Scoping Mortality Research A Report by The Actuarial Profession

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## Summary of key points

The main aim of this report is to provide an overview of the key areas of research into mortality developments across a wide range of disciplines, as well as areas of overlap and gaps in the research. The literature described is compiled from recommendations received by the Mortality Developments Scoping Project Steering Group from experts from different disciplines working in the area of mortality developments.

Key themes identified from recommended literature

- The role of medicine in mortality reduction
- The role of lifestyle and environment in mortality reduction, including smoking, socio-economic conditions and obesity
- Causes of death contributing to mortality reduction, in particular coronary heart disease
- Mortality reduction attributable to differing age groups
- The relationship of active life expectancy to total gains in life expectancy
- Evidence of cohort effects on mortality improvement
- Future trends in mortality developments

Areas of overlap identified from recommended literature

- Overlap between literature examining the role of medicine in mortality decline and the influences on the decline in mortality from coronary heart disease
- Areas of overlap between various disciplines working in the field of mortality developments

Gaps identified in recommended literature

- Lack of recommendations from social policy
- Few papers recommended on the role of lifestyle and behavioural factors on mortality
- Few papers recommended on causes of death other than coronary heart disease
- Few papers recommended on potential threats to future mortality improvement

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## Preface

The Actuarial Profession is currently undertaking a review of its research strategy and has decided to focus more resources on researching mortality developments. It is important that the profession is involved in partnerships with researchers from outside the profession, bringing actuarial expertise into closer contact with other disciplines. We believe that collaboration between these different areas of expertise will provide important new insights in understanding mortality trends. This report represents the first step by the Mortality Developments Scoping Project Steering Group to map current research into mortality developments across a wide range of disciplines. The steering group is aware that the themes and literature discussed in this report are not exhaustive; however it does include areas of research not normally covered by the Actuarial Profession. The steering group welcomes comments on the report and suggestions for any areas which may not yet have been covered.

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#### 1. Introduction

Mortality developments is an area in which the Actuarial Profession has a particular interest and has conducted research. However, at present many within the profession are unaware of research which has been undertaken by other disciplines in the field of mortality developments. The main aim of this report is to provide a multi-disciplinary study of mortality developments research, highlighting the key factors underlying mortality improvements (and impairments) and identifying the core questions which excite the different disciplines studying mortality. In particular any gaps and overlaps in the research will be discussed. It is intended that this report will be of value not only to members of the Actuarial Profession, but also to researchers in other disciplines by providing an overview of the main issues in current mortality research.

## 2. Methods

The time restraints inherent in a scoping project created a number of challenges when developing a methodology to review the large field of mortality developments across several different disciplines. It was decided at an early stage in the project that it would not be practical to perform an in-depth search of several different literature databases to identify high quality, relevant papers. Instead the Scoping Project Steering Group adopted an alternative approach. First, the disciplines which the study intended to cover were identified. These were: medicine, epidemiology, gerontology, demography, health economics, medical sociology, social policy and psychology. It was decided that the researcher would contact key 'experts' working in each of these disciplines to ask them what they believed were the five most important pieces of research in mortality developments at the moment. The original list of experts was devised from suggestions from members of the Scoping Project Steering Group. As the project progressed many of those contacted went on to suggest additional experts who they thought could provide help. In total 38 experts working in the field of mortality developments, in eight different disciplines, were contacted. Of these 22 contributed a list of what they viewed as the five most important pieces of research in mortality developments. Three experts initially agreed to help but did not send in a list of recommendations. A further three expressed an interest in the project but did not feel able to recommend papers to the steering group. Ten of those contacted failed to respond to requests for help. The papers recommended by the experts were entered into a literature database and generated a list of over 90 studies focused on the area of mortality developments, including articles, books and research currently in progress. These studies were reviewed and from these a list of the major themes in mortality developments was compiled. These themes are listed in Section 3. The key issues identified in this review, as

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well as any gaps in, and overlaps with, actuarial research and other disciplines, are discussed in Section 4.

There are a number of strengths and weaknesses associated with the approach which the scoping project took to provide a review of mortality research. The main aim of the project was to provide an overview of the key issues in mortality developments research across a number of different disciplines. Contacting experts working within the field provided an insight into what those at the centre of current research believe is important. As the papers included within this report are derived from experts' recommendations we can be fairly confident that these are high quality, relevant papers. Given the time available to the scoping project it is unlikely that this number of papers would have been identified through the searching of individual literature databases. In addition, the identification of key people working in the field has created an informal network of 'experts' working across a wide range of disciplines that are aware of the Actuarial Profession's interest in mortality developments.

The main drawback of this study is that it is not a comprehensive review of the literature on mortality developments. There are two main risks involved in the methods which this scoping project has adopted. The first is the possibility of bias in the selection of experts working in the field of mortality developments. The second problem may be that not all the key research into mortality developments has been recommended. However, it should be remembered that this is a scoping project aimed at providing an overview of research into mortality developments of disciplines. Several of the experts who were contacted were recommended by a number of different people, suggesting that many of the key people in the field have been identified. These experts represent a wider range of disciplines than those who would normally work with the Actuarial Profession. In addition, many of the key themes discussed in the following section, and indeed many individual papers, were recommended by several different experts, indicating that these issues are regarded as important by many in the field.

#### 3. Themes

The key themes to emerge from the literature recommended to the scoping group are described below.

#### 3.1. The role of medicine

One of the longest running themes in mortality developments is the role which medicine has played in the decline of all-cause mortality. Several studies dealing with this theme were

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recommended to the scoping project from experts in medicine and medical sociology. A number of different methodologies are employed in these studies to assess the relative contribution which medicine has made to all-cause mortality decline.

The origins of the modern debate of the role of medicine lie with the work of McKeown; prior to this the assumption had been that mortality had declined as a result of medical advances. McKeown published most widely in the 1960s and 1970s, culminating in the publication of the book *The Role of Medicine* (1979). McKeown's approach was to calculate what percentage of the total decline in mortality was attributable to specific causes. He established that between the start of death registration in England and Wales in 1848-54 and 1971, 74.4% of the total decline in mortality was attributable to infections and 25.6% to degenerative diseases. Looking at the 20<sup>th</sup> century (between 1901-1971) he argued that 56% of the decline in the infections had occurred before the 1930s which was when sulphonamides, the first effective treatments against a variety of infections, became available. These findings allowed McKeown to argue that medicine was not responsible for the vast majority of the decline in mortality up until the 1970s, as mortality had declined in the absence of effective treatments. Instead McKeown stressed the role played by improving standards of living, and in particular diet, in reducing mortality.

The 'McKeown Thesis', as McKeown's work is now known, has sparked a debate on the role of medicine in the decline of mortality in the late 20<sup>th</sup> and early 21<sup>st</sup> century. Most commentators agree with McKeown's assessment of the role of medicine pre-1971. However, they argue that it is unfair to apply these findings to later time periods when many new technologies have become available. Those studies examining the recent role of medicine which have been recommended to the scoping project are discussed below.

A number of the studies have employed the approach of measuring the contribution of 'amenable or avoidable' mortality to measure the contribution of medicine to the decline of all-cause mortality. The concept of 'amenable or avoidable' mortality was first devised by Rutstein in the 1970s. Essentially this involves a list of those causes of death for which it is accepted that medicine can prevent death. The percentage of the total decline in mortality attributed to these causes is then viewed as having been brought about by medical advances. The number of medical technologies on this list is not rigid, and various studies which have adopted the concept of 'amenable or avoidable' mortality have adapted it to meet their own requirements.

One of the best known studies which has looked at the role of 'amenable or avoidable' mortality is that of Mackenbach (1988, 1996). Mackenbach estimated the contribution of medicine to the decline in mortality in the Netherlands between 1950/54 and 1980/84. Mackenbach complied a list of causes of death for which it could be proven that death could be avoided by adequate preventative or therapeutic interventions, he then attributed the decline in these causes to medicine. He acknowledged that it was possible that not all of the decline in mortality from these conditions could be attributed to medicine, but argued that any over estimation was compensated for by the absence of treatments for ischemic heart disease from his analysis. Mackenbach accredited a gain of 2.96 years in male life expectancy, and 3.95 year gain in female life expectancy, to medicine.

The concept of 'amenable or avoidable' mortality is pursued further in a publication by Nolte and McKee (2004). This publication has two main aims. The first is to provide a review of all studies which have used amenable mortality as a means to empirically measure the role of medicine. A literature review found 72 studies. Nolte and McKee (2004) reviewed these studies to highlight the benefits and drawbacks of using amenable mortality as a measure of the effectiveness of health care systems. In light of these findings Nolte and McKee (2004) then employed a revised concept of amenable mortality to analyse mortality in EU countries during the 1980s and 1990s using routinely available data. The list of amenable mortality compiled by Nolte and McKee consisted of 34 causes of death which they considered amenable to health care. They considered IHD separately as they claimed that the precise contribution of health care to IHD is unresolved, and that the large number of deaths involved with IHD could obscure results.

Nolte and McKee (2004) provide details of their findings for each of the EU countries which they considered. In the case of the UK they calculated that the increase in life expectancy during the 1980s was 1.32 years for men, of which they estimated that declining mortality from amenable causes contributed 32%, for women they calculated that life expectancy increased by 0.80 years in the 1980s, of which 58% was due to amenable causes. However, if the results for IHD are included with those for other amenable causes an even greater percentage of the increase in life expectancy is accounted for, increasing a further 37% for men in the 1980s. Amenable mortality accounted for slightly less of the overall improvement in life expectancy in the 1990s, at only 19% for males and 43% for females, mainly amongst the over 40s. However, once again if the gains in life expectancy associated with IHD are included the combined percentage attributable to amenable and IHD in the 1990s are 60% for males and 70% for females.

Nolte and McKee's (2004) main finding is that there is clear evidence that improvements in access to effective health care have had a measurable impact in many countries during the 1980s and 1990s. They do stress that these results vary between different countries and time periods. In particular, those parts of Europe who began the 1980s with low rates of infant mortality saw a proportionately greater gain in life expectancy amongst those aged over 40.

A different approach to measuring the contribution of medicine to mortality decline was employed by Bunker (1995, 2001). Bunker considered the role of medical treatment on the increase in life expectancy in the USA between 1950-1989. He calculated that life expectancy had increased by 7.1 years. He then devised an inventory approach to calculate the contribution of specific medical treatments to this increase in life expectancy. He identified 13 (clinical) preventative services and 13 curative services. Data from clinical trials and meta analysis was used to establish the effectiveness of these interventions. Bunker then identified the population 'at risk' and estimated the percentage of the population who received the intervention. From this the gain in months or years to life expectancy which may be attributed to specific interventions was estimated. Bunker concluded that 3.5 to 4 years of the gain in life expectancy could be attributed to curative services and 1.5 years to clinical prevention.

An alternative way of viewing the role of medicine in mortality decline is presented in another study which was recommended to the scoping project. Cutler *et al* (2006) considered the role of medicine in the decline of mortality in the USA in terms of financial value. They examine the period 1960 to 2000 during which time life expectancy in the USA increased by 6.97 years, and on average spending on health care increased by 10% per year. This study projects medical spending for four age groups for each decade from 1960 to 2000. It makes the assumption that 50% of total gains in life expectancy are due to medical care.

Overall Cutler *et al* (2006) calculate that life time spending adjusted for inflation increased by \$69,000 between 1960 and 2000, with an overall cost of \$19,000 for every year of life saved, ranging from \$7,400 for each year of life saved in the 1970s to \$36,000 by the 1990s. The cost per year of life saved also varied for each of the age groups, ranging from \$31,600 per year of life gained at age 15 to \$84,700 at 65. Cutler *et al* (2006) conclude that increases in medical spending between 1960 and 2000 have given reasonably good value. However, they emphasise that since 1980 increased spending in medical care for the elderly has been associated with high costs per year of life gained.

## 3.2. Lifestyle and environment

This is a catch-all theme which describes the recommended research on factors which increase the risk of mortality.

#### 3.2.1. Smoking

The impact of smoking behaviour on mortality is also discussed in section 3.3.1 describing the literature on heart disease. However, it is interesting that when asked several of the experts from the Actuarial Profession recommended the work of Doll on smoking dating from the 1950s, illustrating the importance which this work still has on mortality developments research. Doll was one of the first epidemiologists to link smoking behaviour with the incidence of lung cancer (Doll et al, 2004). A number of other papers on smoking were recommended to the scoping project by members of the Actuarial Profession. These include a paper which has attempted to estimate the contribution of smoking related causes of death to hospital admissions and all-cause mortality (The Information Centre, 2006). It was found that in 2004/05 approximately 1.4 million admissions were made to NHS hospitals with a primary diagnosis of a disease which can be caused by smoking. This is a rise of 300,000 admissions since 1995/96. This study also estimated that out of a total of 500,755 deaths in England and Wales in 2004, amongst adults aged over 35, 88,800, or 18%, were caused by smoking. The specific link between smoking and cancer mortality is discussed further in a book recommend to the scoping group (Swerdlow et al, 2001). The relationship of cohort and socio-economic group to smoking behaviour is the subject of another ONS paper recommended to the scoping group (Davy, 2007). Davy found that people born 1926-1950 living in manual households were more likely to become smokers than those in non-manual households. However, both groups later gave up smoking at similar rates. Those cohorts born 1956-1985 were less likely to start smoking, but were also less likely to give up. The rate of giving up amongst the nonmanual group declined slightly; however, the vast majority of manual men and women who started smoking remained smokers. The relationship between socio-economic group and mortality is described further in the following sub-section.

### 3.2.2. Socio-economic circumstances

The relationship between socio-economic group and mortality was the subject of a number of articles recommended to the steering group by experts in medical sociology and demography. Lynch *et al* (2000) discuss the link between income inequality and health. They describe three interpretations of the way in which income inequality can negatively impact on health. The first of these is individual poverty; this is when health and mortality are determined by an individual's income. In psychosocial poverty there are wide inequalities in wealth, and an individual's position in the social hierarchy determines health and mortality. Finally, there is

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neo-materialistic poverty. In this case health and mortality are influenced by individual resources and levels of investment in infrastructure. In this interpretation the dangers associated with lack of personal income can be avoided if sufficient funds are invested in public services to allow equality of access to areas, such as health care, education, transport and housing. Lynch *et al* (2000) recommend that the best way to reduce health inequalities and improve public health in the  $21^{st}$  century is by strategic investment in neo-material conditions via more equitable distribution of public and private resources. The increasing trend of income and health inequality is also discussed by Shaw *et al* (2005). This study considers the impact of New Labour's policies to reduce health inequalities. Shaw *et al* found that although standards of living may have improved amongst some of the poorest in Britain, inequalities in wealth, and health, continue to grow.

A study from the USA, recommended by an expert from the Actuarial Profession and demography, considered whether the impact of socio-economic group decreases with age (Hoffman, 2005). This study found that socio-economic mortality differences remained stable across ages. However, socio-economic differences declined with decreasing health.

#### 3.2.3. Obesity

A paper on obesity was recommended to the scoping project by an expert from demography and the Actuarial Profession. Gibbs (2005) questions the prevailing wisdom that an epidemic of obesity in the US will harm health in the future. He presents a summary of current arguments that the risk of obesity is being exaggerated. This includes one study by Campos who states that the overweight category have a lower risk of premature death than those in the healthy weight category. A recent UK government report (Butland *et al*, 2007) was also recommended by a member of the Actuarial Profession. The Foresight Report is the product of a government obesity project which was set up in 2005. The project modelled data which indicated that by 2050 60% of adult men and 50% of adult women could be obese. In turn this would increase the risk of developing type 2 diabetes, stroke, coronary heart disease, cancer and arthritis, leading to a seven-fold increase in costs to the NHS by 2050. The report also examined the biological and behavioural causes of obesity and the effect of the current environment, in the form of energy dense food, motorised transport and sedentary lifestyles. Population level policies to promote healthier diets and promote walking were recommended to tackle obesity, as well as cultural shifts around food and activity.

### 3.2.4. Diet

No papers recommended.

## 3.2.5. Physical activity

No papers recommended.

## 3.2.6. Alcohol

No papers on alcohol and mortality developments were recommended by the experts contacted by the scoping group. However, members of the scoping group are aware of material published in Health Statistics Quarterly which covers this area. These include data on alcohol related deaths by occupation (Romeri *et al*, 2007) and the geographical variation in alcohol related deaths in the UK (Breakwell *et al*, 2007).

## 3.3. Causes of death

In Section 3.1 those articles which considered the role of medicine on overall mortality decline were described. In this section recommended articles which consider factors influencing the decline of specific causes of death are described.

## 3.3.1. Coronary heart disease (CHD)

CHD is the leading cause of death in the developed world; however, it has been in decline in most developed nations since approximately the 1970s. Articles which have investigated the factors underlying this decline have been recommended to the scoping project by experts from a number of different fields. Of particular note are a series of articles produced by Capewell and colleagues. In some instances experts recommended individual articles in this series, whilst others drew the attention of the steering group to the body of work as a whole. These articles were recommended by experts from medicine, medical sociology, epidemiology, demography and the Actuarial Profession. This was one of the most popular areas of research on mortality developments recommended to the scoping project.

The body of work by Capewell and collegues examines the role which identified medical interventions, for both the primary and secondary prevention, and risk factor reduction has had on the CHD mortality in a variety of geographical locations. To achieve this Capewell and colleagues developed the IMPACT model. This model combines and analyses data on cardiological treatment and risk factors trends. The data employed in this model includes patient numbers, data on uptake of treatment and treatment effectiveness as well as population risk factor trends acquired from social survey data. These calculations allow Capewell and

colleagues to estimate the contribution of each factor to overall changes in mortality within a defined time period.

The IMPACT model was first validated in Scotland (Capewell *et al*, 1999). In this study Capewell *et al* calculated that 6,205 fewer CHD deaths had occurred in 1994 than would have been expected if the death rate had remained the same as it was in 1975. The IMPACT model was then used to calculate how many deaths had been prevented as a result of specific medical and surgical treatments or risk factor reduction. It was estimated that 32% of the decline in CHD in the time period was due to either primary or secondary medical interventions. However, the majority of the decline (60%) was attributed to the changes in rates of smoking, cholesterol, blood pressure, physical activity and poverty. The residual decline was attributed to an 'other' category.

This model was extended to consider the influences on the decline in CHD in England and Wales, where it was calculated that 68,230 fewer CHD deaths had occurred in 2000 compared to the 1981 death rate (Unal *et al*, 2004). The results are similar to those seen in Scotland, with 42% of the decline in mortality being attributed to medical and surgical treatment. Risk factor reduction was credited with 58% of the decline. The number of risk factors considered was extended in this study, although an adverse trend was seen for obesity and diabetes, as well as physical activity. Unal *et al* (2005a) also presented their findings for England and Wales in term of life years gained. They found that modest reductions in major risk factors led to gains in life years four times higher than those for cardiological treatments. Related to this they also considered the relative importance of risk factor reduction amongst the apparently healthy population (primary prevention) and existing patients (secondary prevention) (Unal *et al*, 2005b). It was calculated that of the 45,370 fewer deaths attributed to smoking, cholesterol and blood pressure 81% of the mortality decline had occurred amongst the healthy population and 19% amongst existing patients.

The IMPACT model has also been used to measure the influences on CHD mortality in a population which has seen an increase in mortality. Critchley *et al* (2004) examined CHD mortality in Beijing and calculated that in 1999 there were an additional 1,397 deaths in the age group 35-74 compared to 1984. In this case the model calculated the number of additional deaths which had been prevented due to the introduction of cardiological treatments in this time period. The increase in mortality was attributed to substantial increases in total cholesterol levels, as a result of a growing uptake of a 'western diet', as well as increases in diabetes and obesity.

One of the most interesting features to emerge from the work of Capewell and colleagues is the role which risk factors have played in the reduction of CHD mortality in the UK, and in the case of Beijing the increase in mortality which was seen as risk factors increased. In every study changes in population level risk factor profiles had a greater overall effect on mortality than medical or surgical treatment. Based on these findings Kelly and Capewell (2004) have made recommendations for the way to reduce CHD mortality in the future. They argue that if 80% of eligible patients received appropriate medication this would result in 20,000 fewer CHD deaths each year. However, they believe that modest reduction in smoking, cholesterol and blood pressure could result in 50,000 fewer deaths in England and Wales, or a halving of current levels, with results being seen within 12-24 months, leading to recommendations for population wide policies aimed at risk factor reduction.

A paper recommended to the scoping group by a member of the Actuarial Profession has advanced an alternative approach for CHD mortality reduction. Wald and Law (2003) investigated the potential for developing a single pill, or polypill, designed to reduce cardiovascular disease risk. This study aimed to find a way to simultaneously reduce four of the main risk factors: LDL cholesterol, blood pressure, serum homocysteine and platelet function. A combination of drugs were identified using clinical trial data and meta analyses. These drugs could then be combined into a single pill to be taken daily. Wald and Law (2003) stress that this pill would not only be targeted at an identified high risk population, instead they advocate that it should be taken by all the population aged over 55, as well as any one younger identified as high risk. The use of this treatment amongst the general population is theoretical; however, Wald and Law (2003) argue that its use would have a greater impact than any single cardiovascular disease intervention, leading to an 80% decline in cardiovascular disease.

Another body of work on CHD mortality was recommended by an expert from medical sociology/ epidemiology. This is the global project by the WHO called MONICA which monitors trends and determinants in CHD. At its peak, between the mid 1980s and mid 1990s, this study encompassed 38 populations, in 21 countries, across 4 continents. It measured basic disease, risk factors and medical care measurements (Tunstall-Pedoe, 2003). The study assessed the extent to which changes in risk factors explained the variation in trends in coronary events across populations (Kuulasmaa *et al*, 2000, Tunstall-Pedoe, 2000). It found that between the mid 1980s and mid 1990s there was a 27% fall in CHD mortality, with 21% of the decline due to incidence and 6% to a decline in case fatality. As with the studies conducted by Capewell and colleagues the changes in classic risk factors were seen as partly responsible for the variation in population trends. This led to recommendations in

support of prevention policies based on the classic risk factors, although the study does suggest that there is potential for prevention beyond these.

The prediction of risk of heart disease can be calculated using a variety of different algorithms. A paper was recommended by a member of the Actuarial Profession which has assessed the use of a new cardiovascular risk score (QRISK) for the United Kingdom. Hippesley-Cox *et al* (2007) have validated its performance against the established Framingham algorithm and a newly developed Scottish score ASSIGN. The effectiveness of the algorithms at predicting 10 year risk of developing cardiovascular disease was tested on UK patients aged 35-74 who were initially free of heart disease. The Framingham algorithm over predicted cardiovascular disease risk by 36%, Assign by 36% and QRISK by 0.4%. Both Framingham and ASSIGN tended to over-estimate risk. The authors found that QRISK is likely to provide more appropriate estimates to identify high risk patients, helping to ensure that treatment is directed at those most likely to benefit. However, they also state that the tool requires further validation.

Possibilities for the future of cardiology are considered in a paper recommended by a member of the Actuarial Profession. Flower et al (2000) used current breakthroughs and research, as well as extrapolations from current research, to describe potential future scenarios in the prevention and treatment of heart disease for the first half of the 21<sup>st</sup> century. The first time period considered by Flower et al (2000) is the period up to 2009. In this time the authors predict the initial effects of the unravelling of the human genome on cardiovascular medicine. The results of this may include the ability to identify gene mutations predictive of heart disease via the use of a hand held device, as well as the introduction of powerful new pharmaceuticals. They envisage that surgery will become minimally invasive, and also the beginning of the use of swine hearts in transplant surgery. The next era which Flower *et al* consider is 2009-2024. They foresee a decline in the use of surgery as the genomic revolution leads to the development of drugs designed to bring much of heart disease treatment under pharmaceutical control. Swine hearts may have become common in older people. By 2024-2049 Flower et al (2000) foresee a scenario where heart replacement surgery is almost nonexistent as few hearts become damaged enough to require replacing. Research on the genomic roots of heart disease may bring rapid improvement in prediction, diagnosis and pharmaceutical therapies. The authors do stress that these potential scenarios are speculation; however they are based on current research and the possibilities which this research brings.

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### 3.3.2. Stroke

The WHO MONICA project on stroke was also recommended to the scoping project by another expert from epidemiology. The MONICA project looked at trends in stroke in 15 populations, as stroke and CHD share many of the same risk factors. However, the project found that stroke trends differed from those of CHD mortality in males, whilst there were significant differences in stroke and CHD event rates for both males and females (Truelsen *et al*, 2003). This highlighted the relative difference which risk factors have on the incidence and mortality from stroke and CHD.

The theme of the role of traditional cardiovascular risk factors is explored further in two papers recommended by an expert from epidemiology. Possible explanations for the differing risk factor profile of CHD and stroke are explored in a study by Lawlor and colleagues (Lawlor et al, 2002, Lawlor et al, 2003). This study traced trends in CHD and stroke mortality throughout the 20<sup>th</sup> century. Stroke is made up of two subtypes; cerebral infarct and cerebral haemorrhage. The differential diagnosis of these subtypes on death certificates is frequently inaccurate. Lawlor et al (2002, 2003) were able to calculate the ratio of cerebral infarcts to haemorrhages using data from autopsy studies. These indicate that mortality from cerebral haemorrhage declined throughout 20<sup>th</sup> century, while cerebral infarct mortality increased up to the 1970s before falling. As cerebral infarct follows a similar trend to CHD this suggests that they have common causes. The differing pattern seen for cerebral haemorrhage points to other causes and may explain differing stroke and CHD risk factor profiles. Morris et al (2003) examined the role of traditional risk factors in the north-south mortality gradients for stroke and CHD in the UK. This was a prospective study which covered the 20 years from 1980. It compared age adjusted incidence of major stroke and CHD events in the south of England with the rest of the UK, before and after adjustment for established cardiovascular disease risk factors. They found that incidence of both stroke and CHD was highest in Scottish towns and lowest in southern English towns, but that the magnitude of the gradients diminished once individual risk factors were taken into account, leading once again for recommendations for population wide measures to reduce risk factors.

#### 3.3.3. Cancer

No papers were recommended by experts outwith the steering group. However the steering group is aware of a book by Swerdlow *et al* (2001) which examines cancer incidence mortality in England and Wales. This book brings together data on trends in cancer incidence and mortality. Trends in factors suspected of causing one or more types of cancer are described. A brief description of secular trends, trends by birth cohort, mortality by region and a discussion of these trends are provided for each cancer site.

# 3.3.4. Dementia and neurodegenerative disorders

No papers recommended.

*3.3.5. Chronic obstructive pulmonary disease* No papers recommended.

## 3.3.6. Other causes

No papers recommended.

## 3.4. Age groups

In this section all the papers which were recommended to the scoping project which deal with aspects of age specific mortality developments are described.

## 3.4.1. Childhood and younger adults

No articles covering contemporary developments in mortality amongst children and younger adults were recommended to the scoping group. The effect of early life influences on later life mortality is covered in Section 3.6.

## 3.4.2. Middle age

In Section 3.1. McKeown's study of the role of medicine in the decline of mortality up until 1971 was described. In the time period covered by McKeown the main influence on the increase of average life expectancy was the decline of mortality in infancy and childhood. In England, this situation changed around 1970. During the final three decades of the 20<sup>th</sup> Century, male life expectancy at age 50 increased by more than in the first seven decades. There was a similar, but less dramatic, increase for women. At present there is an absence of research dealing specifically with this area, however, an expert in medical sociology has recommended on-going and proposed research at University College London which focuses on this area. This research hopes to uncover which causes of death have contributed to the increase in life expectancy in middle age and the factors which have influenced their decline; this should aid with the prediction of future changes in life expectancy in middle age.

## 3.4.3. Oldest-old age

A large number of papers were recommended to the scoping group on the theme of oldest-old mortality. These papers were mainly recommended by experts in demography, genetics and the Actuarial Profession. In general this literature refers to mortality developments in the population aged over 80 and covers a wide range of issues, and conflicting views, including

past trends in extreme longevity, potential factors influencing extreme old age and the potential for gains in extreme longevity in the future. These articles are described below.

#### 3.4.3.1. Past trends in extreme longevity

The first group of articles which will be described are those dealing with past trends in oldestold mortality and life expectancy. A study by Kannisto (1994) was recommended to the steering group by members of the Actuarial Profession. Kannisto (1994) begins by stating that in the past octogenarians were unusual and centenarians rare. However, by the late 20<sup>th</sup> century half of all female deaths and a third of male deaths in developed countries occurred in those aged over 80. Kannisto refers to this as a new stage in the mortality transition. In order to study this trend a database was established in 1992 containing death and population counts since 1950 for 30 countries; this allows the estimation of death rates after age 80. In this study Kannisto (1994) presents the initial analyses of these data. His main findings are that in the last two to three decades there has been an unprecedented decline in age specific mortality amongst the oldest-old themselves, leading to an increase in life expectancy at ages 80, 90 and even 100. Aggregated data for 12 countries between 1950-1990 revealed that octogenarians had grown four-fold, nonagenarians eight-fold and centenarians twenty-fold. Kannisto (1994) does stress that the age of onset of this mortality improvement varied between countries, with the improvement generally seen earlier for women than men. This study did not look in depth at factors which may have influenced the decline in oldest-old mortality rates, nevertheless it does suggest possibilities including medical advances and improving living conditions.

Another study investigating past mortality trends was recommended to the scoping project by an expert in demography. Thatcher (1999) agrees with the views expressed by Kannisto (1994) that until recently, although there were spectacular improvements in mortality at lower ages, there was little change in the possibility of dying after age 80. Thatcher (1999) discusses a variety of models for predicting the likelihood of dying, such as the 'law of mortality' discovered by Gompertz in 1825. This showed that the likelihood of dying increases with each successive year soon after age 30. He also describes Fries' theory on rectangularisation. Rectangularisation suggests that as the likelihood of dying at younger ages is reduced the mortality curve becomes more rectangularised as mortality is compressed into a narrow band. Fries advances an upper limit for human life of about 85. In the remainder of this article Thatcher (1999) attempts to model maximum life tables from a variety of historical periods. He concludes that it was likely that the age of 90 was attained in the mediaeval period and that the age of 100 years was probably attained at the end of the 17<sup>th</sup>

century. He uses these findings to claim that there is probably some high age which it is unlikely for humans to exceed, but that it is not predetermined or fixed and definite.

Mesle and Vallin (2006) (recommended by an expert in demography/Actuarial Profession) argue that in most advanced countries child and adult mortality under the age of 60 have fallen so low that further improvements in life expectancy rely on mortality decline at old ages. Mesle and Vallin (2006) are interested in trends in females 65+ life expectancy in high income countries between 1955-96. They claim that although life expectancy has improved in almost all countries some divergence in trends of improvement can be identified. In the case of the USA, the Netherlands, France and Japan they identify a trend of improving life expectancy up until the early 1980s, when the life expectancy of these countries converge. After this point, although life expectancy continued to improve in all four countries, the levels in the USA and the Netherlands were significantly lower than in Japan and France. Mesle and Vallin attempt to explain this divergence in trends by considering the contribution of different causes of death to mortality. They found that up until 1984 the main contributor to mortality decline in all countries was a decline in mortality from cardiovascular diseases. However, between 1984-2000 the USA experienced important increases in mortality from mental disorders, infections and respiratory diseases which jeopardised the gains made from cardiovascular causes. In France and Japan these losses were small. In addition, Japan and France saw an increase in the relative contribution of the decline in mortality at 80+ to the total decline of mortality at 65+ after 1984. Mesle and Vallin (2006) suggest that differences in health care systems and possibly attitudes towards the appropriateness of using medical interventions on the oldest-old may underlie this trend.

The issue of the rectangularisation of the human mortality curve is considered in more depth in a number of papers recommended by an expert in genetics. It has been stated that as deaths become compressed in old age this leads to the rectangularisation of mortality curves, if it is accepted that there is a maximum life expectancy. However, if there is variation in age of death, either from a number of deaths taking place at young ages, or from an increase in the maximum age of death this can lead to less rectangularisation. Wilmoth and Horiuchi (1999) have considered the variability in age of death using data from Sweden during period 1751 to 1991-95. At the start of this time period average life expectancy was 35, however, this disguised enormous variation in age of death, spread from infancy to old age. The rapid reduction in infant and child mortality led to an era of enormous compression from the late 1870s to the early 1950s. However, after this point an unprecedented reduction in late adult mortality led to near constant levels of variability in age of death from 1950 to 1990s. In Wilmoth *et al* (2000) the question of whether there is an immutable life-span limit is

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considered. Again using Swedish data they found that maximum age of death rose from 101 years in the 1860s, to 108 years during the 1990s. They also found that the pace of increase accelerated from 0.44 years per decade before 1969, to 1.11 years per decade thereafter. In addition they attributed only a small part of the increase to increasing size of cohort. The expert who recommended these papers stressed that this indicated that a maximum age at which most deaths would be compressed of 85 is probably wrong.

#### 3.4.3.2. Factors influencing extreme longevity

None of the papers recommended to the scoping project answered satisfactorily the question of why longevity amongst the oldest-old has increased. However, a number of papers have been recommended by experts in epidemiology and genetics which have explored the genetics of ageing, which may help to explain why some individuals live longer than others.

Christensen et al (2006) reviewed the literature on the genetic determinants of longevity. They found that studies of twins reveal that genetic differences account for around a quarter of the variation in adult human lifespan. In most of the studies which they reviewed they found inconclusive evidence for individual genes determining ageing. Possible explanations offered for this were that ageing involves numerous genes which may have small effects, or it may have been due to the small scale of many of the studies reviewed. The only gene which they found to be consistently associated with longevity was APOE. The review also identified studies which found a negative correlation between telomere length and the replicative potential of cultured cells. Telomeres are the protective ends of cell nucleus, each time a cell divides the telomere becomes shorter and eventually the cell dies. However, they found a lack of consistency in the studies' findings. The association between telomere shortening, ageing and mortality is the subject of another article recommended by an expert in epidemiology. Cawthon et al (2003) assessed the association between telomere shortening and mortality amongst individuals aged over 60. Their main finding was that individuals with shorter telomeres in blood DNA had poorer survival, partially due to a higher mortality rate from heart disease. The authors argue that this lends support to the hypothesis that telomere shortening contributes to mortality in many age-related causes of death.

Oxidation, free radical theory and ageing are the subject of two papers recommended by an expert in genetics. The first of these (Tyner *et al*, 2002) considered the relationship between p53 protein, cancer and ageing. P53 regulates cell damage and acts as a tumour suppressor. In this study of mice it was shown that mice with a mutation over-expressing p53 have a reduced incidence of cancer, but also a mortality curve moved to the left. This raises the question of whether p53 has a role in ageing. The second article identifies potential problems

with free radical theory. According to free radical theory ageing occurs as cells accumulate oxidative damage over time. Andziak *et al* (2006) have looked at the naked mole rat, which despite being similar to a mouse has a life span nine to ten times longer, living to around 28 years. The rat tolerates enormous amounts of oxidative damage which the expert who recommended this paper states does not makes sense given current knowledge of cumulative damage, the expert indicated that this strikes at the core of modern gerontology making it important to future research.

#### 3.4.3.3. Future trends in extreme longevity

In this sub-section articles recommended to the scoping project which have attempted to project the future of maximum longevity and the factors which may influence future gains in longevity are described. Once again these papers were recommended by experts from demography, genetics and the Actuarial Profession.

In 2005 Ageing Horizons dedicated an issue to the theme of extreme longevity. In the editorial the findings of the UN long range population projections were described (Howse, 2005). These suggested that by 2300 51 countries will have a life expectancy at birth of over 100, with few countries having a female life expectancy of under 90. These projections are based on the continuation of current trends for the next three centuries. In the remainder of this issue articles are presented which consider the future of extreme longevity.

Experts from demography and the Actuarial Profession recommended the paper by Vaupel and Kistowski (2005). These authors argue that many official forecasts have assumed too low figures for future longevity projections. Vaupel and Kistowski (2005) examined trends in life expectancy since 1840, and argue that there has been a linear rise in life expectancy since that time as a result of the interplay of income, salubrity, nutrition, education and medicine. They extrapolate from this past linear increase that life expectancy will continue to rise, aided by advances in prevention, diagnosis and treatment of age related diseases. Vaupel and Kistowski then consider the view that there is a biological maximum or 'looming limit' to human life expectancy. They refer to theories on senescence, that after a reproductive period humans enter a period of decline. However, Vaupel and Kistowski (2005) argue that, "*there is no empirical evidence of a proximate limit to human longevity*" (p8). They use the example of improving mortality rates in England and Wales amongst the oldest-old from the 1950s, and in particular from the 1970s, to show that improvements in mortality will come from within the elderly population (Vaupel, 1997). In addition they consider the role which calorific reduction and genetic engineering may have on future reductions. The findings of Vaupel and colleagues have been challenged in a number of articles by Olshansky and colleagues (Olshansky, 2005, Carnes et al, 2005); these were recommended to the scoping group by experts from demography and the Actuarial Profession. Olshansky and colleagues argue that there is no scientific evidence to support Vaupel's claim that life expectancy will exceed 100 years in the  $21^{st}$  century. They provide a number of reasons for this opinion. First, they claim Vaupel's estimates are based on flawed methodology. That is his use of extrapolation from past trends to predict future rises in life expectancy, in particular the use of the straight line forecasting to argue that as life expectancy had increased in a linear fashion for the past 160 years it will continue to do so. Olshansky states that these estimates are based on a composite of world records. Olshansky also points out the difficulty of replicating past gains in life expectancy as most of these gains came from the decline of mortality rates in infancy and childhood, which are now low in most developed nations. In addition, Olshansky identifies a number of factors which may threaten future gains in life expectancy. These include the rise in obesity and related causes of death (such as type 2 diabetes, CHD, and cancer) and the rise of the infectious diseases death rate (such as HIV, hospital acquired infections and a potential influenza pandemic). The second part of Vaupel and colleagues' work which Olshansky and colleagues question is their prediction that advances on biomedical technology will accelerate the decline in death rates amongst older persons. Olshansky points out that these technologies do not exist yet and that there is no guarantee that they will in the future.

Olshansky and colleagues also consider whether there is a maximum biological limit to life expectancy. They draw on modern evolutionary theory provided by Medawar, that the body is not immortal, but that genetic information is and is passed on through reproduction. Therefore, the human body is designed to invest in reproduction and not longevity. Under this theory gene mutations cause aging, with the timing of death dependent on when the mutation occurs in the lifespan. Natural selection means that the advantageous genes are brought forward early in the lifespan (to allow reproduction). The senescence of ageing is due to the accumulation of damaging genes in the post-reproductive period of life, or 'genetic dustbin'. Olshansky also refers to the work of Kirkwood, arguing that as, "*external mortality is controlled and survival beyond the end of the reproductive period becomes common occurrence, senescence and senescence-related diseases and disorders have the opportunity to be exposed*" (p22). According to Olshansky this process means there is a natural limit to human longevity with individuals having a 'biological warranty period'.

The possibility of extending this life-span via age-reversal therapies is the subject of an article recommended to the scoping project by an expert in genetics. De Grey (paper in press) has

introduced the concept of the 'longevity escape velocity'. This claims that ageing can be functionally defeated long before there are comprehensive age-reversal therapies, as each improvement buys time for beneficiaries that can be spent developing the next improvement.

Two experts from genetics recommended papers which have considered whether traditional methods of calculating mortality risk are appropriate to the modern population. Based on their investigation of trends in mortality decline in France, Japan, Sweden and the United States, Yashin *et al* (2001) call for a revision of existing theoretical concepts of ageing and mortality. An alternative method for calculating survival/ mortality trajectories is introduced by de Grey (2003).

#### 3.5. Active life expectancy

Related to the work which has been conducted on oldest-old life expectancy is a body of research which has considered active life expectancy. A number of papers in this area were recommended by experts from demography, genetics and the Actuarial Profession. These papers mainly consider the extent to which the increase in life expectancy discussed above has influenced the proportion of the lifespan spent in good health.

Robine and Jagger (2005) argue that as the previous view that life expectancy was fixed at around 85 is no longer tenable, the crucial question is now whether the extra years gained are healthy years. In this study they present the various theories on relationship of healthy life expectancy to total life expectancy which have developed since the 1970s. Gruenberg (1977) predicted an epidemic of chronic diseases as the progression of medical care led to the extension of life of those with disease and disability, as well as the extension of life in to an age when disease and disability are more likely. Fries (1980) proposed an alternate theory where behaviour change and prevention postpone the onset of disease and disability closer to the end of life. According to his prediction that there was a limit to life expectancy of about 85 years this would result in the compression of disability. An intermediate view was advanced by Manton (1982). This was dynamic equilibrium, where the prevalence of disability may increase as mortality falls, but the severity of this disability is reduced.

Robine and Jagger (2005) also consider some of the literature in this area published in recent years. One of the main problems they identified was a lack of consistency in the definitions of healthy life expectancy and also the way in which these definitions are defined; these include active life expectancy (ALE) and disability free life expectancy (DFLE). Their main finding was that the compression of disability, or increase in ALE, is most likely to occur in

those countries where disability was originally high and where life expectancy is increasing slowly. Another area which they consider is the gender gap in life expectancy and ALE. Robine and Jagger (2005) describe the widening of the gender gap in life expectancy throughout the 20<sup>th</sup> century, which meant that by the end of the century females lived on average 7 years longer than males. They found no satisfactory explanation for this gender gap, although the possible influence of traditional masculine and feminine roles in the 20<sup>th</sup> century is considered. That is, that traditional male behaviours, such as smoking, heavy drinking, fast driving, and delaying seeking medical attention, undermine longevity, whilst traditionally female behaviours, such as wearing seat belts, health screening and taking vitamins may improve longevity. Robine and Jagger found that this gap was not present in ALE, or disability. That is, although female may live longer the years of ALE are similar between the sexes. However, few studies have looked at both the longevity gap and disability gap.

Two articles by Manton *et al* (2006a, 2006b) were recommended to the scoping group. In these studies Manton *et al* consider life expectancy and healthy life expectancy in the USA in terms of the contribution of, and the cost to, Medicare, Medicaid and the social security system. Using a number of different sources they considered trends in life expectancy and health life expectancy from the 1930s and predicted trends forward until 2080. They found that between 1935 and 1982 healthy or ALE at age 65 grew at the same rate as life expectancy. However, the rate of decline in disability prevalence accelerated between 1982-1999 from the earlier rate of 0.6% to 0.8%. The effect of this was that the proportion of total life expectancy at age 65 spent in good health increased from 72.8% to 78.5%. These rates are projected to increase further to 84.5% by 2022, and 88.1% by 2080. Manton *et al* also estimated dramatic increases in ALE as a percentage of total life expectancy amongst the over 85s, with the ratio increasing from 23.3% in 1935, to 46.9% in 1999, reaching 63% in 2022 and 75% in 2080.

Based on these findings Manton *et al* made a number of recommendations. The first of these concerned raising the retirement age. When social security was first introduced in the USA in 1935, on average, at age 65 people could expect to live a further 8.8 years in a socially and economically productive state. This compares with 13.9 years by 1999 and a predicted 16.4 years in 2022. Manton *et al* recommend that the retirement age should be raised to 70 for 2005-06, 72 by 2022 and 77 by 2080. These recommendations would still provide the 8.8 years of social security in an active state which the original beneficiaries of social security received in 1935. In the case of Medicare and Medicaid Manton *et al* do not recommend any increase in the age of entitlement as they argue that these measures are partly responsible for

the increases in ALE seen since their introduction. Instead, they suggest that the age of entitlement is lowered as this will help to keep the population healthier at older ages and allow further increases in the retirement age.

### 3.6. Cohort effect

Most of the members of the Actuarial Profession who were asked to recommend papers for the scoping project chose actuarial papers which, at least in part, considered the 'cohort effect'. In the context of actuarial research the cohort effect refers to a specific cohort who were born between 1925 and 1945 who experienced greater improvement in all-cause mortality than those cohorts born before or after. This phenomenon was first described as part of the findings on mortality projections performed by the Government Actuary's Department which looked at the effect of year of birth on mortality improvement (OPCS, 1993).

The cohort effect is explored in a series of working papers by the Actuarial Profession's Continuous Mortality Investigation. These papers describe the process of developing a methodology for future mortality projection, and in particular the significance which this cohort effect may have on future mortality projection. Their main finding was that a cohort effect exists centred upon those born around 1926 who experienced especially rapid improvement in mortality since the early 1980s, and that the cohort effect can be used to project forward (CMI Working Paper 1, 2002, CMI Working Paper 2, 2002, CMI Working Paper 20, 2006, CMI Working Paper 25, 2007).

Richards *et al* (2006) used the methodologies discussed in the Working Papers to analyse the relative importance of the cohort or period effect in predicting mortality. They identified the previously described cohort effect, this time centered on those born in the year 1931. In addition, they identified an increase in mortality improvement with advancing age, that is, there was a greater improvement in mortality within this cohort in 2001 than in 1991. This paper revealed that in the UK cohort effects are more likely to predict mortality improvement than period effects.

In their 2007 paper Richards *et al* investigated whether the cohort effect is unique to the UK. They considered whether the cohort or period effect dominated for seven countries by analysing mortality data for adult populations. This study found that the strength of the cohort effect varies across different countries. In the case of Japan, Germany and the USA

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cohort effects dominated for males. The cohort effect also dominated for females in Sweden, Germany and USA; elsewhere period effects dominated.

In general the papers by the Actuarial Profession have focused on the trends in mortality data as opposed to the factors which may have been driving this trend. Willets (2004) expanded this research to look in more depth at the influences on the cohort effect. Willets again identified the cohort born between 1925 and 1945 (centered on the year 1931). He then conducted a multi-disciplinary review, covering epidemiology, social science and demography, to identify factors which could have influenced this trend. Willets argues that within the 1925-1945 cohort there are two sub-cohorts on which different influences on mortality improvement may have acted. For those born before 1935 Willets points to the role played by smoking behaviour. Different generations have different smoking behaviour with lifetime consumption of cigarettes related to year of birth. Lung cancer is one of the diseases most closely associated with smoking and Willets argues that for males lung cancer deaths increased for those born from 1870 onwards, peaking with those born between 1900-1905, with the greatest improvement in lung cancer mortality amongst those men born in the period 1930-1935. For those born in the later half of the cohort Willets suggests that other factors may be more important, in particular the role which diet and early life influences may have had on declining heart disease mortality.

Although Willets (2004) examined possible factors influencing the 1925-1945 cohort effect overall the Actuarial Profession's interest in cohort effects involves their usefulness in predicting future mortality trends. Experts from epidemiology and medical sociology also recommended papers which looked at cohort effects. These papers differed in a number of ways from the work performed by the Actuarial Profession. First, they do not focus on one particular cohort; instead they tend to look at mortality trends in successive cohorts. Also they focus more on the factors which underlie cohort effects, in particular early life influences.

The role of early influences on later mortality has been considered by Catalono and Bruckner (2006). This study tested the 'diminished entelechy hypothesis'. The bases of this hypothesis is that suffering many or virulent environmental insults during childhood reduces the subsequent lifespan of the survivors of that cohort. In order to test this theory Catalono and Bruckner (2006) measured the association between mortality in the first five years of life, which they used as an indicator of environmental conditions, and life expectancy at age five. Cohort life table data was analysed for those born in Sweden (1751-1912), Denmark (1835-

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1913) and England and Wales (1841-1912). This study concluded that suffering many or virulent environmental insults in childhood did effect subsequent cohort lifespan.

Gerontologists Crimmins and Finch (2006) also examined the link between early life and a cohort's later mortality risk. Although this study acknowledged the link between diet in early life and a cohort's mortality risk in later life, this study focused on the link between inflammation and later life risk. Crimmins and Finch tested the 'cohort morbidity phenotype' theory; that birth cohorts with lower early life mortality due to infections experience lower mortality throughout life. They considered whether exposure to inflammation through the life-course could lead to the development of atherosclerosis, even in the absence of a high fat diet. This study again used childhood mortality as a direct index of high environmental exposure to infections, and so inflammation. This study examined the link between early life mortality and later mortality for four north European countries using data from 1751 to 1899. The study restricted itself to cohorts born before the 20<sup>th</sup> century to avoid the effects of smoking, immunisation and antibiotics. The study concluded that mortality decline amongst older persons occurred in the same cohorts that experienced mortality decline as children.

Some of the studies recommended to the scoping project have examined the role of cohort effects for cause-specific mortality. Davy Smith *et al* (1998) looked at the association between social circumstances in childhood and mortality from coronary heart disease, stroke, lung cancer, stomach cancer and respiratory disease. After adjustments for adult socio-economic circumstances and risk factors this study showed an association between early life and stroke and stomach cancer, and to a lesser degree to coronary heart disease and respiratory disease.

The work of Gavrilov and Gavrilova (2001) on early life influences was recommended by an expert from the Actuarial Profession. Gavrilov and Gavrilova have considered the initial damage which can be done to an individual's DNA. They propose that some individuals are born with a high initial damage load meaning that they are further along the ageing process than others.

One of the main figures in early life influences research is Barker; however, none of the experts contacted by the scoping group specifically recommended any papers by Barker. Barker developed the foetal origins hypothesis. This hypothesis looks at the relationship between foetal undernutrition in middle to late gestation and the risk of developing coronary heart disease in later life. The highest risk was found amongst those who were born small and became heavier during childhood (Barker, 1994). Further literature on the foetal origins

hypothesis is available at the BMJ topics website. It has been proposed that elevated blood cholesterol is one of the outcomes of impaired foetal growth. This relationship is the subject of a systematic review recommended by an expert in genetics. Huxley *et al* (2004) identified 79 relevant studies; however, their main finding was that impaired foetal growth does not have effects on blood cholesterol levels that would have a material impact on vascular disease risk.

#### 3.7. Actuarial views on the future of longevity

All of the members of the Actuarial Profession who were contacted by the scoping group, on the future of mortality, recommended papers by Willets (1999) and Willets *et al* (2004). These documents provide an overview of the profession's main interests in mortality developments, and what the profession thinks is likely to happen to longevity in the near future. One of the most striking features of these reports is that many of the areas covered are included in the themes described above. As these themes are based on the recommendations of experts from a number of different disciplines this suggests that many in the Actuarial Profession are aware of research being conducted elsewhere. However, it is noteworthy that none of the experts from outwith the Actuarial Profession recommended actuarial papers. The paper by Willets *et al* (2004) covers three main areas; past trends in mortality, projections for longevity in the  $21^{st}$  century and the possible financial implications of longevity increase.

One of the main trends highlighted by Willets *et al* has already been described in the previous section. This is the cohort effect, where those people born around 1931 have seen greater improvements in mortality than those generations born on either side. Willets *et al* also consider age and cause specific mortality trends for the latter part of the  $20^{th}$  century. They draw particular attention to the gains seen in the age group 50-79, mainly from heart disease. The international experience of cohort effects and variations in rates of improvement are also discussed. One area which Willets *et al* cover, which was not recommended by experts contacted in other fields, is the potential threat to longevity advance from infectious disease. The risk of disease spread as a consequence of technological advances such as rapid global travel and the emergence of drug resistant disease strains is considered.

Willets *et al* (2004) analyse how mortality is likely to change in the future, drawing out key trends and identifying what they think is likely to drive mortality shifts in the future. They project that it is highly probable that in the first few decades of the 21<sup>st</sup> century mortality rates for the elderly population in the UK will improve faster than ever before, with the expectation of post-retirement lifespan increasing dramatically. Reasons for these potential gains include

the cohort effect, as those born between 1925-1945 enter old age they should see a continuation of the mortality improvement seen amongst this cohort in the past. Based on the past prevalence of smoking they predict falls in smoking-related causes of death, as well as the continuation of the steady trend of falling circulatory and cancer mortality. The accelerating pace of medical advances, as well as the expansion in the use of medical technology amongst the elderly is also highlighted. In addition, life expectancy in the UK is currently relatively low at age 65 compared with other developed countries meaning there is potential for improvement in this age group. Based on these projections Willets *et al* consider the possible financial implications of increasing longevity. However, Willets *et al* also emphasise the uncertainty which is involved in predicting future mortality trends.

#### 4. Discussion

The main aim of this scoping project has been to provide an overview of research being undertaken by a number of different disciplines into the field of mortality developments. In addition, any areas of overlap or gaps in the research were to be identified. The approach taken has been to contact experts working within the field and ask them to nominate what *they* believe are the most important articles, or pieces of research, on mortality developments. This generated a good response and both the content and structure of the report have been based on these recommendations.

The first area of research which was considered was the role of medicine in the decline of all cause mortality. Medical sociologists recommended all the papers in this area. The key questions which emerged from this literature were: what role does medicine play in mortality decline and what role will medicine play in the future of mortality decline? Of particular concern to researchers currently publishing in this field was the need to judge the overall efficacy of medicine on the contribution currently being played by medicine in mortality reduction, as opposed to any role which medicine may have played in the past. The theme heading lifestyle and behaviour was designed to encompass that literature which covered non-medical risk factors on mortality. Somewhat surprisingly there were not many recommendations in this area from the experts contacted by the steering group. A number of papers were recommended on smoking, however, these were all recommended by members of the Actuarial Profession. Very few papers were received covering the other well known health risk factors, such as obesity, diet, physical activity or alcohol and drug abuse. One risk factor which was highlighted by experts from medical sociology and demography was the influence of socio-economic group on mortality risk. The issue of deprivation and risk is one

that is seen in a number of the themes covered by the expert recommended literature, indicating that this is an influence on mortality currently receiving attention.

One of the most popular areas identified by experts was the literature surrounding CHD, in particular the research conducted by Capewell and colleagues. This research appeared to be relatively well known across a number of different disciplines including medical sociology, epidemiology and the Actuarial Profession. Key questions raised in this literature include: what are the main influences on the decline of CHD and what will be the main influences on any future decline? It is of note that the scoping project received very few recommendations for research into the decline of many of the other major causes of death, such as cancer and chronic obstructive pulmonary diseases. There are a number of possible explanations for this. One is that a great deal of research has been conducted on CHD, as it was the leading cause of death in much of the developed world throughout most of the 20<sup>th</sup> century. The large scale epidemiological studies undertaken in the mid 20<sup>th</sup> century, such as Framingham, identified many of the main risk factors for the disease. These studies provided not only a great deal of research directly from their own findings, but provided the background for many other studies looking at the influences on CHD mortality. Cancer, on the other hand, is made up of a large number of individual cancer types, many of which have their own distinct set of risk factors, some of which are currently known whilst the causes of others still remain obscure. This has made it more difficult to carry out large scale research on cancer as a whole, as opposed to CHD with its identified risk factors and good sources of data. It is possible that a body of work does exist which has looked at the overall decline of other causes of death, but that it was not recommended to the scoping project by the experts contacted. However, if this is the case, it is noteworthy that the experts overwhelmingly recommended papers on CHD, indicating that this is an area currently at the forefront of research on mortality developments.

It is interesting how many of the themes covered in Section 3 were dominated by certain disciplines recommending papers. In the case of mortality rates and longevity amongst the oldest-old almost all the papers were recommended by experts from either demography, genetics or the Actuarial Profession. The content of this theme differed from studies looking at influences on overall life expectancy; instead this looked specifically at mortality amongst the oldest-old. Most of the studies recommended agreed that mortality rates had declined, and life expectancy increased amongst the population aged over 80 since around 1950, with an acceleration in this trend after 1970. However, there was a lack of consensus in almost all other areas concerning oldest-old mortality. A number of key issues and questions have emerged from this debate. These include, what has caused the recent increase in longevity amongst the over 80s? What causes ageing? Is ageing a separate condition from disease? Is

ageing an underlying cause of death? Is there a maximum limit to human longevity? Will longevity continue to increase in the future? Will it be possible to extend human lifespan in the future via age-reversal therapies? Many of these questions are still at the stage of theoretical debate as the true nature of ageing and influences on ageing are not yet fully understood.

A number of key issues and questions have also been identified from the literature recommended on the cohort effect. In the case of the Actuarial Profession the key question has been will the cohort born between 1925-44 continue to see greater mortality improvement than those born on either side of these dates? Amongst the papers recommended by experts from medical sociology and epidemiology the key issues are different. Their interest in the cohort effect is mainly in the effect of early life influences on the later mortality of different cohorts, this was a question also raised in the papers recommended on stroke. It is of note that amongst the various papers recommended on the cohort effect and early life, none of the experts recommended any papers by Barker who has published extensively in this area.

Many of the research areas discussed above overlap with each other, with several of the papers reviewed easily falling into more than one category. Perhaps the most obvious area of overlap is between the themes on the role of medicine and on causes of death, in particular influences on the decline of CHD. CHD has been the largest contributor to the decline in mortality in most developed nations, and many of the studies which were recommended considered the role which medicine had in this decline. Another area of overlap is between work carried out by the Actuarial Profession on mortality developments and other disciplines. The most obvious example in this case is the Profession's work on the cohort effect, which was the most commonly recommended area of Actuarial research. It is of interest, however, that although other disciplines research cohort effects, it is only the Actuarial Profession which has focused on the specific cohort born between 1925-1944. Those members of the Profession working on mortality developments, who recommended papers, did seem to be aware of the major areas of research undertaken by other disciplines. Under almost every theme listed in Section 3 (with the exception of the role of medicine) members of the profession recommended papers.

One of the key objectives of the steering group was to identify gaps in the research on mortality developments. This is quite a difficult subject to discuss as the nature of a gap means that no one has recommended it. A number of issues have come to light during the progress of this project. Of note are overall gaps in the knowledge on mortality developments. This was most obviously the case amongst those experts contacted from the field of social policy. Although all those contacted in social policy expressed an interest in the project and a willingness to help, none felt able to recommend papers to the project. The main reason for this appears to be that social policy's interest in mortality lies not in what may be influencing mortality, but in the influence which changes in mortality may have on social policy. For example, the effect which increasing longevity has had on the number of elderly people requiring social care or pensions. This interest led some in social policy to recommend literature which dealt with this area, such as the Wanless Report (2006) which sets out different scenarios for meeting the different care needs for the growing elderly population in the future.

The final type of gap considered by this project concerns overall gaps in the research into mortality developments. Some of these gaps have already been mentioned in the above discussion of the literature recommended by experts. These include, a lack of papers recommended on lifestyle and behavioural influences on mortality and on leading causes of death other than CHD. A number of other potential gaps were identified during discussion within the steering group, these are areas which the multi-disciplinary group wished to know more about but which were not covered in the literature recommended. With regard to causes of death the lack of attention paid to dementia was noted, especially as this is an important cause of death which is often not recorded as a primary cause of death on the death certificate. Related to this was the lack of understanding of some researchers and policy makers regarding the inadequacy of current death certification which does not allow for multiple comorbidities to be listed as the cause of death. In addition members of the steering group wished to know more about other causes of death which may influence mortality decline in the future. Another area which members of the steering group wished to see covered was the relationship between frailty in older people and mortality, and also the relationship between prescribing new drugs and antibiotics and mortality.

As well as factors which may influence the decline in mortality, interest was also expressed in learning more about factors which may retard further declines. This issue was touched on in the work of Olshansky (2005) in respect of the potential role which obesity may play in future mortality rates, as well as the potential re-emergence of infections as a major cause of death. However, no other possible influences which might impede future mortality decline emerged. The role of climate change in future mortality developments was another area which the steering group wished to know more about. Interest was also expressed in the factors underlying the differing trends seen in male and female mortality, as well as the differences in mortality trends seen between the developed and developing world.

It is possible that these gaps are not real but rather reflect the limitations of a scoping project, in that it is not possible to cover all aspects of mortality developments in the limited time available. However, if this research does exist it is interesting that it was not included in the recommendations for the most important research into mortality developments made by the experts contacted by the scoping group.

## 5. Conclusion

This report represents what many of the leading experts working in the field of mortality developments believe to be the key issues in current research. It has been emphasised that this is not a comprehensive list, or discussion, of the literature in the field; however, it does constitute a first step on the part of the Actuarial Profession to map the wide field of mortality developments. The aim in doing this has been to identify gaps and overlaps in the research, as well as gaps in the Actuarial Profession's and other disciplines' knowledge of the respective fields' research. It is the intention that this report will provide a starting point for inter-disciplinary working in the area of mortality developments, and the steering group welcomes comments on any areas which may have been omitted from the report, and suggestions for future research.

### Appendix 1. The work of the Continuous Mortality Investigation

#### Background

The Continuous Mortality Investigation is a research body of the UK Actuarial Profession and carries out research into mortality and morbidity experience.

Traditionally this has encompassed persons covered by long term risk contracts issued by life assurance offices in the United Kingdom and the Republic of Ireland. The investigations cover all the main types of life assurance, annuitant, pensioner, critical illness and income protection insurance contracts offered by the market. The base data is supplied by life offices covering the majority of the market. All dealings with individual offices are confidential.

In June 2006, the CMI also officially took over research into the mortality of members of Self-Administered Pension Schemes (SAPS) based on data submitted by actuarial consultancies.

The CMI is funded by contributions from its members, the majority of whom also submit data. These members receive results on a regular basis.

Some research findings are published. Since 1973 these have been in Continuous Mortality Investigation Reports, which have appeared on average once every eighteen months. In December 2002, the CMI started reporting developments via Working Papers. These papers allow information to be disseminated quickly and facilitate feedback and consultation. All published information can be found in the appropriate section of the website accessed through www.cmib.org.uk

Periodically, the CMI graduates the raw data to produce mortality and morbidity tables that represent the underlying claims experience and are extensively used by UK actuaries in pricing and valuing life insurance and pension scheme risks. The most recent tables, published in 2006, reflect the mortality of life insurance companies in the period 1999-2002 and are called the "00" Series tables.

In recent years, the mortality tables published by the CMI incorporated projections of future mortality. During its work on the "00" Series tables, the CMI undertook extensive research into mortality projections but came to the conclusion that it was unable to present a single view of the future, as had been attempted with preceding mortality tables. The final "00"

Series tables adopted by the UK Actuarial Profession with effect from 1 September 2006 did not contain any projections. It soon became clear that the absence of projections left a gap that caused much debate, both within the Profession and between the Profession and interested external stakeholders. To try to help fill this gap, and to make its earlier research more accessible to actuaries, the CMI published a "library of mortality projections" in draft form in July 2007.

CMI Reports 12, 1991. The analysis of permanent health insurance data.

CMI Working Paper 9, 2004. An analysis of the preliminary results of the mortality of male pensioners of self-administered pension schemes for the period 2000 to 2002 as reported in Working Paper 4.

CMI Working Paper 17, 2005. Report of the preliminary results of an analysis into mortality experience of pensioners of self-administered pension schemes for the period 2000 to 2003.

CMI Working Paper 22, 2006. The graduation of the CMI 1999-2002 mortality experience: final "00" series mortality tables – annuitants and pensioners.

CMI Mortality Committee Working Paper 15, 2005. Projecting future mortality: towards a proposal for a stochastic mortality methodology.

Richards, S, Jones, G, 2004. Financial aspects of longevity risk.

## Appendix 2. The Office for National Statistics

The Office for National Statistics (ONS) publishes a wide variety of mortality data. ONS publish data for England and Wales and at a UK level. Data for Scotland are published by the General Register Office for Scotland. Data for Northern Ireland are published by the Northern Ireland Statistics and Research Agency.

Figures currently published by ONS include:

- National Life Tables for the UK and constituent countries (the Interim Life Tables)
- Life expectancy at birth and at age 65 by area (eg by local authority, by ward level)
- Healthy life expectancy at birth and at age 65
- Life expectancy by social deprivation for selected ages
- Mortality data by cause of death (including a historical series over the 20th century)
- Mortality data by marital status
- Mortality rates by social class
- Projected mortality rates from the national population projections for the UK and constituent countries

(In some cases the mortality data may be grouped rather than by single year of age.)

The ONS also publish two quarterly series, *Population Trends* and *Health Statistics Quarterly*, which often carry articles on particular mortality topics.

*Population Trends* provides population and demographic information. It contains commentary on the latest findings, topical articles on relevant subjects and regularly updated statistical tables and graphs, showing trends and the latest quarterly information on: conceptions, births, marriages, divorces, internal and international migration, population estimates and projections, etc.

*Health Statistics Quarterly* covers the latest trends in the UK's health. It presents an overview of the latest news, and a review of related publications for release and contains commentary on the latest health findings and topical articles. It also highlights trends in health, and details the latest quarterly information on deaths, childhood mortality, cancer survival, abortions, congenital anomalies and morbidity.

These are available both on the ONS website (<u>www.statistics.gov.uk</u>) and as published volumes.

#### Appendix 3. Additional references

This appendix includes those references which did not fall under any of the theme headings in Section 3; this was primarily because they are overarching documents which cover many areas of mortality developments as opposed to specific themes. In addition, any recommendations which were made to the scoping group after the writing of the report have been included here.

Bongaarts, J, 2006. How long will we live? Population and Development Review 32, 605-628.

Caldwell, J. C, 2001. Population health in transition. Bulletin of the WHO 79 159-160.

Caselli, G, Lopez, A, 1996. Health and mortality among elderly populations.

Charlton, J, Murphy, M. (eds) 1997. *The health of adult Britain*, 1841-1994 vol 1 & 2. London: ONS.

Cox, D. R, 1972. Regression models and life tables (with discussion). *Journal of the Royal Statistical Society Series B 34*, 187-220.

Janssen, F, Kunst A. E, The Netherlands Epidemiology and Demography Compression of Morbidity research group, 2005. Cohort patterns in mortality trends among the elderly in seven European countries, 1950-99. *International Journal of Epidemiology 34*, 1149-1159.

Kaplan, E. L, Meier, P, 1958. Nonparametric estimation from incomplete observations. *Journal of the American Statistical Association* 53, 457-481.

Lawlor, D.A, Smith, G. D, O'Callaghan, M, Alati, R, Mamun, A. A, Williams, G. M, *et al.* 2007. Epidemiologic evidence for the fetal over nutrition hypothesis: findings from the materuniversity study of pregnancy and its outcomes. *American Journal of Epidemiology 165*, 418-424.

Lee, R.D, Carter, L, 1992. Modelling and forecasting the time series of US mortality. *Journal of the American Statistical Association* 87, 659-671.

Macdonald, A. S, Gallop, A, Miller, P. K, Richards, S, Shah, J. R, Willets, R, 2005. Projecting future mortality: towards a proposal for a stochastic methodology. *Continuous Mortality Investigation Bureau Working Paper no.* 15. Omran, A.R, 1971. The epidemiologic transition. A theory of the epidemiology of population change. *Milbank Memorial Fund Quarterly 49*, 509-538.

Richards, S., J, Jones, G. L, 2004. Financial aspects of longevity risk. *Staple Inn Actuarial Society*.

Sverdrup, E, 1965. Estimates and test procedures in connection with stochastic models of deaths, recoveries and transfers between different states of health. *Scandinavian Actuarial Journal*, 184-211.

Tuljapurkar, S., N. Li, Boe, C, 2000. A universal pattern of mortality decline in the G7 countries. *Nature* 405, 789-792.

White, K.M, 2002. Longevity advances in high income countries, 1955-96. *Population and Development Review* 28, 59-76.

#### References

Andziak, B, O'Connor, T. P, Qi, W, DeWaal, E. M, Pierce, A, Chaudhuri, A. R, Van Remmen, H, Buffenstein, R, 2006. High oxidative damage levels in the longest-living rodent, the naked mole-rat. *Aging Cell*, *5* (*6*), *463* – *471*.

Barker D. J. P, 1994. Mothers, babies, and disease in later life. London: BMJ.

Breakwell, C *et al*, 2007. Trends in geographical variation in alcohol related deaths in the UK, 1991-2004. *Health Statistics Quarterly, 35, Autumn.* 

Bunker, J. P, 1995. Medicine matters after all. *Journal of the Royal College of Physicians of London 29*, 105-112.

Bunker, J.P, 2001. The role of medical care in contributing to health improvements within societies. *International Journal of Epidemiology 30*, 1260-1263.

Butland, B *et al*, 2007. *The Forsight Report Tackling Obesities: future choices – project report.* Government Office for Science.

Capewell, S, 2006. Commentary: predicting future coronary heart disease deaths in Finland and elsewhere. *International Journal of Epidemiology 35*, 1253-1254.

Capewell, S, Morrison, C. E, McMurray, J, J, 1999. Contribution of modern cardiovascular treatment and risk factor change to the decline in coronary heart disease mortality in Scotland between 1975 and 1994. *Heart, 81, 380-386*.

Capewell, S, Kelly, M (HDA, London, 2004.). Relative contributions of changes in risk factors and treatment to the reduction in coronary heart disease mortality. *NHS Health Development Agency. Briefing Paper*.

Capewell, S., K. MacIntyre, S. Stewart, J.W. Chalmers, J. Boyd, A. Finlayson, *et al.* 2001. Age, sex, and social trends in out-of-hospital cardiac deaths in Scotland 1986-95: a retrospective cohort study. *Lancet 358*, 1213-1217.

Carnes, B, Nakasato, Y, Olshansky, J, 2005. Medawar revisited: unresolved issues in research on ageing. *Ageing Horizons Autumn-Winter*.

Catalano, R, Bruckner, T, 2006. Child mortality and cohort lifespan: a test of diminished entelechy. *International Journal of Epidemiology 35*, 1264-1269.

Cawthon, R. M, Smith, K. R, O'Brien, E, Sivatchenko, A, Kerber, R. A, 2003. Association between telomere length in blood and mortality in people aged 60 years or older. *Lancet 361*, 393-395.

Christensen, K, Johnson, T. E, Vaupel, J 2006. The quest for genetic determinants of human longevity: challenges and insights. *Nature Reviews. Genetics 7*, 436-448.

Continuous Mortality Investigation, 2007. Working Paper 25 - Stochastic projection methodologies: Lee-Carter model features, example results and implications., 1-37.

Continuous Mortality Investigation, 2006. Stochastic Projection Methodologies: Further progress and P-Spline model features, example results and implication Working paper 20., 187-54.

Continuous Mortality Investigation, 2002. An interim basis for adjusting the "92" Series mortality projections for cohort effects. Working Paper 1, 1-47.

Continuous Mortality Investigation, 2002. Responses to the draft report entitled A proposed interim basis for adjusting the "92" Series mortality projections for cohort effects and further commentary thereon. Working Paper 2, 1-12.

Crimmins, E. M, Finch, C. E, 2006. Infection, inflammation, height, and longevity. *Proceedings of the National Academy of Sciences 103*, 498-503.

Critchley, J, Liu, J, Zhao, D, Wei, W, Capewell, S, 2004. Explaining the increase in coronary heart disease mortality in Beijing between 1984 and 1999. *Circulation 110*, 1236-1244.

Cutler, D. M, Rosen, A. B, Vijan, S, 2006. The value of medical spending in the United States, 1960-2000. *New England Journal of Medicine* 355, 920-927.

Davy, M, 2007. Socio-economic inequalities in smoking: an examination of generational trends in Great Britain. *Health Statistics Quarterly, 34, summer, 25 - 34.* 

Davey Smith, G, Hart, C, Blane, D, Hole, D, 1998. Adverse socio-economic conditions in childhood and cause specific adult mortality: prospective observational study. *British Medical Journal 316*, 1631-1635.

de Grey, A, 2003. Critique of the demographic evidence for 'late-life non-senescence'.. *Biochemical Society Transactions 31*, 452-454. Doll, R, Hill, A. B, 2004. The mortality of doctors in relation to their smoking habits: a preliminary report: (Reprinted from Br Med J 1954:ii;1451-5). *BMJ* 328, 7455, 1529-1533.

Flower, J, *et al.* 2000. Technical advances and the next 50 years of cardiology. *Journal of the American College of Cardiology*, 35, 81 - 90.

Gavrilov, L. A, Gavrilova, N. S, 2001. Reliability theory of ageing and longevity. *Journal of Theoretical Biology*, 213, 527 – 545.

Gibbs, W, 2005. Obesity: an overblown epidemic. Scientific American May.

Hippisley-Cox, J, *et al.* 2007. Derivation and validation of QRISK, a new cardiovascular disease risk score for the UK: prospective open cohort study. *British Medical Journal*, 335 (7611) 136.

Hoffmann, R, 2005. Do socioeconomic mortality differences increase with age? *Demographic Research 13*, 35-62.

Howse, K, 2005. Biodemography and longevity. Ageing Horizons Autumn-Winter, 1-5.

Huxley, R, Owen, C. G, Whincup, P. H, Cook, D. G, Colman, S, Collins, R, 2004. Birth weight and subsequent cholesterol levels: exploration of the 'fetal origins' hypothesis. *Journal of the American Medical Association*, 292 (22). 2755 – 2764.

Kannisto, V, 1994. *Development of oldest-old mortality*, 1950-1990. Odense: Odense University Press.

Kuulasmaa, K. H, Tunstall-Pedoe, A, Dobson, S, Fortmann, S, Sans, H. Tolonen, *et al.* 2000. Estimation of contribution of changes in classic risk factors to trends in coronary-event rates across the WHO MONICA Project populations. *Lancet 355*, 675-687.

Lawlor, D, Davey Smith, A. G, Leon, D, Sterne, A. J, Ebrahim, S, 2002. Secular trends in mortality by stroke subtype in the 20th century: a retrospective anaylsis. *The Lancet 360*, 1818-1823.

Lawlor, D. A, Smith, G, D, Leon, D, Sterne, A. J, Ebrahim, S, 2003. Mortality trends by stroke subtype. *Cardiology Review 20*.

Lynch, J.W, Smith, G. D, Kaplan, G. A, House, J. S, 2000. Income inequality and mortality: importance to health of individual income, psychosocial environment, or material conditions. *BMJ 320*, 1200-1204.

Mackenbach, J. P, Looman, C. W. N, Knust, A. E, Habbema, J, O, 1988. Post 1950 mortality trends and medical care: gains in life expectancy due to declines in mortality from conditions amenable to medical intervention in the Netherlands. *Social Science and Medicine*, *27*, 889-894.

Mackenbach, J. P, 1996. The contribution of medical care to mortality decline: McKeown revisited. *Journal of Clinical Epidemiology*, 49, 1207-1213.

Mair, W, Goymer, P, Pletcher, S. D, Partridge, L, 2003. Demography of dietary restriction and death in Drosophila. *Science*, 301 (5640), 1731 – 1733.

Manton, K, Gu, X, Lamb, V, 2006. Change in chronic disability from 1982 to 2004/2005 as measured by long-term changes in function and health in the U.S. elderly population. *103*, 18374-18379.

Manton, K, Gu, X, Lamb, V, 2006. Long term trends in life expectancy and active life expectancy in the US. *Population and Development Review 32*, 81-105.

McKeown, T, 1998. The role of medicine. Oxford: Basil Blackwell.

Mesle, F, Vallin, J, 2006. Diverging trends in female old age mortality: the US and the Netherlands versus France and Japan. *Population and Development Review 32*, 123-145.

Morris, R.W., P.H. Whincup, J.R. Emberson, F.C. Lampe, M. Walker & A.G. Shaper. 2003. North-South Gradients in Britain for Stroke and CHD: Are They Explained by the Same Factors? *Stroke 34*, 2604-2609.

Nolte, E, McKee, M, 2004. Does health care save lives? Avoidable mortality revisited.

Olshansky, J, 2005. The future of human life expectancy. In: *the uncertain future of longevity*. London: Watson Wyatt.

Richards, S., J, J. Ellam R, J. Hubbard, J. Lu C, S. Makin J & K. Miller A, 2007. Twodimensional mortality data: patterns and projections. Richards, S., J, J.G. Kirkby & I. Currie D, 2006. The importance of year of birth in twodimensional mortality data. *British Actuarial Journal 12*, 5-61.

Robine, J, Jagger, C, 2005. The relationship between increasing life expectancy and healthy life expectancy. *Ageing Horizons Autumn-Winter*, 14-21.

Romeri, E, 2007. Alcohol related deaths by occupation, England and Wales, 2001-2005. *Health Statistics Quarterly, 35, Autumn.* 

Shaw, M., G. Davey Smith, D. Dorling, 2005. Health inequalities and New Labour: how the promises compare with real progress. *BMJ 330*, 1016-1021.

Swerdlow, A, dos Santos Silva, I, Doll, R, 2001. *Cancer incidence and mortality in England and Wales: trends and risk factors*. Oxford: Oxford University Press.

Thatcher, A.R, 1999. The long term pattern of adult mortality and the highest attained age (with discussion). *Journal of the Royal Statistical Society Series A 162*, 5-43.

The Information Centre, 2006. *Statistics on smoking: England 2006.* Health and Social Care Centre.

Truelsen, T., M. Mahonen, H. Tolonen, K. Asplund, R. Bonita & D. Vanuzzo, 2003. Trends in Stroke and Coronary Heart Disease in the WHO MONICA Project. *Stroke* 34, 1346-1352.

Tunstall-Pedoe, H, 2003. MONICA's quarter century. *European Journal of Cardiovascular Prevention & Rehabilitation 10*, 409-410.

Tunstall-Pedoe, H., D. Vanuzzo, M. Hobbs, M. Mahonen, Z. Cepaitis, K. Kuulasmaa, *et al.* 2000. Estimation of contribution of changes in coronary care to improving survival, event rates, and coronary heart disease mortality across the WHO MONICA Project populations. *Lancet* 355, 688-700.

Tyner, S. D, Venkatachalam, S, Choi, J, Jones, S, Ghebranious, N, Igelmann, H, Lu, X, Soron, G, Cooper, B, Brayton, C, Hee Park, S, Thompson, T, Karsenty, G, Bradley, A, Donehower, L. A, 2002. p53 mutant mice that display early ageing-associated phenotypes. *Nature 415* (6867) 45 – 53.

Unal, B., J.A. Critchley, D. Fidan & S. Capewell, 2005a. Life-years gained from modern cardiological treatments and population risk factor changes in England and Wales, 1981-2000. *American Journal of Public Health* 95, 103-108.

Unal, B., J.A. Critchley, S. Capewell, 2005b. Modelling the decline in coronary heart disease deaths in England and Wales, 1981-2000: comparing contributions from primary prevention and secondary prevention. *BMJ 331*, 614.

Unal, B., J.A. Critchley, S. Capewell, 2005. Small changes in United Kingdom cardiovascular risk factors could halve coronary heart disease mortality. *Journal of Clinical Epidemiology 58*, 733-740.

Unal, B., J.A. Critchley, S. Capewell, 2004. Explaining the Decline in Coronary Heart Disease Mortality in England and Wales Between 1981 and 2000. *Circulation* 109, 9, 1101-1107.

Vaupel, J.W, Kistowski, K. G. V, 2005. Broken limits to life expectancy. *Ageing Horizons Autumn-Winter*, 6-13.

Vaupel, J.W, 1997. The remarkable improvements in survival at older ages. *Philosophical Transactions of the Royal Society of London - Series B: Biological Sciences 352*, 1799-1804.

Wald, N, M.R. Law, 2003. A strategy to reduce cardiovascular disease by more than 80%. *British Medical Journal 326*, 1419.

Wanless, D, 2006. Securing good care for older people: taking a long-term view.

Willets, R, 1999. Mortality in the next millennium.

Willets, R.C, 2004. The cohort effect: insights and explanations. *British Actuarial Journal 10*, 833-877(45).

Willets, R.C., A.P. Gallop, P.A. Leandro, J.L.C. Lu, A.S. Macdonald, K.A. Miller, *et al.* 2004. Longevity in the 21<sup>st</sup> century *10*, 685-832(148).

Wilmoth, J.R., L.J. Deegan, H. Lundstrom & S. Horiuchi, 2000. Increase of Maximum Life-Span in Sweden, 1861-1999. *Science* 289, 5488, 2366-2368.

Wilmoth, J.R, Horiuchi, S, 1999. Rectangularization Revisited: Variability of Age at Death within Human Populations. *Demography 36*, 475-495.

Yashin, A. I, Begun, A. S, Boiko, S. I, Ukraintseva, S. V, Oeppen, J, 2001. The new trends in survival improvement require a revision of traditional gerentological concepts. *Experimental Gerontology*, *37*(*1*), *157* – *167*.