

## DECREMENT TABLES AND THE MEASUREMENT OF MORBIDITY: II

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### 1. INTRODUCTION

1.1. An earlier paper<sup>(1)</sup> by the author has attempted to describe the theories of multi-state life tables and inhomogeneous Markov chains in their application to the study of morbidity as introduced by Pollard.<sup>(2)</sup> It is the purpose of this paper to extend the model to describe the relationship between the incidence and prevalence of a disease. The implications of certain assumptions about the presence of mortality and of differentials in the level of mortality are also discussed.

1.2. As described earlier, a simple increment-decrement table may be used to represent the flow of new cases of a disease,  $Z$  say, in a community. Figure 1 shows the three states for such a model with the four permissible flows identified.

### 2. INCIDENCE AND PREVALENCE: DEFINITIONS

2.1. The concepts of incidence and prevalence of a disease are widely discussed in the epidemiological and biostatistical literature. A number of different indices have been developed and used, which are defined in § 2.4.

2.2. The definitions relate to the example of a homogeneous cohort of individuals aged  $x$  exact at a particular time origin who are followed up prospectively over the following  $t$  years. Let  $N$  be the initial size of the cohort. The definitions are expressed in terms of a single disease  $Z$  and in terms of individuals suffering from  $Z$ . It is assumed that, at the time origin, individuals suffering from  $Z$  are excluded from the cohort: pre-existing cases are often excluded from epidemiological investigations.<sup>(3)</sup>

2.3. To assist in understanding the definitions presented below, the following symbols are used to denote the composition of the cohort at any point of time,  $s$ , in the follow-up period ( $0 \leq s \leq t$ ):

$a_1(s)$  = number of individuals who are free of  $Z$  at time  $s$  but who have been sick from  $Z$  at some stage in the interval  $(0, s)$ ;

$a_2(s)$  = number of individuals who are free of  $Z$  throughout the interval  $(0, s)$ ;

$b(s)$  = number of individuals who are sick from  $Z$  at time  $s$ ;

$d(s)$  = cumulative number of individuals who have died by time  $s$ .

(If the assumption in § 2.2, concerning the exclusion of those sick from  $Z$  at the

start of the follow-up period, were relaxed, it would be convenient to subdivide the cohort further and to consider separately those persons at time  $s$  who started the period sick but who are free from  $Z$  at time  $s$  having experienced no recurrences.)

Then  $a(s) = a_1(s) + a_2(s)$ .  
 At  $s = 0$ ,  $a_2(0) = N$ , the initial size of the cohort;  
 and  $a_1(0) = 0$ ,  $b(0) = 0$ ,  $d(0) = (0)$ .

2.4. The definitions are as follows:

2.4.1. *The initial incidence rate* for  $Z$  is defined as the number of persons who start at least one episode of sickness due to  $Z$  during the period, divided by the number of persons exposed to the risk of sickness at the start of that period. The denominator is  $N$ , the initial size of the cohort. The numerator counts the first transitions from  $a_2$  to  $b$  during the period, but excludes transitions (i.e. recurrences of  $Z$ ) from  $a_1$  to  $b$ . For the period between ages  $x$  and  $x+t$  the notation  $I_x$  is used for the initial incidence rate. When  $t$  is extended up to  $w-x$ , with  $w$  denoting the highest possible live age, the initial incidence rate is called in some texts the "overall probability of attack from  $Z$ ".

2.4.2. *The central incidence rate* for  $Z$  is defined as the number of persons who start at least one episode of sickness due to  $Z$  during the period divided by the number of person years lived by the cohort over the period. The numerator is as in § 2.4.1. The denominator measures the number of years lived by the total group, i.e. it is an L-type function based on the integral of  $a(s) + b(s)$ . The denominator includes  $b(s)$ , the numbers currently suffering from  $Z$ , and so cannot be interpreted as the numbers exposed-to-risk of sickness from  $Z$ . This will be discussed further in § 7. For the period between ages  $x$  and  $x+t$  the notation  $m_x$  is used for the central incidence rate.

2.4.3. *The point prevalence rate* for  $Z$  is defined as the number of persons who are sick from  $Z$  at a given point in time, divided by the total cohort size at that time, i.e. at time  $s$  it is the ratio of  $b(s)$  to  $a(s) + b(s)$ . At age  $x+s$ ,  $R_{x+s}$  is used to denote the point prevalence rate. The point prevalence rate corresponds to the force of sickness used in textbooks on life and other contingencies.<sup>(4)</sup>

2.4.4. *The period prevalence rate* for  $Z$  is defined as the number of persons who are sick from  $Z$  at some time during the period divided by the number of person-years lived by the cohort over the period. The denominator is as for § 2.4.2. The numerator includes any person who is sick from  $Z$  at any stage during the period, i.e. the integral of  $a_1(s) + b(s)$  over the appropriate values of  $s$ .

2.4.5. *The cumulative prevalence rate* for  $Z$  is defined as the number of persons who are sick from  $Z$  some time during a period and are alive at the end of the period divided by the total cohort size at the end of the period, i.e. at time  $s$  it is the ratio of  $a_1(s) + b(s)$  to  $a(s) + b(s)$ .

2.5. In this paper, attention will be directed at the properties and relationships of the first three of these indices, viz. the initial incidence rate, the central incidence rate and the point prevalence rate.

2.6. These definitions indicate that the concept of incidence relates to the emergence of new cases of a disease whereas prevalence relates to the number of persons who are sick at a point of time or over a period. Thus, incidence rates are 'flow' statistics and prevalence rates are 'stock' statistics, to use demographic nomenclature. A comparison between prevalence and incidence is thus similar to a comparison between modes of data collection and analysis in demography (e.g. the census and the registration of vital events) and in accountancy (e.g. the balance sheet and revenue account).

### 3. MARKOV CHAIN REPRESENTATION: INCIDENCE

3.1. As indicated in §6 of the previous paper, an associated finite-space continuous-time, time-inhomogeneous Markov chain may be defined which corresponds to the increment-decrement table and the states depicted in Figure 1. For convenience the notation of the earlier paper is repeated here.

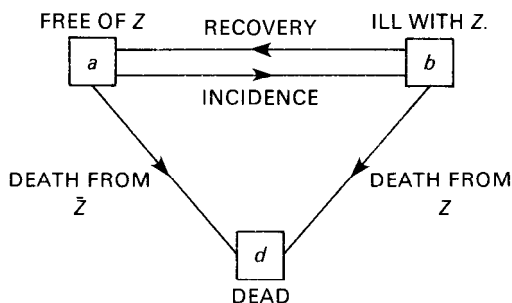


Figure 1. Model for the incidence of disease,  $Z$ .

3.2. A stochastic process  $S(x)$  with continuous-time parameter  $x$  denoting the exact attained age is introduced. The transition probabilities are then

$${}_s^i P_x^j = \Pr[S(x+s) = j | S(x) = i] \text{ where } i = a, b \quad j = a, b, d \quad (1)$$

These depend on the occupancy of a given state at age  $x$ . The transition intensities (or forces) are

$$\left. \begin{aligned} {}^i \mu_x^j &= \lim_{s \rightarrow 0} \left( \frac{{}_s^i P_x^j}{s} \right) \quad i \neq j \quad i = a, b \quad j = a, b, d \\ {}^i \mu_x^i &= -\lim_{s \rightarrow 0} \left( \frac{1 - {}_s^i P_x^i}{s} \right) \quad i = a, b \end{aligned} \right\} \quad (2)$$

These are shown in Figure 2.

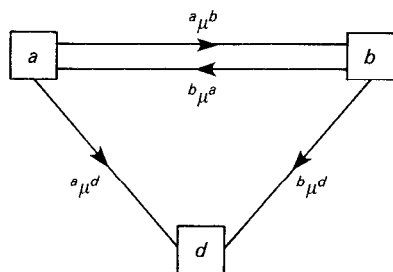


Figure 2. Transition intensities for the model in Figure 1.

3.3. It is assumed for convenience that the recovery rate from  $Z$ , i.e.  ${}^b\mu_x^a$  is sufficiently small for it to be taken equal to zero, in which case  $a_1(s)=0$  for all values of  $s$ . It follows, therefore, from the definitions in §2.4 that the point and cumulative prevalence rates at any age  $x+s$  are equal. In the following sections, reference will be made only to the point prevalence rate.

3.4. It may be proved from the forward Kolmogorov differential equations, quoted in general matrix form in the earlier paper, that, in the absence of recovery, the following equations hold:

$${}_n^aP_y^a = \exp \left( - \int_0^n ({}^a\mu_{y+s}^b + {}^a\mu_{y+s}^d) ds \right) \quad (3)$$

$${}_n^aP_y^d = \int_0^n {}_s^aP_y^a {}_s^a\mu_{y+s}^d ds \quad (4)$$

$${}_n^bP_y^b = \exp \left( - \int_0^n {}^b\mu_{y+s}^d ds \right) \quad (5)$$

$${}_n^aP_y^b = \int_0^n {}_s^aP_y^a {}_s^a\mu_{y+s}^b {}_{n-s}^bP_{y+s}^b ds \quad (6)$$

An example of the derivation, for equation (3), is given in §3.5.

3.5. The definitions of transition intensities imply that as  $h \rightarrow 0$ ,

$${}_h^aP_y^b \rightarrow h {}^a\mu_y^b \quad \text{and} \quad {}_h^aP_y^d \rightarrow h {}^a\mu_y^d$$

Consider the time interval between ages  $y+s$  and  $y+s+h$ , for  $h$  small, so that the probability of one or more transitions is negligible. Then

$$1 = {}_h^aP_{y+s}^a + {}_h^aP_{y+s}^b + {}_h^aP_{y+s}^d \quad \text{for } h \text{ small.}$$

Hence, for  $h$  small,

$${}_h^a P_{y+s}^a = 1 - h({}_y^a \mu_{y+s}^b + {}_y^a \mu_{y+s}^d)$$

Now 
$$\frac{{}_{s+h}^a P_y^a - {}_s^a P_y^a}{h} = \frac{{}_s^a P_y^a ({}_h^a P_{y+s}^a - 1)}{h} = -{}_s^a P_y^a ({}_y^a \mu_{y+s}^b + {}_y^a \mu_{y+s}^d)$$

for  $h$  small, on substituting from the above.

Hence, in the limit as  $h \rightarrow 0+$ ,

$$-\frac{\partial}{\partial s} ({}_s^a P_y^a) = {}_s^a P_y^a ({}_y^a \mu_{y+s}^b + {}_y^a \mu_{y+s}^d) \quad (7)$$

which when integrated, subject to the initial condition that  ${}_0^a P_y^a = 1$  gives (3). Similarly differential equations for the other transition probabilities may be derived.

3.6. Were recoveries to be permitted, the equations in § 3.4 would be more complex as it would be necessary to distinguish the separate non-empty components of  $a(s)$  (in the notation of § 2), i.e.  $a_1(s) + a_2(s)$ . In this situation, for example, the right hand side of (3) would be the probability that an individual remains in state  $a$  throughout the time interval from age  $y$  to  $y+n$ , and *not*  ${}_n^a P_y^a$ .

3.7. Returning to the case of zero recoveries, a further transition probability of interest is  ${}_n^a \bar{P}_y^d = \text{Pr} [S(y+n) = d | S(y) = a \text{ and } S(y+s) = b \text{ for some } 0 < s < n]$ , i.e. the probability that a life in state  $a$  (free of  $Z$ ) at age  $y$  is in state  $d$  at age  $y+n$  having incurred  $Z$  (i.e. dead from  $Z$  rather than  $\bar{Z}$ : causes other than  $Z$ ). The following equation then holds:

$${}_n^a \bar{P}_y^d = \int_0^n {}_s^a P_y^a {}_y^a \mu_{y+s}^b {}_{n-s}^b P_{y+s}^d ds. \quad (8)$$

Because  ${}_{n-s}^b P_{y+s}^d = 1 - {}_{n-s}^b P_{y+s}^b$ , it then follows that

$${}_n^a \bar{P}_y^b + {}_n^a \bar{P}_y^d = \int_0^n {}_s^a P_y^a {}_y^a \mu_{y+s}^b ds \quad (9)$$

3.8. The initial incidence rate  ${}_n I_y$  defined in § 2.4.1 is then equal, by definition, to  $({}_n^a \bar{P}_y^b + {}_n^a \bar{P}_y^d)$ . In the absence of mortality from  $\bar{Z}$  (i.e. for individuals without the disease),  ${}_y^a \mu_{y+s}^d = 0$  and so the expression for  ${}_n I_y$  becomes, on substituting from (3) into (9),

$$\begin{aligned} {}_n I_y &= {}_n^a \bar{P}_y^b + {}_n^a \bar{P}_y^d = \int_0^n {}_s^a P_y^a {}_y^a \mu_{y+s}^b ds \\ &= \int_0^n \exp \left( - \int_0^s {}_y^a \mu_{y+u}^b du \right) {}_y^a \mu_{y+s}^b ds \end{aligned}$$

i.e. 
$${}_n I_y = 1 - \exp \left( - \int_0^n {}_y^a \mu_{y+u}^b du \right) \quad (10)$$

Hence in the absence of mortality from  $\bar{Z}$ ,  ${}_n I_y$  is equal to the total decrement rate in a single decrement table based solely on the incidence of  $Z$  (such a table is called a single decrement incidence table). This assumption of zero mortality

from  $\bar{Z}$  may be appropriate over short age ranges when a dominant cause of death is being investigated, e.g. breast cancer for females at ages under 50.

3.9. With  $I_y$  written for  ${}_nI_y$  with  $n=1$  and  $\tilde{i}_y$  defined by

$$\tilde{i}_y = \prod_{r=0}^{y-x-1} (1 - I_{x+r}) = \exp \left( - \int_0^{y-x} {}^a\mu_{x+u}^b du \right) \quad (11)$$

then  $\tilde{i}_y$  represents the proportion of persons without  $Z$  who have not experienced an attack from  $Z$  by age  $y$ , in the absence of mortality from causes  $\bar{Z}$ . If there is an age  $w$  beyond which no more fresh cases of  $Z$  occur, and if follow-up is continued beyond age  $w$ , then  $\tilde{i}_w$  is the proportion of persons without  $Z$  who never incur it.

3.10. In the absence of mortality from  $\bar{Z}$ , the number of persons in state  $a$  may decrease only by incidence of  $Z$ . Then the difference between the number without  $Z$  at ages  $y$  and  $y+1$  is equal to the number of new cases of  $Z$  between these ages. But the size of the cohort does not change given the above assumptions, so the number without  $Z$  at age  $y$  is proportional to  $\tilde{i}_y$ . We define  $\tilde{j}_y$  as the ratio of the incident cases between ages  $y$  and  $y+1$  to the initial size of the cohort. Then  $\tilde{j}_y = \tilde{i}_y - \tilde{i}_{y+1} = \tilde{i}_y I_y$ , and so

$$I_y = \frac{\tilde{j}_y}{\tilde{i}_y} \quad (12)$$

The quantity  $\tilde{j}_y$  is an estimator for  ${}_y-x P_x^a ({}_y^a P_y^b + {}_1^a \bar{P}_y^d)$ , since all individuals are assumed free of  $Z$  on entry to the study at age  $x$ . Again, only in the absence of mortality for individuals without the disease does this expression reduce to

$$\exp \left( - \int_0^{y-x} {}^a\mu_{x+u}^b du \right) (1 - \exp \left( - \int_0^1 {}^a\mu_{y+u}^b du \right))$$

which is equivalent to the above definition of  $\tilde{j}_y$ , i.e.  $\tilde{i}_y - \tilde{i}_{y+1}$ .

3.11. The series of  $\tilde{j}_y$  provides the age distribution of the  $(\tilde{i}_x - \tilde{i}_w)$  incidences of  $Z$  that would occur in the absence of mortality from  $\bar{Z}$  in a cohort with initial size  $\tilde{i}_x$ . Thus, the series  $\tilde{j}_y/(\tilde{i}_x - \tilde{i}_w)$  constitutes the distribution of ages at first incidence of  $Z$  and may be described by measures of central tendency and of dispersion, as with any other statistical distribution: e.g. mean age at first incidence of  $Z$ , an example of the  ${}^i e_x^j$  functions defined by equation (43) in the earlier paper, under the specific assumptions mentioned above.

#### 4. POINT PREVALENCE RATES

4.1. In general the point prevalence rate of  $Z$  at age  $y=x+s$ , following the definition in §2.4.3, is given by

$$R_{x+s} = \frac{{}_s^a P_x^b}{{}_s^a P_x^a + {}_s^a P_x^b} \quad (13)$$

If there is non-differential mortality i.e.  ${}^a\mu_u^d = {}^b\mu_u^d$  at all ages  $u$  then it can be shown from the above definitions that (13) reduces to

$$R_{x+s} = 1 - \exp\left(-\int_0^s {}^a\mu_{x+u}^b du\right) = 1 - \prod_{r=0}^{s-1} (1 - I_{x+r}) \quad (14)$$

$$\text{i.e.} \quad R_{x+s} = 1 - \tilde{I}_{x+s}$$

Under this assumption, there is therefore a simple and direct relationship between the point prevalence rate and the single decrement incidence table based solely on incidence rates. The above equality is a simple version of a more general relationship derived by Hoem<sup>(5)</sup> in Markov chain theory, i.e. the relationship between partial probabilities in a Markov chain and the derived purged Markov chain.

4.2. Elsewhere, equation (14) has been derived using the assumed equality of  ${}^a\mu_u^d$  and  $\mu_u^d$  where  $\mu_u^d$  is the force of mortality for an individual aged  $u$  irrespective of disease status.<sup>(6)</sup> The similarity between assuming  ${}^a\mu_u^d = {}^b\mu_u^d$  and assuming  ${}^a\mu_u^d = \mu_u^d$  may be established as follows

$$\begin{aligned} \mu_u^d &= \lim_{t \rightarrow 0} \frac{\text{Pr}(\text{death before age } u+t | \text{alive at age } u)}{t} \quad \text{for } u > x \\ &= \lim_{t \rightarrow 0} \frac{1}{t} \left( \frac{{}_tP_{u-u-x}^d {}^aP_{x-x}^a + {}_tP_{u-u-x}^d {}^aP_{x-x}^b}{{}_uP_{x-x}^a + {}_uP_{x-x}^b} \right) \end{aligned}$$

$$\text{i.e.} \quad \mu_u^d = \frac{{}_uP_{u-u-x}^d {}^aP_{x-x}^a}{{}_uP_{x-x}^a + {}_uP_{x-x}^b} + \frac{{}_uP_{u-u-x}^d {}^aP_{x-x}^b}{{}_uP_{x-x}^a + {}_uP_{x-x}^b} \quad (15)$$

So assuming  $\mu_u^d = {}^a\mu_u^d$  is equivalent to assuming  ${}^a\mu_u^d = {}^b\mu_u^d$  (i.e. non-differential mortality) only if  $0 < \frac{{}_uP_{x-x}^b}{{}_uP_{x-x}^a} < 1$ .

4.3. The correspondence demonstrated above between the single decrement incidence table and the point prevalence rate has a parallel in demography where, given a similar set of assumptions, the proportion single in the population and proportion surviving single in the corresponding gross nuptiality table may be proved equal.<sup>(7)</sup>

4.4. So far we assume that the point prevalence of disease  $Z$  among cohorts is measured. In addition, we now assume that, at certain points in time, a count (or census, using demographic terminology) is conducted and the point prevalence rate by current age is measured at each census in time. Consider one such count or census. If the incidence rates in the population under consideration are assumed to have remained unchanged up to the time of the census in question, then that single census may be used as if it represented a series of censuses carried out at annual intervals. When incidence does not change, each cohort has the same series of  $\tilde{I}_y$ . Measuring prevalence at a census is then equivalent to following up a cohort through time; so that

$$R_y = \bar{R}_y \quad (16)$$

where  $\bar{R}_y$  is the point prevalence rate at a census for all persons aged  $y$  in the community. If the conditions for equation (14) are fulfilled (as in §4.1) then

$$\bar{R}_y = 1 - \tilde{\lambda}_y \quad (17)$$

In the absence of time trends a single census may be used as if it presented a series of censuses performed in successive years. This corresponds to the classical demographic device of using cross-sectional indices, in the absence of time trends, as though they refer to 'fictitious' cohorts. In these circumstances, a relationship between the single decrement table and the census prevalence rate,  $\bar{R}_y$ , has been established.

4.5. When the incidence rates of  $Z$  do change over time (as is often the case with, for example, chronic disease), then the use of an equation like (16) will lead to fallacious conclusions (as is well known in demographic examples). The problem is that a calendar period is being used to say something about the cohorts passing through that period without allowance for the difference between these cohorts (caused by the presence of time trends). Thus, if time changes occur within cohorts so that incidence occurs at a younger age then the use of equation (16) would lead to a change in the number of incidences per head (and prevalences per head), even though the ultimate proportion catching the disease were the same in each cohort (i.e.  $\tilde{\lambda}_w$ ).

## 5. OVERALL PROBABILITY OF ATTACK FROM A DISEASE

5.1. When time trends are present in the basic rates, it is still possible to develop relationships between cohort and period data, which are generalizations of, for example, the simple equality expressed in (16). As an illustration of this modification, we consider cohort and period (or census) based formulae for the overall probability of attack from a disease,  $Z$ , as defined in §2.4.1.

5.2. Using the same reasoning as in §3.8, the overall probability of attack from  $Z$  for a cohort (denoted by  $I$ ) is given by the following expression:

$$I = {}_{w-x}P_x^b + {}_{w-x}P_x^d = \int_0^{w-x} \exp \left( - \int_0^u ({}^a\mu_{x+s}^b + {}^a\mu_{x+s}^d) ds \right) {}^a\mu_{x+u}^b du \quad (18)$$

In order to emphasize the dependence on the year of entry (or birth for  $x=0$ ) of the cohort the variable  $T$  (for year of birth) is introduced into the above notation so that (18) becomes

$$I(T) = \int_0^{w-x} \exp \left( - \int_0^u ({}^a\mu_{x+s,T}^b + {}^a\mu_{x+s,T}^d) ds \right) {}^a\mu_{x+u,T}^b du \quad (19)$$

5.3. An expression for  $K(T_0)$ , the overall probability of attack from  $Z$  based on the period experience of the census at time  $T_0$ , is now required. By considering the incidences of  $Z$  per year between the ages of  $t$  and  $t+dt$  at time  $T_0$ , the following expression for  $K(T_0)$  under the assumption of a fixed birth cohort size may be derived:

$$K(T_0) = \int_0^{w-x} \exp \left( - \int_0^u ({}^a\mu_{x+s,T_0-s}^b + {}^a\mu_{x+s,T_0-s}^d) ds \right) {}^a\mu_{x+u,T_0-u}^b du \quad (20)$$



5.4. For comparing these equations two simplifying assumptions may be identified.

### Class 1

If  ${}^a\mu_{x+s,T}^b$  and  ${}^a\mu_{x+s,T}^d$  are independent of cohorts  $T$  then  $I(T)=K(T_0)$ , an intuitive result which corresponds to equation (16).

### Class 2

If  ${}^a\mu_{x+s,T-s}^d$  is independent of  $T$  and equals  ${}^a\mu_{x+s}^d$ , say, but the age-specific incidence rates for  $Z$  change from cohort to cohort, then some progress may be made by assuming a functional form for  ${}^a\mu_{x+s,T-s}^b$ .

If  ${}^a\mu_{x+s,T-s}^b = (a+bT)f(x+s)$  i.e. the incidence rates are a linear function of  $T$  then

$$I(T) = (a+bT) \int_0^{w-x} f(x+u) \exp \left( - \int_0^u ({}^a\mu_{x+s}^d + (a+bT)f(x+s)) ds \right) du \quad (21)$$

and  $K(T_0) =$

$$\int_0^{w-x} (a+b(T_0-u))f(x+u) \exp \left( - \int_0^u ({}^a\mu_{x+s}^d + (a+b(T_0-s))f(x+s)) ds \right) du \quad (22)$$

To simplify the algebra it is assumed that the term involving  $f(x+s)$  in both exponents is small relative to  ${}^a\mu_{x+s}^d$ . The following approximate equations arise from (21) and (22)

$$I(T) \cong (a+bT) \int_0^{w-x} f(x+u) \exp \left( - \int_0^u {}^a\mu_{x+s}^d ds \right) du = (a+bT)X \quad (23)$$

where

$$X = \int_0^{w-x} f(x+u) \exp \left( - \int_0^u {}^a\mu_{x+s}^d ds \right) du$$

and

$$K(T_0) \cong (a+bT_0)X - bY \quad (24)$$

where

$$Y = \int_0^{w-x} u f(x+u) \exp \left( - \int_0^u {}^a\mu_{x+s}^d ds \right) du$$

Both (23) and (24) overestimate the respective values of the  $I$  and  $K$  indices.

If  $T_0 = T + Y/X$  then  $I(T) = K(T_0)$ . Thus  $I$  and  $K$  would be approximately equivalent linear functions of  $T$  but with the origin of the  $T$  axis displaced by an amount equal to  $Y/X$ . This displacement is similar to the concept of demographic translation originally described by Ryder.<sup>(8)</sup>

5.5. An idea of the sensitivity of  $X$  and  $Y$  and their ratio may be obtained by making the (not unreasonable) assumptions that  $f(y)$  and  ${}^a\mu_y^d$  follow Gompertz type functions, i.e.  ${}^a\mu_y^d = ce^{\sigma y}$  and  $f(y) = e^{py}$ . With  $Z$  a chronic degenerative disease, it is sufficient to concentrate on ages over 55. A suitable value of  $\sigma$  might be .092 which is a reasonable approximation to the slope per unit of curves of age specific mortality rates at these ages (i.e. corresponding to a doubling time of 7.5 years). With this  $\sigma$ ,  $Y/X$  is fairly insensitive to changes in  $c$  and  $p$ . Thus either holding  $c$  constant at  $6.0 \times 10^{-5}$  (a reasonable value for the England and Wales

female 1871 birth cohort<sup>(9)(10)</sup> and allowing  $p$  to vary, or holding  $p$  constant at 0.55 (i.e. corresponding to a doubling time of 12.5 years) and allowing  $c$  to vary gives a variation in  $Y/X$  from about 60 to 70 years. Thus, in these special circumstances,  $K$  equals the value of  $I$  for a cohort born about 65 years earlier, whereas the complete cohort information would only be available on those born up to a date about 95 years earlier than time  $T_0$  (for a chronic degenerative disease).

5.6. If as a further simplifying assumption,  $\sigma$  and  $p$  are taken to be equal, then  $Y/X$ , using the approximate equations (23) and (24), reduces to the expectation of life at age  $x$  for the cohort under discussion, and takes values between 45 and 55 years (when  $x=0$ ) for the 1871 and 1886 male and female birth cohorts.<sup>(9-11)</sup> The above development shows that in the presence of time trends simple modifications may be made to the approach to give results which are reasonably robust with respect to variations in the assumptions.

## 6. INDIRECT ANALYSIS USING PREVALENCE RATES

6.1. There are situations in which it is easier practically to derive prevalence rates than incidence rates, for example through a single case-finding survey of a population group or through a study of patient consulting rates in general practice (which approximate to period prevalence rates) as collected, for example, by OPCS and the Royal College of General Practitioners.<sup>(12)</sup>

6.2. It is then possible to make inferences from prevalence rates about the underlying incidence rates if it is assumed, as before, that there is no differential mortality (as in §4.1). Consider the comparison of the incidence experience of two cohorts with respective prevalence and incidence rates  $R_y$  and  ${}^a\mu_{x+s}^b$ ,  $R'_y$  and  ${}^a\mu_{x+s}'^b$  (for all  $s \leq y-x$ ). If the incidence rates are such that, at all ages  $x+s$  less than  $y$ ,  ${}^a\mu_{x+s}'^b = \theta {}^a\mu_{x+s}^b$  for some constant  $\theta$ , then it may simply be proved that:

$$1 - R'_y = (1 - R_y)^\theta \quad (25)$$

Under the assumptions of §4.4 this may be written

$$1 - \bar{R}'_x = (1 - \bar{R}_x)^\theta$$

Hence, given two-point prevalence rates (for different cohorts or at different points of time) the value of  $\theta$  may be determined such that the underlying incidence rates are proportional, by means of the equation

$$\theta = \frac{\log_e (1 - \bar{R}'_x)}{\log_e (1 - \bar{R}_x)} \quad (26)$$

## 7. CENTRAL INCIDENCE RATES

7.1. When incidence rates are computed in longitudinal studies it is customary not to calculate  $I_x$  where new cases of  $Z$  in the follow-up interval are related to the number of persons alive at the beginning of the interval—all of whom are

assumed to be free of  $Z$ . The rate that is commonly used is  ${}_m m_x$ , defined, as in § 2.4.2., by

$${}_m m_x = \frac{\text{no. of new cases of } Z \text{ occurring between ages } x \text{ and } x+t}{\text{no. of years lived by the cohort between ages } x \text{ and } x+t} \quad (27)$$

${}_m m_x$  is a central rate with the denominator referring to a measure of the average population: but not to the average population at risk since the denominator includes persons with  $Z$  already (as discussed in § 2.4.2).  ${}_m m_x$  attempts to measure the average risk of incidence to which the population is subjected during its passage through the period denoted by ages  $x$  to  $x+t$ . It is a different concept from  ${}_I I_x$  which represents the total effect of the incidence of  $Z$  in terms of the proportion who fail to stay free of  $Z$  during this period without reference to the variation of risk over the course of the period. The term 'central incidence rate' is used here in recognition of the similarity of  $m$  to the life table central death rate; however, some biostatisticians prefer the term 'incidence rate'.<sup>(13)</sup>

7.2. There is a further important difference between  ${}_I I_x$  and  ${}_m m_x$ . The denominator of the former is expressed in terms of the starting population at age  $x$ , all of whom are assumed to be free of  $Z$ , whereas the denominator of the latter is expressed in terms of the total population, *including* those with  $Z$ . However, this definition of  ${}_m m_x$  is, nevertheless, natural, for under the assumption of no differential mortality it can be proved that, for any age interval  $y$  to  $y+1$ ,

$$m_y = \tilde{J}_y \quad (28)$$

i.e. the age specific central incidence rates (calculated according to (27)) are equivalent to the incidence column of the single decrement incidence table. Thus, the distinction between renewable and non-renewable events which seems natural (and requires the assumption that the starting population is free of  $Z$  or the exclusion of persons with  $Z$  from the denominator of  ${}_I I_x$ ) has no practical implications if there is non-differential mortality. This approach is similar to calculating parity-specific fertility rates and first marriage rates for cohorts in demography.<sup>(13-15)</sup> The equality (28) has the advantage that it avoids the necessity to have complete information about the denominator, i.e. the number of person-years lived in the various statuses. In general, the important distinction to be made is that between morbid (and demographic) events which are associated with differentials in mortality and those events which are not associated with such differentials, if indeed that are any such events.

7.3. The proof of (28) follows thus: we use  $\mu^d$  as defined in § 4.2 so that the definition of  $m_y$  may be written:

$$m_y = \frac{{}_y - x P_x^a \int_0^1 {}^a \mu_{y+s}^b {}^a P_{y+s}^a ds}{\exp \left( - \int_0^{y-x} \mu_{x+s}^d ds \right) \int_0^1 \exp \left( - \int_y^{y+s} \mu_u^d du \right) ds} \quad (29)$$

where  ${}_y - x P_x^a = \exp \left( - \int_0^{y-x} ({}^a \mu_{x+s}^b + {}^a \mu_{x+s}^d) ds \right)$  as in § 3.4.

If the new cases of  $Z$  are distributed uniformly over the year of occurrence between ages  $y$  and  $y+1$ , then it may be proved, in analogy with the life table equality  ${}_s p_y \mu_{y+s} = q_y$  for  $0 < s < 1$ , that

$${}_y^a \mu_{y+s}^b \exp \left( - \int_y^{y+s} {}_u^a \mu_u^b du \right) = I_y \quad \text{for } 0 < s < 1.$$

Under this assumption

$$m_y = \frac{I_y {}_{y-x}^a P_x^a \int_0^1 \exp \left( - \int_y^{y+s} {}_u^a \mu_u^d du \right) ds}{\exp \left( - \int_0^{y-x} \mu_{x+s}^d ds \right) \int_0^1 \exp \left( - \int_y^{y+s} \mu_u^d du \right) ds}. \quad (30)$$

If  $\mu_{x+s}^d = {}^a \mu_{x+s}^d$  for all  $s$  between 0 and  $y-x$  (which has been shown in § 4.2 to be equivalent to the absence of a mortality differential i.e.  ${}_y^b \mu_{x+s}^d = {}^a \mu_{x+s}^d$ ) then

$$m_y = \frac{I_y {}_{y-x}^a P_x^a}{\exp \left( - \int_0^{y-x} \mu_{x+s}^d ds \right)} = I_y \exp \left( - \int_0^{y-x} {}^a \mu_{x+s}^b ds \right) = I_y \tilde{l}_y = \tilde{j}_y$$

as required, using the definitions in equations (11) and (12).

## 8. CUMULATIVE (CENTRAL) INCIDENCE RATES

8.1. The concept, underlying the definition of (27), of relating the number of events to the total exposed to risk regardless of status, is taken one step further in demographic applications by computing cumulative incidence rates. It has been shown for example that, in the absence of differential mortality, the cumulative incidence rate for a closed cohort represents the prevalence of the event studied—thus the cumulative first-birth incidence rate at age  $x$  for a female cohort may be interpreted as the proportion of the women still alive at age  $x$  who have had a first birth.<sup>(13,15)</sup> It is shown in the following paragraphs that this concept, when applied to morbidity, draws together the themes of §§ 3 and 7.

8.2. Using the notation for the three state incidence model, Hoëm<sup>(5)</sup> has proved that in the case of non-differential mortality, i.e.  ${}_y^a \mu_y^d = {}^b \mu_y^d = \mu_y$  say, then

$${}_s P_y^j = {}_s \tilde{P}_y^j {}_s p_y \quad i, j = a, b$$

where  ${}_s p_y = \exp \left( - \int_0^s \mu_{y+u} du \right)$  and  $\tilde{P}$  is the conditional probability that a person in state  $i$  at age  $y (> x)$  is in state  $j$  at age  $y+s$ , given that he is not in state  $d$  at age  $y+s$ . It is assumed as before that at age  $x$  all persons of the cohort are in state  $a$ .

8.3. Consider  ${}_s \beta_y^j = \int_0^s {}_u^a \tilde{P}_y^i {}_u^j \mu_{y+u} du \quad i, j = a, b \quad i \neq j$  (31)

This represents the expected number of transitions from  $i$  to  $j$  between ages  $y$  and  $y+s$  for a cohort member who survives to age  $y+s$  (from age  $x$ ). If such a transition is a once-in-a-lifetime event, then  ${}_s \beta_y^j$  is the probability that a cohort

member who does survive to age  $y+s$  will then have experienced the event in question, i.e. first incidence of  $Z$  for the case of the incidence model with  $i=a$  and  $j=b$  (or first birth or first marriage in a demographic context).

8.4. In order to investigate further the properties of equation (31) we consider for convenience unit age intervals and let  ${}^iD_y^j$  be the observed number of transitions from state  $i$  to  $j$  during the interval  $(y, y+1)$  and let  ${}^iL_y$  be the total number of person-years lived in state  $i$  during the interval  $(y, y+1)$ . Let  $L_y = {}^aL_y + {}^bL_y$ . Then Hoem<sup>(13)</sup> has shown that an estimator for  ${}^i\beta_y^j$  is  ${}^iB_y^j$  where

$${}^iB_y^j = \sum_{r=0}^{s-1} \frac{{}^iD_{y+r}^j}{L_y} \quad (32)$$

So

$${}^aB_y^b = \sum_{r=0}^{s-1} \frac{{}^aD_{y+r}^b}{L_y}$$

is an estimator for  ${}^a\beta_y^b$ , the expected number of incidences of  $Z$  between ages  $y$  and  $y+s$  for a cohort member who survives to age  $y+s$ . Finnas<sup>(15)</sup> has further shown that cumulative central incidence rates, such as that defined by equation (32), may be used to estimate the transition intensities  ${}^i\mu^j$  for general Markov models in the absence of differential mortality.

If  ${}^a\mu_{y+u}^b$  (for  $0 < u < 1$ ) is assumed to be constant in each sub-interval of age  $(y, y+1)$  and equal to  $v_y$  then it may be shown that a consistent estimator for  $v_y$  is  $M_y$  where

$$M_y = \frac{{}^aD_y^b}{L_y - L_y \sum_{r=x}^{y-1} \left( \frac{{}^aD_r^b}{L_r} \right) - \frac{1}{2} {}^aD_y^b} \quad (33)$$

This estimator may be justified on general reasoning grounds. For

$$L_y \sum_{r=x}^{y-1} \frac{{}^aD_r^b}{L_r}$$

is an estimator for the number of persons remaining at age  $y$  who have had an attack of  $Z$ , so the denominator is an estimator for the number of person-years in the age interval  $(y, y+1)$  lived by those persons free of  $Z$ , as required. Alternatively  $L_y/L_r$  may be viewed as a survival probability. The survival probabilities for all persons in the cohort have been used because of the original assumption of non-differential mortality (§ 8.2).

8.5. The theory of cumulative incidence rates has been extended to allow for several absorbing states (e.g. several causes of death) and for individuals starting at age zero in different statuses.<sup>(16)</sup>

## 9. SUMMARY

This paper, following on from an earlier one, has attempted to draw together

various aspects of the theory of multi-status life tables and Markov chains as they apply to the measurement of morbidity. The relationship between incidence and prevalence has been described and the implications of certain assumptions about the presence of mortality and mortality differentials have been investigated.

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