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COPING WITH MULTIPLE MORBIDITY IN A LIFE TABLE

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One of the applications of the multi-state life table is in the field of Public Health, with states defining various levels of health or functional ability Another approach is to model Public Health by looking at the impact of individual diseases, but, unfortunately, then two practical problems arise there are many diseases, and due to comorbidity people may be in several diseases states simultaneously Both problems tend to make the number of states in the life table impractically large.

In this paper we introduce the proportional multi-state life table It is especially designed to cope relatively easily with a large number of diseases simultaneously, while allowing for comorbidity We provide proof of validity and an example implementation for cardiovascular disease

KEY WORDS Multi-state life table, Illness-death processes, Comorbidity
Submitted by C M Suchindran

1 INTRODUCTION

The life table is a simple and much used instrument for assessment of population health status. The standard life table produces life expectancy at different ages, and the life expectancy at birth is probably still the most employed indicator of Public Health.

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It is also a limited indicator, since it ignores morbidity. This limitation becomes more severe when the burden of disease shifts from acutely fatal, mostly infectious disease, to chronic degenerative, mostly non-communicable disease. After this so called 'epidemiologic transition' (Omran, 1971), that has taken place in the developed and is underway in an increasing number of developing countries, the need for an indicator of population health status that includes morbidity becomes acute.

An important point of interest is the assessment of the health impact of specific diseases, both on morbidity and mortality, and the effect of changes in incidence and survival, caused by autonomous trends and possible interventions. This could help explain observed trends in population health status, make projections of future developments, and perhaps clarify the issue of compression versus expansion of morbidity, that is being debated for quite some time now (Fries, 1980; Olshansky *et al.*, 1991).

Interest arises also from the need for optimal allocation of scarce resources in the health care sector. For example, the 1993 World Development Report from the World Bank made an estimate of the Global Burden of Disease by combining prevalence and mortality data from a large number of diseases with a measure of the seriousness of a disease (the DALY, Disability Adjusted Life Year), and with this indicator compared the cost-effectiveness of various proposed interventions (World Bank, 1993; Murray and Lopez, 1994).

To estimate the total burden of morbidity one has to look at many diseases simultaneously, because, unlike with mortality, people may suffer from various conditions simultaneously (comorbidity), in particular at older ages. The total impact of diseases on population health status and disability does not simply add up: the relation between diseases, health status and disability is a complex one, and more so with comorbidity (Verbrugge *et al.*, 1989). At high ages comorbidity becomes substantial, and it has implications for intervention possibilities and effects, and for the amount of disability caused.

The method of choice for the inclusion of morbidity is the multi-state life table (Schoen, 1987). It is a well established method, backed by a considerable body of theory. In a multi-state life table the inclusion of multiple diseases while taking comorbidity into account is straightforward: just add states defining the combined prevalence of diseases. This works fine for a limited number of diseases, but soon becomes unwieldy when that number increases. For example, with only one state for each disease the number of states to be defined is 2^n-1, with n the number of diseases.

We present the proportional multi-state life table method, that makes the inclusion of multiple diseases better manageable and allows for comorbidity implicitly, without the need to define additional states. We implement the method for heart disease and stroke, and look at the effect of hypothetical but not unrealistic changes in incidence and survival on disease prevalence and comorbidity. Finally we discuss limitations and extensions of the method.

2 METHOD

2.1 Description

Given the large number of diseases, of which many are rare, in practice one will have to limit the number of diseases in the life table to the ones deemed most important. This means that a life table with specific causes of death will always have to include a category 'all other mortality'. This mortality rate from all other causes can be obtained by subtracting the sum of the included disease specific mortality rates from the total mortality rate, as is done in cause elimination life tables. In the remainder we will distinguish two disease specific mortality rates, and one 'all other causes' mortality rate. Of course there will likewise be an 'all other causes' morbidity, for the present study, however, this is ignored.

The basic idea of the proportional multi-state life table method is very simple: express age specific disease prevalence, instead of in numbers, in proportions of diseased among all alive at that age. Under certain independence conditions the comorbidity rate of any number of diseases is then just the product of their respective rates. Sufficient independence assumptions for the case of two diseases and an 'all other mortality' cause of death are listed as A1–A3 in the next section, and they can be summarized as:

- the incidence of each disease should be independent from all causes of death, except its own disease specific mortality (A1);
- disease incidences are independent (A2);
- all causes of death are independent (A3).

The proportional multi-state life table is divided into sections: first a general section, that is in fact a standard cause elimination life table, and secondly, one section for each disease with an independent illness–death process, that describes disease incidence, prevalence, and disease specific mortality. Total mortality in the general section is calculated from an 'all other' mortality rate and the disease specific mortality

rates from the disease sections. Therefore changes in the disease sections that cause a change in its disease specific mortality feed into the total mortality, and thus these disease specific changes are reflected in the total mortality experience of the life table cohort.

Because the disease specific sections are independent and do calculations in rates they need not take into account the mortality from other causes of death: the general section computes for each age the number of deaths from all causes, and the age and disease specific prevalence in numbers is just the prevalence rate of that disease times the number of years lived in the age interval by the cohort. The same holds for the number of incidents and disease specific deaths.

The age specific comorbidity rate from any number of diseases is then the product of their respective prevalence rates, which just like the disease specific prevalence rates can be multiplied by the number of years lived in the age interval in the general section of the life table to obtain comorbidity in numbers. Because each disease specific section does not need to be aware of total mortality or disease specific mortalities from other diseases each section is quite independent from all other disease sections and only linked to the general section by its disease specific mortality.

2.2 Proof

To prove the method described above to be equivalent to a standard life table we must show that prevalence, comorbidity, and mortality thus calculated are identical to results from a standard life table. The following 3 propositions state this more formally (all three propositions concern age specific rates):

(I) The prevalence in the disease section is equal to the prevalence calculated in the presence of other diseases and causes of death.

(II) The comorbidity of the two diseases is the product of their respective prevalences.

(III) The disease specific mortality in the disease section is equal to the disease specific mortality calculated in the presence of other causes of death.

The general independence condition for $n-1$ number of diseases and 1 'all other causes of death' category is:

$$Pr\{A_{\mathrm{I},1} \leq a, \ldots, A_{\mathrm{I},n-1} \leq a, A_{\mathrm{D},1} > a, \ldots, A_{\mathrm{D},n} > a\}$$
$$= Pr\{A_{\mathrm{D},n} > a\} \cdot \prod_{i=1}^{n-1} Pr\{A_{\mathrm{I},i} \leq a, A_{\mathrm{D},i} > a\} \qquad \text{(A)}$$

with

a : index for age
$A_{\mathrm{I},i}$: age at incidence of disease i,
$A_{\mathrm{D},i}$: age at death from disease i,
$A_{\mathrm{D},n}$: age at death from all other causes.

For specific numbers of diseases slightly weaker conditions can be derived from (A) by integration over incidences or causes of death, and without loss of generality we will restrict ourselves to a situation with 2 diseases and an additional 'all other causes' mortality. We will show that in this case the three independence assumptions below are sufficient for proposition I–III to hold.

Incidences and mortalities are independent (except for the same disease):

$$Pr\left\{A_{\mathrm{I},i} \leq a \middle| \bigcap_{j \in S}\{A_{\mathrm{D},j} > a\}\right\} = Pr\{A_{\mathrm{I},i} \leq a | A_{\mathrm{D},i} > a\} \quad \forall i \in Z,$$

$$Pr\left\{A_{\mathrm{D},j} > a \middle| \bigcap_{i \in Z}\{A_{\mathrm{I},i} \leq a\}\right\} = \begin{cases} Pr\{A_{\mathrm{D},j} > a | A_{\mathrm{I},j} \leq a\} & \forall j \in Z, \\ Pr\{A_{\mathrm{D},j} > a\} & j \in S, j \notin Z. \end{cases} \tag{A1}$$

Incidences are mutually independent:

$$Pr\left\{\bigcap_{i \in Z}\{A_{\mathrm{I},i} \leq a\}\right\} = \prod_{i \in Z} Pr\{A_{\mathrm{I},i} \leq a\}. \tag{A2}$$

Causes of death are mutually independent:

$$Pr\left\{\bigcap_{j \in S}\{A_{\mathrm{D},j} > a\}\right\} = \prod_{j \in S} Pr\{A_{\mathrm{D},j} > a\}. \tag{A3}$$

Here Z is the set of diseases and S is the set of causes of death.

Now let:

$Z = \{\mathrm{L}, \mathrm{H}\}, S = \{\mathrm{L}, \mathrm{H}, \mathrm{O}\}$
$N_{\mathrm{L}}(a)$: population prevalence of disease L at age a.
$N_{\mathrm{H}}(a)$: population prevalence of disease H at age a.
$N_{\mathrm{HL}}(a)$: population prevalence of comorbidity of diseases H and L at age a.
$n_{\mathrm{H}}(a)$: prevalence of disease H at age a in disease section.
$M_{\mathrm{H}}(a)$: population disease specific mortality of disease H at age a.

$m_H(a)$: disease specific mortality of disease H at age a in disease section.

PROPOSITION I *The disease section prevalence and the population disease prevalence can be expressed respectively as:*

$$n_H(a) = Pr\{A_{IH} \leq a | A_{DH} > a\}, \tag{1}$$

$$N_H(a) = Pr\{A_{IH} \leq a | A_{DL} > a, A_{DH} > a, A_{DO} > a\}. \tag{2}$$

From Eq. (2) *and* A1 *it follows that:*

$$N_H(a) = Pr\{A_{IH} \leq a | A_{DH} > a\} = n_H(a). \tag{3}$$

PROPOSITION II *The population prevalence of disease* L *and of the comorbidity of* H *and* L *are:*

$$N_L(a) = Pr\{A_{IL} \leq a | A_{DL} > a, A_{DH} > a, A_{DO} > a\}, \tag{4}$$

$$N_{HL}(a) = Pr\{A_{IH} \leq a, A_{IL} \leq a | \ A_{DL} > a, A_{DH} > a, A_{DO} > a\}. \tag{5}$$

By Proposition I *we know that* $N_H(a) = n_H(a)$, *and similarly for disease* L. *Proposition* II *now becomes: are* A1–A3 *sufficient conditions for* (6) *to be true*:

$$n_H(a) n_L(a) = N_{HL}(a). \tag{6}$$

Rewriting (5) *gives*:

$$N_{HL}(a) = \frac{Pr\{A_{IH} \leq a, \ A_{IL} \leq a, A_{DH} > a, A_{DL} > a, A_{DO} > a\}}{Pr\{A_{DH} > a, A_{DL} > a, A_{DO} \leq a\}}. \tag{7}$$

The denominator can be partitioned by using (A3), *to partition the numerator we use, in addition to* (A1) *and* (A2), *the property that incidence of a disease by definition has to occur before its mortality. This property allows us to write*:

$$Pr\{A_{IL} \leq a, A_{DL} > a\} = Pr\{A_{IL} \leq a\} - Pr\{A_{DL} \leq a\}. \tag{8}$$

Equation (7) *then becomes*:

$$N_{HL}(a) = \frac{\left[\begin{array}{l} Pr\{A_{IH} \leq a, A_{IL} \leq a, A_{DH} > a\} - Pr\{A_{IH} \leq a, A_{DL} \leq a, A_{DO} > a\} + \\ Pr\{A_{DH} \leq a, A_{DL} \leq a, A_{DO} > a\} - Pr\{A_{DH} \leq a, A_{IL} \leq a, A_{DO} > a\} \end{array}\right]}{Pr\{A_{DH} > a\} Pr\{A_{DL} > a\} Pr\{A_{DO} > a\}} \tag{9}$$

$$= \frac{Pr\{A_{DO} > a\}Pr\{A_{IH} \leq a, A_{DH} > a\}Pr\{A_{IL} \leq a, A_{DL} > a\}}{Pr\{A_{DL} > a\}Pr\{A_{DH} > a\}Pr\{A_{DO} > a\}} \quad (10)$$

$$= Pr\{A_{IH} \leq a | A_{DH} > a\}Pr\{A_{IL} \leq a | A_{DL} > a\} = n_H(a)n_L(a). \quad (11)$$

PROPOSITION III *The population and disease section probabilities are respectively*:

$$M_H(a) = Pr\{A_{DH} \leq a | A_{DL} > a, A_{DO} > a\}, \quad (12)$$

$$m_H(a) = Pr\{A_{DH} \leq a\}. \quad (13)$$

From A3 *it follows that:*

$$M_H(a) = Pr\{A_{DH} \leq a\} = m_H(a). \quad (14)$$

3 AN EXAMPLE

3.1 A Simple Disease Model

We will illustrate the method with two diseases and an 'all other causes' mortality. Each disease is described by an illness–death process with only one diseased state, consisting of just disease specific incidence, prevalence and mortality, with age specific incidence and mortality rates to be given. Recovery is ignored. This disease model can be described by a continuous time Markov process with three states: h – non-diseased; z – diseased; and d – dead. There are two transition hazards: γ from healthy to diseased; and φ from diseased to dead.

The equations below assume the transition hazards to be constant within age intervals, and to minimize the impact of this assumption the equations use 1-year age intervals. We consider the age interval $[a, a+1)$, with persons distributed over the three health states, and define r_a to be the probability for a person in the healthy state h at exact age a to make two transitions within the age interval: from

healthy to diseased and from diseased to dead. Let U be the time spent in that age interval in the healthy state, and V the time spent in the interval in the diseased state. Two transitions occur in the 1-year interval when the sum of these times is smaller than 1:

$$\begin{aligned} r_a &= P\{U+V\leq 1\} \\ &= \int_0^1 P\{V\leq 1-u|U=u\}P\{U=u\}\,\mathrm{d}u \\ &= \int_0^1 (1-\mathrm{e}^{-\varphi_a(1-u)})\gamma_a \mathrm{e}^{-\gamma_a u}\,\mathrm{d}u \\ &= \begin{cases} \dfrac{\varphi_a(1-\mathrm{e}^{-\gamma_a})-\gamma_a(1-\mathrm{e}^{-\varphi_a})}{\varphi_a-\gamma_a}, & \gamma_a\neq\varphi_a \\ 1-\mathrm{e}^{-\gamma_a}-\gamma_a\mathrm{e}^{-\gamma_a}, & \gamma_a=\varphi_a. \end{cases} \end{aligned} \tag{15}$$

The state variables h_a, z_a, and d_a denote the proportion of the population in the various states at age a. The states at $a+1$ are described by:

$$h_{a+1} = h_a\mathrm{e}^{-\gamma_a}, \tag{16}$$

$$z_{a+1} = h_a(1-\mathrm{e}^{-\gamma_a}-r_a)+z_a\mathrm{e}^{-\varphi_a}, \tag{17}$$

$$d_{a+1} = h_a r_a + z_a(1-\mathrm{e}^{-\varphi_a})+d_a. \tag{18}$$

Prevalence at exact age a is:

$$n_a = \frac{z_a}{1-d_a}. \tag{19}$$

Using Eqs. (16)–(19) we can express prevalence at age $a+1$ as:

$$n_{a+1} = \frac{n_a\mathrm{e}^{-\varphi_a}+(1-n_a)(1-\mathrm{e}^{-\gamma_a}-r_a)}{1-n_a(1-\mathrm{e}^{-\varphi_a})-(1-n_a)r_a}. \tag{20}$$

Mortality probability at a is given by:

$$m_a = \frac{d_{a+1}-d_a}{1-d_a} \tag{21}$$

and incidence density at a by:

$$i_a = 1-\mathrm{e}^{-\gamma_a}. \tag{22}$$

We can now write prevalence at $a+1$ as a function of prevalence, incidence and mortality at a:

$$n_{a+1} = \frac{n_a - m_a + (1 - n_a)i_a}{1 - m_a}. \tag{23}$$

3.2 Life Table Setup

In Table 1 we show the setup of the general section of the life table. The first column contains the 'all other causes' mortality rate, the second adds to this the disease specific mortality rates from the disease sections, and the third converts this to the total mortality probability. From there on the general section is equal to a standard life table.

Table 2 shows the setup of a disease section. The first two columns give the input, the incidence and mortality rates respectively, the latter one is used in the general section to determine total mortality probability. The third and fourth column convert these to probabilities, and the fifth calculates the prevalence.

TABLE 1

The general section of the proportional multi-state life table. Legends: δ^{o} stands for 'all other causes' mortality rate; δ^{d} for a disease specific mortality rate; δ for total mortality rate. Other notation follows standard life table convention

δ_a^o	δ_a	q_a	l_a	d_a	L_a	T_a	e_a
δ_0^o	$\delta_0^o + \sum_d \delta_0^d$	$1 - e^{-\delta_0}$	100 000	$l_0 q_0$	$0.5(l_0 + l_1)$	$\sum_{a=0}^{95} L_a$	$\frac{T_0}{l_0}$
δ_1^o	$\delta_1^o + \sum_d \delta_1^d$	$1 - e^{-\delta_1}$	$l_0 - d_0$	$l_1 q_1$	$0.5(l_1 + l_2)$	$\sum_{a=1}^{95} L_a$	$\frac{T_1}{l_1}$

TABLE 2

A disease specific section of the proportional multi-state life table. Legends: γ is incidence rate; δ the disease specific mortality rate; i the incidence probability; m the disease specific mortality probability; and n the disease prevalence

γ_a	δ_a	i_a	m_a	n_a
γ_0	δ_0	$1 - e^{-\gamma_0}$	$1 - e^{-\delta_0}$	0
γ_1	δ_1	$1 - e^{-\gamma_1}$	$1 - e^{-\delta_1}$	$\frac{n_0 - m_0 + (1 - n_0)i_0}{1 - m_0}$

3.3 Implementation

We have implemented this method, employing a spreadsheet, for heart disease (ischemic heart disease and congestive heart failure combined) and stroke among Dutch males in 1988. Table 3 shows incidence and mortality rates used in the calculations. Incidence of heart disease is based on various studies and a nationwide hospital register (Bonneux *et al.*, 1994), incidence of stroke on a Dutch regional and several international studies (Niessen *et al.*, 1993), disease specific and total mortality rates are from the national bureau of statistics (*Statistics Netherlands,* 1991; *Statistics Netherlands* published annually).

Calculations are done in a full life table (i.e. with 1-year age intervals) because of the crucial assumption, made to be able to subtract and sum mortality rates, that all hazard rates are constant during the age interval (Manton and Stallard, 1988). Table 4 shows part of such a full life table with a general section and a heart disease section. In the latter nothing is happening until, at age 23, the incidence hazard γ_a^d becomes greater than 0. When the heart disease mortality rate δ_a^d is big enough it becomes clear that the total mortality hazard δ_a is the sum of mortality hazard from all other causes (δ_a^o) and the disease specific rate.

TABLE 3

Disease specific incidence and mortality rates for heart disease and stroke, Netherlands, 1989, males. Incidence is defined as incidence rate among the non-prevalent population, heart disease is ischemic heart disease and congestive heart failure combined

Age	Heart disease		Stroke	
	Incidence	Mortality	Incidence	Mortality
25–29	0.000115	0.000012	0.000071	0.000009
30–34	0.000316	0.000048	0.000127	0.000021
35–39	0.001190	0.000175	0.000225	0.000047
40–44	0.003068	0.000462	0.000388	0.000100
45–49	0.005730	0.000943	0.000670	0.000175
50–54	0.009275	0.001710	0.001241	0.000389
55–59	0.013079	0.003478	0.002319	0.000771
60–64	0.016666	0.006122	0.003598	0.001431
65–69	0.021097	0.010198	0.005607	0.002783
70–74	0.028204	0.016316	0.008775	0.005379
75–79	0.038341	0.024833	0.013772	0.009980
80–84	0.051322	0.035256	0.021621	0.018235
85–89	0.068518	0.046781	0.025794	0.025746
90–94	0.098469	0.057755	0.029295	0.033099
95+	0.147829	0.065907	0.031636	0.036967

TABLE 4

Proportional multi-state life table (partly) with a general section and a heart disease section. N_a^d is the product of l_a and n_a^d, all other equations are in Tables 1 and 2

Age	General section					Heart disease section					N_a^d
	δ_a	δ_a	q_a	l_a	d_a	γ_a^d	δ_a^d	δ_a^d	t_a^d	m_a^d	
0	0.0078	0.0078	0.0078	100 000	776	0.00000	0.00000	0.00000	0.00000	0.00000	0
1	0.0011	0.0011	0.0011	99 225	108	0.00000	0.00000	0.00000	0.00000	0.00000	0
2	0.0005	0.0005	0.0005	99 117	51	0.00000	0.00000	0.00000	0.00000	0.00000	0
3	0.0004	0.0004	0.0004	99 066	36	0.00000	0.00000	0.00000	0.00000	0.00000	0
4	0.0003	0.0003	0.0003	99 030	28	0.00000	0.00000	0.00000	0.00000	0.00000	0
5	0.0003	0.0003	0.0003	99 002	25	0.00000	0.00000	0.00000	0.00000	0.00000	0
6	0.0003	0.0003	0.0003	98 977	25	0.00000	0.00000	0.00000	0.00000	0.00000	0
7	0.0002	0.0002	0.0002	98 952	22	0.00000	0.00000	0.00000	0.00000	0.00000	0
8	0.0002	0.0002	0.0002	98 930	19	0.00000	0.00000	0.00000	0.00000	0.00000	0
9	0.0002	0.0002	0.0002	98 911	19	0.00000	0.00000	0.00000	0.00000	0.00000	0
10	0.0002	0.0002	0.0002	98 892	19	0.00000	0.00000	0.00000	0.00000	0.00000	0
11	0.0002	0.0002	0.0002	98 873	19	0.00000	0.00000	0.00000	0.00000	0.00000	0
12	0.0002	0.0002	0.0002	98 854	21	0.00000	0.00000	0.00000	0.00000	0.00000	0
13	0.0002	0.0002	0.0002	98 833	23	0.00000	0.00000	0.00000	0.00000	0.00000	0
14	0.0003	0.0003	0.0003	98 810	26	0.00000	0.00000	0.00000	0.00000	0.00000	0
15	0.0004	0.0004	0.0004	98 784	36	0.00000	0.00000	0.00000	0.00000	0.00000	0
16	0.0005	0.0005	0.0005	98 748	49	0.00000	0.00000	0.00000	0.00000	0.00000	0
17	0.0006	0.0006	0.0006	98 699	54	0.00000	0.00000	0.00000	0.00000	0.00000	0
18	0.0006	0.0006	0.0006	98 645	59	0.00000	0.00000	0.00000	0.00000	0.00000	0
19	0.0007	0.0007	0.0007	98 585	67	0.00000	0.00000	0.00000	0.00000	0.00000	0
20	0.0007	0.0007	0.0007	98 519	70	0.00000	0.00000	0.00000	0.00000	0.00000	0
21	0.0007	0.0007	0.0007	98 449	71	0.00000	0.00000	0.00000	0.00000	0.00000	0

TABLE 4 (*continued*)

Age	General section					Heart disease section					N_a^d
	δ_a	δ_a	q_a	l_a	d_a	γ_a^d	δ_a^d	δ_a^d	t_a^d	m_a^d	
22	0.0007	0.0007	0.0007	98 378	72	0.00002	0.00000	0.00000	0.00000	0.00000	0
23	0.0007	0.0007	0.0007	98 306	73	0.00002	0.00000	0.00002	0.00000	0.00000	0
24	0.0007	0.0007	0.0007	98 233	73	0.00005	0.00000	0.00005	0.00000	0.00002	2
25	0.0007	0.0007	0.0007	98 160	71	0.00007	0.00001	0.00007	0.00001	0.00006	6
26	0.0007	0.0007	0.0007	98 089	71	0.00009	0.00001	0.00009	0.00001	0.00012	12
27	0.0007	0.0008	0.0008	98 018	74	0.00012	0.00001	0.00012	0.00001	0.00021	20
28	0.0007	0.0008	0.0008	97 943	73	0.00016	0.00002	0.00016	0.00002	0.00031	30
29	0.0007	0.0008	0.0008	97 870	74	0.00020	0.00003	0.00020	0.00003	0.00045	44
30	0.0007	0.0008	0.0008	97 796	75	0.00024	0.00003	0.00024	0.00003	0.00061	60
31	0.0008	0.0008	0.0008	97 721	79	0.00028	0.00004	0.00028	0.00004	0.00082	80
32	0.0008	0.0009	0.0009	97 642	86	0.00032	0.00005	0.00032	0.00005	0.00105	103
33	0.0009	0.0009	0.0009	97 556	90	0.00049	0.00007	0.00049	0.00007	0.00132	129
34	0.0009	0.0010	0.0010	97 465	94	0.00067	0.00010	0.00067	0.00010	0.00174	169
35	0.0009	0.0011	0.0011	97 371	102	0.00084	0.00012	0.00084	0.00012	0.00230	224
36	0.0010	0.0011	0.0011	97 269	111	0.00102	0.00015	0.00101	0.00015	0.00302	293
37	0.0011	0.0012	0.0012	97 158	121	0.00119	0.00018	0.00119	0.00017	0.00388	377
38	0.0011	0.0013	0.0013	97 037	126	0.00157	0.00023	0.00156	0.00023	0.00489	475
39	0.0011	0.0014	0.0014	96 911	134	0.00194	0.00029	0.00194	0.00029	0.00622	602
40	0.0012	0.0016	0.0016	96 777	151	0.00232	0.00035	0.00231	0.00035	0.00786	760

The disease prevalence in numbers (N_a^d) is obtained by multiplication of the prevalence rate n_a^d with the l_a column of the general section: both n_a^d and N_a^d are prevalences at exact age a. Note that at these younger ages the difference between hazards and probabilities does not show up in the rounded figures. Also note that by using cross-sectional data in a cohort model the estimated prevalences will not fully comply with observed prevalences in the presence of past trends.

With this life table we first estimated the baseline age specific case fatalities (the disease specific mortality probability, given disease prevalence) from observed disease specific mortality and estimated prevalence, using simply:

$$p_a = \frac{m_a}{n_a}. \tag{24}$$

The resulting baseline values are then used to estimate the impact on disease prevalence and on disease specific and total mortality of changes in incidence and case fatalities.

Cardiovascular disease in the Netherlands (as in many other western countries) has seen declining age specific mortality, for stroke at least since the early sixties, for heart disease since the early seventies. A closer look at the available evidence reveals that this decline is most likely due to a combination of declining incidence and increasing survival (Niessen *et al.*, 1993; Bonneux *et al.*, 1994). We assess the impact of such combined trends by multiplying age specific incidence of both diseases with a factor of 0.9 (all ages), and multiply case fatalities (i.e. 1-survival probability) likewise with 0.8, always comparing outcomes with the 1988 base year. These changes in incidence and survival are compatible with the presumed changes in the past decade.

3.4 Baseline Results

In Table 5 the resulting disease prevalences for the 1988 base year are shown, both in rates and numbers. The prevalence rates are calculated using the average of n_a^d and n_{a+1}^d, the numbers are obtained by multiplication of the average rate with the general sections L_a column, and are therefore higher than the prevalences in Table 4.

3.5 Improved Survival

First we increase survival with heart disease and stroke, while leaving all other parameters at their base value. Figure 1 shows outcome

TABLE 5
Baseline values for the prevalence of heart disease, stroke, and their comorbidity

	Prevalence rates			Prevalence numbers		
Age	Heart	Stroke	Comob	Heart	Stroke	Comob
0–4	0.0000	0.0000	0.0000	0	0	0
5–9	0.0000	0.0000	0.0000	0	0	0
10–14	0.0000	0.0000	0.0000	0	0	0
15–19	0.0000	0.0000	0.0000	0	0	0
20–24	0.0000	0.0000	0.0000	5	3	0
25–29	0.0003	0.0002	0.0000	140	82	0
30–34	0.0013	0.0006	0.0000	624	287	0
35–39	0.0046	0.0013	0.0000	2241	633	3
40–44	0.0137	0.0025	0.0000	6606	1195	17
45–49	0.0318	0.0045	0.0001	15144	2118	70
50–54	0.0612	0.0078	0.0005	28455	3648	229
55–59	0.1003	0.0138	0.0014	44828	6159	629
60–64	0.1441	0.0228	0.0033	60136	9533	1390
65–69	0.1884	0.0349	0.0066	70041	12957	2459
70–74	0.2327	0.0495	0.0115	71426	15201	3555
75–79	0.2785	0.0660	0.0184	62772	14870	4156
80–84	0.3274	0.0816	0.0267	45286	11291	3705
85–89	0.3838	0.0888	0.0341	25242	5841	2241
90–94	0.4640	0.0801	0.0372	10202	1762	814
95+	0.5403	0.0671	0.0363	2819	350	189
Total				445968	85932	19458

expressed as indices (with 1988 = 100) of prevalences by age of heart disease and stroke and of the comorbidity of heart disease and stroke. Both prevalence rates show the same pattern: increases for all age groups, but much more so in older age groups. This pattern is much more visible for stroke than for heart disease, because the base survival of stroke is worse and therefore an equal relative improvement has a larger impact. The comorbidity rate of heart disease and stroke, being the product of the two disease specific prevalence rates, shows the same pattern even more strongly: for the highest age group it is 50% higher than the base line.

The effect of improved disease specific survival on total mortality causes a further strengthening of this pattern when we look at prevalence numbers, because a larger part of the initial birth cohort lives to high age. Comorbidity of heart disease and stroke is 65% higher for the oldest age group.

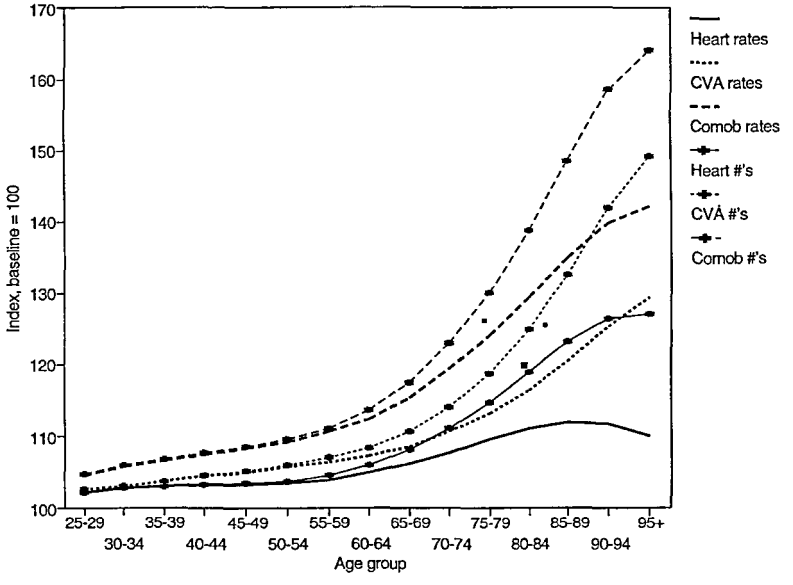

FIGURE 1 Prevalences of heart disease and stroke (rates and numbers) by age after improved survival, index with baseline = 100. Legends: heart rates – prevalence rate of heart disease; CVA rates – prevalence rate of stroke; comob rates – comorbidity prevalence rate of heart disease and stroke; heart #'s – prevalence numbers of heart disease; CVA #'s – prevalence numbers of stroke; comob #'s – comorbidity prevalence numbers of heart disease and stroke.

3.6 Incidence Decline

Secondly we multiplied the age specific incidences with 0.9, again with all other parameters at their base value (Fig. 2). The age specific prevalences at the lowest ages stand at a corresponding 90% of the base rate, but these percentages edge up a bit with age. The lower prevalence rate in any age group results in a larger group at risk for incidence, which counter-acts the lower incidence rate. A similar result for cardiovascular mortality was observed by Rose and Shipley (1990). The effect is stronger for heart disease because the baseline prevalence of heart disease is higher than the one of stroke.

With both diseases at 90% of their prevalence rates for the young, the comorbidity rate of course stands at 81% for those ages, and is also edging up with age. Through the implied lower disease specific mortalities this pattern is more pronounced in prevalence numbers: at the highest age disease prevalences even exceed the baseline value.

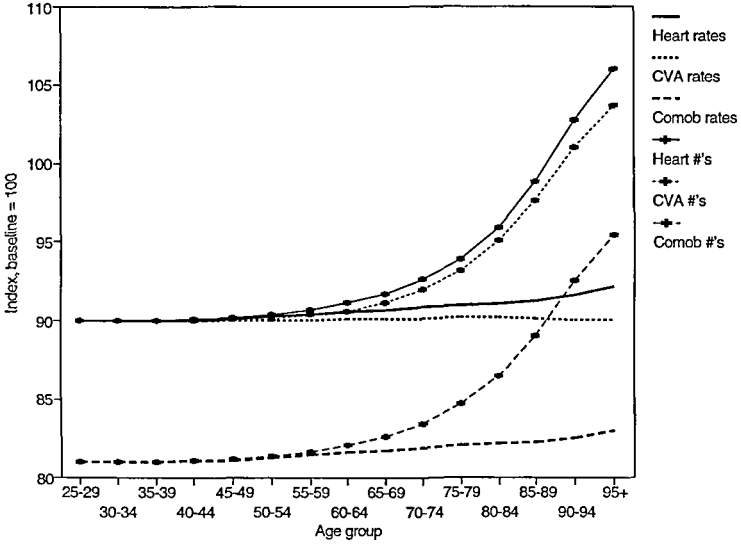

FIGURE 2 Prevalences of heart disease and stroke (rates and numbers) by age after incidence decline, index with baseline = 100. Legends: heart rates – prevalence rate of heart disease; CVA rates – prevalence rate of stroke; comob rates – comorbidity prevalence rate of heart disease and stroke; heart #'s – prevalence numbers of heart disease; CVA #'s – prevalence numbers of stroke; comob #'s – comorbidity prevalence numbers of heart disease and stroke.

3.7 Improved Survival and Lower Incidence Combined

The combined picture of improved survival and lower incidence is shown in Fig. 3. Lower incidence is reflected in 5–10% lower prevalence rates at young ages, and the increased survival causes up to about 15% higher prevalence rates at older ages. The now combined mortality effect pushes up disease prevalence numbers at the highest ages above the improved survival-only case. And comorbidity, while being more than 15% lower for the young, shows a 20% (rates) and 55% (numbers) increase for the oldest age group. The results are tilted index lines, with pivot points somewhere between age 65 and 70.

Summed across ages the lower prevalence at young and higher prevalence at older ages on balance result in somewhat higher prevalence numbers: 3% and 7% for heart disease and stroke respectively. Number of years lived with disease as a percentage of total number of years lived also increases, but a bit less: 2% and 5% respectively.

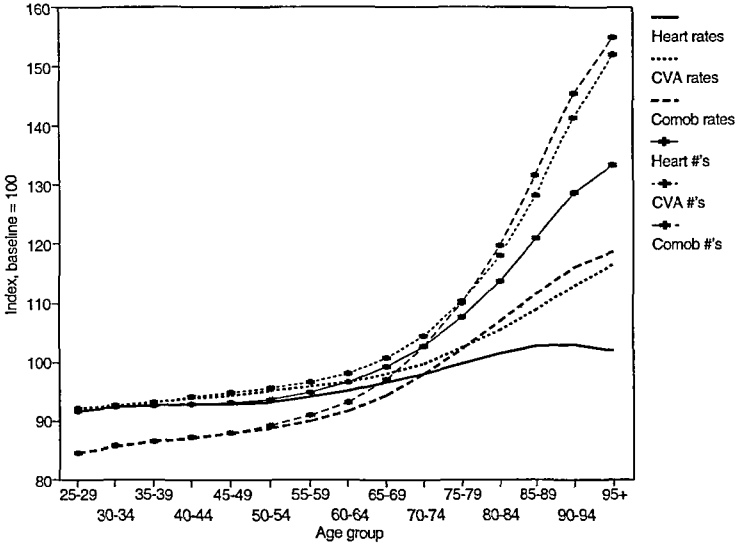

FIGURE 3 Prevalences of heart disease and stroke (rates and numbers) by age after improved survival and incidence decline combined, index with baseline = 100. Legends: heart rates – prevalence rate of heart disease; CVA rates – prevalence rate of stroke; comob rates – comorbidity prevalence rate of heart disease and stroke; heart #'s – prevalence numbers of heart disease; CVA #'s – prevalence numbers of stroke; comob #'s – comorbidity prevalence numbers of heart disease and stroke.

4 DISCUSSION

Improved survival and decreased incidence have, as has been demonstrated above, a similar effect on disease prevalence: a relative shift of the burden of disease towards older ages. With improved survival all age groups have higher prevalences, but the oldest much more so. Declining incidence lowers prevalence for most age groups, but older ages benefit less and the oldest even have a higher prevalence. Combining both changes turns the relative shift into an absolute one: younger age groups experience less disease, older age groups more. In terms of disability this pattern will be even more pronounced because of comorbidity: disability in many cases might be an almost exponential function of the number of comorbid conditions (Verbrugge *et al.*, 1989).

The decline in cardiovascular disease mortality is most likely due to a combination of declining incidence and increasing survival. Declining

incidence may be unique to cardiovascular disease, cancer incidence, for example, has been reported up, albeit based on inconclusive evidence (Adami *et al.*, 1993; Bonneux *et al.*, 1993; 1995). But increased survival probably extends to many other chronic conditions: medical technology has seen more progress in management of chronic disease than in cure. Barring major breakthroughs this pattern is likely to continue.

The question whether morbidity has been compressing or expanding must be seen against the epidemiological background of improved survival for most chronic diseases, with simultaneously decreasing incidences for the large cardiovascular causes of morbidity. Although it is difficult to say what the overall effect of these changes has been, it is likely, in particular when expressed in terms of disability, that there has indeed been an absolute shift in the burden of disease from the young towards the old.

If this pattern of a decreasing prevalence at younger and an increasing one at older ages will indeed turn out to be the prevailing development, it would seem that the debate on compression versus expansion of morbidity is being held in too simplistic terms. While morbidity is compressing in the sense that there is less of it at younger age and it is being concentrated at higher ages, it is at the same time expanding in the sense that there is more of it at older age and in total (both absolute and relative). Perhaps we should rethink our terminology.

The shift in age distribution of disease described above has economic consequences as well: it will inflate health care costs because of increased numbers of patients, who are older on average, have more comorbidity, and therefore are more expensive.

Similar exercises have been done by Crimmins *et al.* (1994). They use a standard multi-state life table with states of varying degrees of dependency, and look at the effects of changes in mortality and morbidity rates. Their results seem compatible with ours, but unfortunately they do not report on changes in the age pattern of dependency, only on expected dependent years and the proportion of total life expectancy in a dependent state.

The proportional multi-state life table method employed in this paper provides a relatively simple method to incorporate several diseases in a life table, and keep track of comorbidity. To be sure, the standard multi-state life table method can handle multiple diseases with comorbidity, but the resulting life table soon becomes awkward when the number of diseases increases. In particular, adding a disease

to an existing standard multi-state life table requires a major update of the life table.

With a proportional multi-state life table, in contrast, only the first two columns of the general section need to be updated, and the four columns of a new disease section added. This aspect makes a step-wise expansion of the life table to incorporate an increasing number of diseases an attractive option.

The price for this relative simplicity and flexibility is assumptions A1–A3 (or a similar set, depending on the number of diseases). They require the diseases to be independent, and the life table cohort to be homogeneous. When other than independent diseases are desirable these can only be modeled by defining additional states. For example, when diabetes and cardiovascular disease are modeled it is imperative to let diabetics have a higher risk on cardiovascular disease incidence, and perhaps also a worse survival. This can be achieved by doubling the number of states of the life table, one set for diabetics and one for non-diabetics. The independence conditions are thus relaxed to local independence. A similar setup can be done for risk factors like smoking and hypertension, but obviously there are practical limits to the number of dependent diseases and risk factors that can thus be accommodated.

Our implementation of the life table used 1-year age intervals. As such this not a requirement, Eqs. (15)–(23) can easily be rewritten for wider intervals, although in particular at higher ages wider intervals will bias results. Minimizing this bias is a good reason for using 1-year intervals, but an additional reason is a wider application of the methodology that avoids a limitation the proportional multi-state life table shares with all life tables: it either describes a single cohort through time, or a population at a single point in time (Shryock and Siegel, 1976).

Often in Public Health it is interesting to look at intervention effects on an entire population through time. *Prevent* is a dynamic population model that links risk factor prevalences with disease specific and total mortality, thus allowing estimates of decreased mortality after risk factor intervention (Gunning-Schepers, 1989; Gunning-Schepers *et al.*, 1989). This model has now been extended to *Prevent Plus* that incorporates multiple morbidity, using dynamic versions of the disease section of the proportional multi-state life table. *Prevent Plus* has a 1-year time step, and to avoid unwanted blending of disease prevalences between adjacent age groups the age interval and time step of the dynamic disease models must be equal.

The proportional multi-state life table method also forms the methodological basis of NIMPH, the Netherlands Integrated Model of Public Health. NIMPH combines the dynamic population and risk factor approach of *Prevent Plus* with dependent diseases (like diabetes and cardiovascular disease) and multi-stage disease models (to allow for duration dependence and differences in severity). This family of models, proportional multi-state life table, *Prevent*, *Prevent Plus*, and NIMPH, with various levels of complexity and data requirements, is used to explore the research field of Public Health, with research question and available data determining which model is most appropriate.

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