QJM Advance Access published May 7, 2014

Q J Med
doi:10.1093/qjmed/hcu083 Advance Access Publication 11 April 2014

Trends in death attributed to myocardial infarction, heart failure and pulmonary embolism in Europe and Canada over the last decade

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Received 19 February 2014 and in revised form 26 March 2014

Summary

Background: Worldwide, cardiovascular diseases and cancer account for ~40% of deaths. Certain reports have shown a progressive decrease in mortality. Our main objective was to assess mortality trends related to myocardial infarction (MI), heart failure (HF) and pulmonary embolism (PE).
Methods: MI, HF and PE were studied as cause of death based on the analysis of death certificates in Canada (C), England and Wales (E), France (F) and Sweden (S). We also used a multiple cause approach. Age-standardized death rates (SDR) were calculated.
Results: The SDR for MI, HF or PE as the underlying cause of death, all decreased during the last decade. The decrease in SDR secondary to MI exceeded that for HF or PE. Concerning multiple cause of death, a greater decrease was also found for MI, compared with HF or PE.
Conclusions: We confirm the beneficial trends in SDR with MI, HF or PE both as underlying or multiple causes in the studied countries. For HF and PE, multiple cause approach seems more accurate to describe the burden of these two pathologies. Our study also suggests that more efforts should be dedicated to HF and PE in order to achieve similar trends than in MI.

Introduction

Worldwide, cardiovascular diseases and cancer account for ∼40% of deaths.[1–4] Regarding cardiovascular diseases, certain reports have shown a progressive decrease in the mortality, but studies were mostly related to a single cardiovascular disease like heart failure (HF)[5,6] or myocardial infarction (MI) and often focused at one country.[7–9] Decreases in mortality over the last decade can be partially attributed to better definition of acute coronary syndromes (ACS), to the implementation of published guidelines in both North America and Europe[10,11] and effective use of specific therapeutic strategies. Similarly, important efforts have been made to improve the knowledge, definitions and management of HF and pulmonary embolism (PE).[12,13] Long lasting therapy of chronic stable heart failure including β-blockers, ACE, aldosterone antagonists have been shown to prevent acute decompensated heart failure and to improve outcome. Acute decompensated heart failure is still associated with high mortality rate and very few therapeutic advances have been made recently.

Accordingly, based on different guidelines implementation and different therapeutic advances in these different diseases, we hypothesize in the current study that improvement in death rate related to MI was more pronounced than the improvement in the death rate of two other major cardiovascular diseases: HF and PE. Lung cancer (LC) another deadly disease, closely related to tobacco consumption, was chosen as a non-cardiovascular comparative.[14,15]

Thus, our main objective was to assess and compare mortality trends related to MI, HF and PE, as the three most frequent cardiovascular causes of death and compare them with LC in Canada and in Europe.

Methods

The causes of death by MI, HF, PE and LC were studied based on the analysis of death certificates in Canada (C), England and Wales (E), France (F) and Sweden (S). In Canada, England and Wales, France and Sweden, all causes of death are reported to the authorities. These data are based on the information provided by medical doctors on each death certificate. This compulsory reporting and certification of death by medical professionals results in the ascertainment of causes of death and is used for the analysis of the trends in various diseases.[16] Using national mortality databases (See Appendix), we obtained, in each of the four countries, detailed data on cause of death from 2001 to 2009. The study was performed according to regulations about privacy.

Methods used for death certificate analysis have been published elsewhere.[5] Briefly, death certificates are standardized among the studied countries and contain two sections in which physicians enter the causes of death. Part I asks for the sequence of events leading directly to death from the 'underlying' cause of death to the direct cause. Part II allows the physician to enter other conditions that indirectly contributed to death (contributing causes of death). The causes of death analysis are usually based on the underlying cause of death. Here, in addition to this method, we used a multiple cause approach. The multiple cause of death for a specific disease is defined if the disease is mentioned anywhere on the death certificate.[5]

Data were retrieved from national mortality databases using the coding rules of the International Classification of Diseases (ICD) 10th revision.[6,17] Supplementary Table S1 indicates the codes used to select the number of annual deaths with MI, HF, PE and LC as underlying or multiple causes that corresponds to any disease mentioned in Parts I and/or II (disease as underlying and/or as associated cause of death). Of note, the multiple causes of death were not yet available for Canada during the study period. In order to compute death rates, resident populations were also obtained for each country and year.

Age-specific mortality rates were computed for each 5-year age group (from 0–4 to 80–84 and above 85 years) and calendar year. Age-standardized death rates (SDR) per 100 000 population were calculated using the direct standardization method, on the basis of the Eurostat, European standard population (Supplementary Table S2). This standardization allows to control age when comparing mortality rates among populations with different age structures.[16] These SDR were calculated per year for each country.

All-cause mortality similarly decreased in all four countries over the last decade (Supplementary Figure S1) at a rate of 2.06% per year (95% CI: 1.86–2.26%) and was similar among all studied countries ($P = 0.07$). This corresponds to 11.1 deaths per 100 000 population per year. When considering the underlying cause of death, the four studied diseases (HF, MI, PE and LC) represent 16.6% of all deaths in 2001. Of note ICD codes used to retrieve the number of deaths were: I50 for HF, I21 for acute MI, C34 for malignant neoplasm of bronchus and lung and I26 for PE.

Measures of mortality include the number of deaths, mean age at death and SDR for the total population when analyzing the underlying cause of death. When considering the multiple cause of death, SDR were computed for the population of the European countries. We also computed SDR by gender and for two age categories (0–74 years, ⩾75 years). These data were computed for each disease in each country separately and for the total study population.

Statistical analysis

We compared SDR trends by disease, country, sex and age at death using contingency tables. Depending on the question, models including year, gender, age category, country and their interaction were fitted. Association between mortality rates and covariates were assessed using a partial Wald test or maximum likelihood ratio tests. The percentage of SDR increase or decrease was calculated considering the value in 2001 equal to 100 for each category. Similar linear models were performed. Impact of year on age at death was evaluated using a linear model with a pathology interaction. All tests were at the 0.05 level and are two sided. All analyses were performed using *R* 2.15 (http://www.R-project.org).

Results

Table 1 and Figure 1a show that the SDR for MI, HF or PE as the underlying cause of death, all decreased during the last decade, whereas LC remained stable. The decrease in SDR secondary to MI as an underlying cause exceeded that for HF or PE [−5.4% vs. −3.1% ($P<0.001$) and −3.9% ($P=0.001$) per year, respectively]. The absolute decrease in SDR due to MI (−2.7 deaths/100 000/year) was 5- to 10-fold greater than the decrease in SDR due to HF (−0.5 deaths/100 000/year, $P=0.003$) or PE (−0.2 deaths/100 000/year, $P<0.001$) (Table 2).

Concerning multiple causes of death, a greater decrease was also found in the SDR due to MI (−5% per year), compared with that of HF (−2.5% per year) or PE (−2.4% per year), ($P<0.001$) (Figure 1b). The corresponding decrease in the absolute number of deaths was −2900 for MI, −1900 for HF ($P=0.28$) and −300 for PE ($P=0.006$). In 2009, the absolute number of deaths due to HF were 2-fold greater than MI and 5-fold greater than PE. Figure 1d shows the mean age at death from MI, HF and PE. Mean age of death was 4 years more in HF as compared with MI and PE over the study period. We observed a

Table 1 Age-adjusted death rate with diseases as underlying or multiple cause of death in 2001 and 2009 and death rates evolution expressed in percentage from 2001 to 2009

		Underlying cause			Multiple cause		
		2001	2009	Evolution (%)	2001	2009	Evolution (%)
Myocardial infarction	England and Wales	58.8	30.3	**−48.5**	64.2	34.8	**−45.8**
	France	27.9	16.8	**−39.8**	35.3	22.3	**−36.8**
	Sweden	70.0	44.1	**−37**	79.2	51.4	**−35.1**
	Canada	50.8	31.1	**−38.8**			
Heart failure	England and Wales	10.9	7.5	**−31.2**	70.9	49.7	**−29.9**
	France	21.8	15.7	**−28.0**	71.5	54.8	**−23.4**
	Sweden	16.8	15.6	**−7.1**	89.1	85.3	**−4.3**
	Canada	11.2	7.6	**−32.1**			
Pulmonary embolism	England and Wales	3.7	3.3	**−10.8**	15.4	13.7	**−11.0**
	France	5.2	3.9	**−25.0**	15.8	11.9	**−24.7**
	Sweden	4.4	2.5	**−43.2**	10.7	9.2	**−14.0**
	Canada	1.9	1.4	**−26.3**			
Lung cancer	England and Wales	40.6	37.8	**−6.9**	43.1	40.3	**−6.5**
	France	34.8	36.0	**+3.4**	37.9	39.2	**+3.4**
	Sweden	25.3	24.7	**−2.4**	26.6	26.1	**−1.9**
	Canada	49.0	45.0	**−8.2**			
All cause mortality	England and Wales	672.1	551.7	**−17.9**			
	France	603.5	511.3	**−15.3**			
	Sweden	599.5	520.4	**−13.2**			
	Canada	594.2	507.2	**−14.6**			

Age-adjusted death rates are given in number of deaths per 100 000 population.

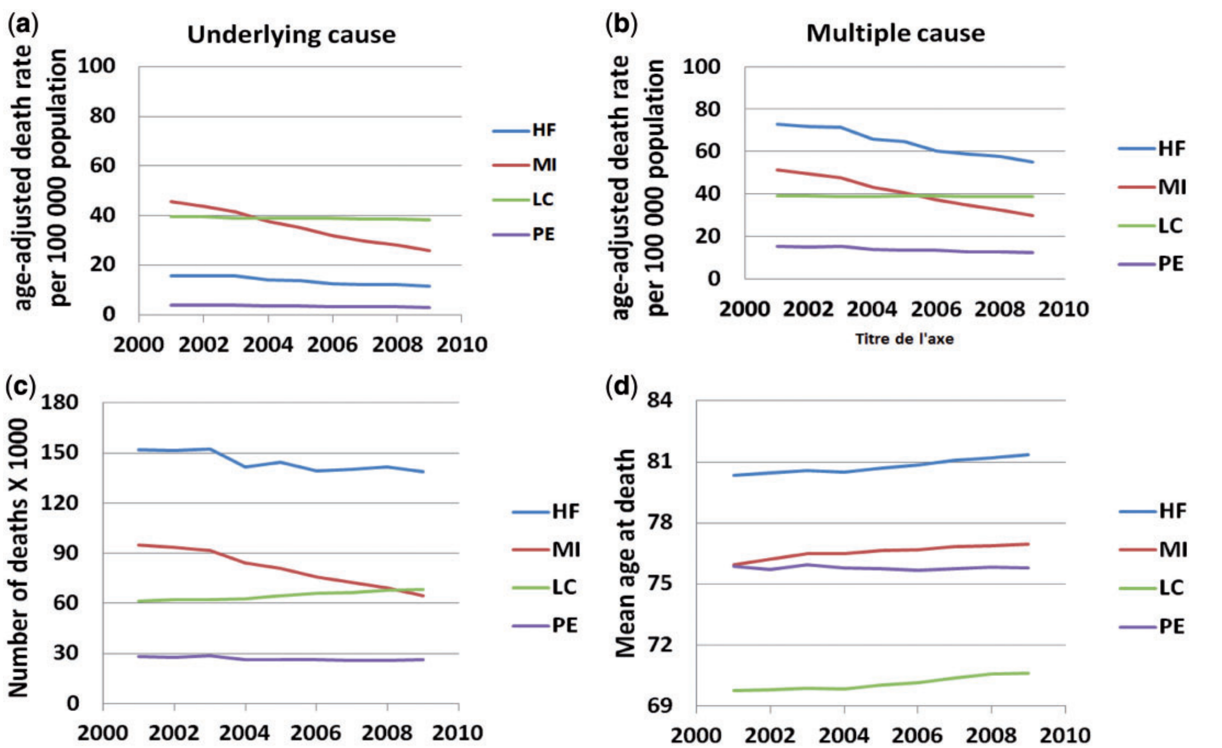

Figure 1. Trends in death characteristics in recent years. (**a**) Age-standardized death rates with diseases as underlying cause in the four studied countries considered as a whole. (**b**) Age-standardized death rates with diseases as multiple cause (i.e. mentioned anywhere on the death certificate) in the three European countries considered as a whole, (**c**) number of deaths with diseases as multiple cause in the three European countries considered as a whole and (**d**) mean age at death with each disease as a multiple cause of death in the three European countries considered as a whole.

Table 2 Slopes and total percent decrease in age-adjusted death rates. Data are presented with the three cardiovascular diseases as underlying or multiple causes of death

	MI		HF				PE			
	Slope	Percent	Slope	*P*-value*	Percent	*P*-value*	Slope	*P*-value*	%	*P-value**
Underlying cause	−2.7	−5.4	−0.5	0.003	−3.1	<0.001	−0.2	<0.001	−3.9	0.001
Multiple cause	−2.9	−5	−1.9	0.28	−2.5	<0.001	−0.3	0.006	−2.4	<0.001

**P*-value when comparing slopes or total percent decrease with MI taken as a reference. Age-adjusted death rates are given in number of deaths per 100 000 population.

parallel increase in the mean age at death for HF and MI by an average of 1 year over the study period ($P = 0.15$). For PE, however, the age at death was stable over the study period ($P < 0.0001$).

LC, a leading cause of death in Canada and Europe, had a similar SDR, as compared with MI, in 2001. However, trends were markedly divergent, being stable for LC as underlying (0.2% per year, $P = 0.5$) or multiple cause (0.5% per year, $P = 0.18$).

Though the baseline values were different among studied countries, the above mentioned death rate decline was homogeneous for all countries in our analysis (Supplementary Figure S2 for cardiovascular diseases as underlying cause of death and Supplementary Figure S3 for multiple causes of death).

Figure 2 exhibits SDR trends with HF, MI, PE and LC as multiple causes of death by age category, below and above 75 years and by gender. We observed a near 40-fold difference in the absolute levels of SDR for MI, HF, PE or LC as multiple causes between <75 years and ⩾75 years. Furthermore, the decrease in SDR with MI or HF as multiple causes was more pronounced in patients <75 years than ⩾75 years (−5.6%/year vs. −4.4%/year, $P < 0.001$ for MI, −3.6%/year vs. −2.1%/year, $P = <0.001$ for

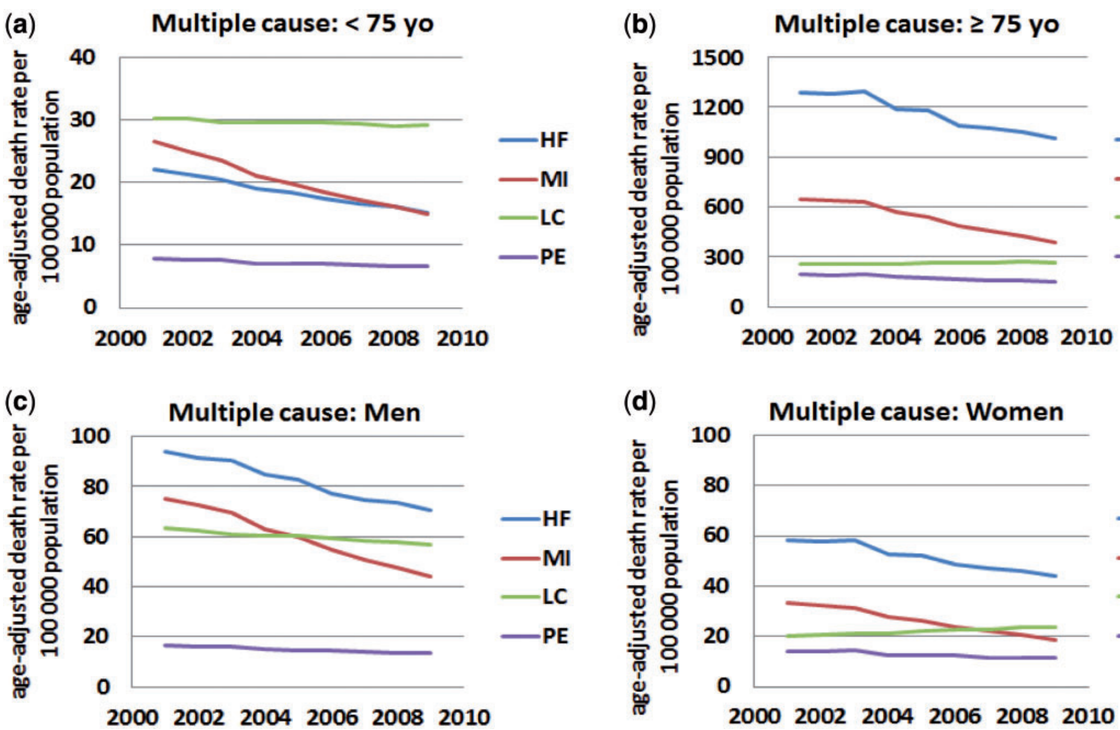

Figure 2. Age-adjusted death rates with diseases as multiple causes of death. By age category and by gender. (**a**) <75 yrs. (b) ⩾75 yrs (**c**) Men and (d) Women.

Table 3 Percentages of decrease in age-adjusted death rates

		Men (%)	Women (percent)	*P*-value	<75 years (%)	⩾75 years (%)	*P* value
Underlying cause	MI	−5.3	−5.3	0.81	−5.2	−5.3	0.73
	HF	−3.3	−3.3	0.92	−2.7	−2.8	0.06
	PE	−4	−4	0.98	−4	−4	0.31
Multiple cause	MI	−5.1	−5.1	0.91	−5.6	−4.4	<0.001
	HF	−2.8	−2.6	0.64	−3.6	−2.1	<0.001
	PE	−2.2	−2.2	0.95	−2.2	−2.3	0.67

Data are presented with the three cardiovascular diseases as underlying or multiple cause by age category and by gender. *P*-value is calculated when comparing age categories or genders.
Age-adjusted death rates are given in number of deaths per 100 000 population.

HF). However, no difference was found as a function of age in SDR for PE as multiple cause, the observed decrease was similar in the two age categories (−2.2% and −2.3% per year, $P = 0.67$) (Table 3).

Figure 2 also showed similar trends in SDR for the three cardiovascular diseases between genders (Table 3).

We then decided to calculate for each disease and for the year 2009, the following ratio: number of cases with disease coded as multiple causes divided by the number of cases with disease coded as underlying cause of death. Obtained results were for MI: 1.16 in England and Wales, 1.34 in France and 1.16 in Sweden; very similar to ratios obtained for LC: 1.07 (E&W), 1.10 (F) and 1.06 (S). Ratios were higher for HF: 5.99 (E&W), 3.35 (F) and 5.00 (S) and PE: 3.94 (E&W), 2.99 (F) and 3.61 (S).

Discussion

Our study is one of the first to compare recent trends in cardiovascular deaths at a disease level in Canada and Europe.[18] We found that the percent decrease in SDR, when taking 2001 as reference, with MI as underlying or multiple causes was much greater than that seen for HF or PE in the last decade for the selected developed countries. Furthermore, the improvement in SDR with MI and HF as cause of death was more pronounced in patients <75 years than in those aged >75 years. Another strength of this study is to consider not only the single underlying cause of death, but to also report in those cases where multiple causes were contributory to the final outcome.[19,20] The observed ratios with number of cases with disease coded as multiple cause divided by the number of cases with disease coded as underlying cause of death are very close to 1 for MI and LC, whereas these ratios are constantly >2.5 for HF or PE. Our interpretation is that the number of cases with diseases as underlying cause of death seems to be robust and can possibly describe the burden for certain diseases like MI or LC. However, for other diseases like HF and PE, considering multiple causes of death is more accurate to describe the burden of these two pathologies as they are more often coded as contributing cause of death.[5,21]

Our study confirms the persistence of beneficial trends in SDR with MI, HF or PE both as underlying or multiple causes in each of the four studied countries in recent years. The improvement in SDR slope with MI as underlying cause of death was more pronounced, 5- to 10-fold greater, than for both HF and PE. This great improvement in MI mortality trends can possibly be explained by a better management of this disease including early management in the pre-hospital setting, improvement in early pharmacological treatment and increased use of reperfusion therapy, in particular, percutaneous coronary intervention (PCI). These factors, coupled with improvement in research infrastructure and joint efforts of Emergency Department (ED) physicians and cardiologists, have resulted in significant progress in reducing the deaths related to acute coronary syndrome (ACS). Our hypothesis is in line with the results of a recent publication analyzing survival after ACS in four French registries from 1995 to 2010.[22] These results strongly suggest that efforts started years ago on the management of MI[23,24] have led to tremendous success and should be continued. Our study also suggests that much more efforts should be dedicated to HF and PE management in order to achieve successful trends in mortality, similar to those observed with MI. This includes more research for the early diagnosis and the early management of HF or PE both in the ED and later during hospitalization. Those increasing efforts should be started very rapidly as the prevalence of HF has been increasing in the past years in developed countries.[25,26]

No difference was found, when comparing SDR trends with MI, HF or PE as underlying or multiple causes between genders. Our data are also in line with the general decrease of cardiovascular mortality in developed countries.[27,28]

Limitations

The use of mortality data in evaluating disease burden has limitations. Mortality rate is an incomplete indicator of disease burden. Such indicators depend on the quality of the medical certification and the level of detail of the coding system, which is not standardized across countries. The main potential issue is due to the reliability of death certification and validity in various countries.[16,29] Inaccuracies in death certificates are potential limitations in the interpretation of mortality trends. However, because death is an objective endpoint ultimately reflective on the quality of care delivery within a country, the use of death certificates to assess outcomes is common in various areas of medicine.[30–32] Another limitation using death certificates in our analysis is that it is purely descriptive, without any mean to ascribe observed SDR trends to the evolution of the health care system. Death certificates are increasingly used in research on cardiovascular diseases.[33–35] Furthermore, no change in ICD version occurred during the study period.

In summary, this study showed a continuous decrease in mortality trends for three major cardiovascular diseases over the last decade, confirming, at a disease level, the improvement of cardiovascular mortality in developed countries. This is especially true for MI in which large research and delivery of care efforts have been made to include the pivotal role of ED physicians in the very early management (golden hours) and to speed up admission to the catheterization lab. However, improvement in HF and PE mortality is moderate compared with the striking improvement in outcome in MI and no change in mortality was seen in LC. Those results urge medical community to maintain or even increase efforts to cure those diseases.

Supplementary material

Supplementary material is available at *QJMED* online.

Acknowledgements

Authors would like to thank the following persons who helped for data collection: Claudia Wells, Centre for Health Analysis and Life Events | Office for National Statistics, England and Wales. Charlotte Bjorkenstam, Socialstyrelsen, The National Board of Health and Welfare, Sweden. S.L. and A.M. worked

on the conception and design of the study, analysis and interpretation of data, drafting of manuscript. A.A., H.J. and M.E. performed data acquisition and critical revision of the manuscript. W.F.P., J.M., J.A.E., A.C.S. and P.P. did a critical revision of the manuscript. E.J. worked on the conception and design of the study and critical revision of the manuscript. M.R.R. conducted the statistical analysis.

Conflict of interest: None declared.

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