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# Modelling Coronary Heart Disease Mortality declines in the Republic of Ireland, 1985–2006

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ABSTRACT

*Background:* Consistent declines in coronary heart disease (CHD) death rates have been previously observed in Ireland since1985.
*Aims & Methods:* To use the previously validated Irish IMPACT CHD mortality model to further examine the subsequent CHD mortality falls from 1985 through to 2006, and to determine the contribution of risk factor changes and "evidence based" treatments to this decline by age and gender.
*Results:* CHD mortality rates fell by 68% in men (63% in 65–84 years) and by 69% in women (66% in 65–84 years). This resulted in approximately 6450 fewer CHD deaths than if mortality rates had not changed. Overall, approximately 40% *(38% in men; 45% in women)* of the CHD mortality decline could be attributed to improvements in treatment uptake, particularly secondary prevention (12%), angina (9%), and heart failure therapies (8%).
Approximately 48% of the CHD mortality decline was attributable to risk factor improvements (*54% in men; 37% in women);* the biggest contributions came from falls in population systolic pressure (28%), cholesterol (24%), and physical inactivity levels (10%). Negative trends in diabetes and obesity levels generated an estimated 17% additional CHD deaths.
The largest benefits from improvements in risk factors were seen in men aged 25–64 years, while the greatest treatment benefits occurred in women aged 65–84 years.
The model explained approximately 88% of the observed mortality declines.
*Conclusion:* Falls in CHD mortality have continued in both sexes in Ireland, but with notable gender and age differences. The continued increase in diabetes and obesity levels is particularly worrying.


## 1. Introduction

Cardiovascular disease continues to be the dominant cause of death in most European countries, including Ireland. Deaths from coronary heart disease (CHD) have been declining in the Republic of Ireland since the mid-1980s, with 50% fewer deaths in 2000 compared to 1985 [1]. Our previous research had suggested that this decline could be attributed equally to reductions in adverse risk factors and to improvements in medical and surgical interventions over this time [1]. Data from Northern Ireland and a number of other developed countries have shown further declines in CHD mortality rates in recent years [2–6]. The Republic of Ireland has implemented a major cardiovascular disease prevention strategy since the year 2000 [7], updated in 2010 [8].

A recent study in the Republic of Ireland observed an overall 27% decline in hospitalization rates of acute myocardial infarction (AMI) between 1997 and 2008. There were marked declines in ST elevation MI (STEMI) patients but a 122% increase in non-STEMI admissions [9]. Recent studies in the UK, Australia, and in the US have shown flattening of CHD mortality declines in younger age groups [10–12]. It is, however, uncertain whether Republic of Ireland has maintained the same rate of CHD mortality decline as over the 1985–2000 periods. Moreover, the relative importance of risk factor changes and increased uptake of cardiology treatments on recent CHD mortality trends in men and women and in younger and older age groups has not been addressed in detail in previous work. It is also uncertain how CHD trends in the Republic of Ireland between the mid 1980's and the last decade compare with those recently reported from Northern Ireland, an important issue given the significant differences in health service provision between these two jurisdictions.

The aim of this study was therefore to use the previously validated IMPACT CHD mortality model [2,13,14], to examine the long-term CHD mortality trends in Ireland between 1985 and 2006, paying particular attention to variation in CHD trends by gender and age group. The findings will permit comparison with those from Northern Ireland [2], and will potentially inform future prevention strategies.

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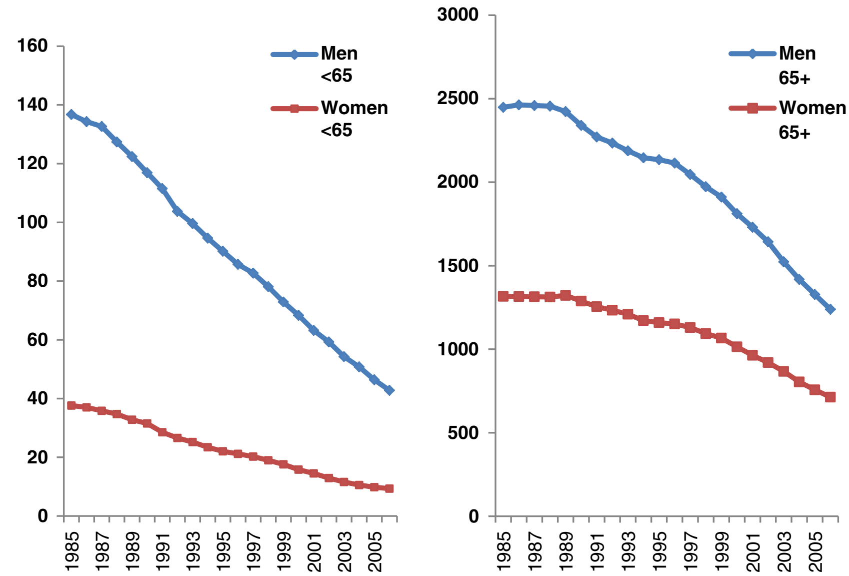


**Fig. 1.** Age-standardized coronary heart disease (CHD) mortality rates per 100,000 in Ireland by two broad age-groups and by gender distribution, 1985–2006.

## 2. Methods

"The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology".

Because of the nature of aggregated data utilized in this study with no identifiers, no ethical approval was sought.

The cell-based IMPACT CHD mortality model in Microsoft Excel has been described in detail elsewhere [1]. The Irish IMPACT CHD mortality model has been further refined and updated to include recent data on changes in risk factors and improvements in 'evidence-based' interventions [see Appendices I–III].

We identified and incorporated data for men and women aged 25 to 84 years in the total Irish population of ~4.2 million, stratified by age and sex, detailing:

a) CHD patient numbers (ICD 9 codes 410–414) categorised by disease sub-group
b) Use of specific medical and surgical treatments,
c) Population trends in major cardiovascular risk factors (smoking, total cholesterol, systolic blood pressure, obesity, diabetes, and physical inactivity),
d) Effectiveness of specific cardiology treatments,
e) Effectiveness of population cardiovascular risk factor changes.

### 2.1. Risk factors

In brief, the model employs regression coefficients for quantifying the association between population risk factor changes and subsequent CHD mortality based on meta-analyses and cohort studies [15–18]. For each risk factor, the subsequent reduction in deaths in 2006 was estimated as the product of the specific regression coefficient, the relative risk factor reduction, and the number of CHD deaths observed in 1985, the base year [1]. Relative risk estimates were taken from the INTERHEART study [19].

Age–sex specific data on risk factors such as total cholesterol, diabetes prevalence, etc was obtained from various regional and national lifestyle surveys [see Appendix II].

### 2.2. Treatment data: sources of data and cardiology treatment uptake levels

Details of the sources of data considered in this study are shown in Appendices I and III. Data on the effectiveness of therapeutic interventions were obtained from published randomised controlled trials, meta-analyses and cohort studies.[1] Medical treatment data was available from the Heath Service Executive-Primary Care Reimbursement Services (HSE-PCRS) prescribing databases [20], the Heartwatch programme in secondary prevention therapy in primary care [21], the EUROASPIRE II and III [22,23], and the EUROHeart Failure I and II surveys [24,25].

The number of deaths prevented or postponed by each intervention in each group of CHD patients in the year 2006 was calculated by multiplying the number of people in each diagnostic group by the proportion of those patients who received a particular treatment, by the case-fatality rate over 1 year, and by the relative reduction in 1–year case-fatality by the administered treatment [26].

We assumed that compliance, the proportion of treated patients actually taking therapeutically effective levels of medication, was 100% among hospital patients, 70% among symptomatic community patients, and 50% among asymptomatic community patients. To avoid double counting of patients treated, we identified potential overlaps between different groups of patients and made appropriate adjustments. To address the potential effect on relative reduction in case-fatality rate for individual patients receiving multiple treatments, we used the Mant and Hicks cumulative relative benefit approach as previously [1].

### 2.3. Model validation: comparison of estimated V observed changes in mortality

The model produces estimates of the total number of deaths from coronary heart disease prevented or postponed attributable to each treatment and to changes in each specific risk factor. These estimates were then summed and compared with the observed changes in mortality for men and women in each specific age group. Any shortfall in the overall estimate from the model is presumed to be attributable to inaccuracies in our methods. In particular, there may be biased input data and insufficient accounting for time lag. Additional potential causes of this shortfall include other unmeasured risk factors, such as psychosocial ones or dietary habits (including salt reductions or fruit or vegetable consumption patterns).

### 2.4. Sensitivity analyses

All the above assumptions were tested in a multi-way sensitivity analysis with the analysis of extremes method [27]. For each model parameter, we assigned a lower and upper value using 95% confidence intervals where available or otherwise ±20% values (for numbers of patients, uptake of treatment, and compliance).

## 3. Results

Between 1985 and 2006, CHD mortality rates fell by 68% in men and 69% in women in the Republic of Ireland. This resulted in some 6450 fewer CHD deaths than if mortality rates had persisted unchanged. Fig. 1 shows the age-standardized CHD mortality rates in both sexes across two broad age-groups between 1985 and 2006. The rate of decline decreased slightly towards the end of the period of study in men and women in both age groups. Happily, the gender gap in CHD mortality narrowed in both the younger and older age groups (Fig. 1).

Table 1 presents the trends in risk factors both as absolute values (weighted across age and gender) and relative changes. Table 1 also highlights variations in risk factor levels by two broad age-groups: <65 years of age and above. In general, the relative percentage changes among the older individuals (≥65 years of age) have shown a greater decline in all the major risk factors except for diabetes and BMI levels (Table 1).

Table 2 shows the number and percentage of deaths prevented or postponed (DPPs) attributed to changes in risk factors and improvements in treatment uptake overall and by gender. Of the 6450 CHD deaths prevented between 1985 and 2006 approximately 40% can be attributed to improvements in uptake of treatments (minimum estimate 14%, maximum estimate 88%), with the largest contributions coming from secondary prevention (12%), and treatments for chronic angina (8%) and hospital and community heart failure (8%) (Table 2). Approximately

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**Table 1**
Absolute and relative changes in age-standardized population risk factor levels in Ireland, overall and by gender and age distribution (1985–2006).

| | Overall | | | | Men | | | | Women | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Population risk factor | 1985 | 2006 | Absolute change | Relative change (%) | 1985 | 2006 | Absolute change | Relative change (%) | 1985 | 2006 | Absolute change | Relative (%) |
| Total cholesterol (mmol/l) | 5.88 | 5.39 | −0.49 | −8.3 | 5.89 | 5.43 | −0.46 | −7.8 | 5.88 | 5.35 | −0.53 | −9.0 |
| 25–64 years | 5.80 | 5.42 | −0.38 | −6.6 | 5.86 | 5.50 | −0.36 | −6.1 | 5.74 | 5.34 | −0.40 | −6.9 |
| 65–84 years | 6.35 | 5.19 | −1.16 | −18.3 | 6.05 | 5.00 | −1.05 | −17.3 | 6.61 | 5.36 | −1.25 | −18.9 |
| Smoking (%) | 32.3 | 28.2 | −4.1 | −12.7 | 31.0 | 29.9 | −1.1 | −3.5 | 33.5 | 26.4 | −7.1 | −21.2 |
| 25–64 years | 32.1 | 30.5 | −1.6 | −4.9 | 29.1 | 32.1 | +3.0 | 10.3 | 35.2 | 28.9 | −6.3 | −17.9 |
| 65–84 years | 33.2 | 15.0 | −18.2 | −54.8 | 42.9 | 16.9 | −26.0 | −60.6 | 25.0 | 13.4 | −11.6 | −46.4 |
| SBP (mm Hg) | 137.0 | 136.0 | −1.0 | −0.7 | 141.0 | 143.0 | +2.0 | 1.4 | 134.0 | 129.0 | −5.0 | −3.7 |
| 25–64 years | 134.1 | 134.3 | +0.2 | 0.15 | 137.7 | 142.5 | +4.8 | 3.5 | 130.5 | 125.8 | −4.7 | −3.6 |
| 65–84 years | 155.0 | 145.7 | −9.3 | −6.0 | 159.2 | 147.6 | −11.6 | −7.3 | 151.4 | 144.2 | −7.2 | −4.8 |
| Physical inactivity (%) | 24.5 | 18.7 | −5.8 | −23.7 | 24.8 | 18.5 | −6.3 | −25.4 | 24.1 | 18.9 | −5.2 | −21.6 |
| 25–64 years | 20.6 | 16.6 | −4.0 | −19.4 | 22.4 | 17.2 | −5.2 | −23.2 | 18.7 | 16.0 | −2.7 | −14.4 |
| 65–84 years | 45.5 | 30.3 | −15.2 | −33.3 | 39.0 | 26.0 | −13.0 | −33.3 | 51.0 | 34.0 | −17.0 | −33.3 |
| Diabetes (%) | 1.79 | 3.21 | +1.42 | 79.3 | 2.15 | 3.28 | +1.13 | 52.6 | 1.43 | 3.14 | +1.71 | 119.6 |
| 25–64 years | 1.41 | 2.26 | +0.85 | 60.3 | 1.76 | 2.31 | +0.55 | 31.3 | 1.06 | 2.22 | +1.16 | 109.4 |
| 65–84 years | 3.85 | 8.42 | +4.57 | 118.7 | 4.47 | 9.14 | +4.67 | 104.5 | 3.31 | 7.81 | +4.50 | 135.9 |
| BMI (kg/m2) | 25.4 | 28.5 | +3.1 | 12.2 | 25.9 | 27.3 | +1.4 | 5.4 | 24.9 | 29.7 | +4.8 | 19.3 |
| 25–64 years | 25.5 | 28.8 | +3.3 | 12.9 | 26.2 | 27.7 | +1.5 | 5.7 | 24.8 | 29.8 | +5.0 | 20.2 |
| 65–84 years | 25.1 | 27.0 | +1.9 | 7.6 | 24.3 | 25.0 | +0.7 | 2.9 | 25.8 | 28.8 | +3.0 | 11.6 |

48% of the 6450 CHD deaths prevented between 1985 and 2006 could be attributed to improvements in risk factor levels (minimum estimate 34%, maximum estimate 59%). The largest contributions were from reductions in population systolic blood pressure (28%) and cholesterol levels (24%), followed by reductions in physical inactivity levels (10%). However, there was an increase in the rates of both diabetes and obesity contributing to an increase of 17% in CHD DPPs (Table 2). Table 2 shows independent effects of both population systolic blood pressure and anti-hypertensive treatments, and of total cholesterol levels and statins treatment.

### 3.1. CHD deaths in men and women

Women in general showed a greater relative decline in three of the major risk factors (smoking, cholesterol, and in SBP levels) but worsening in the relative changes to the remaining two risk factors (diabetes and BMI levels; Table 1). Table 2 shows that there were approximately 3900 DPPs in men, and 1750 DPPs in women from 1985 to 2006, thus explaining approximately 90% and 82% of the observed mortality declines in men and women respectively. Fewer CHD deaths were attributable to improvements in treatments in men (37%) than in women (54%), while conversely improvements in risk factors accounted for bigger mortality reductions in men (45%) than in women (38%). Increasing obesity and diabetes together contributed to approximately 15% additional CHD deaths in men and 21% in women. Fig. 2 shows the proportional distribution of DPPs contributing to CHD fall by gender and age. Among both men and women the estimated contribution of risk factor improvements declined with age and there was a corresponding increase in the relative contribution of treatment with age.

Fig. 3 shows that the modelled mortality estimates closely corresponded to the observed CHD deaths across all age-groups in both men and women, thus validating the model estimates. Also, the proportional contributions of specific risk factors and treatments category to the observed CHD declines remained relatively consistent in rigorous sensitivity analyses (Figs. 4–5).

## 4. Discussion

Between 1985 and 2006, a substantial downward trend in CHD mortality has continued in both men and women in the Republic of Ireland. This fall has resulted in some 6450 fewer CHD deaths in 2006 than would otherwise have occurred if the rates observed in 1985 had persisted. Approximately half of this mortality decline was attributable to improvements in population level risk factors, mainly systolic blood pressure and cholesterol level [1]. A further 40% was attributable to the increased uptake of cardiology interventions, particularly treatments for secondary prevention, chronic angina and heart failure. These contributions were reassuringly similar to an earlier study [1].

However, these positive effects were partly negated by the additional CHD mortality attributable to increasing levels of both diabetes and obesity, particularly in women. Compared to the previous study [1], the present study shows that trends in obesity levels have been increasing, particularly amongst women. The problem of increasing obesity and overweight is not unique to Ireland, but is common amongst most developed countries [28,29]. Also, more recent estimates of diabetes prevalence from cohort studies in Ireland are of concern [30]. Furthermore, the decline in CHD mortality rates among those aged over 65 years has notably slowed and compounds the recent Irish study on AMI hospitalization rates [9]. However, it is noteworthy that the estimated proportion of adults who are physically inactive has fallen in Ireland over the study period [31], particularly in the older age group where it has fallen from 45% to 30%. Overall the positive changes in physical inactivity accounted for over 10% of the fall in CHD deaths.

The progression of CVD reflects a complex interplay between genetic, biological, economic and social determinants. DPPs in the 25 to 64 years age group were mainly attributed to risk factor level improvements, while DPPs in the over 65 age group were largely attributed to treatment effects. This might be expected given that prevention of CHD deaths among the relatively young depends largely on primary prevention whereas in the elderly the benefits of treatment (secondary prevention) are likely to be more evident.

The estimated absolute fall in smoking prevalence between 1985 and 2006 (less than 5%) is disappointing. The early effects of the comprehensive smoke-free legislation in March 2004 were less evident than those seen in other countries. However, the effects of changes in smoking prevalence may be underestimated in the current model due to the limitations of the available data. There is some evidence that the volume of cigarettes smoked in Ireland following the smoke-free policy had fallen and positive health effects of the Irish smoke-free policy have been documented [32–35]. In particular, a positive impact of the smoke-free policy on hospital presentations with acute coronary syndrome (ACS) was observed, with a significant 12% reduction in admissions in the year following implementation of the ban. A further reduction in ACS admissions of similar magnitude was observed 2 years after implementation of the ban [34]. Despite these encouraging trends it is clear that more comprehensive tobacco control policies such as the introduction of pictorial or

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**Table 2**
Results from IMPACT CHD mortality model 1985–2006: factors contributing to the total deaths prevented or postponed (DPPs) by gender.

| Risk factors | DPPs (M; W) | % of total DPPs (M; W) |
|---|---|---|
| Smoking (self-report) | 182 (113; 69) | 2.8% (2.6%; 3.2%) |
| Population blood pressure (physical exam) | 1803 (1307; 496) | 28.0% (30.5%; 23.1%) |
| Population cholesterol (physical exam) | 1561 (1011; 550) | 24.2% (23.6%; 25.6%) |
| Physical inactivity (self-report) | 669 (533; 136) | 10.4% (12.4%; 6.3%) |
| Diabetes (self-report) | −820 (−543; −277) | −12.7% (−12.6%; −12.8%) |
| Obesity (physical exam) | −291 (−117; −174) | −4.5% (−2.7%; −8.1%) |
| Total risk factors | 3104 (2304; 800) | 48.2% (53.7%; 37.2%) |
| **Treatments** | **DPPs (M; W)** | **% of total DPPs (M; W)** |
| AMI treatments | 226 (156; 70) | 3.5% (3.6%; 3.3%) |
| Secondary prevent post-AMI | 572 (370; 202) | 8.9% (8.6%; 9.4%) |
| Secondary prevent post-CABG/PTCA | 228 (159; 69) | 3.5% (3.7%; 3.2%) |
| Chronic angina | 532 (315; 217) | 8.3% (7.3%; 10.1%) |
| Unstable angina | 45 (29; 16) | 0.7% (0.67%; 0.74%) |
| Heart failure (hospital) | 259 (165; 94) | 4.0% (3.8%; 4.4%) |
| Heart failure (community) | 249 (136; 112) | 3.9% (3.2%; 5.4%) |
| Hypertension | 223 (140; 83) | 3.4% (3.3%; 3.8%) |
| Statins primary prevention | 250 (142; 108) | 3.9% (3.3%; 4.9%) |
| Total treatments | 2584 (1612; 972) | 40.2% (37.6%; 45.3%) |
| Total treatments & risk factors (minus statins & high BPs) | 5688 (3916; 1772) | 88.3% (91.2%; 82.4%) |

Negative value indicates an increase in CHD deaths; M; Men; W: Women.

graphic warning on cigarette packs and stringent fiscal measures are required to accelerate the fall in smoking rates in Ireland [35].

Although no substantial changes in mean SBP levels were seen in men, women showed a significant decline from an average SBP of 134 mmHg to 129 mmHg between 1985 and 2006. Such population-level changes contributed significantly to the decline in CHD mortality overall, and may partly reflect improvements in diet (including reduced salt intake) [36,37] over the period and the increased use of anti-hypertensive therapy in Ireland in recent years [38]. However, the putative effects of favorable dietary trends on population blood pressure are speculative and require further investigation. A recent study in the UK demonstrated that stricter dietary policies (no industrial trans fats, reduction in saturated fats and salt and substantial increases in fruit and vegetable intake) could result in approximately 30,000 fewer cardiovascular deaths [39].

An additional 40% of the decline in CHD mortality was attributed to improvements in the uptake of treatments particularly secondary preventive therapies, treatments for heart failure (both hospital and community), and community angina therapy. The findings are broadly similar to those reported previously [1] but certainly compliance has improved over the years. The HSE-PCRS reports an almost 6-fold increase in prescription items, under the largest community drug scheme in Ireland, for cardiovascular disease and antithrombotic agents from 2000 to 2006 [20]. A proportion of this increase is due to the introduction to the scheme of free medical care to all those aged 70 years and over in July 2001. Ireland has been amongst the highest prescribers of statins across Europe [40] and in prescribing of most secondary preventive therapies according to the EUROASPIRE II and III studies [22,23]. Contributions from revascularisation were small, reflecting the relatively small size of this patient group.

The current Irish IMPACT CHD model employed is more refined, with detailed analyses by gender and age-groups along with more recent robust population-level risk factor data. Three distinct features in relation to the previous study [1] are noted: First, there have been no further improvements in overall population smoking rates since 2000, despite the introduction of a comprehensive smoke-free policy in 2004, thus reducing the contribution of changes in smoking prevalence to the overall CHD mortality decline. Second, unlike the previous model where UK estimates were employed, more recent Irish physical inactivity level data were available showing an improvement in overall physical inactivity levels (using less strict criteria of 'no' physical exercise in an average week) [31] thus reversing the negative trend reported earlier [1]. Finally, obesity estimates were based on mean BMI in the present study, as opposed to the cruder metric of obesity prevalence % in the earlier study [1]. No detailed analysis on age and gender-specific CHD mortality decline was reported in the previous study [1].

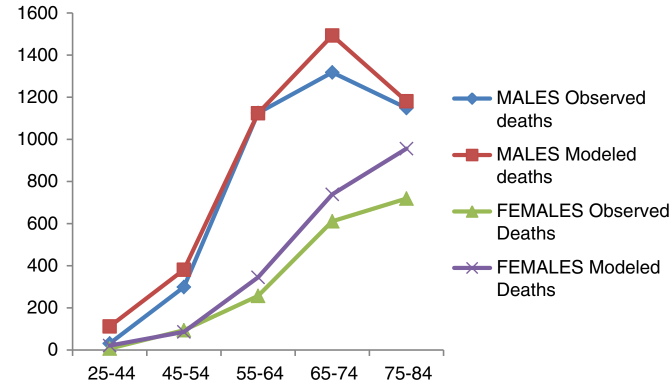


**Fig. 3.** Validation of the Irish CHD IMPACT mortality model (observed vs. modelled CHD death estimates) by age and gender distribution.

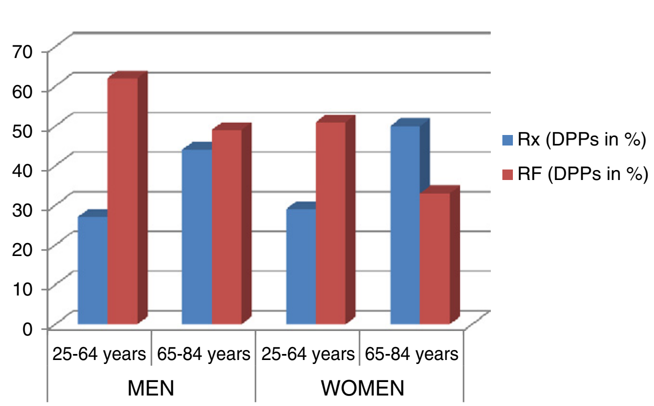


**Fig. 2.** CHD deaths prevented or postponed (DPPs) by percentage contribution across two age-groups in both sexes for risk factor and cardiology treatment.

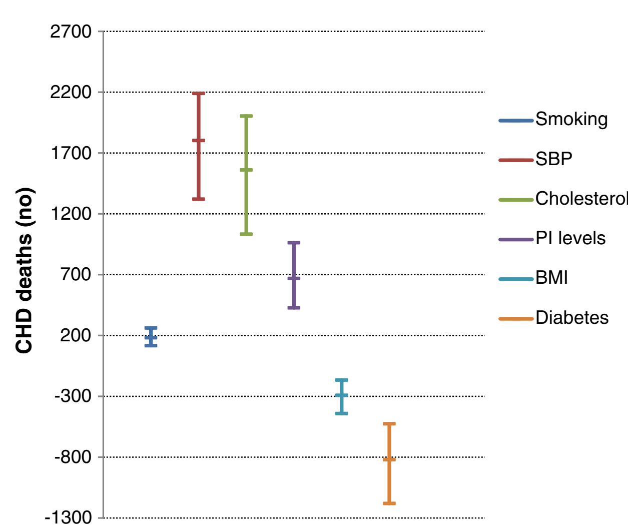


**Fig. 4.** Proportional contributions of risk factor changes to CHD deaths in Ireland—a sensitivity analysis.

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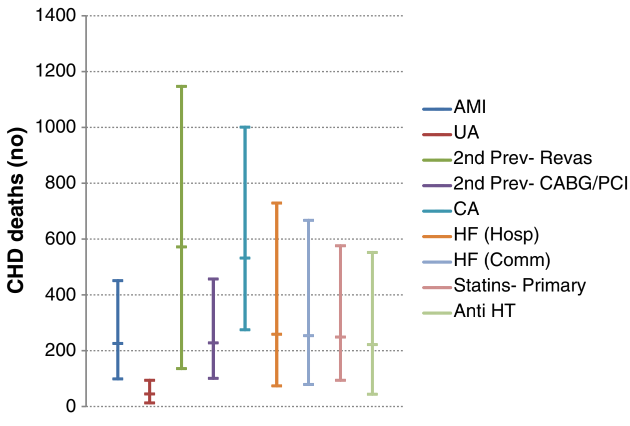


**Fig. 5.** Proportional contributions of specific treatments to CHD deaths in Ireland—a sensitivity analysis.

### *4.1. Comparisons with recent trends in Northern Ireland*

During the period of this study, there has been a higher level of investment in health services and greater access to care in Northern Ireland compared to the Republic of Ireland. This reflects differences between the tax-funded National Health System and a mixed public/private system with user fees for primary care in the two jurisdictions respectively. Previous work has documented important differences in secondary prevention prescribing [41] and cost-effectiveness of secondary prevention in these two jurisdictions [42]. Comparison of trends in the North and the Republic of Ireland is therefore potentially instructive. The Northern Ireland study reported a greater decline in crude CHD rates in women (60%) compared to men (52%) between 1987 and 2007 aged 25–84 years [2]. However, consistent with the findings from the current study, the Northern Ireland model suggested that 35% of the observed fall in CHD deaths was attributable to beneficial treatment effects and 60% of the fall was due to improvements in risk factors. There were some differences between the two jurisdictions. The Northern Ireland study showed a greater relative decline in the classical cardiovascular risk factors (cholesterol, smoking, and SBP) compared to the Republic of Ireland. By contrast, a steeper increase in diabetes prevalence was observed in the Northern Ireland study (+126%) compared to the present study (+79%) over the same period.

Reassuringly, however, major differences in health service organisation and provision were not evident in this comparison of trends in CHD mortality between Northern Ireland and the Republic of Ireland.

### *4.2. Limitations of the study*

As with all modelling studies, the limitations reflect the assumptions made and the accuracy and quality of the data available. In some cases, data were not available on those aged <45 years and these were therefore extrapolated using the data for the older age groups. Polypharmacy and the potential overlapping of treatment groups were also explicitly addressed. The IMPACT model assumes that estimates of efficacy from randomized controlled trials can be generalized to effectiveness in clinical practice. However, it is reassuring that only 12% of the decline remains unexplained through this modeling study. This gap has previously been attributed to an imperfect quantification of measured factors, plus unmeasured factors such as dietary changes, alcohol, affluence and life course exposures which have not been included in the model. Although this seems reasonable, further development work is clearly needed. Overall, it is also reassuring that a diverse range of countries have demonstrated similar results when the IMPACT CHD model was applied [2–6].

## 5. Conclusions

In conclusion, the decline in CHD mortality in Ireland has continued in both men and women. Important contributions have come from reductions in systolic blood pressure and total cholesterol levels in the population, and from increased medical interventions. However, obesity and diabetes prevalence have increased significantly in recent years, especially among women. These adverse trends clearly need to be aggressively tackled with age and gender-specific public health strategies targeting diet and physical activity. Effective, evidence-based public health policies exist and should now be implemented more energetically.

## Funding

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## Authors' contributions

ZK, JC, SC and KB conceived the idea; ZK performed the analyses and drafted the first manuscript, with inputs from IJP, JC, SC and KB. MOF refined the original IMPACT model, with inputs from JC and SC. All authors contributed to the interpretation and final draft of the manuscript. ZK and KB have access to full data sets. KB is the guarantor of the manuscript.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ijcard.2013.03.007.

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