Comparative Morbidity — What Are The Prospects?

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Thanks to the efforts of many illustrious medical directors and actuaries, comparative mortality was developed in the early part of this century as the indispensable tool for life insurance underwriting of individual applicants. The work of Rogers and Hunter culminated in the publication of the numerical rating system. Over the years results of many insurance mortality studies of impaired risks have provided the basis for underwriting manuals that are in use in all companies offering individual life insurance[1]. More recently follow-up studies have been culled from the medical literature and the mortality systematically presented in a comparative format[2]. Thus the risk classification of applicants with all degrees of excess mortality has been steadily refined since the early years of this century.

Health insurance protection has evolved much more recently, from small beginnings prior to World War 2, burgeoning rapidly in the 1950s, and expanding to provide hospital expense and other benefits to a high percentage of the U.S. population. The bulk of this health insurance is provided on a group basis by insurance companies and Blue Cross or Blue Shield associations, but some of the providers continue to offer health insurance to individual applicants. This means underwriting and assessment of a morbidity instead of a mortality risk. Although I have had only peripheral exposure to health insurance underwriting in my career in insurance medicine, what I have seen leads me to picture underwriting as still being in an early stage of development, with manuals that are based much more on opinion than they are on the application of follow-up studies of morbidity. Do you think I am right in this impression? If so, what accounts for this failure to develop a truly scientific basis for health insurance underwriting during the 50 years or so in which it has been practiced?

In my opinion there are two principal reasons for the lack of development of health insurance underwriting: the passive attitude of health insurance companies in not aggressively going ahead with intercompany morbidity follow-up studies tailored to their own needs, and the absence of successful innovation among medical directors and others responsible for such underwriting, innovation displayed to such a remarkable degree by our predecessors in the first two decades of this century. This phenomenon is definitely not due to the lack of a methodology with which to carry out morbidity follow-up studies, nor is it due to lack of such studies reported in the medical literature. It is my objective in this article to demonstrate how easily familiar life table methodology can be applied to morbidity follow-up, and to cite examples of articles of this sort from the abundant supply in current medical literature. Instead of the usual mortality abstract, I have submitted to our willing Editor a Morbidity Abstract on recurrent myocardial infarction (MI), to accompany and illustrate this article.

Application of Life Table Methodology to Morbidity Follow-up

Although the traditional use of life tables has been in data on human mortality and survival, there is absolutely no mathematical requirement for this. With a human population series one can readily substitute for death a morbid event as the object of study. From the biological point of view, life table methodology can be applied to a follow-up cohort of any living species, not just Homo sapiens. Finally, life table methodology has often been applied to non-living groups, such as failure rates of light bulbs, in quality control of industrial products. This application has been widely used since World War 2. The mathematical principle is to start with a defined cohort and to follow in time the rates of occurrence of a defined event, and the complementary survival rates of members free of this event. This involves counting in each time interval the number of members entering the interval, the number of events during the interval, and the average number of members exposed to risk during the interval. In a mortality study exposure is calculated as 1 - 0.5w, where w is the number of subjects withdrawn alive during the interval, because of loss to or end of follow-up, or other valid reason, such as dropping out a treatment plan that was a basis for definition of the group being followed. In a morbidity study exposure is calculated in the same way, but now includes deaths during the period, since this removes the member from being at subsequent risk for the defined morbid event. The symbols, definitions and rate calculations can be summarized for mortality and morbidity follow-up studies in the accompanying Table.

When the exposures are all in units of person-years, the total E, and total d or n can be obtained by adding values of any set of consecutive intervals, and the aggregate mean $\check{q}$ calculated as (total d)/(total E), or the aggregate mean $\check{r}$ calculated as (total n)/(total E). When the numbers of deaths or events in each interval, such as one year, are very small, it may be desirable to pool the data over 5 years , for example, in order to calculate a mean with a larger number of events and smaller random error. If full life table data are not available but cumulative survival curves are given in the published article, then a geometric mean annual $\check{q}$ or $\check{r}$ can be calculated as the complement of the 5th root, for

FACTOR DEFINED	MORTALITY	MORBIDITY
Number available for FU at start of interval	ℓ	ℓ
Number of events during interval	d = deaths	n = morbid events
Number of event-free withdrawn from exposure to risk during interval	w = all alive (deaths excluded)	w = both alive and deaths during interval (but n excluded)
Number exposed to risk of event during interval	E = 1 - 0.5w	E = 1 - 0.5w
Interval event rate (observed)	q = d/E = interval mortality rate	r = n/E = interval morbid event rate
Interval event rate (expected)	q' from age/sex matched mortality table	r' from age/sex-matched data
Number of expected events during interval	d' = (q') (E) (expected deaths)	n' = (r') (E) (expected events)
Interval observed event-free survival rate	p = 1 - q = interval survival rate	p = 1 − r = interval event-free survival rate
Interval expected event-free survival rate (observed)	p' = 1 − q'	p' = 1 − r'
Cumulative event-free survival rate (observed)	$P = (p_1')\ (p_2')\ (p_3')\ldots$	$P = (p_1')\ (p_2')\ (p_3')\ldots$
Cumulative event-free survival rate (observed)	$P = (p_1')\ (p_2')\ (p_3')\ldots$	$P = (p_1')\ (p_2')\ (p_3')\ldots$
Cumulative event rate (observed)	Q = 1 − P	R = 1 − P
Cumulative event rate (expected)	Q' = 1 − P'	R' = 1 − P'
Percentage event ratio	Mortality ratio MR = 100d/d' = 100q/q'	Morbidity ratio MR = 100n/n' = 100r/r'
Excess event rate	Excess death rate EDR = 1000(q − q')	Excess event rate EER = 1000(r − r')
Cumulative survival ratio	SR = 100P/P'	SR = 100P/P'

example, of the 5-year period survival rate. All of this is set forth in the Methodology Chapter of Medical Risks[2], and in the homework material for the Mortality Seminars, and lecture notes for the Board of Insurance Medicine courses. The above table covers the same ground, with the addition of a few new symbols for the morbidity application of the life table methodology, to replace d, d', q, and q'.

For clinical investigators this application of life table methodology has been reported in a 1974 paper in the Journal of Surgical Research[3], and in a later 1977 article[4]. The authors were associates, including a biostatistician, of Dr. Albert Starr, developer of the caged ball device widely used in valve replacement surgery. Not only cardiothoracic surgeons but surgeons and investigators in other specialties often refer to these reports as the basis of their life table methodology, not only for mortality and survival, but also for morbid events. The methodology is a time- honored one for actuaries, and many descriptive articles have appeared in the medical literature long before 1974. One reason for the interest in morbid events displayed by Dr. Starr and others involved in valve replacement surgery is the importance of characterizing the mean rate of occurrence of long-term complications of valve replacement: embolic stroke, serious hemorrhage due to anticoagulation, bacterial endocarditis, and valve failure. All of these are serious complications, but not 100% fatal, and they are best measured as morbid events. Tabular data on the incidence of these complications have been given in abstracts 667-673 of the new Medical Risks volume 5, abstracts which also deal with comparative mortality following valve replacement surgery.

Examples of Morbidity Follow-up Studies

The first study I wish to cite is Section 32 of the series of Framingham Study detailed reports of data, as distinct from the profusion of articles published in the medical literature about this unique long-term follow-up of a defined segment of a Massachusetts town population[6]. This 150-page section contains 51 tables and 13 graphs of follow-up data on cardiovascular (CV) diseases and deaths occurring after first

myocardial infarction (MI) or angina pectoris, during the first 20 years' observation of the Framingham cohort, in which 21% of the men and 11% of the women developed their first evidence of CV disease. The morbid events, as distinct from death, sudden death and CV death, were MI, angina pectoris without MI, coronary attack, coronary insufficiency, cerebrovascular accident, and congestive heart failure. Section 32 also contains mortality and morbidity on the Framingham cohort still free of CV disease at the time of the last biennial examination. These data provide the needed expected rates of MI incidence. Please refer to the abstract for my chief illustrated application of life table methodology to MI as a morbid event. The table footnotes and text provide some detail of the calculations, which I will not discuss further. The reader who makes a careful study of Section 32 and the MI Morbidity Abstract will be rewarded with a better understanding of the wealth of information available from the Framingham Study, and a detailed illustration of how comparative morbidity results can be derived from the observed data.

Two CV morbidity studies will be cited from a plethora of recent articles I have on file. Herlitz et al. have reported on a 5-year morbidity (and mortality) follow-up of patients with suspected MI or chest pain in three hospitals in Goteberg, Sweden[7]. There were four diagnostic categories: possible MI, angina, chest pain of uncertain origin, and nonischemic chest pain. Baseline characteristics and outcomes are reported in great detail, of potential significance for underwriting. Rehospitalization, anginal pain, dyspnea and cessation of working in patients under age 65 were some of the morbid events studied. Hospital mortality was only 0.7% for all patients, but the 5-year cumulative mortality appeared to me to be elevated for all groups except those with chest pain of uncertain origin. Nevertheless, 40% of the 181 latter patients developed anginal pain with an attack frequency at least once a week, and 26% were hospitalized during the 5-year follow-up. The second example is a very detailed report by Flemma et al on observation for more than 10 years of 785 patients with valve surgery involving the tilting disc (Bjork-Shiley) valve[8]. This group of cardiovascular surgeons in Milwaukee has maintained an excellent computerized file of operated patients, and provided additional data to supplement previous articles at the time of a visit I made in 1982, and these data were used in abstracts 669 and 672 of volume 2. Dr. Flemma kindly provided a typescript of this updated study in response to Ed Lew's inquiry last January, and Ed passed on a copy to me. It was too late to revise the abstracts, but mortality and morbidity results in this latest article certainly deserve the preparation of new abstracts. Follow-up results are given for three different age and four valve groups, with tabular data of events, total exposure and mean annual event rates, as well as survival and event-free survival curves. For example, in patients age 50-59 years the exposure, E, was 2356 patient-years, there were 39 events involving the complication of clotted valve and arterial emboli, four involving clotted valve without embolus, and 7 each involving paravalvular leak and endocarditis. The corresponding mean annual morbid event rates for these complications were 17, 1.6, 7.0 and 7.0 per 1000 pt.-yrs., respectively. Such data are additive with respect to both events and rates, as the exposure is the same, so the total for these complications is 57, for a mean event (complication) rate of 24 per 1000 per year.

Four recent morbidity articles can be quickly cited from the Framingham Study, one of which is not concerned with CV disease. One deals with cigarette smoking and cardiovascular morbidity in women over 50, with or without the use of estrogens. Estrogen use was associated with an increase in stroke morbidity rate in smokers and nonsmokers, but the increase in overall CV morbidity was found only in estrogen users who also smoked[9]. A 1988 article has examined in greater detail cigarette smoking as a risk factor for stroke in both men and women[10]. Blood pressure at the biennial examinations was analyzed for 95 subjects who had received drug therapy for hypertension but were normotensive at the first examination after treatment was stopped[11]. The event-free survival curve for these subjects consisted of the cumulative percentage of those remaining free of hypertension (blood pressure under 140/90). Only 32% remained normotensive without medication at 2 years, and only 14% at 4 years, illustrating the importance of continued medication to control blood pressure in most patients with responsive hypertension. (Seminar graduates, can you calculate a geometric mean annual relapse rate, r, from these lapse-free survival rates?) In another recent paper[12] postmenopausal estrogen usage was found to be associated with a reduced incidence of hip fracture: only 3 fractures in 1799 person-years with recent use of estrogen, for a rate of 1.7 per 1000, significantly less than the rate of 7.3 per 1000 (135 fractures in 18,326 person-years) among women who never used estrogen. In some of the articles cumulative incidence (R) is used for a period such as 8 years, contrasting the rates when a factor is present versus not present. Often adjustment is made in R for age, sex and other factors. The variety of formats used in presenting results is a challenge to anyone eager to apply them to our formal view of comparative morbidity. Sometimes relative risk as a decimal is used, and this is analogous to a morbidity ratio. All of these articles contain a wealth of morbidity information, much of it of potential value to the health insurance underwriter.

One very recent article[13] provides data on cancer recurrence, a subject I have always been interested in because of its importance for the length of the waiting period before the applicant with a history of complete removal of an internal cancer can be accepted with a rating. The Local Cancer Study Group reported a retrospective (more accurately, an historical prospective) follow-up of 1532 patients with "complete" surgical removal of non-small-cell lung cancers, in which there were 98 patients with metastatic recurrence in the brain, only after a maximum follow-up of 8 years. Tabular data are given for annual "hazard rate" (recurrence rate) per patient-year, and hazard or morbidity ratios are presented for four other groups against T_1N_0 (smallest tumor size, no lymph node extension) as the "expected" lowest recurrence rate. Life table data (without E) for the combined experience are given up to 8 years; these show 64 recurrences in the first year, 27 in the second, and only 13 in durations

2-8 years. An article based on data from the first National Health and Nutrition Examination Survey and a follow-up study of this NHANES cohort showed that shorter stature in adults was associated with a significantly reduced occurence of cancer, especially in men[14]. Bone sarcomas occurring after two-year survival from an earlier cancer of any type in children were reported to be related to dose of radiation and to use of chemotherapy for the initial cancer[15]. Table 1 gives comparative morbidity data (except for E values), including n, n', relative risk (n/n'), and "absolute excess risk" (excess events per 10,000 patient-years). Cumulative event curves are also shown up to 25 years. This paper deserves study by the medical director interested in the methodology of morbidity follow-up in children with a history of cancer. An epidemiologic study was carried out in three plants in Sweden in which workers were exposed to ethylene oxide [16]. Eight cases of leukemia were observed in circumstances with only 0.8 cases expected.

Side-effects of antihypertensive drugs were investigated in the Stepped-Care category of patients enrolled in the Hypertension Detection and Follow-up program[17]. Patients were divided into four age groups, and over a five-year follow-up number of side-effects and cumulative incidence (R) were reported for six antihypertensive drugs, and for a long list of individual side effects. Definite effects, sufficient to result in discontinuance of the drug, were observed in 9.3% of cases, cumulative overall to five years. Another study, of recurrence of seizures after withdrawal of anticonvulsant drugs in patients with epilepsy[19]. Of the 92 patients who have been seizure-free for two years when medication was withdrawn, 31 relapsed and 61 remained seizure-free in a maximum follow-up of five years. The morbid event of a recurrent seizure is one that can be well defined.

Conclusion

Perhaps I have raised many difficult questions, for which answers are better attempted by medical directors much more experienced in the practical problems of health insurance underwriting than I am. One important question is how to translate the impact of a single excess event rate into overall excess morbidity. Another is to account for the cost of the benefit, which is not fixed as is the benefit in the life insurance contract. Disability income, not discussed at all in this brief review, has its own adverse claim incentives that affect the cost in ways very difficult to predict. However, we do not know that these problems are insoluble; we are certain only that not enough has been done to gather the data that might lead to their solution and to a scientific basis for health insurance underwriting. Medical directors, actuaries and underwriters of the health insurance world unite, and devise a cooperative program to accomplish this! Perhaps this small initial step will provide a needed stimulus to get moving.

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