ABSTRACT OF THE DISCUSSION

The President (Mr J. S. R. Ritchie, O.B.E., F.F.A.): The subject of this meeting is 'The Impact of Medical Advances and Lifestyle on Mortality'. There will be three presentations, followed by a discussion. We have on our panel Professor Macdonald, Professor Waters, Dr Macdonald, Mr Chatterjee and Mr Roche.

Professor Macdonald joined the Department of Actuarial Mathematics and Statistics at Heriot-Watt University in 1989, where he obtained his PhD in 1995, and became Professor of Actuarial Mathematics in 2000. He set up the Genetics and Insurance Research Centre in 1999. Since then it has contributed most of the quantitative research on this topic. His other research interests include survival models and insurance solvency. He was the first Director of the Maxwell Institute for Mathematical Sciences, and was elected a Fellow of the Royal Society of Edinburgh in 2006.

Professor Waters moved to Heriot-Watt University in 1975, and became a Professor in 1990. He has visiting appointments at the University of Copenhagen, the University of Melbourne and the University of Waterloo.

Dr Macdonald graduated in history from Stirling University, and she has worked as a research assistant at both Glasgow and Glasgow Caledonian Universities. She then undertook a PhD at Edinburgh University. Her thesis considered the relative contribution of medicine and standards of living to the decline of mortality in Scotland since 1950, which is extremely relevant to the presentation. She has continued her interest in the influences on mortality with her work with the Actuarial Profession's Mortality Developments Scoping Project.

Mr Chatterjee is a Bachelor of Statistics from the Indian Statistical Institute, Kolkata, India. He became a Master of Statistics in 2000 and gained a Postgraduate Diploma in Actuarial Science in 2001 from Heriot-Watt University. He is both a Fellow of the Faculty of Actuaries and an Associate of the Institute of Actuaries in India.

Mr Roche studied theoretical physics at Trinity College in Dublin, and now works for New Ireland Life Assurance in Dublin, a division of the Bank of Ireland. Professor Macdonald was his MSc supervisor during the summer of 2007, while he was studying for his MSc at Heriot-Watt.

Professor Capewell will contribute to the discussion immediately after the presentations. He qualified from Newcastle University, and subsequently worked in clinical medicine in Cardiff, Oxford and Edinburgh. He 'discovered' Public Health in the Scottish Office. I am not quite sure what that means, but maybe we will find out! Then he moved to Glasgow University before his appointment to the University of Liverpool Chair of Clinical Epidemiology in 1999.

Professor Capewell managed a research programme involving various aspects of clinical epidemiology, mainly coronary heart disease, and he has produced over 100 peer-reviewed papers in the past decade. He contributes to the public health policy nationally and internationally, mainly by working for the British Heart Foundation, the Faculty of Public Health, the Department of Health and the National Institute for Health and Clinical Excellence (NICE).

Professor H. R. Waters, F.I.A., F.F.A. (introducing the topic)**:** This discussion pulls together several strands of research, linked by our common interest in mortality and how it is changing. Actuaries have had an unfairly disappointing press over the past few years, because we have been seen to have been unable to predict changes in future lifetimes which have now occurred. To be fair to actuaries, I do not think that anybody else predicted the changes on the scale which we have seen. As actuaries, we have been working hard to put our house in order, and this meeting is part of that process.

There are two major strands to the discussions. The more recent of the two is the Mortality Scoping Project, about which Dr Macdonald will speak. It is a rather broad brush approach to mortality improvement.

Some years ago, the Social Policy Board set up what it called the Actuaries' Panel on Medical Advances (APMA), whose terms of reference were: "To identify major medical advances

and changes in environment or habits that have altered levels of mortality and health needs ...'' That is rather ambitious, and is the other major strand to be discussed. I have worked as a member of the APMA for the past few years, and we have been trying to address the issues.

I could characterise the first approach, the mortality scoping project, as a macro approach to the subject; trying to look at things in a broad sense, and bringing in many aspects. The APMA approach is very much a micro approach — concentrating on the details — but both have the same goal. Within the study, we will be looking here at two particular research projects. The first one concerns heart disease and stroke, and we shall concentrate on the applications of a model to smoking, statins and obesity. We shall also look at breast cancer. This is a study in which Mr Roche and Professor Macdonald have been involved, — looking at the effect of Herceptin on future lifetimes for breast cancer sufferers.

Dr C. Macdonald (a visitor; presenting the Mortality Scoping Project)**:** I shall discuss briefly the findings of the first draft report of the Actuarial Profession's Mortality Developments Scoping Group (Macdonald, 2009). This was set up in late 2006, and includes members from various different specialties — including the Actuarial Profession, medicine, medical sociology, demography and the Office for National Statistics.

The aim of the scoping group has been to map the main areas of current research (and interest) in mortality developments across a wide range of disciplines. These include: the Actuarial Profession, medicine, epidemiology, gerontology, demography, health economics, medical sociology, social policy and psychology.

Basically, the scoping project hoped to provide an overview of research undertaken across a wide range of disciplines, which would highlight areas of overlap with the research undertaken by the Actuarial Profession and between the various disciplines included in the study. Also of central importance to the scoping group was the identification of any gaps in the current research into mortality developments.

The first challenge which the group faced was how to identify, review and draft a report covering all the research on mortality developments conducted by the wide range of disciplines which had been selected for inclusion, within the six months which were available to the project.

It was decided that it would be impossible to conduct a comprehensive review of the various literature databases for each discipline. Instead, the scoping group decided to contact key experts working in each discipline, and to ask them to recommend what they believed were the five most important pieces of research on mortality developments. The experts who were contacted initially came from suggestions from within the scoping group. Many of them also recommended additional names.

We are aware that this approach has a number of potential weaknesses as well as strengths, the most obvious weakness being that we have not done a comprehensive review of the literature. Also, there is the possibility of bias in the selection of the experts. In fact, many of the people whom we contacted were recommended by several sources, so, we are reasonably confident that we have contacted many of the key people.

This is a scoping project, designed as a first step at mapping the field of mortality developments; it was never the intention to produce a definitive list of all current research. We believe that our approach of asking experts to recommend research has a number of strengths. In particular, the fact that they are experts working in the area means that they are aware of the key research. This approach also gives us an impression of what people working in the area think are the most important issues. We can also be relatively confident of the quality of this literature, as it has been recommended by experts. It would not have been possible to assemble this list of literature in the timeframe by traditional methods. Finally, having contacted these people, a wide range of individuals are now aware of the Actuarial Profession's interest in mortality developments.

In total, we contacted 38 experts. Of these, 22 agreed to contribute a list of recommendations to the scoping group. This generated a list of over 90 pieces of research, mainly in the form of articles, although some books were recommended, as well as research currently being undertaken.

The structure of the report has been guided by the literature recommended. The rest of this presentation provides a brief summary of the main themes which we identified from this literature.

My first theme is headed 'The Role of Medicine'. This includes research which has looked at the overall role of medicine in the decline of all causes of mortality. The research under this heading was recommended by experts from medicine and medical sociology, and includes the work of Thomas McKeown, who published mainly in the 1960s and 1970s. McKeown's main argument was that, taken as a whole, medicine had contributed little to the decline in mortality up until the 1970s — instead, he emphasised the role played by improving standards of living. A number of the papers recommended considered the more recent contribution of medicine to the decline of mortality in a number of geographical settings.

The next theme is 'Lifestyle and Environment'. This was designed as a catch-all theme, which covers non-medical influences on the decline of all-cause mortality. The literature in this section was recommended by experts from the Actuarial Profession, medicine, medical sociology and demography. This included papers on smoking and mortality — including the works of Sir Richard Doll. A number of papers also considered the effect of socio-economic circumstances on mortality. Very few papers were recommended on the effect of either obesity or alcohol on mortality — and the experts whom we contacted did not recommend any papers which looked specifically at the relationship between diet and physical activity and mortality.

The next theme is 'Causes of Death'. In this category we placed all the research which looked at mortality from specific causes of death. One of the most interesting features of this category is that the majority of recommendations were for papers covering two causes of death — coronary heart disease and stroke. We were recommended the work of Swerdlow and Doll, on cancer, by a member of the scoping group. However, we received no recommendations for any other major causes of death.

Papers which examined mortality from coronary heart disease were recommended by experts from a number of disciplines, including medicine, medical sociology, epidemiology, demography and the Actuarial Profession. Coronary heart disease received the greatest number of recommendations of any subject recommended, and, of these, the majority were for the body of work carried out by Capewell and colleagues. This investigates the relative contribution of medicine and risk factor reduction to the decline of mortality.

Several papers considered mortality within specific age groups. There were no papers which looked specifically at children and younger adults, but on-going research into the influences on the decline of mortality in middle age was covered.

A large number of papers recommended from experts in demography, genetics and the Actuarial Profession looked at mortality amongst the very elderly — this included literature which described past trends in oldest-old mortality. A number considered what factors may be influencing the increase in longevity amongst the oldest-old — none of which could satisfactorily answer why this is occurring. Finally, several papers looked at future trends in extreme longevity — including whether there is a biological age limit to which humans can live, and the potential for future gains in longevity.

Related to the increase in life expectancy amongst the oldest-old were a number of papers which explored the issue of active versus inactive life expectancy. These papers mainly considered the degree to which the increase in life expectancy was spent in good health.

The next theme is 'The Cohort Effect'. In the case of papers recommended by members of the Actuarial Profession, this refers to research conducted by the Profession. This identified a specific cohort — that is, those born between 1925 and 1944 — who have seen a greater improvement in their mortality rates than those cohorts born on either side of these dates.

The literature recommended by other disciplines refers to the cohort effect in a different way — and in many cases this involved looking at the effects which early life influences may have on successive generations of older people. This includes papers which considered the relationship between environmental influences on early life — such as maternal welfare, diet, housing, infection — and the risk of mortality in later life.

The final theme which we included is 'Actuarial Views on the Future of Life Expectancy',

and this includes those papers which were recommended by members of the Actuarial Profession which provide an overview of the Profession's main interests in mortality developments, in particular past trends in mortality, projections for longevity in the 21st century, and the possible financial implications of a longevity increase. The most commonly recommended papers in this category were those by Willets and colleagues.

From this initial review of the literature recommended by the experts, the scoping group identified a number of questions which are prominent in current research. These include: "What role does medicine play in mortality decline and what role will medicine play in any future declines?" and "What is the relative contribution of medicine and risk factor reduction to the decline in mortality from coronary heart disease?"

A number of questions were raised in the literature on the oldest-old, including: "What is it that causes ageing?" "Is ageing a separate condition from disease?", "Is ageing an underlying cause of death?", "Is there a maximum limit to human longevity?", and "Will longevity continue to increase in the future?"

One of the main questions raised in research conducted by the Actuarial Profession was whether the 1925 to 1944 cohort will continue to see greater mortality improvement than those born on either side of these dates.

As I stated at the start of this presentation, the scoping group wanted to identify overlaps and gaps in the research on mortality developments amongst the various relevant disciplines. Although this project is only a first step in mapping this area, the literature recommended to the study by experts working in the field has highlighted a number of issues.

Regarding areas of overlap, two different types of overlap were evident to the scoping group. The first was the overlap in the areas of research being conducted by the various disciplines. The second area of overlap was amongst papers recommended by experts from different disciplines. In many instances experts from a variety of disciplines would recommend research from the same area, and, in some cases, the same paper was recommended by several different experts. This was most evident in the research conducted by Capewell and colleagues, which was recommended to the scoping group by experts from many of the disciplines which we contacted. In the case of the literature on mortality amongst the oldest-old, the overlap in recommendations was amongst the Actuarial Profession, genetics and demography.

The identification of gaps in the research was one of the main objectives of the scoping group, but this is one of the most difficult subjects to discuss, because, by their nature, there is no research in those areas. It is possible to see gaps under the theme headings suggested for the report. For example, the lack of papers which considered the impact of diet, obesity, alcohol and physical activity on mortality trends, and also the lack of recommendations for causes of death other than heart disease and stroke.

A number of suggestions for gaps were also generated from discussion within the scoping group, and these included a lack of attention paid to dementia as a significant cause of death, and, related to this, was concern regarding the inadequacy of current death certificates for allowing co-morbidities to be listed as causes of death. The scoping group also wished to know more about factors which may have an adverse effect on future longevity — including the effects of obesity and the potential for the re-emergence of infection as a major cause of death. In addition, it wanted to know more about the effect of climate change on future mortality.

Given the methodology used in this project, of using only those papers recommended by experts, it is possible that some of these gaps are not real, but, rather, that the research exists, but was not recommended to the scoping group. However, if this is the case, it is nonetheless interesting that the experts did not recommend papers in these areas. This may suggest that they may regard other research as more relevant.

The scoping project is one of the first steps towards identifying these gaps in mortality research. By contacting people working in the area, we can get an indication of what are seen, currently, as the most important issues in mortality research. It is hoped that the scoping project will act as a starting point for suggestions and collaborations for future research on mortality developments.

Professor Waters (presenting the topic of the modelling of heart disease and stroke)**:** I shall be speaking about some modelling work which Mr Chatterjee, Professor Macdonald and I have been doing over the past three years. I would like to acknowledge the Framingham Heart Study people in America, who, very kindly, gave us some of their data; the Engineering and Physical Sciences Research Council, a publicly-funded research council, for financing the study; and the Actuarial Profession, which has backed this through the Social Policy Board and particularly through the APMA. That was very important to us, because it has facilitated the meetings of the APMA to oversee this project. The panel consisted of about eight members, most of whom were actuaries, some of whom were doctors. Their advice was invaluable to us in guiding us through this project.

The aim of the project was to produce an individual life history model which included ischaemic heart disease (IHD), stroke and death, and the perceived risk factors for these. I shall not go into too much detail about the model, which is a multiple state model, with many different states. These models are very flexible, and very useful, but they require a great deal of data to parameterise them. We were fortunate that the data from the Framingham Heart Study extended for over 50 years. You need a particular type of data to parameterise these models, which follow the individuals through for a period of time, rather than snapshot data, as in the Health Survey for England (2003). We calibrated our model using the Framingham Heart Study, and then we adjusted the parameterisation so that it fitted, as best we could, the Health Survey for England data in 2003. We looked at several risk factors: age; sex; smoking habits; body mass index (BMI), as a measure of obesity; diabetes; hypertension; and hypercholesterolaemia (high cholesterol levels). Note that, whilst body mass index, diabetes, hypertension and hypercholesterolaemia, are measured on a continuous scale, we have allocated them into a number of different discrete bands.

The first application of this is smoking. Having analysed the data and read the literature, our conclusion (guided by the panel, including our doctors) is that smoking is a direct risk factor for heart disease; for stroke; and, independently of those two, for mortality. None of this is surprising. We are interested in modelling the relative risk of heart disease, stroke or mortality for someone who is a current smoker, compared to someone who has never smoked, and also for someone who has given up smoking (when the relative risk will depend on, among other things, how long ago it was when they gave up smoking). The relative risks of these things depend on whether the person is a current smoker, whether the person has never smoked, or the duration since they stopped smoking. The models which we developed from the information which we had did not depend on sex or age. There was evidence in the literature that this was the case, and this was supported by evidence in our data. The models, also, do not depend on the number of cigarettes smoked, either by the current smokers or by the people who have stopped smoking when they were smokers. The literature, I have to say, was mixed on that. We did not have the right kind of detailed data to analyse whether this mattered, so we took the easy option. Furthermore, our models do not depend on how many years somebody spent as a smoker, although this may well be a relevant risk factor.

Figure D.1 shows the relative risk of the three events. The three events are: dying, myocardial infarction (heart attack) and hard stroke, ruling out transient ischaemic attacks. Transient ischaemic attacks are strokes which do not have an effect beyond 24 hours. What we are doing here is to measure the relative risk compared to someone who has never smoked (whose relative risk is set at one). For a current smoker (duration since giving up is zero), the relative risk of myocardial infarction is about three and a half times. If they give up smoking then, the relative risk of myocardial infarction declines very, very quickly. It goes down to almost, but not quite, one (about 1.1). There is always a residual extra risk of heart attack for someone who has given up smoking, but two years after giving up they are down to around half the relative risk of a current smoker.

The same is true for strokes, where, if you give up smoking, the relative risk of a stroke, which for a current smoker is about 2.2 times that of a person who has never smoked, drops very, very quickly, and again levels out at about 1.1.

For mortality, the picture is different. This is mortality after allowing for heart attacks and
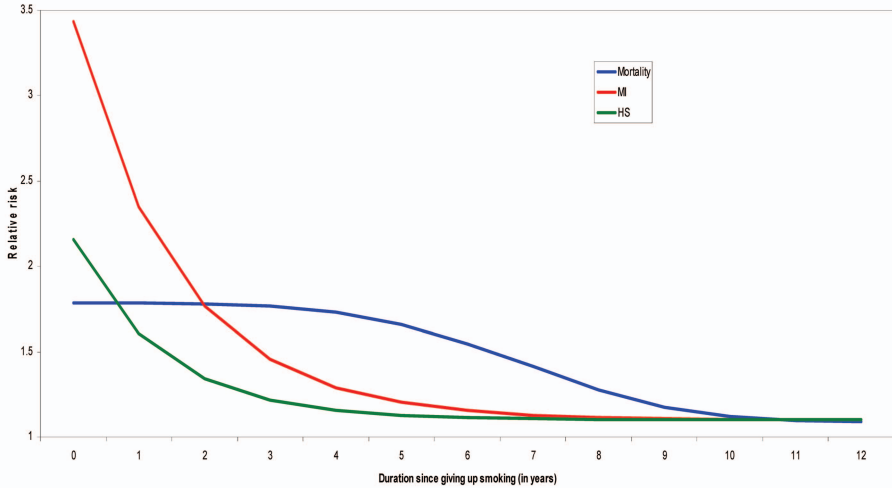
Figure D.1.   Application — smoking; relative risk of events after quitting smoking

strokes. The effect here is that, if you give up smoking, the effect of smoking on mortality, the relative risk, stays with you for a much longer period, before declining slowly down to about 1.09. This mortality effect comes from lung diseases, particularly lung cancer. Whilst giving up smoking does reduce the impact of these diseases, in terms of mortality, it takes a while before the effects really kick in, whereas for heart disease and stroke the effects are much more rapid.

Let us look at some figures. Table D.1 shows the expected future lifetimes from age 20 (based on 20 year olds in England in 2003), for males and females, dependent upon their smoking history. Looking at someone who never smokes, for a male the expected future lifetime in our model is 58.6 years, and for a non-smoking female it is longer, at 62.4 years.

Then we used our model to answer various questions. First: "What would happen if this person is a smoker and always smokes?" The difference is fairly dramatic. For the male, life expectancy drops from 58.6 years to 51.5 years — over seven years' expected future lifetime lost because this person always smokes. For a female the drop is about 6.3 years. Then we said: "What would happen if our 20 year old was a smoker at age 20, continued to smoke until aged

Table D.1.   Application — smoking; expected future lifetimes

Smoking profile	Expected future lifetime from age 20		Expected future 'event free' lifetime from age 20	
	Male	Female	Male	Female
Never smokes	58.6	62.4	53.2	58.2
Gives up at age 30	57.2	61.2	51.8	56.9
Gives up at age 50	55.8	60.2	50.0	55.7
Gives up at age 70	52.7	57.8	46.8	53.0
Always smokes	51.5	56.1	45.8	51.4

30, and then gave up?'' Of course, the person may die before then, but, if they get to age 30, they give up and there is then, from age 20, an increase in their expected future lifetime from 51.5 years, if they never give up, to 57.2 years, almost the same as for the person who never smoked, just by giving up at age 30. If they give up at ages 50 or 70, there are still benefits to be gained. This is mainly because of the rapid decline in the relative risk of heart attack and stroke. The same pattern is seen for females.

Dr Macdonald mentioned active life expectancy. We looked at the expected future lifetime until the first to occur of death, heart disease or stroke. We called this the expected future event-free lifetime from age 20. This must be necessarily less than, or at least no greater than, the expected future lifetime.

We can see in Table D.1, for males who have never smoked, that the expected future event-free lifetime is 53.2 years compared to 58.6 years of expected future lifetime, dropping for a smoker down to 45.8 years. If you give up smoking, there are definite benefits along the way. For a male, even if you continue smoking to age 70 and then give up, your expected future event-free lifetime from age 20 would be a year greater than if you never gave up. For a female, the difference is slightly greater.

Let us move on to the next application, statins. Interestingly, this is where the APMA started looking at this project. The panel were informed by the late Sir Richard Doll that statins were going to have a major effect on the health of people in the United Kingdom and elsewhere, and, if we were looking for medical advances, we should be looking at statins.

Statins are drugs which reduce cholesterol in the body. In particular, they reduce low-density lipoproteins (LDL). This is the 'bad' cholesterol. I do not want to get too technical, but a standard dose reduces LDL by 1.8 mmol/L. By taking statins, there is a reduction in the relative risk of heart disease and stroke, whatever the initial level of cholesterol. You do not have to have high cholesterol or high LDL for statins to be of benefit. That is important for what will come in a moment. Statins were first licensed in the U.K. in 1987, but the drug industry does not stand still. They have been developed on a regular basis ever since. Statins have been widely prescribed in the U.K. since the mid 1990s.

Let us think about the effect of a standard dose of statins. We are interested in the reduction in the relative risk of heart disease and stroke. The paper by Wald & Law (2003) states that the reduction in the relative risk of stroke is immediate and constant at 17%. That is interesting, because high cholesterol, itself, is not actually a risk factor for stroke, but statins seem to have a beneficial effect in terms of stroke. For heart disease, in particular for heart attacks, the effect is more gradual, and depends on how many years of treatment there have been. The reduction in the relative risk of a heart attack after one year of taking statins is about 19%. After two years it is 39%; after three to five years it is 51%; and after six plus years it is 55%. These figures come from Wald & Law's research.

Consider the effect of taking statins for six or more years, which is a reduction of 55% in the relative risk of suffering a heart attack. This is good news, but statins, particularly in their most recent form, have not been around that long. A recent statin, Rosuvastatin, was first licensed in 2003. We have not had six or more years of data on the effect of this drug. So, these figures involve a fair amount of extrapolating into the future. That is going to be very important for the next section of this presentation.

Table D.2 looks at the effect of statins on expected future lifetimes from age 20. I have taken figures for someone who has never smoked. The effect is similar for someone who is a smoker or who gives up. Looking at the expected future lifetime from age 20 for males and for females, and also at the expected future, event-free lifetime, before heart disease, stroke or death, our model here assumes that there is mass medication: every male aged 50 or more and every female aged 60 or more is given statins.

This mass medication was suggested recently by Professor Boyle, the National Director for Heart Disease and Stroke. Statins are predicted to have the same effect in terms of reducing relative risk, whatever the initial level of cholesterol which you have. So, there are reasons for using mass medication. Whether the public in the U.K. is ready for mass medication is another matter. The figures in Table D.2 show that, if we do not give statins, then we have the same

Table D.2.   Application — statins; expected future lifetimes

	Expected future lifetime from age 20*		Expected future 'event free' lifetime from age 20*	
	Males	Females	Males	Females
Treated	59.2	62.7	54.3	58.8
Untreated	58.6	62.4	53.2	58.2

* Never smokes

Treatment protocol: males aged 50+; females aged 60+
(Professor R. Boyle, National Director for Heart Disease and Stroke, July 2007)

figures as those which we saw in Table D.1, 58.6 years of expected future lifetime for a non-smoking 20 year old male. With statins, the life expectancy goes up: for males, by a little over half a year; and for females, by just under half a year. The effect on event-free lifetimes is a little more: just over one year for males; and just over half a year for females.

So, you can form your own opinion. You might think that the effect of statins is not very impressive, but this is one class of drugs for one condition, high cholesterol, and it is having an effect on everybody. We are not focusing on people with heart disease here. So, these drugs, in themselves, given our figures, will push this expected future lifetime up by half a year — a little bit more/a little bit less for males/females.

The third application which I now consider is obesity. We have measured obesity by the body mass index (BMI). This is your weight in kilograms divided by the square of your height in metres. There is plenty of literature which says that this is not the best measure of obesity. The waist to hip ratio may well be a better measure, and we do not dispute that, but we do not have data on that to put into our models.

We have categorised obesity into five categories, depending on the BMI, and these are shown in Table D.3. The lowest we have called underweight. The next one is lightweight. This is called by some authors the ideal BMI. In one official Government publication it is called the desirable range. We then have what is usually called overweight, and we have split the obese category, as is usually done, into the moderately obese, a BMI between 30 and 40, and then the morbidly obese, a BMI in excess of 40. Note that we were guided by medical experts on this.

The BMI is a direct risk factor for three conditions. The higher your BMI, the more likely you are to develop diabetes, to have high blood pressure (hypertension), and it is a direct risk factor for mortality, although the relationship is not monotonic, as we will see in a moment. It is an indirect risk factor (but not a direct risk factor according to our data) for heart disease, because diabetes and hypertension, themselves, are direct risk factors for heart disease.

Table D.3.   Application — obesity; body mass index

Category	BMI range
Underweight	$BMI \leq 18.5$
Lightweight	$18.5 < BMI \leq 25$
Overweight	$25 < BMI \leq 30$
Moderately obese	$30 < BMI \leq 40$
Morbidly obese	$40 < BMI$

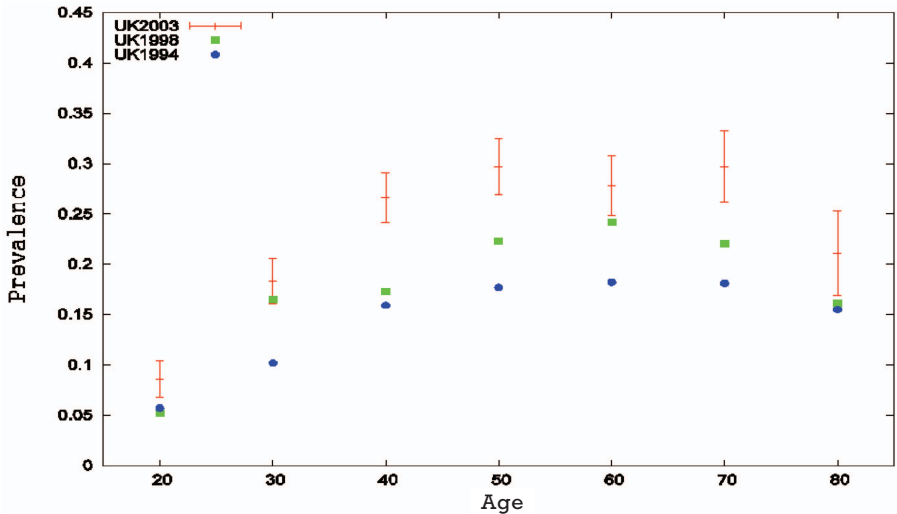Body Mass Index $=$ (Weight in kgs)/(Height in mtrs)^2

Figure D.2.   Application — obesity; prevalence of obesity (BMI > 30 kg/m^2) in England for males

The prevalence of obesity is increasing in the U.K. We can see this in Figure D.2. We have the prevalence of obesity plotted by age, 20 to 80 year olds, where we are putting the two categories (moderately obese and morbidly obese) of obesity together (people with a BMI in excess of 30). The blue spot is taken from the prevalence figure for England in 1994. For 20 year olds it is about 5% in 1994. For 30 year olds it goes up to nearly 10%, rising to nearly 15%, and then falling away a little.

The green squares are the same figures, but for 1998 in England, and we can see that this is very similar. The middle point of the red bar is the 2003 figure for England. We can see that it has risen again. We have also put here plus or minus two standard errors to give you an idea of the sampling variability. We can see that, for 40 year olds it has gone up quite a lot.

The BMI is a direct risk factor for mortality, and Figure D.3 shows the relative risks of mortality for different age groups by BMI category. Everything is scaled, so that the relative risk for the underweight is one at each age. The lowest line in Figure D.3 shows 35 year olds. Underweight people have a much higher relative risk of mortality than the morbidly obese. This is after factoring out everything else: heart disease, diabetes, and so on. As we increase the age from 35 to 50 to 65 to 80, we see the development of a U shape. Remember that, at age 80, the actual levels of mortality are much higher. The absolute level of mortality for a 35 year old is very low. All that Figure D.3 is recording is the relative risk.

For an 80 year old the level of mortality itself is much higher, but still, for the morbidly obese, it is actually lower than for the underweight. This surprised us when we first found it in the data. We looked through other data, did a great deal of literature searching, and talked to doctors about it. One explanation is that we are measuring BMI just before death. If, as many do, people die of cancer, then quite often the body will waste away before death, and so the BMI, when the person dies, is actually very low.

The other explanation which we have been given for this is that, if you have a little bit of 'padding' on you, then you may, particularly in later years, be better able to fight off infections which otherwise might have a more serious effect on you. Whether these explanations are correct, I do not know. When you look at Figure D.3, it looks as if category two comes out the winner. That is the one which is officially called overweight.
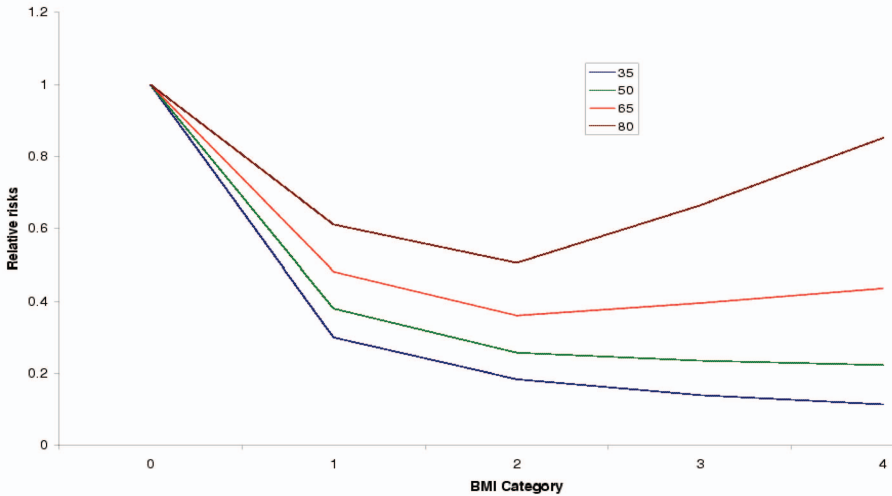
Figure D.3.   Application — obesity; BMI effect on mortality at different ages

We were concerned that the BMI is dynamic in its nature, and is changing, so we wanted to build into our model the scope for change. We developed three models. Model I had no calendar time trend. So, there is no change in time as you go through the years. There is change as you age, but an 80 year old now has the same chance of being obese as an 80 year old in ten, 15 or 20 years' time.

We then tried to match the changes in prevalence which have been seen between 1994 to 2003. This is not a very precise science. The changes were quite dramatic in our models. We looked at two scenarios when projecting forwards this calendar time trend: Model II assumes that the trend continues for 20 years, and then levels off; and Model III assumes that the trend continues indefinitely. If we do that, we get some pretty remarkable figures. Table D.4 shows the prevalence of obesity for females in England in 2003, at ages 20, 40, 60 and 80. Model I tries to match these, starting from age 20 (so that we match these perfectly), and gives a reasonably close match at all ages.

Model II has this built-in increase in prevalence. We start from the same point at age 20, but, as people get older, the prevalence of obesity at these ages, 40, 60, 80, just shoots through the roof. It is getting up to 80%, or even 82.3%, at age 60.

Table D.4.   Application — obesity; predicted prevalence (%) of obesity for females, starting from age 20

	Age			
	20	40	60	80
England 2003	13.1	22.2	27.9	26.3
Model I	13.1	23.3	29.9	30.7
Model II	13.1	60.4	82.3	80.0
Model III	13.1	60.4	93.5	97.5

Table D.5.   Application — obesity; expected future lifetime and prevalence of diabetes, hypertension and IHD/stroke at age 70; males, non-smokers, starting from age 20

BMI model	EFL years	Diabetes %	Hypertension %	IHD/stroke %
I	58.6	12.6	56.0	19.2
II	58.2	17.4	64.1	20.1
III	57.9	18.5	65.4	20.2

Model III has no limits to it. By the time when you get to 80, if you are still alive, you are lucky if you are not obese. We do not put model III forward as a sensible model. We wanted an extreme model to show what would happen.

Table D.5 shows the expected future lifetimes in years for a 20 year old male in 2003. In Model I, as you would expect, the figure is 58.6 years. Under Model II, the expected future lifetime goes down, but by less than half a year. With Model III, which really is a very extreme model, it goes down again, but it still has not gone down by a year from Model I. So, increasing obesity is not having that much effect on expected future lifetime.

If we do a different calculation, and say what the future prevalence of diabetes at age 70 is for our population, then our Model I matches the 2003 prevalence. If we go for the increased obesity under Model II, this will go up by around 50%, and it goes up further under the extreme Model III. The prevalence of hypertension will go up quite considerably as well. This is because the BMI is a direct risk factor for these two conditions. Although we do not see the reduction in expected future lifetime, we do see a far less healthy population in terms of diabetes and high blood pressure. We are not saying that being overweight is an ideal way of life. It may be all right in terms of expected future lifetime, but, in terms of these other things, it is not so good.

The effect on the prevalence of IHD and stroke is not so dramatic with the increase in obesity. The reason for this is that these models predict a much higher prevalence of the BMI, but, for it to have an effect on heart disease and stroke, you have to go through the process of developing diabetes or of developing high blood pressure, and then developing heart disease and stroke, because the BMI is only an indirect risk factor for these two conditions.

<div align="center">REFERENCE</div>

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Professor A. S. Macdonald, F.F.A. (presenting the topic of the work relating to the treatment of breast cancer with Herceptin): I begin by acknowledging the work carried out by the members of the APMA panel and, in particular, Dr Virginia Warren, who suggested this topic, and also the Faculty and Institute Research Steering Committee, which funded it in the form of an MSc prize project, which was undertaken by Mr Roche.

You may not have heard of Trastuzumab, but you almost certainly will have heard of Herceptin, because it has been in the news a good deal recently. They are, for our purposes, one and the same. One is a generic name, the other is a trade name.

The story begins with the HER2 gene, which promotes cell division, and, therefore, is a potential oncogene, since cancer is cell division running out of control. The HER2 gene can be amplified in breast tumours, meaning that there are multiple copies of the gene in the tumour cells, and so its activity is heightened. This gives rise to a more aggressive tumour and a worse prognosis.

Unlike the genetics and insurance topics which we have discussed previously, this is not a heritable feature which is passed on from one generation to the next. It is a property of the

tumour, not of the person. So, any person could develop a HER2-positive tumour (in which this amplification is occurring), and that happens in about 15% to 25% of cases.

The fact that a genetic mechanism underlies this particular route to tumour development makes it a target for the development of new genetic therapies, such as Trastuzumab, better known as Herceptin. It is one of the first major applications of a radically new class of treatments called monoclonal antibodies, which could not have been discovered and developed without the most recent developments of human molecular genetics. So, this is, genuinely, the newest expression of genetic medicine. It targets the HER2 gene expression, therefore over-expression in an HER2-positive tumour.

It is not a treatment on its own; it follows the normal treatment of surgery, radiotherapy and chemotherapy, and is known as an adjuvant treatment. I said that, probably, you have heard of it, because it has recently received much publicity. NICE was not able to recommend Herceptin for widespread use in the National Health Service (NHS), simply because it had not completed its studies. This attracted much political campaigning, even leading to ministerial interference in what is meant to be an independent body.

In the event, when it completed its studies, NICE recommended that Herceptin be widely used at suitable stages of treatment. Nevertheless, NICE had hit the headlines, and, indeed, was in the news again in the past few days, because a parliamentary committee recommended that NICE might adopt the process used in Scotland, which is a bit more rough and ready, but considerably faster.

Dr Warren drew this to our attention at the beginning of 2006, because it was beginning to yield epidemiology. This was not epidemiology like the Framingham study, which has been running since the 1940s, but very new epidemiology from a study and three years of follow up involving about 5,000 women, of whom about 3,200 could be compared directly in terms of treatment or non-treatment.

The first results suggested that three-year survival probabilities were about 92% in the treated group and about 90% in the untreated group. This does not seem to be large, but, over three years of follow-up, it is a significant result, and it was described by one expert as being of the same order of magnitude as the previous blockbuster treatment for breast cancer, and a real breakthrough, given that this was the first of many possible applications of monoclonal antibodies.

Our model is shown in Figure D.4. From a healthy state it is possible to develop one of two forms of breast cancer, which are suitable for treatment with Herceptin: locally advanced breast cancer (LABC), and early breast cancer (BC). A tumour can be either HER2-positive or HER2-negative. As I mentioned, this is a property of the tumour, not of the person who develops it. Since we are interested in life insurance, we measure mortality after onset. Our existing models, based on the population before the availability of Herceptin, gave us the baseline. From the results of the Herceptin adjuvant trial, we could model the effects of Herceptin treatment, and follow that through to the impact on life insurance premiums. The samples which we chose were ordinary term insurance premiums up to age 60.

We have given two sets of results, depending on what allowance is made for the fact that HER2-positive tumours are more aggressive and have a worse prognosis in the absence of treatment with Herceptin. This is not very well quantified, so is best regarded as a sensitivity test, and is shown in Figure D.5.

The scale on the left axis goes from below 99.2% up to 100%, and it expresses the life insurance premiums, with Herceptin treatment being available, as a percentage of the life insurance premiums with no Herceptin treatment being available. The greatest effect is at about age 30, and the effect is a reduction in life insurance premiums of a little less than 1%. The results are simply expressed. The question is: "Is 1%, in this context, a small number or a big number?" It seems to be small, but this results just from one treatment for one disease, which is hailed as being the pioneer of a whole new class of treatments.

There is huge uncertainty about a study like this. It is based on three years of data. Professor Waters alluded to similar uncertainty with some recent results from treatment with more modern forms of statins. It seems that this is a lesson for the APMA. This degree of uncertainty is
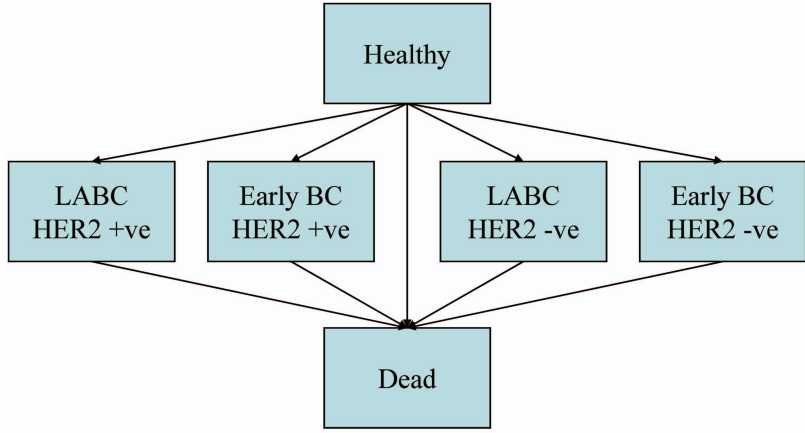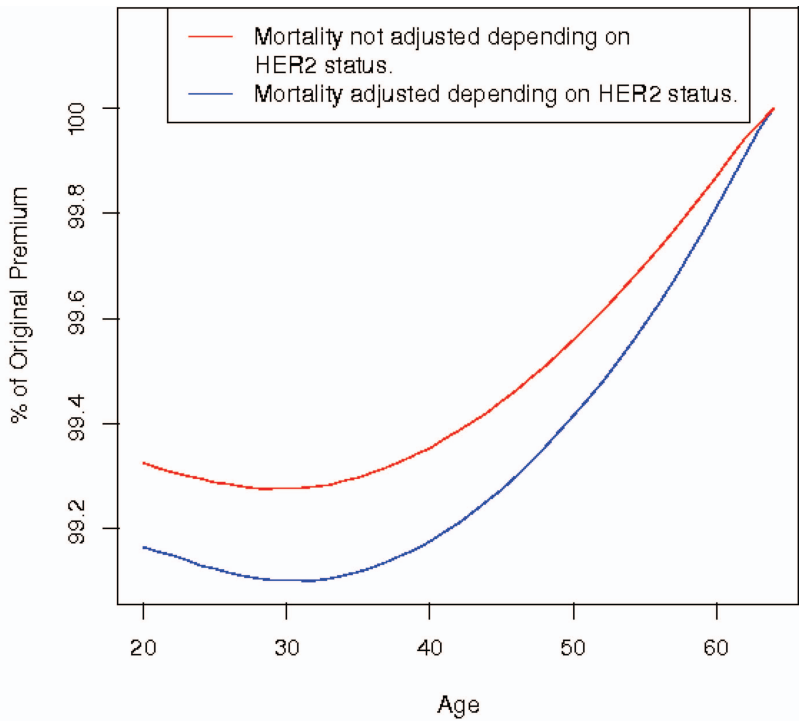
Figure D.4.   Model for breast cancer

Figure D.5.   Sensitivity test for mortality after onset of breast cancer; ordinary term insurance premiums to age 60

unavoidable if you try to look at recently developed treatments or recent medical advances, which, after all, was what the APMA was set up to do.

Another lesson from this study is that, although it was possible to commence the study relatively quickly (as soon as epidemiological studies on Herceptin became available), that depended on the underlying model of the disease process being readily available. We could take the epidemiology and plug it into existing models. The effort which had gone into the development of those models is measured in person-years, not in person-months. Had we started this study from scratch, we would not be showing you results for another two or three years.

Beyond the APMA, we most often hear about modelling disease processes and predicting their future impact when discussing longevity. Modelling different causes of death and predicting future changes in the causes of death is often held up as the way forward in projecting longevity. Much has been said about that here and in other places in connection with pensions and annuities. It would be ideal if it could be done, but it is a very difficult thing to do at any level of detail, the more so when the epidemiology is at an early stage. It will be very interesting to revisit this project in a few years' time, when more mature studies of the epidemiology of Trastuzumab are available.

Professor S. Capewell (a visitor; University of Liverpool)**:** I acknowledge many colleagues who have helped me over the past decade, and the funding which we have had from the Medical Research Council, from the British Heart Foundation, and from a number of other kind agencies.

We have already heard about the trends in coronary heart disease (CHD) in westernised countries. Figure D.6 shows death rates for men, from 1968 through to 2003. There is a very consistent trend. A long time ago we were stimulated to ask the question: "Why have mortality rates for heart disease halved in so many countries?"

We looked at a variety of populations. Looking at England and Wales, we have to try to explain why, in the year 2000, there were 68,000 fewer deaths from heart disease than you would
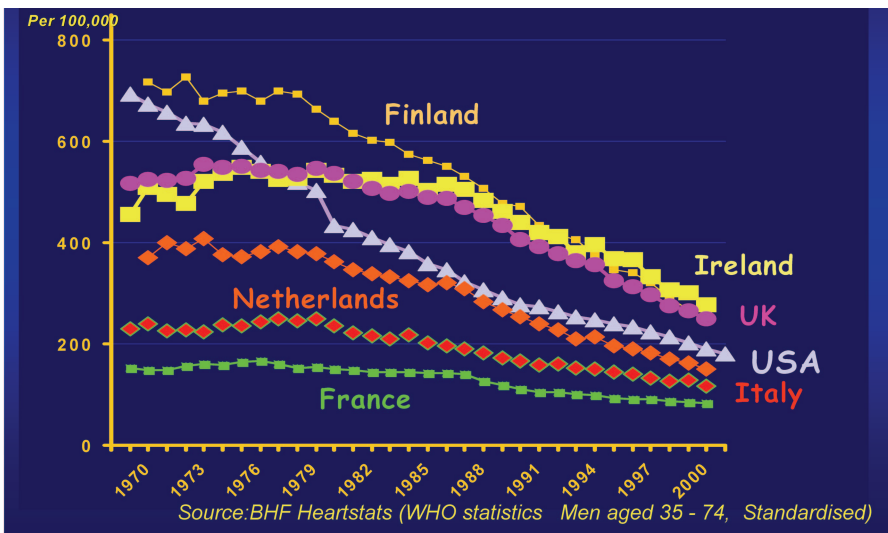

Figure D.6.   International mortality trends, 1968 to 2003, men, coronary heart disease (CHD)
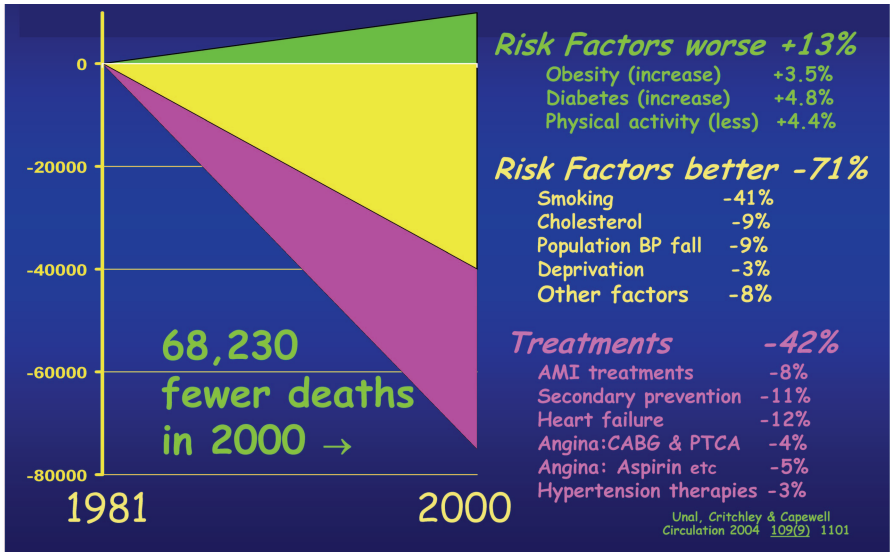
Figure D.7. Explaining the fall in coronary heart disease deaths in England and Wales, 1981 to 2000

have expected if things had stayed the same from 1981. Because of the ageing of the population, you might actually have expected the death rates — at least, the numbers of deaths — to have increased.

We built a model called IMPACT (see Unal *et al.*, 2004), and we found that medical treatments probably explain about 40% of the fall in deaths. Improvements in risk factors explain about 70%, and some risk factors are actually getting worse, which otherwise would have increased deaths by about 13%. The details are given in Figure D.7.

There are no prizes for guessing what kinds of things were going on in the U.K. population in that time. Obesity was going up, diabetes was going up, and people were less active than before. In general terms, for the risk factors improving, smoking rates halved during these two decades. Cholesterol levels and blood pressure came down a little. So, smoking in this population played a major role in reducing deaths. In terms of treatments, it was fairly evenly split between treatments for heart attack, secondary prevention for other forms of heart disease and heart failure.

Most of the money was spent on revascularisation, coronary artery bypass grafting surgery, and for angioplasty. The model suggested that all of that activity contributed only 4% or 5% of the fall in deaths, and, indeed, a number of independent studies, using different methodologies, have come up with very similar findings.

So, we find that risk factors are clearly very powerful. They are obviously important in explaining the falls, but was it the tablets or was it the lifestyles which made the big difference? In the paper Unal *et al.* (2005), we showed that, in fact, it was the lifestyles.

Figure D.8 shows the number of deaths prevented or postponed on the *y* axis. The left side shows the fall in deaths due to cholesterol, overall. There are about 8,000 fewer deaths to explain: population diet changes explain about 4,000; diet in patients with established heart disease explains another 2,000; statins in patients with heart disease account for about 2,500; which leaves barely 500 for high-risk statins, in other words individuals before they get their first
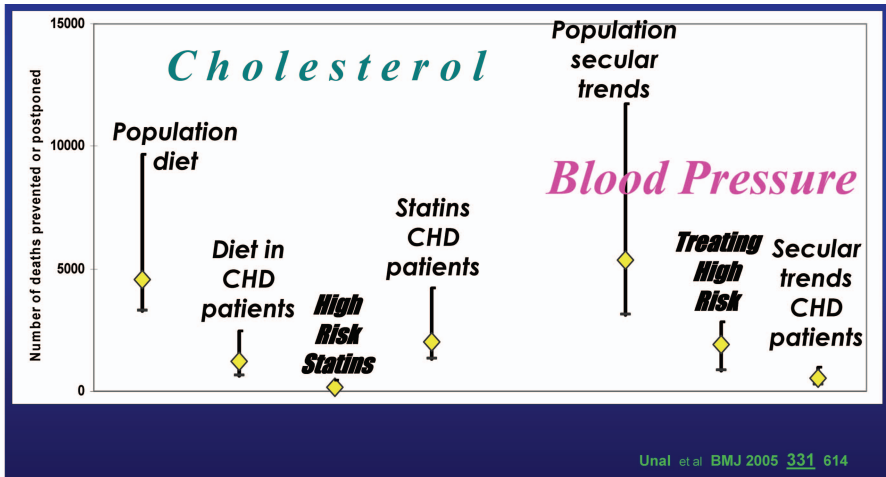
Figure D.8.   CHD prevention in England and Wales, 1981 to 2000; population v. high risk strategies; deaths prevented or postponed (sensitivity analysis)

cardiac event. It was certainly not the tablets which reduced the cholesterol in that population at that time.

Also, blood pressure tablets fared much the same, as is shown on the right side of Figure D.8. Overall, there are about 8,000 fewer deaths to explain. Most of these are because of secular trends in the whole population, mostly diet, in particular reduced salt intake. Blood pressure tablets for individuals account for only 2,000 fewer deaths, with some further benefit for patients once they have presented with their first heart attack or attack of angina.

We found very similar results when we looked at other countries. An article Ford *et al.* (2007), looked at the United States of America between 1980 and 2000. Treatments explained about 47%, improvements in risk factors about 65%, and the Americans are getting fatter faster than we are, so there was an even bigger dent (around 17%) from that adverse trend.

We also compared our results with those for many other populations around the world, as shown in Figure D.9. The risk factors consistently contributed over 50%, and up to 76% in Finland. Having built a model like IMPACT, we can test it against other populations, and see if it works. Reassuringly, it does. We have looked at populations, such as China, with rising heart disease mortality rates, and have tried to explain them. We can also look at life years gained, cost effectiveness, or treatments, and I would like to focus on the latter for this particular talk.

We found that, even in the year 2000 in the U.K., only about 50% of NHS patients, on average, were getting the therapies which were actually proposed for them. That was postponing 25,000 to 26,000 deaths. If, however, the NHS framework target was achieved, if at least 80% of the patients received what they should get, that would postpone another 20,000 to 21,000 deaths.

Figure D.10 shows those 25,000 to 26,000 deaths which were prevented, and the extra gains if we got tablets to everybody who might benefit. So, you can see the big areas for postponing death are heart failure and secondary prevention. I should like to emphasise that getting statins to people before their first heart attack would involve treating about eight million people, and it would gain only 2,000 deaths postponed: quite a high effort; quite a high cost; for quite a low return.
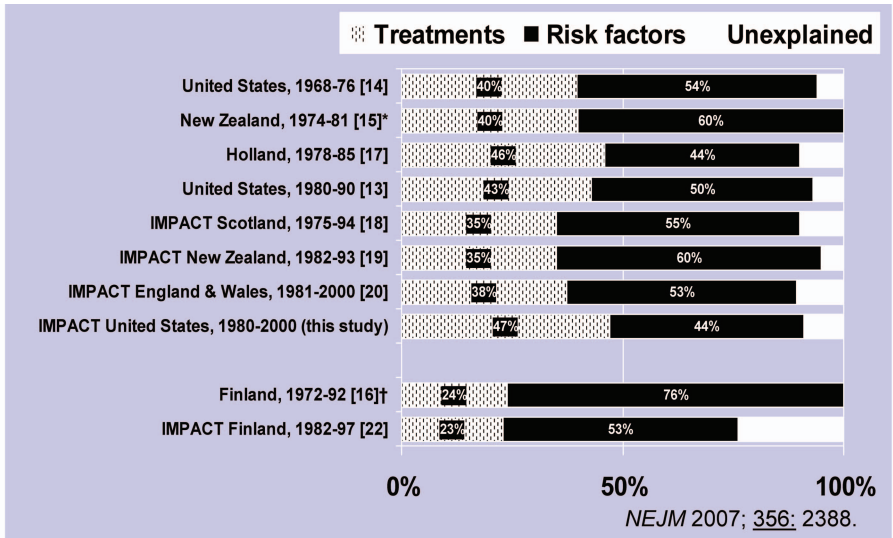
	Treatments	Risk factors	Unexplained

United States, 1968-76 [14] — 40% — 54%
New Zealand, 1974-81 [15]* — 40% — 60%
Holland, 1978-85 [17] — 46% — 44%
United States, 1980-90 [13] — 43% — 50%
IMPACT Scotland, 1975-94 [18] — 35% — 55%
IMPACT New Zealand, 1982-93 [19] — 35% — 60%
IMPACT England & Wales, 1981-2000 [20] — 38% — 53%
IMPACT United States, 1980-2000 (this study) — 47% — 44%

Finland, 1972-92 [16]† — 24% — 76%
IMPACT Finland, 1982-97 [22] — 23% — 53%

0%   50%   100%

NEJM 2007; 356: 2388.

Figure D.9.   Comparisons with studies in various countries; percentage CHD mortality falls
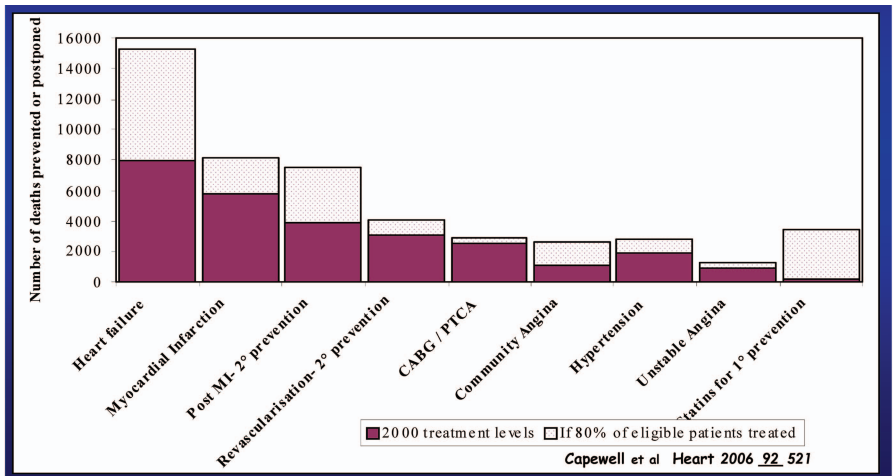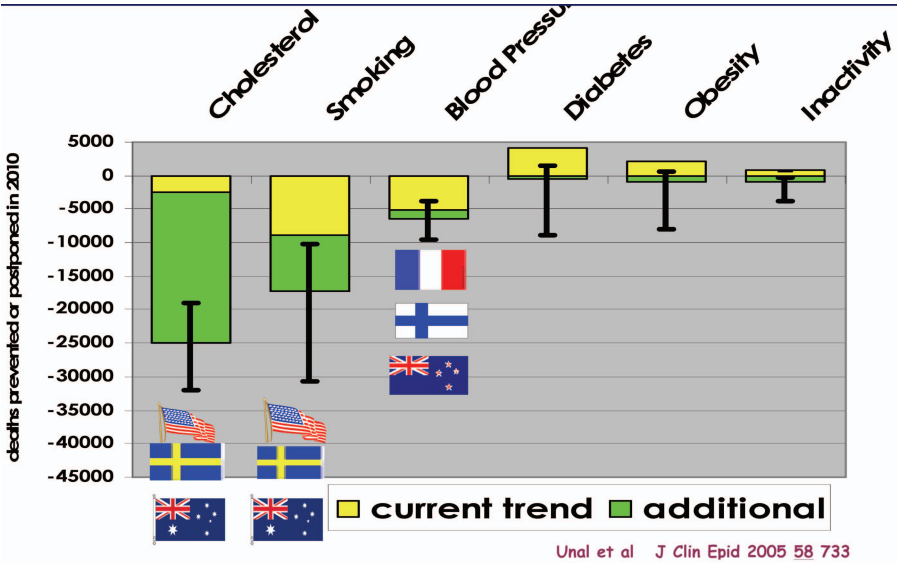

Figure D.10.   Impact of treatment uptakes in England and Wales

Figure D.11.   Potential changes in CHD mortality in England and Wales between 2000 and 2010; if risk factors: (a) continue recent trends; or (b) include additional reductions already achieved elsewhere

We can do other what-if games with a model like this. We can look at risk factors. In answer to the question: "What would happen in England and Wales between 2000 and 2010?", we looked at two different scenarios: if recent trends in risk factors continue in the same way; or, alternatively, if we looked at additional reductions. We chose very realistic values, that is to say levels already seen in other industrialised countries. These are shown in Figure D.11.

Cholesterol levels are coming down slowly in England and Wales, and even in Scotland, but if we got the cholesterol down to 5.2, as already achieved in some other countries, that would be 25,000 fewer cardiac deaths. Smoking related deaths are reducing quite nicely, but we can still double the mortality benefit, maybe 16,000 to 17,000 fewer deaths, if we got down to a more reasonable smoking prevalence, such as is seen in, say, California or Finland. With blood pressure, there could be some benefit, but for diabetes, obesity and physical activity there are only small potential gains. This is very much consistent with what Professor Waters said earlier. Part of the problem is that these risk factors are difficult to change in populations. However, the other, more important, message is that these are minor risk factors. With the big ones, cholesterol, smoking and blood pressure, if you make a change, you get a big return. If we had the modest additional risk factor reductions already seen in other countries, then we could perhaps halve cardiac deaths in England and in Scotland.

Is the party over? I suggest that, perhaps, it is. For instance, Figure D.12 shows the male and female mortality rates for heart disease in the U.S.A. Over the period from 1983 to 2002, the rates for over 35 year olds, as a whole, were decreasing steadily, so you may think that everything is fine. Actually, all is not well. If, instead, we analyse the data by different age groups, we get a very different message, as shown in Figure D.13. In the youngest age group, the 35 to 44 year olds, we have a steady fall to about 1990, but then a clear flattening. For women there has actually been a rise. Likewise, for ages 45 to 54, there is a clear fall to about 1990, then flattening out until about 2000 for both males and females.
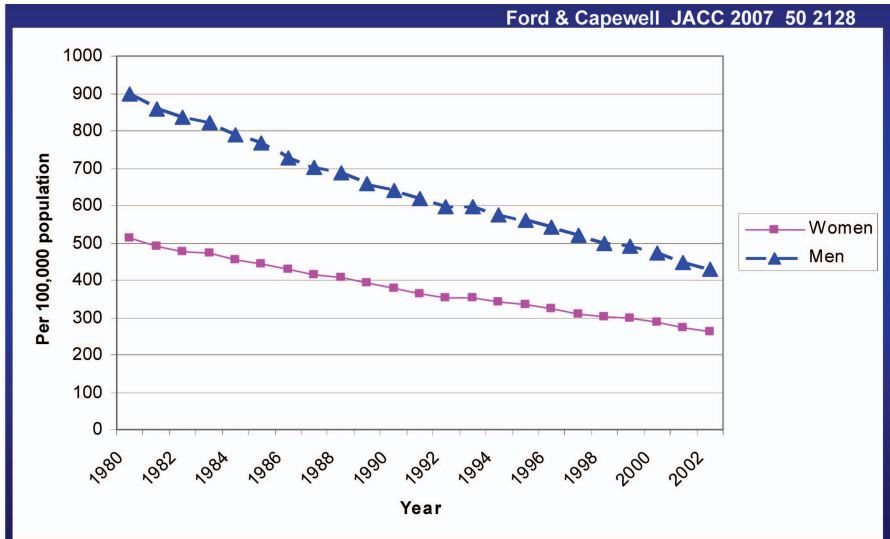
Figure D.12.   U.S. trends in age-adjusted CHD mortality rates; men and women; aged $\geqslant$ 35 years

This is not just an American phenomenon; it is also happening in the U.K. Figure D.14 shows the trends in England and Wales up to 2004 for both men and women. The youngest age group for men, 35 to 44, shows definite flattening from about 1999 to 2000, and likewise for women, a flattening in the youngest groups, perhaps a year or two earlier. The only question is: "Are we going to do something about it, or will the effect only apply to older age groups in the future?"

So, I suggest that the big falls in heart disease deaths, which dominate cardiovascular disease trends, and make a major contribution to total mortality trends (some 25%, or even 50% in some countries), can be explained by evidence-based therapies. However, in the majority of countries, a larger part (50% to 75% in Finland), can be explained by risk factor reductions, particularly from smoking and cholesterol; in other words, diet.

That is the message to take home; further small reductions in risk factors in the U.K. could actually halve coronary deaths, and so we believe that healthy diet and tobacco control should remain the top policy priorities.

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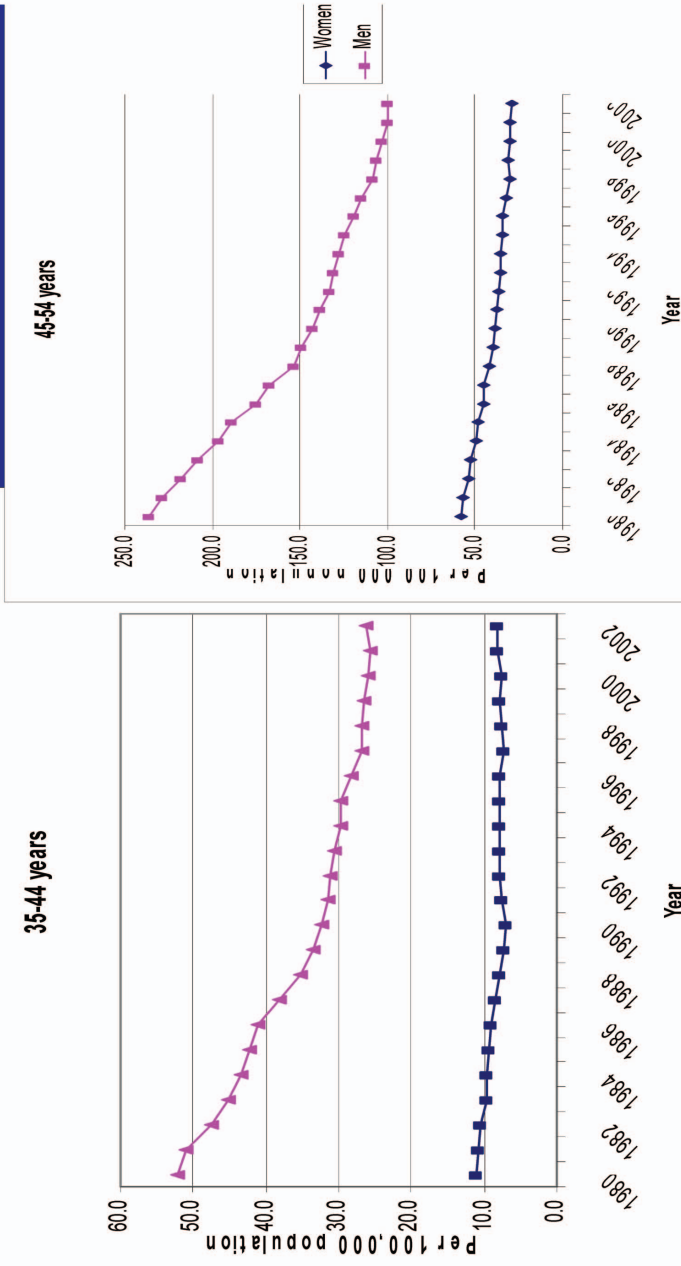
Figure D.13.   U.S. trends in age-specific CHD mortality rates; men and women; aged ≥ 35 years
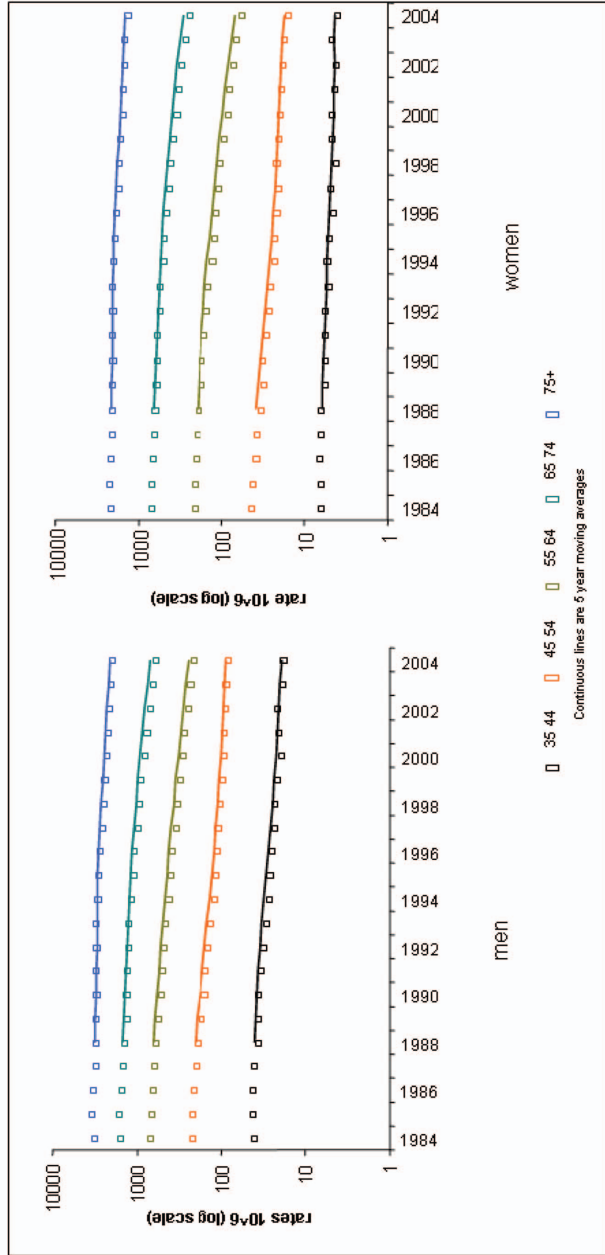
Figure D.14. Trends in age-specific CHD mortality rates; England and Wales; 1984 to 2004

Mr R. R. Ainslie, F.F.A.: The comments which Professor Waters made about the impact on mortality, as we moved through the various BMI categories which appear in Table D.3 and Figure D.3, has made me wonder whether I may be looking at this in an over-simplified fashion. It seemed as though what he was saying was that it is better to be moderately obese, i.e. have a BMI between 30 and 40, than to have an ideal weight. Is the interpretation as straightforward and as simple as that, or are there other risk factors which distort the true picture?

Also, I also have a question for any doctors present, in that I should be interested in how much a course of statins costs each year. During Professor Capewell's presentation, in Figure D.7, there is a reference to aspirin, which is cheap. Are statins an inexpensive or an expensive treatment?

Professor Waters: The analysis of mortality by BMI category is not as simple as Mr Ainslie expressed it. We have taken out all other causes of mortality according to the models: heart disease, high blood pressure, high cholesterol, strokes, and diabetes. Then we are left with the effect of the BMI on its own. You are right that, on this basis, moderately obese is better than underweight. If we were to do the modelling differently, and leave all these other factors in, I expect that we would see a much greater relative mortality at the higher BMI levels.

If you are moderately obese, for example, you are more likely to have developed diabetes or to have high blood pressure. Also, if you are a diabetic, or if you have high blood pressure, then you are more likely to die at a given age, and so on.

So, these factors are indirect effects of higher BMIs, which are not in Figure D.3. That figure, in a simple way, exaggerates the effect of the underweight, or disguises the effect of the higher BMI.

On the cost of statins, I do not know the cost of treatment. The earlier statins are now out of patent, so my understanding is that they are not expensive. It is an interesting point about which somebody else may have more information.

Mr B. P. Ridsdale, F.F.A.: I should like to thank the Profession for its consistent support for these two substantial initiatives through the APMA and the Mortality Scoping Project.

Looking first at the APMA, I tried to get my head around the different improvement factors about which Professor Waters spoke. What really interested me were the differences in the units of measure and the ways in which we communicate these issues, and how important it is that, if we are talking with the general public, we get these into focus. I can understand a seven year addition to life expectancy for non-smokers as against smokers, and an increase of a half to one year on the whole population, if the whole population were treated with statins, but, quite clearly, more substantial improvements for those people who really need to be treated with them.

Considering obesity, for the extremely obese there is, quite clearly, a very substantial increase in mortality. Also, looking at the Herceptin figure for breast cancer, a 3% improvement in three year survival probabilities brings survival up from 90% to 93%, or, the other way round, it means that it is bringing down the number of deaths in three years from 10% to 7%. So, there is a 30% reduction in deaths in the first three years. If we can find ways of communicating these units of measure more effectively, it would be really helpful.

Turning to Dr Macdonald's research for the Mortality Scoping Group (Macdonald, 2008), the intention is that we finalise this draft paper and take it to a multi-disciplinary seminar, to be chaired by an Honorary Fellow, Professor Tom Kirkwood, with invitations to a variety of medical people, gerontologists, statisticians, and so on. The meeting will focus on developing the agenda for discussion, and on how we might start the research. It will be supported by the Economic and Social Research Council and the Engineering and Physical Sciences Research Council, which already sponsor the Profession's Quantitative Finance Network.

We hope that a potential outcome will be working towards a forum, and then, potentially, to a conference in about 18 months' time, which could be widely represented with actuaries and all those in the other disciplines who might focus on areas of research, remembering that one of the most important aspects for us is to establish: where there is a need for research; where we can interface with the other professions involved; who the users might be; and who those people who

would fund the research might be. It will only be attractive if, as well as highlighting gaps and areas for research, we can also indicate who might fund the research.

Understanding improvements in mortality is clearly vital for the Profession and for our 'customers', if this leads to better projections of future changes in mortality and better approaches at improving mortality, for ourselves, for our families and for the nation.

Mr D. G. Robinson, F.F.A.: It seems to me that, for at least the past 20 years or so, the Profession has been seeking so-called wider fields in which we actuaries can deploy our skills. Certainly, the range of disciplines in which actuaries are now employed is very wide indeed — much wider than before.

However, what these presentations, the background paper and the substantial body of work which has been described have made me, and I expect made others, realise is that, whilst the grass in these wider fields may well be enriching for those actuaries who are venturing there, we simply must not overlook the fact that there is very fertile ground to be explored in the very area which was the foundation of actuarial work over 250 years ago; namely the study of human mortality. These areas are not simply of academic interest, nor are they relevant just to insurance, they are relevant to a whole raft of problems which society faces today, and which will be of increasing relevance in the future.

These issues cannot be tackled optimally by just one profession on its own, they need a multi-disciplinary approach, such as the one which we are experiencing in this meeting. I was pleased to hear the comments of Mr Ridsdale in that respect, and the way in which a multidisciplinary approach is being taken forward.

I now consider two of the key themes identified in the draft report: the role of medicine in mortality reductions; and (related to the first) future trends in mortality developments. These are both of huge societal importance.

If we, as actuaries, are to refine our projections of population mortality and longevity, traditional graduation and projection techniques, on their own, will not be sufficient. We need to get beneath the surface of the crude rates and to identify and to quantify the medical and other drivers of mortality change. However, as the authors have, no doubt, found, a major problem with modelling mortality in this way is the lack of sufficient, good quality data. Specifically, there are very few good longitudinal studies of sufficient scale. The Framingham study is one of the best known, but even it has only 5,000 lives in it. So, the results do need to be used with some caution, as the authors recognise.

Another problem relates to the way in which data are collected in medical research studies. All too often, in my experience, age groupings are very crude, e.g. under 65, 65 and over, and, occasionally, even males and females are lumped together. I think that it is perfectly understandable, in the context of research studies being conducted to test the efficacy of different treatments, but it is unhelpful for actuaries and other researchers looking for more granular results, varying by age and sex.

I do not know enough about the subject myself, but I wonder if there are protocols for the collection of data for medical research studies. If not, then, perhaps, this is an area where the Actuarial Profession might be able to work together with the medical profession with mutual benefits.

Something which I was pleased to see very recently was the establishment of a U.K. longitudinal study of the nation's health, the U.K. BioBank Study, which is going to cover half a million lives. From what I have seen, this does seem to be constructed on very sound, scientific, statistical lines, although, given the importance of the waist to hip ratio, I was surprised to learn that this is not one of the measures which the BioBank Study is incorporating in its work.

I believe that Professor Macdonald has some knowledge of this study, and I would like to ask him to indicate to what extent the Actuarial Profession has been, and can be in future, involved in it. Half a million lives going forward for a very long time will create a very valuable resource. I can understand the reticence of the medical profession and also data subjects, of which I am one, in having their data out in the public domain, but, if the Profession could be involved at a

macro level and have access to these research data, then I think that that would be a very positive result.

I have a further question for Professor Macdonald, and it relates to the 'Longitudinal Study of GPs', going back over 60 years, on smoking and health. When the study was first set up, smoking was not the factor which was suspected as being the cause of an increase in lung cancer, but something entirely different. Professor Macdonald recently revealed to me the real suspect, and he might like to reveal that to us.

I also have a comment on the conclusions being drawn in relation to obesity. I think that this is quite dangerous territory, and we need to act carefully and responsibly here. I have previously been critical that we have not, as a Profession, made enough of the link between smoking and health, in particular getting that information out into the public domain in a way which the general public can digest and act on. If we see newspaper headlines like, 'It is Better to be Fat than Thin', then that is dangerous, and, I suggest, not in the public interest. It is clear from the data that there are linkages between a high BMI index and coronary heart disease and diabetes. These are the diseases from which people die through being overweight; rather than being overweight, *per se*, being a cause of higher mortality. To interpret the data as suggesting that a high BMI is associated with low mortality is odd, and, I suggest, that it is rather misleading for the general public.

Professor Macdonald: Sir Richard Doll and Professor Austin Bradford Hill originally suspected that factors involved in the expansion of road travel were to blame for the rise in lung cancers which had been seen since the First World War. They discovered the link with smoking as a by-product, because they asked about that as a covariant, in order to control for its effect. They then found out that it *was* the effect.

Mr Robinson mentioned the BioBank Study, and asked what actuarial involvement there has been, and what actuarial involvement there might be. I can answer that there will be no involvement of the insurance industry. It was part of the draft BioBank protocol that no data would be provided in any form to the insurance industry or to any related concern.

Both Mr Robinson and Mr Ridsdale made a good point in alluding to the reasons for setting up the scoping study. We realise that the Profession is one of many disciplines which have an interest in mortality, disease and longevity. Coming at the question from many different angles, we all tend to focus on different questions, and apply different methodologies, and attach significance to different answers. For example, in medical statistics the outcome may be some short-term/medium-term improvements offered by one treatment over another, and so the key statistics are things like five-year survival probabilities, ten-year survival probabilities, and so on. The actuary's problem is that anybody of any age can come along and buy an insurance policy covering anything you like over some term. We need detailed estimates of the impact of a particular risk factor at all ages.

This is much more detailed than is needed to answer questions of clinical importance. It is one reason why actuaries are short of data. Important questions in medicine can be answered by much simpler statistics, so why set up expensive studies which over-engineer the question? This will always be an issue for us. It is probably up to actuaries to learn as much as we can about what other disciplines are doing, and how best to adapt their results, in whatever approximate ways we can, to our own purposes.

Mr P. J. Sweeting, F.I.A.: I was interested to see, in the introductory paper, the list of questions which need to be answered. The authors have managed to give a clear and concise list of the outstanding information which we still need.

I have two questions. First, the information relating to the BMI was reassuring in terms of the life expectancy at different levels of obesity, but I wonder how it would look if deaths from cancer were excluded. To what extent does cancer have an effect on the relative mortality at those different levels of the BMI?

The other question relates to the relative mortality at different durations since giving up smoking, and the fact that there seems to be some residual mortality, even for people who gave

up smoking a very long time ago. I wonder to what extent this is thought to be caused by damage which had been done by smoking, or whether there were any other fundamental differences between people who smoked and people who did not smoke, which were not picked up in the data. For example, were there differences in the BMI between the former smokers and the people who had never smoked?

Professor R. Bhopal (a visitor; University of Edinburgh)**:** I am Professor of Public Health at the University of Edinburgh. These presentations could have been made at any public health conference or epidemiology conference, or even at a medical statistics conference, which tells me that our interests are very closely tied, so we need to spend more time listening to each other, talking to each other and working with each other.

I have two specific comments. With a colleague, I reviewed all the cardiovascular cohort studies in North America and Europe, and we found 71 of them. If you look worldwide, you could probably double that number. Similarly, if you include cancer studies and others, there are, perhaps, 500 major cohort studies across the world.

There are also other large longitudinal datasets, birth cohorts in the country going back to 1946. There is the Office for National Statistics (ONS) longitudinal study of half a million people from 1991 onwards, including cancer mortality and deaths. In Scotland there is a longitudinal study of 250,000 people linked to the 1991 census, and a new linkage starting in 2001, for which I am partly responsible, of 4.6 million people in Scotland linked to all hospitalisations, all cancers and all deaths. So, there are many public health epidemiological datasets with linked data.

I encourage your group to turn what has been a review based on expert advice to one which is, perhaps, a more thorough search of what is actually available. I think that you would find a great deal of extra information which will be very valuable to your project.

As a member of the Science Committee of BioBank U.K., I think that I am in a position to comment on the view that actuaries will be excluded from the BioBank in any way. That is quite wrong. The truth is that everyone will be excluded from getting individual data, but statistical aggregated data are going to be available to anyone in the world, whether they are actuaries or not. There will be small charges to defray the costs of the BioBank. It will be open to industries of any kind and any bona fide researcher to access the Bio Bank database, according to protocols, of course.

Mr T. Chatterjee, F.F.A.: In reply to the question by Mr Sweeting about the BMI and cancer, we accept that cancer is not one of the explanatory variables discussed. This is because it did not fit in with the aims of the study, as statins do not have a beneficial effect on cancers.

We have not carried out any research on cancer and obesity. In the literature study they were not sure, but guessed that the reason for underweight mortality is because of cancer or the wasting of the body just before death from cancer. My guess would be that the U-shape which we saw, or the high levels of mortality for underweight, may come down if we include cancer as a covariant. Unless we do a much more detailed study, we cannot say, but that is likely.

Regarding smoking, the effects of smoking are twofold: one is the short-term effect; one is the longer-term effect. The short-term effects are from things such as carbon monoxide, and, once you stop smoking, those effects go down very quickly, in about six months or so. The long-term effects are due to atherosclerosis, tar getting deposited in the arteries. Some of these remain with you throughout your life. That is why you see that heart disease (which is due to the short-term effects) goes down very quickly within the first five years of giving up. The long-term effects of atherosclerosis remain for ever, so there will always be a difference in mortality compared to those who have never smoked.

Professor Waters: I was very interested in Professor Bhopal's comments. The people who were guiding our study and giving us advice did point us to various longitudinal studies in the U.K. and elsewhere.

The data requirements for our modelling were very specific. We found that there was no longitudinal study in the U.K. which was suitable in any way. Even the Framingham data — and

we have not gone into detail here, but you will understand that there was the original cohort and then the offspring and spouses' cohort — is becoming less suitable, because examinations are about every six years for the offspring and spouses, whereas they were every two years for the original cohort.

For the kind of modelling which we want to do, we want to collect information on a lot of variables, and we want to collect it very frequently on the same individuals. Many of the longitudinal studies have very long gaps between examinations. That makes them unsuitable. We did not look at 500, but we looked at several.

There is a message here about obesity. The message which we are putting out, which is from our research — and you can read our papers — is not out of line with the research which we see from other parts of the world. It is very much in line with the research which Professor Capewell is reporting to us. If you get your information only from the popular press, then you might well be confused. Once it was perceived as bad to be anything other than 'size zero'. Now, suddenly, it is better to be fat! It is not as simple as that. There is a lot going on here, and it is a complicated message.

The President (Mr J. S. R. Ritchie, O.B.E., F.F.A.): We have had excellent presentations and discussion, a very intensive communication of facts and opinions. I should like you to join me in congratulating all our contributors for their excellent work.