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Using structural equation modeling to investigate change in health-related quality of life

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CHAPTER 3

The Analysis of Multivariate Longitudinal Data: An Instructive Application of the Longitudinal Three-Mode Model

Structural equation modeling is a common technique to assess change in longitudinal designs with a limited number of measurement occasions (e.g., two or three). However, these models can become of unmanageable size with many more measurement occasions. One solution is the imposition of Kronecker product restrictions to model the multivariate longitudinal structure of the data. The resulting longitudinal three-mode models (L3MMs) are very parsimonious and have attractive interpretation. In this study, L3MMs were applied to health-related quality of life (HRQL) data obtained from 682 patients with painful bone metastasis, with 8 measurements at 13 occasions (104 variables); before and every week after treatment with radiotherapy. Using the Kronecker product restrictions we will illustrate (1) how to model the multivariate longitudinal structure of the data, (2) how to interpret L3MM parameters, and (3) how to test substantive hypotheses. Compared to the ordinary common factor model with 1270 parameter estimates, the L3MM restrictions lead to more parsimonious models (with a total number of parameter estimates between 1118 and 132) that provide a close fit to the longitudinal HRQL data. Results indicated that patients' functional limitations increased over time, while their health impairments decreased. In addition, the change patterns suggest that patients became more homogenous in their answers to the questionnaires. We conclude that the L3MM provides a convenient model for multivariate longitudinal data, as it not only facilitates the analysis of complex longitudinal data but also the substantive interpretation of the dynamics of change.

This chapter is based on: Verdam, M. G. E., & Oort, F. J. (2015). *The analysis of multivariate longitudinal data: An instructive explanation of the longitudinal three-mode model*. Manuscript submitted for publication.

Introduction

Longitudinal studies in the life-sciences involve multiple observations at multiple measurement occasions, yielding multivariate longitudinal data sets. Structural equation modeling (SEM) offers a general and versatile framework for the analysis of such data. Compared to usual regression methods, SEM allows for the use of latent variables and measurement error of observed variables, and provides tests for overall goodness of fit, and for specific hypotheses about relationships between variables and longitudinal developments. The longitudinal factor model (LFM; Tisak & Meredith, 1990; Oort, 2001) may include multiple latent variables, with multiple indicators from multiple measurement occasions, and thus enables investigation of complex longitudinal relations. However, the LFM becomes progressively large and unmanageable when the number of measurement occasions increases. For example, when the data-structure consists of 9 indicators of 3 common factors (e.g., studying the development of three different social or behavioral constructs), the LFM requires estimation of 78 parameters when it includes 2 measurement occasions, 228 parameters when it includes 4 measurement occasions, and 450 parameters when it includes 6 measurement occasions (see Appendix 3A for the calculation of the numbers of parameters). Estimation of model parameters may be difficult with such large models. Also, it has been argued that the trustworthiness of results decreases when the number of parameter estimates increases in relation to the sample size (Bentler & Chou, 1978; Jackson, 2003; Kline, 2011). Moreover, it becomes more difficult to arrive at a meaningful interpretation of findings when the number of model parameters is larger. For the interpretation of relations between the common factors from 2, 4 or 6 measurement occasions in the situation above, the LFM provides 15, 66 or 153 correlation estimates respectively (see Appendix 3A). Such large numbers of parameter estimates complicate a meaningful interpretation of change in the relationships between common factors across time.

The increasing complexity of multivariate longitudinal models with multiple measurement occasions can be reduced by imposing additional restrictions on model parameters. The longitudinal three-mode model (L3MM; Oort, 2001) imposes so-called Kronecker product restrictions on model parameters to describe the three-mode structure of the data. The three modes refer to the subjects, the measurement occasions and the variables. The Kronecker product is an operation that can be applied to two matrices **A** and **B** of arbitrary size, and results in a block matrix that contains the matrices **B** pre-multiplied by each element of **A** (see Appendix 3B). With Kronecker products, relationships between all variables from all measurement occasions are decomposed into parameters that describe the relationships between variables that apply to all measurement occasions, and parameters that describe the relationships between measurement occasions that apply to all variables. Using this multiplicative decomposition, the L3MM describes all relationships between all variables from all measurement occasions, but requires only the estimation of a much smaller number of parameters. In the example described above, imposition of Kronecker-product restrictions on the relations between the common factors would require

only 6, 13 or 24 estimates for the interpretation of 15, 66, or 153 correlations between common factors from 2, 4 or 6 measurement occasions respectively. The L3MM thus substantially reduces the number of parameter estimates (i.e., leading to more parsimonious model), especially with larger numbers of measurement occasions. In addition, the substantive interpretation of change in the relations between common factors is facilitated as the L3MM yields separate estimates for the relationships between (observed and latent) variables and the relationships between the measurement occasions (i.e., the change in the relationships between the variables over time).

The aim of the present paper is to provide an instructive application of L3MMs. We will apply the L3MM to health-related quality of life (HRQL) data obtained from 682 patients with painful bone metastasis, with 8 measurements at 13 occasions (104 variables); before and every week after treatment with radiotherapy. Part of these data have been analyzed before using simple repeated measures analyses to compare the development of HRQL between two different treatment regimens (Steenland et al., 1999), or using between group analyses to compare scores from only one specific measurement occasion (van der Linden et al., 2004). A comprehensive analysis of the multivariate longitudinal development of HRQL is possible through SEM, by imposing Kronecker product restrictions. Using the example of bone metastases we will illustrate (1) how to take into account the multivariate longitudinal structure of the data, (2) how to interpret L3MM parameters, and (3) how to test substantive hypotheses.

Method

Sample

The sample in the current study is a subset from the sample from the Dutch Bone Metastasis Study (DBMS; Steenland et al., 1999; van der Linden et al., 2004; van der Linden et al., 2006). In the DBMS, a total of 1157 patients (533 women) with painful bone metastases from a solid tumor were enrolled from 17 radiotherapy institutes in The Netherlands. Purpose of the study was to prove the equal effectiveness of single fraction versus multiple fraction radiation therapy for patients with painful bone metastases; endpoint of the study was response to pain. The Medical Ethics Committees of all participating institutions approved the study and all patients gave their informed consent. For the present study only patients who survived at least 13 weeks were included, which resulted in a total sample size of 682 patients (354 women). Patients' primary tumor was either breast cancer ($n=321$), prostate cancer ($n=181$), lung cancer ($n=106$), or other ($n=74$). Ages ranged from 33 to 90, with a mean of 64.2 (standard deviation 11.5).

Measures

Health-related quality of life questionnaires were administered before treatment (T0), and during the first 12 weeks of follow-up, patients completed weekly HRQL questionnaires by mail (T1 through T12). Eight health-indicators were computed using the available data (for

more information, see Verdam, Oort, van der Linden & Sprangers, 2015), and were modeled to be reflective of two common factors: functional limitations and health impairments (see Figure 1). The squares represent observed variables (scale scores), the circles on the top represent the common factors, and the circles on the bottom represent residual factors. Functional limitations are measured by three observed variables, health impairments are measured by six observed variables, with one observed variable in common.

Statistical Analyses

The program OpenMx (Boker et al., 2011) was used to run the statistical analyses. OpenMx is free and open source software for use within R that allows estimation of a wide variety of advanced multivariate statistical models. It was used because it allows for an operation of the structural equation model using matrix specifications, and therefore the Kronecker product restrictions can be easily applied. Syntaxes of all analyses that are reported in this paper are provided as online supplementary material.¹

Evaluation of Goodness-of-Fit

To evaluate goodness-of-fit the chi-square test of exact fit (CHISQ) was used, where a significant chi-square indicates a significant difference between model and data. As an alternative, the root mean square error of approximation (RMSEA; Steiger & Lind, 1980; Steiger, 1990) was used as a measure of approximate fit, where an RMSEA value below .05 indicates 'close' approximate fit, and values below .08 indicate 'reasonable' approximate fit (Browne & Cudeck, 1992). Additionally, the expected cross-validation index (ECVI; Browne & Cudeck, 1989) can be used to compare different models for the same data, where the model with the smallest ECVI indicates the model with the best fit. For both the RMSEA and ECVI 95% confidence intervals were calculated using the program NIESEM (Dudgeon, 2003). We also calculated the Comparative Fit Index (CFI; Bentler, 1990), where the model of interest is compared to the independence model, i.e., a model where all covariances in Σ are assumed zero. The CFI ranges from zero to one, and as a general rule of thumb values above 0.95 are indicative of relatively 'good' model fit (Hu & Bentler, 1999).

With different tests and indices to evaluate model fit, providing decision rules on whether the fit of a model is 'good' is complicated by the fact that one might find inconsistent results (e.g., a significant exact chi-square test, but close approximate fit according to the RMSEA). The researcher then has to make a decision on which fit index is most appropriate for the data and hypotheses under study. For example, although the chi-square test of exact fit is the most commonly used, it is also generally acknowledged that it tends to become significant in larger samples and favors highly parameterized models. Indices of approximate fit are less dependent on sample size and reward model parsimony, but they usually do not provide a test of model fit. In our example of bone metastasis the sample size is large and the model has many degrees of freedom. This might cause the chi-square test of exact fit to have high power to detect small, but

¹ Syntaxes can be retrieved from the first authors' Open Science Framework page at osf.io/kzyvh

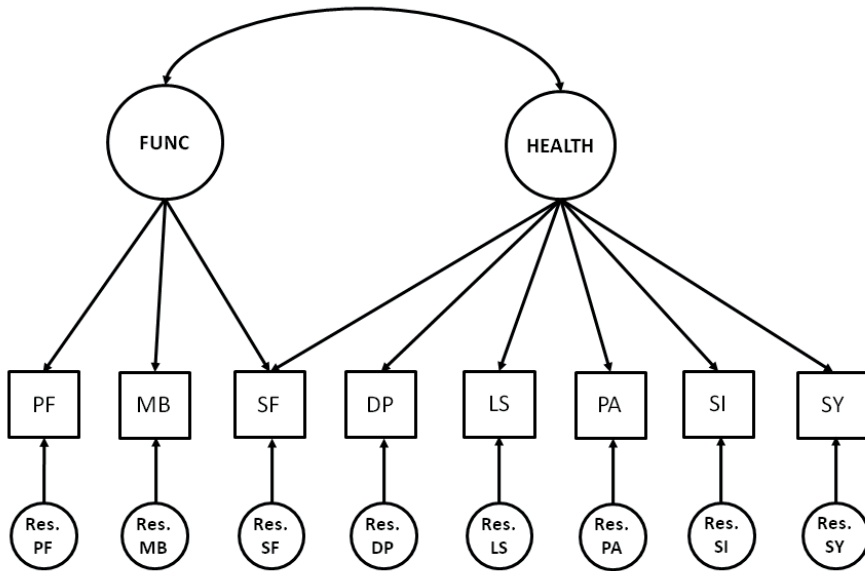


Figure 1 | The measurement model

Notes: Circles represent latent variables (common and residual factors) and squares represent observed variables (the scale scores). FUNC = functional limitations, HEALTH = health impairments, PF = physical functioning, MB = mobility, SF = social functioning, DP = depression, LS = listlessness, PA = pain, SI = sickness, SY = treatment related symptoms, and Res. = Residual factors.

trivial, differences between model and data. Therefore, in this paper we will base our evaluation of overall model fit on indices of approximate fit and will substantiate decisions on model fit evaluation in case of inconsistent results. A more extensive discussion about model fit evaluation is provided in the discussion paragraph at the end of this paper.

Evaluation of Differences in Model Fit

To evaluate differences between hierarchically related models the chi-square difference test ($CHISQ_{diff}$) can be used, where a significant chi-square indicates a significant difference in model-fit. The ECVI difference ($ECVI_{diff}$) can be used to test equivalence in approximate model fit, where a value that is significantly larger than zero indicates that the more restricted model has significantly worse approximate fit. In addition, it has been proposed that the difference between CFI values (CFI_{diff}) can be used to evaluate measurement invariance and more generally, the difference in model fit between two nested models (Cheung & Rensvold, 2002). As a rule of thumb CFI_{diff} values larger than 0.01 are taken to indicate that the more restricted model should be rejected. As confidence intervals are not available for CFI values, the CFI_{diff} cannot be used to test whether the difference in model fit is significant.

Evaluation of differences in model fit is complicated for similar reasons as described above. When comparing different models for the same data, one has to decide on the trade-off between a deterioration of model fit and a gain in model parsimony. Such decisions should be guided by the evaluation of differences in model fit, but depend also on the substantive considerations with regards to interpretation of the model or model parameters. For example, the imposition of Kronecker product restrictions to take into account the multivariate longitudinal structure of the data generally leads to a large gain in model parsimony. When one considers the assumption of the multivariate structure of the data to be reasonable, one might not want to have too much power to detect small, but trivial, differences between model and data. However, when testing specific substantive hypotheses one might consider high power to detect small differences to be beneficial. In this paper we will report results of all tests for differences in model fit that are explained above and will provide a rationale for the decision that is being made.

The Longitudinal Three-Mode Model (L3MM)

In order to facilitate interpretation of the longitudinal three-mode model (L3MM) we build upon the longitudinal factor model (LFM) to explain the imposition of Kronecker product restrictions one step at a time. In addition, we use the example of bone metastases data to explain how the imposition of Kronecker product restrictions increases model parsimony and facilitates interpretation of parameters. Using an integration of both general model formulations and the data example we aim to optimize the explanation of L3MMs.

The Longitudinal Factor Model

To explain how the L3MM can be used to model the multivariate longitudinal structure of the data, we will first describe the LFM and show how Kronecker product restrictions can be applied to yield the L3MM. In our example of bone metastases data, eight health-indicators ($K = 8$) are measured at 13 consecutive measurement occasions ($J = 13$), resulting in a total of 104 variables ($JK = 104$). The eight health-indicators are modeled to be reflective of two common factors ($R = 2$), so that the total number of common factors in the longitudinal model is 26 ($JR = 26$). Following the LFM, the means and covariances of the observed variables in our example are given by:

$$E(\mathbf{x}) = \boldsymbol{\mu} = \boldsymbol{\tau} + \boldsymbol{\Lambda} \boldsymbol{\kappa}, \quad (1)$$

and:

$$\text{Cov}(\mathbf{x}, \mathbf{x}') = \boldsymbol{\Sigma} = \boldsymbol{\Lambda} \boldsymbol{\Phi} \boldsymbol{\Lambda}' + \boldsymbol{\Theta}, \quad (2)$$

where $\boldsymbol{\tau}$ is a JK -vector of intercepts (of dimensions 104×1 , containing 104 parameters that are free to be estimated), $\boldsymbol{\Lambda}$ is a $JK \times JR$ matrix of common factor loadings (of dimensions 104×26 , in this case containing 117 parameters that are free to be estimated), $\boldsymbol{\kappa}$ is a JR -vector of common factor means (of dimensions 26×1 , containing 26 parameters), $\boldsymbol{\Phi}$ is a $JR \times JR$ symmetric matrix containing the variances and covariances of the common factors (of dimensions 26×26 ,

containing 351 non-redundant parameters), and Θ is a $JK \times JK$ symmetric matrix containing the variances and covariances of the residual factors (of dimensions 104×104 , containing 728 parameters). To achieve identification of all model parameters, scales and origins of the common factors can be established by fixing the common factor means at zero and the common factor variances at one (leaving no free parameters in κ and 325 free parameters in Φ).

Imposition of Kronecker Product Restrictions

The L3MM can be described by restrictions on the parameter matrices that feature in the mean and covariance structures of the longitudinal factor model. We will explain these restrictions on each of the parameter matrices, and how further restrictions can be imposed to test substantive hypotheses. Specifically, we will explain the imposition of Kronecker product restrictions on (1) factor loadings and intercepts (Λ and τ) to comply with longitudinal measurement invariance; (2) residual factor variances and covariances (Θ), and additional restrictions to test equality of variances, correlations and covariances across occasions; (3) common factor variances and covariances (Φ), and additional restrictions to test equality of variances, correlations and covariances across occasions; (4) common factor means (κ), and additional restrictions to test a linear trend of common factor means; and (5) we will explain more restrictive longitudinal structures such as the autoregressive model and latent curve model. The order of the imposition of Kronecker product restrictions was chosen because the Λ and τ restrictions (1) are the most logical starting point from the researchers perspective, as longitudinal measurement invariance is required for the comparison of common factors means, the Θ and Φ restrictions (2, 3) are most effective in increasing model parsimony and facilitating parameter interpretation, while the κ and other restrictions (4, 5) can be used to test specific hypotheses regarding the common factor means while profiting from the model parsimony yielded by the earlier restrictions.

Step 1: Longitudinal Measurement Invariance. With longitudinal data, the structure of matrix Λ is a block diagonal matrix containing matrices of factor loadings of each measurement occasions on the diagonal ($\Lambda_1, \Lambda_2, \dots, \Lambda_j, \dots, \Lambda_j$; see Table 1), where each of the Λ_j is a $K \times R$ matrix containing the factor loadings of occasion j . Vector τ consists of stacked vectors of intercepts from all measurement occasions ($\tau_1, \tau_2, \dots, \tau_j, \dots, \tau_j$; see Table 1), where each of the τ_j is $K \times 1$. To test substantive hypotheses about the common factors, it is required that the meaning of these factors is the same across occasions. The requirement of longitudinal measurement invariance entails that the common factor loadings (Λ_j) and the intercepts (τ_j) are invariant across occasions (i.e., $\Lambda_j = \Lambda_0$, and $\tau_j = \tau_0$ for all j). The usual longitudinal measurement invariance restrictions, that is, equality restrictions on factor loadings and intercepts across time, can be written as a Kronecker product constraint:

$$\Lambda = \mathbf{I} \otimes \Lambda_0, \quad (3)$$

$$\tau = \mathbf{u} \otimes \tau_0, \quad (4)$$

where Λ_0 is a $K \times R$ matrix of invariant common factor loadings, τ_0 is a $K \times 1$ vector of invariant intercepts, \mathbf{I} is a $J \times J$ identity matrix, \mathbf{u} is a $J \times 1$ vector of ones, and the symbol \otimes denotes the Kronecker product (see Table 1). The Kronecker product operations in equations (3) and (4) impose the restriction that factor loadings Λ_0 and intercepts τ_0 apply to all measurement occasions.

Table 1 | Imposition of measurement invariance restrictions on factor loadings and intercepts using the Kronecker product

Factor loadings (Λ), assuming $\Lambda_j = \Lambda_0$ for all j		
$\Lambda_{(JK \times JR)}$ 104 x 26	$\mathbf{I}_{(JJ)}$ 13 x 13	$\Lambda_{0(K \times R)}$ 8 x 2
$\left \begin{array}{cccc} \Lambda_{1(K \times R)} & & & \\ \Lambda_2 & & & \\ & \Lambda_3 & & \\ & & \dots & \\ & & & \Lambda_J \end{array} \right $	$= \left \begin{array}{cccc} 1 & & & \\ & 1 & & \\ & & 1 & \\ & & & \dots \\ & & & & 1 \end{array} \right $	$\otimes \left \begin{array}{cc} \lambda_{11} & \\ \lambda_{21} & \\ \lambda_{31} & \lambda_{32} \\ & \lambda_{42} \\ & \lambda_{52} \\ & \lambda_{62} \\ & \lambda_{72} \\ & \lambda_{82} \end{array} \right $
Intercepts (τ), assuming $\tau_j = \tau_0$ for all j		
$\tau_{(JK \times 1)}$ 104 x 1	$\mathbf{u}_{(JJ)}$ 13 x 1	$\tau_{0(K \times 1)}$ 8 x 1
$\left \begin{array}{c} \tau_{1(K \times 1)} \\ \tau_2 \\ \tau_3 \\ \dots \\ \tau_J \end{array} \right $	$= \left \begin{array}{c} 1 \\ 1 \\ 1 \\ \dots \\ 1 \end{array} \right $	$\otimes \left \begin{array}{c} \tau_1 \\ \tau_2 \\ \tau_3 \\ \tau_4 \\ \tau_5 \\ \tau_6 \\ \tau_7 \\ \tau_8 \end{array} \right $

Notes: Λ_0 and τ_0 contain invariant factor loadings and intercepts of one measurement occasion that are applicable to all measurement occasions, \mathbf{I} and \mathbf{u} are an identity matrix and unity vector with dimensions equal to the number of measurement occasions, and the symbol \otimes denotes the Kronecker product.

Step 2: Residual Factor Variances and Covariances. Matrix Θ is a symmetric $JK \times JK$ matrix, consisting of $K \times K \Theta_{jj'}$ matrices that contain the covariances of the residual factors on occasion j with the residual factors on occasion j' . Residual factors do not correlate with other residual factors, but are allowed to correlate with the same residual factors across occasions. Thus, all $\Theta_{jj'}$ matrices are diagonal. In our example, the complete Θ matrix has dimensions 104 x

104 and contains 728 free parameters, thus adding a large number of parameters to the model. Imposition of the Kronecker product restriction entails:

$$\Theta = \Theta_T \otimes \Theta_V, \quad (5)$$

where the full $JK \times JK$ matrix (Θ) is decomposed into two smaller matrices that describe the relations between the measurement occasions (Θ_T ; a symmetric matrix of dimensions $J \times J$) and the variances of the residual factors (Θ_V is a diagonal matrix of dimensions $K \times K$, containing within occasion correlations between residual factors). The subscripts ‘T’ and ‘V’ refer to ‘time’ and ‘variable’. Instead of estimating all 728 parameters of Θ , we now estimate the parameters of Θ_T (of dimensions 13×13 , containing 91 non-redundant free parameters) and Θ_V (of dimensions 8×8 , containing 8 free parameters; see Table 2). To achieve identification at least one parameter of Θ_T or Θ_V needs to be fixed at a non-zero value. We choose to fix the first element of Θ_T to unity, which is a convenient choice for the interpretation of parameter estimates. Matrix Θ_V then contains the residual factor variances at the first measurement occasion, and Θ_T contains coefficients of proportionate change. Imposing the Kronecker product restriction implies that the changes in variances and covariances of the residual factors across occasions are proportionate for all residual factors. In our example of bone metastases, it may be reasonable to assume that the residual variances of the observed indicators are either invariant or change proportionately over time (e.g., patients may show more or less variability and co-variability over time, where this change is proportionally equal for all observed variables).

To further facilitate interpretation of parameter estimates it is convenient to use a reparameterization that decomposes the residual factor variances and covariances of Θ into correlations Θ^* and standard deviations Δ :

$$\Theta = \Delta \Theta^* \Delta, \quad (6)$$

where Δ is a $JK \times JK$ diagonal matrix containing the standard deviations of the residual factors, and $\text{diag}(\Theta^*) = \mathbf{I}$, so that the off-diagonal elements of Θ^* contain the correlations between the residual factors. This, in turn, enables the imposition of Kronecker product restrictions on residual factor correlations, using:

$$\Theta^* = \Theta_T^* \otimes \Theta_V^*, \quad (7)$$

where the full correlation matrix (Θ^*) is decomposed into two smaller matrices that describe the correlations between the measurement occasions (Θ_T^*) and the correlations between residual factors (Θ_V^*). As residual factors do not correlate with other residual factors, $\Theta_V^* = \mathbf{I}$. Instead of estimating 624 parameters of Θ^* , we now only estimate the 78 parameters of Θ_T^* (see Table 2). The reparameterization therefore allows investigation of the Kronecker product restrictions on residual factor correlations, while allowing each residual factor to have a unique standard deviation. In our example of bone metastases, it may be reasonable to assume that the relations between the residual factors are either invariant or change proportionately over time.

In addition, Kronecker product restrictions can be imposed on the standard deviations of the residual factors, using:

$$\Delta = \Delta_T \otimes \Delta_V, \quad (8)$$

where Δ_T is a $J \times J$ diagonal matrix that describes the proportionate change in standard deviations across occasions (of dimensions 13×13 , containing 13 parameters, with the first parameter fixed at unity for the purpose of identification), and Δ_V is a diagonal $K \times K$ matrix that contains the standard deviations of the residual factors at the first occasion (of dimensions 8×8 , containing 8 parameters; see Table 2). Imposition of Kronecker product restrictions on both Θ^* and Δ is equivalent to the imposition of the Kronecker product restriction directly on Θ (as in Equation 5).

Substantive hypotheses. Further restrictions enable hypothesis tests about the equality of residual factor correlations, variances, and covariances. In our example of bone metastases it may be of interest to test whether the variances of the residual factors are invariant across time.

Equality of residual factor correlations of the same lag is investigated by imposing a banded structure on Θ_T^* in Equation 7 so that all elements of the same diagonal are equal. This restriction implies that correlations between residual factors at the first occasion and residual factors at the second occasion are equal to correlations between residual factors at the second and third occasion, and so on.

Equality of residual factor standard deviations is investigated by imposing:

$$\Delta = \mathbf{I} \otimes \Delta_0, \quad (9)$$

where \mathbf{I} is a $J \times J$ identity matrix and Δ_0 contains the invariant standard deviations of the residual factors of one measurement occasion that are applicable to all measurement occasions.

Equality of residual factor covariances across occasions of the same lag is tested by imposing both restrictions described above. This is equivalent to the imposition of the Kronecker product to Θ (as in Equation 5), where the banded structure is imposed on Θ_T .

Step 3: Common Factor Variances and Covariances. The procedure of imposing Kronecker product restrictions on the matrix of common factor variances and covariances is largely similar to the procedure for imposing Kronecker product restrictions on the matrix of residual factor variances and covariances described above.

Matrix Φ is a $JR \times JR$ symmetric matrix, consisting of $R \times R$ Φ_{jj} matrices that contain the covariances of the common factors at occasion j with the common factors at occasion j' . In our example of bone metastases data (with $J = 13$ and $R = 2$) the complete Φ matrix is of dimensions 26×26 containing 351 parameters. Imposition of the Kronecker product restriction implies that the change in relations between the common factors across occasions is proportionate for all common factors:

$$\Phi = \Phi_T \otimes \Phi_V, \quad (10)$$

Table 2 | Imposition of Kronecker product restrictions on residual factor variances and covariances

Residual factor variances and covariances (Θ)											
$\Theta_{(JKsJK)}$ 104 x 104				$\Theta_{T(JsJ)}$ 13 x 13				$\Theta_{V(KsK)}$ 8 x 8			
$\Theta_{11(KsK)}$	Θ_{21}	Θ_{22}	...	Θ_{J1}	Θ_{J2}	...	Θ_{JJ}	=	θ_{T11} θ_{T21} θ_{T22} ... θ_{TJ1} θ_{TJ2} ... θ_{TJJ}	\otimes	θ_{V11} θ_{V22} ... θ_{VKK}
Residual factor correlations (Θ^*)											
$\Theta^*_{(JKsJK)}$ 104 x 104				$\Theta^*_{T(JsJ)}$ 13 x 13				$\Theta^*_{V(KsK)}$ 8 x 8			
$I_{(KsK)}$	Θ^*_{21}	I	...	Θ^*_{J1}	Θ^*_{J2}	...	I	=	1 θ^*_{T21} 1 ... θ^*_{TJ1} θ^*_{TJ2} ... 1	\otimes	1 1 ... 1
Residual factor standard deviations (Δ)											
$\Delta_{(JKsJK)}$ 104 x 104				$\Delta_{T(JsJ)}$ 13 x 13				$\Delta_{V(KsK)}$ 8 x 8			
$\Delta_{1(KsK)}$	Δ_2	...	Δ_J	=	δ_{T11} δ_{T22} ... δ_{TJJ}	\otimes	δ_{V11} δ_{V22} ... δ_{VJJ}				

Notes: Residual factor covariances (Θ), correlations (Θ^*) and standard deviations (Δ) are decomposed using the Kronecker product (\otimes), where Θ_T, Θ_T^* and Δ_T represent relationships between measurement occasions of residual factor covariances, correlations and standard deviations; and Θ_V, Θ_V^* and Δ_V represent residual factor variances, correlations and standard deviations of one measurement occasion.

where Φ_T is a $J \times J$ symmetric matrix that describes the relationships between the measurement occasions (of dimensions 13×13 , containing 91 parameters), and Φ_V is a $R \times R$ symmetric matrix that describes the relationships between the variables (of dimensions 2×2 , containing 3 parameters). Thus, imposition of the Kronecker product restriction requires estimation of 94 parameters to compute all 351 parameters of Φ (see Table 3). For the purpose of identification, the first element of Φ_T is fixed at unity so that Φ_V contains the common factor variances and covariances at the first measurement occasion, and Φ_T contains coefficients of proportionate change. In our example of bone metastasis, it could be interesting to test whether the change in the variances and covariance of the underlying factors is proportionate over time.

Table 3 | Imposition of Kronecker product restrictions on common factor variances and covariances

Common factor variances and covariances (Φ)		
$\Phi_{(JR \times JR)}$ 26×26	$\Phi_{T(J \times J)}$ 13×13	$\Phi_{V(R \times R)}$ 2×2
$\left \begin{array}{cccc} \Phi_{11(R \times R)} & & & \\ \Phi_{21} & \Phi_{22} & & \\ \dots & \dots & \dots & \\ \Phi_{J1} & \Phi_{J2} & \dots & \Phi_{JJ} \end{array} \right $	$=$	$\left \begin{array}{ccc} \phi_{T11} & & \\ \phi_{T21} & \phi_{T22} & \\ \dots & \dots & \dots \\ \phi_{TJ1} & \phi_{TJ2} & \dots & \phi_{TJJ} \end{array} \right \otimes \left \begin{array}{cc} \phi_{V11} & \\ \phi_{V21} & \phi_{V22} \end{array} \right $
Common factor correlations (Φ^*)		
$\Phi^*_{(JR \times JR)}$ 26×26	$\Phi^*_{T(J \times J)}$ 13×13	$\Phi^*_{V(R \times R)}$ 2×2
$\left \begin{array}{cccc} \Phi^*_{11(R \times R)} & & & \\ \Phi^*_{21} & \Phi^*_{22} & & \\ \dots & \dots & \dots & \\ \Phi^*_{J1} & \Phi^*_{J2} & \dots & \Phi^*_{JJ} \end{array} \right $	$=$	$\left \begin{array}{ccc} 1 & & \\ \phi^*_{T21} & 1 & \\ \dots & \dots & \dots \\ \phi^*_{TJ1} & \phi^*_{TJ2} & \dots & 1 \end{array} \right \otimes \left \begin{array}{cc} 1 & \\ \phi^*_{V21} & 1 \end{array} \right $
Common factor standard deviations (Γ)		
$\Gamma_{(JR \times JR)}$ 26×26	$\Gamma_{T(J \times J)}$ 13×13	$\Gamma_{V(R \times R)}$ 2×2
$\left \begin{array}{ccc} \Gamma_{1(R \times R)} & & \\ & \Gamma_2 & \\ & & \dots \\ & & & \Gamma_J \end{array} \right $	$=$	$\left \begin{array}{ccc} \gamma_{T11} & & \\ & \gamma_{T22} & \\ & & \dots \\ & & & \gamma_{TJJ} \end{array} \right \otimes \left \begin{array}{cc} \gamma_{V11} & \\ & \gamma_{V22} \end{array} \right $

Notes: Common factor covariances (Φ), correlations (Φ^*) and standard deviations (Γ) are decomposed using the Kronecker product (\otimes), where Φ_T , Φ_T^* and Γ_T represent relationships between measurement occasions of common factor covariances, correlations and standard deviations; and Φ_V , Φ_V^* and Γ_V represent common factor variances, correlations and standard deviations of one measurement occasion.

In addition, it is convenient to use the following reparameterization:

$$\Phi = \Gamma \Phi^* \Gamma, \quad (11)$$

where Γ is a $JR \times JR$ diagonal matrix containing the standard deviations of the common factors, and $\text{diag}(\Phi^*) = \mathbf{I}$ so that all off-diagonal elements of Φ^* are correlations between the common factors. This, in turn, allows for imposition of the Kronecker product restriction on the correlations between common factors (Φ^*) and the common factor standard deviations (Γ) separately:

$$\Phi^* = \Phi_T^* \otimes \Phi_V^*, \quad (12)$$

and:

$$\mathbf{\Gamma} = \mathbf{\Gamma}_T \otimes \mathbf{\Gamma}_V, \quad (13)$$

where $\mathbf{\Phi}_T^*$ contains the correlations between measurement occasions, $\mathbf{\Phi}_V^*$ contains the correlations between common factors irrespective of the measurement occasions, $\mathbf{\Gamma}_T$ contains coefficients of proportionate change in standard deviations across occasions (where the first element of $\mathbf{\Gamma}_T$ to unity for identification), and $\mathbf{\Gamma}_V$ contains the standard deviations of the common factors at the first measurement occasion (see Table 3). Imposition of Kronecker product restrictions on both $\mathbf{\Phi}^*$ and $\mathbf{\Gamma}$ is equivalent to the imposition of the Kronecker product restriction directly to $\mathbf{\Phi}$.

Substantive hypotheses. Equality of common factor variances, correlations and covariances across occasions can be tested by further restricting the L3MM matrices. In our example of bone metastases it could be of interest to test whether the variances of functional limitations and health impairments are invariant across time (i.e., equality of common factor variances), or whether the relationship between functional limitations and health impairments is invariant across time (i.e., equality of common factor correlation across time).

The hypothesis of equal common factor correlations across occasions of the same lag is investigated by imposing a banded structure on $\mathbf{\Phi}_T^*$ in Equation 12 so that all elements of the same diagonal are equal. Because $\mathbf{\Phi}_V^*$ is a symmetric matrix, this restriction entails that both the correlations between the common factors of one measurement occasion are equal across occasions, and that correlations between common factors at the first and second measurement occasions are equal to correlations between common factors at the second and third measurement occasions, and so on.

The hypothesis of equality of common factor variances across occasions is investigated by imposing:

$$\mathbf{\Gamma} = \mathbf{I} \otimes \mathbf{\Gamma}_0, \quad (14)$$

where \mathbf{I} is a $J \times J$ identity matrix and $\mathbf{\Gamma}_0$ is a $R \times R$ matrix that contains the invariant standard deviations of the common factors of one measurement occasions that apply to all measurement occasions. Equality of common factor covariances across occasions of the same lag is tested by imposing both restrictions described above, which is equivalent to imposing a banded structure directly on $\mathbf{\Phi}_T$ in Equation 10.

Step 4: Common Factor Means. The $JR \times 1$ vector $\boldsymbol{\kappa}$ consists of stacked $R \times 1$ $\boldsymbol{\kappa}_j$ vectors, containing the common factor means of occasion j . Instead of estimating all common factor means in $\boldsymbol{\kappa}$ (in our example of bone metastases data, 26 parameter estimates), the imposition of the Kronecker product restriction requires only estimation of $\boldsymbol{\kappa}_T$ and $\boldsymbol{\kappa}_V$:

$$\boldsymbol{\kappa} = \boldsymbol{\kappa}_T \otimes \boldsymbol{\kappa}_V, \quad (15)$$

where $\boldsymbol{\kappa}_T$ is $J \times 1$ vector that contains coefficients of proportionate change in common factor means across occasions (with dimension 13×1 , containing 13 parameters; where the first

element is fixed at unity for identification requirements) and $\boldsymbol{\kappa}_v$ is a $R \times 1$ vector that contains the common factor means at the first measurement occasion (with dimensions 2×1 , containing 2 parameters) (see Table 4).

Substantive hypotheses. To test and facilitate interpretation of (possible) changes in common factor means across time, we may impose various restrictions on $\boldsymbol{\kappa}$. For example, to test for linear development of common factor means, we can impose:

$$\boldsymbol{\kappa} = \mathbf{u} \otimes \mathbf{a} + \mathbf{t} \otimes \mathbf{b}, \quad (16)$$

where \mathbf{u} is a $J \times 1$ unity vector, \mathbf{a} is a $K \times 1$ vector of intercepts, \mathbf{t} is a $J \times 1$ vector with some coding for the time of the occasions (for example 0, 1, 2, ... J), and \mathbf{b} is a $K \times 1$ vector of slope parameters (see Table 4). The slope parameters then give an indication of the change across time for each common factor (instead of having to interpret all separate estimates of common factor means). In addition, to test invariance of common factor means we can fix the slopes at zero (i.e., $\mathbf{b} = \mathbf{0}$).

Table 4 | Imposition of Kronecker product restrictions on common factor means

Common factor means ($\boldsymbol{\kappa}$)								
$\boldsymbol{\kappa}_{(K \times J)}$		$\boldsymbol{\kappa}_{T(J \times 1)}$		$\boldsymbol{\kappa}_{V(K \times 1)}$				
26×1		13×1		2×1				
$\left \begin{array}{c} \boldsymbol{\kappa}_{1(K \times 1)} \\ \boldsymbol{\kappa}_2 \\ \dots \\ \boldsymbol{\kappa}_J \end{array} \right $	=	$\left \begin{array}{c} \boldsymbol{\kappa}_{T1} \\ \boldsymbol{\kappa}_{T2} \\ \dots \\ \boldsymbol{\kappa}_{TJ} \end{array} \right $	\otimes	$\left \begin{array}{c} \boldsymbol{\kappa}_{V1} \\ \boldsymbol{\kappa}_{V2} \end{array} \right $				
Linear trend of common factor means ($\boldsymbol{\kappa}$)								
$\boldsymbol{\kappa}_{(K \times J)}$		$\mathbf{u}_{(J \times 1)}$		$\mathbf{a}_{(K \times 1)}$		$\mathbf{t}_{(J \times 1)}$		$\mathbf{b}_{(K \times 1)}$
26×1		13×1		2×1		13×1		2×1
$\left \begin{array}{c} \boldsymbol{\kappa}_{1(K \times 1)} \\ \boldsymbol{\kappa}_2 \\ \dots \\ \boldsymbol{\kappa}_J \end{array} \right $	=	$\left \begin{array}{c} 1 \\ 1 \\ \dots \\ 1 \end{array} \right $	\otimes	$\left \begin{array}{c} a_1 \\ a_2 \end{array} \right $	+	$\left \begin{array}{c} 0 \\ 1 \\ \dots \\ 12 \end{array} \right $	\otimes	$\left \begin{array}{c} b_1 \\ b_2 \end{array} \right $

Notes: Common factor means ($\boldsymbol{\kappa}$) are decomposed using the Kronecker product (\otimes), where $\boldsymbol{\kappa}_t$ represents relationships between measurement occasions, $\boldsymbol{\kappa}_v$ represents common factor means of one measurement occasion, \mathbf{u} is a unity vector, \mathbf{a} is a vector of intercept parameters, \mathbf{t} is a vector with a time coding for the time of measurement, and \mathbf{b} is a vector of slope parameters.

Step 5: Longitudinal Structures of Common Factors. To further test substantive hypotheses regarding the common factors, we can apply longitudinal structures to both the covariance and mean structures of the common factors. Examples of these longitudinal structures are the autoregressive model and the latent curve model. We will introduce these models below and explain how they

can be applied to the L3MM. For a more extensive explanation of these models, including possible variations and examples of hypotheses testing, the reader is referred to Oort (2001).

Autoregressive model. The basic autoregressive model is used to describe the mean and covariance structures of the common factors using a path-model, where the scores of the common factors at occasion j are explained by the scores of the common factors at occasion $j - 1$. We can apply the autoregressive model to the full Φ and κ matrices, but in the L3MM we can also apply the autoregressive model to the matrices that describe the relationships between the measurement occasions, using:

$$\Phi_T = (\mathbf{I} - \mathbf{B})^{-1} \Psi (\mathbf{I} - \mathbf{B})^{-1}, \quad (17)$$

and:

$$\kappa_T = (\mathbf{I} - \mathbf{B})^{-1} \alpha, \quad (18)$$

where \mathbf{I} is a $J \times J$ identity matrix, \mathbf{B} is a square $J \times J$ matrix containing regression coefficients (that consists of diagonal β_{jj-1} elements only), Ψ is a $J \times J$ diagonal matrix containing the variances of the innovation factors (representing everything that happened between occasions j and $j - 1$, uncorrelated with the scores of the common factor on occasion $j - 1$), and α is a $J \times 1$ vector that contains the means of the innovation factors. Because Φ_T and κ_T are a function of Ψ , \mathbf{B} and α , we use the first element of Φ_V and κ_V for identification. Application of the basic autoregressive model to Φ_T and κ_T implies that the autoregressive structure is proportionate for all common factors.

Latent curve model. The latent curve model is a special case of the common factor model, where scores of repeated measurements are explained using latent curve factors. When the curve is linear, there is only one curve factor that represents the development over time (or slope), and the factor loadings are used to define the linear trajectory (e.g., by fixing the values to 0, 1, 2, ..., J). In addition, there is a curve factor that represents the initial status, where all factor loadings are fixed at unity to define this factor as the intercept of the developmental trajectory. Other types of curves can be defined using different values for the factor loadings of the development factor (e.g., logistic curves), or by using additional curve factors (e.g., quadratic curves). In Kronecker product restricted models, we can apply the linear latent curve model to the matrices Φ_T and κ_T , by imposing:

$$\Phi_T = \Lambda_{II} \Phi_{II} \Lambda'_{II} + \Theta_{II}, \quad (19)$$

and:

$$\kappa_T = \Lambda_{II} \kappa_{II}, \quad (20)$$

where Λ_{II} is a $J \times 2$ matrix that contains the (fixed) factor loadings of the curve factors, Φ_{II} is a 2×2 symmetric matrix that contains the variances and covariances of the curve factors, Θ_{II} is a $J \times J$ diagonal matrix that contains the variances of the residual factors (representing variance of the common factors that is not explained by the latent curve model), and κ_{II} is a 2×1 vector that contains the means of the curve factors. The Kronecker product restriction implies that the latent curve model is proportionate for all common factors.

Results

The measurement model of Figure 1 was the basis for a structural equation model for baseline and follow-up measurements without any across occasion constraints. This model yielded a chi-square test of exact fit that was significant but the RMSEA measure and CFI indicated close fit (see Model 1.1, Table 5). The number of model parameters to be estimated was 1274. As the number of parameter estimates exceeds the sample size ($N = 682$), we should be very cautious when interpreting measures of fit and parameter estimates.

L3MMs were applied to the 104 variables from 13 measurement occasions to investigate change in HRQL. Kronecker product restrictions were imposed on (1) factor loadings and intercepts (Λ and τ) to comply with longitudinal measurement invariance; (2) residual factor variances and covariances (Θ), (3) common factor variances and covariances (Φ), and (4) common factor means (κ). Substantive hypotheses were tested at each consecutive step.

Step 1: Longitudinal Measurement Invariance

The model with both factor loadings and intercepts restricted to be equal across occasions yielded a chi-square test of exact fit that was significant, but the RMSEA and CFI measures indicated close and good fit respectively (Model 2.1, see Table 5). To test whether the assumption of longitudinal measurement invariance holds, the model fit of this model can be compared to the model fit of the LFM without restrictions. Both the chi-square difference test and the ECVI difference test are significant ($\text{CHISQ}_{diff}(156) = 658.8, p < .001$; $\text{ECVI}_{diff} = 0.43$ 95% CI: 0.29 – 0.59), indicating that the restrictions of invariant factor loadings and intercepts across occasions may not be tenable. However, the difference in CFI values indicates that the hypothesis of invariance should not be rejected ($\text{CFI}_{diff} = 0.005$). Moreover, overall model fit of the measurement invariance model is considered to be close (RMSEA = 0.03). As longitudinal measurement invariance is required for testing substantive hypotheses regarding common factors, we will retain the model with measurement invariance restrictions on both factor loadings and intercepts. The number of free parameters in the longitudinal measurement invariance model (1118) is still larger than the sample size and therefore measures of model fit and parameter estimates (see Table 6) should still be interpreted with caution.

Step 2: Residual Factor Variances and Covariances

The imposition of the Kronecker product restriction on the residual factor correlations (Model 2.2a, see Table 5) and residual factor standard deviations (Model 2.2b) yielded close fit according to the RMSEA and CFI. Although the overall model fit is considered to be good, the deterioration in model fit as compared to the measurement invariance model (Model 2.1) is significant ($\text{CHISQ}_{diff}(630) = 2168.8, p < .001$; $\text{ECVI}_{diff} = 1.00$ 95% CI: 0.74 – 1.27; $\text{CFI}_{diff} = 0.015$). The number of degrees of freedom that is gained with these L3MM restrictions is considerable (630) and leads to a total number of parameter estimates (488) that is lower than the sample size ($N = 682$).

Table 5 | Goodness of overall fit of the longitudinal three-mode models

Model	P	Df	CHISQ	CFI	RMSEA [95% CI]	ECVI [95% CI]
<i>Measurement model</i>						
1.1 No restrictions	1274	4290	7002.34	0.975	0.031 [0.029 ; 0.032]	14.71 [14.30 ; 15.13]
<i>L3MM restrictions</i>						
2.1 $\Lambda = \mathbf{I} \otimes \Lambda_0; \tau = \mathbf{u} \otimes \tau_0$	1118	4446	7661.17	0.971	0.033 [0.031 ; 0.034]	15.13 [14.70 ; 15.59]
2.2 a $\Theta = \Delta(\Theta_T^* \otimes \mathbf{I})\Delta$	572	4992	9471.75	0.959	0.036 [0.035 ; 0.038]	15.90 [15.40 ; 16.41]
b $\Theta = \Theta_T \otimes \Theta_V$	448	5076	9829.93	0.956	0.037 [0.036 ; 0.038]	16.13 [15.62 ; 16.66]
c Equal ϵ variances	476	5088	9846.17	0.956	0.037 [0.036 ; 0.038]	16.11 [15.60 ; 16.64]
d Equal ϵ correlations	422	5142	10690.4	0.949	0.040 [0.039 ; 0.041]	17.16 [16.62 ; 17.72]
e Equal ϵ covariances	410	5154	11413.6	0.943	0.042 [0.041 ; 0.044]	18.18 [17.62 ; 18.77]
2.3 a $\Phi = \Gamma(\Phi_T^* \otimes \Phi_V^*)\Gamma$	242	5322	10486.0	0.953	0.038 [0.037 ; 0.039]	16.24 [15.71 ; 16.78]
b $\Phi = \Phi_T \otimes \Phi_V$	230	5334	10515.3	0.952	0.038 [0.037 ; 0.039]	16.24 [15.71 ; 16.79]
c Equal ξ variances	218	5346	10552.9	0.952	0.038 [0.037 ; 0.039]	16.25 [15.73 ; 16.80]
d Equal ξ correlations	166	5400	10820.4	0.950	0.038 [0.037 ; 0.040]	16.47 [15.93 ; 17.02]
e Equal ξ covariances	152	5412	10854.5	0.950	0.038 [0.037 ; 0.040]	16.47 [15.93 ; 17.02]
2.4 a $\kappa = \kappa_T \otimes \kappa_V$	218	5346	10579.3	0.952	0.038 [0.037 ; 0.039]	16.29 [15.76 ; 16.84]
b Linear t trend κ	208	5356	10611.4	0.952	0.038 [0.037 ; 0.039]	16.30 [15.77 ; 16.85]
c Equal κ	206	5358	10637.2	0.952	0.038 [0.037 ; 0.039]	16.34 [15.80 ; 16.89]

Notes: $N = 682$; P = number of free parameters in the model; Df = degrees of freedom; κ , Φ , and Θ are common factor means, common factor covariances and residual factor covariances and the subscripts 'T' and 'V' refer to matrices that contain relationships between different measurement occasions or variables respectively, Δ and Γ are standard deviations of residual factors and common factors, and Λ and τ are common factor loadings and intercepts.

Therefore, we will retain these L3MM restrictions in favor of model parsimony and use this model as the reference model in subsequent model comparisons below.

Substantive hypotheses. Models 2.2c, 2.2d, and 2.2e are used to test hypotheses about equality of residual factor variances, correlations and covariances respectively. These restrictions have been imposed, one at a time (see Table 5). It appears that the residual factor variances are invariant across occasions ($\text{CHISQ}_{diff}(12) = 16.2, p = .18; \text{ECVI}_{diff} = -0.02; \text{CFI}_{diff} < 0.001$), but the hypotheses about equal correlations and thus covariances across occasions must be rejected according to the chi-square difference and ECVI difference tests ($\text{CHISQ}_{diff}(66) = 860.4, p < .001; \text{ECVI}_{diff} = 1.05$ 95% CI: 0.88 – 1.24). The CFI difference indicates that the hypothesis of equal correlations might be tenable ($\text{CFI}_{diff} = 0.007$), but that the hypothesis of equal covariances must be rejected ($\text{CFI}_{diff} = 0.014$), although the overall model fit for both models is not considered to be good ($\text{CFI} < 0.95$). Therefore, in our example of bone metastases only the hypothesis of equal residual variances seems tenable.

Table 6 | Three-mode model parameter estimates for the factor loadings and intercepts (Model 2.1)

Invariant factor loadings (Λ_0)											
	PF	MB	SF	DP	LS	PA	SI	SY			
FUNC	1.00	0.71	0.31								
HEALTH			0.69	1.00	1.10	0.78	0.93	0.49			
Invariant intercepts (τ_0)											
	PF	MB	SF	DP	LS	PA	SI	SY			
	0.00	-0.07	-0.09	0.00	0.09	0.35	0.62	0.48			
Computation of factor loadings (Λ), where $\Lambda = \mathbf{I} \otimes \Lambda_0$											
	PF _{T0}	MB _{T0}	SF _{T0}	...	PF _{T1}	MB _{T1}	SF _{T1}	...	PF _{T13}	MB _{T13}	SF _{T13}
FUNC	1.00	0.71	0.31		1.00	0.71	0.31		1.00	0.71	0.31
HEALTH			0.69				0.69				0.69
Computation of intercepts (τ), where $\tau = \mathbf{u} \otimes \tau_0$											
	PF _{T0}	MB _{T0}	SF _{T0}	...	PF _{T1}	MB _{T1}	SF _{T1}	...	PF _{T13}	MB _{T13}	SF _{T13}
	0.00	-0.07	-0.09		0.00	-0.07	-0.09		0.00	-0.07	-0.09

Notes: \mathbf{I} and \mathbf{u} are an identity matrix and unity vector with dimensions equal to the number of measurement occasions.

Interpretation of parameter estimates. For interpretation of parameter estimates of residual factor variances and covariances from a Kronecker product restricted model, we will look at the parameter estimates of Model 2.2c (see Table 7). The first element of Δ_0 contains the estimate of the standard deviation of the residual factor of physical functioning ($\Delta_{011} = 0.46$), which results in an estimate of the residual variance of 0.21 (0.46^2) for all indicators of physical functioning across occasions. Estimates of Θ_T^* are the correlations between measurement occasions. The factor by which the relationships

Table 7 | Three-mode model parameter estimates for the residual factor variances and covariances (Model 2.2c)

Standard deviations of residual factors ($\text{diag}(\Delta_0)$)													
	PF	MB	SF	DP	LS	PA	SI	SY					
	0.46	0.43	0.69	0.43	0.35	0.61	0.48	0.25					
Correlations between measurement occasions (Θ^*_T)													
	T0	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10	T11	T12
T0	1.00												
T1	0.64	1.00											
T2	0.57	0.71	1.00										
T3	0.52	0.65	0.74	1.00									
T4	0.49	0.61	0.67	0.76	1.00								
T5	0.48	0.61	0.65	0.71	0.78	1.00							
T6	0.47	0.60	0.63	0.68	0.73	0.80	1.00						
T7	0.48	0.59	0.62	0.65	0.71	0.77	0.81	1.00					
T8	0.46	0.56	0.59	0.62	0.67	0.72	0.76	0.81	1.00				
T9	0.46	0.55	0.58	0.62	0.66	0.71	0.75	0.78	0.81	1.00			
T10	0.43	0.53	0.56	0.60	0.64	0.68	0.72	0.74	0.77	0.81	1.00		
T11	0.43	0.52	0.56	0.60	0.62	0.65	0.69	0.72	0.74	0.77	0.82	1.00	
T12	0.42	0.51	0.54	0.58	0.61	0.63	0.66	0.69	0.71	0.74	0.77	0.82	1.00
Computation of parameter estimates in Θ , where $\Theta = \Delta(\Theta^*_T \otimes \mathbf{I})\Delta$, and $\Delta = \mathbf{I} \otimes \Delta_0$													
	PF _{T0}	MB _{T0}	SF _{T0}	...	PF _{T1}	MB _{T1}	SF _{T1}	...	PF _{T13}	MB _{T13}	SF _{T13}		
PF _{T0}	0.21												
MB _{T0}		0.18											
SF _{T0}			0.47										
...	...												
PF _{T1}	0.13												
MB _{T1}		0.12											
SF _{T1}			0.30										
...	...												
PF _{T13}	0.09												
MB _{T13}		0.08											
SF _{T13}			0.20										

between the residual factors change across occasions are equal for all residual factors, but the actual covariances between the residual factors across occasions may differ because they are dependent on the standard deviations of the indicators. Also, it is now easy to see that correlations between measurement occasions decrease as the lag between the occasions becomes larger (i.e., the correlation between the first and second measurement occasion is larger than the correlation between the first and third measurement occasion, and so on). In addition, correlations between

measurement occasions of the same lag increase over time, i.e., the correlation between the first and second measurement occasion is smaller than the correlation between the second and third measurement occasion, and so on. This pattern of correlations explains why the restriction of equal correlations of the same lag (i.e., Model 2.2d) was not tenable. It might be, for example, that patients get used to the repeated assessments and therefore answer the questions in a more homogenous way.

Step 3: Common Factor Variances and Covariances

The model with Kronecker product restrictions imposed on both the common factor correlations and the common factor standard deviations yielded close fit according to the RMSEA and CFI (Model 2.3b, Table 5) and can be considered to show equivalent approximate fit compared to the model with free common factor variances ($\text{CHISQ}_{\text{diff}}(258) = 685.3, p < .001$; $\text{ECVI}_{\text{diff}} = 0.11$ 95% CI: $-0.03 - 0.26$; $\text{CFI}_{\text{diff}} = 0.004$). Therefore, this model is retained and used as the reference model in subsequent model comparisons below. This result indicates that the changes in the standard deviations of the common factors functional limitations and health impairments and their correlation, change proportionately over time. The total number of free parameters in this model (288) is considerable lower than the sample size ($N = 682$).

Substantive hypotheses. Models 2.3c, 2.3d and 2.3e are used to test equality of common factor variances, correlations and covariances respectively. The hypothesis of equal common factor variances across occasions should be rejected based on the chi-square difference test, but based on the ECVI difference test and the CFI difference the model with equal common factor variances can be retained ($\text{CHISQ}_{\text{diff}}(12) = 37.6, p < .001$; $\text{ECVI}_{\text{diff}} = 0.01$, 95% CI: $-0.01 - 0.06$; $\text{CFI}_{\text{diff}} < 0.001$). Moreover, the overall model fit of this model is still considered to be good. The hypotheses about equal correlations and thus covariances across occasions must be rejected based on the chi-square difference and ECVI difference tests, but might be retained based on the CFI difference ($\text{CHISQ}_{\text{diff}}(64) = 305.2, p < .001$; $\text{ECVI}_{\text{diff}} = 0.23$ 95% CI: $0.13 - 0.34$; $\text{CFI}_{\text{diff}} = 0.002$). Taken together, these results indicate that only the hypothesis of equal common factor variances is tenable.

Interpretation of parameter estimates. The L3MM parameter estimates for common factor variances and covariances of Model 2.3c are given in Table 8. The estimates of the standard deviations of the common factors functional limitations and health impairments (Γ_0) are 0.83 and 0.51 respectively, and the correlation between the two common factors (Φ_V^*) is 0.44. The covariance between the two common factors of one measurement occasion is thus 0.19 (i.e., $0.44 * 0.83 * 0.51$). Correlations between measurement occasions (Φ_T^*) show the change in correlations between measurement occasions across time, e.g., correlation between measurement occasions decrease as the lag between measurement occasions becomes larger. Although correlations between measurement occasions apply to both common factors, actual covariances between common factors across occasions differ as they are dependent on the standard deviations of the common factors. Similar to the pattern of correlations between

measurement occasions of residual factors, the result of the common factors shows a decrease in correlations between measurements as the lag between the occasions becomes larger, while correlations between measurement occasions of the same lag increase over time. This indicates that patients become more homogenous in their answers to the observed variables of physical limitations and health impairments over time.

Table 8 | Three-mode model parameter estimates for the common factor variances and covariances (Model 2.3e)

Standard deviations of common factors ($\text{diag}(\Gamma_0)$)													
	FUNC	HEALTH											
	0.83	0.51											
Correlations between common factors (Φ_V^*)													
	FUNC	HEALTH											
FUNC	1.00												
HEALTH	0.44	1.00											
Correlations between measurement occasions (Φ_T^*)													
	T0	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10	T11	T12
T0	1.00												
T1	0.89	1.00											
T2	0.86	0.93	1.00										
T3	0.83	0.88	0.92	1.00									
T4	0.80	0.86	0.89	0.93	1.00								
T5	0.80	0.83	0.87	0.90	0.93	1.00							
T6	0.77	0.80	0.85	0.87	0.90	0.93	1.00						
T7	0.75	0.79	0.82	0.86	0.89	0.91	0.95	1.00					
T8	0.74	0.79	0.82	0.84	0.88	0.90	0.92	0.94	1.00				
T9	0.71	0.76	0.80	0.82	0.85	0.89	0.90	0.91	0.95	1.00			
T10	0.68	0.74	0.77	0.80	0.82	0.86	0.88	0.90	0.94	0.95	1.00		
T11	0.67	0.74	0.76	0.78	0.80	0.84	0.86	0.87	0.92	0.92	0.95	1.00	
T12	0.64	0.72	0.74	0.76	0.79	0.81	0.84	0.85	0.89	0.90	0.92	0.95	1.00
Computation of parameter estimates in Φ , where $\Phi = \Gamma(\Phi_T^* \otimes \Phi_V^*)\Gamma$, and $\Gamma = \mathbf{I} \otimes \Gamma_0$.													
	FUNC _{T0}	HEALTH _{T0}	FUNC _{T1}	HEALTH _{T1}	...	FUNC _{T13}	HEALTH _{T13}						
FUNC _{T0}	0.70												
HEALTH _{T0}	0.19	0.26											
FUNC _{T1}	0.62	0.17	0.70										
HEALTH _{T1}	0.17	0.23	0.19	0.26									
...								
FUNC _{T13}	0.44	0.12	0.50	0.14	...	0.70							
HEALTH _{T13}	0.12	0.16	0.14	0.19	...	0.19	0.26						

Step 4: Common Factor Means

The model with Kronecker product restrictions on the common factor means yielded close fit according to the RMSEA, and good fit according to the CFI (Model 2.4a, see Table 5). The model that imposes a linear trend on the means of the common factors (Model 2.4b) can be considered to show equivalent approximate fit ($\text{CHISQ}_{diff}(10) = 32.1, p < .001; \text{ECVI}_{diff} = 0.01$ 95% CI: -0.01 – 0.05; $\text{CFI}_{diff} < 0.001$), whereas the model that imposes equality of common factor means across occasions (Model 2.4c) shows a significant deterioration in model fit according to the chi-square difference and ECVI difference tests, but should not be rejected based on the CFI difference ($\text{CHISQ}_{diff}(12) = 57.9, p < .001; \text{ECVI}_{diff} = 0.04$ 95% CI: 0.01 – 0.09; $\text{CFI}_{diff} < 0.001$). These results indicate that there is a significant change in the common factor means across time, and that this change can be described using a linear trend.

Interpretation of parameter estimates. L3MM parameter estimates for common factor means of Model 2.4c are given in Table 9. The intercept parameters (\mathbf{a}_1 and \mathbf{a}_2) are common factor means at the first measurement occasion. The slope parameters (\mathbf{b}_1 and \mathbf{b}_2) are the (linear) change in common factor means across occasions, where the means of the common factor functional limitation increase across occasions ($\mathbf{b}_1 = 0.04$), while the means of the common factor health impairments decrease across occasions ($\mathbf{b}_2 = -0.06$). The complete vector of common factor means is computed as a function of time of measurement (see Table 9).

Table 9 | Three-mode model parameter estimates for the common factor means (Model 2.4b)

Intercept parameters common factor means (\mathbf{a})						
FUNC	HEALTH					
2.57	1.80					
Slope parameters common factor means (\mathbf{b})						
FUNC	HEALTH					
0.04	-0.06					
Computation of common factor means ($\boldsymbol{\kappa}$), where $\boldsymbol{\kappa} = \mathbf{u} \otimes \mathbf{a} + \mathbf{t} \otimes \mathbf{b}$						
FUNC _{T0}	HEALTH _{T0}	FUNC _{T1}	HEALTH _{T1}	...	FUNC _{T13}	HEALTH _{T13}
2.57	1.80	2.57	1.79	...	2.62	1.73

Notes: \mathbf{u} is a unity vector; the time coding for the time of measurement (\mathbf{t}) that was used was 0, 0.1, 0.2, 0.3 etc.

Discussion

The longitudinal three-mode model (L3MM) is a valuable tool for the assessment of change in situations where there are many measurement occasions. Kronecker product restrictions yield very parsimonious models, enabling the application of SEM to large longitudinal data sets. In the present paper we explained and illustrated the imposition of Kronecker product restrictions on the parameter matrices of (1) factor loadings and intercepts to comply with the assumption of longitudinal measurement invariance; (2) residual factor covariances and correlations, and additional restrictions to test equality of variances, correlations and covariances across occasions; (3) common factor covariances and correlations, and additional restrictions to test equality of variances, correlations and covariances across occasions; (4) common factor means, and additional restrictions to test a linear trend of common factor means; and (5) longitudinal structures such as the autoregressive model and latent curve model. In addition, we explained how the resulting parameter estimates can be interpreted. This paper therefore serves as an instructive explanation of L3MMs in order to facilitate their applications for complex longitudinal data and to enhance the substantive interpretation of model parameters.

In our example of bone metastases, the Kronecker product restrictions imposed on factor loadings and intercepts to comply with measurement invariance yielded deterioration in model fit. We still retained the model because longitudinal measurement invariance is required for testing substantive hypotheses regarding common factors, and the overall fit of the measurement invariance model was considered to be good. It was not the aim of the present paper, but it would be interesting to investigate which model parameters show violations of measurement invariance (i.e., measurement bias). However, because the invariant model parameters in the L3MM are a function of parameter estimates, the detection of measurement bias in Kronecker product restricted models requires alternative methods. A procedure for measurement bias detection in Kronecker product restricted models has been proposed (Verdam & Oort, 2015a), where additional parameter matrices are introduced to accommodate possible violations of measurement invariance. This procedure enables the investigation of measurement bias, to account for apparent bias, and use partial measurement invariance to investigate change in common factor means in L3MMs.

L3MMs are applied to assess change in multivariate longitudinal data with many measurement occasions. The size of these types of models is usually large in terms of observed variables and model parameters. For example, in our sample of 682 patients with bone metastases we modeled 104 observed variables measured over 13 measurement occasions, which resulted in a measurement model that required estimation of 1274 model parameter with 4290 degrees of freedom. Evaluation of model fit is complicated by the fact that the chi-square test of exact fit is dependent on sample size and number of degrees of freedom (i.e., with increasing sample size and equal degrees of freedom the chi-square value increases) and tends to favor highly parameterized models (i.e., the chi-square value decreases when parameters are added to the model). Indices of approximate fit are less dependent on sample size and reward model parsimony. In our illustration

with the L3MMs the evaluations of overall model fit indicated that none of the models showed exact fit according to the chi-square test, while all models showed close approximate fit ($RMSEA < 0.05$). The CFI index seemed to be somewhat more discriminative as not all models showed good fit ($CFI > 0.95$), but without confidence intervals for these values the precision of the index is unknown. Therefore, this raises the question of how informative these overall model fit measures are in the case of highly parsimonious models. As these type of models will only become more prevalent in the presence of large data sets, it would be worthwhile to investigate the behavior of overall model fit indices as a topic of future research.

The imposition of Kronecker product restrictions leads to more parsimonious models, and thus to deterioration in model fit. To test whether the restrictions are tenable we can test differences in model fit. As the imposition of Kronecker product restrictions usually leads to a large gain in number of degrees of freedom, evaluation of difference in model fit complicated for the same reasons as described above. As an alternative to the chi-square difference test we used the difference in ECVI and CFI values to evaluate differences in model fit. An advantage of the ECVI difference is that the associated confidence interval provides information about the precision of the estimate and allows to test the equivalence in approximate model fit. In our application, the chi-square difference test showed the highest power, rejecting all the L3MM restrictions (i.e., Kronecker product restrictions on parameter matrices), and all but one of the additional restrictions on L3MM parameter matrices to test substantive hypotheses. The ECVI difference test showed that some of the L3MM restrictions and substantive hypotheses could be retained based on the evaluation of equivalence in approximate fit, whereas the CFI difference showed the least discriminative power as almost all models could be retained based on the rule of thumb for this index ($CFI_{diff} = 0.01$). Thus, the results of the evaluation of differences in model fit differ between the evaluation methods, which again raises the question of how these fit indices can be used in an informative way. These results also emphasize that statistics alone are not sufficient to guide decisions regarding these type of model evaluations, and that such decisions require substantive guidance as well.

For example, the evaluation of difference in model fit can be used to test the trade-off between model fit and model parsimony, but may also be affected by interpretability of results. In our illustration we incorporated Kronecker product restrictions on residual factor variances and covariances, even though these restrictions yielded deterioration in model fit. In part, we chose to incorporate these restrictions in favor of model parsimony and interpretability of results. Instead of yielding 104 estimates of residual factor variances and 624 estimates of residual factor covariances, the L3MM yielded 8 estimates of residual factor variances, and 90 estimates that represent the proportional change in residual factor variances and covariances over time. These restrictions thus facilitate the substantive interpretation of model parameters. Therefore, the decision of whether to incorporate Kronecker product restrictions might not only be guided by evaluation of differences in model fit, but also by the improved substantive evaluation of findings. With regard to the imposition of additional restrictions on L3MM parameter matrices

however, the decision of whether to incorporate these restrictions might not be guided by the same considerations of model parsimony and interpretability of findings. As these restrictions are imposed to test specific substantive hypotheses, it might be more desirable to have a high power to detect differences in parameter estimates. Therefore, substantive decisions play an important role in the evaluation of differences in model fit, and might even require the use of different fit indices or different decision rules that are guided to the purpose of the analysis.

As a recommendation for research and practitioners that apply these type of models, we would suggest to: (1) use several tests and indices of model fit in order to find support for the robustness of the result in their communalities, (2) keep in mind that some fit indices are more appropriate in certain circumstances than others (e.g., specifically developed to take into account model parsimony), and (3) take into account substantive considerations when making decisions on model fit evaluation (e.g., using theory to establish an appropriate measurement model in addition to relying on model fit tests or indices to guide the specification of a measurement model).

To conclude, this paper provides an instructive explanation of how the L3MM can be applied to multivariate longitudinal data from many measurement occasions. Kronecker product restrictions are used to model the multivariate longitudinal structure of the data, which yields models that are more parsimonious and have attractive interpretation. Application of the L3MM therefore facilitates the analysis of complex longitudinal data and can provide meaningful interpretation of the dynamics of change.

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Appendix 3A

Calculation of the number of free parameters of a longitudinal factor model

Below we give specific calculations for the number of free parameters in a longitudinal factor model with simple measurement structure that consists of 9 indicators and 3 common factors, when it includes two, four or six measurement occasions.

Two measurement occasions: The matrix of factor loadings (Λ) is of dimensions 18×6 and contains 18 parameters (9 factor loadings for each measurement). The matrix of common factor variances and covariances (Φ) is of dimension 6×6 and contains 21 parameters (6 common factor variances on the diagonal, and 15 common factor covariances on the off-diagonal). The matrix of residual factor variances and covariances (Θ) is of dimensions 18×18 and contains 27 parameters (18 residual variances, and 9 residual covariances between the same indicators across occasions). The vector of intercepts (τ) is of dimensions 18×1 and contains 18 parameters (one intercept for each observed indicator). The vector of common factor means (κ) is of dimensions 6×1 and contains 6 parameters (one mean for each common factor). The total number of parameters is thus 90. For the purpose of identification one can fix the common factor means to zero and the common factor variances to unity. This amounts to a total of 78 free parameters in the model.

Four measurement occasions: The matrix of factor loadings (Λ) is of dimensions 36×12 and contains 36 parameters (9 factor loadings for each measurement). The matrix of common factor variances and covariances (Φ) is of dimension 12×12 and contains 78 parameters (12 common factor variances on the diagonal, and 66 common factor covariances on the off-diagonal). The matrix of residual factor variances and covariances (Θ) is of dimensions 36×36 and contains 90 parameters (36 residual variances, and 54 residual covariances between the same indicators across occasions). The vector of intercepts (τ) is of dimensions 36×1 and contains 36 parameters (one intercept for each observed indicator). The vector of common factor means (κ) is of dimensions 12×1 and contains 12 parameters (one mean for each common factor). The total number of parameters is thus 252. For purpose of identification one can fix the common factor means to zero and the common factor variances to unity (alternatively, one can fix one intercept per common factor to zero and one factor loading per common factor to unity). This amounts to a total number of 228 free parameters in the model.

Six measurement occasions: The matrix of factor loadings (Λ) is of dimensions 54×18 and contains 54 parameters (9 factor loadings for each measurement). The matrix of common factor variances and covariances (Φ) is of dimension 18×18 and contains 171 parameters (18 common factor variances on the diagonal, and 153 common factor covariances on the off-diagonal). The matrix of residual factor variances and covariances (Θ) is of dimensions 54×54 and

contains 189 parameters (54 residual variances, and 135 residual covariances between the same indicators across occasions). The vector of intercepts (τ) is of dimensions 54×1 and contains 54 parameters (one intercept for each observed indicator). The vector of common factor means (κ) is of dimensions 18×1 and contains 18 parameters (one mean for each common factor). The total number of parameters is thus 486. For purpose of identification one can fix the common factor means to zero and the common factor variances to unity. This amounts to a total of 450 free parameters in the model.

Appendix 3B

Explanation of the Kronecker product operation

The Kronecker product of two matrices, \mathbf{A} ($m \times n$) and \mathbf{B} ($p \times q$), is defined as:

$$\mathbf{A} \otimes \mathbf{B} = \begin{bmatrix} a_{11}\mathbf{B} & \cdots & a_{1n}\mathbf{B} \\ \vdots & \ddots & \vdots \\ a_{m1}\mathbf{B} & \cdots & a_{mn}\mathbf{B} \end{bmatrix},$$

where the result is a $mp \times nq$ block matrix that contains mn submatrices $a\mathbf{B}$.

More specifically:

$$\mathbf{A} \otimes \mathbf{B} = \begin{bmatrix} a_{11}b_{11} & a_{11}b_{12} & \cdots & a_{11}b_{1q} & \cdots & \cdots & a_{1n}b_{11} & a_{1n}b_{12} & \cdots & a_{1n}b_{1q} \\ a_{11}b_{21} & a_{11}b_{22} & \cdots & a_{11}b_{2q} & \cdots & \cdots & a_{1n}b_{21} & a_{1n}b_{22} & \cdots & a_{1n}b_{2q} \\ \vdots & \vdots & & \vdots & & & \vdots & \vdots & & \vdots \\ a_{11}b_{p1} & a_{11}b_{p2} & \cdots & a_{11}b_{pq} & \cdots & \cdots & a_{1n}b_{p1} & a_{1n}b_{p2} & \cdots & a_{1n}b_{pq} \\ \vdots & \vdots & & \vdots & \ddots & & \vdots & \vdots & & \vdots \\ \vdots & \vdots & & \vdots & & & \vdots & \vdots & & \vdots \\ a_{m1}b_{11} & a_{m1}b_{12} & \cdots & a_{m1}b_{1q} & \cdots & \cdots & a_{mn}b_{11} & a_{mn}b_{12} & \cdots & a_{mn}b_{1q} \\ a_{m1}b_{21} & a_{m1}b_{22} & \cdots & a_{m1}b_{2q} & \cdots & \cdots & a_{mn}b_{21} & a_{mn}b_{22} & \cdots & a_{mn}b_{2q} \\ \vdots & \vdots & & \vdots & & & \vdots & \vdots & & \vdots \\ a_{m1}b_{p1} & a_{m1}b_{p2} & \cdots & a_{m1}b_{pq} & \cdots & \cdots & a_{mn}b_{p1} & a_{mn}b_{p2} & \cdots & a_{mn}b_{pq} \end{bmatrix}.$$

A numerical example:

$$\begin{bmatrix} 2 & 4 \\ 5 & 8 \end{bmatrix} \otimes \begin{bmatrix} 3 & 6 \\ 7 & 1 \end{bmatrix} = \begin{bmatrix} 2 * \begin{bmatrix} 3 & 6 \\ 7 & 1 \end{bmatrix} & 4 * \begin{bmatrix} 3 & 6 \\ 7 & 1 \end{bmatrix} \\ 5 * \begin{bmatrix} 3 & 6 \\ 7 & 1 \end{bmatrix} & 8 * \begin{bmatrix} 3 & 6 \\ 7 & 1 \end{bmatrix} \end{bmatrix} =$$

$$\begin{bmatrix} 2 * 3 & 2 * 6 & 4 * 3 & 4 * 6 \\ 2 * 7 & 2 * 1 & 4 * 7 & 4 * 1 \\ 5 * 3 & 5 * 6 & 8 * 3 & 8 * 6 \\ 5 * 7 & 5 * 1 & 8 * 7 & 8 * 1 \end{bmatrix} = \begin{bmatrix} 6 & 12 & 12 & 24 \\ 14 & 2 & 28 & 4 \\ 15 & 30 & 24 & 46 \\ 35 & 5 & 56 & 8 \end{bmatrix}$$