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A cross-national study of transitions in deficit counts in two birth cohorts: Implications for modeling ageing

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Abstract

Generally, health does not improve with age, and many physical and physiological functions are known to decline. These changes do not occur uniformly, however; for many reasons, some people experience significant improvement in their health over non-trivial time intervals. Earlier, we showed that 5-year transitions in health status in elderly people (age 65+ years) can be modeled as a stochastic process, using a modified Poisson distribution with four readily interpretable parameters. The original description was based on follow-up of a single cross-sectional study, thus mixing age and cohort effects. Here, we again used a multistate Markov chain to model 5-year deficit accumulation in relation to frailty in both a Swedish birth cohort (aged 70 years at inception) and, from the original cross-sectional study, a Canadian birth cohort, aged 69–71. In both datasets, we found again that a modified Poisson describes the transition in health status with high precision. The parameters of the model though different, are close to each other, even though the cohorts are from different countries, were assembled 20 years apart, and counted different deficits. The model suggests that all health transitions, including health improvement, worsening, and death, can be summarized in a unified stochastic model with a few interpretable parameters.

Keywords: Ageing; Health transitions; Multistate stochastic model; Markov chain; Frailty

1. Introduction

Ageing is associated with the accumulation of deficits. At the sub-cellular level, a range of altered proteins have been identified (Hipkiss, 2006). In humans, individuals accumulate deficits (symptoms, diseases, disabilities) at an average rate that is similar across developed countries (Mitnitski et al., 2005), and that has characteristic maximum limits (Rockwood and Mitnitski, 2006). Still, the number of deficits present in given individuals varies considerably between people of the same age, which likely reflects varying degrees of fitness and frailty (Rockwood et al., 2004). In general, the more deficits an individual has, the frailer that person is. This level of frailty is reflected by an increased risk of adverse health outcomes, including death (Mitniski et al., 2001; Goggins et al., 2005) institutionalization (Mitnitski et al., 2005; Rockwood et al., 2006) and the use of hospital and community service (Jones et al., 2005; Woo et al., 2006). These relationships hold even though the items used to calculate the frailty index vary between samples, suggesting that, as at subcellular levels, deficit accumulation itself is an important – and measurable – phenomenon for individuals. In a series of publications, summarized in a forthcoming review (Rockwood and Mitnitski, accepted) we have also demonstrated that it has characteristic changes with age in its distribution, a decline in relative variability with age, and the ability to be readily summarized for clinical use.

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Although in general ageing is highly correlated with deficit accumulation, individuals can improve their health – for example, by taking up exercise (United States Department of Health and Human Services, Centers for Disease Control and Prevention, 1996). Such improvement can be captured in our model by a decrease in the deficit count. Recently, we demonstrated that the transitions between the number of deficits – both increases (worsening) and decreases (improvement) – can be modeled as a Markov chain (Mitnitski et al., 2006). There, transitions between health states were represented by a modified Poisson distribution with 4 parameters. Those data, however, came from the follow-up of a cross-sectional study, and thus are susceptible to bias from age effects. Here, we extend the analyses to two birth cohorts, where the impact of frailty, expressed as variable deficit accumulation is clearer. Our objective was to compare the 5-year transitional probabilities between two national datasets.

2. Methods

2.1. Population and variables

The Canadian Study of Health and Aging (CSHA) is a representative cohort study of 10,263 people aged 65+ in 1990–91 (Canadian Study of Health and Aging Working Group, 1994); their frailty characteristics and consecutive assessments have been described elsewhere (Rockwood et al., 2005; Mitnitski et al., 2006). Here, we used 31 variables from the CSHA that were recorded in a self-report questionnaire, and that were available for both waves as evaluated previously (Mitnitski et al., 2006). The questionnaires were administered to 1036 people (including 660 women) aged 69 to 71. Of these 1036, 151 died in 60 months; all 885 survivors completed these questionnaires again in 1995–1996. The variables were almost evenly distributed between diseases and disabilities (Mitnitski et al., 2006), (Appendix 1A).

The longitudinal Gothenburg study of 70-year-olds (H70) (Steen and Djurfeldt, 1993; Skoog et al., 1993) evaluated a birth cohorts of people aged 70 in 1971–72, who were followed up in 1976–77. Of 973 people (including 518 women) 965 had complete data, of whom 209 died in 60 months. Of the 130 available health related variables, we selected 31, to correspond to the same number as in the CSHA data sample. Although some variables were similar to those used in the CSHA dataset, others were different (e.g., laboratory abnormalities and social interactions) (Appendix 1B). The fact that the two cohorts used different variables matters less than might be assumed. For example, we have shown that, however constructed, these variables reveal characteristic rates of accumulation of deficits (Mitnitski et al., 2005). Recently too, we compared variable compositions of the frailty index between these two birth cohorts. Obviously, we found that comparability of estimates in longitudinal studies requires that, within any given cohort, the same variables are used to count deficits at baseline and at follow-up. Less obviously, we also found that, in general, the nature of the variables selected is less important than the number of variables that is presented – in other words, that the variables which make up the set to be considered as deficits can be chosen from the larger set *at random*, with comparable results in estimating the risk of adverse outcomes (Rockwood et al., 2006).

2.2. Statistical analysis

To estimate the parameters of the model and their confidence intervals, a nonlinear fitting procedure was used. The codes were written in Matlab 7.1 (Matworks Inc.). Goodness of fit was evaluated using R^2.

3. Results

Fig. 1 illustrates the general schema as a Markov chain of transitions between the different health states (S_i, $i = 0,1,2,3,\ldots$) including death (D). Let the health status of an individual be represented by the number of deficits, 'n' present at the time of the baseline assessment. Let P_{nk} be the probability that an individual with n deficits at the baseline assessment has 'k' deficits at the time of the follow-up assessment, and let P_{nd} be the probability to die before the follow-up assessment. We have suggested (Mitnitski et al., 2006) that the transition probabilities between the different numbers of deficits can be approximated as follows:

$$P_{nk} = \frac{\rho_n^k}{k!} A_n \cdot (1 - P_{nd}), \tag{1}$$

where A_n is the normalization constant:

$$A_n = (1 - P_{nd}) / \sum_k \frac{\rho_n^k}{k!}. \tag{2}$$

If a large number of deficits is allowed, the transition probabilities P_{nk} can be further approximated as a modified Poisson distribution (Mitnitski et al., 2006):

$$P_{nk} = \frac{\rho_n^k}{k!} \exp(-\rho_n) \cdot (1 - P_{nd}), \tag{3}$$

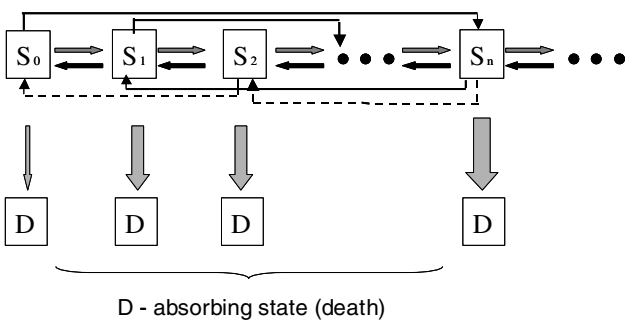

Fig. 1. Schematic representation of the chain transitions between different health states (S_i, $i = 0,1,2,3,\ldots$) differed by the number of accumulated deficits, and death (D). The width of the vertical arrows corresponds to an increasing chance of death.

Table 1
Estimates of parameters, and goodness of fit, for the transitional probabilities and death according to Eqs. (1)–(4)*

	H70 (age 70)	CSHA (age 69–71)	CSHA (age 65+)
ρ_0	2.31 (2.06, 2.56)	1.79 (1.52, 2.07)	1.77 (1.67,1.87)
β_1	0.67 (0.60, 0.74)	0.79 (0.69, 0.88)	0.82 (0.78, 0.86)
$\ln(P_{0d})$	−2.22 (−2.42, −2.03)	−2.84 (−3.19, −2.50)	−2.15 (−2.23,−2.07)
β_2	0.12 (0.09, 0.14)	0.19 (0.15, 0.22)	0.16 (0.15, 0.17)
r	0.93	0.91	0.99
R^2	0.87	0.83	0.98

* Parameters in the last columns were obtained for the whole CSHA sample (Mitnitski et al., 2006).

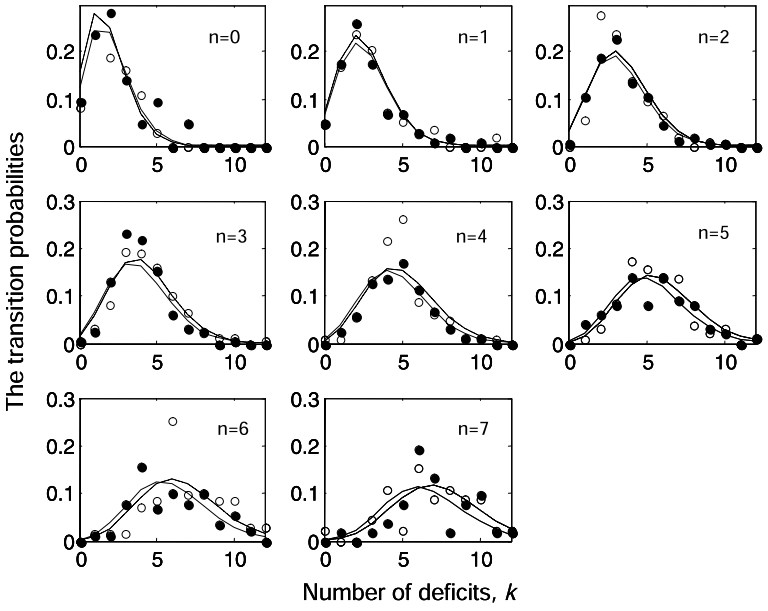

Fig. 2. The probability of transition from n to k deficits in relation to the starting n deficits (the first seven transitions are presented). Circles represent observational data of 5-year transitions for CSHA (empty circles) and H70 (filled circles) and lines represent the model fit (dashed lines for CSHA, and solid lines for H70). Note that as the graph represents absolute probabilities, the areas under the curve decrease with the starting number of deficits, reflecting the increased risk of death.

where ρ_n is positive parameter that depends on the current state n and linearly increases with n: $\rho_n = \rho_0 + \beta_1 n$, and the probability of death increases exponentially:

$$P_{nd} = P_{0d}\exp(\beta_2 n) \tag{4}$$

($P_{nd} \leqslant 1$). The parameters: ρ_0,P_{0d}, (*the background components*) and β_1, and β_2 (*the increments*) can be estimated from observational data (these supplementary data are available at http://myweb.dal.ca/amitnits/trans2.htm). Of note, fewer than 5% of people had more than 11 of the maximum 31 deficits.

Table 1 shows the estimates of the parameters for the model for each dataset; for comparison, the whole-sample CSHA estimates are also presented. The parameters for the CSHA cohorts are close to each other, except the background mortality, which is lower for those aged 69–71 cohort than in the entire cohort. In contrast, the parameters for H70 cohort are different from the age 69–71 cohort, except the increment parameter β_1. The probabilities of 5-year transitions between the different numbers of deficits are displayed in Fig. 2 as is the probability mortality by 5 years.

4. Discussion

How to model ageing as a stochastic process using actual biomedical data – and not just demographic information – is a question of some interest. In each of the two population-based cohorts considered here, the process of ageing, summarized as the transition probabilities between health states, could be modeled by a modified Poisson distribution with very good accuracy (Table 1). While the parameters of the distributions are different between the two samples, the differences are not dramatic (Fig. 2) especially given the relatively small sample sizes. Moreover, the cohorts are from two different countries, and were assembled about 20 years apart (Fig. 3).

Our data must be interpreted with caution. We have combined items across levels of deficit severity, without differential weighting. In general, our experience is that weighting items (for example, assigning a higher weight

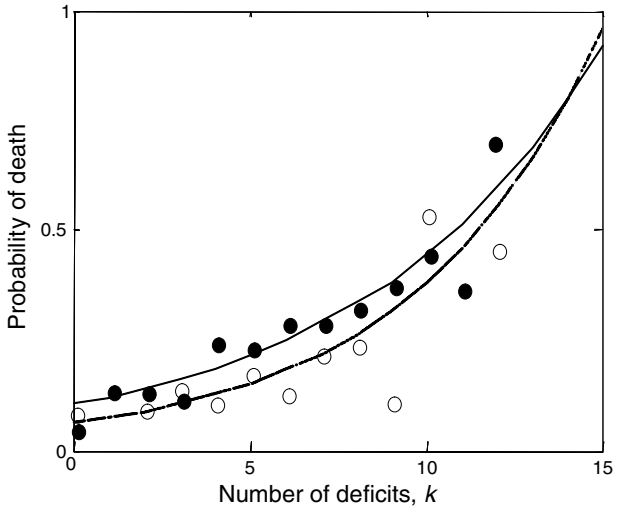

Fig. 3. The 5-year probability of death, given n deficits at baseline. Circles represent observational data of 5-year transitions for CSHA (empty circles) and H70 (filled circles) and lines represent the model fit (dashed lines for CSHA, and solid lines for H70).

to cancer than to skin disease) can increase the accuracy of mortality prediction, but at the expense of limited generalizability (Song et al., 2004). It is also important to remember that our goal is not mortality prediction, but a parsimonious description of how changes in health occur with age. Moreover, the very high fit of our model suggests that the method works well enough as a first approximation, considering the nature of the data. In addition, we have only considered transitions at five years. How these transitions extend over shorter periods is not yet clear.

That the change in the number of deficits that people have should conform to a stochastic process is not surprising. General theoretical models that include essential stochastic components have been proposed (Gavrilov and Gavrilova, 2001; Yashin et al., 2001) and a stochastic accumulation of sub-cellular deficits represents a chief theory of ageing (Kirkwood et al., 2000; von Zglinicki et al., 2001). Still, how best to model specific stochastic processes of changes in health at the level of the whole organism has not been clear. Here, we have suggested a multistate model of health transitions that is based on biomedical characteristics at the level of whole organism. In contrast to some earlier models, we have not speculated about the processes underlying these changes in health states. On the other hand, such speculations about mechanism typically introduce additional, theoretical parameters in order to make the model fit, whereas we have restricted ourselves to observable data, and yet have still obtained excellent fit with few parameters. Their generalization is more likely, given that these few parameters appear to be reproducible, and still hold when age as a source of variability has been eliminated by the cohort design.

In addition, the generalizability of our approach is aided by the comprehensibility of the results. For example, given the number of deficits for a 70 years old person, the expected number of deficits he or she is likely to have five years later is linearly predictable. For a person with n deficits, the expected number of deficits at age 75 is $2.31 + 0.67n$ for H70 data; and $1.79 + 0.79n$ for CSHA data. It is of interest that a limit is observed here, as before (Rockwood and Mitnitski, 2006) – Canadians with more than seven deficits and Swedes with more than eight deficits (from the total 31 deficits considered) are hardly likely to increase their number of deficits very much, as the mortality rate at these deficit levels more than quadruples from the baseline risk to about 33% in 5 years. The probability of dying P_{nd} depends on the number of deficits at baseline $P_{0d} = e^{a_2}$ and therefore $P_{nd} = P_{0d}e^{b_2 n}$ ($P_{0d} = 0.108$ for H70 and 0.058 for CSHA). Thus for a Swede with 5 deficits at baseline, the probability of dying of $0.108e^{0.116(5)} = 0.19$; for a Canadian with 5 deficits at baseline, the probability of dying of $0.058e^{0.187(5)} = 0.15$.

The background mortality of Canadians is lower than Swedes, which might reflect secular trends – for example, the fact that Canadians were assessed just over 20 years later than the Swedes. Despite these differences, the general law governing transitions in relative health states satisfy the same modified Poisson stochastic mechanisms we observed earlier. An additional implication of our model is that, at any state of health, improvement is possible. By allowing transitions to states with fewer deficits, we can quantify the chance of health improvement. For example, the probability of moving to the state of zero deficits exponentially decreases with n: $P_{n0} = e^{-(\rho_0 + b_1 n)}(1 - P_{0d}e^{b_2 n})$.

Our data are consistent with the view that the ageing process might be characterized based on the dynamics of deficit accumulation. In principle, the stochastic processes that might result in damage to macromolecules and thereby give rise to deficit accumulation at the cellular and tissue levels can be so modeled. Whether, the model that we have described generalizes to these levels requires additional elaboration, and is motivating further inquiries by our group.

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Appendix 1A. List of deficits CSHA

1. Eyesight
2. Hearing
3. Help to eat
4. Help to dress & undress
5. Ability to take are of the appearance
6. Help to walk
7. Help to get in & out of bed
8. Help to take a bath or shower
9. Help to go to bathroom
10. Help to use the telephone
11. Help to get to place out of walking distance
12. Help to shopping
13. Help to prevent own meals
14. Help to do housework
15. Ability to take medicine
16. Ability to handle own money
17. Self rating of health
18. High blood pressure
19. Heart and circulation problems
20. Stroke or effect of stroke
21. Arthritis or rheumatism
22. Parkinson's disease
23. Eye trouble
24. Ear trouble
25. Chest problems
26. Trouble with stomach
27. Losing control of bladder
28. Losing control of bowels
29. Diabetes
30. Fracture
31. Living alone

Appendix 1B. List of deficits H70

1. Difficulty with take care of self
2. Difficulty with taking care of house
3. Feels health is not good
4. Feels tired
5. Low appetite
6. Headache
7. Stomachache
8. Sick/vomiting
9. Chest pain
10. Coughing/breath
11. Rising difficulties
12. Needs to use aid to walk
13. Respiratory problem
14. Abdominal problem
15. Prostate problems
16. Rigidity
17. Hearing problem
18. Diabetes
19. Hypertension
20. Asthma
21. Angina pectoris
22. Gastric-ulcer
23. Arthritis
24. Cancer
25. BMI > 20
26. High glucose (highest quartile) >102
27. High cholesterol (highest quartile) >6.84
28. Difficult socializing
29. Difficult retirement
30. Problem with being disturbed
31. Living alone

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