Modeling Disease Elimination

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The effect of the elimination of mortality from heart disease and cancer was modelled mathematically to allow for the effect of other competing causes of death. The model allows for potential dependence between heart disease or cancer and other causes of death by using cupola functions, which analyse the individual risk itself and the dependence structure between causes of death by using correlation coefficients. As the strength of these risk associations is unknown, the study investigated both full positive and negative dependence and compared this with no dependence. Depending upon the degree and type of correlation assumed, positive or negative, the life expectancy at birth is increased by between 3 months and 6.5 years if cancer mortality was eliminated, and between 5 months and 7.5 years in the case of heart disease. In addition, estimates of these effects on life insurance premia can be made with the greatest reduction for women with the elimination of cancer mortality. These figures provide a range of improvements in life expectancy and the consequent effect on life insurance risk premium rates which elimination of either of these important diseases would produce.

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Two hundred years ago the pattern of mortality was substantially different from that observed today. Infectious diseases claimed three lives in every five and tobacco-related cancers were infrequent because smoking was rare. Because of improvements in public health, more hygienic living conditions and the introduction of population-wide immunisation, diseases such as tuberculosis, cholera and typhoid are now uncommon in many parts of the globe. The new killers are cardiovascular disease and tobacco-related cancer, which account for over half of all deaths in the developed world.

The first half of the 20th century saw a gradual rise in heart disease fatalities, considered to be due partly to an increase in smoking, changes in diet and exercise patterns (Figure 1). During the last quarter of the 20th century, advances in medicine and a reduction in smoking habits have been associated with a marked decline in cardiovascular mortality. Cancer has undergone a similar pattern, albeit with a less dramatic peak and a less marked decline. The limited decline for cancer could be a result of increased use of screening and a delayed impact of the reduced prevalence of smoking.

How will this graph look in another 50 years? Like infectious disease, could cancer or heart disease be largely eradicated with further progress in the field of genetic science? A recent report from the National Service Framework group in the United Kingdom highlights the decline in coronary heart disease (CHD) mortality rates and then pro-
ceeds to extrapolate the mortality rates to zero by 2013 (Figure 2).

The improvements in life expectancy in the last 100 years are a result of the changes in the mortality pattern for individual diseases. However, can we identify how each disease contributes to life expectancy? If we could eliminate or cure cancer or the trends in CHD mortality continued as depicted in Figure 2, how long would it be before we died from some other cause?

**DISEASE ELIMINATION: ALTERNATIVE APPROACHES**

Life expectancy is estimated from mortality tables. Traditional methods of analysing the effect of cause of death elimination on life expectancy assume that causes of death are independent. These methods use cause-eliminated mortality tables derived from standard tables after the removal of one or more cause-specific death rates based on actual observa-
tions. Cause-eliminated life expectancy is then estimated from the revised mortality tables.

However, causes of death are infrequently independent. One or more antecedent risk factors such as obesity or smoking may contribute to more than one cause of death. In addition, with increasing age, death is more likely to be caused by a combination of diseases rather than a single identifiable cause. Thus reduction or elimination of a risk factor may reduce cancer and CHD mortality simultaneously. Furthermore, cardiovascular risk factors such as diabetes mellitus not only increase the risk of myocardial infarction (MI), but also case fatality rates for MI are higher in diabetics than in those without diabetes mellitus. Cause elimination studies that assume independence will therefore miss the effect of such interactions.

Cause elimination reflects cause-specific mortality although incidence is important. While a variable proportion of the substantial reduction in CAD mortality in the last 30 years is a result of reducing incidence, as much as 50% of the remainder is a result of reduced case fatality rates. In addition, cancer screening programmes may increase the reported incidence of individual cancers such as prostate or breast cancer but reduce cancer fatality rates by early detection. Analysing cause elimination in respect of a particular disease, such as cancer, does not assume that people are no longer at risk of developing it, but that it is no longer fatal.

Eliminating death caused by cancer with limited impact on the incidence of cancer will increase the number of people with a past history of the disease with potential co-morbidities from treatment and the systemic effects of cancer. This may increase the risk that people die from another cause. Assuming this to be the case, the gains in life expectancy from the elimination of any one disease may not be as great as the numbers implied in the mortality tables, which use simple cause-independent elimination techniques, would suggest.

As a result, any cause-elimination model needs to be able to take into account the dependencies or interaction between different causes of death. Such a model has been developed in association with the Cass Business School at London’s City University. The objective of this report is to quantify how changes to life expectancy could result from the elimination of disease specific fatality while taking into account full and zero dependence between cancer and CHD with regard to other causes of death.

**METHODS**

The Mathematical Model

If the causes of death are assumed to be mutually independent, then the overall survival function can be represented as a product of net survival functions. However, assuming dependence means that the degrees of correlation between various causes of death need to be quantified. The mathematical model employed for this purpose uses copula functions, which are based on Spearman's rank correlation.

Copula is a Latin word meaning to connect or join together. In statistics, the copula function is a method, which describes association or dependency among random variables. The copula function is an alternative approach to correlation. Unfortunately, correlation using linear models based upon normal distributions is often an inadequate measure of multivariate dependency for the more complicated approach needed to describe real-world phenomena. The copula function quantifies dependencies between two or more variables by splitting a set of dependent risks into two parts: the individual risk itself and the dependence structure between them.

This study is based on a mathematical framework that models the effect of elimination of cancer or heart disease fatalities on life expectancy under the initial assumption that causes of death are mutually dependent. It involves the following steps:

1) Construction of an overall survival function from a mortality table
2) Derivation of net survival functions for
The individual causes of death (cancer and IHD) from the overall survival function
3) Simulation of the partial/complete elimination of a cause of death by modifying the net survival function pertaining to that cause
4) Rebuilding the overall survival function using the modified and other net survival functions

The Correlation Coefficients Used in the Copula Function

The correlation coefficient ($\rho$) defines the relationship between the future life times due to the two causes of death $i$ and $j$ as $\rho (T_i, T_j)$. For example, a fully positive correlation means that the observed future life times due to cause $j$ can be expected to be at the same level as the observed future life times due to cause $i$. In such a case, removal of cause $i$ does not affect the overall future lifetime. Since overall survival function is defined as $P[\min(T_1, T_2, \ldots, T_m) < t]$, if $\min(T_1, T_2, \ldots, T_\nu, T_\nu, T_\nu, \ldots, T_m) = T_i$ (say), removal of cause $i$ would not significantly affect the overall survival, as $T_j$ would also be expected to be close to the minimum value.

Correlation Coefficients for the Model

The definition of net survival functions is based on lifetime vectors for each cause of death. As these lifetime vectors are not directly measurable, it is difficult to calculate rank correlation coefficients between various causes of death. The correlation possibilities range from positive to negative (including neutral correlation or independence). In modelling, an assumption is required about the degree of correlation between the causes of death, which ranges from $-1$ (full-negative correlation) through zero (neutral correlation or independence) to $+1$ (full-positive correlation). The analysis investigated two causes of death, cancer and heart disease, compared with other causes. The correlation coefficient was set to create a range of values within which life expectancy could be expected to be affected from full-positive to full-negative correlations, as well as an assumption of independence for comparison.

Datasets Used

The study is based on two data sets. One is a general population life table from the United States (US Decennial Life Tables for 1989–91) in which the data are grouped by causes of death. The second set is based on the select insured mortality table 1990–95 (US Society of Actuaries) with transformation of the data using the pattern of cause-specific mortality in the Decennial Life Table.

RESULTS

The range of effects on life expectancy based on the correlation assumptions used in the model is given in Figure 3. The effects of eliminating cancer or heart disease deaths on life expectancy depend upon which of the extreme scenarios are investigated:

- A positive correlation (ie, eliminating cancer or heart disease renders death from other causes in any future year more probable)
- A negative correlation (ie, eliminating cancer or heart disease renders death from other causes in any future year less probable)
- The effect of independence (or neutral correlation), where cancer or heart disease is eliminated but there is no effect on the probability of death from other causes, is also provided for comparison.

Depending on the correlation assumed, the life expectancy at birth is increased by between 3 months and 6.5 years if cancer were eliminated, and between 5 months and 7.5 years in the case of heart disease (Figure 3). Eliminating heart disease results in a higher gain in life expectancy as more people die from heart disease than from cancer. This is especially true in the case of men who have a higher rate of heart disease fatality compared with women.
A negative correlation between either cancer or heart disease and all other causes of death results in the highest overall gain in life expectancy as removing either cause of death reduces the chances of dying from other causes. However, as the correlation between causes of death increases from neutral to positive, the gains in life expectancy decline. At the extreme, where both causes of death are highly and positively correlated, the removal of any one cause appears to have a negligible impact on life expectancy. This is because the number of lives saved from removing that cause is offset by an increase in the number of deaths from other causes.

**DISCUSSION**

These data provide a range of estimates for changes in life expectancy with the elimination of two major causes of death, cancer and heart disease. Disease elimination with independence has a maximum gain in life expectancy of 4 years (males, heart disease), which increases to 7.5 years with a fully negative correlation and reduces to about 5 months with a fully positive correlation.

Life insurers and pension providers are exposed to changes in the risk landscape for mortality. Accounting for the effects of the outcomes of medical and public health interventions is clearly a topic of interest for the insurance industry, particularly when it comes to pricing life assurance and annuities. A longer life expectancy may be welcome news for life assurance providers but will have less favourable consequences for companies who primarily write annuity business. Modelling the differing effects of disease elimination according to a variable degree of interdependence between causes of death produces a range of estimates, which can serve to limit excessive assumptions about ongoing improvements in life expectancy. Using the data in Figure 1, an estimated decrease in premiums for a typical life assurance product in the United States can be developed (Figure 4).

Women aged between 40 and 60 can be expected to benefit from a greater reduction in premium from the elimination of cancer than would be the case with the elimination of heart disease. Women in this age group are at greater risk of dying from cancer than from heart disease. The opposite is true for men.

Analysing mortality trends caused by the elimination of disease specific fatality provides little information about any effect on disability rates. There is ongoing debate about whether in parallel with declining mortality rates there is a reduction in the prevalence of chronic disability, also called the compression of morbidity. Evidence remains mixed with some developed countries showing reduced age-specific rates of disability while other countries show no change in the prevalence of disability, especially if less severe forms of disability are included.
Both heart disease and cancer are important causes of disability in developed countries but the effect of elimination of either of these would be subject to the uncertainties of correlation between causes of disability. Heart disease and cancer tend to be unitary causes of death, whereas disability may also arise because of treatment (cancer) or co-morbidity (cancer and heart disease). There is evidence that an increased life expectancy from the elimination of a fatal disease can mean that more people are exposed to disorders that can cause disability with consequent increases in healthcare costs. However, because healthcare expenditure is greatest during the last 2 years of life this expenditure may be postponed rather than increased.

As more is understood about the correlation, or otherwise, between causes of death, risk factors and chronic diseases, life and health insurers will be better able to manage their risk exposures. In considering the elimination of mortality risk associated with individual diseases, actuaries can re-examine the pricing assumptions, and underwriters can reconsider the data required to assess the mortality risk. Protective value studies carried out using the results of studies such as these will assist with this process.

Editor’s Note: This article is based on an article first written by Swiss Re for The Review, Worldwide Reinsurance.

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