A factor mixture model for multivariate survival data. An application to the analysis of lifetime mental disorders

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TITLE:

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ABSTRACT:

The assessment of the lifetime prevalence of mental disorders under comorbidity conditions is an important area in mental health research. Because information on lifetime disorders is usually gathered retrospectively within cross-sectional studies, the information is necessarily right-censored and this should be taken into account when setting up models for the estimation of lifetime prevalences. We propose a factor-analytic discrete-time survival model combining mixture item response theory and discrete-time hazard functions to describe disorder associations while accounting for censoring. This model is used for describing the life-time prevalence and comorbidity of eight depression and anxiety disorders from the ESEMeD study.

KEY WORDS:

disorder diathesis; cure fraction; Internalising disorders; Item response theory; latent classes; Psychiatric comorbidity;

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Background and aims

The prevalence of a disease in a population is defined as the percentage of diseased subjects at any time during a certain time span. In mental health, the typical prevalence measures refer to the last 30 days, the last 12 months, or the lifetime. Measures based on short time spans (e.g. 12 month) provide information on the current-status of the disease, while lifetime prevalence relates to the lifetime spread of the disease within the population. Lifetime prevalence encompasses the proportion of the population proportion fulfilling diagnostic criteria for the disorder, regardless of the age of onset, duration, severity and environmental factors.

Prevalence information on psychiatric disorders is most frequently gathered using cross-sectional study designs, in which the lifetime disorder information is collected retrospectively. The lifetime disorder information obtained from this type of study is intrinsically right censored because no information is available on the occurrence of mental disorders beyond the time of the interview. As a result, direct computation of lifetime prevalences yields an underestimation of these prevalences. An alternative is to use statistical techniques that take into account that individuals who did not have a disorder up to the moment of the interview time are still at risk of suffering from it in their remaining life.

Epidemiological studies about lifetime disorders typically do not use adequate analysis methods. Even though the data are clearly right-censored, most studies proceed as if complete data were obtained. Lifetime estimation is often conducted assuming that an individual's lifetime equals his/her age at the time of the interview (e.g. Alonso et al. 2004a). Such a procedure inevitably leads to systematic underestimation of lifetime prevalence.

More recently, actuarial survival methods (also known as life-table methods) have been used to take into account right censorship. These are non-parametric methods used when it is known that the event occurred within a time-interval (Hosmer and Lemeshow 1999), which can estimate the lifetime prevalence as the projected

lifetime risk for a specific age (Bonnewyn et al. 2007; Kessler et al. 2005a). A limitation of this approach when dealing with multiple disorders is, however, that it cannot take the correlation between disorders into account; that is, it cannot deal with what is usually referred to as comorbidity. Another limitation is that it is not possible to perform parametric inference such as the estimation and testing of covariate effects on life time prevalence.

Lifetime mental comorbidity implies that a person has suffered from two or more disorders during his life, regardless of whether the disorders overlap in time. Studies focusing on mental comorbidity provide information that remains invisible in single disorder studies. For example, it has been shown that mental comorbidity is related to increased severity, longer duration of a disorder, greater functional disability, and increased use of healthcare services (e.g., Bijl and Ravelli 2000; Roy-Byrne et al. 2000). These and other studies indicate that considering comorbidity allows for a better understanding of a patient's health state and better identification of individuals with high disease severity. However, the right-censoring caused by using a cross-sectional study design may have even larger biasing effects on multivariate comorbidity estimates than on univariate prevalence estimates (Kraemer et al. 2006).

This article proposes a methodology for estimating lifetime disorder prevalence and comorbidity using right-censored data from cross-sectional studies. The proposed factor-mixture survival model takes into account simultaneously the comorbidity associations between disorders and the reported disorders censorship by combining mixture factor-analytic tools and discrete-time survival techniques. The mixture part is used to model a qualitative distinction between 2 types of individuals, those who do not suffer from any disorder and those who may do. The proposed model is illustrated with an application using the mood and anxiety disorders from the ESEMeD study, yielding a description of the European population in terms of lifetime internalising diathesis as well as providing accurate estimates for lifetime disorder prevalences and comorbidities.

Internalising diathesis

A psychiatric explanation for disorder onset and comorbidity is that individuals' non-observable psychological states determine their vulnerability to develop psychopathological disorders in response to a sufficiently stressful environment. This vulnerability is referred to as diathesis (Clark 2005). According to Clark and Watson (1991), diathesis is chronic in nature; that is, it is intrinsic to the individual and has lifetime implications. Thus, rather than conceiving common mental disorders as dichotomous entities, disorders are conceived as extreme points on continua spanning a range of emotional and behavioural functions (Krueger 1999).

One important example of mental diathesis is the mental health dimension called "internalising", which explains emotional and mood related mental states. The internalising dimension is assumed to explain the presence and comorbid association among mood and anxiety disorders (Cerda et al. 2008; Krueger 1999). The internalising factor structure has been confirmed using item response theory models (IRT) on a variety of datasets (e.g. Almansa et al. 2011; Cerda et al. 2008), obtaining similar results in terms of measurement parameters (intercepts and factor loadings from the factor models) in different target populations, irrespective of the time period considered (lifetime or 12-month disorders). In the case of lifetime disorders, the continuous latent factor serves as a measure for an individual's internalising diathesis, which may produce internalising disorders at any time in their lives.

Statistical model

Discrete-time event history analysis for univariate survival data

Event history analysis makes it possible to determine at what time periods the event of interest is most likely to occur, taking into account the time-to-event duration and the

existence of censored information (Vermunt 2009; Tekle and Vermunt 2012). Time measurement can be continuous or discrete, but discrete-time methods are widely used in psychological research as well as in other social and behavioural sciences because events of interest are often observed retrospectively and recorded in discrete intervals of time due to the difficulty of knowing the exact time in which the events appear. Additionally, discrete-time techniques are computationally and conceptually simpler than the continuous-time ones.

Let T denote the variable measuring the time at which an event first occurs, for example, the age of first occurrence of a mental disorder. The distribution of the time of non-occurrence of the event of interest is described by the survival function $S(t)$,

$$S(t) = P\left[T > t\right]. \tag{1}$$

In the discrete-time case the underlying continuous time is discretized, so T takes on a finite number of discrete values $T = \left\{t_1, t_2, \ldots, t_{max}\right\}$ referring to equal-size time intervals (Vermunt 2009). Another important function in survival analysis is the *hazard function*, which defines the probability of experiencing the event during a specific time-interval given that the event has not yet occurred. The discrete-time hazard function is:

$$h(t_l) = P\left[T = t_l \,\middle|\, T \geq t_l\right] \tag{2}$$

The discrete survival function can be obtained from the discrete-time hazard as follows:

$$S\left(t_l\right) = \prod_{t=t_1}^{t_l}\left[1 - h(t)\right] \tag{3}$$

It has been shown that a discrete-time survival analysis can be performed by modelling the hazard function using standard logistic regression analysis after arranging the data in an appropriate way (Efron 1988; Singer and Willett 1993; Muthén and Masyn 2005). The data should be in person-period format so that for each individual we have as many records as time-intervals observed up to the event or censored time. The dependent variable takes the value 1 for the time interval during which a person experienced the event of interest (the last record for individuals with uncensored event

times) and 0 for all other time intervals. Note that the probability of experiencing an event in time-interval t computed with this data-arrangement yields an estimate of the hazard rate for each time point: it is the proportion of events at $T = t$ for those who did not experience the event before the time-interval concerned. The logistic discrete-time hazard model can be expressed as a piecewise constant model:

$$\text{logit}\left[h\left(t\right)\right] = \beta_t \qquad t = \left\{t_1, t_2, \ldots, t_{max}\right\} , \tag{4}$$

that is, as a logistic model with a time-specific intercept β_t.

Factor-mixture model for multivariate survival data

Now we deal with the situation in which there are J different events of interest. These events are correlated because they share a common underlying factor θ; that is, some subjects will be more likely than others to experience each of the events of interest as a result of unobserved subject-specific risk factors captured by θ. In this application, θ is assumed to measure an individual's diathesis towards internalising lifetime mental disorders. This unobserved heterogeneity in the hazard is often referred to as shared frailty (Hougaard 1984, 1995).

A common way to deal with unobserved heterogeneity is to define a time-invariant subject-specific random effect (Tekle and Vermunt 2012), which in our case represents an individual's latent internalising diathesis. Typically, hazard rates are assumed to be proportional, which implies that the effect of the latent variable on the disorder hazards is assumed to be constant across time intervals. Expanding equation (4), the hazard for the onset of disorder j $\left(j = 1,2,..,J\right)$ during age interval t for individual i can be expressed as follows:

$$\text{logit}\left[h_{ij}\left(t\right)\middle|\theta_i\right] = \beta_{jt} + \lambda_j \cdot \theta_i \ . \tag{5}$$

The intercept β_{jt} captures the age-dependency of the hazard for disorder j, and the slope λ_j the association between the latent diathesis factor and the log-odds of

disorder onset. The latent factor θ is assumed to be normal distributed. The J hazard (and survival) functions are correlated because they depend on the same diathesis variable θ_i.

The factor-survival model described in equation (5) is in fact an extended IRT model (De Boeck 2004); that is, a two-parameter logistic model with time-varying intercepts β_{jt}. Similar latent variable models for survival responses, possibly combined with categorical responses, have been proposed by Moustaki and Steele (2005) and Vermunt (1997, 2002). Other relevant applications of latent class models on longitudinal data can be found in Lin et al. (2002), Larsen (2004) and Masyn (2009).

In a general population the majority of individuals do not develop mental disorders. Thus, when dealing with samples that are representative of a general population, it makes sense to assume that the latent diathesis distribution differs across "at-risk" and "not-at-risk" subgroups. More specifically, it can be expected that there is a discontinuity in diathesis scores between individuals at risk of suffering from any disorder and others who are not at risk. This idea can be translated into a mixture model with two latent classes, in which one class contains individuals with a risk of experiencing the disorders, and the second class the individuals with a zero risk. Finite mixture variants of survival and IRT models have been proposed which permit accounting for such qualitative distinctions between individuals in the investigated population (Larsen 2004; Davier and Rost 2007; Tay et al. 2011).

We propose using a 2-class mixture model for distinguishing between individuals with and without risk of lifetime mental disorders. Let ν be the categorical variable indicating the latent class membership. The factor-analytic hazard model of interest can be defined as follows:

$$\begin{aligned} \text{logit}\left[h_{ij}\left(t\right)\middle|\theta_{i|\nu}\right] &= \beta_{jt}+\lambda_j\cdot\theta_{i|\nu} \\ \text{logit}\left[P\left(\nu=1\right)\right] &= \tau \end{aligned} \tag{6}$$

where the latent score distributions are assumed to be $\theta|\nu = 1 \sim N\left(0,1\right)$ for the "at-risk" class and $\theta|\nu = 2 \sim N\left(-a,0\right)$, with $a \gg 0$, for the "not-at-risk" class, and where the τ determines the class proportions. Note that latent class 2 has a degenerate distribution of θ at a very low diathesis level. Assuming that the latent diathesis value is large negative for the "not-at-risk" class implies that its occurrence probability is close to zero for all disorders. Although it is most logical to fix the value of $-a$ a priori so that the occurrence probabilities are exactly 0, it is also possible to estimate this parameter freely to confirm the existence of a "not-at-risk" class. Note that in class 2 the survival probability equals 1 for all t, which is why such individuals are also referred to as long-term survivors (Farewell, 1982; Vermunt 1997). A similar model with a continuous latent variable and a two-class mixture has been proposed by Steele (2003) for modelling multilevel survival data with long term survivors, and by Almansa et al. (2011) for the analysis of mental health states at a single time point.

The 2-class mixture model described above can be expanded to include two different types of covariates. The first group of covariates ($\mathbf{z}^C$) predict class membership. The logit model for the latent class proportions is then modelled as

$$\text{logit}\left[P\left(\nu = 1\right)\right] = \tau + \boldsymbol{\gamma}^C\mathbf{z}^C, \tag{7}$$

where τ and $\boldsymbol{\gamma}^C$ are the regression intercept and slope parameters, respectively. The second group of covariates ($\mathbf{z}^F$) predict the factor scores (diathesis severity) for people belonging to the "at-risk" class using a linear regression model:

$$\theta|\nu = 1 \sim N(\boldsymbol{\gamma}^F\mathbf{z}^F, 1) \tag{8}$$

As can be seen, for class 1 ("at-risk") the factor mean varies depending on the covariate values $\mathbf{z}^F$, typically indicating differences in mental health diathesis across socio-demographic groups. For individuals belonging to class 2 the factor score is degenerate at a very large negative value ($-a$), so no severity covariates need to be considered.

Prevalence Estimation

Let D_{ij} denote a binary variable indicating whether the disorder j is or will ever be manifested in individual i. The lifetime prevalence of disorder j in the studied population is the percentage of non-survivors at the end of the life, $100 \times P(D_{\cdot j} = 1)$, where $P(D_{\cdot j} = 1)$ is the average of the individual probabilities $P(D_{ij} = 1)$. Below we show how $P(D_{\cdot j} = 1)$ can be obtained from the model parameters.

The hazard probability for disorder j at time point t for individual i belonging to class ν equals

$$\hat{h}_{ij}\left(t \mid \theta_{i|\nu}\right) = \frac{\exp\left[\beta_{jt} + \lambda_j \cdot \theta_{i|\nu}\right]}{1 + \exp\left[\beta_{jt} + \lambda_j \cdot \theta_{i|\nu}\right]}, \tag{9}$$

and the probability this individual experiences disorder j during his\her lifetime is

$$P\left(D_{ij} = 1 \mid \theta_{i|\nu}\right) = 1 - S_{ij}\left(t_{\max} \mid \theta_{i|\nu}\right) = 1 - \prod_{t=1}^{t_{\max}}\left[1 - \hat{h}_{ij}\left(t \mid \theta_{i|\nu}\right)\right]. \tag{10}$$

Then, the lifetime prevalence estimate is obtained by integrating over latent variables and averaging over individuals. For the latter we take into account the sampling weights w_i, which are scaled to sum to the sample size: $\sum_i^N w_i = N$. More specifically,

$$P(D_{\cdot j} = 1) = N^{-1} \sum_{i=1}^{N} w_i \left\{ \begin{array}{r} \int P\left(D_{ij} = 1 \middle| \theta_{i|\nu=1}\right) f\left(\theta \middle| \nu = 1, \mathbf{z}_i^F\right) \hat{P}\left(\nu = 1 \middle| \mathbf{z}_i^C\right) d\theta \\ + P\left(D_{ij} = 1 \middle| \theta_{i|\nu=2} = -a\right) \hat{P}\left(\nu = 2 \middle| \mathbf{z}_i^C\right) \end{array} \right\} \tag{11}$$

where $\hat{P}\left(\nu \middle| \mathbf{z}_i^C\right)$ is the class proportion

$$\begin{aligned} \hat{P}\left(\nu = 1 \middle| \mathbf{z}_i^C\right) &= \frac{\exp\left[\hat{\tau} + \hat{\boldsymbol{\gamma}} \mathbf{z}_i^C\right]}{1 + \exp\left[\hat{\tau} + \hat{\boldsymbol{\gamma}} \mathbf{z}_i^C\right]} \\ \hat{P}\left(\nu = 2 \middle| \mathbf{z}_i^C\right) &= 1 - \hat{P}\left(\nu = 1 \middle| \mathbf{z}_i^C\right) \end{aligned} \tag{12}$$

Note that the expression in equation (11) could be simplified further by making use of the fact that $P\left(D_{ij}=1\middle|\theta_{i|\nu=2}=-a\right)\approx 0$.

Estimation of factor scores and hazard functions

Latent factor (diathesis) scores can be estimated from the factor posterior distribution using the Expected a Posteriori (EAP) method (Vermunt and Magidson 2005), weighted by posterior class membership probability.

$$\hat{\theta}_i=\sum_{\forall\nu}\hat{P}\left(\nu\middle|\mathbf{T}_i,\mathbf{z}_i\right)E\left[\theta\middle|\mathbf{T}_i,\nu,\mathbf{z}_i\right] \tag{13}$$

where $\mathbf{T}_i$ is the observed (multivariate) time to event data for the individual i, and $\hat{P}\left(\nu\middle|\mathbf{T}_i,\mathbf{z}_i\right)$ is the posterior class membership probability.

The expected disorder-specific hazard functions can also be estimated from (6) as marginal hazards with respect to the latent variables:

$$\hat{h}_{\bullet j}\left(t\right)=N^{-1}\sum\nolimits_{i=1}^{N}w_i\left\{\begin{array}{r}\int\hat{h}_{ij}\left(t\mid\theta_{i|\nu=1}\right)f\left(\theta\middle|\nu=1,\mathbf{z}_i^F\right)d\theta\cdot\hat{P}\left(\nu=1\middle|\mathbf{z}_i^C\right)\\ +\hat{h}_{ij}\left(t\mid\theta_{i|\nu=2}=-a\right)\cdot\hat{P}\left(\nu=2\middle|\mathbf{z}_i^C\right)\end{array}\right\} \tag{14}$$

The integral is solved by Latent GOLD using Gauss-Hermite numerical integration (Vermunt and Magidson 2005).

Model assumptions

The statistical assumptions of the proposed factor-analytic model for multivariate right-censored disorder data are the following:

a) Related to the Factor component

We assume the existence of a lifetime-invariant underlying diathesis factor affecting the occurrence of internalising disorders (Clark 2005; Clark and Watson 1991). Moreover, the measurement of mental diathesis is assumed to be invariant across ages and periods; that is, the λ_j parameters are not influenced by any temporal effect.

Moreover, invariance is assumed in a wider sense: the measurement parameters (λ_j and β_{jt}) do not vary across subpopulations (Lubke et al. 2003; Tay et al. 2011). The internalising factor is already a well-established construct in psychiatry, and a previous study has shown its measurement invariance for "last 12-month" disorder data (Almansa et al. 2011). Measurement invariance implies that estimated factor scores are comparable across time, age periods and subpopulation groups.

Another assumption is the local independence assumption: conditional on the latent variables, the disorder timing and occurrence is independent across disorders. The local independence assumption implies that the factor and the classes capture all common time-invariant sources of variation in disorders.

b) *Related to the Survival component*

Turning to the survival part of the model, the most important assumption is that censoring is non-informative; that is, the censoring rate should be unrelated to the hazard rate, conditional on the factors which are controlled for. In cross-sectional studies, where event history data are collected retrospectively, it is reasonable to assume that right-censoring is non-informative because it depends on the timing of the survey, which is not related to a person's hazard rate.

We are also assuming proportional hazards; that is, the effect of diathesis on the hazard probabilities (see equation (5)) is assumed to be the same across different age-of-onset time periods. Note that this is similar to the assumption of measurement equivalence discussed above since the proportional hazards assumption implies that the factor loadings are constant across time periods.

c) *Sampling design*

One additional assumption concerns the sampling design rather than the model. Some people who were born within the number of years considered for 'lifetime' (for example, the 90 previous years) could not be included in the sample because they died or were

institutionalized before the interview time. This truncation is assumed to be unrelated to the disorder probabilities.

Application

ESEMeD Data

The ESEMeD Project was a cross-sectional survey based on a stratified, multi-stage, clustered area probability sample. Individuals were assessed in person at their homes using computer-assisted interview (CAPI) techniques. The target population was the non-institutionalized adult population (aged 18 years or older) of Belgium, France, Germany, Italy, the Netherlands and Spain, providing data between January 2001 and August 2003. For the present analysis, a representative ESEMeD subsample was used (N=8,796). Mental disorders assessment was based on version 3.0 of the World Health Organization Composite International Diagnostic Interview (CIDI 3.0) (Kessler and Ustun 2004), a fully structured lay administered diagnostic interview that generates diagnoses according to the DSM-IV criteria (American Psychiatric Association 2000). Individuals were weighted to adjust for their population representativeness. A detailed description of the methods and the participants of the ESEMeD project are provided elsewhere (Alonso et al. 2004c). Table 1 shows some socio-demographic information about this dataset. Further basic descriptives of the disorders included in the ESEMeD data can be found elsewhere (Alonso et al. 2004b; Alonso et al. 2004a).

[- Insert Table 1 by here -]

The variables used in our analysis indicate whether a mental disorder was present in any time previous to the interview, according to the DSM-IV criteria. The eight disorders considered are: major depression episode (mde), dysthymia (dys), general anxiety disorder (gad), post-traumatic stress disorder (ptsd), agoraphobia with or without panic (ago), specific phobia (sp), social phobia (so), panic disorder (pd).

The ESEMeD study provides retrospective information on the age of onset for those who fulfil the criteria for mental disorders. Individuals were questioned regarding the age of onset of mental symptoms, using a series of questions designed to avoid implausible response patterns. The sequence began with a question designed to emphasize the importance of accurate responses: "Can you remember your exact age the very first time you had the syndrome?". Respondents who answered "no" were probed for a bound of uncertainty by moving up the age range incrementally (e.g., "Was it before you first started school?", "Was it before you became a teenager?", etc). Age of onset was set at the upper end of the bound (e.g., age 12 years for respondents who reported that onset was before they became a teenager). This set of questions helped respondents to recall remote events in order to minimize possible recall bias (Knauper et al. 1999; Simon and VonKorff 1995).

The age of onset of a disorder defines the metric for the survival functions. These onset values were coded in the dataset in years, yielding a discrete-time measurement. Moreover, given that mental disorders are quite infrequent events, time units were grouped into larger time intervals. The age of onset variable, then, was coded as five equal-size intervals of 20 years each. Even with rather wide time intervals, some disorders had no observed events (disorder onset) in the last age of onset periods (Table 2). For these periods, the parameters associated with the hazard (β_{jt}) were fixed to the large negative value -15.

[- Insert Table 2 by here -]

Analysis

First, a standard hazard model was estimated in which the disorders are assumed to be independent of one another; that is, a model without an underlying common factor (or equivalently $\lambda_j = 0$). This model, which served as a baseline model to assess the improvement of fit when moving to the more complex models, is obtained as:

$$\text{logit}\left(h_{ij}\left(t\right)\right) = \beta_{jt} \ . \quad (15)$$

Then, the continuous latent factor assumed to capture the associations between the internalising disorders was included, as expressed in equation (5). The next step involved the addition of the two-class mixture defining "not-at-risk" and "at-risk" populations, as expressed in (6), with $a = 10$, implying that the "not-at-risk" group had a degenerate value of -10: $\theta \left| \nu = 2 \sim N\left(-10, 0\right)\right.$, which yields a hazard rate very close to 0. As a final step, latent class covariates were included to obtain a better prediction of an individual's class membership, and factor covariates were included to determine whether diathesis differences could be explained within the "at-risk" class – as expressed by equations (7) and (8). The selected covariates are all assumed to be time constant, such as gender, year of birth and country (although individuals may have changed their country of residence, we assumed that sampled individuals were representative of their current country population at the interview time).

Once the final model had been chosen, EAP factor scores and their standard deviations were estimated for each individual. This scoring method provides a measure on a continuous scale of the internalising lifetime diathesis. Lifetime prevalences and hazard functions were also estimated for each disorder.

Model comparison was mainly done using the Bayesian information criterion (BIC) (Raftery 1995). We also examined another comparative fit index for decision-making, the Akaike's information criterion (AIC) (Akaike 1974). Using these indexes it is possible to choose the best fitting model among a set of nested and/or non-nested alternative models.

In order to obtain unbiased estimates and standard errors, the complex sample design was taken into account in all analysis by using a linearization variance estimator (Alonso et al. 2004c; Vermunt and Magidson 2005). All models were estimated using maximum likelihood, with 125 different start values to avoid local-optima, using the

syntax module of version 4.5 of the Latent GOLD program (Vermunt and Magidson, 2008). The specification of the final 2-class mixture factor survival model in Latent GOLD is provided in the appendix.

RESULTS

The internalising factor model fitted the data better than the model assuming independent disorders (Table 3), supporting the adequacy of a dimensional internalising structure. The addition of a latent class variable defining “not-at-risk” and “at-risk” subpopulations led to a large improvement in goodness-of fit (lower BIC and AIC values). The socio-demographic covariates gender, country and birth-year were found to be significant predictors of class membership. Country and birth-year were also significant predictors of severity-diathesis, that is, they had a significant effect on the factor mean within latent class 1 (the “at-risk” class).

[- Insert Table 3 by here -]

Table 4 shows the estimates of the measurement parameters (intercepts and loadings) obtained with the selected mixture-IRT model, while Table 5 shows the estimates of the covariate effects on class membership and on severity diathesis. Males had lower probability of belonging to the “at-risk” class than females. Italy and Spain had significantly lower “at-risk” class proportions than the other countries, while for France the “at-risk” class proportion is higher. The oldest individuals showed a low “at-risk” class membership probability and those born between 1950 and 1964 showed the highest “at-risk” class proportion. Regarding the factor covariates, France and The Netherlands had the highest internalising diathesis levels within the “at-risk” class, while Germany had the lowest values. An interesting age-cohort effect was found: within the “at-risk” class, the level of diathesis increased with year of birth. Thus, the oldest group not only showed lower proportions of “at-risk” individuals, but also lower levels of diathesis.

It is also possible to interpret the effects of these factor (severity) covariates using hazard odds ratios. For example, in class 1 ("at-risk") the odds of experiencing major depression in the Netherlands are on average 2.1 times higher than the odds in Spain. The corresponding hazard odds ratio for social phobia (so) is equal to 1.4. And the hazard odds ratio for those born after 1975 against those born in 1950-64 is 2.4 for major depression – and 1.5 for social phobia.

The proportion in the "not-at-risk" class was estimated as 52.3%, which implies that just over half of the population is expected to never display any internalising lifetime disorder.

[- Insert Table 4 and 5 by here -]

Disorder hazard functions were estimated using the parameter estimates from the final model. Figure 1 depicts the estimated marginal hazards of disorder onset for four of the internalising disorders (major depression episode, dysthymia, social phobia and specific phobia) - computed using equation (14). Specific and social phobia had very high hazard values at the early age-of-onset interval compared to the subsequent intervals, indicating that these disorders appear mainly before adulthood. Depression disorders (major depression and dysthymia) appear most frequently during midlife. For the remaining disorders, the shapes of the hazard functions were generally similar to the hazard for depression.

[- Insert Figure 1 by here -]

One of the most important goals in our analyses was to obtain estimates of the lifetime disorder prevalences taking into account comorbidity and censoring. As can be seen from Table 6, major depression (18.4%) and specific phobia (8.6%) are most prevalent lifetime disorders. It can also be seen that the estimated prevalences obtained with our model are much higher that the observed prevalences, except for those disorders with early onsets (such as social and specific phobia). The size of the difference between the observed and estimated lifetime prevalence depends on the time-dependence of

the hazard rates: the higher the hazard at older ages, the larger the underestimation in the lifetime prevalence when censoring is ignored. The IRT model that ignores the data censorship reproduced exactly the observed cross-sectional data prevalences.

[- Insert Table 6 by here -]

A simple descriptive analysis of the estimated factor scores can be used as a rough indication of the overall impact of covariates on psychiatric diathesis (Table 7). This shows that, on average, women and the population of northern countries are more vulnerable for internalising disorders.

The two roles of the covariates (class and factor/severity) in the mixture-IRT model yielded a more detailed explanation for these diathesis differences. The gender diathesis difference is due to a larger proportion of women affected by internalising disorders compared to men, but no significant differences in severity levels were found between genders (on average, “at-risk” men and “at-risk” women had the same levels of diathesis severity). Regarding countries, the lower diathesis levels in southern Europe countries (Italy and Spain) can also be explained by the lower proportion in the “at-risk” class for these two countries. The proportions of “at-risk” individuals in The Netherlands and Germany were both close to the European average, but the diathesis levels were significantly higher in The Netherlands and lower in Germany.

[- Insert Table 7 by here -]

Discussion

Lifetime mental disorder is an important indicator in psychiatric epidemiology. In this article we have shown how to build a multivariate statistical model of mental comorbidity that takes into account censorship and comorbidity. The model explains disorder associations using an IRT-type latent structure, with discrete-time survival functions that model the age of onset of the disorders. We applied this model to data on mood and anxiety mental disorders from the ESEMED study (Alonso et al. 2002),

implementing a conceptual internalising model (Cerda et al. 2008; Clark 2005). The proposed factor-analytic model yields a realistic estimation of the lifetime prevalences and provides an estimate of the individuals' inherent vulnerability (diathesis) towards internalising mental disorders, which summarizes the comorbidity pattern data, excluding the random comorbidity association, referred to as *pseudocomorbidity* (Kraemer et al. 2006).

The fact that the estimated lifetime disorder prevalences were often substantially higher than the observed prevalence shows that the bias introduced by ignoring censorship is not trivial. The estimated factor scores clearly indicated socio-demographic differences in the internalising mental vulnerability. Moreover, the two types of covariates (class and factor/severity) included in the mixture-IRT model may serve as a source for generating hypotheses explaining mental health differences across countries. For example, the model can distinguish between two quite different medical scenarios with similar factor means; that is, a large group of "at-risk" individuals with low severity versus a smaller group of "at-risk" individuals but with higher severity.

One of the main advantages of the method described here is that all relevant epidemiological measures can be obtained from a single model, including the prevalence of the disorders, hazard functions, risk factors assessment, socio-demographic differences and the severity level of each comorbidity pattern. The model provides a joint description of variables (how disorders relate to each other through a factor structure) and individuals (factor scores, disorder prevalence, class membership, etc.). All estimates are already adjusted by the covariates and the factors included in the model. Whereas epidemiological studies usually estimate separately the disorder prevalences, risk factors and comorbidity assessment (Alonso et al. 2004b; Alonso et al. 2004a; Kessler et al. 2005b), the method proposed here allows different research questions to be tested within a common framework.

We presented only part of the information that can be derived from the final model. One may for instance also estimate the hazard functions for different subpopulations or for different increments in the diathesis level, investigate how diathesis varies with the age-of-onset of the disorders, get the expected diathesis score for each realised disorder pattern, or estimate the joint prevalence for pairs of disorders. The model can also provide the probability of lifetime disorders for individuals who have not yet shown an onset.

Limitations

Mental disorders are infrequent events in the general population. The low prevalences forced us to use relatively large age-of-onset time intervals for the discrete survival models rendering the hazard functions quite imprecise for describing the onset of disorders. Nevertheless, our main goal was not to understand the process of appearance of the disorders during an individual's lifetime, but to correct for the data right-censorship when estimating diathesis and lifetime prevalences. With the logistic discrete survival procedure, wide time intervals ensure a reasonable number of events per age-of-onset interval, but may lead to bias if the true hazard varies within intervals. Taking smaller age-of-onset time intervals would lead to a large increment in the number of time-points without events. Possible extensions of the discrete-hazard model may include the selection of different numbers of time-points across disorders (so that hazard functions from disorders with higher prevalence could be described in more detail), or the use of a binary-type outcome in the logistic discrete-hazard models, in order to take into account the exact number of years that censored cases are observed (Almansa et al. 2010; Almansa et al. (accepted)), which would allow a slightly more precise estimation of the latent scores. But, if detailed description of disorder-onset process is a main research interest, a different and more complex survival approach may be used, such as smoothing techniques or penalized maximum likelihood (Ambler G et al. 2010; Rondeau et al. 2003; Pritscher and Tutz 1996).

Lifetime data obtained from cross-sectional surveys in a retrospective fashion has been criticized, mainly because of memory bias underestimating past mental problems (Streiner et al. 2009). Thus, the interpretation of age-cohort effects should be interpreted with caution. We found a trend in which younger individuals showed higher levels of diathesis, but given the above-mentioned caveat, it is not clear whether this age-trend is real or whether this is caused by memory bias of older respondents.

The presented factor-analytic discrete-survival methodology can be extended to deal with more complex factor structures (e.g. a 2-factor internalising structure and an externalising dimension (Krueger 1999)). The consideration of more detailed psychiatric conceptual models, including a wider range of disorders, would undoubtedly lead to a richer description of mental health diathesis in general populations.

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Table 1. Socio-demographic descriptives and observed prevalence of any internalising lifetime disorder. Weighted percentages (to adjust for the population representativeness).

	Whole sample		Any lifetime disorder	
	N	%	N	%[1]
Gender				
Male	3689	48.2	1273	17.0
Female	5107	51.8	2684	28.8
Age				
18-24	664	11.4	272	24.2
25-34	1599	18.3	710	21.7
35-49	2669	27.8	1327	26.2
20-64	2197	21.8	1039	25.0
+65	1667	20.7	609	17.7
Mean (SE)	47.0	(0.31)	45.6	(0.45)
Country				
Belgium	1043	3.8	486	24.2
France	1436	20.5	858	35.9
Germany	1323	31.5	534	20.5
Italy	1779	22.4	626	17.8
Netherlands	1094	6.1	600	27.0
Spain	2121	15.6	853	17.6
TOTAL	8796	100.0	3957	23.1

[1] Percentage of individuals with observed lifetime internalisng disorder.

Table 2. Number of onsets of each disorder in age intervals.

Time	Age	mde	dys	gad	pts	ago	pds	so	sp
1	0-19	660	216	126	133	74	105	299	837
2	20-39	1479	414	286	198	76	210	75	75
3	40-59	691	258	125	87	21	66	12	25
4	60-79	153	68	19	23	5	7	0	8
5	80-99	4	2	0	1	0	0	0	0

Table 3. Comparative goodness of fit indices for model selection

Hazard models	Covariates	LogLikelihood	BIC	AIC	Npar
Independence		-14905.5	30119.8	29879.0	34
IRT		-13695.0	27771.5	27474.0	42
Mixture IRT[1]		-13667.6	27725.7	27421.2	43
	Class covariates				
Mixture IRT	Gender	-13584.3	27568.2	27256.6	44
	+ Country	-13472.1	27389.2	27042.2	49
	+ Birth-Year	-13406.4	27294.1	26918.8	53
Mixture IRT with class covariates[2]	*Factor covariates*				
	Gender	-13403.3	27297.1	26914.7	54
	Country	-13382.5	27291.8	26881.1	58
	Birth-Year	-13374.0	27265.6	26861.9	57
	Country + Birth-Year	-13351.6	27266.3	26827.2	62

[1] Mixture IRT: 2-class model defining “at-risk” and “not-at-risk” latent classes.
[2] Mixture IRT model with 3 class covariates: Gender, country and Birth-Year.

Table 4. Estimates of measurement parameters in the final model with standard errors in brackets.

	Intercepts					factor loading
	β_{j1}	β_{j2}	β_{j3}	β_{j4}	β_{j5}	λ_j
mde	-3.73 (0.23)	-2.26 (0.21)	-1.90 (0.22)	-2.16 (0.26)	-3.56 (0.66)	1.84 (0.16)
dys	-4.72 (0.25)	-3.94 (0.23)	-3.18 (0.22)	-3.40 (0.26)	-5.11 (0.79)	1.43 (0.15)
gad	-5.03 (0.29)	-4.19 (0.24)	-4.29 (0.25)	-4.71 (0.38)	-15 (.)	1.40 (0.15)
pts	-4.59 (0.21)	-4.04 (0.21)	-3.99 (0.25)	-4.30 (0.33)	-4.44 (1.03)	0.97 (0.13)
ago	-5.19 (0.36)	-5.10 (0.38)	-6.04 (0.38)	-7.02 (0.64)	-15 (.)	1.23 (0.24)
pds	-5.05 (0.22)	-4.38 (0.22)	-4.80 (0.28)	-5.84 (0.44)	-15 (.)	1.10 (0.15)
so	-3.26 (0.20)	-4.81 (0.29)	-6.10 (0.38)	-15 (.)	-15 (.)	0.82 (0.13)
sp	-1.72 (0.10)	-4.17 (0.20)	-5.04 (0.32)	-5.88 (0.45)	-15 (.)	0.39 (0.06)

Table 5. Estimates of covariate parameters, coded as sum-zero dummies, in the final model with standard errors in brackets.

	Class 1[1]		**Severity**[2]	
Class size	47.7%			
Gender				
Male	-0.57	(0.06)		
Female	0.57	(0.06)		
Country				
Belgium	0.16	(0.25)	-0.03	(0.12)
France	0.73	(0.17)	0.20	(0.09)
Germany	0.17	(0.23)	-0.41	(0.11)
Italy	-0.52	(0.14)	0.00	(0.08)
The Netherlands	-0.11	(0.16)	0.33	(0.09)
Spain	-0.44	(0.17)	-0.08	(0.10)
Birth-Year				
–1934	-0.54	(0.17)	-0.41	(0.10)
1935-49	0.11	(0.16)	-0.27	(0.08)
1950-64	0.46	(0.15)	-0.10	(0.08)
1965-74	-0.18	(0.15)	0.41	(0.09)
1975–	0.15	(0.23)	0.37	(0.14)

[1] Class 1 (“at-risk”) membership probability. Class covariates use class 2 (the “not-at-risk”class) as reference category.
[2] Effect on the factor mean within class 1 (“at-risk”).

Table 6. Observed and model-estimated lifetime prevalences, and median of age of onset.

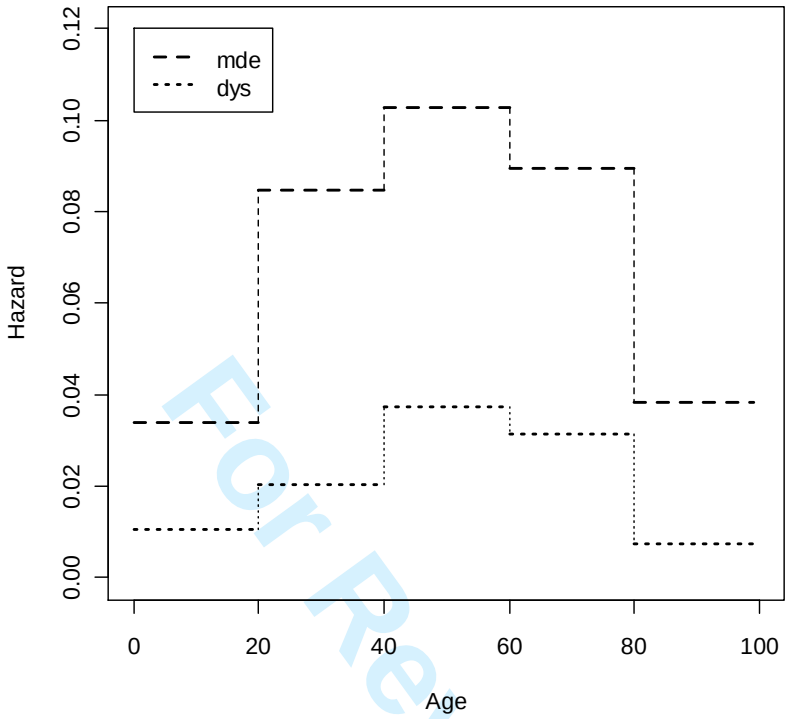
	Observed	Estimated	Age of onset
	N	% (SE)	% (SE)	Median
Dysthymia	958	4.4 (0.21)	8.2 (0.07)	31
Major Depression	2987	13.4 (0.37)	18.7 (0.14)	29
Post Traumatic Stress	442	2.6 (0.20)	4.6 (0.04)	26
General Anxiety Disorder	556	2.8 (0.20)	4.2 (0.04)	26
Agoraphobia	176	1.2 (0.14)	1.4 (0.01)	20
Panic disorder	388	1.8 (0.13)	2.3 (0.02)	25
Social Phobia	386	2.8 (0.24)	2.9 (0.02)	12
Specific Phobia	945	8.3 (0.43)	8.6 (0.05)	6

Table 7: Mean of factor (diathesis) scores and class 1 (“at-risk”) membership proportion by sociodemographic categories.

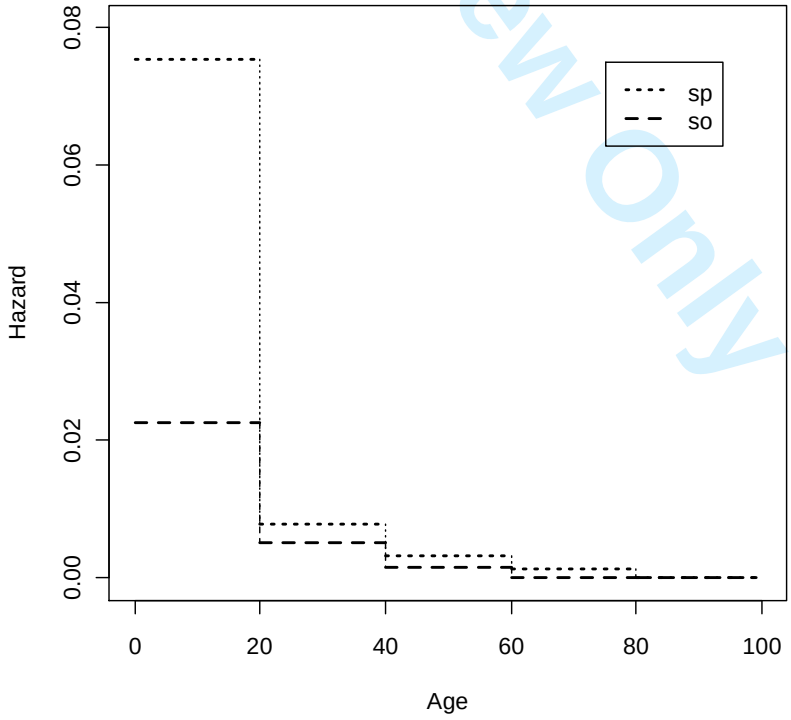
	Diathesis mean (SE)	**Class 1 % (SE)**
Overall sample	-5.27 (0.05)	47.7 (0.4)
Gender		
Male	-6.56 (0.06)	34.7 (0.6)
Female	-4.08 (0.06)	59.8 (0.5)
Birth Year		
–1934	-6.46 (0.10)	37.2 (0.9)
1935-49	-5.27 (0.09)	49.0 (0.9)
1950-64	-4.43 (0.08)	56.7 (0.8)
1965-74	-5.60 (0.11)	42.5 (1.0)
1975–	-5.00 (0.14)	48.6 (1.3)
Country		
Belgium	-4.93 (0.15)	50.9 (1.4)
France	-3.54 (0.13)	63.4 (1.2)
Germany	-5.08 (0.09)	51.4 (0.9)
Italy	-6.46 (0.08)	35.5 (0.7)
The Netherlands	-5.32 (0.15)	45.3 (1.4)
Spain	-6.30 (0.09)	37.3 (0.9)

Figure 1. Estimated hazard of onset disorder functions, for *(a)* major depression (mde), dysthymia (dys) and *(b)* specific phobia (sp), social phobia (so)

(a)



(b)



References

Akaike, H. (1974) A new look at the statistical model identification. *IEEE Transactions on Automatic Control,* 19 (6), 716–723.

Almansa, J., Forero, C.G., Vermunt, J.K. & Alonso, J. (conditionally Accepted) Estimation of lifetime outcomes models in cross-sectional desings using Partially Weighted Likelihood IRT: an application in the ESEMeD Surveys. Psycometrika.

Almansa, J., Vermunt, J.K., Forero, C.G., Vilagut, G., & Alonso, J. (2010) IRT models with censored binary indicators, application on European lifetime mental health comorbidity assessment. *31st Annual Conference of the International Society for Clinical Biostatistics. 29 August-2 September 2010, Montpellier, France*.

Almansa, J., Vermunt, J.K., Forero, , C.G., Vilagut, G., de Graaf, R., de Girolamo, G., & Alonso, J. (2011) Measurement and description of underlying dimensions of comorbid mental disorders using Factor Mixture Models: results on the ESEMeD project. International Journal of Methods in Psychiatric Research, 20(2),116-133

Alonso, J., Angermeyer, M. C., Bernert, S., Bruffaerts, R., Brugha, T. S., Bryson, H., de Girolamo, G., Graaf, R., Demyttenaere, K., Gasquet, I., Haro, J. M., Katz, S. J. (2004a) Prevalence of mental disorders in Europe: results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) project. *Acta Psychiatr. Scand*, 109, 21-27.

Alonso, J., Angermeyer, M. C., Bernert, S., Bruffaerts, R., Brugha, T. S., Bryson, H., Girolamo, G., Graaf, R., Demyttenaere, K., Gasquet, I., Haro, J. M., Katz, S. J. (2004b) 12-Month comorbidity patterns and associated factors in Europe: results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) project. *Acta Psychiatr Scand*, 109, 28-37.

Alonso, J., Angermeyer, M. C., Bernert, S., Bruffaerts, R., Brugha, T. S., Bryson, H., Girolamo, G., Graaf, R., Demyttenaere, K., Gasquet, I., Haro, J. M., Katz, S. J. (2004c) Sampling and methods of the European Study of the Epidemiology of Mental Disorders (ESEMeD) project. *Acta Psychiatr Scand*, 109, 8-20.

Alonso, J., Ferrer, M., Romera, B., Vilagut, G., Angermeyer, M., Bernert, S., Brugha, T. S., Taub, N., McColgen, Z., de Girolamo, G., Polidori, G., Mazzi, F. (2002) The European Study of the Epidemiology of Mental Disorders (ESEMeD/MHEDEA 2000) project: rationale and methods. *Int. J. Methods Psychiatr. Res.*, 11, 55-67.

Ambler G, Seaman, S., Rumana O. (2010) Developing risk models for survival outcomes when the number of events is small. *31st Annual Conference of the International Society for Clinical Biostatistics.29 August-2 September 2010, Montpellier, France.*

American Psychiatric Association (2000) *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), Fourth Edition*. Washington, DC: American Psychiatric Association

Bijl, R. V. and Ravelli, A. (2000) Current and residual functional disability associated with psychopathology: findings from the Netherlands Mental Health Survey and Incidence Study (NEMESIS). *Psychol Med*, 30, 657-668.

Bonnewyn, A., Bruffaerts, R., Vilagut, G., Almansa, J. and Demyttenaere, K. (2007) Lifetime risk and age-of-onset of mental disorders in the Belgian general population. *Soc Psychiatry Psychiatr Epidemiol*, 42, 522-529.

Cerda, M., Sagdeo, A. and Galea, S. (2008) Comorbid forms of psychopathology: key patterns and future research directions. *Epidemiol. Rev.*, 30, 155-177.

Clark, L. A. (2005) Temperament as a unifying basis for personality and psychopathology. *J. Abnorm. Psychol.*, 114, 505-521.

Clark, L. A. and Watson, D. (1991) Tripartite model of anxiety and depression: psychometric evidence and taxonomic implications. *J. Abnorm. Psychol.*, 100, 316-336.

Davier, M. V. and Rost, J. (2007) Mixture distribution Item Response Models. In *Handbook of Statistics*, vol. 26 Elsevier, pp. 643-661.

De Boeck, P. (2004) *Explanatory item response models: a generalized linear and nonlinear approach*. New York : Springer-Verlag.

Efron, B. (1988) Logistic Regression, Survival Analysis, and the Kaplan-Meier Curve. *J Am Stat Assoc*, 83, 414-425.

Farewell, V.T. (1982) The use of mixture models for the analysis of survival data with long-term survivors. *Biometrics*, 38, 1041-1046.

Hougaard, P. (1984) Life table methods for heterogeneous populations: Distributions describing the heterogeneity. *Biometrika,* 71(1), 75-83

Hougaard, P. (1995) Frailty Models for Survival Data. *Lifetime Data Analysis,* 1, 255-273

Hougaard, P. (2000) *Analysis of Multivariate Survival Data*. New York: Springer.

Hosmer, DW Jr, Lemeshow, S. (1999) *Applied Survival Analysis: Regression Modeling of Time to Event Data.* New York: John Wiley.

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R. and Walters, E. E. (2005a) Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*, 62, 593-602.

Kessler, R. C., Chiu, W. T., Demler, O., Merikangas, K. R. and Walters, E. E. (2005b) Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*, 62, 617-627.

Kessler, R. C. and Ustun, T. B. (2004) The World Mental Health (WMH) Survey Initiative Version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). *Int J Methods Psychiatr Res*, 13, 93-121.

Knauper, B., Cannell, C. F., Schwarz, N., Bruce, M. L. and Kessler, R. C. (1999) Improving the accuracy of major depression age of onset reports in the US National Comorbidity Survey. *Int J Methods Psychiatr Res*, 8, 39-48.

Kraemer, H. C., Wilson, K. A. and Hayward, C. (2006) Lifetime prevalence and pseudocomorbidity in psychiatric research. *Arch Gen Psychiatry*, 63, 604-608.

Krueger, R. F. (1999) The structure of common mental disorders. *Arch Gen Psychiatry*, 56, 921-926.

Larsen, K. (2004) Joint analysis of time-to-event and multiple binary indicators of latent classes. *Biometrics*, 60(1), 85-92.

Lin, H., Turnbull, B., McCulloch, C., & Slate, E. (2002) Latent class models for joint analysis of longitudinal biomarker and event process data: Application to longitudinal prostate-specific antigen readings and prostate cancer. *Journal of the American Statistical Association,* 97(457), 53- 65.

Lubke, G. H., Dolan, C. V., Kelderman, K. and Mellenberg, G. J. (2003) On the relationship between sources of within - and between-group differences and measurement invariance in the common factor model . *Intelligence*, 31 , 543-566.

Masyn, K. (2009) Discrete-time survival factor mixture analysis for low-frequency recurrent event histories. *Research in Human Development*, 6(2), 165-194.

Moustaki, I. and Steele, F. (2005) Latent Variable Models for Mixtures of Categorical and Survival Responses, with an Application to Fertility Preferences and Family Planning in Bangladesh, *Statistical Modelling,* 5(4), 327-342.

Muthén, B. and Masyn, K. (2005) Discrete-Time Survival Mixture Analysis. *J Educ Behav Stat*, 30, 27-58.

Pritscher L, Tutz G (1996). Nonparametric Estimation of Discrete Hazard Functions. *Lifetime Data Analysis*, 2, 291-308.

Raftery, A. E. (1995) Bayesian model selection in social research. *Sociol Methodol*, 25, 111-163.

Rondeau, V., Commenges, D. and Joly, P. (2003) Maximum penalized likelihood estimation in a gamma-frailty model. *Lifetime. Data Anal.*, 9, 139-153.

Roy-Byrne, P. P., Stang, P., Wittchen, H. U., Ustun, B., Walters, E. E. and Kessler, R. C. (2000) Lifetime panic-depression comorbidity in the National Comorbidity Survey. Association with symptoms, impairment, course and help-seeking. *Br J Psychiatry*, 176, 229-235.

Simon, G. E. and VonKorff, M. (1995) Recall of psychiatric history in cross-sectional surveys: implications for epidemiologic research. *Epidemiol Rev*, 17, 221-227.

Singer, J. D. and Willett, J. B. (1993) It's about time: Using discrete-time survival analysis to study duration and the timing of events. *Journal of Educational Statistics*, 18, 155-195.

Steele, F. (2003) A Multilevel Mixture Model for Event History Data with Long-term Survivors: An application to an Analysis of Contraceptive Sterilisation in Bangladesh. *Lifetime Data Analysis*, 9, 155-174.

Streiner, D. L., Patten, S. B., Anthony, J. C. and Cairney, J. (2009) Has 'lifetime prevalence' reached the end of its life? An examination of the concept. *Int. J. Methods Psychiatr. Res.*, 18, 221-228.

Tay, L., Newman, D.A., and Vermunt, J.K. (2011). Using mixed-measurement item response theory with covariates (MM-IRT-C) to ascertain observed and unobserved measurement equivalence. *Organizational Research Methods*. 14(1), 147-176.

Tekle, F.B., and Vermunt, J.K. (2012). Event history analysis. In *APA Handbook of Research Methods in Psychology*.(eds. Harris Cooper et al.), Volume 3, section 4, pp. 267-290, Washington, DC, US: American Psychological Associatio

Vermunt, J.K. (1997) *Log-linear models for event histories*. Thousand Oaks: Sage.

Vermunt, J.K. (2002) A general latent class approach to unobserved heterogeneity in the analysis of event history data. In *Applied latent class analysis* (eds. J. Hagenaars and A. McCutcheon), 383-407. Cambridge, UK: Cambridge University Press.

Vermunt, J. K. (2009). Event history analysis. In *Handbook of Quantitative Methods in Psychology*, R. Millsap and A. Maydeu-Olivares (eds.),London: Sage, pp. 658-674.

Vermunt, J. K. and Magidson, J. (2005) *Technical Guide for Latent GOLD 4.0: Basic and Advanced*. Belmont Massachussets: Statistical Innovations, Inc.

Vermunt, J. K. and Magidson J. (2008) *LG-Syntax User's Guide: Manual for Latent GOLD 4.5 Syntax Module*, Belmont, MA: Statistical Innovations Inc.

APPENDIX

This appendix shows how the models proposed in this article can be specified with the Latent GOLD syntax (Vermunt and Magidson,2008). It should be noted that the data is in person-period format with at most 5 records per individual, where each record corresponds to a 20-year time period. Of course, an id variable is used to connect the multiple record of the same individual. The variables used in the model are defined before providing the equations. The variable “time” is a categorical predictor taking on values between 1 and 5, indicating which of the 5 time intervals the record concerned refers to. The dependent variables are labelled “y1” to “y8”, and “theta” and “nu” are defined to be a continuous latent variable and a two-class categorical latent variable respectively. Gender, country and birthyear are categorical predictors. The equations defining the final mixture-IRT model are as follows (// means that the line concerned is a comment):

```
// logistic regression equation for nu
nu <- 1 + gender + country + birthyear;

// linear regression equation for theta, with parameters
// that vary across classes, which is indicated with “| nu”
theta <- (m) 1 | nu + (g1) country | nu + (g2) birthyear | nu;

// variance of theta, which also depends on nu
(s) theta | nu;

// logistic regression equations for response variables
// which intercepts that vary across time points
y1 <- (b1) 1 | time + theta;
y2 <- (b2) 1 | time + theta;
y3 <- (b3) 1 | time + theta;
y4 <- (b4) 1 | time + theta;
y5 <- (b5) 1 | time + theta;
y6 <- (b6) 1 | time + theta;
y7 <- (b7) 1 | time + theta;
y8 <- (b8) 1 | time + theta;

// restrictions on hazard logits for time periods without events
b3[5]=-15;
b5[5]=-15;
b6[5]=-15;
b7[4]=-15; b7[5]=-15;
b8[5]=-15;

// restrictions on class-specific means/intercepts and
// variances of theta
s[1]=1; s[2]=0;
m[1]=0; m[2]=-10;

// factor covariate effects are fixed to 0 for class 2
g1[2]=0; g2[2]=0;
```