

A Case Study of the Application of a Multilevel Growth Curve Model and the Prediction of Health Trajectories

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Abstract

This case study provides guidance on the application of a multilevel growth curve model and the prediction of health trajectories. Using our secondary data analysis as an example, we introduce definitions of the multilevel growth curve model, random intercept and slope, and the intraclass correlation coefficient. We discuss time centering and time metrics, marginal effects for drawing frailty trajectories, as well as multiple imputation for handling missing values.

Learning Outcomes

By the end of this case, students should be able to

- Learn what the multilevel growth curve model is
- Learn how we fit a multilevel growth curve model for assessing the relationship between employment histories and frailty trajectories
- Learn methodologies for the prediction of frailty trajectories
- Learn the methodological challenge we met in analysis

Project Overview and Context

This study was part of the work undertaken by the Well-being, Health, Retirement and the Lifecourse (WHERL) Interdisciplinary Consortium funded by the cross-Research Council Lifelong Health and Well-being (LLHW) program under Extending Working Lives (ES/L002825/1). This study was conducted in 2015 as Dr. Wentian Lu's MSc dissertation (supervised by Professor Amanda Sacker). Although the focus here is on the statistical methodologies used, we briefly introduce the rationale of this study.

Given the policy changes that expect people to work for longer in England, we set out to investigate whether people's lifetime exposure to work affects their health in later life. This can be treated as a lifecourse approach—a diverse range of social, economic, and environmental factors during adulthood influence an individual's health and well-being in later life. A lifecourse approach of exploring the relationship between employment histories during adulthood and individual health in later life could inform the debate on the public health impacts of working longer. Frailty is a clinical syndrome among the elderly associated with various adverse health outcomes including morbidity, incident disability, hospitalization, institutionalization, and mortality. A frailty index (FI) has been developed based on a range of health indicators such as chronic conditions, pain, depression, cardiovascular diseases, falls, fractures, and joint replacement, measuring individual health multidimensionally. Before our study, no studies have investigated how paid employment histories before retirement are associated with frailty in later life. Arising from this, we aimed to understand the relationship between employment histories and frailty trajectories in later life in England.

Section Summary

- A lifecourse approach can investigate whether people's lifetime exposures affect their health and well-being in older age.
- Frailty is a clinical syndrome and can be developed based on various health indicators to measure individual health multidimensionally.

Research Design

Our investigation was based on secondary data analysis. Data from the English Longitudinal Study of Ageing (ELSA) in England were used ([Steptoe et al., 2013](#)). ELSA is a longitudinal panel study that began in 2002 (Wave 1), recruiting around 12,000 participants aged 50 or more, and has revisited the sample every 2 years since then. ELSA integrates information about the economic, social, psychological, community, and health experiences of older people in England. Our study included a subsample of 4,386 ELSA respondents aged 60 (for women) or 65 (for men) to 90 years in Wave 2 (2004–2005) who also completed the life history questionnaire in Wave 3 (2006–2007). There were 2,765 female participants in our sample. Respondents in our study were followed up until Wave 6 (2012–2013). The analysis included data in Waves 2, 4 (2008–2009), and 6.

We derived each participant's history of labor force participation based on his or her employment history (EH) data in Wave 3. An optimal matching analysis was employed. This case study will not cover details for this method. Students could refer to a further introduction of this method in [Corna et al. \(2016\)](#). Eventually, we generated five categories of employment histories for men (employed full-time throughout, not employed throughout, full-time throughout until early exit at 49 or at 60 years, and late start of paid work and exit at 60 years) and seven categories for women (employed full-time throughout, not employed throughout, weak attachment to the labor market and early exit, long or short career break followed by part-time employment, family care to full-time work and full-time to part-time work).

We developed the FI for each participant using 60 health deficits in Waves 2, 4, and 6. This case study will not cover details for those health deficits. Students could refer to Supplementary Table S1 in our article for details. Each deficit was dichotomized or organized into quartiles and then standardized to the interval of 0 to 1. For each participant, the deficit points were summed and divided by the total number of deficits measured to yield an FI ranging from 0 to 1. Higher scores indicate more frail status.

Confounders known to be associated with work and health were included for adjustment, including father's social class at 14 years, self-rated health during childhood, education, occupation, marital history, fertility history, partnership, smoking, alcohol consumption, index of multiple deprivation, and nonpension wealth.

Section Summary

- Conducting a longitudinal analysis is based on multiple waves of data collection.

- The temporality should be clear—exposure precedes outcome (i.e., in our study, we collected individuals' employment histories before 60/65 years old and assessed their frailty status after 60/65 years).
- The repeated measures of health outcome from multiple waves of data collection should be used for predicting health trajectories (i.e., our study included frailty measures at Waves 2, 4, and 6 of ELSA).

Method in Action

Defining a Multilevel Growth Curve Model

Our dataset included repeated measures of FI and covariates over time. Therefore, we chose to use multilevel modeling to estimate growth curve models of frailty by employment histories among men and women, separately. Multilevel modeling was originally developed to recognize data hierarchies by allowing for residual components at each level in the hierarchy, such as children nested within classrooms, or schools clustered within areas. Multilevel modeling can also be equivalently applied to fit a growth curve model as repeatedly measured data over time could be treated as observations for each wave of data collection (Level 1) being nested within each individual (Level 2), allowing for the estimation of between-individual differences in within-individual change (Curran et al., 2010). Growth curve models are suitable for research questions such as “what is the trajectory for the population,” “are there distinct trajectories for each participant,” or “if participants have distinct trajectories, what variables predict these individual trajectories.” For our study, we hypothesized that both male and female participants have distinct aging trajectories by different categories of employment histories.

The following is an example of a multilevel growth curve model with covariates for age, age-squared, and EH only (Equations 1–3). Here FI_{ij} indicates the FI in wave i for individual j . EH_j is the time-invariant EH categorical variable for individual j . age_{ij} is time-varying. In Equation 1, every individual's frailty trajectory is modeled as a function of age, EH, and an interaction between the two

(1)

$$FI_{ij} = \beta_{0j} + \beta_{1j}age_{ij} + \beta_2EH_j + \beta_3EH_j * age_{ij} + \varepsilon_{ij}$$

$$FI_{ij} = \beta_{0j} + \beta_{1j}age_{ij} + \beta_2EH_j + \beta_3EH_j * age_{ij} + \varepsilon_{ij}$$

(2)

$$\beta_{0j} = \gamma_{00} + U_{0j}$$

$$\beta_{0j} = \gamma_{00} + U_{0j}$$

(3)

$$\beta_{1j} = \gamma_{10} + U_{1j}$$

$$\beta_{1j} = \gamma_{10} + U_{1j}$$

Therefore, the intercept β_{0j} is made up of two parts: a fixed part γ_{00} representing the mean intercept and a random part U_{0j} representing individual deviations from the mean intercept (Equation 2). Similarly, the coefficient for age, β_{1j} , is made up of two parts: a fixed part γ_{10} representing the mean slope and a random part U_{1j} representing individual deviations from the mean slope (Equation 3). The time-specific residual term or random error for each individual, ε_{ij} , is assumed to be normally distributed with a mean at zero. If the residual term is not normally distributed, it is possible that the confidence interval used to capture the value of the process parameter becomes shorter than its necessary range of interval, leading to inaccurate conclusions being drawn about the process. However, the normality assumption for the residual term is not needed if sample size increases, especially if we consider repeated sampling at the population level (Bartlett, 2013). The random coefficients, U_{0j} and U_{1j} are not estimated directly; instead, the variance of U_{0j} and U_{1j} captures individual variation in baseline FI and changes of FI with age, respectively. The coefficient β_2 is the fixed effect of EH at baseline (i.e., when age is equal to zero; see more below). The coefficient β_3 is the fixed effect of the interaction between EH and age and signifies whether aging trajectories depend on an individual's EH. However, students should bear in mind that, for some datasets, there will only be enough power to fit a random intercept model implying that the rate of change in FI with age is the same for everyone.

Section Summary

- The multilevel growth curve model estimates between-individual differences in within-individual change using repeated-measures data over time.
- The multilevel growth curve model allows for random intercepts, implying that the intercepts of the trajectories are different across individuals.
- Some multilevel growth curve models have enough power to fit random slopes, implying that the rates of change in trajectories over time are different across individuals.

Fitting a Multilevel Growth Curve Model

Time Centering and Time Metrics

We applied a quadratic growth curve model to estimate the frailty trajectories by employment histories among men and women separately. First, we centered age on 65 for men and 60 for women. The ages of 65 and 60 were normal pension ages for men and women in our sample at that time, respectively. Centering age variables gives the intercept a more meaningful interpretation. In our study, the intercept indicates the average value of the FI at 65 years for men or at 60 years for women (i.e., at State Pension Age). Centering the time variable can reduce collinearity in quadratic and higher-order polynomial models; it will also change the estimates of intercept variance and intercept–slope covariance, depending upon in-/out-of-subject-specific slopes (Allerhand, 2016). However, in longitudinal studies, heterogeneity in time measures is common (i.e., when individuals vary in age at different occasions, or the time of onset of a disease varies between individuals).

A high degree of heterogeneity in the mean times of measurement between individuals might lead to an overestimation of the within-person time effect and an underestimation of the variance in the random time effect when the location of time was common across individuals (Blozis & Cho, 2008). When conducting multilevel growth curve models, apart from centering age at a particular age as we did, students could also center age either at the mean baseline age or at the overall mean age. The meaning of the intercept will also change accordingly, indicating the expected response of the dependent variable either at the mean baseline age or at the overall mean age.

Second, we considered the application of the Age-Period-Cohort (APC) model for data analysis. The APC model is a nonparametric regression (or additive) model where the predictor is a sum of age, period, and cohort effects. The APC model has been widely used in epidemiological studies, as many health outcomes change with age but are also affected by risk factors at different time periods and across birth cohorts. However, the age, period, and cohort effects are intertwined; the inclusion of all three effects results in perfect collinearity (Fannon & Nielsen, 2018). Therefore, researchers can choose to drop one of the three time variables for estimation. Any pair of the three factors is independent. If period is the metric of time, students could choose to control for year of birth or age at baseline (cohort) to build the Period-Cohort (PC) model (repeat wave model controlling for cohort). If age is the metric of time, students could choose to either control for any period effects using wave to build the Age-Period (AP) model (repeat age model controlling for wave), or control for the cohort effect using year of birth to build the Age-Cohort (AC) model (repeat age model controlling for cohort). The AP, AC, and PC models are all submodels of the APC model.

This can be based on a priori knowledge about the relative importance of age, period, and cohort. Alternatively, the likelihood ratio test can help decide which APC model to use through comparing the log likelihoods of different models. For our study, we eventually chose to fit the AP model, controlling for wave and our set of time-invariant and time-varying covariates.

Results of the multilevel growth curve model consist of both fixed and random effects. The fixed effects represent the mean frailty trajectory (intercept and slope) pooled across all individuals within the sample, ignoring any between-individual variation in effects of employment histories and other covariates on frailty. The random effects are expressed in terms of the variance of the mean intercept and slope, representing the between-individual variations in individual baseline frailty and individual frailty trajectories thereafter. In results, these are shown as random-effects parameters for residuals within (Level 1) and across (Level 2) individuals.

The likelihood ratio test also helped identify potential confounders for adjustment. Our final model included terms for age, age-squared, wave, all other covariates, as well as the interaction between employment histories and age. Please refer to Table 3 in our original article for details.

Stata offers a number of commands for the application of multilevel modeling. The command “xtmixed” can be used for the multilevel growth curve model. The basic syntax is given by “xtmixed depvar [fe_equation] [[[re_equation].” In our case, the depvar term was *FI*, the fe_equation listed all the independent variables in the

model, and the `re_equation` was of the form “`levelvar: [varlist]`,” where `levelvar` is the variable `ID` containing individual identification numbers and `varlist` is our centered age variable `agecen`. Students could refer to Stata manuals for more details ([StataCorp, 2008](#)).

Section Summary

- Age can be centered at a particular age, at the mean baseline age, or at the overall mean age.
- The AP, AC, and PC models are three types of multilevel growth curve models that have been widely used in epidemiological studies.
- Results of the multilevel growth curve model consist of both fixed and random effects.

Intraclass Correlation Coefficient

Some researchers like to calculate the intraclass correlation coefficient (ICC) based on the variations at Levels 1 and 2 to describe the proportion of the total variance at Level 1 (individual level). The equation for the calculation of ICC is

(4)

$$\rho = \sigma_u^2 / (\sigma_u^2 + \sigma_e^2)$$

$$\rho = \sigma_u^2 / (\sigma_u^2 + \sigma_e^2)$$

where σ_e^2 and σ_u^2 are the variations at Levels 1 and 2, respectively; $\sigma_u^2 + \sigma_e^2$ is the total variation. Possible values for ρ lie between 0 and 1 ([Srivastava & Keen, 1988](#)). However, students should bear in mind that although the ICC can be calculated, it cannot be interpreted for multilevel growth curve models with random slopes. Fitting a growth curve model with random slopes results in the estimation of two random terms at the individual level: a set of intercept residuals and a set of residuals for each set of random slopes. Therefore, the ICC's simplicity as a measure of clustering is diminished as it becomes a function of several predictor variables if they have random coefficients at either level ([Goldstein et al., 2002](#)).

Section Summary

- ICC is to describe the proportion of total variance at individual level.
- However, ICC cannot be interpreted for multilevel growth curve models with random slopes.

Predicting Health Trajectories

Predicting frailty trajectories by employment histories with the increase in age after 60/65 years old could be very useful for the interpretation of the nonlinear effects of age and interactions between age and employment histories. We calculated the marginal effects of the employment histories on frailty at each year after 60 (for women) and 65 (for men) years old, separately. The marginal effect for continuous variables measures the instantaneous rate of change in a dependent variable that will be produced by a one-unit change in

an independent variable, when other covariates are assumed to be constant. There are three types of the marginal effect: average marginal effect (AME), marginal effect at the mean (MEM), and marginal effect at representative values (MER). If we hold each covariate at the observed value for each individual in the sample, calculate the relevant predicted marginal effect for each individual, and then take the average over all cases, we will obtain AME. If we calculate the marginal effect by setting the values of other covariates to their respective sample means, we will obtain MEM. Alternatively, if we choose specific values instead of mean values for covariates to calculate marginal effects, we will obtain MER ([Williams, 2012](#)).

Researchers argued that the AME approach is superior to the MEM approach as the latter approach seeks to understand the effect of the independent variable on the dependent variable for the average case in a sample, whereas the former approach aims to obtain an estimate of the average effect of the independent variable in the population. Using the MEM approach to predict marginal effects may introduce prediction bias, especially when predicting the marginal effects for cases in a very small subsample group. The reason is that predictions based on the sample means across all independent variables may not represent typical cases and may not even be observed in a population. The AME approach is able to buffer the bias brought by skewed sample distributions ([Hanmer & Kalkan, 2013](#)).

However, the approaches of AME and MEM both produce a single estimate of the marginal effect of an independent variable. With the MER approach, we can choose ranges of values for one or more covariates to assess how the marginal effects differ across that range. In our analysis, we set the values of age between 60/65 and 90, to predict the marginal effects of employment histories on frailty at each year of age after 60 (for women) and 65 (for men) years old, separately. Please refer to Figures 1 and 2 in our 2017 article for marginalized frailty trajectories. In a complicated model with many covariates, it might be impossible to specify representative values for each covariate. For those variables of least interest, students could set them to either their mean values or observed values.

Stata offers a number of commands for the prediction of the marginal effect for both linear and nonlinear models. The command “margins” can calculate the marginal effect in the presence of random effects, which is followed by the command “marginsplot” to visualize the marginalized trajectories. The option “atmeans” can tell Stata to estimate margins at the mean values of covariates, whereas the option “at(asobserved)” can tell Stata to estimate margins at observed values of covariates. Students could refer to Stata manuals for details ([StataCorp, 2013](#)).

Section Summary

- The calculation of marginal effects is an approach for the prediction of health trajectories.
- The AME, MEM, and MER are three types of the marginal effect.
- With the MER approach, we can choose ranges of values for one or more covariates to assess how the marginal effects of an explanatory variable differ across that range.

Handling Missing Data

Missing data in employment histories, FIs, and other covariates is the main methodological challenge we met. We employed multiple imputation (MI) to deal with missing data through chained equations. MI has become a popular approach to handle missing data by replacing each missing value with multiple imputed values. The assumption is that all missing values in each wave are missing at random ([Azur et al., 2010](#)). In reality, it might be inapplicable testing the assumption of missing at random. However, students could consider employing a pattern mixture model via MI to detect the robustness of the results ([Little, 1994](#)). In our study, we only imputed nonresponse items in each wave. In longitudinal studies where individuals' characteristics are measured repeatedly across waves, it is recommended to impute missing items within a wave that an individual responded to and not impute items for a wave where the individual did not respond. For example, across three waves, if a person attended only the first two waves and then dropped out of the study, his or her information in the third wave is not imputed. The application of the multilevel growth curve model is actually able to handle attrition and wave nonresponse ([Curran et al., 2010](#)).

There is also a debate over whether or not to apply imputed values of dependent variables in statistical analysis. Imputed outcome values might introduce bias because of simulation error. Some researchers also suggest including auxiliary variables in the imputation model. In survey research, if a variable is available for all units in a population but not a variable of interest for the analysis model, it can be employed to enhance estimation of missing values for the variables of interest and is called an auxiliary variable ([Cohen, 2011](#)). To impute the dependent variable in the analysis model, the auxiliary variable must be highly correlated with the dependent variable. If a set of auxiliary variables is included, imputation can be considerably more efficient than complete case analysis, resulting in more precise estimates and narrower confidence intervals ([Roderick, 1992](#)). However, some researchers have argued that including many auxiliary variables in a small sample could lead to a downward bias of regression coefficients and, especially, decrease precision. The reason is that when including many auxiliary variables, the ratio of observations to variables will become low, resulting in overparameterization of the imputation model. In that case, the regression model may become unstable. Therefore, it has been suggested that the number of observations with complete data should be at least three times the number of variables included in the imputation model ([Hardt et al., 2012](#)). In our study, we developed the FI for each individual using 60 health indicators in physical capabilities, depressive symptoms, self-reported chronic conditions, cognitive function, falls, and pain (please refer to Supplementary Table S1 in our article). The inclusion of a large number of health indicators for the construction of the FI made the selection of extra health indicators as auxiliary variables difficult. We were also concerned that potential auxiliary variables that were highly correlated with FIs might differ between men and women. Therefore, we decided to use imputed values for employment histories and covariates, and original values of the FI for statistical analysis.

Researchers have also developed another approach to MI—the twofold fully conditional specification (FCS). Records with imputed values for nonrespondents in each wave can be automatically excluded. Students can refer to an article for details ([Nevalainen et al., 2009](#)).

Section Summary

- MI has been widely used to handle missing data by replacing each missing value with multiple imputed values.
- It is recommended to impute missing items within a wave that an individual responded to and not impute items for a wave where the individual did not respond.
- There is debate over whether or not to use imputed values of dependent variables in subsequent statistical analysis.

Practical Lessons Learned

In the previous section, we specifically introduced what the multilevel growth curve model is, how we fit a multilevel growth curve model, methodologies for the prediction of frailty trajectories, and the methodological challenge in our analysis. In this section, we will summarize some practical tips based on the previous section for students who wish to apply multilevel modeling and predict health trajectories in their research.

First, the multilevel growth curve model estimates between-individual differences in within-individual change using repeated-measures data over time. In epidemiological studies, growth curve models are suitable for research questions about the prediction of population and individual trajectories of health outcomes by different risk factors.

Second, when fitting a multilevel growth curve model, centering the time variable is recommended, especially in quadratic and higher-order polynomial models. For example, age can be centered at certain particular age, at the mean baseline age, or at the overall mean age. After centering the time variable, the intercept of the model means the expected response of the dependent variable at the centering time. When applying the APC model, we suggest trying to build different submodels (PC, AP, or AC models) and selecting the best-fit model by comparing the log likelihoods of different models. Students could add random intercept and slope to the model; but please bear in mind that some datasets have only enough power to fit a random intercept model. Besides, the calculation of ICC is not applicable for models with random slopes. The command “xtmixed” in Stata can be used for the multilevel growth curve model.

Third, in terms of the prediction of health trajectories, the calculation of the marginal effect is recommended. There are three types of the marginal effect: AME, MEM, and MER. Students can calculate MER to predict health trajectories over time. For example, if students wish to draw health trajectories as people age by education, they could choose a range of values for age to calculate the marginal effects of education on health at each value of that age range. In a model with many covariates, it might be impossible to specify representative values for each covariate. For those variables of least interest, students could set them to either their mean values or observed values. Students can also calculate the marginal effect based on nonlinear models. The commands “margins” and “marginsplot” in Stata can be used for the prediction of the marginal effect and the visualization of the marginalized trajectories, respectively.

Last, both chained equations and twofold FCS algorithm can be applied for handling missing data. For longitudinal analysis, the principle of imputing nonresponse items within a wave but not imputed values for a full set of items for nonresponders of a wave should be noted. One advantage of the multilevel growth curve model is that it is capable of handling attrition and wave nonresponse. There is debate over whether or not to use imputed values of dependent variables in subsequent statistical analysis. Before making a decision, students should consider the sample sizes of their studies, as well as the feasibility of the inclusion of appropriate auxiliary variables in MI.

Section Summary

- The multilevel growth curve model is an approach for the prediction of population and individual trajectories of health outcomes.
- Time centering, time metrics, random intercepts and slopes, as well as ICC are several important components to consider when fitting a multilevel growth curve model.
- The calculation of MER values can be applied to predict health trajectories over time.
- Both chained equations and twofold FCS algorithm are approaches for handling missing data; however, issues of imputing full items for nonresponders in a wave and using imputed values of dependent variables should be noted.

Conclusion

In conclusion, this case study provides some guidance for the application of the multilevel growth curve model and the prediction of health trajectories. Using our own longitudinal analysis as an example, apart from introducing basic concepts and principles, we touched on a few of the important pragmatic issues associated with growth curve modeling and trajectory prediction, including time centering, selection of time metrics, calculation of ICC and MER, as well as imputation of missing outcomes, to help students gain a better understanding of multilevel modeling and build appropriate multilevel models for their studies.

Classroom Discussion Questions

Classroom Discussion Questions

1. What is the multilevel growth curve model? Based on your research areas, can you give examples of research question which are suitable for its application?
2. If age is the time variable, please list three ways of centering age.
3. What are the metric of time and the control for the AP, AC, and PC models, respectively?
4. List three types of the marginal effect and explain how to draw health trajectories by education with the increase in age.

Declaration of Conflicting Interests

The Authors declare that there is no conflict of interest.

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Web Resources

<http://www.bristol.ac.uk/cmm/learning/multilevel-models/>

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