A parametric approach to modeling health transitions

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Abstract
We present a novel approach to summarizing health transitions as a stochastic process of changes in health states. Instead of analyzing health transitions separately in each direction (improvement, worsening and death) we suggest a general parametric approach which allows estimating the probabilities of changes as a function of the current state. From the four population specific parameters, two represent health transition of survivors, and two represent the probability of death. The approach is illustrated in the representative Canadian population: (i) transitions in general health status (deficits accumulation), (ii) transitions in cognitive states represented by the errors in the Modified Mini Mental Scale Examination Score, and (iii) transitions between cognitive impairments of different degrees. The performances of the models are very high, R^2 ranging from 0.89 to 0.99, and robust across settings. This approach has a potential for the wide range of applications in analyzing age-related health transitions.

Background
We have modeled health related changes between two assessments as a stochastic process of the accumulation of deficits and demonstrated in different settings that a modified four-parametric Poisson model fitted the large amount of observational data with very high precision (R^2 >0.95). As cognitive impairment increases with age, as do deficits in general, we wondered whether the patterns of general deficit accumulation might also obtain with decrements in cognition. As the accuracy of the Poisson model in representing transitions in health is limited when the number of states is small (<~10), we therefore also investigated changes in the model to replace the Poisson model with a more general binomial model.

Methods
Population
The data come from the Canadian Study of Health and Aging (CSHA). Briefly, in 1990-91, during the first wave of the study (CSHA1) 9,008 community-dwelling people age 65 and over were assessed using a self-report questionnaire, of whom complete data are available for 5,586 survivors for the second wave (CSHA-2, conducted in 1995-1996) and 3,211 for the third wave (CSHA-3, conducted in 2000-2001). Complete mortality follow-up is available, so we know that 1,821 people died in the 60-month interval between CSHA-1 and CSHA-2, and an additional 1,488 between CSHA-2 and CSHA-3. Of 2,305 people in clinical examination sample, 2199 people had information about the Modified Mini Mental State examination (3MS), 1024 of them died within 5 years follow up. The cognitive diagnoses were available for 1,072 at baseline (517 without cognitive impairment, 319 with some cognitive changes but no dementia, 98 with mild dementia, 97 with moderate and 47 with severe dementia). Of these 1,072 people 518 died before the next assessment.

Measures

Deficit accumulation count: Thirty one health related variables were available for each of the three waves of the study. The variables are almost evenly distributed between diseases and disabilities [1]. The state is defined by the number of deficit present and thus, the number of states including death is thirty two.

3MS-errors: We consider the errors on the 100-point 3MS score grouped as sequential 2-error states. Thus, we consider that the "0" state is defined as 0, 1 error (corresponding to 3MS scores=100, 99). Likewise, the "1" state represents 2, 3 errors and so on until 3MS≤49 after which low numbers of people with those scores meant that they were combined in the 26th sate. The number of states including death is twenty seven.

Diagnostic classes: No cognitive impairment (coded as a zero state), Cognitive impairment but no dementia (coded as a 1-state), mild, moderate/severe dementias coded as 2,and 3-states respectively. The number of state including death is five.

The empirical transition probability matrices between the different states of health were calculated from the survey data.

The Poisson model

The transitions between the states were modeled using a modified Poisson distribution [Mitnitski et al., 2006; Mitnitski et al., 2007a,b; Mitnitski and Rockwood, 2008]:

$$P_{nk} = \frac{\bar{k}_n^{\,k}}{k!}\exp(-\bar{k}_n)\cdot(1-P_{nd}), \qquad (1)$$

where $\bar{k}_n$ is a positive parameter (which is the mean number of deficits after transition from the state with n deficits) that linearly increases with n:

$$\bar{k}_n = \alpha_1 + \beta_1 n \qquad (2)$$

and the probability of death is a linear function of n:

$$P_{nd}=\exp(\alpha_2+\beta_2 n) \qquad (3)$$

($P_{nd}\leq 1$). The Poisson model, by its nature, can be applied when the number of states is relatively large (>10) otherwise more general binomial model is considered.

The binomial model

If the number of states is small (e.g.,<10) a modified binomial model is proposed:

$$P_{nk} = \binom{N}{k}^{k} p_n^k (1-p_n)^{N-k}(1-P_{nd}) \qquad (4)$$

where p_n is the one-step transition probability which depends linearly of n:

$$logit\,(p_n)=\alpha_1+\beta_1 n \qquad (5)$$

and the probability of death is the same as in equation (3).

Each model has four parameters, the background parameters: α_1, α_2, and the increments: β_1, β_2. The parameters were estimated from observational data using a nonlinear least squares fitting procedure in Matlab 7.4. Goodness of fit of the model was evaluated using R^2.

Results & Discussion

Table 1, shows the estimates of the parameters for three models: (i) the Poisson model for the general deficits accumulation, (ii) the Poisson model for the 3MS errors, and (iii) the binomial model for the dementia diagnoses. For the binomial model, the value of the first background parameter α_1 =-2.35 corresponds to p_0=0.095. The probabilities of 5-year transitions in the 3MS-error states are shown in Figure 2 A, and the probability of death as a function of cognitive state is shown in Figure 1B. The result of modeling transitions between different dementia states is shown in Figure 2 (panel A for transitions among the survivors and panel B for the probabilities of death).

Our approach of summarizing changes of health over time and capturing both degradation and repair is equally applicable to transitions in general health status (as (represented by deficits accumulations) and to cognitive changes. The probability of the changes in any direction (improvement or worsening to any degree, and death) are calculated, given the initial health and cognitive state. Four population specific parameters can be characterized and compared. The model fit is high in all settings suggesting its generalizability.

Our results are consistent with the view that changes in health might be characterized based on the dynamics of these measures. These dynamics indicate that the similar stochastic process underlies such changes. What this stochastic mechanism is and how it can be revealed for the other measures requires additional elaboration, and is motivating further inquires by our group.

Acknowledgements

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References

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Table1 1

Estimates of parameters, and goodness of fit for the transitional probabilities and death according to equations (1)-(5)

	Deficits accumulation Index	3MS-errors	Clinical diagnoses (dementias)
α_1	1.77 (1.67, 1.87)	0.70 (0.54, 0.87)	-2.35 (-2.75,-1.96)
β_1	0.82 (0.78, 0.86)	1.07 (1.02, 1.13)	1.61 (1.37, 1.85)
α_2	-2.15 (-2.23, -2.07)	-1.02 (-1.07, -0.96)	-0.77 (-0.87, -0.67)
β_2	0.16 (0.15, 0.17)	0.03 (0.02, 0.03)	0.08 (0.04, 0.11)
r	0.99	0.94	0.98
R^2	0.98	0.89	0.97
N*	9,008	2,199	1,072

*N is the number of people in the sample at baseline.

Figure 1 Panel A. The probability of transition (vertical axis) from a given 3MS-error state *n* (shown in each subplot) to *k* deficits (horizontal axis). Dots represent observed transitions between two assessments. The lines show the model's fit according to equations (1)-(3). The data are truncated at state 11. Panel B. The probability of death as a function of the cognitive state. Dots are observational data and the line is the models fit (equation (3)).

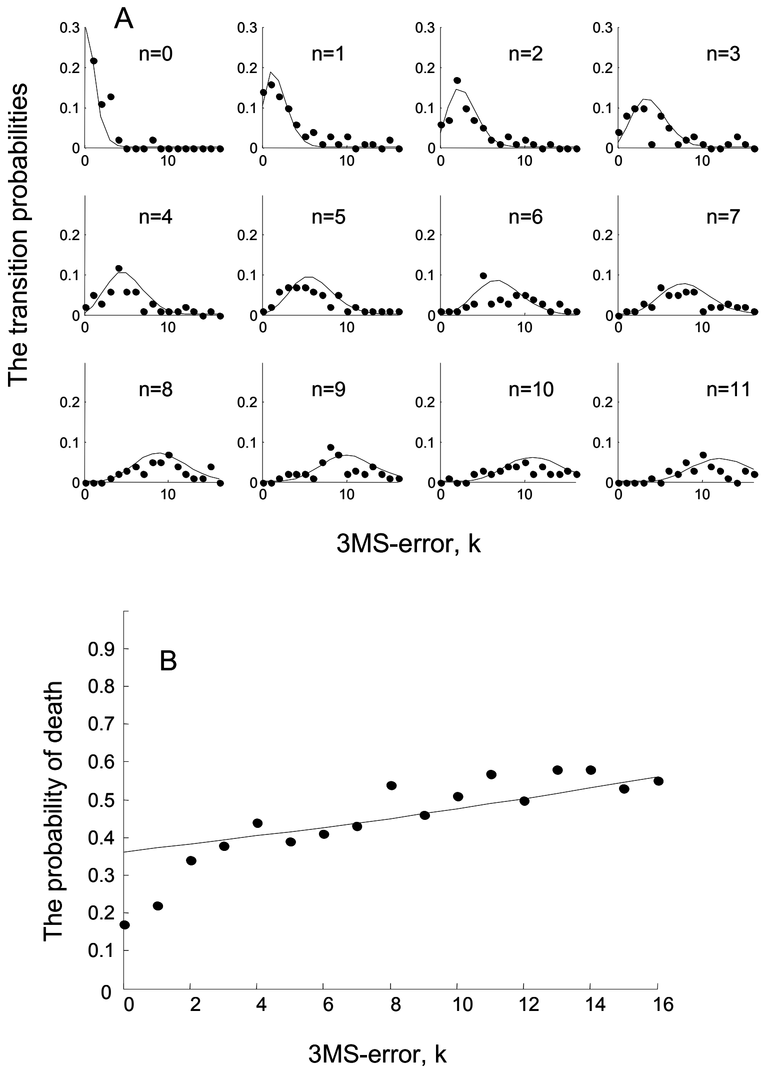

Figure 2 Panel A. The probability of transition (vertical axis) from a given diagnostic state *n* (shown in each subplot) to the other state (horizontal axis). Solid circles represent observed transitions between two assessments. The empty circles (connected with the dotted lines) show the model's fit according to equations (3)-(5). Panel B. The probability of death as a function of the diagnostic state. Dots are observational data and the line is the models fit (equation (3)).