

BMJ Open Frequency of data collection and estimation of trajectories of physical functioning and their associations with survival in older men: analyses of longitudinal data from the Manitoba Follow-Up Study

Yixiu Liu,¹ Depeng Jiang ,¹ Robert Tate ,¹ Philip St. John²

To cite: Liu Y, Jiang D, Tate R, *et al.* Frequency of data collection and estimation of trajectories of physical functioning and their associations with survival in older men: analyses of longitudinal data from the Manitoba Follow-Up Study. *BMJ Open* 2022;**12**:e054385. doi:10.1136/bmjopen-2021-054385

► Prepublication history for this paper is available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2021-054385>).

Received 10 June 2021
Accepted 03 April 2022



© Author(s) (or their employer(s)) 2022. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

¹Department of Community Health Sciences, University of Manitoba, Winnipeg, Manitoba, Canada

²Department of Internal Medicine, University of Manitoba, Winnipeg, Manitoba, Canada

Correspondence to

Dr Depeng Jiang;
depeng.jiang@umanitoba.ca

ABSTRACT

Objective In studies of trajectories of physical functioning among older people, the data cannot be measured continuously, but only at certain time points in prespecified cycles. We examine how data collection cycles can affect the estimation of trajectories and their associations with survival. **Study design and setting** Longitudinal data from the Manitoba Follow-Up Study (MFUS), with 12 measurements collected annually from 2004 to 2015, are analysed using a summary measures of physical functioning from the Short Form-36 questionnaire. Based on the joint models of the functioning trajectories and risk of death, we compare the estimations among models using different frequency of data collection (annually, biennially and triennially).

Results Our 2004 baseline includes 964 men who were survivors from the original MFUS cohort with mean age of 84 years and range between 75 and 94 years. Results from analysis of annual data indicate that the mean physical functioning is significantly decreasing over time. Further, the rate of decline is increasing over time. The current value of physical functioning is significantly associated with the hazard of death ($p < 0.001$), whereas the association between the change rate and mortality is marginally significant ($p < 0.10$). Results from analysis of biennial and triennial data reveal similar trajectory patterns of physical functioning, but could not reveal the association between the change rate of physical functioning and mortality. The frequency of data collection also impacts substantially on the estimation of heterogeneity of functioning trajectory. The prediction of mortality risk obtained using annual measurements of physical functioning are better than using biennial or triennial measurements, while the predictions obtained using biennial or triennial measurements are almost equivalent.

Conclusion The impact of frequency of data collection depends on the shape of functional trajectories and its linking structure to survival outcome.

INTRODUCTION

The role of frequency of data collection for the estimation of change in physical functioning

Research in the field of functional trajectory among older people remains challenging due

Strengths and limitations of this study

- Use annually collected physical functioning data up to 12 years from the Manitoba Follow-Up Study (MFUS). In its 73rd year, MFUS is among the longest running studies of health and ageing and enjoys very low non-mortality attrition and very high survey response rates.
- Use of advanced statistical methods, joint models, which allow us to explore the trajectories of physical functioning among older men with non-random participant truncation due to death.
- This is the first study to examine the impact of data collection frequency on the estimations using joint models of longitudinal and survival data.
- Our findings based on a cohort of male aircrew recruits from the Royal Canadian Air Force during World War II and self-reported physical functioning are not necessarily generalisable to other populations and other functioning measures.

to the longitudinal drop-out rates, complex endpoints and higher risk of death. Planning a longitudinal study of functional trajectory raises many concerns related to cost and efficiency of the study. It is important to determine an efficient length of data collection cycle given that the total time period of study is fixed, because it directly affects our inference about the true patterns of change over time from the observed change trajectory. Collecting data too frequently may place undue burden on participants and may lead to more drop-outs and non-responses. The drop-outs and missingness are considered as a loss of information and thus reduce the power of a study.¹ Moreover, the number of data waves determines the functional forms of changing trajectories that are able to



be investigated. For example, linear change requires a minimum of three time points, while quadratic requires at least four points.^{2,3} Ideally the time points are spaced in such a way that it allows the true pattern of change over time to be observed during the period of study. If we collect data too rarely, the observed time interval would be too long as compared with the optimal time interval and in turn we might not be able to discover the true change trajectory. However, a larger number of time points is not always better or more accurate than a small number of time points,² because the observed data may have measurement errors, that, in turn, might lead to unreliable or invalid estimation of change trajectory.

Considerations for optimal frequency of data collection

The optimal frequency of data collection depends on research objectives of a longitudinal study. For diseases such as AIDS that have rapid changes over time, data need to be collected frequently with time intervals ranged from 2 weeks to 2 months.⁴ For those that should take longer time to manifest changes such as functional trajectories, longer time intervals of 1 or 2 years may often be appropriate.² The optimal frequency may also depend on the response scale type in terms of reliability, validity and responsiveness. The estimation of trajectories of self-reported physical functioning requires measures with psychometrically sound reliability and validity. The responsiveness or sensitivity to change is an important merit for a functioning measure because it quantifies the propensity of measures to detect changes in physical functioning. The more responsive a measure is, the more confident researchers can be that the measure will be sensitive to functioning change. The proper frequency depends on the target population as well. For instance, the trajectory of functional and cognitive status may differ in older populations compared with younger ones.⁵ Researchers also need to face funding and other resource limitations which directly affect the number of data waves that can be collected. However, a general rule for deciding data collection cycles when developing longitudinal studies does not essentially exist and careful considerations in each specific study context are needed.⁶

The physical functioning trajectories in general

There is strong evidence that physical functioning is a marker of the current and future health, and the risk of mortality.^{7,8} The physical functioning declines with advancing age, particularly in very old age.⁹ Functional decline is characterised by an increased inability to perform basic activities of daily living.¹⁰ Physical functioning declines throughout adulthood and exhibits progressively steeper decrements throughout old age.^{11,12} Substantial individual variabilities have been reported in both onset of limitations in functioning and progression of decline over time.¹³ Decline in physical functioning was steeper in individuals who were older and closer to death and change in physical functioning is more strongly affected by time to death than by chronological age.¹⁴

Declining trajectories of physical functioning were found in a variety of cohorts in older populations. A linear changing pattern was found among older adults with four waves of data collected over 8 years.⁷ A quadratic trajectory was revealed with four waves of annually collected data.¹⁵ A linear declining trend was found to have the best performance using data collected with a varied length of time intervals.¹⁶ These and other longitudinal studies have adopted trade-offs of the time interval to be 2, 3, 4 or varied years.

The necessity of joint models for linking physical functioning trajectories to mortality

A meta-analysis revealed consistent evidence that better physical functioning was associated with a lower rate of all-cause mortality among older population.⁸ Recent research has highlighted the change in physical functioning as a short-term predictor of mortality. Andrasfay found that conditional on baseline functioning, those with steeper declines in physical functioning typically have higher mortality in the subsequent 4 years.¹⁷ Hirsch *et al* also found that the rates of change in stride length and grip strength provide important prognostic information for late-life disability and death.¹⁸ But the studies in the meta-analysis and most of empirical studies on functional trajectories applied traditional statistical models such as Cox proportional hazard models^{18–20} and growth curve models (GCMs).^{7,15,16} Both these traditional statistical approaches have limitations. Separate analysis of the longitudinal process of the physical functioning trajectory and the mortality-related process might fail to capture true change of longitudinal outcome and the association between them.²¹ The joint model for longitudinal and survival data which simultaneously analyses the two processes is more appropriate to reflect the true changing pattern of functional trajectory and its linkage with survival.

Decreasing grip strength was found to be strongly related to risk of death using the basic joint model with seven waves of data collected through a varied length of intervals (ie, 2–4 years).²² Both the changing rate and accelerating rate of change in memory performance were found to be significant predictors of risk of death with five waves of data using a 2-year interval of data collection strategy.²³ According to a meta-analysis, the application of joint models in healthcare fields has been increasing noticeably since 2012.²⁴ However, no empirical study has been conducted to examine the impact of the data collection cycle on the estimation of joint model of functional trajectory and its linkage to mortality.

The rationale and significance of this study

To the best of our knowledge, whether and how the different length of interval of the data collection strategy affects the estimations of functional trajectory and its impact on mortality risk has not been discussed in the literature. Thus, there are outstanding issues—First, is joint modelling a better approach to describe the

association of physical functioning trajectory with death? Second, the optimal sampling frequency for estimating the shape of trajectory and predicting risk of death is also unclear. In this study, we use data from one of the longest running studies of health and ageing to illustrate the impacts of using different amounts of longitudinal information (annually, biennially and triennially) on the estimation of trajectory of physical functioning and its associations with death. This will provide a guidance for selecting the proper frequency and spacing of data collection in age-related longitudinal study to ensure that the true functional trajectory and association with risk of death could be revealed.

METHODS

Data source

Data are from the Manitoba Follow-Up Study (MFUS) in Canada, one of the longest running longitudinal studies of health and ageing in the world. This longitudinal study began in 1948 with a cohort of 3983 former World War II male veterans with mean age of 31 years.²⁵ The process of signed, informed consent was not requested for the study participants in 1948. However, it has been acknowledged by the Human Research Ethics Board of the University of Manitoba that the continued response from MFUS members to surveys and requests for medical examinations can be seen as consent to participate in the study.²⁵ By spring of 2019, 107 original cohort members were alive with a mean age of 96 years, living across Canada with a geographic distribution similar to that of the national older male population. Since the inception of the cohort, the participants have been actively engaged in the study and only 46 participants have been lost to follow-up.

The Successful Ageing Questionnaire (SAQ) was added in 1996 and conducted again in 2000, 2002 and annually since 2004.²⁵ The core components of the SAQ in all

study years include living arrangement, marital status, items of social engagement, self-rated health, items of life satisfaction, the ability to perform basic and instrumental activities of daily living, definition and self-assessment of successful ageing and the Short Form-36 (SF-36).^{26–28}

The data used for the current study include the annual SAQ and mortality data from 2004 to 2015. Therefore, as far as this study is concerned, participants were still alive in 2004 and completed the SAQ questionnaire himself (or with help from his family member) for at least one time during the 11 years. At 2004 baseline, there were 964 men at a mean age of 84 years, with range from 75 to 94 years. Response rates for all waves are very high. If a respondent was missing for one wave, attempts were made to contact for a following wave until we know he had died. This aspect of the survey coupled with high response rates means that overall non-mortality attrition is low. Of 964 participants at 2004 baseline, only 11 (1%) were alive but lost to follow-up by 2015. More information about the study sample including the percentage of missing SAQs, and number of deaths is given in [table 1](#). The average number of observations over 12 waves is 6. If we take death into consideration that no measurement would be collected after death, the average percentage of response is over 83%. Nevertheless, we conducted analyses to compare those participants with complete data to those with non-mortality missing data, no significant differences in physical functioning scores and mean age were found for almost all study years. Therefore, our analysis assumed that non-mortality missingness is missing at random.

Study variables

The SF-36 is a widely used, easily administered measure of health-related quality of life which is sensitive to change. It contains the Physical Component Score (PCS), which considers physical functioning, and the Mental

Table 1 Sample size, number of deaths, percentage of received SAQs and mean of age in each survey year

| Year | Sample size | Mean age | No of deaths | No of drop-outs | Per cent of drop-out | Per cent of received SAQs | Per cent of non-responses |
|------|-------------|----------|--------------|-----------------|----------------------|---------------------------|---------------------------|
| 2004 | 964 | 83.83 | 28 | 0 | 0.00 | 84.08 | 15.92 |
| 2005 | 936 | 84.65 | 44 | 2 | 0.21 | 85.65 | 14.16 |
| 2006 | 892 | 85.57 | 70 | 3 | 0.34 | 89.66 | 10.01 |
| 2007 | 822 | 86.3 | 71 | 0 | 0.00 | 81.23 | 18.77 |
| 2008 | 751 | 87.26 | 78 | 0 | 0.00 | 76.67 | 23.33 |
| 2009 | 673 | 87.97 | 53 | 0 | 0.00 | 75.32 | 24.68 |
| 2010 | 620 | 88.82 | 78 | 1 | 0.16 | 71.40 | 28.47 |
| 2011 | 542 | 89.74 | 102 | 1 | 0.18 | 73.64 | 26.20 |
| 2012 | 440 | 90.71 | 70 | 0 | 0.00 | 71.89 | 28.11 |
| 2013 | 370 | 91.45 | 65 | 2 | 0.54 | 67.87 | 31.35 |
| 2014 | 305 | 92.21 | 59 | 1 | 0.33 | 68.70 | 31.02 |
| 2015 | 246 | 93.02 | 46 | 1 | 0.41 | 61.50 | 38.19 |

SAQ, Successful Ageing Questionnaire.

Component Score, which considers mental health functioning. In this study, we use the PCS as an illustrating example for investigating the functional trajectories of older people and their impact on survival. The PCS is normalised on a unitless scale with a mean of 50 and SD of 10. The death date of those who are known to have died have been collected through questionnaires, administrative database or direct phone calls to physicians or family.

Joint models

Two main approaches to study how a longitudinal process predicts the survival time are the extended Cox model²⁹ and joint modelling.²¹ The Cox proportional hazard regression model links the covariates to the survival time through the hazard function while the extended Cox model is an extension of the Cox model to handle time-varying covariates.²⁹ The time-varying covariates in the extended Cox model are required to be measured without error, remained constant and only updated at measurement times.^{30 31} However, many time-varying covariates especially for self-reported data (eg, physical functioning) do not meet the requirement. If the extended Cox model is conducted, the parameter estimation can be biased and unreliable.²¹ Joint modelling of longitudinal and survival data may complement the Cox models by providing a more accurate representation of the quantitative influence of time-varying factors such as physical functioning, on the time to an event such as death.²¹

The joint model consists of two submodels, mixed-effect model for longitudinal outcome and the Cox model for survival outcome. An underlying random effects structure links the survival and longitudinal submodels and allows for individual-specific predictions. Suppose we have n subjects, who are followed up for a time period $[0, T]$. For each subject i , repeated measurements $y_i(t)$ are collected at time t . The observed event time T_i equals the minimum of the true event time T_i^* and the censored time C_i for subject i . The indicator for event is $\delta_i = I(T_i^* \leq C_i)$, which means $\delta_i = 0$ if the subject is censored before the end the study or the event does not happen through the whole study period.

The formula of the longitudinal submodel takes the form:

$$\begin{aligned} y_i(t) &= m_i(t) + \varepsilon_i(t) \\ &= x_i^T(t)\beta + z_i^T(t)b_i + \varepsilon_i(t), \end{aligned} \quad (1)$$

where $m_i(t)$ indicates the true value of longitudinal outcome for subject i at time point t ; $x_i^T(t)$ and $z_i^T(t)$ denote the design matrix for the fixed effects β and random effects b_i , respectively. The random effects b_i and the error term $\varepsilon(t)$ are assumed to have the multivariate normal distribution $\mathfrak{N}(0, G)$ and $\mathfrak{N}(0, I_{\sigma^2})$, respectively, and they are mutually independent, where G is the variance-covariance matrix of random effects, σ^2 is the variance of error terms and I_{σ^2} denotes identity matrix with σ^2 on the diagonal and zero off diagonal.

The formula of the survival submodel takes the general form²⁹:

$$h_i(t | \mathfrak{M}_i(t), \omega_i) = h_0(t) \exp\{\gamma^T \omega_i + \alpha W_i(t)\},$$

where $\mathfrak{M}_i(t) = \{m_i(s), 0 \leq s \leq t\}$ denotes the history of the true repeated measurements up to time t ; $h_0(t)$ is the baseline hazard function; ω_i is a vector denoting the baseline covariates; $W_i(t)$ denotes the linking approach of the longitudinal and survival processes. The association between the longitudinal outcome and the risk of death is reflected by the parameter α . The piecewise constant model which was evidenced to work well²¹ was used in this study to model the baseline hazard function.

Six different linking approaches were compared using Akaike information criterion (AIC) and Bayesian information criterion (BIC).

Model (a): $h_i(t | \mathfrak{M}_i(t), \omega_i) = h_0(t) \exp\{\alpha_1 m_i(t)\}$

Model (b): $h_i(t | \mathfrak{M}_i(t), \omega_i) = h_0(t) \exp\{\alpha_1 m_i(t) + \alpha_2 m_i'(t)\}$

Model (c): $h_i(t | \mathfrak{M}_i(t), \omega_i) = h_0(t) \exp\{\alpha_2 \int_0^t m_i(s) ds\}$

Model (d): $h_i(t | \mathfrak{M}_i(t), \omega_i) = h_0(t) \exp\{\alpha_1 m_i(t) + \alpha_2 \int_0^t m_i(s) ds\}$

Model (e): $h_i(t | \mathfrak{M}_i(t), \omega_i) = h_0(t) \exp\{\alpha_2 \int_0^t \varpi(s) m_i(s) ds\}$

Model (f): $h_i(t | \mathfrak{M}_i(t), \omega_i) = h_0(t) \exp\{\alpha_1 m_i(t) + \alpha_2 \int_0^t \varpi(s) m_i(s) ds\}$

Model (a) is the basic joint model linking the two processes through adding the true current value of longitudinal outcome into the survival submodel. Model (a) assumes that the hazard of survival outcome is affected by the current true value of the longitudinal outcome, $m_i(t)$, and parameter α_1 quantifies this effect. Model (b) assumes that not only the current true value, $m_i(t)$, but also the change rate, denoted by the derivative of $m_i(t)$, affects the hazard of survival outcome. Model (c) assumes that the hazard of survival outcome is affected by the whole history of longitudinal outcome (cumulative values of longitudinal outcomes, denoted by the integral of $m_i(t)$). Model (d) assumes that both current value and cumulative value affect the hazard of survival outcome. The more recent values of longitudinal outcome might have stronger impact on the hazard of survival outcome than the values earlier in time. Therefore, a weight function $\varpi(s)$ is added to Model (c) and Model (d) to represent different impact of previous values, leading to Model (e) and (f), respectively.

We identified the best joint model that described the functional trajectories and risk of death using all the measurements collected annually from 2004 to 2015. Then the same best joint model was fitted using every other measurement (biennially), that is, the measurements collected in 2004, 2006, 2008, 2010, 2012 and 2014. Similarly, we fitted the same model using the triennially collected measurements, that is, the measurements in 2004, 2007, 2010 and 2013. We can imagine that these represent three different scenarios of data collection cycles (annually, biennially and triennially). Two measures of model performance, the mean absolute error (MAE) for longitudinal outcome and the area under the receiver operating characteristic curve (AUC), were used to compare models using different amounts of longitudinal information. MAE was used to measure the accuracy of

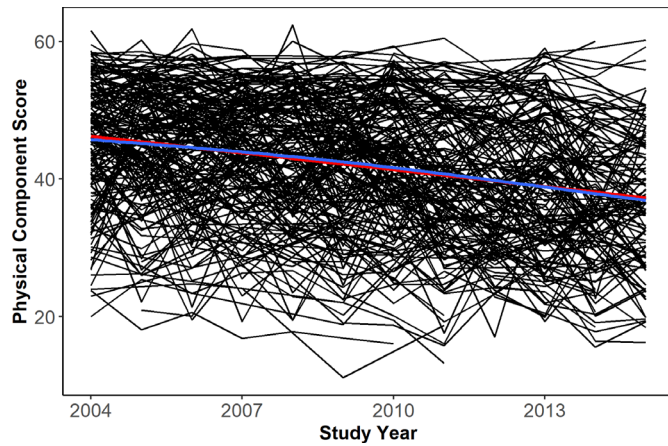


Figure 1 Individual trajectories of physical functioning for the 200 survivors by the year of 2015.

prediction for longitudinal outcomes. AUC was used for discrimination ability for survival process. Smaller MAEs and larger AUCs indicate better model performance.

Patient and public involvement

There was no patient or public involvement in the study.

RESULTS

The mean PCS at the baseline was 42.5 in our sample of men aged from 75 to 94. This is similar to the Canadian normative data for the SF-36 health survey being reported by Hopman and colleagues.³² To examine how physical functioning changes over time among survivors, GCMs were conducted on the cohort of those 200 males who were still alive by the end of 2015. **Figure 1** presents empirical individual growth plots of the physical functioning for the 200 males, along with the superimposed ordinal linear regression trajectory (red line) and smoothed trajectory (blue line) across 200 survivors. The preliminary analyses indicated that the declining physical functional trajectory among older men can be described as a quadratic function of time. We compared the model with the physical functioning over study year to that over age. The results are shown in **table 2** and **figure 2**. The goodness-of-fit index for model selection did not result in an overwhelmingly clear determination of which model is better. According to a measure of proportional reduction in residual variance (ie, R^2 in **table 2**) and AIC, the model with time in study is better than the model with age, whereas the model with age is better according to BIC. However, two models (modelling physical functioning over time vs over age) indicated a similar patterns of findings and supported consistent conclusions that the mean physical functioning is significantly decreasing over time, and the rate of decrease is increasing over time. Moreover, the results from the variance components of both models indicated that there are significant variations among participants in the baseline value of physical functioning, declining rate and accelerating rate over time.

Table 2 Results from modelling physical functioning over study year versus age (N=200)

| Parameter | Over time in study | Over age |
|----------------------------------|--------------------|-----------------|
| Fixed effects | | |
| Intercept | 45.53 (0.60)*** | 44.53 (0.58)*** |
| Time | -0.49 (0.16)** | -0.65 (0.09)*** |
| Time \times time | -0.03 (0.015)* | -0.02 (0.01)* |
| Variance components | | |
| Level 1 | 25.55 (0.99)*** | 26.69 (1.03)*** |
| Level 2 variance | | |
| Intercept | 54.98 (7.30)*** | 59.62 (6.68)*** |
| Time | 1.80 (0.53)*** | 0.57 (0.15)*** |
| Time \times time | 0.015 (0.01)*** | 0.004 (0.002)* |
| Level two covariance | | |
| Intercept and time | 0.02 (1.47) | 1.72 (0.70)* |
| Intercept and time \times time | -0.11 (0.13) | -0.29 (0.09)*** |
| Time and time \times time | -0.14 (0.05)** | -0.03 (0.02) |
| Goodness of fit | | |
| -2LogLik | 12 465.7 | 12 485.7 |
| AIC | 12 485.7 | 12 505.7 |
| BIC | 12 518.7 | 12 505.8 |
| R^2 | 0.225 | 0.219 |

Cells format—parameter estimation (SE) significance level; year was centred at 2004 and age was centred at 84, the average age at baseline (2004). The R^2 in the mixed-effect model was calculated using the approach suggested by Xu.³⁴
* $P < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

AIC, Akaike information criterion; BIC, Bayesian information criterion.

For the joint model analyses, we will just model change of physical functioning over study year.

With this quadratic growth as the longitudinal submodel in which the intercept and linear and quadratic slopes have random effects, the six joint models, referred as

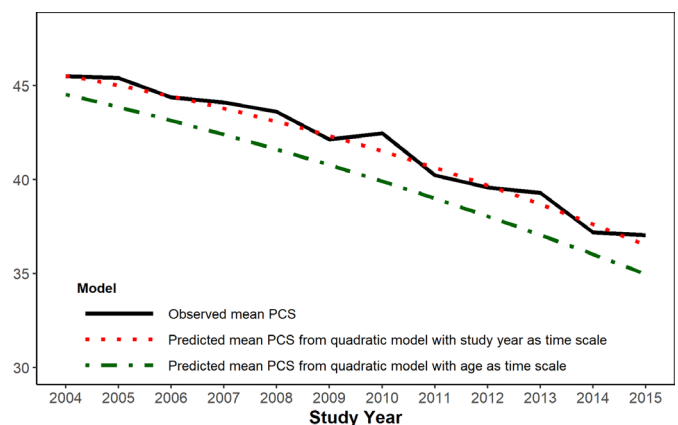


Figure 2 Predicted and observed mean trajectories of Physical Component Score (PCS) (N=200).

Table 3 Log-likelihood, AICs and BICs of the six joint models

| Model | Log-likelihood | AIC | BIC |
|-----------|----------------|--------|--------|
| Model (a) | -20 491 | 41 018 | 41 106 |
| Model (b) | -20 329 | 40 696 | 40 789 |
| Model (c) | -20 563 | 41 162 | 41 249 |
| Model (d) | -20 478 | 40 994 | 41 086 |
| Model (e) | -20 553 | 41 142 | 41 230 |
| Model (f) | -20 472 | 40 982 | 41 075 |

Model a is the basic joint model with the true longitudinal measurement of physical functioning in the survival submodel; Model b includes both the true value and the changing rate of physical functioning in the survival submodel; Model c only contains the history of physical functioning while Model d contains both the true value and history of physical functioning in the survival submodel; Model e incorporates weighted history of physical functioning while Model f incorporates both the true value and weighted history of physical functioning in the survival submodel. N=964.

AIC, Akaike information criterion; BIC, Bayesian information criterion.

model (a) to (f) above, were fitted on all measurements collected annually from 2004 to 2015. The goodness of fit of these models are reported in [table 3](#) where, model (b) was identified as the best joint model, indicating that not only the current physical function but also its change rate was associated with the risk of death.

The best joint models were fitted on three scenarios of data collection cycles (annually, biennially and triennially). The results of longitudinal and survival submodels are reported in [tables 4 and 5](#), respectively. Reported in [tables 4 and 5](#) are the change in parameter estimate from using annual data to using biennial or triennial data. [Table 4](#) reveals the differences between models in estimates of linear and quadratic slopes were larger than the estimates of intercept, so were the variances of these estimates. The SEs of these estimates became larger when model using the biennial and triennial data than the model with annual data. [Table 5](#) reveals that the estimations of the association between current PCS and hazard of death were similar across models using different cohort data. However, there was considerable variation in the estimation of the association between the change rate of PCS and hazard of death. This indicates that data collection cycles have relatively small influence on the association between current PCS and the risk of death but significant influence on the association between changing rate of PCS and hazard of death.

[Figure 3](#) shows the accuracy of prediction for longitudinal functional outcomes. The predictions by model using the annually collected data had the lower MAE than models using biennial or triennial data. The difference of MAEs from models using biennial and triennial data was negligible. [Figure 4](#) shows AUC estimates calculated annually based on these models. The AUCs of prediction of risk of death in the next year were calculated since

2005 to ensure at least one measurement of PCS. Except in 2010, the AUCs based on annually collected data was the highest. The difference between AUCs in biennial and triennial data were not significant except in 2014. The predictions of risk of death obtained using annual measurements are better than using biennial or triennial measurements, while the predictions obtained using biennial or triennial measurements are almost equivalent.

DISCUSSIONS AND CONCLUSIONS

In this research, we used a practical example to illustrate the influence of data collection cycles on the estimation of physical functioning trajectory and its relationship with mortality risk among older men. Our results reveal that the impact of data collection frequency on estimations of parameters for describing the functional trajectory is minimal as long as we have enough data points to estimate the individual shape of trajectory (eg, three points for linear and four points for quadratic GCMs). The frequency of data collection has a large impact on the estimation of heterogeneity of functioning trajectories and more frequent data collection is desirable for more accurate estimation of heterogeneity. The influence of data collection frequency on the estimation of the association of functioning trajectory and mortality risk depends on how the two processes are linked. We found when both the current physical function and its change are connected to the risk of death, to get more accurate estimation of the association between the change rate of physical functioning and mortality risk, we need to collect data more frequently.

The predictions of mortality risk obtained using annual measurements of physical functioning were better than using biennial or triennial measurements, while the predictions obtained using biennial or triennial measurements were almost equivalent. Analysis of annual data revealed that the association between the change rate of physical functioning and the hazard of death was marginally significant. Analysis of biennial or triennial measurements could not reveal this association. To increase the accuracy of the prediction of survival or the power to detect the association between physical functioning and mortality, more frequent data may need to be collected.

Joint modelling is often preferred for analysing a longitudinal process and survival time. To the best of our knowledge, no study has been conducted to explore the impact of data collection frequencies on the estimation of joint models in longitudinal studies of ageing. In fact, in a longitudinal study, enough data waves need to be collected to ensure the true change pattern can be reflected by the statistical analysis. Our results reveal that the marginal-significant effect of the rate of change in the physical functioning on the hazard of death cannot be captured in a study design with data collection intervals longer than 1 year. The intersubject variation in the trajectories of physical functioning over time could be substantially underestimated based on a less frequent

Table 4 Parameter estimations of the longitudinal process of the three study designs

| Model 2b | | Annual | Biennial | Change from annual | Triennial | Change from annual |
|----------------|----------------------------|------------------------------|------------------------------|--------------------|------------------------------|--------------------|
| | | Estimate (SE) ^{sig} | Estimate (SE) ^{sig} | | Estimate (SE) ^{sig} | |
| Fixed effects | $\hat{\beta}_{00}$ | 42.52 (0.28) ^{***} | 42.50 (0.21) ^{***} | -0.05% | 42.56 (0.33) ^{***} | 0.09% |
| | $\hat{\beta}_{01}$ | -1.18 (0.10) ^{***} | -0.98 (0.11) ^{***} | -16.95% | -0.93 (0.13) ^{***} | 21.19% |
| | $\hat{\beta}_{02}$ | -0.01 (0.01) | -0.007 (0.01) | -30% | -0.011 (0.02) | 10.00% |
| Random effects | $\hat{\sigma}_\varepsilon$ | 5.35 (0.01) [*] | 5.21 (0.02) [*] | 2.62% | 5.04 (0.03) [*] | 5.79% |
| | $\hat{\sigma}_{b_0}$ | 8.76 (0.03) [*] | 8.52 (0.03) [*] | 2.74% | 8.86 (0.03) [*] | 1.14% |
| | $\hat{\sigma}_{b_1}$ | 1.38 (0.003) [*] | 1.05 (0.002) [*] | 23.90% | 1.23 (0.003) [*] | 10.87% |
| | $\hat{\sigma}_{b_2}$ | 0.09 (0.05) | 0.08 (0.05) | 11.11% | 0.06 (0.06) | 33.33% |

Cells format—parameter estimation (SE)^{significance level}; $\hat{\sigma}_\varepsilon$ is the estimated variation of within subject residuals; $\hat{\sigma}_{b_0}$ is the estimated variation of intercept across subjects; σ_{b_1} is the estimated variation of changing rate across subjects; σ_{b_2} is the estimated variation of the accelerating rate across subjects; $\hat{\beta}_{00}$ is the estimated intercept indicating the baseline average physical functioning measurement (PCS); $\hat{\beta}_{01}$ is the estimated changing rate of physical functioning at the baseline; $\hat{\beta}_{02}$ is the estimated accelerating rate of physical functioning over time. N=964.

*P<0.05, **p<0.01, ***p<0.001.

data collection strategy. Collecting data more frequently improves the predictions of mortality risk.

This study has several strengths and limitations. Among the strengths of this study are the use of the annually collected physical functioning data up to 11 years from the MFUS, one of the longest running studies of health and ageing. MFUS has experienced very low non-mortality attrition and very high survey response rates. The advanced statistical approaches, joint models, are used to examine the trajectory of physical functioning, which allow us to address non-random participant truncation due to death. One limitation of this study is that our results are based on the physical functioning data. Quality of life scales other than the physical functioning—or indeed the underlying factor that they measure—may differ in their responsiveness to change. Physical functioning may be more or less variable than some other measures. For example, immune functioning often changes relatively quickly (in a matter of weeks) whereas depressive symptoms often change more slowly (in a matter of months). Caution is therefore needed in extrapolating our findings to other measures of health functioning.

Another limitation of this study is our sample selectivity. MFUS began in 1948 with a cohort of aircrew recruits from the Royal Canadian Air Force during World War II. Our findings are not necessarily generalisable to other male populations, nor to women. MFUS members may have been more highly selected relative to those of other arms of service. The cohort is similar to Canadian men of the same age in terms of functional status, mortality, geographic distribution and marital status.

Moreover, no other covariates are considered in our analyses. This may lead to the low AUCs with all values below 0.7. Although there is no gold standard for a good value of AUC, incorporating more relevant covariates such as demographic information could increase the discrimination ability of a model. The joint modelling analyses on the biennial or triennial data were based on individuals with maximum of 6 or 4 observations over 12 survey waves. There was a high proportion of individuals with only one single observations because of early death or non-response. This high proportion of individuals with fewer observations limited our possibilities of data analyses, for example, specifying cubic change patterns in

Table 5 Parameter estimations of the survival process of the three study designs

| Model 2b | | Annual | Biennial | Change from annual | Triennial | Change from annual |
|----------|------------------|------------------------------|------------------------------|--------------------|------------------------------|--------------------|
| | | Estimate (SE) ^{sig} | Estimate (SE) ^{sig} | | Estimate (SE) ^{sig} | |
| | $\hat{\alpha}_1$ | -0.06 (0.005) ^{***} | -0.05 (0.005) ^{***} | 16.67% | -0.06 (0.006) ^{***} | 0 |
| | $\hat{\alpha}_2$ | -0.09 (0.05) [†] | 0.03 (0.05) | 133.33% | 0.05 (0.08) | 155.56% |

Cells format—parameter estimation (SE)^{significance level}; $\hat{\alpha}_1$ is the estimation of the association between current physical functioning measurement and the log hazard of death; $\hat{\alpha}_2$ is the estimation of the association between the changing rate of physical functioning and the log hazard of death. N=964.

***P<0.001.

†p<0.10



Figure 3 MAE of models using different amounts of longitudinal measurements. MAE, mean absolute error.

physical functioning or including more baseline or time-varying covariates. This also limited the statistical power to detect the association between physical functioning and mortality. Future empirical and simulation studies could be conducted to investigate the impact of using a different amount of measurement occasions on the estimation of functional trajectories.

Finally, we studied the influence of data collection frequency only based on data from an existing cohort. This might not solve the general problem of determination of the reasonable number of longitudinal measures needed for prediction of quality-of-life trajectory and mortality risk. Simulation studies might be required to investigate the incremental benefit of more frequent data collection. Our study, as with most longitudinal ageing studies, focuses on intraindividual changes, which relies on sequences of widely spaced repeated single measurements. This implies that we cannot examine how short-term within-person relationships (eg, emotional reactivity to daily stress) change over time. If the research focus is on daily or momentary intraindividual variability, it would require repeated bursts of daily diary or experience sampling assessments that spanned several years.³³

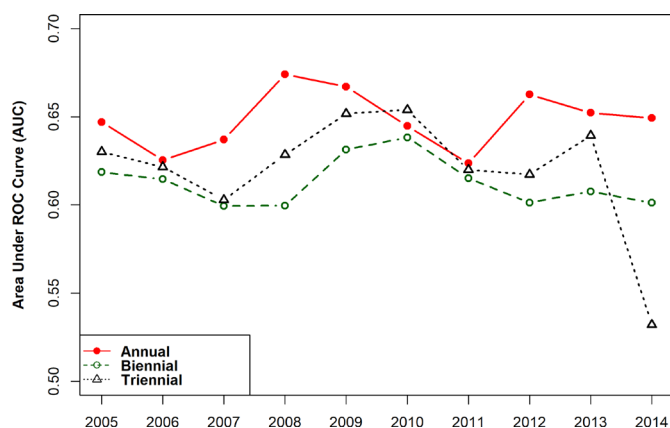


Figure 4 AUC estimates for 1-year predictions from models using different amounts of longitudinal measurements. ROC, Receiver Operating Characteristic.

In summary, the impact of study design on estimation of parameters depends on the complexity of the longitudinal process and its link to survival outcome. In general, more frequent measurement might be required to study low-frequency events (eg, emotional functioning) than higher-frequency events (eg, physical functioning). Collecting data annually might bring negligible improvement compared with collecting data biennially or triennially if the focus is on the estimation of mean changes in physical functioning for those far from death. If we focus on the estimation of the association between change rate of physical functioning and mortality or changes in physical functioning within a shorter distance to death, collecting data annually appears superior in assessing the association or changes than collecting data biennially or triennially. This study provides a reference for selecting the follow-up strategy in a longitudinal study of ageing when focusing on the trajectories of physical functioning and its linkage to the survival probability using joint models.

Contributors YL led the conception and design of the study, analysis and interpretation of the data and drafted the article. DJ provided guidance on the conception and design of the study, assisted in the analysis and interpretation of the data and was involved in revising the article. RT provided guidance on the conception of the study, provided access to the study data, and assisted in interpretation of the data. PSJ provided guidance on the conception and design of the study, assisted in the analysis and interpretation of the data and was involved in revising the article. All authors read and approved the final manuscript.

Funding This work was supported by the Canadian Institute for Health Research (CIHR) (378073, 2016) and the Children's Hospital Research Institute of Manitoba (CHRIM) Foundation (OG2019-19).

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by Health Research Ethics Board (HREB) of the University of Manitoba has approved this study (HS2019:286). The process of signed, informed consent was not requested for the study participants in 1948. However, it has been acknowledged by the Human Research Ethics Board of the University of Manitoba that the continued response from MFUS members to surveys and requests for medical examinations can be seen as consent to participate in the study.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iDs

Depeng Jiang <http://orcid.org/0000-0002-7060-4892>

Robert Tate <http://orcid.org/0000-0002-0624-8264>

REFERENCES

- 1 Cook NR, Ware JH. Design and analysis methods for longitudinal research. *Annu Rev Public Health* 1983;4:1–23.
- 2 Wang M, Beal DJ, Chan D, et al. Longitudinal research: a panel discussion on conceptual issues, research design, and statistical techniques. *Work Aging Retire* 2017;3:1–24.

- 3 Chan D. The conceptualization and analysis of change over time: an integrative approach incorporating longitudinal mean and covariance structures analysis (LMACS) and multiple indicator latent growth modeling (MLGM). *Organ Res Methods* 1998;1:421–83.
- 4 Abrams DI, Goldman AI, Launer C, *et al.* A comparative trial of didanosine or zalcitabine after treatment with zidovudine in patients with human immunodeficiency virus infection. The Terry Beinr community programs for clinical research on AIDS. *N Engl J Med* 1994;330:657–62.
- 5 Hsu H-C, Jones BL. Multiple trajectories of successful aging of older and younger cohorts. *Gerontologist* 2012;52:843–56.
- 6 Taris TW, Kompier MAJ. Cause and effect: optimizing the designs of longitudinal studies in occupational health psychology. *Work Stress* 2014;28:1–8.
- 7 Hu Y, Pikhart H, Paják A, *et al.* Education, material condition and physical functioning trajectories in middle-aged and older adults in central and eastern Europe: a cross-country comparison. *J Epidemiol Community Health* 2016;70:1128–35.
- 8 Cooper R, Kuh D, Hardy R, *et al.* Objectively measured physical capability levels and mortality: systematic review and meta-analysis. *BMJ* 2010;341:c4467.
- 9 Wettstein M, Schilling OK, Wahl H-W. "Still feeling healthy after all these years": The paradox of subjective stability versus objective decline in very old adults' health and functioning across five years. *Psychol Aging* 2016;31:815–30.
- 10 Stenholm S, Westerlund H, Salo P, *et al.* Age-related trajectories of physical functioning in work and retirement: the role of sociodemographic factors, lifestyle and disease. *J Epidemiol Community Health* 2014;68:503–9.
- 11 Morack J, Infurna FJ, Ram N, *et al.* Trajectories and personality correlates of change in perceptions of physical and mental health across adulthood and old age. *Int J Behav Dev* 2013;37:475–84.
- 12 Sargent-Cox KA, Anstey KJ, Luszcz MA. Patterns of longitudinal change in older adults' self-rated health: The effect of the point of reference. *Health Psychology* 2010;29:143–52.
- 13 Hardy SE, Dubin JA, Holford TR, *et al.* Transitions between states of disability and independence among older persons. *Am J Epidemiol* 2005;161:575–84.
- 14 Wettstein M, Spuling SM, Cengia A. Trajectories of functional health and its associations with information processing speed and subjective well-being: the role of age versus time to death. *Psychol Aging* 2020;35:190–203.
- 15 Payette H, Gueye NR, Gaudreau P, *et al.* Trajectories of physical function decline and psychological functioning: the Quebec longitudinal study on nutrition and successful aging (nuage). *J Gerontol B Psychol Sci Soc Sci* 2011;66B:i82–90.
- 16 Garcia MA, Reyes AM. Physical functioning and disability trajectories by age of migration among Mexican elders in the United States. *J Gerontol B Psychol Sci Soc Sci* 2018;73:1292–302.
- 17 Andrasfay T. Changes in physical functioning as short-term predictors of mortality. *Journals Gerontol Ser B* 2020;75:630–9.
- 18 Hirsch CH, Buzková P, Robbins JA, *et al.* Predicting late-life disability and death by the rate of decline in physical performance measures. *Age Ageing* 2012;41:155–61.
- 19 Andrasfay T. Changes in physical functioning as short-term predictors of mortality. *J Gerontol B Psychol Sci Soc Sci* 2020;75:630–9.
- 20 Mutambudzi M, Chen N-W, Howrey B, *et al.* Physical performance trajectories and mortality among older Mexican Americans. *J Gerontol A Biol Sci Med Sci* 2019;74:233–9.
- 21 Rizopoulos D. Joint Models for Longitudinal and Survival Data With Application in R. Chapman & Hall/CRC biostatistics series 2012.
- 22 Peterson MD, Zhang P, Duchowny KA, *et al.* Declines in strength and mortality risk among older Mexican Americans: joint modeling of survival and longitudinal data. *J Gerontol A Biol Sci Med Sci* 2016;71:1646–52.
- 23 Muniz Terrera G, Piccinin AM, Matthews F, *et al.* Joint modeling of longitudinal change and survival. *GeroPsych* 2011;24:177–85.
- 24 Sudell M, Kolamunnage-Dona R, Tudur-Smith C. Joint models for longitudinal and time-to-event data: a review of reporting quality with a view to meta-analysis. *BMC Med Res Methodol* 2016;16:1–11.
- 25 Tate RB, Cuddy TE, Mathewson FAL. Cohort profile: the Manitoba follow-up study (MFUS). *Int J Epidemiol* 2015;44:1528–36.
- 26 Alshammari M. Response Shift in Health-Related Quality of Life in Older Men : The Manitoba Follow-Up Study, 2015. The University of Manitoba. Available: <http://hdl.handle.net/1993/30715>
- 27 St John PD, Jiang D, Tate RB. Quality of life trajectories predict mortality in older men: the Manitoba follow-up study. *J Aging Health* 2018;30:247–61.
- 28 Tate RB, Swift AU, Bayomi DJ. Older men's lay definitions of successful aging over time: the Manitoba follow-up study. *Int J Aging Hum Dev* 2013;76:297–322.
- 29 Fisher LD, Lin DY. Time-Dependent covariates in the COX proportional-hazards regression model. *Annu Rev Public Health* 1999;20:145–57.
- 30 Kalbfleisch JD, Prentice RL. The survival analysis of failure time data. Wiley series in probability and statistics 2002;439.
- 31 Henderson R, Diggle P, Dobson A. Joint modelling of longitudinal measurements and event time data. *Biostatistics* 2000;1:465–80.
- 32 Hopman WM, Towheed T, Anastassiades T, Papadimitropoulos E. Canadian normative data for the SF-36 health survey. *CMAJ* 2000;163:265–71.
- 33 Sliwinski MJ. Measurement-burst designs for social health research. *Soc Personal Psychol Compass* 2008;2:245–61.
- 34 Xu R. Measuring explained variation in linear mixed effects models. *Stat Med* 2003;22:3527–41.