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Contributions of specific causes of death to lost life expectancy in severe mental illness

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ABSTRACT

Life expectancy gap between people with severe mental illness (SMI, schizophrenia, schizoaffective disorder and bipolar disorder) and general population remains. This study aims to estimate contributions of specific causes of death to the gap.

All-cause death in the observation period was used to calculate the life expectancy at birth for people with SMI by gender. Hypothetical changes in life expectancy were then re-calculated after equalling each cause-specific death rate to that in the general population of England & Wales in 2010.

Overall, natural causes (i.e. discounting suicide and other external causes) took 79.2% (female) and 78.6% (male) lost life-years respectively. Deaths from circulatory disorders accounted for more life-year lost in women than men (2.24 years, 22.0% of contributed person-years versus 1.82 years, 17.4% of person-years, respectively), as did deaths from cancer (8.1% versus no contribution). Less contribution was detected among females for respiratory disorders (13.7% versus 16.5%). Similar contributions were found for digestive disorders (9.9% versus 8.8%), suicide (13.6% versus 13.4%), and other external causes (7.2% versus 8.0%).

Loss of life expectancy in people with SMI is accounted for by a broad range of causes of death with specific gender differences. Interventions focused on multiple rather than individual causes of death should be prioritised accordingly.

INTRODUCTION

Premature death among people with mental disorders is an international concern [1]. Individuals with severe mental illness (SMI) with psychotic symptoms, including schizophrenia, schizoaffective disorder and bipolar disorder, experience particularly higher all-cause mortality and lower life expectancy [2,3]. This is an important indicator for policy development to improve on current health inequality; however, contributions of individual causes of death to the life expectancy gap remain unclear, seriously limiting the evidence. Previous research has suggested excesses of both natural and unnatural causes of death, and that the excess of natural causes may cross several mental disorder groups [4]. Nevertheless, standardised mortality ratios cannot be translated into the more important construct of life expectancy, because the latter indicator emphasising age pattern of death. Using data from a large clinical cohort, we estimated the contribution of the major groups of causes of death to shortened life expectancy in people with SMI, delineating to what extent this gap could conceivably be closed if mortality rates for each cause of death could be equalised with those in the general population.

METHODS

Data sources and cohort

The South London and Maudsley NHS Foundation Trust (SLAM) is one of Europe's largest secondary mental healthcare providers, serving a single geographic catchment of approximately 1.36 million residents in four southeast London boroughs. In 2006, fully electronic health records were implemented across all SLAM services, and, in 2008, the Clinical Record Interactive Search (CRIS) system, supported by the National Institute of Health Research (NIHR) Biomedical Research Centre for Mental Health at SLAM, was developed to allow search and retrieval of anonymised but complete medical records within a robust patient-led governance framework [5,6]. Using CRIS, individuals who received a primary diagnosis of SMI (schizophrenia, ICD-10 coded F20; schizoaffective

disorder, F25, or bipolar affective disorder, F31) during the period between 1st Jan 2007 and 31st Dec 2012 were included in this analysis. Recorded primary diagnoses in structured fields of the record were supplemented by a natural language processing application developed using Generalised Architecture for Text Engineering (GATE) software to identify diagnostic statements in open text fields (i.e. correspondence letters and clinical notes) [6,7].

Mortality

Date and primary cause of death for our study subjects in the same period (2007-2012 inclusive) were retrieved from a CRIS linkage to death certifications, held by the UK Office of National Statistics which is updated regularly [8], by NHS numbers through an anonymised process. The same data source (i.e. UK Office of National Statistics), but this time via online data files, was used to obtain age-, gender, and cause-specific mortality for England & Wales population in 2010 [9]. Since an SMI diagnosis is unlikely to be given to subjects under the age of 15 years, we assumed equal mortality rates up to that point as to those in the general population of England & Wales in 2010.

Baseline life expectancy at birth

Using Microsoft Excel software, life expectancy at birth was estimated using Chiang's abridged life-table method [10]. In brief, the accumulated person-years were calculated by gender based on age- and gender-specific mortality experienced by a specified male / female cohort in five-year age bands, and then divided by the total number of male / female cohort subjects at baseline. Because of dynamic nature of our cohort during the six-year follow-up period (2007-2012), we weighted the number of deaths observed by the average at-risk period of each age and gender band. We also estimated the life expectancy at birth for the England & Wales population using 2010 data for the purpose of validation on Chiang's abridged method [10,11].

Re-calculated life expectancies by equalising mortality rates

A life expectancy simulation was used to examine the contribution of major causes of mortality to the elevated mortality in people with SMI. Death rates in SMI cohort for each major primary cause

category were sequentially replaced with England and Wales gender- and age-specific rates for that cause of death, obtained from UK Office of National Statistics [9]. The expected number of deaths in each five-year age band was then re-calculated using these national gender- and age-specific rates. These re-estimations were carried out for cause-of-death categories by the order of number of deaths observed in the SMI study cohort: i) circulatory diseases, ii) cancer, iii) respiratory diseases, iv) digestive diseases, v) suicide, vi) deaths due to other (non-suicide) external causes, and vii) all remaining causes of death. Where there was a reverse association identified for any cause-of-death category (i.e. a lower life expectancy for SMI subjects following equalisation of a specific cause-of-death category to general population), its contribution to loss of life expectancy was set zero. Percentage of person-year contribution to the gap for each category of death was then calculated accordingly. In sensitivity analysis, the adjustment for cancer was re-applied taking into account reference to cancer anywhere on the death certificate rather than the primary cause of death.

RESULTS

Calculating by Chiang's method, the life expectancy at birth for the England and Wales population in 2010 was 78.5 (95% CI 78.1-78.8) years for males and 82.4 (95% CI 82.1-82.7) years for females, which were identical to what reported by the UK ONS [11]. In the SLAM cohort, there were 1,558 deaths during the observation period among 19,106 subjects with SMI (816 deaths among 10,414 males and 742 deaths among 8,692 females). The life expectancy at birth in people with SMI was estimated to be 67.9 years (95% CI 67.1-68.6) for men and 72.2 years (95% CI 71.5-72.8) for women – i.e. reduced by 10.6 years for men and 10.2 years for women. Summarised in Table 1, the leading cause of death in those with SMI was circulatory diseases, followed by cancer, respiratory disease, gastrointestinal disorders, suicide, and other external causes.

Figures 1 and 2 represent the incremental improvements to life expectancy by gender when major cause of death's category was sequentially replaced with the England and Wales population rates in

2010 one by one. The incremental changes to hypothetical male life expectancy from the baseline 67.9 years were: 69.7 years by equalising circulatory disease death rates to those in the general population, 69.7 years (i.e. no change) by further equalising cancer mortality, 71.4 years equalising respiratory disease, 72.3 years equalising gastrointestinal diseases, 73.6 years equalising suicide, 74.5 years equalising all other external causes, and finally attaining the national level of 78.5 years by equalising all remaining causes. The corresponding changes to the life expectancy at birth for females from the baseline 72.2 years were: 74.4 years (circulatory diseases), 75.2 years (cancer), 76.6 years (respiratory diseases), 77.7 years (gastrointestinal diseases), 79.1 years (suicide), 79.8 years (other external causes), and 82.4 years (all remaining causes). These increments are visually displayed in Figures 1-2 and are expressed in terms of life years gained and as proportions of the life expectancy gap in Table 1.

To further address the issue if position of cancer on death certificate varied between people with SMI and general population, another set of sensitivity analysis was carried out. This was done by equalising mortality rates where cancer was recorded anywhere on the death certificate and we found this did not change the findings substantially: resulting in a 0.06 year reduction of life expectancy among males with SMI and an improvement of life expectancy for females by 0.22 years when comparing rates from cancer as primary cause of death or as a contributory factor (details not shown).

DISCUSSION

With a large cohort of people with SMI, we investigated the contributions of causes of death underlying the reduced life expectancy, which has been well-recognised in this vulnerable group. Our aim was to estimate the improvements in life expectancy which might be achieved if people with SMI could experience the same age- and gender-specific mortality rates as the general population. The main finding was that the gap in life expectancy was accounted for by a wide range of underlying causes of death, rather than just one or two predominating ones. Meanwhile, some elements in the

pattern of contribution differed between men and women. The results drew an alternative picture of individuals with SMI having high mortality risk across all causes of death.

When assessing the specific contribution from each cause of death to life expectancy on where the greatest impact and least impact by gender lies, it was difficult to identify a single group or two that affects a specific gender. As single groups of causes, circulatory and respiratory were highest in males and females, but when we grouped all causes other than circulatory, respiratory, cancer, digestive, external and suicide, the rest causes of death still contributed 35.9% for male and 25.5% for female to the gap, displaying its highly heterogenic nature.

As stated, life expectancy is a more meaningful construct than standardised mortality for public health, as it takes into account not only the level of mortality but also age distributions. Disorders affecting mortality at younger age therefore have a higher impact on life expectancy, even if associated mortality rates are similar or even lower than those of later-life disorders. Estimated life expectancies at birth for male and female cohort members in our analysis were comparable to those previously reported from the CRIS database [3]. Both are substantially lower than the life expectancy at birth for men and women in the England & Wales population in 2010 (78.5 and 82.4 years, respectively). The importance of ‘natural’ causes (i.e. rather than suicide or violence) accounting for the mortality gap is increasingly recognised. For example, in a population of 292,585 people in contact with mental health services, 77.7% of excess deaths were found to be accounted for by physical conditions, of which cardiovascular illnesses contributed 29.9% and cancers contributed 13.5%, compared to 13.9% of excess deaths caused by suicide [12]. In that study, excess mortality by cause was defined as the difference between the observed number of deaths (the total person-years in the cohort of psychiatric patients) and the expected number of deaths (expected numbers of deaths in the cohort by major cause of death using cause-specific death rates by age group, sex, and time period) [12]. Kessing *et al* (2015) also found that among men with SMI, 74% of life years lost after age 15 were due to natural causes and, among female counterparts, figure was 80% [13]. In our cohort, natural causes accounted for 78% and 77% respectively. Suicide clearly remains an important

adverse outcome in SMI with a 5% lifetime risk estimated for people with schizophrenia [14]. It accounted for approximate 1.4 life years lost for both genders (13.4% in men and 13.6% in women for its contribution) in our sample.

Our findings revealed a minor effect of deaths from cancers, especially for male SMI subjects. Other studies have also shown increase in mortality due to cardiovascular diseases and infectious diseases, but, unlike in our study, their subjects also experienced increases to deaths of cancer with up to 1.4 to 2.0 folds of increasing risks [15]. The explanation is simply that cancer deaths happen later than other causes, resulting in less impact on life expectancy among people with SMI. Our study remains unique for its methodology emphasising the impact of mortality pattern for each major death cause categories, rather than comparing summed risks for people with mental illness as the above studies. Our study provides an overview of all cancer deaths in the SMI population in the given time period, in response to our previous finding of similar patterns in presentation / diagnosis of cancer to that of general population [16].

Despite the well-recognised importance of deaths from natural causes in SMI, investigations and suggested interventions have tended to focus on specific causes of death such as cardiovascular disease, although comparable morbidity has been reported in other systems [17]. Our findings suggest that this is over-simplistic and that a range of recorded causes potentially underlie the gap in premature mortality. The widening mortality gap between people with and without SMI is primarily accounted for by progressively improving survival rates in the general population which are not being experienced by people with SMI, rather than by rising absolute mortality in SMI [4]. Furthermore, risk factors for mortality have high prevalence in people with SMI include smoking, alcohol, recreational drug use, poor diet and lack of exercise [18-22]. These are potentially implicated in a number of causes of death and their associations with mortality have been found to be stronger than expected in SMI [22]. General health promotion activities are therefore most likely to have an impact on life expectancy, including improvements in the availability and accessibility of prevention and risk management services, as well as addressing inequalities in treatment receipt where life-threatening

conditions are present [23]. It is also clearly important to consider side effects of some psychotropic medications, such as the weight gain and hyperlipidaemia which affect a high proportion of patients during initiation or maintenance of antipsychotic treatment [21]. Improving the availability and accessibility of prevention and risk management services could be an important means to minimise the mortality gap, but broader attention is also needed to address profound socio-economic inequalities.

Although 13% of deaths for this cohort were due to cancer, the third leading cause of death, there was no improvement to life expectancy at birth among men when England and Wales cancer mortality rates were substituted. We considered the possibility that cancer was a potential underlying cause of death but not always considered or recorded as the primary cause in death certificates (e.g. because of deaths from respiratory disease in people with advanced cancer). However, there was minimal alteration in findings when mortality rates were substituted where cancer was recorded anywhere on the death certificate. Of all cancer mortality in women with SMI, the commonest cause in our sample was breast cancer (n=179) leading to a mean age at death of 67.7 years followed by lung cancer (n=110) with mean age at death of 71.7 years. For males, the commonest cancer causing death was lung cancer (n=128) with mean age at death of 70.9 years followed by prostate cancer (n=101) with mean age at death of 78.0 years. The younger age of deaths from breast cancer could therefore explain the greater impact on life expectancy among females. Our finding for cardiovascular disease accounting for a higher proportion of life expectancy in women was similar to those of another study findings with higher contributions from cardiovascular disease to excess deaths in female compared to male patients with mental disorders (35.2% and 26.2%, respectively) [12].

Strengths of our study include the large sample size and linkage to nationwide mortality, with up to six years of follow up. This study adds to the literature by showing contribution of each major cause of death to its current life expectancy compared to England and Wales which provides a full picture of difference in mortality compared to excess mortality alone. Generalisability of our analysis might need to be further considered, as the findings for life expectancy at birth clearly refer to people with

these mental disorders who had made contact with secondary mental health services within the specified time period. In this respect, the secondary healthcare setting is unlikely to bias findings to a large extent as SMIs by nature are disorders where most cases will have received secondary care input. The limitations of this study may come from its inclusion criteria as it included anyone with a SMI diagnosis whether or not they had other mental health diagnoses as well. This was done to ensure the study was most inclusive to patients experiencing psychotic symptoms and had a diagnosis of F20, F25 or F31 ICD-10 conditions. There is potential for introducing survivor bias with the individuals that survive the longest, the highest risk period potentially being after first diagnosis, being included. However, the aim of this study is to highlight the patterns of mortality as estimated by life expectancy. Although SLAM is a major academic as well as clinical centre, mental disorders defined from its records are likely to be broadly generalisable to other UK urban and suburban settings. An important consideration in drawing inferences from our findings concerns the assumptions. These presupposed independent processes did not take into account the potential for interaction among causes of death or competing risks of death (e.g. that equalising cancer mortality might have less impact than expected on life expectancy because of persisting cardiovascular diseases). The estimated contributions to the life expectancy gap therefore need to be viewed cautiously, although the principal finding of multiple contributions remains.

We carried out this study to improve understanding of premature mortality which has been a long-lasting problem among people with severe mental illness and described as "... at worst, a form of lethal discrimination" [24]. While we agree with the other opinion in this area that the time has come to shift efforts towards interventions to improve survival, we believe that the observational data remains deficient as an evidence base. In particular, our findings suggest that prioritised interventions should be those which demonstrably have an impact on multiple causes of death, as clearly addressing a single cause will only have a small effect on life expectancy. In addition to receiving optimum mental healthcare, it is thus imperative that individuals with severe mental illnesses should receive a package of care to help improve lifestyle, diet, and proper medication management. It is also important to bear in mind current thinking on achieving health improvements through reducing health

inequalities and minimising the impact of socio-economic status on health advantages [25]. Failure to appreciate these challenges may result in resources being used inefficiently as what is most beneficial might be to tackle the issue in a systematic way.

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Figure 1. Changes in the estimated life expectancy of men with SMI following successive equalisation of primary causes of death with rates of England and Wales in 2010 (N = 10,414)

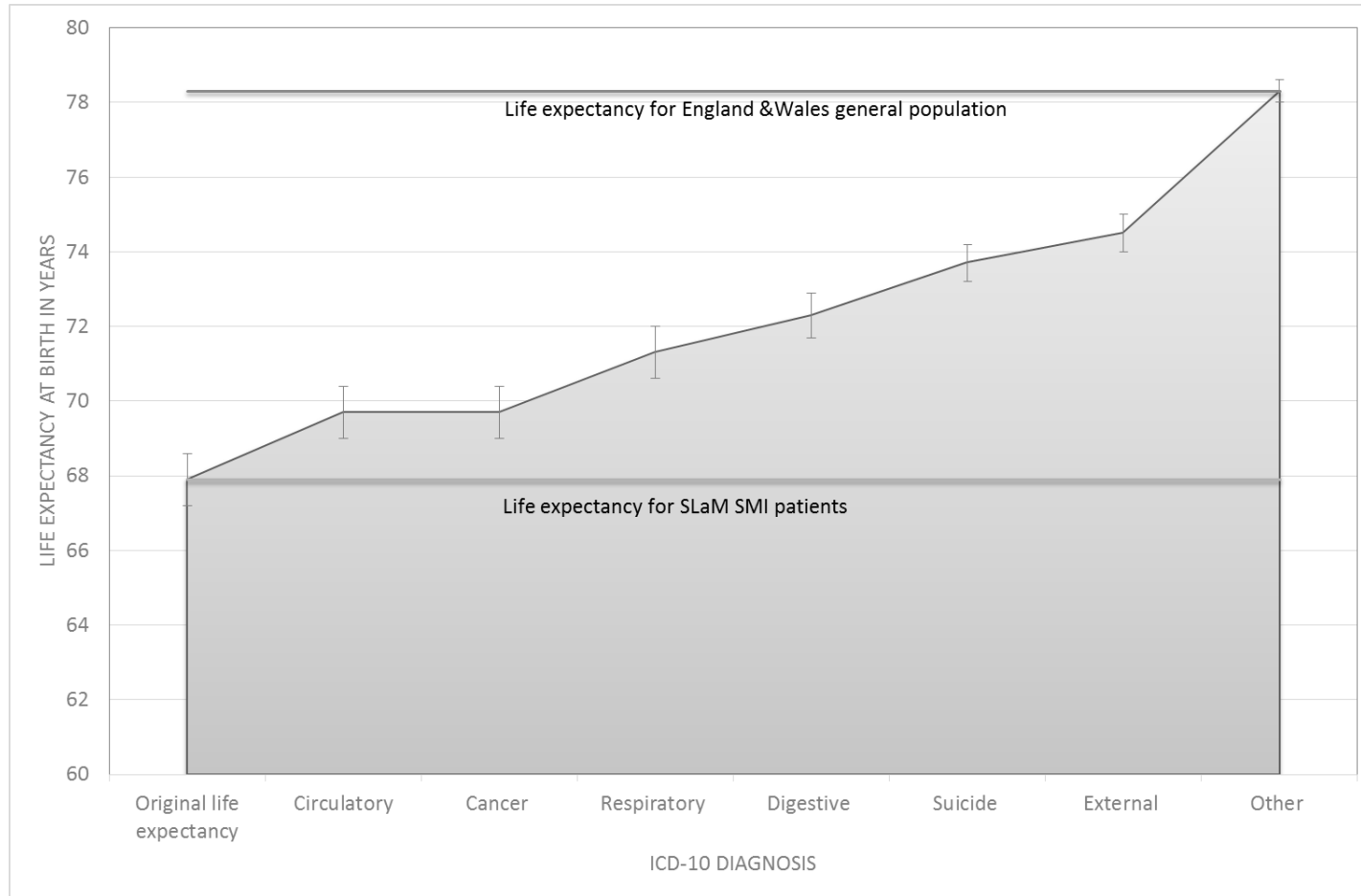


Figure 2. Changes in the estimated life expectancy of women with SMI following successive equalisation of primary causes of death with rates of England and Wales in 2010 (N = 8,692)

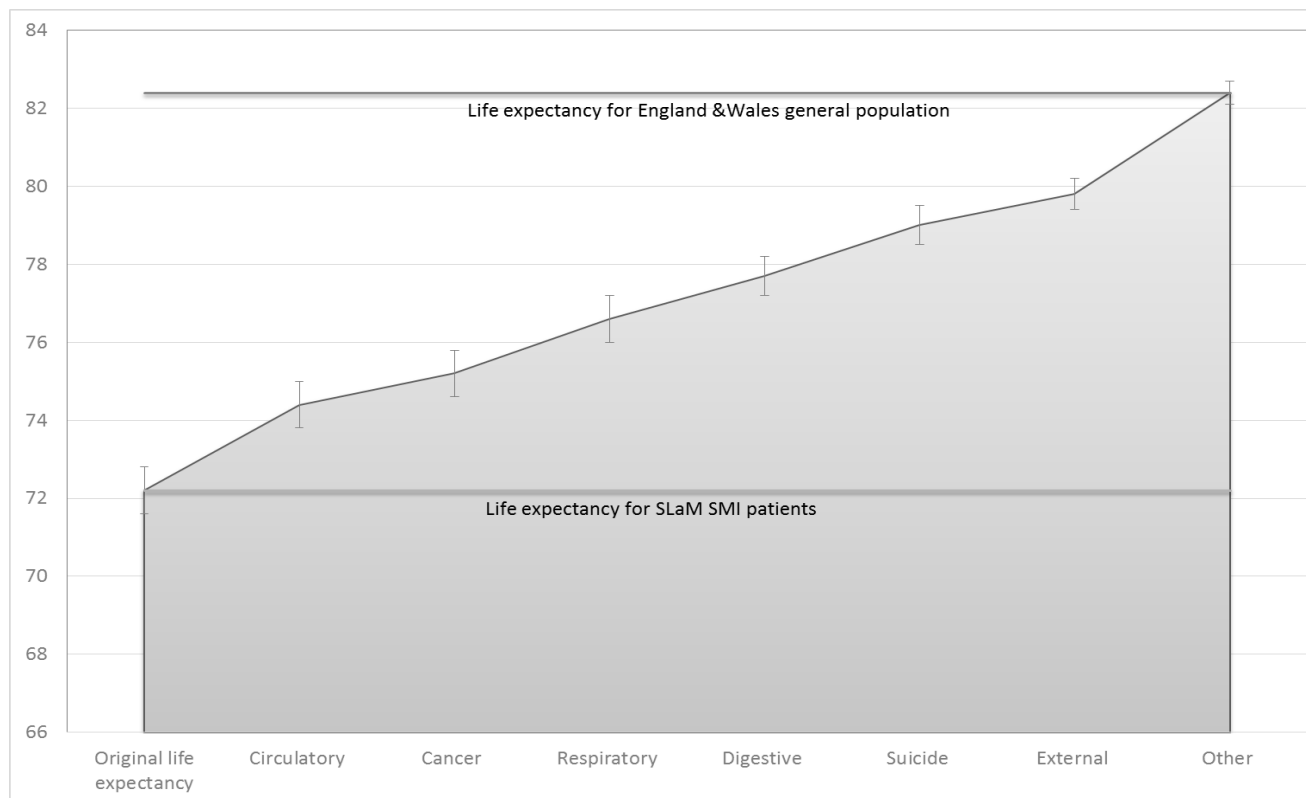


Table 1. Number of deaths by primary cause (ICD-10 categories) in people with SMI and the hypothetical change in life expectancy following equalisation of these to England and Wales cause-specific mortality rates in 2010

Gender	Primary cause of death	Number of deaths during 2007-2012 (% of all deaths)	Life expectancy improvement in years by	
			equalising causes of death with those in general population	Percentage of contribution to the gap of person-years
Males	Circulatory (I00-I99)	195 (23.9)	1.82	17.4
	Cancer (C00-D48)	110 (13.5)	-0.02*	--
	Respiratory (J00-J99)	132 (16.2)	1.73	16.5
	Digestive (K00-K93)	55 (6.7)	0.92	8.8
	Suicide (X60- X84, Y10-Y34)	55 (6.7)	1.40	13.4
	Other external (V01- Y98)	57 (7.0)	0.84	8.0
	All other causes	212 (26.0)	3.76	35.9
	Females	Circulatory (I00-I99)	205 (27.6)	2.24
	Cancer (C00-D48)	148 (19.9)	0.83	8.1
	Respiratory (J00-J99)	114 (15.4)	1.40	13.7

Digestive (K00-K93)	40 (5.4)	1.01	9.9
Suicide (X60- X84,Y10-Y34)	33 (4.4)	1.39	13.6
Other external (V01- Y98)	28 (3.8)	0.74	7.2
All other causes	174 (23.4)	2.60	25.5

* Replaced by zero in the consecutive calculations