THE PROPAGATION OF UNCERTAINTY IN HUMAN MORTALITY PROCESSES

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ABSTRACT

Human mortality and aging have frequently been modeled as stochastic diffusion processes. Estimates of the parameters of these processes have been made from various longitudinal studies. This paper shows how the stochasticity intrinsic to those processes will propagate through time and generate uncertainty about the future physiological state of the population. Variance expressions are derived for the future values of the physiological variables; and for the conditional survival functions and conditional life expectancies which reflect the uncertainty in the future values of the physiological variables. The results show that a major component of uncertainty is due to mortality. This suggests that the limits to forecasting may be different in physiological systems subject to systematic mortality than in physical systems such as weather.

I. INTRODUCTION

In the physical sciences, especially in meteorology, there are well developed theories about the limits to forecasting because of the propagation of uncertainty in initial conditions and because of the stochasticity of the process during the forecast period. This paper examines a similar problem for biological systems and establishes certain analytic results concerning the limits on the ability to forecast changes in health status and mortality rates in human populations. To establish such limits, one must first specify the form of the process under consideration and then, for the specific process, determine how uncertainty (i.e., the variance of the forecasted quantity) increases with time.

The development of our analytic model proceeds along different avenues than other investigations. For example, Matis and Wehrly (1979) developed expressions for the variances of certain conditional parameters in stochastic compartmental systems (e.g., the conditional survival probability) based upon models which included various combinations of effects due to four distinct classes of stochasticity. Two of these classes (R1, R2) of stochasticity referred to random changes a.) in initial values, or b.) in hazard rates, between replications of an entire experiment (population). However, we wish to focus on a single population (experiment), and will not pursue this type of stochasticity. Two other classes (P1, P2) of stochasticity referred to random effects a.) due to discrete numbers of particles in the system or b.) due to random rate coefficients of the particles. In the limit, as the sample size tends to infinity the P2-stochasticity gives rise to a continuous distribution which is isomorphic to the fixed frailty model presented in Vaupel et al. (1979) and in Manton and Stallard (1980, 1981, 1984a,b). Matis and Wehrly (1979) noted this point and suggested that their system could be extended to include a class of stochastic models with random differential equations, but they did not

pursue this avenue.

This paper considers the class of stochasticity due to stochastic differential equations for the particular case of multivariate Gaussian diffusion processes of the type defined in Woodbury and Manton (1977) and Yashin et al. (1985a). For this special case, it is shown that these processes give rise to a form of P2-stochasticity in which the rate coefficients are random among particles but for which the assumption of fixed frailty is not made. This suggests that these new models will be more biologically realistic than the fixed frailty models in two important aspects. First, we know from clinical and epidemiological evidence that the risk of death depends upon the physiological state of the individual. Consequently, a substantial component of the uncertainty in the risk of death will be due to the effects of this physiological heterogeneity. Second, we know that such physiological variables evolve over time in a manner that can be described by a multivariate diffusion process. Thus, an additional component of the uncertainty in the risk of death in our mortality forecast will be due to the effects of diffusion. Thus, we need to determine the variance, and its change over time, of the parameters of a conditional life table whose parameters are themselves functions of a multivariate diffusion process in survival-relevant physiological variables.

The stochastic process model we have selected is due initially to Woodbury and Manton (1977). This model describes the evolution of mortality risks as a two component process governed by the Kolmogorov-Fokker-Planck equation. The special case of a multivariate Gaussian diffusion process can be described by a.) a linear autoregressive model of change in the physiological variables, and b.) a quadratic function describing the relation of the hazard rate to the values of the physiological variables. This two component process and the functional forms selected for

each component (i.e., linear dynamics and quadratic hazard dependency) have been found to describe human physiological change and mortality in a number of epidemiological studies of chronic disease (Manton and Woodbury, 1983, 1985; Manton et al., 1985). For example, there is considerable epidemiological evidence to suggest the appropriateness of the quadratic hazard function for total mortality (Tyroler et al., 1984). The quadratic hazard function also is consistent with the physiological dynamics of several general theories of human aging and mortality (Woodbury and Manton, 1977, 1983a,b).

Yashin et al. (1985a) considered this stochastic process model in detail and extended it to the case where not all the variables defining the physiological state relevant to survival were measured. Yashin et al. (1985b) considered the problem of producing maximum likelihood estimates for parameters when both observed and unobserved variables were assumed to influence mortality and presented a maximum likelihood estimation strategy. This paper considers the stochasticity of the survival curves generated by this process; shows that this is a form of P2-stochasticity (Matis and Wehrly, 1979) in which the mortality rates are random because they are functions of a stochastic process; and discuss certain limits to forecasting under such a process.

II. STOCHASTIC PROCESS MODEL

We will take the model of human mortality developed by Woodbury and Manton (1977, 1983a,b) and extended by Yashin et al. (1985a) as the basis for our analysis of the uncertainty of future mortality rates. This model is composed of a stochastic process with two distinct components. One component describes the evolution of the physiological status of survivors. The second component describes the risk of death among persons with specific physiological characteristics. The first component can be defined by specifying that the change in Y_t, the stochastic process describing physiological status, satisfies the following stochastic differential

equation,

$$dY_t = [a_0(t) + a_1(t)\ Y_t]dt + b(t)dW_t \ , \tag{1}$$

where $t \geq 0$, W_t is k-dimensional Wiener process, Y_0 is an n-dimensional vector of Gaussian random variables with joint distribution $N(m_0, \gamma_0)$; the elements of the vector $a_0(t)$ and the matrices $a_1(t)$ and $b(t)$ are bounded functions of time.

The second component can be defined by assuming that the mortality rate for individuals in each cohort is a nonnegative definite quadratic function of the process Y_t as follows,

$$\mu(t, Y_t) = Y_t' Q(t) Y_t + \mu_0(t) \ . \tag{2}$$

This function was called the conditional mortality rate in Yashin et al. (1985a). The unconditional or observed mortality rate $\bar{\mu}(t)$ is the mathematical expectation of $\mu(t, Y_t)$, given by

$$\bar{\mu}(t) = E[\mu(t, Y_t) \mid T>t] \tag{3a}$$

$$= tr[Q(t)\ \gamma_t] + m_t' Q(t)\ m_t + \mu_0(t) \ , \tag{3b}$$

where T denotes time of death, where Y_t is distributed as $N(m_t, \gamma_t)$, and m_t and γ_t are the solutions of the following ordinary differential equations,

$$\frac{dm_t}{dt} = [a_0(t) + a_1(t)\ m_t] - 2\ \gamma_t\ Q(t)\ m_t \tag{4}$$

$$\frac{d\gamma_t}{dt} = a_1(t)\ \gamma_t + \gamma_t\ a_1'(t) + b(t)\ b'(t) - 2\ \gamma_t\ Q(t)\ \gamma_t. \tag{5}$$

If the parameters $a_0(t)$, $a_1(t)$, $b(t)$, $Q(t)$ and $\mu_0(t)$ are specified as known functions of time (or are known constants) one can forecast future mortality simply using Eqs. (3), (4), and (5). These forecasting equations can produce projected trajectories for the survival probability and the parameters of the distribution $N(m_t, \gamma_t)$ of survivors. However, these equations say nothing about the variability of the conditional

mortality rates, nor of the trajectories of the conditional survival probabilities. In the following section we derive the variances of these conditional survival quantities.

III. VARIANCE ESTIMATES FOR MORTALITY FORECASTS

In order to characterize the uncertainty of future mortality rates we need to derive estimates of the variance of certain forecasted quantities. In this section we derive expressions for the variance of the conditional mortality rate, $\mu(t, Y_t)$, the conditional survival probability, $\ell(t, Y_0^t)$, and the conditional life expectancy, $e(0, Y_0^\infty)$, where $Y_0^t = \{Y_s | s \in [0,t]\}$ denotes the entire trajectory of the stochastic process over the interval $[0,t]$.

A. Variance of the Conditional Mortality Rate

By definition, a forecasted future mortality rate refers to mortality in the subpopulation of individuals still alive at the targeted time of the forecast. This means that the variance of the forecasted conditional mortality rate at time t should be calculated conditionally both on the physiological characteristics of the population (Y_t) and on the event $\{T>t\}$ where T is the time of death. The conditional Gaussian property of the distribution of the process (i.e., $Y_t \sim N(m_t, \gamma_t)$) and the quadratic dependence of $\mu(t, Y_t)$ on Y_t allow us to determine the formula for the variance of the conditional mortality rate. The results can be formulated in the following theorem:

Theorem: Let the conditional mortality rate $\mu(t, Y_t)$ depend upon the process Y_t as specified in equation (2). Let $V_\mu(t)$ denote the conditional variance of $\mu(t, Y_t)$ given $\{T>t\}$. Then,

$$V_\mu(t) = E\{[\mu(t, Y_t) - \bar{\mu}(t)]^2 | T>t\} \tag{6a}$$

$$= 2\, tr[Q(t)\, \gamma_t\, Q(t)\, \gamma_t] + 4\, m_t'\, Q(t)\, \gamma_t\, Q(t)\, m_t, \tag{6b}$$

where m_t and γ_t satisfy Eqs. (4) and (5).

The proof of this theorem is based on the results for calculating the variance of the quadratic form for independent random variables given by Seber (1977). This we generalized to the case where the random variables are not independent but can be transformed as indicated in the Appendix.

B. Variance and Covariance of the Conditional Survival Probability

We now consider the calculation of the variance and covariance of the conditional probability of survival. Let $\ell(t, Y) = \ell(t, Y_0^t)$ be the conditional survival function,

$$\ell(t, Y) = P(T>t|Y_0^t) \tag{7a}$$

$$= \exp\{-\int_0^t \mu(u, Y_u)du\} \tag{7b}$$

$$= \exp\{-\int_0^t [Y_u' Q(u) Y_u + \mu_0(u)]du\}; \tag{7c}$$

and let $\ell(t)$ be the unconditional survival function,

$$\ell(t) = P(T>t) \tag{8a}$$

$$= \exp\{-\int_0^t \bar{\mu}(u)du\} \tag{8b}$$

$$= \exp\{-\int_0^t [tr[Q(u) \gamma_u] + m_u' Q(u) m_u + \mu_0(u)]du\}, \tag{8c}$$

where m_u and γ_u are the solutions of the differential equations (4) and (5). Let $V_\ell(t) = C_\ell(t, t)$ denote the variance of $\ell(t, Y)$:

$$V_\ell(t) = E[\ell(t, Y) - \ell(t)]^2 \tag{9a}$$

$$= E[\ell^2(t, Y)] - \ell^2(t), \tag{9b}$$

and let $C_\ell(s,t)$ denote the covariance of $\ell(s,Y)$ and $\ell(t,Y)$. Then for $s \leq t$,

$$C_\ell(s,t) = E[\ell(s,Y) \ell(t,Y)] - \ell(s) \ell(t) \tag{10a}$$

$$\begin{aligned} &= \exp\{-\int_0^t [tr[Q^{(s)}(u) \gamma_u^{(s)}] + m_u^{(s)'} Q^{(s)}(u) m_u^{(s)} + \mu_0^{(s)}(u)]du\} \\ &- \exp\{-\int_0^t [tr[Q^{(s)}(u) \gamma_u] + m_u' Q^{(s)}(u) m_u + \mu_0^{(s)}(u)]du\}, \end{aligned} \tag{10b}$$

where

$$\overset{(s)}{Q}(u),\ \mu_0^{(s)}(u) = \begin{cases} 2\,Q(u),\ 2\,\mu_0(u), & \text{if } u \le s \\ Q(u),\ \mu_0(u), & \text{if } u > s\ ; \end{cases} \tag{11}$$

and where $m_u^{(s)}$ and $\gamma_u^{(s)}$ are the solutions of the following ordinary differential equations

$$\frac{dm_t^{(s)}}{dt} = [a_0(t) + a_1(t)\, m_t^{(s)}] - 2\,\gamma_t^{(s)}\,\overset{(s)}{Q}(t)\, m_t^{(s)}\ , \qquad (m_0^{(s)} = m_0) \tag{12}$$

$$\frac{d\gamma_t^{(s)}}{dt} = a_1(t)\,\gamma_t^{(s)} + \gamma_t^{(s)}\,a_1'(t) + b(t)\,b'(t) - 2\,\gamma_t^{(s)}\,\overset{(s)}{Q}(t)\,\gamma_t^{(s)}, \quad (\gamma_0^{(s)} = \gamma_0). \tag{13}$$

C. Variance of the Conditional Life Expectancies

Life expectancy at birth (time t = 0) can be calculated easily when the age (time t) specific mortality rates are known. The conditional life expectancy $e(0, Y) = e(0, Y_0^\infty)$ is the average survival time for a specific trajectory of the stochastic process Y_t, or

$$e(0, Y) = \int_0^\infty \ell(t, Y)dt. \tag{14}$$

The average life expectancy at birth e(0) can be calculated by taking the mathematical expectation of the expression for e(0, Y):

$$e(0) = E[e(0, Y)] \tag{15a}$$

$$= \int_0^\infty \ell(t)\ dt. \tag{15b}$$

Let $V_e(0)$ denote the variance of e(0, Y). Then

$$V_e(0) = E[e^2(0, Y)] - e^2(0) \tag{16a}$$

$$= \int_0^\infty \int_0^\infty C_\ell(s, t)\ ds\ dt. \tag{16b}$$

D. Life Table Parameters

The sequence of survival function values $\ell(t)$, $t \in \{0,1,2,\ldots\}$ may be used to form the forecasted cohort life table using the following standard formulas (Chiang, 1984):

$$d(t) = \ell(t) - \ell(t+1) \tag{17}$$

$$q(t) = 1 - \ell(t+1)/\ell(t) \tag{18}$$

$$L(t) = \int_t^{t+1} \ell(u)\ du \tag{19}$$

$$T(t) = \int_t^\infty \ell(u)\ du \tag{20}$$

$$e(t) = T(t)/\ell(t). \tag{21}$$

Replacing $\ell(t)$ in (17)-(21) with $\ell(t, Y)$ results in a corresponding life table for the trajectory Y_0^∞ with parameters $d(t,Y)$, $q(t,Y)$, $L(t,Y)$, $T(t,Y)$, and $e(t,Y)$ whose expectations are $d(t)$, $q(t)$, $L(t)$, $T(t)$, and $e(t)$, respectively, and whose variances are:

$$V_d(t) = V_\ell(t) + V_\ell(t+1) - 2\, C_\ell(t, t+1) \tag{22}$$

$$V_q(t) \simeq \{V_\ell(t+1) + [1 - q(t)]^2 V_\ell(t) - 2[1 - q(t)]\, C_\ell(t, t+1)\}/\ell^2(t) \tag{23}$$

$$V_L(t) = \int_t^{t+1} \int_t^{t+1} C_\ell(s,u)\, ds\, du \tag{24}$$

$$V_T(t) = \int_t^\infty \int_t^\infty C_\ell(s,u)\, ds\, du \tag{25}$$

$$V_e(t) \simeq [V_T(t) + e^2(t)\, V_\ell(t) - 2\, e(t)\, C_{\ell T}(t)]/\ell^2(t), \tag{26}$$

where $C_{\ell T}(t)$ denotes the covariance of $\ell(t, Y)$ and $T(t, Y)$, given by

$$C_{\ell T}(t) = \int_t^\infty C_\ell(t, u)\, du. \tag{27}$$

IV. APPROXIMATIONS BASED ON A DISCRETE TIME MODEL

Calculation of the life table parameters in (17)-(21) requires only that we have the correct values of $\ell_t = \ell(t)$, m_t, and γ_t at integer values of t. These may be estimated using the discrete time form of the model described in Manton et al. (1985). In this form of the model, the continuous time parameters $a_0(t)$, $a_1(t)$, $b(t)$, $Q(t)$, and $\mu_0(t)$ are replaced with the discrete time parameters a_{0t}, a_{1t}, $\Sigma_t = b_t\, b_t'$, Q_t, and μ_{0t}; and Eqs. (1) and (2) are replaced by:

$$Y_{t+1} = a_{0t} + (I + a_{1t})Y_t + b_t\, W_t \tag{28}$$

$$\mu_t(Y_t) = Y_t'\, Q_t\, Y_t + \mu_{0t}. \tag{29}$$

Let $\bar{\mu}_t$ be the mathematical expectation of $\mu_t(Y_t)$. Then

$$\bar{\mu}_t = E[\mu_t(Y_t) \,|\, T>t] \tag{30a}$$

$$= tr[Q_t\, \gamma_t] + m_t'\, Q_t\, m_t + \mu_{0t}. \tag{30b}$$

Let $V_{\mu t}$ be the conditional variance of $\mu_t(Y_t)$ given $\{T>t\}$. Then, following

the arguments leading to (6b) one can show that

$$V_{\mu t} = 2\ \mathrm{tr}[Q_t\ \gamma_t\ Q_t\ \gamma_t] + 4\ m_t'\ Q_t\ \gamma_t\ Q_t\ m_t, \tag{31}$$

where m_t and γ_t satisfy Eqs. (4) and (5).

Let $\ell_t(Y) = \ell_t(Y_0^t)$ be the conditional survival function in the discrete time model,

$$\ell_t(Y) = P(T>t\,|\,Y_0^t) = \exp\{-\int_0^t \mu_u(Y_u)du\}, \tag{32}$$

and let ℓ_t be the unconditional survival function,

$$\ell_t = P(T>t) = \exp\{-\int_0^t \mu_u\ du\}\ . \tag{33}$$

Then a necessary and sufficient condition that $\ell_t = \ell(t)$ for integer values of t, as assumed above, is

$$\int_0^t \mu_u\ du = \int_0^t \bar{\mu}(u)\ du \qquad t\ \varepsilon\{0,1,2,\ldots\} \tag{34a}$$

$$\leq \int_0^t \bar{\mu}_u\ du. \tag{34b}$$

The inequality (34b) is a form of Jensen's inequality (Matis and Wehrly, 1979).

Let $C_{\ell s,t}$ denote the covariance of $\ell_s(Y)$ and $\ell_t(Y)$ in the discrete time model. Then, for $s \leq t$

$$C_{\ell s,t} = E[\ell_s(Y)\ \ell_t(Y)] - \ell_s\ \ell_t \tag{35a}$$

$$= \ell_t^{(s)} - \ell_s\ \ell_t\ , \tag{35b}$$

where $\ell_t^{(s)}$ is obtained from iterative application of the following equations (Woodbury and Manton, 1983a; Manton et al., 1985):

$$\gamma_{t+1}^{(s)} = \Sigma_t + (I+a_{1t})\ (I+2\ \gamma_t^{(s)}\ Q_t^{(s)})^{-1}\ \gamma_t^{(s)}\ (I+a_{1t})', \qquad (\gamma_0^{(s)} = \gamma_0) \tag{36}$$

$$m_{t+1}^{(s)} = a_{0t} + a_{1t}\ m_t^{(s)*}\ , \tag{37}$$

$$\ell_{t+1}^{(s)} = \ell_t^{(s)}\,|I+2\ \gamma_t^{(s)}\ Q_t^{(s)}|^{-\frac{1}{2}} \exp\{-2\ \mu_t^{(s)}\left(\frac{m_t^{(s)} + m_t^{(s)*}}{2}\right) + \left(\frac{\mu_t^{(s)}(m_t^{(s)}) + \mu_t^{(s)}(m_t^{(s)*})}{2}\right)\}, \qquad (\ell_0^{(s)} = 1) \tag{38}$$

where

$$m_t^{(s)*} = m_t^{(s)} - 2(I+2\,\gamma_t^{(s)}\,Q_t^{(s)})^{-1}\,\gamma_t^{(s)}\,Q_t^{(s)}\,m_t^{(s)}, \qquad (m_0^{(s)} = m_0). \tag{39}$$

The functions $\mu_t^{(s)}$ and $Q_t^{(s)}$ are:

$$Q_t^{(s)},\ \mu_{0t}^{(s)} = \begin{cases} 2\,Q_t,\ 2\,\mu_{0t}, & \text{if } t \le s \\ Q_t,\ \mu_{0t}, & \text{if } t > s, \end{cases} \tag{40}$$

$$\mu_t^{(s)}(Y_t) = Y_t'\,Q_t^{(s)}\,Y_t + \mu_{0t}^{(s)} \quad . \tag{41}$$

The variance of $\ell_t(Y)$ is obtained from $V_{\ell t} = C_{\ell t,t}$.

The discrete time model life table parameters d_t, q_t, L_t, T_t, and e_t are defined by replacing $\ell(t)$ in (17)-(21) with ℓ_t; the corresponding life tables for the trajectory Y_0^∞ with parameters $d_t(Y)$, $q_t(Y)$, $L_t(Y)$, $T_t(Y)$, and $e_t(Y)$ are defined by replacing $\ell(t)$ in (17)-(21) with $\ell_t(Y)$. The integration of ℓ_t and $\ell_t(Y)$ in (19) and (20) can be performed with the trapezoidal rule, yielding, for the means of $L_t(Y)$ and $T_t(Y)$:

$$L_t \simeq (\ell_t + \ell_{t+1})/2 \tag{42}$$

$$T_t \simeq \tfrac{1}{2}\,\ell_t + \sum_{u=t+1}^{w-1} \ell_t, \qquad (\ell_t \simeq 0,\ t \ge w); \tag{43}$$

and, for the variances of $L_t(Y)$ and $T_t(Y)$:

$$V_{Lt} \simeq (V_{\ell t} + V_{\ell t+1})/2 + C_{\ell t,t+1} \tag{44}$$

$$V_{Tt} \simeq h^{[t]'}\,C_\ell^{[t]}\,h^{[t]} \tag{45}$$

where $h^{[t]'} = (\tfrac{1}{2},1,\ldots,1)$ is the $(w-t)$ vector containing $\tfrac{1}{2}$ in the first element and 1's elsewhere and $C_\ell^{[t]}$ is the $(w-t) \times (w-t)$ submatrix obtained by deleting the first t rows and columns of $C_\ell = \{C_{\ell s,u}\}$. Corresponding formulas for the variances of $d_t(Y)$, $q_t(Y)$ and $e_t(Y)$ are obtained by replacing the continuous time functions in (22), (23) and (26) with the corresponding discrete time analogues, i.e., $V_{\ell t}$, $C_{\ell s,t}$, q_t, ℓ_t, V_{Tt}, e_t and $C_{\ell Tt}$, where $C_{\ell Tt}$ denotes the covariance of $\ell_t(Y)$ and $T_t(Y)$, i.e.,

$$C_{\ell Tt} = \sum_{u=t}^{w-1} h_u^{[t]} C_{\ell t,u} \quad . \tag{46}$$

V. OBSERVATIONS ON THE LIMITS TO FORECASTS OF SURVIVAL

The evolution of uncertainty in the forecasts of mortality is complex and does not admit readily to pure analysis because of the interdependence of the multiple aspects of the process. For example, Manton et al. (1985) studied how various combinations of diffusion (Σ_t) and regression (a_{0t} and a_{1t}) would affect the trajectory of the observed mortality rate (μ_t). It was found that the mortality rate was relatively insensitive to the magnitude of diffusion as long as diffusion and regression were in approximate equilibrium. Indeed, the trajectory of the mortality rate seemed to be more sensitive to the total variance of the physiological variables than to the particular combination of diffusion and regression which generated that variance. Nonetheless, we can make certain important qualitative observations from an analysis of the variance expressions and their arguments, provided above. Specifically, Eqs. (12) and (13) represent the basic differential equations for the process. For the stable case, when coefficients a_0, a_1, b and Q are constants, one can find the solution of these equations for the conditions $\frac{dm_t}{dt} = 0$ and $\frac{d\gamma_t}{dt} = 0$.

Depending upon the initial conditions, m_0 and γ_0, the time evolution of the variance of both the conditional survival function (Eq. (10)) and the conditional life expectancy (Eq. (26)) can occur over time in complex ways. For example, since the variance calculations in (10) involve the force of selection (i.e., Q), the variance of the conditional survival probability $\ell(t, Y)$ is initially $V_\ell(0) = 0$, followed by an increase to some peak value, followed by a decline ultimately to $V_\ell(\infty) = 0$. We note that the variance of $\ell(t, Y)$ also is governed, in part, by the process governing change in the means and covariances of the physiological variables. In Eq. (10) we have quadratic forms involving both $m_t^{(s)}$ and $\gamma_t^{(s)}$ as well as m_t and γ_t (compare (4) and (5) with (12) and (13)).

The expressions $m_t^{(s)}$ and $\gamma_t^{(s)}$ correspond to the survival function associated with the mortality rate $\mu^{(s)}(t, Y)$ in (7b). For $V_\ell(t)$, the coefficients for this expression will be twice as large (i.e., 2 Q(t) and 2 $\mu_0(t)$) as the normal hazard rate $\mu(t, Y)$. Since $E[\ell(t,Y)\ \ell(t,Y)]$ is the first term in (10) this means that increases in age specific mortality will tend to decrease the age at which the peak value of $V_\ell(t)$ occurs. This effect is further promoted by the process governing change in $m_t^{(s)}$ and $\gamma_t^{(s)}$ (i.e., (12) and (13)). Again, mortality operates to reduce both sets of parameters. This is because the terms involving mortality rates in (12) and (13) are twice as large as in (4) and (5). Thus mortality selection will tend to have a strong variance controlling effect--both through the direct effect of mortality and through the indirect effect of risk factor dynamics on the expectation of the squared conditional survival function, $\ell(t, Y)$. This suggests that the time dependence of the variance of the conditional survival probabilities is more complex than in the case of physical systems because of the changing equilibrium with time and age of mortality and risk factor dynamics.

VI. EXOGENOUS FACTORS AND THEIR EFFECT ON MORTALITY FORECASTS

To this point we have discussed uncertainty which results from individual heterogeneity and the evolution of individual characteristics over time. It is apparent that there are many factors that are exogeneous to the individual that will impact upon his survival. For example, environmental pollution may adversely affect the survival chances of an individual, as may changes in economic conditions. Since these forces are often observable it will be useful to include their effects in mortality forecasts and in estimates of the uncertainty of the mortality forecasts. This can be done simply by extending the vector Y_t to include such environmental factors.

For example, suppose that climatic factors influence human mortality.

We could include temperature and other climatic variables in the vector Y_t. The equations describing changes in the exogenous component of Y_t would be those that describe seasonal and other changes in temperature, whereas the changes in the endogenous component of Y_t could be modeled as dependent on the exogeneous component. If, as a first approximation, we assume that all persons are affected equally by changes in temperature then we only need to estimate one term in the quadratic hazard for temperature. On the other hand, it is more likely that temperature would have a greater effect on certain population groups (e.g., the elderly) in which case interaction terms involving temperature and age (or other relevant variables) would have to be included in the hazard function. This would imply a more rapid selection of certain groups under certain changes in the temperature component of Y_t. The dynamic equations describing the change of temperature (or some other exogeneous factor) would not, however, be affected by mortality selection so that no further modification of the time series equations for forecasting temperature would be necessary. Similarly the effects of a whole range of exogenous factors might be represented in mortality forecasts and in estimates of the uncertainty of those forecasts, where the added stochasticity was not due to the diffusion process describing the physiological changes of the individual but to the uncertainty of the climate forecasts. Similarly macro-economic variables could be included as elements of Y_t, where each person is impacted by economic factors, where mortality does not affect Y_t, and where estimates of the trajectory and uncertainty of the economic components are generated by a macro-economic simulation analysis.

VII. DISCUSSION AND SUMMARY

We have developed variance formulas for the conditional mortality rates, conditional probabilities and conditional life expectancies for the case where mortality depends upon a set of physiological variables whose

change is driven by a Gaussian diffusion process. This represents a considerable extension of the variance formulas for P2-stochasticity provided by Matis and Wehrly (1979) for the case of a fixed frailty life table model, and recognizes the variability of forecasts due to the physiological heterogeneity of the population and the diffusion of that heterogeneity.

The formulas derived can be easily calculated and the coefficients of the basic process can be estimated using maximum likelihood procedures for longitudinal data (e.g., Manton et al., 1985; Yashin et al., 1985b). Thus the model represents a potentially useful tool for the empirical analysis of the uncertainty of mortality in a human cohort. Moreover, an evaluation of the form of the equations shows that the uncertainty in forecasts of human mortality processes propagates very differently through time than does the uncertainty of forecasts of the future state of certain physical systems, e.g., weather. This is because the interaction of risk factor dynamics and selective mortality represents a more complex set of dynamic forces. For example, in our analysis of Eqs. (10) - (13) we showed that one effect of mortality selection will be that the variance of $\ell(t, Y)$ will decrease after an initial rise. These equations suggest that models for forecasting uncertainty in human survival will require the development of analytic approaches different from those used in many physical systems.

The variance calculations presented in this paper can be extended to the case where mortality is influenced by factors exogenous to the physiology of the individual organism. For example, certain variables at the societal level (e.g., sanitation, environmental quality, water quality, level of health services, level of economic development) can have an effect on mortality. If one can specify the form of the dependency of mortality on these exogenous factors, then their effects on the mortality forecasts and on the uncertainty of those forecasts can be determined from the

equations above in two ways. First, one can assume that such exogenous factors affect all persons equally (i.e., their effect on the population is homogeneous). In this case we can include an exogenous component in the set Y_t which is the same for all persons but which changes according to some specified process, with some associated diffusion or uncertainty. Thus both the uncertainty and secular trend of exogeneous factors may be included in the mortality forecasts and in their anticipated uncertainty. Second, one may introduce the exogenous factors into the set Y_t and assume that there is a differential effect on mortality or on endogeneous risk factor dynamics over the population. In this case a population component more sensitive to economic or sanitary conditions may be more rapidly selected from the population. Thus the variance computations provided herein can reflect uncertainty arising from both physiologically endogenous and exogeneous processes.

REFERENCES

Chiang, C.L. 1984. "The Life Table and Its Application," Robert E. Krieger, Malabar, Florida.

Manton, K.G., and Stallard, E. 1980. A stochastic compartment model representation of chronic disease dependence: Techniques for evaluating parameters of partially unobserved age inhomogeneous stochastic processes, Theor. Pop. Biol. 18, 1, 57-75.

Manton, K.G., and Stallard, E. 1981. Methods for evaluating the heterogeneity of aging processes in human populations using vital statistics data: Explaining the black/white mortality crossover by a model of mortality selection, Human Biol. 53, 1, 47-67.

Manton, K.G., and Stallard, E. 1984a. "Recent Trends in Mortality Analysis," Academic Press, Orlando, Florida.

Manton, K.G., and Stallard, E. 1984b. Heterogeneity and its effect on mortality measurement, Chapter 12 in "Methodologies for the Collection and Analysis of Mortality Data," Vallin, J., Pollard, J.H., and Heligman, L., Eds., International Union for the Scientific Study of Population Ordina Editions, Leige, Belgium, pp. 265-299.

Manton, K.G., Stallard, E., and Woodbury, M.A. 1985. Chronic disease evolution and human aging: A general model for assessing the impact of chronic disease in human populations, Internat. J. Math. Modeling, Special Issue on Mathematical Modeling of Diseases, Witten, M., Ed., forthcoming.

Manton, K.G., and Woodbury, M.A. 1983. A mathematical model of the physiological dynamics of aging and correlated mortality selection: II. Application to the Duke Longitudinal Study, J. Gerontol. 38, 4, 406-413.

Manton, K.G., and Woodbury, M.A. 1985. A continuous-time multivariate Gaussian stochastic process model of change in discrete and continuous state variables, in "Sociological Methodology, 1985", Tuma, N., Ed., Jossey-Bass, forthcoming.

Matis, J.H., and Wehrly, T.E. 1979. Stochastic models of compartmental systems, Biometrics, 35, 199-220.

Seber, G.A. 1977. "Linear Regression Analysis," Wiley, New York.

Tyroler, H.A., Knowles, M.G., Wing, S., et al. 1984. Ischemic heart disease risk factors and 20-year mortality in middle age Evans County black males, Am. Heart J., 108, 3, 738-746.

Vaupel, J.W., Manton, K.G., and Stallard, E. 1979. The impact of heterogeneity in individual frailty on the dynamics of mortality, Demography 16, 3, 439-454.

Woodbury, M.A., and Manton, K.G. 1977. A random-walk model of human mortality and aging, Theor. Pop. Biol. 11, 1, 37-48.

Woodbury, M.A., and Manton, K.G. 1983a. A theoretical model of the physiological dynamics of circulatory disease in human populations, Human Biol. 55, 2, 417-444.

Woodbury, M.A., and Manton, K.G. 1983b. A mathematical model of the physiological dynamics of aging and correlated mortality selection: I. Theoretical development and critiques, J. Gerontol. 38, 4, 398-405.

Yashin, A.I., Manton, K.G., and Vaupel, J.W. 1985a. Mortality and aging in a heterogeneous population: A stochastic process model with observed and unobserved variables, Theor. Pop. Biol. 27, forthcoming.

Yashin, A.I., Manton, K.G., and Stallard, E. 1985b. Evaluating the effects of observed and unobserved diffusion processes in survival analysis of longitudinal data; in review at J. Applied Probability.

APPENDIX

The proof of the theorem is facilitated by the following auxiliary lemma (Seber, 1977).

Lemma. Let $z' = (z_1,\ldots,z_n)$ be independently Gaussian distributed according to $N(0, \sigma^2 I)$ where I is the n x n identity matrix, and let A be an n x n symmetric matrix. Then

$$E[(z'A\,z)^2] = 2\,\sigma^4\,\mathrm{tr}\,A^2 + \sigma^4(\mathrm{tr}\,A)^2 .$$

Proof. Switching to scalar notation, we have

$$E[(z'A\,z)^2] = \sum_i \sum_j \sum_k \sum_\ell a_{ij}\,a_{k\ell}\,E(z_i\,z_j\,z_k\,z_\ell).$$

Observe that the independence of the components of z yields

$$E(z_i\,z_j\,z_k\,z_\ell) = \begin{cases} \sigma^4, & \text{for } i=k,\ j=\ell,\ j\neq k \\ \sigma^4, & \text{for } i=\ell,\ j=k,\ j\neq \ell \\ \sigma^4, & \text{for } i=j,\ k=\ell,\ j\neq k \\ m_4, & \text{for } i=j=k=\ell \\ 0, & \text{otherwise,} \end{cases}$$

where m_4 is the fourth moment of the distribution of z_i. This allows one to write

$$E[(z'A\,z)^2] = \sigma^4 \sum_i \sum_j a_{ij}^2 + \sigma^4 \sum_i \sum_j a_{ij}\,a_{ji} + \sigma^4 \sum_i \sum_k a_{ii}\,a_{kk} + (m_4 - 3\,\sigma^4) \sum_i a_{ii}^2 .$$

Switching back to matrix notation, one can see that the first term is σ^4 tr A^2, as is the second term, because $a_{ji} = a_{ij}$; the third term is $\sigma^4(\mathrm{tr}\,A)^2$; the fourth term is zero, because $m_4 = 3\sigma^4$ in the case of a Gaussian distribution. Making these changes, one obtains the result.

Corollary. Let $x' = (x_1,\ldots,x_n)$ be independently Gaussian distributed according to $N(\theta, \sigma^2 I)$, and let A be an n x n symmetric matrix. Then

$\mathrm{Var}(x'A\,x) = 2\,\sigma^4\,\mathrm{tr}\,A^2 + 4\,\sigma^2\,\theta'\,A^2\,\theta.$

Proof. From the definition of variance, we have

$$\mathrm{Var}(x'A\,x) = E[(x'A\,x)^2] - E^2(x'A\,x). \tag{C1}$$

Let $z = x-\theta$, so that $z \sim N(0, \sigma^2 I)$. We evaluate each term in (C1) separately.

$$\text{(a)}\quad E(x'A\,x) = E[z'A\,z + 2\,\theta'A\,z + \theta'A\,\theta]$$

$$= \sigma^2\,\mathrm{tr}\,A + \theta'A\,\theta \tag{C2}$$

$$\text{(b)}\quad E[(x'A\,x)^2] = E[(z'A\,z)^2 + 4\,(\theta'A\,z)^2 + 2\,\theta'A\,\theta\,z'A\,z$$

$$+ (\theta'A\,\theta)^2 + 4\,\theta'A\,z\,z'A\,z + 4\,\theta'A\,\theta\,\theta'A\,z]. \tag{C3}$$

The first term in (C3) is given in the lemma; the second term evaluates to $4\,\sigma^2\,\theta'\,A^2\theta$; the third term evaluates to $2(\theta'A\,\theta)\,\sigma^2\,\mathrm{tr}\,A$; the fourth term evaluates to $(\theta'A\,\theta)^2$; the fifth and sixth terms evaluate to zero because $E(z_i) = 0$ and $E(z_i\,z_j\,z_k) = 0$, all i, j, k. Hence,

$$E[(x'A\,x)^2] = 2\,\sigma^4\,\mathrm{tr}\,A^2 + 4\,\sigma^2\,\theta'\,A^2\theta + \sigma^4(\mathrm{tr}\,A)^2$$

$$+ 2\,(\theta'A\,\theta)\,\sigma^2\,\mathrm{tr}\,A + (\theta'A\,\theta)^2. \tag{C4}$$

Observe that the sum of the third, fourth, and fifth terms is equal to the square of $E(x'A\,x)$ in (C2). Hence, from (C1), the first two terms of (C4) give the variance.

Proof of the Theorem. In this proof we suppress the index t for notational simplicity. By assumption, $Y' = (Y_1,\ldots,Y_n)$ is Gaussian distributed according to $N(m,\gamma)$, where γ is an n x n positive definite symmetric matrix. Hence, there exists a nonsingular n x n matrix R and a random vector $x' = (x_1,\ldots,x_n)$ such that

$\gamma = R\,R'$ and $Y = R\,x$,

where x is independently Gaussian distributed according to $N(R^{-1}\,m,\ I)$.

Let Q be an n x n nonnegative definite symmetric matrix and let the matrix $A = R'Q\,R$. It follows that A is also an n x n nonnegative definite symmetric

matrix.

Let $\mu(Y)$ be the nonnegative definite quadratic function of Y:

$$\mu(Y) = Y' Q Y + \mu_0$$

$$= x' A x + \mu_0.$$

In accordance with the result of the corollary to the lemma, one can write:

$$\text{Var}[\mu(Y)] = \text{Var}[x'A x]$$

$$= 2 \text{ tr } A^2 + 4 m'(R^{-1})' A^2 R^{-1} m$$

$$= 2 \text{ tr } (R' Q R R'Q R) + 4 m' Q R R' Q m.$$

By replacing tr(R' Q R R'Q R) with tr (Q R R' Q R R') and R R' with γ, one obtains the result of the theorem given in Eq. (6b).