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INTERVENTION EFFECTS AMONG A COLLECTION OF RISKS

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ABSTRACT

To describe the long-term effects of changes that affect health, including aging, risk factors must be included in actuarial computations. This is problematic when there are multiple risk factors that interact with one another and that change over time.

In this paper risk-factor-dependent multiple decrements and actuarial cost functions are initially described as a general compartment model, that is, a discrete time and discrete state stochastic model of morbidity and mortality processes for risk factor strata. For situations with large numbers of risk factors, the compartment model is extended to its natural continuous time and continuous state form, which represents risk factor dynamics and interactions as a system of first-order stochastic differential equations. By deriving the stochastic differential equations as a generalization of multiple-decrement models, both the relationship between decrement rates and the relationship among the parameters of the dynamic equations are made explicit, as are the actuarial cost functions for both the continuous and the discrete models. The methodology is illustrated by using data from the Framingham heart study.

I. INTRODUCTION

Actuarial practice frequently requires a prediction of the morbidity or mortality experience of groups of individuals. Because of changing conditions or interventions, previous experience cannot be used naively to make forecasts. A "collection of risks" is a set of individuals (for example, block of business, group of insured persons, and so on) for which estimates of intervention effects are required. By "intervention effects" we mean the effects of any variation that would cause the health experience of the set of individuals to change (for example, aging, introduction of a new medical treatment, an antismoking campaign, and so forth). Current methods involve discretely stratifying the "collection of risks" by risk factors and then estimating actuarial functions—often using simulation.

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Stratification is often termed "classification of risks" (see Cummins et al. [3]). Risk factor stratification of life (or decrement) tables to reflect increased (or decreased) risks of death can be based upon medical studies (see, for example, Lew and Gajewski [10]) as well as primary data. The creation of risk strata is difficult when there are a large number of risk factors (see, for example, Gunning-Schepers [6]). Further complications occur when (a) risk factors interact (that is, risk associated with one factor is contingent upon the level of another factor), (b) individuals change strata over time, (c) risk varies as a continuous function of the risk variables—not discretely, and (d) transitions between strata occur continuously.

Continuous risk factors (or time) may be approximated by defining large numbers of risk factor strata (or by finely dividing time). This, however, aggravates the multiple variable problem. For example, five risk factors (such as smoking, blood pressure, body weight, serum cholesterol, and age), each divided into three levels, define fifteen categories without interactions and $5^3 = 125$ categories with interactions. For some variables, such as age, three levels may not fully characterize a risk factor's effect.

To deal with the stratification problem, we propose extending the multiple-decrement life table model to a continuous state and continuous time stochastic process in which risk is described by a multivariate function. Changes in the risk factor distribution are represented by stochastic differential equations that are derived naturally from the multiple-decrement model as the number of discrete risk strata is increased to infinity. Thus, the stochastic differential equation model is a natural generalization of the actuarial practice of risk classification. Cost functions can be generalized similarly. Furthermore, because health events naturally occur in continuous time (it is observation that generates *data* in discrete time and in discrete states), the stochastic differential equations provide a basis for evaluating approximations used in discrete models.

The effects of shifts in the distribution of risk factors on health costs have to be accounted for in both public and private actuarial practice. In the public domain, the assignment of limited resources to health care programs and projects requires analysis of the future costs and benefits of those programs. In the private sector, changes in either risk factor exposure or the treatment of disease may affect the morbidity costs and mortality rates for a large portion of the insured lives. When such changes are restricted to particular groups of insured lives, their negative financial impacts might be offset by reserves, reinsurance, or risk-sharing pools. For future business, both positive and negative changes that continue to influence mortality and morbidity

costs will have an impact on premium calculations, the valuation of liabilities, and the determination of reserves. An insurer who benefits from reduced costs because of changes in morbidity or mortality will have a surplus to distribute to shareholders or to offset other actuarial losses. On the other hand, insurers who plan to provide preventive care as a benefit must recapture costs through actuarial gains. In all cases, expected costs must be accurately estimated.

In addition, efficacy is often not adequately measured by "current cost" estimates. Primary prevention programs require managing and reducing risk factor exposure, and the benefits, measured by decreased morbidity or disability, require time to emerge because prevention affects the onset of disease. Persons who already have the disease may not be susceptible to the intervention and continue to progress through the course of the disease. Thus, intervention studies frequently require five to ten years to show significantly reduced morbidity and mortality risks. As a consequence of these lengthy periods, the demographic profile of the beneficiary population may shift (for example, the population may become older with time) or those with adverse risk factor values may die early. In such cases some of the observed benefits are not the result of interventions but of population shifts in the distribution of risk factors. When "benefits" are negative, the intervention may be manifest only in a reduction of the negative effects (for example, reducing age-specific morbidity rates may partly offset the aging of persons to higher age categories in which chronic prevalence is high). Thus determining the benefits of a risk factor management program requires separating cost savings attributable to risk factor modification from costs attributable to demographic shifts and mortality selection.

We present two strategies for modeling risk factor interventions. The first generalizes standard increment-decrement life table models (see, for example, Jordan [8]) to "compartment" models (that is, discrete state and discrete time models of health processes) to represent movement between risk factor states. The states in the compartment model can represent death, disability, or an adverse (or beneficial) risk factor status. Interventions are represented by changes in risk factor states; for example, interventions modify transition rates between certain risk factor and mortality states and change the number of individuals in those states. The costs and benefits of the intervention are calculated by standard actuarial procedures. A multivariate continuous state model arises directly from the compartment model as the number of risk strata increases. Actuarial cost functions are presented for this continuous state model.

II. A DISCRETE STATE MODEL OF HEALTH INTERVENTION

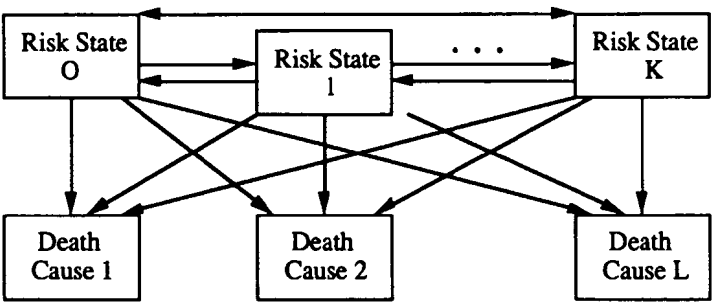
A compartment model of morbidity-mortality processes is illustrated in Figure 1. An individual resides in only one risk factor state although he/she can move to any other state at time t. The risk factor states can represent chronic illness, disability and risk factor exposure (for example, smoker versus nonsmoker, hypertensive versus not hypertensive, and so on). The "well" state is defined as the state with no risk factors. Though an individual can be only in one state at any time, the definitions of states need not be exclusive; for example, an individual may be in a hypertensive state, a smoking state, or a hypertensive and smoking state. We define the following terms:

t = time interval ($t=1, 2, \ldots, T$)
K = number of risk factor states (besides the well state). Risk factor state "0" is the "well" state
L = number of causes of death ($l=1, 2, \ldots, L$)
a = index for age groups
$n_k(a,t)$ = number of individuals in age group a at beginning of t in state k
$p_{kj}(a,t)$ = probability that an individual in risk factor state k and age a at time t will move to risk factor state j at time $t+1$
$q_{kl}(a,t)$ = probability that a person in age group a in state k at t will die of cause l during the year
$q_l(a,t)$ = probability that a person in age group a at t dies of cause l,

$$= \sum_k q_{kl}(a,t)\, n_k(a,t) / \sum_k n_k(a,t). \tag{1}$$

FIGURE 1

COMPARTMENT MODEL SCHEMATIC OF MORBIDITY-MORTALITY PROCESS WITH DISCRETE RISK STATES



III. THE MARKOV ASSUMPTION

Multiple increment or decrement life tables are special cases of the compartment model in Figure 1. Consequently, methods to estimate multiple-decrement life table parameters are easily extended to the compartment model. Applying those methods for many risk factor states and causes of death, however, requires a huge volume of data. Problems in evaluating actuarial functions arise because (i) all possible pathways that result in the contingent event of interest must be determined and (ii) the probabilities associated with each of these pathways must be assessed. The problems are simplified if the model in Figure 1 can be assumed to be Markovian; that is, the probability of changing states depends only on the two states (the state the individual is coming from and the state he/she is going to) and not on any previous states the individual has been in nor length of time in the current state.

The Markov assumption seems unreasonable because age, length of illness, and prior illness are determinates of the risks of many causes of death and diseases. The Markov assumption can be made more reasonable by several strategies. First, risk factor states can be defined to represent multiple diseases. A risk factor state may also be defined as increased length of time with a particular risk factor. For example, a person enters the "smoked 0–5 years" risk state when he/she begins to smoke. In five years he/she moves to a "smoked 5–10 years" risk state if he/she still smokes and has not died. Or he/she may enter a "hypertensive *and* smoked 5–10 years" state if his/her blood pressure rises and he/she continues to smoke. Alternatively if he/she stops smoking, he/she may enter the "smoked only 5 years" state. Age can be treated similarly; that is, Figure 1 can be viewed as applying to a specific age group with risk factor states defined for each subsequent age group. Individuals move between states as they age.

Assuming that the Markov assumption holds for Figure 1, movement between states can be described by a matrix of transition probabilities. If π_{ij} is the probability of moving from state i to state j in a year, the transition matrix is

$$\Pi = \begin{pmatrix} \pi_{00} & \pi_{01} & \cdots & \pi_{0R} \\ \cdot & & & \\ \cdot & & & \\ \cdot & & & \\ \pi_{R0} & \pi_{R1} & \cdots & \pi_{RR} \end{pmatrix}, \tag{2}$$

where the total number of states is $R+1=K+L+1$ including the "well" and death states. The π_{ij} are estimated from $n_k(a,t)$ and $q_{kl}(a,t)$. To determine the population in each state after m years, let n_i be the number of individuals in state i at time 0. The row vector $\mathbf{N}=(n_0, n_1, \ldots, n_R)$ of these counts is called the state vector. The vector $\mathbf{N}^{(m)}$ of counts in each state after m years is

$$\mathbf{N}^{(m)} = \mathbf{N}\Pi^m \tag{3}$$

where Π^m is product of Π with itself $m-1$ times (that is, the m-th power of Π). The vector $\mathbf{N}^{(m)}$, $m=1, 2, \ldots$, is the basis for all actuarial functions.

The model can be used in different ways. First, it could relate future morbidity and mortality experience data with risk factor data from follow-up studies in which changes are defined by Π. Second, the model is useful for forecasting future contingent outcomes and for evaluating actuarial functions associated with morbidity and mortality outcomes under various interventions or changes in the insured population. Because the current model is more biologically plausible than simply "alive-dead" and "standard-substandard risk" classifications, the actuarial estimates will be more accurate. By selecting a sufficient number of risk factor and mortality states, any finite combination of risk factors can be modeled. A model representing the interactions of risk factors and chronic conditions is more defensible than risk-scoring methods that do not represent those interactions (see Cummins et al. [3]).

IV. RELATION TO HEALTH STUDIES

The different types of risk measures used in epidemiological and public health studies are reviewed to illustrate how they can be used to estimate the parameters in Figure 1 (that is, the q_{kl} and n_k values).

Incidence rate is the rate per unit of time that cases occur in the population. For example, the annual "incidence" rate of lung cancer deaths among smokers age a at t is $q_{kl}(a,t)$, where k represents the "smoking" risk factor state and l represents the "death by lung cancer" state. Alternately, incidence may represent onset of a chronic disease. The incidence rate of, for example, diabetes for those over age 50 at t is

$$\sum_{j\in\bar{K}} \sum_{k\in K} \sum_{a>50} n_k(a,t)\, p_{kj}(a,t)/n$$

where K is the set of all indexes of risk states that do not include diabetes in their definition and $\bar{K}$ is the set of risk factors states that include diabetes

in their definition. The total population of individuals over 50 who are *not* diabetic is

$$n = \sum_{k \in K} \sum_{a > 50} n_k(a,t).$$

Prevalence is the number of *cases* in a population or sample at t. The prevalence of state k among individuals who are age a at t is $n_k(a,t)$. The prevalence rate does not refer to transitions but to the proportion of the population in a certain state (or set of states) at t. Thus, prevalence rates give information only on $n_k(a,t)$.

Relative Risk (or Risk Ratio or Rate Ratio) is the ratio of the incidence of an event from two different risk factor states (see, for example, Breslow and Day [2]). The events can be onset of morbidity or death by specific causes. The risk of death from cause l at time t for those with risk factor k_1 relative to the same risk for those with risk factor k_2 is, for age a,

$$\text{Relative Risk} = \frac{q_{k_1 l}(a,t)}{q_{k_2 l}(a,t)}.$$

With the relative risk, the ratio of certain probabilities of death can be estimated. This does not provide an estimate of a transition probability—only a ratio.

In case control studies, relative risk is defined by prevalence (see, for example, Monson [12]). In this case, samples are selected from two different risk factor states and the prevalence of a disease examined. The relative risk of the disease is the ratio of the prevalence of disease in two risk factor states. Because this relative risk is based on prevalence, it does not provide estimates of transition probability ratios, but ratios of *counts*. Explicitly, the relative risk (prevalence based) at t of a chronic illness for individuals in risk factor state k_1 and k_2 is

$$\text{Relative Risk} = \frac{n^*_{k_1}(a,t)}{n_{k_1}(a,t)} \cdot \frac{n_{k_2}(a,t)}{n^*_{k_2}(a,t)},$$

where $n^*_{k_1}(a,t)$ represents persons *with* the disease aged a and in state k_1 at t and $n_{k_1}(a,t)$ represents all those without and with the disease.

This type of relative risk is used to determine risk factor states. For example, if we separated "smokers" into those with chronic obstructive lung disease (COLD) and those without, a relative risk measure provides information on the counts in the new "smoker–COLD" state relative to a "nonsmoker–COLD" state.

Excess Mortality is the additional chance of dying due to the presence of a risk factor, say k_1, relative to a second risk factor, say k_2,

$$\text{excess mortality} = q_{k_1}(a,t) - q_{k_2}(a,t).$$

This measure also can be used to calculate the excess risk of a chronic disease by replacing $q_l(a,t)$ with $p_{kl}(a,t)$.

Cross Product Ratio ("Odds Ratio") is the ratio of the "odds" of an event, in one risk factor state relative to the odds in a second risk factor state. For example, the age-specific cross product ratio of death for smokers to nonsmokers at t is r_1/r_2, with

$$r_1 = \sum_{k \in K_1} \sum_j q_{kj}(a,t) \Big/ \left[1 - \sum_{k \in K_1} \sum_j q_{kj}(a,t) \right]$$

where K_1 is the index set for smoker risk factor states and r_2 is defined similarly for K_2, the index set for nonsmokers.

Cross product ratios can also be used with prevalence data, for example, the odds ratio of smokers and nonsmokers who have COLD is r_1/r_2, where

$$r_1 = \sum_{k \in K_1} n_k(a,t) \Big/ \sum_{k \in K_1^*} n_k(a,t)$$

and K_1 is the set of risk factor states that include both smokers and persons with COLD and K_1^* is the set of risk factor states that include smokers and persons without COLD.

Attributable Risk (or Etiologic Fraction) is the portion of deaths caused by a risk factor over what would have occurred without the risk factor (see Miettinen [11]). The attributable risk of smoking for lung cancer deaths is

$$\text{Attributable Risk} = \frac{\sum_{k \in K} n_k(a,t)\, q_{kl}(a,t)}{\sum_j \left(\sum_{k \in K_j} n_k(a,t) \right) q_{jl}(a,t)}$$

where K is the index set of risk factor states that include smoking. K_j is the index set of risk factor j across all levels of smoking; that is, K_j represents all risk factors states that would have been in the risk factor state without stratifying on smoking, for example, "hypertensive nonsmoker," "hypertensive light smoker," and "hypertensive heavy smoker" are three states that would have been a "hypertensive" state. In this case $q_{jl}(a,t)$ is the annual mortality rate for hypertensive nonsmokers. The index l refers to the

death by lung cancer state. Attributable risk can also be defined for chronic diseases.

These morbidity and mortality measures are commonly used in epidemiological and public health literature. Published results from such studies, in conjunction with national mortality data, can be used to construct relatively complex compartment models of risk and mortality. Given the wide range of risk measures, estimating the parameters for the model from secondary studies with a mixture of measures requires complex algebraic manipulation and approximation.

V. AN EXAMPLE OF A MULTISTATE COMPARTMENT MODEL

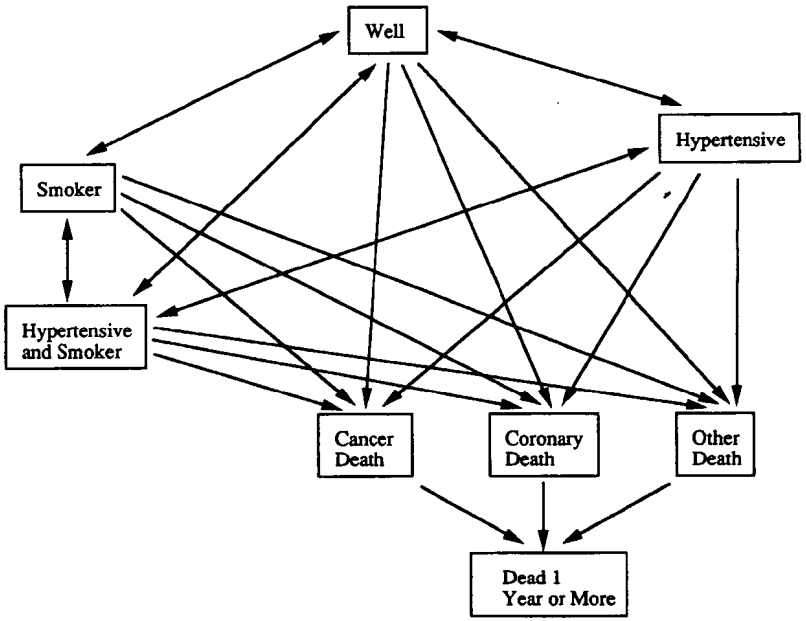
To illustrate these concepts, consider the example in Figure 2. For simplicity, all transitions are assumed to be independent of age. The compartments labeled "smoker" and "hypertensive" are risk factor states. Persons who are not hypertensive and who do not smoke are in the "well" state. When a "well" person begins to smoke, he/she enters the "smoking" state. Similarly, a well person who becomes hypertensive enters the "hypertensive" state. The "hypertensive and smoking" state represents individuals with both risk factors. Figure 2 allows for movement from risk factor states back to the "well" state. Transitions are effected by medical treatment (for example, for hypertension) or behavior modification (for smokers).

Causes of death are denoted by the "lung cancer death," "coronary death" and "other death" states. The "dead 1 year or more" state enables calculation of actuarial functions associated with mortality; that is, an insurer can expect to incur costs in the year of death, but not subsequent years. The "dead 1 year or more" state identifies individuals with no further insurance risk. The transition rates for this model are

$$\Pi = \begin{array}{c|cccccccc|l}
 & \text{0. well} & \text{1. smoker} & \text{2. hypertensive} & \text{3. hypertensive smoker} & \text{4. lung cancer death} & \text{5. coronary death} & \text{6. other death} & \text{7. died 1 year or more} & \\
\hline
 & p_{00} & p_{01} & p_{02} & p_{03} & q_{01} & q_{02} & q_{03} & 0 & \text{Well} \\
 & p_{10} & p_{11} & p_{12} & p_{13} & q_{11} & q_{12} & q_{13} & 0 & \text{Smoker} \\
 & p_{20} & p_{21} & p_{22} & p_{23} & q_{21} & q_{22} & q_{23} & 0 & \text{Hypertensive} \\
 & p_{30} & p_{31} & p_{32} & p_{33} & q_{31} & q_{32} & q_{33} & 0 & \text{Hypertensive smoker} \\
 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & \text{Lung cancer death} \\
 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & \text{Coronary death} \\
 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & \text{Other death} \\
 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & \text{Dead 1 year or more}
\end{array}$$

FIGURE 2

SIMPLE EXAMPLE OF THE COMPARTMENT MODEL FOR MODELING HEALTH STATES UNDER THE MARKOV ASSUMPTION



In Π the "smoker" state is denoted state 1, the "hypertensive" state 2, and so on. The transition probabilities are

$$p_{ii} = 1 - \sum_{j \neq i} p_{ij} - \sum_{k} q_{ik}. \tag{4}$$

The probability of going to the "dead 1 year or more" state from the dead by any cause states is a certainty (that is, $\pi_{47} = \pi_{57} = \pi_{67} = 1.0$).

We require estimates for each transition probability; these can be generated from published results. For example, Peto [13] gives a formula relating smoking to lung cancer. This provides estimates of q_{01} and q_{11}. The probability of coronary death for smokers is estimated to be about twice that of nonsmokers. Under this assumption, $q_{12} = 2q_{02}$. Other relationships might be assumed such as (see, for example, Bumgarner [1]):

$$q_{21} = q_{01}$$
$$q_{22} = 2q_{02}$$
$$q_{23} = 4q_{02}$$
$$q_{03} = q_{13}$$
$$p_{10} = p_{21} = 0.03$$

The vector of the number of individuals in each health state is $\mathbf{N} = (n_0, n_1, \ldots, n_7)$. If everyone starts "well," then $n_1 = n_2 = \ldots = n_7 = 0$. The number of individuals in each state after m years, $\mathbf{N}^{(m)}$, is

$$\mathbf{N}^{(m)} = \mathbf{N}\Pi^m. \tag{5}$$

From (5) the present value of total costs for, say, state 2, discounted at 6 percent interest and by the contingency of the event is

$$\text{cost}_h = c \sum_{m=0}^{\infty} (1.06)^{-m} n_2^{(m)}, \tag{6}$$

where c is the annual health cost for an individual who is hypertensive and $n_2^{(m)}$ is the third element of the vector $\mathbf{N}^{(m)}$.

Other costs are similarly calculated from powers of the transition matrix Π. For example, the mortality costs for lung cancer death are

$$\text{cost}_d = c_d \sum_{m=0}^{\infty} (1.06)^{-m} n_4^{(m)}, \tag{7}$$

where c_d is the cost of death from lung cancer. The sequence $n_1^{(1)}$, $n_1^{(2)}$, ... , $n_1^{(m)}$ represents the number of individuals who smoke and who, consequently, may incur additional medical costs. Costs may also be expressed as demands for resources, not as monetary units discounted by interest and contingency. Such resource measures (for example, the number of beds required per year, health manpower requirements) might be useful for resource allocation in health service systems with fixed global budgets (for example, hospitals or HMOs). Introducing age dependency in the transition probabilities increases the size of Π, though it does not add conceptual difficulty. The costs and benefits of interventions are estimated by altering the transition probabilities, or cost functions, and performing the matrix computations.

Our primary interest is the evaluation of risk factor interventions. To simulate an intervention in Figure 1, the probabilities of transition into or out of certain states are altered; that is, the π_{ij} parameters in the transition

matrix are changed starting at $t=0$. For example, an intervention may reduce the rate at which people start smoking by 25 percent. Though the effect of the intervention on the transition probabilities is clear, how the intervention operates over time depends on all parameters of the Markov model.

The example shows advantages and disadvantages of the compartment model. First, the vectors, $n_i^{(m)}$, are the basis for calculating actuarial cost functions for state i. Knowledge of $\mathbf{N}^{(m)}$, over values of m, and the costs associated with each state allow estimation of actuarial functions for the process. Changes in transitions, in turn, alter the entries in $\mathbf{N}^{(m)}$ from which the financial consequence of the intervention is assessed. Thus the $\mathbf{N}^{(m)}$ are "sufficient statistics" for the compartment model; that is, all discrete time actuarial functions can be calculated once the compartment model is specified.

To use the compartment model to calculate actuarial functions for contingent events, two assumptions are made. The first is that the occurrence of a contingent event at t is equivalent to an individual being present in a state at the *end* of t. By appropriate construction of states, absorbing transitions (for example, death by a specific cause) can be modeled. Morbidity and health-related actuarial functions are easily modeled by such states. The second assumption is that an appropriate cost for the contingent event can be assigned to the state (or states) indicating the occurrence of an event. This assumption is satisfied by determining costs on a present value basis, for example, present value at year's end for health care costs for the year.

The disadvantage of the approach, despite familiarity to actuaries, is that the number of risk factor states that can be represented is limited. In the example, there are 24 transition probabilities and 6 cost functions. If this were applied to a cohort grouped into five-year categories for ages 30 to 90, there are 12×24, or 288, transition probabilities. Thus, estimation of such models (Weinstein et al. [16]) may require unrealistic assumptions (for example, that risk factors operate independently). In the example in Section X, nine risk factors are examined. A discrete state model of this complexity requires more data than are generally available.

A second limitation is the need to approximate continuous risk factors by discrete risk states. For example "hypertensive" or "high blood cholesterol" are not defined until the blood pressure or cholesterol threshold for each is specified. Often standards are set up by national or international organizations, but different standards might classify both values of 200 and 240 as "high," though the risks of cardiovascular failure in these two cases vary considerably. Similarly, smoking two cigarettes a day and smoking two

packs a day are different risks that are not distinguished by classifying individuals as "smokers."

VI. THE CONTINUOUS STATE GENERALIZATION OF THE MULTIPLE DECREMENT/COMPARTMENT MODEL

When continuous risk factors (for example, age, blood pressure) are represented as *discrete* states, there is a loss of information. In this section we generalize the compartment model to represent continuous risk factors and time to avoid this loss. The advantages of generalizing the compartment model are:

1. The response of many diseases to risk factor exposures is naturally continuous.
2. Rules for describing discrete risk factor states are often arbitrary.
3. The data requirements of discrete state models exceed those for a model of continuous risk factors.
4. Fewer simplifying assumptions are required than in complex compartment models in which transitions often have to be estimated from multiple independent published studies.

Conversely, it is easy to use discrete risk factors (for example, gender) in the continuous model. For variables that are discrete (and cannot be represented by a continuous surrogate risk factor variable), the process is made specific to the discrete state. For example, continuous state models could be sex-specific—or apply only to those individuals who have (or have not) had a coronary event. For coronary heart disease, an individual can be viewed as "jumping" from one continuous state model to another (probably with very different parameters) when a coronary event occurs. In addition, discrete risk factors may be replaced by continuous variables that are surrogates for the event. This is useful when information is gathered at discrete points in time.

A second generalization of the compartment model represents transitions in continuous, not discrete, time. This has two advantages. First, it is more realistic. Even when data are gathered at discrete time points, both mortality and morbidity processes are operating in continuous time. Second, the equations describing the number of individuals at each risk factor level are easier to solve in continuous time. Under mild regularity conditions, the function describing the number of individuals at each level of the risk factors is described by a specific type of differential equation (for example, Gillespie [5]).

More formally, to generalize the compartment model, we replace the discrete states with a vector of continuous risk factors for person w denoted as $\mathbf{r}_w(t)$. Thus $\mathbf{r}_w(t)$ describes the level of smoking, blood pressure, cholesterol, and so on of individual w at *exact* time t. The values that a person has at t describe his/her "state" as a point in a risk factor continuum. Changes in $\mathbf{r}_w(t)$ are described by a continuous time, vector stochastic process; that is, the health "state" of the individual, represented by $\mathbf{r}_w(t)$, is governed by a random process—as are movements between discrete states in the compartment model. The discrete state of an individual (for example, gender) is indexed by d.

Following the Markov assumption $\mathbf{r}_{dw}(t+\Delta)$, the "state" of individual w at time $t+\Delta$, given that individual w was in "state" $\mathbf{r}_{dw}(t)$ at t, is an outcome whose probability depends only on $\mathbf{r}_{dw}(t)$ and not on $\mathbf{r}_{dw}(t-s)$ (for $s>0$). Thus, the "state" of an individual is defined jointly by the risk factor vector $\mathbf{r}_w(t)$ and the discrete state d. Both can change at any t. For example, risk factor $\mathbf{r}_w(t)$ may increase. The individual may have a heart attack, which changes d. The realization of this process at time t for the w-th individual represents the w-th individual's risk factors.

To understand the probabilistic mechanism describing changes in risk factors, denote h_i as the i-th element of the difference $\mathbf{r}_{dw}(t+\Delta)-\mathbf{r}_{dw}(t)$, for a small value of Δ. The process is represented by changes in the h_i values over time. Specifically we assume the following first two moment conditions, given that the value of $\mathbf{r}_{dw}(t)$ is known to be $\mathbf{x}$:

$$E[h_i|\mathbf{r}_{dw}(t) = \mathbf{x}] = g_{di}(\mathbf{x},t)\Delta + o(\Delta) \tag{8}$$

and

$$E[h_ih_j|\mathbf{r}_{dw}(t) = \mathbf{x}] = A_{dij}(\mathbf{x},t)\Delta + o(\Delta), \tag{9}$$

where $o(\Delta)$ is such that $o(\Delta)/\Delta \to 0$ as $\Delta \to 0$. The third assumption is:

$$E[h_ih_jh_k|\mathbf{r}_{dw}(t) = \mathbf{x}] = o(\Delta). \tag{10}$$

Collectively, the assumptions in (8), (9), and (10) indicate that for small time intervals (small Δ), the average expected change in the risk factors is a function of the current risk factor level times the length of the time interval; a similar relation holds for the second moment as described by Equation (9). All moments higher than the second are assumed to decrease faster than Δ as Δ goes to zero. The vector containing the $g_{di}(\mathbf{x},t)$ values can be denoted $\mathbf{g}_d(\mathbf{x},t)$ and the matrix containing the $A_{dij}(\mathbf{x},t)$ values as $\mathbf{A}_d(\mathbf{x},t)$ where these quantities are functions of the discrete state d. With these conditions and

regularity conditions on the correlation of the random vector process $\mathbf{r}(t+\Delta) - \mathbf{r}(t)$, $\mathbf{r}(t)$ satisfies the stochastic differential equation

$$d\mathbf{r}(t) = \mathbf{g}_d[\mathbf{r}(t),t]\, dt + \sigma_d(\mathbf{x},t)\, d\xi\, [\mathbf{r}(t), t], \tag{11}$$

where $\xi\,[\mathbf{r}(t),t]$ is a Gaussian vector process (see Kushner [9]) and $\sigma_d(\mathbf{x},t)$ is the "square root" of $\mathbf{A}_d(\mathbf{x},t)$. The parameters on the right-hand side of (11) are dependent on d. Equation (11) assumes that the individual did not change states during the interval $(t,t+\Delta)$.

To understand (11), let $\mathbf{a}_w(\mathbf{x},t,\Delta)$ denote the risk factor values that are statistically *expected* for individual w at time $t+\Delta$ given that he/she remains in discrete risk factor state d and has continuous risk factor values $\mathbf{r}(t)=\mathbf{x}$ at t. Then $\mathbf{a}_w(\mathbf{x},t,\Delta)$ is calculated from the distribution of the risk factor process at $t+\Delta$ given that the value of the process at t is $\mathbf{x}$. This expectation is similar to the compartment model in which the state that an individual is expected to be in at $t+1$ is calculated conditionally on the state the individual was in at t. The function $\mathbf{g}_d[\mathbf{r}(t),t]$ in (11) is (see Schuss [15])

$$\mathbf{g}_d[\mathbf{r}(t),\, t] = \frac{\partial}{\partial t}\, \mathbf{a}_w\, [\mathbf{r}(t),\, t,\, \Delta]\, |_{\Delta \to 0^+}. \tag{12}$$

Consequently, Equation (11) describes changes in risk factors as changes in the conditional mean of the risk factor and the "differential" of random noise within each discrete state or compartment.

To illustrate (11), consider insured persons with two risks: smoking and hypertension. For this population during a year, suppose smoking increases 3 percent with a standard deviation of 2 percent. Suppose hypertension rises 1 percent, with a standard deviation of 1/2 percent. Assume, for convenience, that changes in smoking and hypertension are linear in time and independent. Using the notation above,

$$\mathbf{r}(t) = \begin{pmatrix} \text{smoking level} \\ \text{hypertensive level} \end{pmatrix} = \begin{pmatrix} r_1(t) \\ r_2(t) \end{pmatrix}.$$

If the instantaneous rate of change is constant over the year, then

$$g(\mathbf{x},t) = \begin{pmatrix} 0.03\, x_1 \\ 0.01\, x_2 \end{pmatrix}$$

and the matrix $\mathbf{A}(\mathbf{x},t)$ is given by

$$\mathbf{A}(x,t) = \begin{bmatrix} (0.01\,x_1)^2 & 0 \\ 0 & (0.005\,x_2)^2 \end{bmatrix}$$

Equation (11) replaces the compartment model transitions between risk factor states. In the compartment model, a number of discrete states are required to describe the levels of smoking and hypertension. In the continuous case, only two equations are required.

VII. JUMP PROCESS

Equation (11) represents how continuous risk factors change over time given that individuals remain in state d. However, individuals will not remain in the same discrete states. Some will enter the different discrete disease/risk states by suffering a heart attack, stroke, and so on. Others die. In this section we describe how these discrete changes are represented for the continuous state process.

Assume that the probability individual w is in discrete state d is $P_w[d|\mathbf{r}(t),t]$. Then, in addition to changes in $\mathbf{r}_w(t)$, the individual's risk profile can change by jumping from one discrete state to another. For small Δ, the probability of jumping from d to d' $(d \neq d')$ is

$$\text{Prob}\,[d,d'|\mathbf{r}(t),\,t] = \lambda_{dd'}\,[\mathbf{r}(t)]\Delta + o(\Delta), \tag{13}$$

where λ is the Poisson rate parameter. We assume the other Poisson assumptions for jumps: Jumps are independent in nonoverlapping time intervals and independent between individuals; there is a small probability of two (or more) jumps in a short interval of time. All independence assumptions are conditional on $\mathbf{r}(t)$. Equations (11) and (13) are similar to the compartment model except that certain risk factor states are converted into a continuous vector $\mathbf{r}_w(t)$ and generalized to continuous time as $\Delta \to 0$. Intrinsically discrete states are still modeled as discrete except that individuals jump from state to state with Poisson rate, λ, rather than with annual probability, π_{ij}.

The concept that parallels the state vector $\mathbf{N}(t)$ in the discrete model is the distribution of risk factors $\mathbf{r}_d(t)$ for each d. Denote the probability density function for $\mathbf{r}_d(t)$ for discrete state d at time t, given that at time $\tau < t$ the risk factor was $\mathbf{x}_\tau$ in discrete state d_τ, is $f_t(\mathbf{x},\, d,\, \mathbf{x}_\tau,\, d_\tau)$. For any function $\phi(\mathbf{x})$ that has all derivatives, we can write

$$\int f_t(\mathbf{x}, d, \mathbf{x}_\tau, d_\tau)\,\phi(\mathbf{x})\,d\mathbf{x} = \int f_t(\mathbf{x}, d, \mathbf{x}_\tau, d_\tau)\left[\phi(\mathbf{x}_\tau) + \sum_i (x_{it} - x_{i\tau})\left.\frac{\partial\phi(\mathbf{x})}{\partial x_i}\right|_{\mathbf{x}=\mathbf{x}_\tau} + \sum_i\sum_j (x_{it} - x_{i\tau})(x_{jt} - x_{j\tau})\left.\frac{\partial^2\phi(\mathbf{x})}{\partial x_i \partial x_j}\right|_{\mathbf{x}=\mathbf{x}_\tau} + \ldots\right] d\mathbf{x}. \tag{14}$$

We assume τ is "close" to t and that jumps occur at the end of the interval. Given (8), (9), (10) and (13), we can rewrite (14) as

$$\int f_t(\mathbf{x}, d, \mathbf{x}_\tau, d_\tau)\,\phi(\mathbf{x})d\mathbf{x} = \int f_t(\mathbf{x}, d, \mathbf{x}_\tau, d_\tau)\theta_{d_\tau d_t}\left[\phi(\mathbf{x}_\tau) + \Delta\sum_i g_i(\mathbf{x}_\tau,\tau)\left.\frac{\partial\phi(\mathbf{x})}{\partial x_i}\right|_{\mathbf{x}=\mathbf{x}_\tau} + \Delta\sum_i\sum_j A_{ij}(\mathbf{x}_\tau,\tau)\left.\frac{\partial^2\phi(\mathbf{x})}{\partial x \partial x_j}\right|_{\mathbf{x}=\mathbf{x}_\tau} + o\Delta)\right] d\mathbf{x} \tag{15}$$

where $\Delta = t - \tau$, and $\theta_{d_\tau d_t}$ is the probability of jumping from discrete state d_τ to d_t in the interval (τ,t) given in (13). The probability of jumping is a function of $\mathbf{x}_\tau$.

Equation (15) holds for any $\varphi(\mathbf{x})$ that has derivatives of all orders (Iranpour and Chacon [7]). Consequently, the density function, $f_t(\mathbf{x},d,\mathbf{x}_0,d_0)$, is the solution to the differential equation,

$$\begin{aligned}\frac{\partial f_t(\mathbf{x}, d, \mathbf{x}_0, d_0)}{\partial t} = &-\sum_i \frac{\partial[f_t(\mathbf{x}, d, \mathbf{x}_0, d_0)g_{di}(\mathbf{x}, t)]}{\partial x_i} \\ &+ \sum_i\sum_j \frac{\partial^2[f_t(\mathbf{x}, d, \mathbf{x}_0, d_0)A_{dij}(\mathbf{x}, t)]}{\partial x_i \partial x_j} \\ &+ \sum_{k\neq d} \lambda_{kd}(\mathbf{x})\, f_t(\mathbf{x}, k, \mathbf{x}_0, d_0) \\ &- \left[\sum_{k\neq d} \lambda_{dk}(\mathbf{x})\right] f(\mathbf{x}, d, \mathbf{x}_0, d_0).\end{aligned} \tag{16}$$

In (16), $g_{di}(\mathbf{x},t)$ is the i-th element of the vector $\mathbf{g}_d(\mathbf{x},t)$ and $A_{dij}(\mathbf{x},t)$ is the i,j-th element of $A_d(\mathbf{x},t)$.

Equation (16) represents the distribution of the risk factors and discrete states given the initial state $(\mathbf{x}_0,d_0)$. This equation is similar to the Fokker-Planck equations for continuous processes (Iranpour and Chacon [7]). In

(16), however, individuals can move between states according to the jump process in (13).

Equation (16) is useful for simulating changes in the distribution of risks and numbers of individuals in each discrete state. This is done by incrementally changing the initial distribution according to (16). Equation (16) can be used to construct likelihood models for observed data.

VIII. CALCULATION OF COSTS

In Section V, actuarial functions were calculated by using the number of individuals in each state at t. In continuous time, actuarial functions are derived from the *expectation* of the number of individuals with risk factor profile $\mathbf{r}_{dw}(t)$. For risk factor profile $\mathbf{r}_{dw}(t)$, the instantaneous medical cost and/or mortality costs at time t are denoted $c[\mathbf{r}_{dw}(t),t]$. The instantaneous cost at time t for a collection of N risks in a population described by (11) and (13) is

$$\text{Cost}(t) = N \sum_{d} \int f_t(\mathbf{x}, d)c(\mathbf{x}, t)\, d\mathbf{x}, \tag{17}$$

where $f_t(\mathbf{x},d)$ is marginal probability density at time t over all "states" $\mathbf{r}(0)$, d_0 at time 0. The present value of the costs accumulated over time, starting at $t=0$, is

$$\text{Present Value of Future Costs} = \int_0^\infty \exp(-\delta t)\ \text{Cost}\ (t)\, dt \tag{18}$$

where δ is the force of interest. The distribution function $f_t(\mathbf{x},d)$ plays the same role as $n_i(t)$ in the actuarial functions.

Costs for a collection of risks can be calculated under dynamic situations by determining the value of f_t over time. One method of doing this is to start from a given distribution of risk factors at a fixed point in time. Then, future values of f_t are determined by using Equation (16). Both dynamic risk factor processes and jumps from state to state are represented. In many situations this approach is simpler than constructing a large number of discrete states. Besides the reduced computational burden, it is often easier to specify a distribution of risk factors and trends than it is to detail each transition probability as required in the compartment model case.

IX. ESTIMATION

Even though, for most risk factors, studies relate risk factor distributions to the risk of death for specific causes, those studies may not describe all risk factor dynamics. It is desirable, therefore, to estimate all components of the dynamic model from a single, extensive follow-up study. One method (Woodbury and Manton [17]) has been applied to the Framingham heart disease study.

The function f_t, describing change in risk factors over time, can be estimated if specific functions are selected to describe mortality and risk factor dynamics. Woodbury and Manton [17] assumed that the mortality rates (that is, the hazard functions) are specific to cause of death. The only discrete states were alive or dead by a specific cause. The hazard for cause of death m is denoted $\mu_m[\mathbf{r}(t)]$. The mortality function μ is assumed to be a quadratic function of the factors $\mathbf{r}_w(t)$,

$$\mu_m[\mathbf{r}_w(t)] = \{a_0 + b\mathbf{r}_w(t) + 1/2\ \mathbf{r}'_w(t)\ B\mathbf{r}_w(t)\}\ (\alpha\ e^{\theta t})_m \qquad (19)$$

where a_0, b and B are scalar, vector and matrix constants, respectively. The Gompertz scaling term, $e^{\theta t}$, represents the average effects of unobserved factors on the hazard. The function $\mu_m[\mathbf{r}(t)]$ represents a specific assumed form of the function $\lambda\ [\mathbf{r}(t)]$ for the jumping process described previously. In this case, however, the only jumps are deaths.

The Gompertz term transforms the equations that describe the change in risk factors over time into the mortality conditions of a select population, where the change is estimated from relatively rare long-term longitudinal data (for example, Framingham). Changes in the proportional mortality structure of the population are represented by altering α. Changes in the age dependence can be represented by θ. These transformations make the hazard function applicable to a wide range of populations. For example, the hazards in six developing countries have been successfully modeled by scaling the cause-specific Gompertz proportionality and age-dependence parameters by using either national vital statistics data or data from specific health clinics and hospitals (for example, Dowd and Manton [4]).

In addition, the distribution of risk factor or physiological variables, $\mathbf{r}(t)$, is assumed to change as a "linear" function of the prior risk factor state:

$$r_{it+1} = u_{0i} + \beta_1\, r_{it} + \beta_2 \times \text{Age} + \beta_3(\text{Age} \times r_{it}) + e_{it}. \qquad (20)$$

Equation (20) is linear in its coefficients. The variables may be nonlinear functions of time, age, or interactions. Age is explicitly introduced, both as a linear term and as an interaction with the prior risk factor values.

Equations (19) and (20) can be estimated (as in our example) from longitudinal study data (Equation (19) by maximum likelihood, Equation (20) by least squares). With parameters estimated for those two equations, the differential equations can be solved to yield life table survival parameters, age-specific changes in risk factors, and cost functions. Risk factor values, $\mathbf{r}_w(t)$, are calculated from (20), and conditional on these values, the hazard is estimated from (19). Thus the two sets of equations interact over time. The parameters in the two sets of equations can be derived from multiple sources. Equation (16) can be used to examine the change in the distribution, $f_t(\mathbf{x},d)$, of risk factors over time under different intervention scenarios. Explicitly, if health interventions were introduced at $t=0$, the distribution of a risk factor, say smoking, will be altered. The effect of this alteration diffuses throughout the distribution of other risk factors in the cohort over time according to (16)—analogous to taking the M-th power of Π. The corresponding health effect is seen by changes in mortality experience for causes of death for which smoking is a risk factor. The impact of the intervention may take many years to emerge, even assuming that the physiological effect of smoking cessation is immediate.

X. APPLICATION

The continuous state model can be used to simulate a wide range of interventions by modifying a number of features of the dynamic equation. In each case, we can calculate life tables that reflect interventions in risk factor values for survivors to age x and the values of actuarial functions. For example, we may wish to determine the change in the present value of an annuity associated with a 10 percent reduction in blood pressure of an insured group.

Consider results obtained from 20-year follow-up data on males from the Framingham heart study in which measurements were made biannually on systolic and diastolic blood pressure, smoking, serum cholesterol, body mass index, hemoglobin, blood sugar, vital capacity index, and age. Using this data, we simultaneously modeled changes in the risk factor variables and the effects of the risk factors on cause-specific mortality (discrete, absorbing states) under the assumptions of Equations (19) and (20). In addition, we determined the effects of interventions by manipulating different features of the dynamic equations in (16) and the hazard function (19).

In Table 1 we present the male life table calculated for the Framingham population.

TABLE 1

OBSERVED (BASELINE) AND CAUSE ELIMINATION LIFE TABLE VALUES ASSUMING NO CHANGE IN RISK FACTORS (INDEPENDENCE) AND ALTERING THE RISK FACTOR DISTRIBUTION (DEPENDENCE): CIRCULATORY DISEASE ELIMINATION, MALES, FRAMINGHAM HEART STUDY

	l	d	q	e	Age ($t+30$)	Pulse Pressure	Diastolic Blood Pressure	Quetelet Index	Cholesterol	Blood Sugar	Hemoglobin	Vital Capacity Index	Cigarettes per Day
Baseline	100,000	260	0.003	43.80		45.83	79.57	261.88	215.22	79.55	142.11	139.29	13.24
Dependence	100,000	122	0.001	53.98	30.00	45.83	79.57	261.88	215.22	79.35	142.11	139.29	13.24
Independence	100,000	122	0.001	54.88									
Baseline	98,209	563	0.006	34.50		41.13	83.20	273.20	241.50	78.37	147.76	138.16	14.46
Dependence	99,263	210	0.002	44.34	40.00	41.14	83.21	273.35	241.56	78.39	147.76	138.16	14.48
Independence	99,264	210	0.002	45.25									
Baseline	94,289	1,203	0.013	25.70		47.62	83.40	277.11	241.12	83.70	149.63	127.60	12.61
Dependence	97,798	461	0.005	34.92	50.00	47.64	83.42	277.26	241.27	83.76	149.64	127.59	12.67
Independence	97,801	460	0.005	35.84									
Baseline	85,976	2,569	0.030	17.65		55.26	83.31	274.24	233.01	91.00	150.42	114.42	9.13
Dependence	94,493	1,069	0.011	25.94	60.00	55.34	83.37	274.40	233.28	91.17	150.44	114.29	9.27
Independence	94,508	1,063	0.011	26.90									
Baseline	68,166	5,355	0.079	10.79		62.97	82.85	266.77	222.97	98.27	150.74	100.90	4.78
Dependence	86,685	2,552	0.029	17.76	70.00	63.25	83.01	266.37	223.39	99.07	150.74	100.32	5.09
Independence	86,789	2,498	0.029	18.78									
Baseline	35,532	7,278	0.205	5.82		70.39	82.04	257.70	213.13	105.78	150.96	88.44	0.00
Dependence	68,613	5,462	0.080	10.96	80.00	71.21	82.41	255.04	213.67	107.06	150.82	86.52	0.47
Independence	69,388	4,930	0.071	12.09									
Baseline	5,818	2,722	0.468	2.86		77.34	80.87	250.65	204.64	111.89	151.91	78.01	0.00
Dependence	36,316	7,325	0.202	6.00	90.00	79.36	81.68	242.69	205.59	115.04	151.30	73.30	0.00
Independence	39,670	6,756	0.170	7.17									
Baseline	56	44	0.772	1.55		83.36	79.58	249.33	197.13	116.80	153.60	71.51	0.00
Dependence	6,520	2,848	0.437	3.10	100.00	87.75	81.05	232.38	200.48	123.51	152.48	61.55	0.00
Independence	10,599	3,508	0.331	4.24									
Baseline	0	0	0.947	1.11		88.01	78.50	254.14	188.80	120.75	155.69	70.35	0.00
Dependence	113	80	0.710	1.76	110.00	96.18	80.52	225.99	198.91	133.32	154.35	53.14	0.00
Independence	776	401	0.516	2.68									

Note: Mean values under independence are the same as those under the baseline model.

In the life table, in addition to the standard survival parameters (for example, l_x, e_x, d_x), age-specific means (υ_x) and variances (V_x) of the risk factors are presented. These are calculated from the time series change of the risk factors, Equation (20), as it interacts with mortality, Equation (19). Thus, the ability of the mean to describe the experience of the population is evaluated not only by survival but also by the ability to reproduce age changes in multiple risk factors. This greatly increases the information used in evaluation. In addition, we present the life tables if a specific disease (CVD) is eliminated both (a) as an independent cause (that is, it does not affect the age-specific risk factor values) and (b) as a dependent cause. The dependent risk model shows that, at advanced ages, the independent risk model overstates the effects of the disease on survival because reducing the reduction of mortality at early ages allows more risk-susceptible persons to survive.

In addition, we modified the dynamic equation to represent specific interventions. In Table 2, we present changes in age-specific life expectancies at select ages (that is, 30, 40, 50, 60, 70, 80) induced by modifying the parameters of the risk factor dynamics.

TABLE 2

CHANGE IN LIFE EXPECTANCY UNDER DIFFERENT RISK FACTOR INTERVENTIONS, FRAMINGHAM MALES

Intervention	Age					
	30	40	50	60	70	80
Baseline values of life expectancy	44.52	35.17	26.35	18.34	11.53	6.39
Control of the age increase of pulse and diastolic blood pressure	1.09	1.08	1.11	1.22	1.33	1.30
Reduction of the variability of pulse and diastolic blood pressures	2.08	1.98	1.80	1.50	1.07	0.58
Elimination of the age increase and the variability of pulse and diastolic blood pressures	3.00	2.90	2.78	2.63	2.37	1.90
Control of the age increase of cholesterol	0.12	0.12	0.11	0.10	0.12	0.14
Control of the variance of cholesterol	0.64	0.61	0.55	0.46	0.33	0.20
Both age increase and variance control for cigarette smoking (mean = 0)	1.48	1.33	1.10	0.75	0.36	0.06
Control of the age increase of vital capacity	1.14	1.16	1.19	1.22	1.19	1.03
Control of the age increase of blood sugar	0.43	0.43	0.45	0.46	0.44	0.36
Control of the age increase of all variables	4.36	4.25	4.09	3.95	3.85	3.59

Three risk factor interventions are represented in Table 2. The first involves preventing the j-th risk factor from increasing with age (that is, the

values are fixed at their age 30 levels—these values may not optimize survival at all ages so that alternative values at later ages may have greater survival improvement). In this intervention, we adjust the A_{ij} terms to maintain the variance of the distribution of the risk factor at approximately the same level as in the model before the intervention.

Not allowing systolic and diastolic blood pressure values to rise with age produces bigger increases in life expectancy above age 60—consistent with hypertension being a risk factor for causes of death more prevalent at advanced ages, that is, stroke and heart disease.

The second intervention allows risk factor means to change with age, but eliminates the variance of the risk factor distribution representing interventions that affect only persons with extreme risk factor values. This intervention produces a bigger effect on life expectancy at early ages (that is, at age 30, 2.08 years versus 1.09 years). The effect of reducing the variance of blood pressure decreases with age.

In the third example both interventions are introduced. For blood pressure, the simultaneous control of the two aspects of blood pressure dynamics produced nearly additive effects.

Imposing interventions on both the mean and variance of cholesterol produced relatively small effects on life expectancy. Eliminating increases in blood sugar with age also had a small effect. Control of cigarette smoking (with mean and variance set to zero) has most of its effect before age 70. In contrast, controlling vital capacity has a constant effect over age. The simultaneous control of the age increase of all variables (with mean and variance of cigarette smoking set to zero) produces a large effect on life expectancy. Overall, variance control, which implies reducing extreme risk factor values, has a larger effect at younger ages, whereas controlling the age change of risk factors is more important at advanced ages.

We translated the person-year changes in Table 2 into their age-specific direct and indirect mortality cost implications using the cost functions of Rice and Hodgson [14]. These are presented in Table 3.

The table shows that the pattern of effects on indirect costs is quite different from that of the effects on life expectancy. This is because the age-specific cost function used in the calculations is derived from current wage rates and employment patterns, assuming a current general retirement age of 65 and low general retirement ages (Rice and Hodgson [14]). If one wishes to determine what the relative costs and benefits would be if increases in

TABLE 3

CHANGE IN THE DIRECT AND INDIRECT COST OF DISEASE AND MORTALITY UNDER DIFFERENT RISK FACTOR INTERVENTIONS, FRAMINGHAM MALES

Intervention	Age					
	30	40	50	60	70	80
Indirect Costs						
Baseline value of indirect cost	$10,800	$12,809	$11,670	$6,856	$3,315	$1,554
Control on the variability of pulse and diastolic blood pressures	198	164	171	332	333	194
Control on the variability of pulse and diastolic blood pressures	2,025	2,440	2,204	1,180	427	116
Both types of intervention on pulse and diastolic blood pressure	1,968	2,440	2,016	1,303	684	292
Control of the age increase of cholesterol	54	128	92	18	25	23
Control of the variability of cholesterol	657	777	698	371	135	39
Both types of intervention on smoking	2,274	2,553	2,051	868	196	12
Control of the age increase of vital capacity	183	342	537	526	343	164
Control of the age increase of blood sugar	60	124	211	214	142	63
Control of the age increase of all variables	2,445	2,812	2,465	1,514	848	413
Direct Costs						
Baseline value of indirect cost	$1,050	$1,696	$2,636	$3,918	$5,490	$7,103
Control on the variability of pulse and diastolic blood pressure	31	52	92	180	318	437
Control on the variability of pulse and diastolic blood pressure	118	179	249	305	303	213
Both types of intervention on pulse and diastolic blood pressures	135	208	308	447	592	645
Control of the age increase of cholesterol	4	9	11	13	27	47
Control of the variability of cholesterol	37	56	77	95	95	70
Both types of intervention on smoking	107	150	182	178	115	20
Control of the age increase of vital capacity	36	67	119	202	298	353
Control of the age increase of blood sugar	13	26	46	79	116	126
Control of the age increase of all variables	174	271	402	591	847	1,096

life expectancy also implied increases in retirement age, then the cost function would require modification to represent the implied changes in age-specific earnings.

In Table 3 we present the direct costs of mortality fixed at $10,000. These costs increase with age due to the shorter times for the discount rates to operate. Because smoking-related mortality tends to occur at younger ages, the combined control on smoking has a relatively smaller impact on direct costs than on indirect costs. In contrast, the combined dynamic and variance control of blood pressure has a larger relative effect on direct costs.

In Table 4 we present the present value of a cost of $1,000 per death prior to age 75 (6 percent discount rate) under baseline conditions (no intervention) and with the elimination of smoking. In addition, we present the

ratio of the values under the two scenarios. There is a 26 to 30 percent reduction in the present value of a death under smoking elimination. Thus, there is a considerable cost reduction for a life insurance program due to an effective antismoking intervention program. The change produced by eliminating smoking was at the population level and not the elimination for a subpopulation with a specific level of smoking (for example, the elimination of smoking among persons who consume two packs of cigarettes per day). The effects on the subpopulation are much larger.

TABLE 4

PRESENT VALUE OF A COST OF $1,000 PER DEATH PRIOR TO AGE 75 WITH INTERVENTION AND NO INTERVENTION BY 5-YEAR AGE GROUPS. VALUES ARE CALCULATED ASSUMING 6% ANNUAL INTEREST RATE.

Age Group	Present Value of $1,000 at Death		
	No Smoking Intervention	Intervention Eliminating Smoking	Ratio
30–35	$ 83.27	$ 64.55	1.29
35–40	88.86	68.40	1.30
40–45	112.98	86.69	1.30
45–50	141.14	108.67	1.30
50–55	171.71	134.33	1.28
55–60	182.13	144.79	1.26

XI. SUMMARY

We have shown how standard multiple-decrement models for calculating the direct and indirect costs of disease can be generalized from a discrete state to a continuous state form. This latter type of model has the advantages of representing (a) the stochastic evolution of the risk factors, (b) the interdependence of risk factors, (c) the interdependence of competing causes of death, and (d) the effects of a large number of different risk factor variables. The cost calculations for this model also use more information from time series data on risk factor changes, so that intervention effects for a wide range of risk factors can be calculated by using moderate sized (for example, 2,000 to 10,000 cases) populations. The presence of diffusive and regressive forces in the model suggests that the estimates of long-term costs in the population will be more accurately calculated than by using models that represent the effects of risk factors as only a small number of discrete strata.

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