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The Entropy of Health and Disease: Dementia in Canada

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Abstract

The object of this paper is to combine two concepts which have developed on the interface between public health and demography: health expectancy and the analysis of linkage in demographic models. The paper addresses, in the general case, the question: what are the marginal effects of changes in incidence or mortality rates on the expectation of life with, and without, a particular irreversible, non-communicable disease or type of disability? A simple model of disease in a population is described, and general solutions for the two components of the expectation of life are obtained. Formulae for the entropies (elasticities) of these expectations in relation to changes in incidence and mortality rates are derived. It is shown that, under certain conditions, the entropy of the expectation of disease free life, with respect to changes in incidence, can be approximated by an extension of Sullivan's index. Data on dementia among elderly Canadians, obtained from the Canadian Study of Health and Aging, are used for illustration.

Résumé:

Le présent article combine deux concepts issus de l'interface entre la santé publique et la démographie : les attentes en mati@re de santé et l'analyse de liens dans les modèles démographiques. En termes généraux, il s'interroge sur les répercussions marginales des changements de taux d'incidence ou de mortalité sur l'espérance de vie, en présence ou en l'absence d'une maladie chronique non transmissible ou d'un handicap donné. Il décrit un modèle de maladie simple dans une population et obtient des solutions générales pour les deux éléments de l'espérance devie. Des formules permettant de déterminer l'entropie (indice) du gain d'information sont dérivées. Il est démontré que, dans certaines conditions, l'entropie de l'espérance de vie exempte de maladie, par rapport aux changement du taux d'incidence, peut être approchée au moyen de l'index de Sullivan. L'auteur utilise des données relatives à la démence parmi les Canadiens âgés (Étude sur la santé et le vieillissement au Canada) à titre d'exemple.

Key Words: *entropy, health expectancy, dementia*

Introduction

The object of this paper is to combine two concepts which have developed on the interface between public health and demography : disease (or disability) free life expectancy, and the analysis of linkage in demographic models. The paper addresses, in the general case, the question - what are the marginal effects of small changes in incidence or mortality rates on the expectation of life with, and without, a particular irreversible, non-communicable disease or type of disability?

The paper begins with a brief review of the historical development of these concepts. A simple mathematical model of disease is then described and general solutions for the two components of the expectation of life are obtained. Formulae for the entropies (elasticities) of these expectations in relation to changes in incidence and mortality rates are derived. It is shown that the entropy of the expectation of disease-free life can be approximated by an extension of Sullivan's index. Data on dementia among elderly Canadians, obtained from the Canadian Study of Health and Aging (CSHA), are used for illustration.

Historical background

The history of the development of the life table has been described by many authors (e.g. Farr, 1843; Greenwood, 1948; Benjamin and Haycocks, 1970; Smith and Keyfitz, 1977; Pearson, 1978; Chiang, 1984; Impagliazzo, 1985). Halley (1693) was the first to calculate a population-based life table using sound methods, but it was Deparcieux (1760) who showed how to calculate the expectation of life, and to advocate its use for comparing mortality in different populations. However it was Farr (1843) who, using the national census and death registrations, established the use of the expectation of life as the most important single index of public health.

Attempts to find a broader index of health, incorporating morbidity as well as mortality, began in the 1930's (Chen and Bryant, 1975) under the auspices of the League of Nations, and later the World Health Organization. The momentum for this grew with the development of population-based health surveys and medical record systems in developed countries (Swaroop, 1960). The most frequent approach is to use these morbidity data to partition the population, at any point in time, into two or more "states", to each of which was attributed a weight based on the degree of "health". A single index is then obtained by the weighted average of the proportion of the population in the different states, using prevalence data or multistate life table methods (Fanshel and Bush, 1970; Chiang and Cohen, 1973; Torrance, 1987). The simplest of these approaches (Gordon, 1953; Sullivan, 1971) is to define two states, healthy and diseased or disabled. The total expectation of life is then partitioned into two components : the expectation of disease-free life (health expectancy) and the expectation of life with disease.

Sullivan (1971) estimated these components by calculating direct age-standardized prevalence rates for the two states using the stationary population of the current life table as the standard. The use of Sullivan's method to estimate health expectancy expanded in the 1980's (Wilkins and Adams, 1983; Colvez and Blanchet, 1983), and is now the topic of an international research network (Mathers and Robine, 1992). Wolfson (1991) and Wolfson and Manton (1992) have reviewed the recent literature on models of population health expectancy, including multistate models and the use of simulation. Newman (1988) has provided a theoretical justification for the use of Sullivan's intuitive method.
The study of the sensitivity of intrinsic rates and age distributions to perturbations in the age-specific mortality and fertility rates has a long history (Keyfitz, 1971). An expression for the proportionate decrease in the expectation of life produced by a proportionate increase in mortality, equal at all ages, was derived by Keyfitz (1977). In a notation corresponding to that to be used later in this paper and that of Hakkert (1987), if E is the expectation of life produced by a mortality function Km(t) at age t, and x(t) is the proportion surviving to age t, then the required expression is

$$H = -d(\ln E) / d(\ln K) = \int_0^\infty x(t).\ln[x(t)]dt / E$$

Following Demetrius (1974) H is called the entropy of the survival curve. In economic parlance it is the elasticity of E with respect to changes in K.

Mitra (1978) provided a useful approximation for H in terms of the average age of the stationary population. Further contributions to this literature were made by Goldman and Lord (1986) and Hakkert (1987). Estimates of H for Canadian life tables were published by Nagnur (1986), and for historical cohort life tables by Hill (1993). The topic is closely related to that of cause-deleted life tables (Tsai, Lee and Hardy, 1978; Newman, 1986; Vaupel, 1986; Nagnur and Nagrodski, 1987).

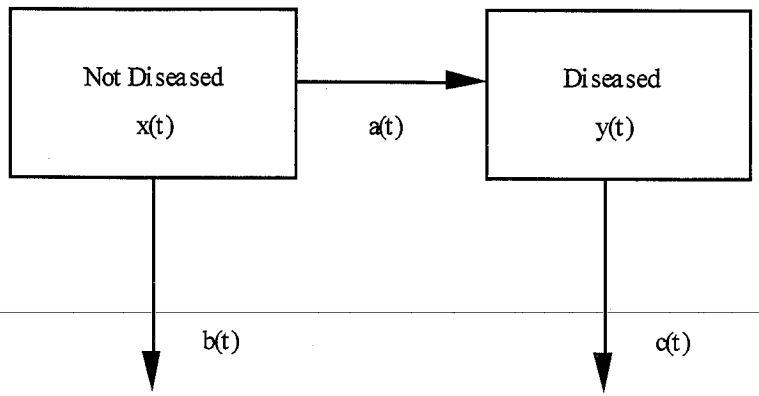
Mathematical models of communicable disease began with the work of Farr (1840) on the smallpox epidemic of 1837-39. The subsequent historical development of work in this area has been described by Bailey (1975). Models of the prevalence of exposure to endemic zoonotic infections such as yellow fever, which are similar to the model described below, were formulated by Muench (1955). Mathematical models of survival from non-communicable diseases such as cancer were introduced by Fix and Neyman (1951) and Zahl (1955). For more recent work on models of chronic diseases see Beck (1988), Manton and Stallard (1988) and Morgenstern et al (1992).

Model of an irreversible, non-communicable disease

Figure 1 shows a model of an irreversible, non-communicable disease or disabling condition (D) in a closed cohort of individuals of the same age, not necessarily zero, at time zero. If the cohort is a birth cohort then the disease is not congenital. If the age of the cohort at time zero is greater than zero then the incidence of the disease is zero at ages prior to that at time zero. All five functions of time shown in Figure 1 are non-negative. The model is deterministic in the sense that the transition rates are descriptive functions of aggregates, and no probabilistic model of the movement of individuals is implied. It is assumed that the size of the initial cohort is large enough to ensure that the five functions can be treated as continuous.

Since D is a disease or disability we can assume that the mortality of those with D, c(t), is not less than that of those without D, b(t). However, the results could also be applied to a situation where $c(t) < b(t)$, for example if D were defined as "ever married". Within the context of disease and disability, the case of equality, or near equality, of the two mortality functions would be relevant to diseases such as arthritis, and to causes of functional disability such as blindness and deafness.

Figure 1 Model of Irreversible, Non-communicable Disease



x(t) = proportion of cohort not diseased at time t
y(t) = proportion of cohort diseased at time t
a(t) = rate of incidence of disease at time t
b(t) = mortality rate among those not diseased at time t
c(t) = mortality rate among those diseased at time t
initial conditions : x(0) = 1, y(0) = 0

The model is solved in terms of the proportion of the cohort without disease, x(t), and with disease, y(t), and the corresponding expectations of life:

$$E_x = \int_0^\infty x(t)dt \text{ and } E_y = \int_0^\infty y(t)dt$$

Define the cumulative transition rates :

$$A(t) = \int_0^t a(s)ds,\ B(t) = \int_0^t b(s)ds,\ C(t) = \int_0^t c(s)ds.$$

Then it is straightforward to show that:

$$x(t) = \exp[-\{A(t)+B(t)\}] \qquad (1)$$
$$y(t) = \int_0^t a(s)x(s)\exp[-\{C(t)-C(s)\}]ds.$$

It is helpful to define three ancillary functions :

$$u(t) = \exp[-A(t)]$$

$$v(t) = \exp[-B(t)] \qquad (2)$$

$$w_s(t) = \exp[-\{C(t) - C(s)\}].$$

Then $x(t) = u(t)v(t)$ (3)

$$y(t) = a(s)x(s)w_s(t)ds$$

$$E_x = u(t)v(t)dt$$

$$E_y = \int_0^{\infty} \int_0^{t} a(s)x(s)w_s(t)dsdt.$$

Further define functions of the form :

$$i(x,u;t) = -x(t)\ln[u(t)] \qquad (4)$$

$i(x,x;t) = -x(t)\ln[u(t)]$ etc., and let

$I(x,u) = i(x,u;t)dt$ etc.

Then denoting the entropy of E_x with respect to a(t) [i.e. the proportional decrease in E_x produced by a uniform proportional increase in a(t)] by H(x,a), and similarly for H(x,b), H(y,a), H(y,b), H(y,c), the following results can be derived :

$$H(x,a) = I(x,u)/E_x$$

$$H(x,b) = I(x,v)/E_x.$$

Note that since $\ln[x(t)] = \ln[u(t)] + \ln[v(t)]$

$$i(x,x;t) = i(x,u;t) + i(x,v;t)$$

$$I(x,x) = I(x,u) + I(x,v).$$

Hence $H(x,a) + H(x,b) = I(x,x)/E_x$.[1] (5)

Note also that $x(t)\ln[u(t)] = x(t)\ln[x(t)] - x(t)\ln[v(t)]$

$$= x(t)\ln[x(t)/v(t)].$$

If the incidence of D is small, or the mortality with D is equal to that without D, then v(t) approximates the survivor function of the cohort as a whole. Writing $p(t) = x(t)/v(t)$ for the proportion of the cohort which is "disease-free" at time t we obtain:

$$H(x,a) = - \int_0^\infty v(t)p(t)\ln[p(t)]dt/E_x.$$

Sullivan's Index estimates E_x as $v(t)p(t)dt$, so that an estimate of the entropy of the disease-free expectation of life in relation to change in incidence is :

$$H(x,a) = - \int_0^\infty v(t)p(t)\ln[p(t)]dt \Big/ \int_0^\infty v(t)p(t)dt.$$

The expressions for the entropies of E_y are more complicated:

$$H(y,a) = \int_0^\infty \int_0^t a(s)i(x,u;s)w_s(t)dsdt / E_y - 1$$

$$H(y,b) = \int_0^\infty \int_0^t a(s)i(x,v;s)w_s(t)dsdt / E_y$$

$$H(y,c) = \int_0^\infty \int_0^t a(s)x(s)i(w_s,w_s;t)dsdt / E_y$$

Note that:

1. $H(y,a) < 0$ (i.e. increasing incidence increases E_y) if $i(x,u;t) < x(t)$ for all t, which is true if $A(t) < 1$

2. $H(y,a) + H(y,b) = a(s)i(x,x;s)w_s(t)dsdt / E_y - 1$

In the special case where D does not affect mortality, i.e. $b(t) = c(t)$, the entropies of E_y reduce to simpler expressions :

$$H(y,a) = - I(x,u) / E_y$$

$$H(y,b) = [I(v,v) - I(x,v)] / E_y$$

and we note that $H(y,a) + H(y,b) = [I(v,v) - I(x,x)] / E_y$. Also, if we write $z(t) = x(t) + y(t)$, and the total expectation of life $E_z = E_x + E_y$, we have, in this special case :

$$H(z,a) = 0, \text{ and } H(z,b) = I(v,v)/E_z$$

Example : Dementia in Canada

To illustrate the use of these results let D = dementia, and take the age at time zero to be 60 years. In 1991 the Canadian Study of Health and Aging (CSHA) recruited a sample of 10,250 Canadians age 65 and over and estimated the prevalence of dementia among them by clinical examination following a psychometric screening test (Canadian Study of Health and Aging Working Group, 1994).

In 1993 the subjects in the CSHA, or their relatives, were contacted again by telephone. This was done in anticipation of a follow-up study (beginning in 1996) to determine the incidence of dementia. From the information obtained at the second contact it was possible to derive mortality rates for those who were demented in the initial survey, and for those who were not. Estimates of the rates of incidence of dementia in Canada will not be available until the follow-up of CSHA is complete. Data from a Swedish study (Hagnell, Ojesjo, Rorsman et al, 1992) have been used in the interim.

Gompertz functions were fitted to the age-specific incidence and mortality rates at ages 60 and over:

$$a(t) = \exp(.116t - 6.55)$$

$$b(t) = \exp(.075t - 4.55)$$

$$c(t) = \exp(.053t - 2.84)$$

These functions gave the following results:

$E_x = 20.03$ years	$E_y = 1.10$ years
$H(x,a) = .092$	$H(y,a) = -.798$
$H(x,b) = .344$	$H(y,b) = .654$
$H(y,c) = .699$	

The approximation using the modified Sullivan approach gives 20.95 years for E_x, and .057 for H(x,a). However in the hypothetical situation where the mortality among those with dementia is the same as that among those without dementia the approximation is closer to the actual values : $E_x = 20.05$ years, and $H(x,a) = .092$. The following results are also obtained in this special case:

$$E_y = 2.19 \text{ years}$$

$$H(y,a) = -.822$$

$$H(y,b) = .596$$

$$H(y,c) = .437$$

Discussion

The general expressions for the solution of the two-state model given by (1) and (3) are useful, even when the functions are such that analytical expressions cannot be found. It is easier to evaluate the integrals numerically, using the trapezium rule (as in the example) or Simpson's rule, than to solve the system of two differential equations using Runge-Kutta methods, or by the piecewise methods used for multi-state life tables. It is possible to extend the formulae to the situation in which there is a chain of states, for example the stages of a progressive disease, but the algebra soon becomes formidable.

The ancillary functions defined in (2) are survivor functions: u(t) is the proportion surviving to time t of a hypothetical cohort subject only to depletion by the incidence rate a(t); v(t) is the proportion surviving subject only to b(t) (i.e. with D eliminated); and $w_s(t)$ is the proportion surviving to time t of a cohort which entered D at time s. The model described here is deterministic, but in the corresponding probabilistic model it would be necessary to specify independent hazards and homogeneity. With these restrictions the solutions, in terms of expected values, are intuitive.

The introduction of the "bivariate" version (4) of the numerator of the entropy function seems to be a productive advance, which could be used for models including more than two states. The additive nature of the entropies seen in (5) and note 1 is interesting, and is reminiscent of the similar property of the entropy function in probability theory (Khinchin, 1957).

The results for dementia should not be taken as definitive, since the incidence rates were taken from a Swedish study, which may not reflect the Canadian experience. However, the overall expectation of life at age 60 of 21.13 years is not too different from the published life table figure of 21.83 years.

The entropies allow us to quantify potential changes in the impact of dementia on the elderly population. Currently a cohort of 1,000 Canadians reaching their 60th birthday would experience $L_x = 20{,}030$ person years without dementia and $L_y = 1{,}100$ person-years with dementia. With a 1 per cent reduction in the incidence of dementia, L_x would increase by 18 person-years and L_y would decrease by 9 person-years. With a 1 per cent reduction in mortality without dementia, L_x would increase by 18 person-years but L_y would also increase by 7 person-years. With a 1 per cent reduction in mortality with dementia, L_x would remain unchanged while L_y would increase by 8 person-years. Clearly a reduction in incidence is the most favourable event in terms of the burden of dementia. A reduction in mortality from causes other than dementia increases L_x, but at the "cost" of increasing L_y also. A reduction in mortality due to dementia merely increases L_y without any compensating increase in L_x.

The most important type of dementia in the elderly is Alzheimer's disease, which accounts for 64 per cent of the total dementia in Canada (Canadian Study of Health and Aging Working Group, 1994). The etiology of Alzheimer's disease is not fully understood, but there is increasing evidence that exposure to

aluminum in drinking water may be implicated (Forbes and McLachlan, 1996). Based on data from a study in Ontario, it has been estimated that 23 per cent of Alzheimer's disease can be attributed to drinking water containing more than 100 micrograms/litre of aluminum. If the association is causal then reducing the level of aluminum below this critical level would decrease the incidence of dementia by about 15 per cent. Since about 90,000 people in Ontario reach the age of 60 in a given year such a reduction in incidence would increase their years lived without dementia by about 1,620 person-years, and reduce their years lived with dementia by about 810 person-years.

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Endnote:

1. This result can be extended to any number of competing hazards from a single state, say $m_j(t)$, $j = 1,2 \ldots n$.

Define $M_j(t) = m_j(s)ds$, $u_j(t) = \exp[-M_j(t)]$,

$i(x,u_j;t) = -x(t)\ln[u_j(t)]$, $I(x,u_j) = \int_0^\infty i(x,u_j;t)dt$.

Then $x(t) = \Pi_j \; u_j(t)$, $H(x,m_j) = I(x,u_j) / E_x$, and

$\Sigma_j \; H(x,m_j) = I(x,x) / E_x$

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