TITLE: Explaining the Fall in Coronary Heart Disease Mortality in the Republic of Ireland between 2000 and 2015 - IMPACT Modelling Study

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ABSTRACT

Around 200 words (word count 198)

Background: To investigate the contribution of individual and population determinants to reduced coronary heart disease (CHD) mortality rates in Ireland between 2000 and 2015.

Methods: The Irish IMPACT CHD model was utilized with CHD Deaths Prevented or Postponed (DPPs) as outcome.

Results: CHD mortality rates in Ireland in those aged 25-84 years fell by -56% (-63% in women vs. men -53%), with 4060 fewer deaths than expected in 2015.

Improvements in CHD risk factors explained ~30% of the observed decline (785 DPPs in men; 425 in women): [population systolic blood pressure (-25%), mean cholesterol serum levels (-11%) and smoking prevalence (-5%)]. However, additional mortality came from rises in diabetes prevalence (+6% DPPs), BMI (+4%) and physical inactivity (+2%).

Increased cardiology treatments explained ~60% of the decline (1620 DPPs in men; 825 in women), particularly secondary prevention and heart failure treatments. Some 10% was unexplained.

Conclusion: CHD mortality declined in Ireland between 2000 and 2015, with some two thirds attributable to increased cardiology treatments uptake and just one third to improvements in population risk factors, partly reflecting adverse trends in obesity, diabetes and physical inactivity. Additional investments in prevention policies and treatments will be necessary to reduce future CHD deaths.

BACKGROUND

Coronary Heart Disease (CHD) is defined as disease of the blood vessels supplying the heart muscles and is a leading cause of death in the world contributing to 7.4 million of all global deaths in 2015. (1) However, CHD mortality rates have been decreasing in developed countries in the recent years unlike low to middle income countries. (1) Although Ireland has one had large reductions over the past 30 years, lower mortality rates do not necessarily equate to lower disease burden. (2) Improved survival leads to a higher disease burden and to more hospital admissions. In 2015, CHD cost Ireland approximately 158 million euros. (3) In our previous studies, we have shown a continued decline in CHD mortality rates from 1985 onwards until 2006. In this study, we examined if such a decline in CHD continued from 2000 until 2015 in Ireland, and to provide explanations for any changing pattern with regard to contributions of risk factor and treatment uptake.

METHODOLOGY

The methods employed here are similar to our previous CHD modelling studies published elsewhere (4,5). Data sources have been appended (Appendix 1-3).

IMPACT CHD Model

Previous studies have used the validated CHD IMPACT model to explain the contributions of treatments and CHD risk factors on CHD mortality rates in different populations through merging epidemiological data that is available for each country.(4,6)

Population data

Data on the population of Republic of Ireland (ROI) and CHD deaths of those aged between 25-84 years in 2000 (baseline year) and 2015 were collected and stratified by age and gender (see Appendix 1 for details on sources). Individuals older than 84 years were not included because of potential unreliability of cause of death.(5)

CHD Deaths

The International Classification of Diseases (ICD) codes (ICD9 (410–414) and ICD10 (I20– I25) were used. Age-standardised CHD mortality rates were calculated in 10-year age group intervals and gender specific analyses were performed.

Mortality rates in 2000 were calculated and used as base year for the indirect age standardisation of expected CHD deaths in 2015 if the mortality rates in 2000 have been stable. The expected number of CHD deaths was calculated by multiplying age and gender specific mortality rates in 2000 by the population size for each 10 year age-gender stratum in 2015. The number of deaths prevented/postponed (DPPs) were determined by subtracting the actual numbers of CHD deaths in 2015 from the expected numbers in 2015 if the age and gender specific mortality rates in 2000 persisted using the IMPACT model which accounted for the increasing life expectancy.

Risk Factors

The CHD risk factors analysed in this study consist of population total blood cholesterol, population mean systolic blood pressure (SBP), body mass index (BMI) as measurement for obesity, prevalence of tobacco smoking, (lack of) physical activity and diabetes mellitus (see Appendix 2). The expected number of CHD deaths in 2015 was estimated for a particular risk factor (see Appendix 4).

Use of medical/surgical interventions

Data was gathered on the CHD diagnostic groups and uptake of treatments (5) through different databases (details can be found in Appendix 3 and 5). If current data was unavailable through registries or databases, high quality literature was sought i.e. meta-analyses, randomised controlled trials or cohort studies containing the necessary data (see Appendix 1-3).

Compliance, defined as the percentage of eligible patients taking the medications effectively, was assumed to be 100% in hospital patients, 70% in symptomatic community patients and 50% in asymptomatic community patients.(4) Sensitivity analyses were conducted to test these assumptions.(4) Potential double counting of patient data was addressed by making adjustments. (4,5).

Polypharmacy was examined using the Mant and Hicks cumulative benefit approach. (5) The relative reduction was calculated by subtracting the relative benefit (%) from the additive value.

The effectiveness of medical/surgical interventions was calculated by estimating the DPPs for at least a year attributable to each CHD treatment within a disease subgroup (stratified by age and gender) (for further details see Appendix 5).

Results

CHD death rates decreased from 590 deaths/100000 in the year 2000 to 260 deaths/ 100000 in the year 2015 reflecting a decline of 56% in CHD death rate. A total of 2844 CHD deaths were reported by the Central Statistics Office (CSO) in 2015 for the age group 25-84 years. We estimated that 6900 CHD deaths would have occurred in 2015 if the mortality rates for 2000 had persisted, which equates to 4060 deaths prevented or postponed or DPPs. Our model explained 90% of the observed DPPs which were attributable to both improvements in cardiology treatment and in population risk factors (Table 1 and 2, Appendix 6).

CHD mortality rates fell by 53% among men aged 25-84 years, (780 per 100000 in 2000 to 370 per 100000 in 2015) and by 63% mortality rates among women (from 410 per 100000 in 2000 to 150 per 100000 in 2015). That mortality fall represented approximately 2425 DPPs in men and 1235 DPPs in women.

Changes in the major risk factors for CHD explained approximately 1210 fewer CHD deaths (785 fewer deaths in men, 425 fewer deaths among women), representing some 30% of the observed fall in CHD mortality (see Table 1).

Lower population SBP contributed the most to the fall in DPPs, followed by a decreased population cholesterol and smoking prevalence, contributing -25%, -11% and -5% respectively. However, increases in diabetes prevalence, population BMI and physical inactivity levels generated increases in mortality of +6%, +4% and +2% respectively. Medical interventions for coronary heart diseases have prevented or postponed approximately 2445 CHD deaths (min estimate 840, max estimate 5280) representing approximately 60% of the CHD mortality decline (see Table 2).

Discussion

CHD mortality in Ireland continued to decline from 2000 to 2015, falling by 56% in those aged 25-84 years, and was greater in women (63%) than in men (53%).

Compared to our previous trend analyses from 1985 onwards observations (4,6), the current study has shown that recent improvements in population cardiovascular modifiable risk factors have been relatively modest, thus diminishing their contribution to the overall mortality CHD decline.

This specific observation is crucial for both the Irish cardiovascular health strategy and also for the newly developed Sláintecare report (7). The diminishing risk factor contribution represents a huge opportunity cost compounded by a failure to counteract escalating obesity, diabetes and inactivity. Prevention programmes addressing the most powerful population CHD risk factors (blood pressure, smoking, cholesterol and obesity), therefore need to be urgently strengthened.

An early meta-analysis reported a doubling of diabetes prevalence among Irish adult population in the last two decades.(8) has now been succeeded by more encouraging recent figures showing a deceleration in childhood obesity trends (9). However, 65% of Irish adults overweight or obese, and thus at high risk of future type 2 diabetes and CHD. Comprehensive multi-component obesity prevention strategies will thus be necessary to further decrease CHD deaths in Ireland.

These structural population level approaches should include bold regulatory legal and fiscal policy interventions, to reduce smoking prevalence below 5%, implement more comprehensive sugar reduction across the food system and strengthening salt reformulation of processed foods.(11–13) Conversely, the recent weakening of the Food Standards Agency (FSA) salt reduction programme in UK has generated an additional 35 000 extra CVD cases and £1.1billion additional health care costs within the next decade. (14) Furthermore, targeted interventions might have a role in complementing structural policies by stimulating the reduction of health inequalities and tackling diseases less amenable for structural prevention.(15)

Policy-makers, health providers and knowledge users therefore need to be cognisant of the study findings to inform successful strategic planning and thus transform population health and well-being. This would maximise return on investments from population level preventive interventions rather than costly treatments.

This analysis has a number of strengths and weaknesses....

In conclusion, further investment in structural policies to improve population risk factors, especially diets and physical activity will be necessary to consolidate and accelerate recent health gains, and to reduce gender inequalities in Ireland.

BIBLIOGRAPHY

- WHO [Internet]. [cited 2017 Mar 2]. Available from: http://www.who.int/cardiovascular_diseases/publications/global_brief_hypertension/en
- Hartley A, Marshall DC, Salciccioli JD, Sikkel MB, Maruthappu M, Shalhoub J. Trends in Mortality From Ischemic Heart Disease and Cerebrovascular Disease in Europe: 1980 to 2009. Circulation [Internet]. 2016 May 17;133(20):1916–26. Available from:

http://www.ncbi.nlm.nih.gov/pubmed/27006480

- Wilkins E, Wilson L, Wickramasinghe K, Bhatnagar P, Leal J, Luengo-Fernandez R, Burns R, Rayner M TN. European Cardiovascular Disease Statistics 2017 [Internet]. European Heart Network, Brussels. 2017 Oct. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24014390
- Kabir Z, Perry IJ, Critchley J, Flaherty MO, Capewell S, Bennett K. Modelling Coronary Heart Disease Mortality declines in the Republic of Ireland , 1985 – 2006. Int J Cardiol [Internet]. 2013;168(3):2462–7. Available from: http://dx.doi.org/10.1016/j.ijcard.2013.03.007
- Bennett K, Kabir Z, Unal B, Shelley E, Critchley J, Perry I, et al. Explaining the recent decrease in coronary heart disease mortality rates in Ireland, 1985-2000. J Epidemiol Community Health [Internet]. 2006;60(4):322–7. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2566167&tool=pmcentrez& rendertype=abstract
- Flaherty MO, Bandosz P, Critchley J, Capewell S, Guzman-castillo M, Aspelund T, et al. Exploring potential mortality reductions in 9 European countries by improving diet and lifestyle : A modelling approach. Int J Cardiol [Internet]. 2016;207:286–91. Available from: http://dx.doi.org/10.1016/j.ijcard.2016.01.147
- Committee on the Future of Healthcare. Slaintecare report ; An Coiste um Chúram Sláinte sa Todhchaí Tuarascáil maidir le Cúram Sláinte [Internet]. 2017. Available from: file:///Users/vive/Downloads/270718095030-1134389-Slaintecare-Report-May-2017 (2).pdf
- Tracey ML, Gilmartin M, O'Neill K, Fitzgerald AP, McHugh SM, Buckley CM, et al. Epidemiology of diabetes and complications among adults in the Republic of Ireland 1998-2015: a systematic review and meta-analysis. BMC Public Health. 2016;16(1):132.
- 9. Keane E, Kearney PM, Perry IJ, Kelleher CC, Harrington JM. Trends and prevalence of overweight and obesity in primary school aged children in the Republic of Ireland

from 2002-2012 : a systematic review. 2014;

- Nichols M, Townsend N, Scarborough P, Rayner M. Trends in age-specific coronary heart disease mortality in the European Union over three decades: 1980-2009. Eur Heart J. 2013;34(39):3017–27.
- 11. Department of Health. Tobacco Free Ireland [Internet]. 2013. Available from: https://health.gov.ie/wp-content/uploads/2014/03/TobaccoFreeIreland.pdf
- Novotny TE. The Tobacco Endgame: Is It Possible? PLOS Med.
 2015;12(5):e1001832.
- Hyseni L, Elliot-Green A, Lloyd-Williams F, Kypridemos C, O'Flaherty M, McGill R, et al. Systematic review of dietary salt reduction policies: Evidence for an effectiveness hierarchy? PLoS One [Internet]. 2017;12(5):e0177535. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28542317
- 14. Laverty A, Kypridemos C, Seferidi P, Vamos EP, Pearson-Stuttard J, Collins B, et al. Quantifying the impact of the Public Health Responsibility Deal on salt intake, cardiovascular disease and gastric cancer: interrupted time series and microsimulation study. J Epidemiol Community Heal. 2019;(In press).
- Kypridemos C, Allen K, Hickey GL, Guzman-Castillo M, Bandosz P, Buchan I, et al. Cardiovascular screening to reduce the burden from cardiovascular disease: microsimulation study to quantify policy options. BMJ [Internet]. 2016 Jun 8;353:i2793. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27279346

TABLES

TABLE 1. Changes in CHD risk factors and DPPs by gender (approximations-rounded to the closest integer)*

Risk Factors	2000*	2015*	DPPs (%)**	DPPs(Males)	DPPs(Females)

Smoking	29%	23%	190 (-5.0)	110	80
Mean SBP*	131	125	1030 (-25.0)	825	205
Total cholesterol	5.6	5.3	455 (-11.0)	250	205
Physical inactivity	31.1%	38.8%	-65 (1.5)	-45	-20
Mean BMI*	26.8	27.6	-165 (4.0)	-130	-35
Diabetes	2.9%	3.6%	-235 (5.5)	-225	-10
Total			1210 (30.0%)**	785 (19%)**	425 (11%)**

*Abbreviations: CHD=Coronary Heart Disease, DPPs=Deaths prevented or postponed, SBP=Systolic blood pressure, BMI=Body Mass Index

** Percentages are depicted with the total DPP (N=4060) as denominator. Note that when risk factors improved, the DPP were positive and when risk factors deteriorated, the DPP were negative.

TABLE 2. Medical Interventions for CHD and DPPs by gender*

Medical Interventions	Overall N (%)**	Male	Female
Overall AMI treatments	270 (6 5)	200	70
	270 (0.0)	200	10
Secondary prevention	810 (20.0)	560	250
post AMI*			

Total treatments	2455 (60 %)**	1620 (40%)**	825 (20%)**
Anti-hypertensive drugs	20 (0.5)	5	15
prevention			
Statins for primary	55 (1.0)	25	30
community			
Heart failure in the	405 (10.0)	220	185
hospital			
Heart failure in the	205 (5.0)	135	70
Unstable angina	65 (1.5)	45	20
angina			
Community (chronic)	220 (5.5)	140	80
post CABG* or PTCA*			
Secondary prevention	395 (10.0)	290	105

* Abbreviations: CHD=Coronary Heart Disease, DPPs=Deaths prevented or postponed AMI=acute myocardial infarction, CABG=coronary artery bypass graft, PTCA=Percutaneous transluminal coronary angioplasty

** Percentages are depicted with the total DPP (N=4060) as denominator