prevalence increased from 9% to 11%, which resulted in approximately 2,600 (900 to 4,500) additional deaths, representing some 3.5% (1.2% to 5.9%) of the total deaths (Table 2). Increases in mean BMI from 22.5 in 1980 to 23.2 in 2012 contributed approximately 2,000 (1,600 to 2,400) extra deaths, an additional 2.7% (2.1% to 3.2%) of total CHD deaths (Table 2). Increases in mean cholesterol (4.93 to 5.22 mmol/L) accounted for approximately 1,600 (760 to 2,600) additional deaths corresponding to 2.2% (1.0% to 3.4%) of the total CHD deaths (Table 2). This effect was blunted by subtraction of statin benefits (4.0% [3.4% to 4.6%] corresponding to 3,000 [2,600 to 3,500] fewer CHD deaths)(Table 3). The contribution of all risk factors and treatments and their uncertainty are presented in Supplemental Figure 1.

Discussion

Principal findings

Between 1980 and 2012, the age-adjusted CHD mortality rates in Japan decreased by 61%, resulting in 75,700 fewer CHD deaths. The IMPACT Japan model explained approximately 91% of this mortality fall. Changes in medical treatments accounted for 56% (95% UI: 54% to 59%) of the mortality decrease. Additionally, favourable risk-factor changes accounted for approximately 35% (28% to 41%), in spite of adverse trends in cholesterol, BMI, and diabetes.

Relation to previous studies

Medical and surgical treatments

Cardiology treatments developed rapidly during the period of study in Japan (1980–2012). The

fewer CHD deaths in Japan were attributable to medical and surgical treatments representing 56% (95% UI: 54% to 59%) of the total mortality fall, which was higher than that of the UK (42%) [11] and the US (47%) [8]. This could be due to differences in healthcare systems. Japan has utilized universal health coverage that charges fees per service similar to the UK but could be less restrictive; however, the US did not have a similar system [19]. On the other hand, results from the IMPACT model in Portugal show that approximately 50% of the CHD mortality reduction was due to changes in medical treatments, similar to our present results [13]. Possible reasons for this similarity can be that both Japan and Portugal had lower age-standardized CHD mortality and had also utilized universal health coverage [13,19].

Improvements in chronic angina management in Japan represented 21.1% (20.5% to 21.8%) of the mortality reduction, similar to Canada [9]. Community-based treatments for hypertension (9.5% [7.7% to 11.4%]), heart failure (7.2% [6.4% to 8.1%]), and statins (4.0% [3.4% to 4.6%]), also played major roles, similar to the US, the UK, Canada, and Sweden [8,9,11,12,20].

Furthermore, the contribution of those treatments to the decline of CHD deaths is likely explained by the Japanese universal health coverage by which most people can obtain health services without suffering financial hardship [19]. However, room for improvement still exists from ACE/ARBs treatment for AMI as follows. Twelve percent of the mortality reduction could be attributed to ACE/ARBs treatment that is expensive compared to cheaper alternatives, but freely affordable under the Japanese universal health coverage [19]. The 3.8% (3.6% to 4.7%) of DPPs explained by AMI treatments in Japan was lower than the UK (7.7%) and the US (6.3%) [8,11], while 2.8% (2.6% to 2.9%) explained by unstable angina treatments which fell in the UK (1.5%) and the US (4.0%) [8,11]. In Japan, beta-blockers and ACE/ARB for AMI have not been prescribed frequently, especially in small hospitals; the use of both treatments might further increase.

Major cardiovascular risk factors

Net changes in major cardiovascular risk factors explained approximately 35% (28% to 41%) of the CHD mortality fall between 1980 and 2012. Some 24.4% (19.7% to 29.4%) was explained by decreased population blood pressure, even more than the US and Canada, both of which had around 20%[8,9]; this likely reflects the dramatic decrease in salt reduction attributable to public health interventions and westernised dietary patterns [21,22,23]. Smoking prevalence in Japan declined from 35% (1980) to 21% (2012) and prevented approximately 8,400 (5,900 to 10,600) fewer CHD deaths, some 11.1% (7.8% to 14.0%) of the total mortality fall, similar to Canada (9.5%) [9] and Sweden (9.1% in the entire population, 6.8% in the population without CHD for the primary prevention of CHD, and 6.9% in CHD patients for the secondary prevention of CHD) [12,24] but lower than the UK (48.1% in the entire population, 83.0% in the population without CHD for the primary prevention of CHD, and 17.0% in the population with CHD for the secondary prevention of CHD) [11, 25].

Increases in BMI and diabetes mirrored trends elsewhere and generated 6.2% of additional deaths. Mean cholesterol at population level had fallen in almost all Western countries except for Japan where total cholesterol increased steadily from 4.93 to 5.22 mmol/L to reach U.S levels [7,26]. This rise generated approximately 1,600 (760 to 2,600) additional CHD deaths, in spite of statin treatments. This cholesterol rise probably reflects a progressive Westernisation of the healthy traditional Japanese diet and consumption of sugar, animal product, total fats, and oil increased four-fold from 1965 to 2005 [27,28]. Consumption of meat, milk, and dairy products also rose, increasing the ratio of saturated fatty acids to total energy intake [23], while vegetable intake remained constant [29] (Figure 1 in Appendix II). National nutritional surveys showing lower intake of vegetable, fruit, and seafood in younger age-groups raise concern for future increases in CHD, as in other populations [1,14,30].

Strengths and weaknesses of the present study, and unanswered questions and future work

Our study has several strengths. Firstly, this is the first study to use high quality, nationally representative datasets to quantify the factors driving coronary mortality trends in Japan. For example, all hospital cardiac arrest cases were captured through the All-Japan-Utstein Registry, which is already validated [31,32]. Risk factor distribution was obtained through the national nutritional survey, which was based on the randomly sampled nationwide population[33]. Second, our validated IMPACT model can transparently integrate and simultaneously consider huge amounts of data from many sources.

Our study also has limitations. We used a validated methodology to adjust for the different version of ICD coding and. However, we might still have overestimated mortality rates in the 1980s. Additionally, we were unable to perform sensitivity analyses to estimate the effect of change in ICD coding on our results by using data in 1995 or 1996 (the coding method was changed in 1995 in Japan) instead of data in 1980 because we did not have enough data in 1995 and 1996 to perform the IMPACT model. Second, diabetes prevalence in 1980 was defined as a casual blood sugar >200 mg/dl or as treated diabetes, though diabetes prevalence in 2012 was calculated by multiplying that which was based on HbA1c in 2012 by the ratios of diabetes prevalence in 2010 based on casual blood sugar to that based on HbA1c. For the details, please see the methods section. However, the relative change observed was compatible with other studies [34,35]. Third, we might have overestimated angina in the community due to the high prevalence of vasospastic angina in Japanese populations. However, we explicitly adjusted for this peculiarity of angina epidemiology in Japan (see Appendix). Fourth, the elderly, aged 85 and above, were not included in the model due to lack of data. Fifth, we optimistically assumed that treatment effectiveness in the population equalled the efficacy reported in randomised trials, likely overestimating treatment benefits. Sixth, the IMPACT model used CHD mortality as the endpoint, and did not consider CHD morbidity. Thus, the estimation of DPPs could be improved by considering the burden of CHD morbidity. Finally, our model could not explain the overall 9% decline in CHD mortality. This perhaps reflected imprecision

of the model, or omission of other risk factors, such as psychosocial stress, alcohol, or fish omega-3 fatty acid consumption. That may also reflect that our model omitted stroke deaths (as a potential competing risk), of which mortality and prevalence were higher in Japan than in European countries and the US. For example, there may have been several people who would have died from CHD if they had not died from stroke. Thus, the present results should be interpreted by considering these limitations.

Public health implications

Preventive approaches, particularly population-based policies, are consistently more effective than healthcare-based primary prevention [36]. Current efforts to prevent cardiovascular disease in Japan are based on the national health check-up promotion programs (see Appendix). However, such individual-level interventions appear less effective and equitable than population-wide structural interventions. [37,38] Population level policy approaches should therefore be considered as a potentially powerful and likely cost-saving strategy. In Japan, actions on salt have been extremely effective. For example, recently, Japanese Hypertension Society conducted a campaign for reducing salt by many publications such as recipe books, and successfully changed labels of salt contents in processed foods that consumers could easily understand [21,22]. However, no regulation currently exists for reducing trans-fatty acids in Japan, which would be an effective intervention [39]. Tobacco control policy could also be strengthened, along with mandatory salt reformulation in processed foods and sugar-sweetened beverage taxation.

Finally, these results can be cautiously generalized to other countries in the Asia-Pacific region, such as countries like South Korea that have a similar epidemiological profile where AMI incidences increase due to an aging society and westernisation of lifestyle, especially for diet [40,41].

In conclusion, the declining trend in CHD deaths in Japan was explained by policies reducing blood pressure and smoking, and by considerable application of evidence-based

treatment for CHD. However, these successes have been partly offset by the increase in diabetes, BMI, and cholesterol levels. Additionally, effective population-based policy approaches may therefore now be required to reduce the future burden of CHD in Japan.

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Table 1. Population aged from 35 to 84, observed coronary heart disease deaths, age-standardized rates for 1980 and 2012, and deaths prevented or postponed (DPPs) in Japan.

	Men and women		Men		Women	
Year	1980	2012	1980	2012	1980	2012
Population	53,026,428	79,457,000	25,119,073	38,445,000	27,907,355	41,012,000
Observed CHD deaths	41,572	49,273	31,226	32,838	18,102	16,435
Age-standardized rate (per 100,000) †	78.4	37.5	96.2	54.1	62.2	22.5
Expected deaths††	-	124,955	-	80,710	-	44,245
DPPs‡	-	75,682	-	47,872	-	27,810
% of expected deaths prevented	-	60.60%	-	59.30%	-	62.90%

†The direct method of age-standardized rates was used with the Japanese population aged 35-85 (ten-year age-bands) in 1980 as standard to calculate the age-standardized rates according to the aim of the present study.

†† Expected deaths = the number of CHD deaths in 2012 was calculated on an assumption that age and sex-specific CHD mortality rates in 1980 continued through 2012.

‡DPPs = expected – observed deaths in 2012.

Abbreviations: CHD, coronary heart disease; DPPs, deaths prevented or postponed.

Table 2. Coronary heart disease deaths prevented or postponed (DPPs) due to changes in total treatment, and changes in prevalence and levels of risk factors between 1980 and 2012 in Japan.

	DPPs (95% uncertainty interval*)	% of total DPPs (95% uncertainty interval*)
Total treatments and risk factors prevalence	75,682	NA
Explained by changes in total treatments	42,336 (40,868 to 44,652)	56% (54% to 59%)
Explained by changes in risk factor prevalence and risk factor levels	26,280 (21,191 to 31,030)	35% (28% to 41%)
Systolic blood pressure† (decreased by 8.87 mmHg in the period)	18,445 (14,909 to 22,251)	24.4% (19.7% to 29.4%)
Total cholesterol‡ (increased by 0.28 mmol/L in the period)	-1,645 (-2,573 to -757)	-2.2% (-3.4% to -1.0%)
Body mass index (increased by 0.68 kg/m^2 in the period)	-2,013 (-2,422 to -1,589)	-2.7% (-3.2% to -2.1%)
Smoking (decreased by 14.0% in the period)	8,407 (5,903 to 10,595)	11.1% (7.8% to 14.0%)
Physical inactivity (decreased by 18.5% in the period)	5,714 (4,465 to 6,736)	7.5% (5.9% to 8.9%)
Diabetes (increased by 1.6% in the period)	-2,627 (-4,465 to -908)	-3.5% (-5.9% to -1.2%)
Unexplained by the present IMPACT model	7,065	9% (NA)

Abbreviations: DPPs, deaths prevented or postponed.

*95% uncertainty interval corresponds to 2.5th and 97.5th percentiles limits of uncertainty analysis.

†After subtracting DPPs due to antihypertensives in primary prevention.

‡After subtracting DPPs due to statin treatment in primary prevention.

Table 3. Coronary heart disease deaths prevented or postponed (DPPs) due to changes in specific treatment between 1980 and 2012 in Japan.

Treatments by patient groups	DPPs (95% uncertainty interval*)	% of total DPPs (95% uncertainty interval*)
Total treatments	**42,336 (40,868 to 44,652)**	**56% (54% to 59%)**
Acute myocardial infraction†	**2,842 (2,725 to 3,557)**	**3.8% (3.6% to 4.7%)**
Aspirin	564	0.70%
ACE inhibitors	131	0.20%
Beta-blockers	61	0.10%
CABG	29	0.00%
PTCA	683	0.90%
Rehabilitation	184	0.20%
Community CPR	297	0.40%
Hospital CPR	51	0.10%
PTCA (NSTEMI)	774	1.00%
Clopidogrel	69	0.10%
Unstable angina†	**2,102 (1,968 to 2,195)**	**2.8% (2.6% to 2.9%)**
Aspirin	501	0.70%
Aspirin & Heparin	7	0.00%
ACE inhibitor	80	0.10%
Beta blockers	71	0.10%
Spironolactone	212	0.30%
IIb/IIIa	14	0.00%
CABG	143	0.20%
PTCA (STEMI)	806	1.10%
Rehabilitation	28	0.00%
Community CPR	28	0.00%
Hospital CPR	1	0.00%
Clopidogrel	212	0.30%
Secondary prevention post myocardial infarction†	**1,478 (1,211 to 1,741)**	**2.0% (1.6% to 2.3%)**
Statins	380	0.50%
Aspirin	272	0.40%
Warfarin	47	0.10%
ACE inhibitor	285	0.40%
Beta blockers	272	0.40%

Rehabilitation	221	0.30%
Secondary prevention post revascularisation†	**811 (681 to 984)**	**1.1% (0.9% to 1.3%)**
Statins	213	0.30%
Aspirin	183	0.20%
Warfarin	34	0.00%
ACE inhibitor	147	0.20%
Beta blockers	149	0.20%
Rehabilitation	85	0.10%
Angina in the community†	**15,993 (15,515 to 16,499)**	**21.1% (20.5% to 21.8%)**
Statins	1,699	2.20%
Aspirin	996	1.30%
ACE inhibitor	7,356	9.70%
Beta blockers	4,848	6.40%
Spironolactone	610	0.80%
CABG	484	0.60%
Heart failure in patients requiring hospitalisation†	**3,441 (3,254 to 3,633)**	**4.5% (4.3% to 4.8%)**
Aspirin	666	0.90%
ACE inhibitor	348	0.50%
Beta blockers	1,473	1.90%
Spironolactone	954	1.30%
Heart failure in the community†	**5,459 (4,844 to 6,130)**	**7.2% (6.4% to 8.1%)**
Aspirin	1,350	1.80%
ACE inhibitor	623	0.80%
Beta blockers	2,919	3.90%
Spironolactone	567	0.70%
Primary prevention therapies: Statins†	**2,996 (2,573 to 3,481)**	**4.0% (3.4% to 4.6%)**
Primary prevention therapies for high blood pressure†	**7,213 (5,828 to 8,628)**	**9.5% (7.7% to 11.4%)**

*95% uncertainty interval corresponds to 2.5th and 97.5th percentiles limits of uncertainty analysis for the 9 disease groups and total treatments.

†Subtotals (in rows) for coronary heart disease patient groups.

Abbreviations: ACE, angiotensin converting enzyme; ARB, angiotensin receptor blockers;

CABG, Coronary artery bypass graft; PTCA, percutaneous transluminal coronary angioplasty; DPPs, deaths prevented or postponed.

What is already known this topic

· Age-adjusted mortality of coronary heart disease (CHD) has declined since 1980 in many developed countries.

· This mortality fall in Japan occurred in spite of recent increases in obesity and cholesterol, marking population aging, and Westernised dietary changes.

· Those results have suggested that the decline of the age-adjusted CHD mortality may be explained by key factors other than obesity and total cholesterol in Japan.

What this study adds

· In Japan, the declining trend in CHD deaths was explained by policies in reduction of prevalence of smoking, elevated levels of systolic blood pressure, and by implementation of evidence-based treatment for CHD.

· These successes have been partially offset by adverse increases in prevalence of diabetes and elevated levels of body mass index and cholesterol.

· Japan should continue with their control policies for blood pressure and tabaco, and build an effective strategy to prevent diabetes and elevated levels of body mass index and cholesterol diabetes to prevent CHD deaths in the future.