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# Explaining Structural Change in Cardiovascular Mortality in Ireland 1995-2005: A Time Series Analysis

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*Abstract*: **Background:** Deaths from circulatory respiratory causes among older age groups in Ireland fell sharply between 1995 and 2005 as did the seasonality of deaths from these causes.**Objective:**To examine whether a structural break has occurred in deaths from circulatory causes in Ireland between 1995 and 2005 and test whether this can be explained by changes in the prescribing of cardiovascular medications during the same period controlling for weather trends. **Methods:** Grouped logit Time series models were used to identify if and at which quarter a structural break occurred in Irish circulatory deaths between 1995 and 2005. Data on cardiovascular prescribing and temperature within the quarter were entered into the trend-break model to examine whether the structural break could be explained. **Results:** There was a reduction in circulatory deaths of 0.82%/quarter among men 1995-2005 which increased by 0.5%/quarter after the final quarter of 1999. The 25% excess winter deaths among men fell by 9% after Q4 1999. Among women the long term decline in deaths of 0.53%/quarter increased by 0.48% after Q1 2000 and seasonality was reduced by 6.8%. The structural break in trend and seasonality was higher among those aged 85+. Controlling for temperature, beta-blocker, ace-inhibitor and aspirin medications rendered the structural break indicator insignificant among all age groups for men. Diuretic, statin and calcium channel blocker medications could not explain the break point for men aged 75 to 84. Beta blocker, aspirin and calcium channel blocker medications explained mortality trends among all age groups among women. Ace inhibitor and statin could not explain trends amongst women aged 65-74 and nitrates and diuretics did not explain trends for any age group. **Conclusions:** Models suggest that cardiovascular prescribing significantly reduced circulatory mortality among men and women aged 65+ after 1999 in Ireland but the effect of prescribing was lower among women than men. Beta-blocker, ace inhibitor and aspirin medications were more successful than statin, diuretic and nitrates at explaining trends.

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# Explaining Structural Change in Cardiovascular Mortality in Ireland 1995-2005: A Time Series Analysis

## 1. INTRODUCTION

As elsewhere in the EU15, all cause death rates have been falling steadily in Ireland since the 1970s but the rate of improvement has been particularly pronounced since the turn of the 21st century. Between 1996 and 1999 all cause death rates in Ireland fell by 5.2%, but by 26.2% between 2000 and 2004. The trend change can largely be explained by lower death rates from circulatory and respiratory causes (Layte et al 2007). Death rates from circulatory causes fell by 29.6% between 2000 and 2005 and deaths from respiratory causes by 29.1%. Research (Bennett et al 2006) suggests that the long term downward trend in circulatory death rates prior to 2000 in Ireland can be explained by changes in lifestyle and diet in combination with improved secondary prevention. No research to date has explained the acceleration in the trend in circulatory deaths since 2000 but trends in lifestyle factors since 2000 are challenging and cannot explain the change. Although the steep fall in respiratory death rates may also be related to the processes discussed in this paper[1] we confine our analyses here to trends in circulatory deaths rates and leave trends in respiratory deaths to a future paper.

Previous analyses (Walsh 2007) have shown that a significant proportion of the fall in mortality rates can be explained by a decrease in the extent of excess winter deaths, that is, the size of the increase in mortality in winter months over summer months each year (Wilmhurst, 1994, Healy 2000, Healy 2003). Together, the extent of the fall in deaths after 1999 and the fall in seasonality from that point would suggest that there has been a structural break in Irish mortality trends but to date no explanation has been put forward for either the timing or nature of the change.

[1] The extent of comorbidity between COPD and cardiovascular disease may mean that deaths attributed to respiratory disease may have their origin in cardiovascular events. Mascarenhas et al (2008) found that almost 40% of patients who were post AMI also had a diagnosis of COPD. Given this, better control of the symptoms of heart failure would reduce respiratory mortality as well as circulatory mortality.

The change in the seasonality of deaths could suggest that meteorological factors in the form of warmer winter weather, perhaps associated with global warming trends may play a role. An alternative explanation could be the change which occurred in patterns of prescribing for cardiovascular disease in the late 1990s in Ireland in combination with an increase in access to care which occurred after 2001. 'Building Healthier Hearts' (BHH), the report of the Irish cardiovascular health strategy group was published in 1999 (DOHC 1999). This recommended a set of priorities including a structured approach to the primary and secondary prevention of cardiovascular disease. The recommendations were widely adopted within Irish general practice but were also accompanied by increased investment in cardiology manpower in the Irish hospital sector, an increase in the volume of CABG and PTCA surgery[2] carried out and the establishment of a 'shared care' system between GPs and out patient departments for heart failure. Within primary care BHH recommended the adoption of the guidelines of European task force on coronary prevention and this was formalised in one fifth of GP practices who participated in the 'Heart Watch' programme which established a system of secondary prevention. Together these developments may have contributed to a steep increase in the volume of cardiovascular drugs prescribed after 1999. Between the summer of 1999 and end of 2003 prescribing rates of beta blockers increased by 109%, ace inhibitors by 89% and statins by 206%.

The increase in the volume of drugs prescribed was aided by the change in eligibility rules for medical cards in the third quarter of 2001. GP visits and associated prescribing is free to roughly 30% of the population in Ireland who have a medical card[3]. Until July 2001 only those eligible on the basis of a means test or involvement in specific government training scheme had access to a medical card. From July 2001 on however, all those aged 70 or over were given access to free primary care and pharmaceuticals[4]. The timing of the change in prescribing practices and the fact that the medications may well interact with other drivers of cardiovascular mortality such

[2] Coronary artery bypass graft and percutaneous transluminal coronary angioplasty.
[3] GP fees per visit vary widely but average 60EURO. Charges for prescribed medications are capped at 110 euro per month for the whole population through the Drug Payment Scheme.
[4] Non-medical card holders are entitled to free in patient and out patient care on the same basis as medical card holders except for the payment of a relatively small per diem charge for inpatient care.

as season and temperature could mean that this development was responsible for the fall in circulatory mortality and seasonality which was observed after 1999.

A review of clinical trials of cardiovascular drug efficacy during the period from 1970 (Weisfeldt and Zieman 2007) concluded that pharmaceutical agents played a major role in the prevention of atherosclerosis and its consequences and that the introduction of new classes of cardiovascular drugs often has positive population health consequences. A series of papers by Lichtenberg (2006; 2007; 2009) has also shown that the introduction of new classes of cardiovascular medication reduce other types of medical expenditure, hospital expenditure and, most importantly in the context of this paper, death rates from circulatory causes. As far as we are aware no research to date has examined the role of cardiovascular prescribing on the seasonality of death rates although it is reasonable to expect that specific classes of drugs may lessen the probability of thrombotic disease, the major cause of excess winter mortality alongside respiratory disease (Donaldson and Keatinge 2002).

There is also now a well developed literature examining the composition of change in cardiovascular mortality using the IMPACT CHD mortality model (Unal et al 2004; Capewell et al 1999; Capewell et al 2007) including a paper applying this model to the Irish context (Bennett et al 2006). Irish IMPACT models suggest that approximately 44% of the decline in CHD deaths between 1985 and 2000 can be attributed to improvements in the uptake of treatments, particularly secondary prevention (18%) and treatments of chronic angina (8.4%). This model also attributes 30% of the fall in CHD mortality to reductions in population cholesterol, probably as a result of changes in diet. Bennett (et al) also estimate that reductions in smoking contributed 26% of the reduction in cardiovascular deaths over the same period whilst population trends in physical activity, obesity and diabetes all contributed to worsening trends. It is interesting to note that all the main population risk factors for cardiovascular disease - smoking, physical activity, obesity, diabetes and population

blood pressure, have all worsened in Ireland since 2000 with the exception of population cholesterol[5] (Morgan et al 2008).

The IMPACT CHD mortality model does not attempt to directly test whether changing treatments and lowered population cholesterol explain the timing and extent of the trend in CHD deaths. Instead it uses international evidence on the impact of different treatments and risk factors combined with demographic data to decompose the observed falls in cardiovascular mortality over the approximate time period under examination. In this paper we adopt a more direct approach and use time series analysis to test whether the increased levels of prescribing of CHD medications can account for the timing and extent of the change in CHD mortality.

The paper is structured as followed. The next section details the various data sources that will be used in the paper whilst the third section of the paper discusses the methodology used in the paper. The fourth section describes our results including a descriptive analysis of mortality trends, weather patterns and cardiovascular prescribing in Ireland 1995-2005. The section then goes onto test whether a structural break in mortality trends occurred in Ireland before examining our hypotheses about cardiovascular prescribing using grouped logit models. In the fifth section we discuss the results of the analyses and their limitations before outlining possible future directions.

## 2. DATA

Ideally we would test the role of cardiovascular drug prescribing by regressing individual risk of death from cardiovascular causes against prescriptions of cardiovascular medications controlling for confounding factors at the individual level. Unfortunately such data are not available in the Irish context. Our only option is to use aggregated data on deaths disaggregated by cause, sex and age group. Our data on mortality are death registrations in the Republic of Ireland from 1995 to 2005 supplied by the Irish Central Statistics Office (CSO). Deaths from 1995 to 2005 were grouped

[5] There is a high likelihood that the increased prescribing of lipid lowering medications since 1999 may well have contributed to this fall in population cholesterol.

by quarter (44), sex, cause of death (circulatory [ICD-9-CM codes 390-459] and three age groups (65 to 74, 75 to 84 and 85+ and an all 65+ group) for analysis. As previously commented upon we focus on those aged 65 or more for whom the change after 1999 was most pronounced. Population totals for each age and sex group were also obtained from the CSO and used to calculate the death rate per 1000 population.

A change in weather patterns in the form of warmer winter temperatures is also a possibility that we need to examine and control for. Temperature data were obtained from Met Eireann, the Irish Meteorological Service. Although it would be possible to get temperature readings from different locations, the use of aggregate data in this paper means that only a single measure of temperature can be used. Different formulations of temperature at Dublin Airport, Ireland (average temperature in quarter, average minimum temperature in quarter and overall minimum temperature in quarter) by quarter between January 1995 and December 2005 were obtained for analysis.

The main hypothesis examined is that the impact of changing prescribing practices on mortality rates. Information on prescribed cardiovascular medicines for the period from January 1995 to December 2005 were obtained from the Health Care Executive Primary Care Reimbursement Service (HSE-PCRS). The HSE-PCRS collates data on medicines prescribed under the three Community Drugs Schemes – the General Medical Services Scheme (GMS), the Drugs Payment Scheme (DPS) and the Long Term Illness Scheme (LTI). The GMS is by far the largest of these schemes and accounts for almost 75% of publicly funded prescriptions. Those eligible for a medical card receive free primary care and prescribing via an income means test, through particular health needs, or participation in an approved Government training and employment scheme (Primary Care Reimbursement Service, 2007). In 1998 67% of those aged 65 or more were holders of a medical card or had access to one via a close relative. With effect from July of 2001 all those aged 70 or more became entitled to a medical card and this saw the proportion in receipt of a card increase to almost 87%. Although contemporary HSE-PCRS data cover prescriptions received free under the GMS as well as the DPS and LTI schemes, available longitudinal data do not include prescriptions under DPS and LTI schemes. Due to changes in coding procedures only data for the Eastern Region Health Authority (ERHA) are available

for the observation period used in this paper. The ERHA region covers approximately one-third of the Irish population (The Health Board regions were superseded by the Health Services Executive Regions in 2005). Nonetheless trends in this region should be representative of trends in the Republic of Ireland overall. Data supplied by the PCRS in relation to cardiovascular drug prescriptions for persons within the ERHA aged 65 and over were adjusted to rates per 1,000 of the population.

## 3. METHODS

We assess the relationship between aggregate data on mortality, temperature, respiratory discharges and cardiovascular prescribing through time series analysis of 44 quarterly observations. The simplest model for this is:

$$y_t=\alpha+\beta_1 T_t+ \beta_2 D_t+\varepsilon$$

where the death rate at time t ($Y_t$) is a function of temperature (T) and rate of cardiovascular drug use in the population (D) all at time t, plus error ($\varepsilon$). This could be estimated using ordinary least squares (OLS) or weighted least squares (WLS) methods. However OLS or WLS will produce predictions <0 for some values of the independent variables. Instead we use grouped logit methods which are more appropriate:

$$Z=\log(p/(1-p))$$

We thus estimate the log of the number dying from a circulatory cause in quarter t divided by the proportion not dying from this cause in the quarter, As we are using grouped data we assume that all cases at t have the same values of the explanatory variables at t.

A central issue in time series analysis is the extent to which the data auto-correlated, that is, a process:

$$Yt = rY_{(t-1)} + u_t$$

is said to be autocorrelated for where r is equal or greater than 1. A Durbin-Watson (DW) test varies between 0.38 and 0.84 for male circulatory deaths (depending on age) suggesting strong autocorrelation. However, controlling for the long term

downward trend in circulatory deaths and the seasonal nature of deaths produces a DW of between 1.96 to 2.4, a more acceptable result. Examination of autocorrelation and partial correlation plots for an OLS model of circulatory death rates for men aged 65 or more controlling for the trend in deaths and the seasonal variation shows relatively low and random autocorrelation and minimal partial correlation suggesting that our models are stationary. Dickey-Fuller unit root tests were negative.

**Modelling Strategy**

The analysis strategy we adopt is to first establish whether and at which point there is a structural break in the death rate from circulatory causes in Irish death rates by sex and age group. We do this by fitting 128 ordinary least squares (OLS) models of circulatory deaths which use alternative break points between the first quarter of 1998 and the last quarter of 2001 by each age/sex group (16 possible break points x 4 age groups x 2 sexes) which include the overall trend in deaths (a linear representing each year quarter 1995 to 2005 running from 1 to 44), three variables representing year quarter (omitting quarter one), a term for the interaction of the structural break point and the overall trend and three other terms interacting the year quarter with the structural break point (see Appendix Table 1 for definitions of variables used). We use OLS models rather than grouped logit models in this instance to facilitate the comparison of non-nested models[6]. We select the break point for each age/sex combination by choosing the point at which the explained variance is highest as measured by an $R^2$ statistic.

Having established the break point, we then fit a variable representing each drug to the basic model of death rate trend, seasonal pattern and break point whilst also controlling for temperature fitted as the lowest temperature at t. If the quantitative variable expressing the cardiovascular drug effect can render the variable representing the structural change, or break point in death rates insignificant and reduce its coefficient we then take this as giving support to the hypothesis that the new trend pattern can be explained to an extent by cardiovascular prescribing trends.

[6] Use of grouped logit models would necessitate the use of an information criterion approach such as the Bayesian or Akaike Information Criterion. There is still some debate about the efficacy of such approaches (Bernham and Anderson 2002).

## 4. RESULTS

### Trends in Circulatory Death Rates

Figures 1 and 2 show male and female circulatory death rates between 1995 and 2005 for four age categories: 65-74 years, 75-84 years and 85+ years plus all 65+ years. These show that mortality from circulatory disease in Ireland displays a strong seasonal pattern, with the highest mortality rates occurring in quarter one, and the lowest in quarter three. In relation to cardiovascular deaths, male mortality is generally higher than female mortality across all age groups. For both sexes, in addition to the higher amplitude of fluctuations, the rate is highest amongst the oldest age group aged 85 and over. The first quarter of 1999 exhibited the highest rates of mortality in this group, with males recording 34.3 deaths per 1,000 of the population aged 85 and over, compared to slightly lower 28.1 deaths per 1,000 of the female population aged 85 and over. The figures below,

FIGURES 1 and 2 ABOUT HERE

These mortality figures indicate that post 2000, the seasonal pattern has modified, with less amplitude in the differences between quarter one and quarter three. Previous research (Walsh, 2007) commented on the strong seasonality effects in circulatory mortality in Ireland. This is also strongly evident in our graphs which plot the quarterly death rates over the period 1995-2005.

Appendix Table 2 gives the adjusted $R^2$ associated with each of the break points and shows that among men the break point which explains the most variance in the mortality data occurs in Q4 1999 for those aged 64 to 74 and 85+ (as well as all 65+), whilst for those aged 75-84, a break point in the last quarter of 2000 explains more of the variance in the data. For women the break point occurs around a year later in the third and fourth quarters of 2000. These break points are adopted in the main analysis of our variables of interest.

TABLE 1 ABOUT HERE

Table 1 shows the results for grouped logit models of circulatory deaths by sex and age group. This shows that for men aged 65 to 84 there is a significant structural break in the time trend plus a structural break in the seasonality trend for those aged 75 to

84. For men aged 85+ on the other hand there is evidence only of a structural break in the seasonality accounting for the overall decrease in mortality rates for circulatory disease. Table 1 shows the significant downward trend in death rates for all age and sex groups plus the strong seasonality in deaths with Q3 each year having the lowest rate of deaths and Q1 the highest. Transformed, the results for men aged 65+ show a 0.82% fall in deaths/000 per quarter 1995-2005, increasing by 0.5% per quarter after Q4 1999. They also show a strong seasonal variation with 25% less deaths/000 in Q3 than Q1[7]. There is a 9% reduction in Q3 seasonality post Q4 1999. For women the structural break in the main time trend is significant for all age groups whereas there is evidence for the break in seasonality only for women aged 75 to 84. Transformation of the results in Table 1 for women aged 65+ suggest a 0.53% fall in deaths/000 per quarter 1995-2005, increasing by 0.48% after Q1 2000. Seasonality among women is just as pronounced as among men with 25.2% less deaths in Q3 than Q1 although there is a smaller reduction in this proportion after Q1 2000 of 6.8% relative to 9% among men.

Among the oldest age groups (85+) the over downward trend was stronger with a 0.68% reduction among men per quarter and 0.54% among women, a fall which decreases by 0.37% among men and 0.26% among women after the break point. Seasonal variation is higher among the oldest age group with men experiencing 29.3% fewer deaths in Q3 compared to Q1 and women 24.7%. These seasonal fluctuations decrease by 10.6% among men and 4.2% among women after the break point.

**Temperature**

Figure 3 shows the Met Eireann data on the average minimum temperature, minimum temperature and mean temperature which were recorded in each of the quarterly time periods from 1995-2005.

FIGURE 3 ABOUT HERE

The differences across seasons fluctuate between lows in quarter one, to highs in quarter three, for the average minimum temperature and mean temperature. The

[7] Healy (2003) found a 21% increase in winter mortality for Ireland using data from 1988 to 1997 using a slightly different measure, the coefficient of seasonal variation in mortality (CVSM).

lowest minimum temperature was often lowest in quarter four. The greatest fluctuation between season one and season three occurred in 1995 for mean temperature when the temperature fluctuated between a minimum of 5.7 degrees in season one to a maximum of 16.2 degrees in quarter three. The lowest temperature was recorded in the first quarter of 2001 when temperature fell to a mean low of 4.7 degrees which was also the quarter when the lowest minimum temperature was recorded (-8.0 degrees Celsius).

The suggestion that milder winters (Walsh, 2007) may have had an effect on the fall in death rates, the temperature data does not reflect the decline that was witnessed in mortality post 2000. Fitting each of these variables (average minimum temperature, mean temperature and minimum temperature) into our model, alongside the trend, and structural break variables yields mainly insignificant results across all age groups and disease categories. Where there were significant results, they were negative, for example, after fitting minimum temperature into the model, the effects for males aged 65 and over in the circulatory disease group fell by 0.2 per cent.

**Cardiovascular Drug Prescribing**

Figures 4 and 5 show the prescribing rates for different CHD medications for the period 1995 to 2005 for men and women. Across almost all the medications there is a gradual increase from the beginning of the series followed by a steepening increase after 1999 followed by a pronounced change in the prescribing trend post 2001. This coincides with the timing of the provision of medical cards to all those aged 70 years and over in the third quarter of 2001, irrespective of means.

FIGURES 4 AND 5 ABOUT HERE

**Modelling the Impact of CHD Prescribing**

Table 2 shows that the introduction of the variables representing cardiovascular prescribing (controlling for temperature) has an important impact, both in terms of the effects of the drugs themselves and their impact on the significance and coefficient for the terms representing the trend-break point in the time series. However, the impact of the cardiovascular drugs varies considerably both by type and between the sexes. The impact of the drug variables is highest among men with the drug terms for beta-blocker, ace inhibitor and aspirin rendering the trend-break variable insignificant

across all age groupings. Diuretic, statin, calcium channel blocker and nitrates fail to explain the trend-break for men aged 75 to 84.

Among women, beta-blocker, aspirin and calcium channel blocker explain the trend-break terms for all age groups. Ace inhibitor and statin fail to explain the trend break for those aged 65-74 and diuretic and nitrates fail to explain the trend in any age group.

The impact of the drug effects on the trend-break coefficient varied by drug and sex. For men, aspirin and beta blocker produced the largest fall in the trend-break coefficient at 82% followed by statin (77%). Diuretic, calcium channel blocker and nitrate medications reduced the trend-break coefficient by 62%, 63% and 58% respectively. The variable representing rates of ace inhibitor use produced the lowest fall in the coefficient at 25% largely because of its lack of impact for the 65 to 74 year age group among men. Among men aged 75 to 84 ace inhibitor produced a 45% fall in the trend-break coefficient, rising to 78% among men aged 85+. The mean reduction in the trend-break coefficient masks substantial variation between age groups. The mean fall in the coefficient for men aged 65 to 74 and 75 to 84 is 50% and 49% respectively but this rises to 92% among men aged 85+.

Among women the medication variables produce substantially smaller falls in the female trend-break variables with statin producing the largest fall at 47% followed by ace inhibitor (42%), beta blocker (41%), aspirin (38%), calcium channel blocker (23%), nitrate (12%) and diuretic (8%). As with the male results, the female results vary by age group with the largest fall occurring among women aged 75 to 84 at 63% followed by women aged 85+ at 28%. This proportion falls to less than 1% among women aged 65 to 74.

The coefficients for the effect of the drugs on mortality vary also with beta blocker, ace inhibitor and calcium channel blocker reducing the odds of death from circulatory causes by 0.3% for each increase rate per thousand prescribed the medications. Statin, diuretic and aspirin have impacts on the probability of death of roughly half this size at 0.15% per rate point increase. Nitrate results prove to be positive, i.e. increase the probability of death (0.49% per rate point increase). Among women coefficients are larger for calcium channel blocker (0.42%) and beta blocker (0.37%), but smaller for ace inhibitor (0.25%). As among men, aspirin (0.16%) and diuretic (0.18%) have a

lower impact. Nitrate and diuretic appear to have a positive effect on deaths among women with the nitrate effect particularly large at 1.6% per rate point increase.

## 5. DISCUSSION

This paper was motivated by the pronounced fall in mortality from circulatory and respiratory causes observed around the turn of the last century in Ireland. Our estimates suggest that male deaths from circulatory causes were already falling by 3.3% a year until the fourth quarter of 1999 at which point the rate proportionate fall increased to 5.3% a year. Among women the extent of change was not as large but the first quarter of the year 2000 saw the yearly fall in circulatory deaths essentially double from 2.1% to 4%. Similar pronounced and sudden changes were observed in the seasonality of circulatory deaths. Before the fourth quarter of 1999/first quarter 2000 circulatory deaths in the third quarter of the year were typically 25.2% lower than in the first quarter among both men and women. After this point however, the peak summer fall in mortality dropped to 18.4% among men and 20.2% among women. This change in mortality has attracted much comment in Ireland and further afield but up to this point attempts to explain the change in trend have been few in number and met with limited success (Walsh 2008). This paper has shown that the structural break in the trend can be explained by changes in the pattern of cardiovascular drug prescribing in Ireland after 1998. Our analyses show that variables representing the trend break across different age/sex groups can be rendered insignificant, and a high proportion of their coefficient explained by quantitative variables measuring the increase in prescribing of cardiovascular drugs between 1995 and 2005. Variations in this effect across the sexes and between drugs deserves some comment.

Just as the fall in circulatory deaths was largest among men, our models also showed that the impact of circulatory drugs was also more significant among men with drug variables both more likely to render the trend-break variable insignificant and reducing its coefficient by a larger amount. Whilst there is no evidence to show that the cardiovascular medications examined in this paper are less effective among women there is some evidence internationally to suggest that women may be prescribed such medications at a lower level of risk than among men (Stocks et al

2004). If replicated among our Irish sample such over prescribing would lead to the slope coefficient for cardiovascular prescribing among women to be reduced.

Our analyses also showed differential impacts among the different medications. Among men, beta blocker, aspirin and ace inhibitor medications were most effective at explaining the structural break in the mortality trends and reducing its effect. Among women, all drug variables failed to completely explain the trend break across all age groups. The rather small effect for statin in this context is difficult to understand given its efficacy in randomised control trials. Once again however, it may be that overprescribing of statin to individuals at a lower level of risk may lead to lower levels of effect than would be expected from trials.

Our research clearly had a number of drawbacks. Ideally, longitudinal data on circulatory mortality alongside individual specific data on prescribing would be used for this analysis. Unfortunately this is not available for Ireland at present. In its absence we are forced to use aggregate data and time series methods within which we have a limited number of degrees of freedom to examine the hypotheses at issue. First and foremost this means that our estimates of the effects of the cardiovascular medications are not as precise as we would like. But it also means that we cannot test for the independent effects of different medications and combinations thereof without experiencing unacceptable levels of autocorrelation.

Secondly, our data are not as representative of the population as we would like. Our data on cardiovascular medications measure prescribing patterns only for medical card holders over the age of 64. This partial coverage is not as problematic as it would be among the younger population as 67% of those over the age of 64 had access to a medical card in the late 1990s rising to 87% after 2001 with 100% coverage of those over 70. Nonetheless this partial coverage introduces error into the analysis of the probability of death from cardiovascular causes which is based on national data. Ideally data on prescribing for the total population would be used although this is not available at present.

A factor which we have not examined in this paper but which it is possible played a role in the change in mortality trends may have been the wider availability of influenza vaccine after 1998. Campaigns to increase levels of flu vaccination in winter

months among older Irish people began in 1998 and were accompanied by free flu vaccine for all those aged over 65. The timing of this policy initiative fits well with the observed time trend in death rates as does the fact that influenza infection has been shown to be a contributing factor to increased death rates from thrombotic and respiratory disease (Donaldson and Keating 2002). The fall in the seasonality of deaths from respiratory and circulatory disease also suggests that this hypothesis has promise since influenza and other respiratory infections are more common from December to February. Data on the extent of take up of vaccine among older age groups is not available from the Primary Care Reimbursement Service at present but it would be important to be able to control for this factor in future analyses.

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# Figures and Tables

**Figure 1: Male Circulatory Death Rates by Age Group, Year and Quarter 1995-2005**

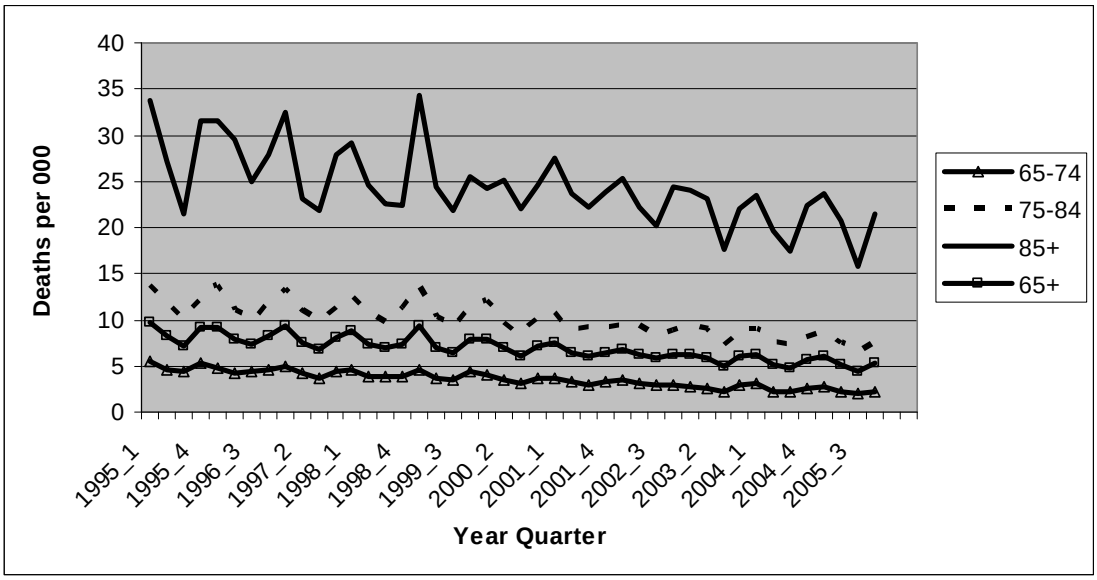



**Figure 2: Female Circulatory Death Rates by Age Group, Year and Quarter 1995-2005**

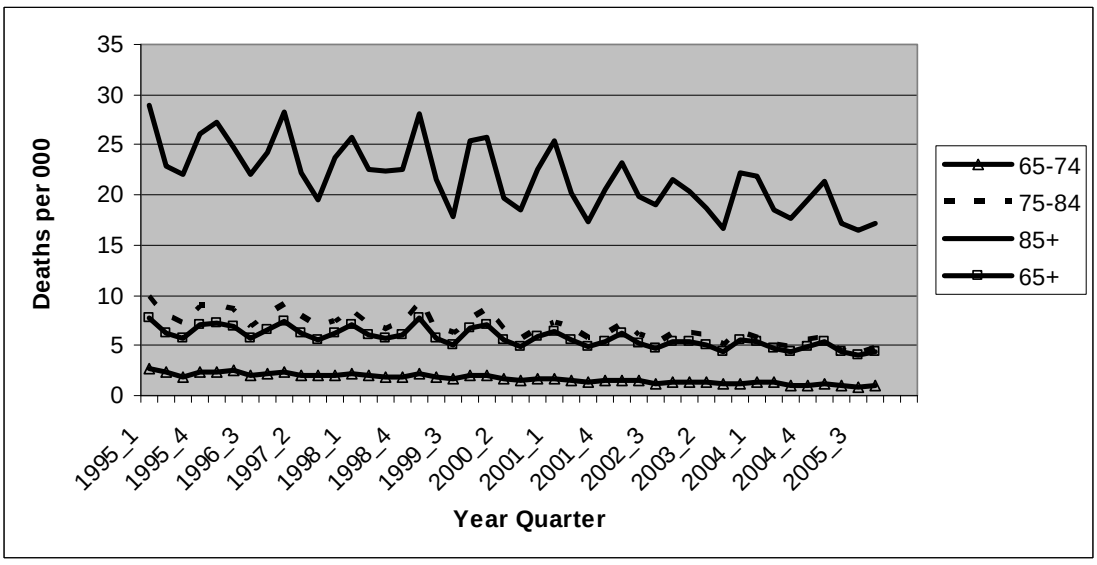


**Figure 3: Average Minimum, Minimum Temperature and Mean Temperature at Dublin Airport by Quarter 1995-2005**

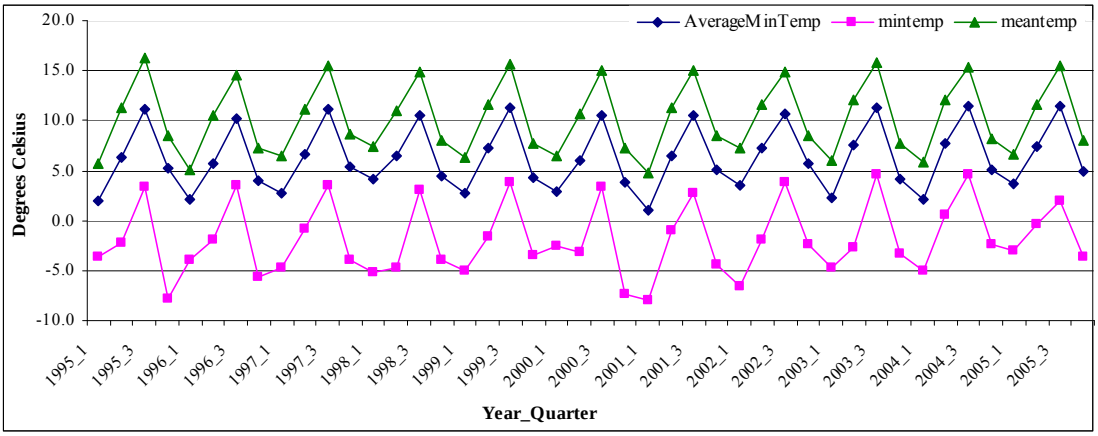
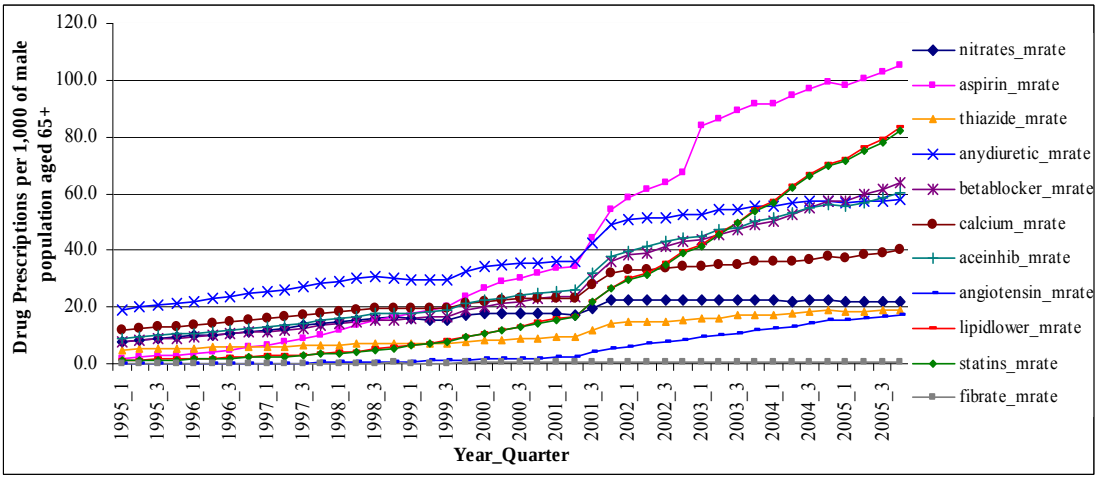
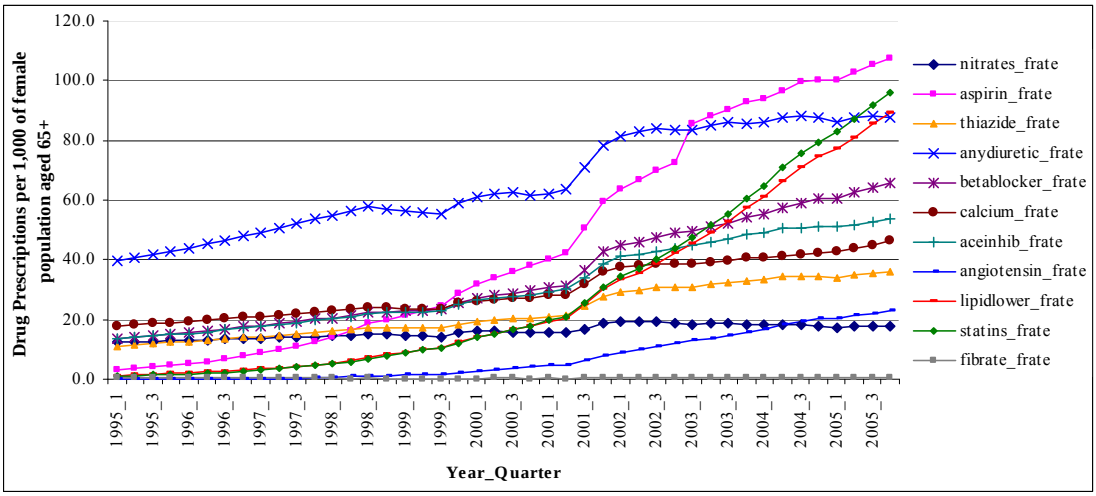



**Figure 4: Cardiovascular Prescribing for Males Aged 65+ per 1,000 Male Population**




Source: Primary Care Reimbursement Service, Eastern Region Health Area Data

**Figure 5: Cardiovascular Prescribing for Females Aged 65+ per 1,000 Female Population**




Source: Primary Care Reimbursement Service, Eastern Region Health Area Data

**Table 1: Grouped Logit Model of Male Circulatory Deaths by Age Group 1995-2005**

| Male | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Aged 65-74 | | Aged 75-84 | | Aged 85+ | | Aged 65+ | |
| | β | Sig. | β | Sig. | β | Sig. | β | Sig. |
| Trend | -0.015 | *** | -0.007 | *** | -0.007 | ** | -0.008 | *** |
| Q2 | -0.174 | *** | -0.200 | *** | -0.221 | *** | -0.199 | *** |
| Q3 | -0.215 | *** | -0.314 | *** | -0.347 | *** | -0.290 | *** |
| Q4 | -0.053 | n.s | -0.124 | *** | -0.161 | *** | -0.115 | *** |
| Trend_Int | -0.004 | * | -0.005 | *** | -0.004 | n.s | -0.005 | *** |
| Q2_Int | 0.071 | n.s | 0.089 | * | 0.125 | ** | 0.089 | *** |
| Q3_Int | 0.045 | n.s | 0.130 | *** | 0.101 | * | 0.086 | *** |
| Q4_Int | 0.036 | n.s | 0.046 | n.s | 0.120 | * | 0.063 | ** |
| Constant | -5.163 | *** | -4.228 | *** | -3.345 | *** | -4.587 | *** |
| Psuedo $R^2$ | 0.0047 | | 0.0030 | | 0.0026 | | 0.003 | |
| N | 5071600 | | 2581600 | | 523200 | | 8176400 | |
| Female | | | | | | | | |
| | Aged 65-74 | | Aged 75-84 | | Aged 85+ | | Aged 65+ | |
| Trend | -0.015 | *** | -0.009 | *** | -0.005 | *** | -0.005 | *** |
| Q2 | -0.093 | ** | -0.205 | *** | -0.196 | *** | -0.186 | *** |
| Q3 | -0.215 | *** | -0.323 | *** | -0.284 | *** | -0.290 | *** |
| Q4 | -0.067 | n.s | -0.149 | *** | -0.112 | *** | -0.132 | *** |
| Trend_Int | -0.005 | ** | -0.005 | *** | -0.003 | * | -0.005 | *** |
| Q2_Int | 0.026 | n.s | 0.102 | ** | 0.020 | n.s | 0.063 | ** |
| Q3_Int | 0.015 | n.s | 0.107 | ** | 0.041 | n.s | 0.066 | ** |
| Q4_Int | -0.042 | n.s | 0.088 | ** | 0.032 | n.s | 0.061 | ** |
| Constant | -5.915 | *** | -4.578 | *** | -3.510 | *** | -4.835 | *** |
| Psuedo $R^2$ | 0.0051 | | 0.0034 | | 0.0022 | | 0.0021 | |
| N | 5680800 | | 384 0400 | | 1204400 | | 10725600 | |

Note: See Appendix Table 1 for variable definitions & section 4 for year/quarter of each structural break point.
Sig Key: n.s – Not Significant; *=P<0.05; **=P<0.01; ***=P<0.001

**Table 2: Grouped Logit Model of Circulatory Death Rates By Age Group and Sex (Controlling for Minimum Temperature in Quarter)**

| | | Male | | | | Female | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | 65-74 | 75-84 | 85+ | 65+ | 65-74 | 75-84 | 85+ | 65+ |
| a. Beta-Blocker | B | -0.0055 | -0.003 | -0.0006 | -0.0037 | -0.0016 | -0.0059 | -0.0001 | -0.0037 |
| | Sig. | ** | n.s | n.s | *** | n.s | * | n.s | ** |
| b. Trend_int | B | -0.0005 | -0.0019 | -0.0002 | -0.0015 | -0.004 | -0.0004 | -0.0019 | -0.002 |
| | Sig. | n.s | n.s | n.s | n.s | n.s | n.s | n.s | * |
| a.Ace-Inhibitor | B | -0.0058 | -0.0029 | -0.0008 | -0.004 | -0.0017 | -0.0039 | -0.0015 | -0.0025 |
| | Sig. | ** | n.s | n.s | ** | n.s | n.s | n.s | n.s |
| b. Trend_int | B | -0.0005 | -0.0021 | -0.0002 | -0.0015 | -0.0052 | -0.0017 | -0.0023 | -0.0027 |
| | Sig. | n.s | n.s | n.s | n.s | * | n.s | n.s | ** |
| a. Diuretic | B | -0.0031 | -0.0004 | -0.0013 | -0.0028 | 0.0036 | 0.0016 | 0.0013 | 0.001 |
| | Sig. | n.s | n.s | n.s | n.s | n.s | n.s | n.s | n.s |
| b. Trend_int | B | -0.002 | -0.0032 | -0.0001 | -0.0023 | -0.0055 | -0.0031 | -0.0022 | -0.0036 |
| | Sig. | n.s | ** | n.s | ** | *** | ** | * | *** |
| a. Statin | B | -0.0029 | -0.0014 | -0.0003 | -0.0018 | -0.0015 | -0.0027 | -0.0005 | -0.0018 |
| | Sig. | ** | n.s | n.s | *** | n.s | *** | n.s | *** |
| b. Trend_int | B | -0.0009 | -0.0022 | -0.0002 | -0.0018 | -0.0035 | -0.0006 | -0.0016 | -0.002 |
| | Sig. | n.s | * | n.s | * | * | n.s | n.s | ** |
| a. Aspirin | B | -0.0029 | -0.001 | -0.0006 | -0.0019 | -0.0008 | -0.002 | -0.0002 | -0.0016 |
| | Sig. | ** | n.s. | n.s. | *** | n.s | n.s. | n.s. | n.s. |
| b. Trend_int | B | -0.0003 | -0.0024 | 0 | -0.0014 | -0.004 | -0.0011 | -0.0018 | -0.002 |
| | Sig. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | n.s. | * |
| a. Calcium | B | -0.0064 | -0.0012 | -0.0018 | -0.0051 | 0.0021 | -0.0059 | -0.0001 | -0.0042 |
| | Sig. | n.s. | n.s. | n.s. | * | n.s | n.s. | n.s. | n.s. |
| b. Trend_int | B | -0.0019 | -0.0031 | -0.0002 | -0.0023 | -0.0052 | -0.0016 | -0.0019 | -0.0026 |
| | Sig. | n.s. | ** | n.s. | ** | n.s. | n.s. | n.s. | ** |
| a. Nitrates | B | 0.0113 | 0.006 | -0.0027 | 0.0057 | 0.0196 | 0.0191 | 0.0095 | 0.0163 |
| | Sig. | * | n.s. | n.s. | n.s. | n.s. | ** | n.s. | ** |
| b. Trend_int | B | -0.0021 | -0.0031 | -0.0005 | -0.0026 | -0.005 | -0.0031 | -0.0022 | -0.0038 |
| | Sig. | n.s. | *** | n.s. | *** | *** | ** | * | *** |

NOTE: a – Cardiovascular medication coefficient and significance
b – Trend-break point interaction coefficient and significance controlling for cardiovascular medication a.

# Appendix

**Appendix Table 1: Variable Description**

| Variable | Description |
|---|---|
| Trend | =Integer from 1 to 44 identifying Year/Quarter 1995-2005 |
| Q2 | =1 if 2nd Quarter of Year |
| Q3 | =1 if 3rd Quarter of Year |
| Q4 | =1 if 4th Quarter of Year |
| Trend_Int | = Trend * post break point period |
| Q2_Int | =2nd Quarter * post break point period |
| Q3_Int | =3rd Quarter * post break point period |
| Q4_Int | =4th Quarter * post break point period |
| Mintemp | =Minimum temperature measured in quarter t |
| β-Blocker | =Sex specific rate of prescribing of β-Blocker in quarter t |
| Ace Inhibitor | =Sex specific rate of prescribing of Ace Inhibitor in quarter t |
| Diuretic | =Sex specific rate of prescribing of any Diuretic in quarter t |
| Statin | =Sex specific rate of prescribing of Statin in quarter t |
| Aspirin | =Sex specific rate of prescribing of Aspirin in quarter t |
| Calcium | =Sex specific rate of prescribing of Calcium Channel Blocker in quarter t |
| Nitrates | =Sex specific rate of prescribing of Nitrates in quarter t |

**Appendix Table 2: Model Fit (Adjusted $R^2$) Statistics for Different Structural Break Points**

| | Males | | | | Females | | | |
|---|---|---|---|---|---|---|---|---|
| | 65-74 | 75-84 | 85+ | 65+ | 65-74 | 75-84 | 85+ | 65+ |
| 98_1 | 0.9548 | 0.9284 | 0.8038 | 0.9498 | 0.9513 | 0.9120 | 0.8646 | 0.9119 |
| 98_2 | 0.9552 | 0.9278 | 0.8083 | 0.9500 | 0.9511 | 0.9142 | 0.8626 | 0.9121 |
| 98_3 | 0.9534 | 0.9267 | 0.8052 | 0.9477 | 0.9504 | 0.9123 | 0.8579 | 0.9062 |
| 98_4 | 0.9545 | 0.9266 | 0.8157 | 0.9490 | 0.9507 | 0.9143 | 0.8618 | 0.9092 |
| 99_1 | 0.9553 | 0.9492 | 0.8233 | 0.9620 | 0.9526 | 0.9240 | 0.8697 | 0.9224 |
| 99_2 | 0.9565 | 0.9484 | 0.8268 | 0.9626 | 0.9521 | 0.9257 | 0.8693 | 0.9219 |
| 99_3 | 0.9575 | 0.9504 | 0.8272 | 0.9641 | 0.9525 | 0.9268 | 0.8711 | 0.9238 |
| 99_4 | 0.9578 | 0.9545 | 0.8296 | 0.9656 | 0.9559 | 0.9260 | 0.8678 | 0.9235 |
| 00_1 | 0.9574 | 0.9585 | 0.8144 | 0.9604 | 0.9587 | 0.9382 | 0.8698 | 0.9356 |
| 00_2 | 0.9570 | 0.9572 | 0.8068 | 0.9603 | 0.9581 | 0.9382 | 0.8692 | 0.9343 |
| 00_3 | 0.9575 | 0.9604 | 0.8011 | 0.9614 | 0.9581 | 0.9403 | 0.8718 | 0.9348 |
| 00_4 | 0.9576 | 0.9606 | 0.8030 | 0.9614 | 0.9601 | 0.9399 | 0.8718 | 0.9339 |
| 01_1 | 0.9550 | 0.9309 | 0.8144 | 0.9500 | 0.9540 | 0.9158 | 0.8618 | 0.9143 |
| 01_2 | 0.9547 | 0.9272 | 0.8057 | 0.9483 | 0.9523 | 0.9169 | 0.8650 | 0.9161 |
| 01_3 | 0.9549 | 0.9383 | 0.8006 | 0.9523 | 0.9534 | 0.9218 | 0.8657 | 0.9178 |
| 01_4 | 0.9548 | 0.9316 | 0.8016 | 0.9491 | 0.9553 | 0.9206 | 0.8639 | 0.9132 |

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