Modelling Hierarchically Clustered Longitudinal Survival Processes with Applications to Childhood Mortality and Maternal Health

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Abstract

This paper merges two parallel developments since the 1970s of new statistical tools for data analysis: statistical methods known as hazard models that are used for analyzing event-duration data and statistical methods for analyzing hierarchically clustered data known as multilevel models. These developments have rarely been integrated in research practice and the formalization and estimation of models for hierarchically clustered survival data remain largely uncharted. I attempt to fill some of this gap and demonstrate the merits of formulating and estimating multilevel hazard models with longitudinal data.

Résumé

Cette étude intègre deux approches statistiques de pointe d'analyse des données quantitatives depuis les années 70: les méthodes statistiques d'analyse des données biographiques ou méthodes de survie et les méthodes statistiques d'analyse des données hiérarchiques ou méthodes multi-niveaux. Ces deux approches ont été très peu mis en symbiose dans la pratique de recherche et par conséquent, la formulation et l'estimation des modèles appropriés aux données longitudinales et hiérarchiquement nichées demeure essentiellement un champ d'investigation vierge. J'essaye de combler ce vide et j'utilise des données réelles en santé publique pour démontrer les mérites et contextes de formulation et d'estimation des modèles multi-niveaux et multi-états des données biographiques et longitudinales.

Introduction

Longitudinal studies in the social and biomedical sciences have been major instruments for measuring compositional and structural changes in individual and group behaviour. Of interest in this paper are two parallel developments of statistical tools since the 1970s for analyzing longitudinal data. One has focused on statistical methods, known as hazard models, for analyzing event-duration data generated by failure-time processes (Cox, 1972; Kalfleisch and Prentice, 1980; Baltagi, 1995). The other has centred on statistical methods, known as multilevel models, for analyzing hierarchically clustered data (Mason et al., 1983; Bryk and Raudenbush, 1992; Goldstein, 1999; Snijders and Bosker, 1999; Heck and Thomas, 2000). These two developments have rarely been integrated, and research practice that formulates and estimates models for hierarchically clustered survival data is still under development.

This study formulates hierarchically clustered survival models and demonstrates the importance and relevance of using those models for data analysis, with applications to real-life event-duration data from Africa. The next section outlines some general issues in modelling survival or duration-response data within a multilevel framework, and briefly describes multilevel event-duration data to be used for illustrative purposes. Then, I shall outline the general formulations of the hierarchically clustered survival models, followed by illustrations for analyzing hierarchically clustered longitudinal single spell

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survival data (with an application to the study of child survival) and multiple spell survival data (with an application to the study of maternal health). Finally, I shall formulate the model for discrete state space, and apply it to examine individual, familial and area influences on infant mortality for different geographic regions in Africa.

Multilevel Event-duration Data or Hierarchically Clustered Survival Data

The expression "multilevel event-duration data" or "hierarchically clustered survival data" refers to data with explanatory/outcome variables and the timing and sequencing of events for individuals situated in both time and contexts. Generally speaking, such multilevel survival data are rarely, if ever, collected in surveys or population laboratories, despite growing efforts in longitudinal data collection. There is a need for contextual longitudinal surveys through which information is collected over time, contexts and states occupied by the individuals in the sample. When such data are available for analysis, it is essential that researchers have a good understanding of the complexities of data organization involved as well as the methods for multilevel modelling of failure-time processes.

The most frequent type of data available for multilevel survival analysis are multilevel life histories. These can be repeated measurements at discrete and fixed occasions on the same individuals several times during an observation period, or multi-occasion measurements that include retrospective questioning on the timing of events and capture contextual, compositional, and structural changes experienced by individuals and various groups they constitute. The time intervals and the number of occasions may vary across individuals.

Conventional multilevel analysis of longitudinal data has centred on describing and attempting to explain the average pattern of changes over time and its between-individuals variation (for a review, see Yang and Goldstein, 1996). A weakness of this approach is that time is used simply as another explanatory variable without recognition of its special nature as the domain in which qualitative changes in states take place in a dynamic way within specific contexts. Features and complexities of longitudinal data create additional difficulties in analyzing changes over exposure time using conventional multilevel approaches. Most processes are both duration- and context-dependent. Therefore, models that explicitly recognize state and duration dependencies and the possibility of an autocorrelation structure among the error terms within a multilevel survival framework are called for. Obviously, further complications arise when one is interested in modelling multilevel longitudinal event-duration data in the presence of dropouts.

As for illustrations, I shall take advantage of the data from *Enquête sur la Mortalité Infantile et Juvénile* (EMIJ), collected prospectively by the United Nations' *Institut de Formation et de Recherche Démographiques* (IFORD) based in Yaounde (Cameroon). A representative sample of 9,774 children born to 9,592 resident women of Yaounde who gave birth throughout the year 1978 were followed for two years or until the death of the newborn or other form of losses to observation. The first stage of data collection was the constitution of the sample of children born to resident mothers during a 12-month period. The second stage consisted of seven rounds of follow-up interviews at 1, 4, 8, 12, 16, 20, and 24 months post-partum. Evaluative studies of these data show that they are of good quality and can help us in our understanding of influences on maternal and child health within a multilevel framework (Kuate-Defo, 1992). These repeated measurements on child survival provide an opportunity to illustrate the modelling of single-spell multilevel duration data.

Besides collecting information on infant and child mortality, the EMIJ also collected information on women's health (or maternal health), namely the episodes of illness experienced by women following childbirth. Morbidity for each woman was assessed using qualitative and quantitative descriptions of illness, including symptoms, as reported by the women to female interviewers. Classification of causes of morbidity was based on lay reporting, a procedure generally followed in longitudinal population-based studies (Halabi et al., 1992). Following the baseline health status at the time of childbirth, the episodes of illnesses were collected prospectively over a-two year period, at 1, 4, 8, 12, 16, 20 and 24 months postpartum. Contrary to the conventional study of women's health only at/around birth, this life-cycle information enables us to study maternal health over a two-year postpartum period. This is consistent with empirical evidence from many studies that have shown that full recovery from childbirth encompasses more than restoration of pre-pregnancy physiological state and generally takes more than 6 months (Kuate-Defo, 1997). These repeated measurements data provide a useful source for illustrating the modelling of multiple-spell multilevel duration data.

The second data set used for illustrations in this paper comes from the most recent Demographic and health Surveys of 15 African countries with comparable information on putative risk factors of infant and child mortality at the child-level, mother-level, household-level, and community-level. These countries are: Morocco (for North Africa), Côte d'Ivoire, Burkina Faso, Mali, Senegal, Niger, and Nigeria (for West Africa), Cameroon and Central Africa Republic (for Central Africa) and Kenya, Malawi, Uganda, Tanzania, Madagascar and Zimbabwe (for East and Southern Africa). The data were pooled by these geographic regions and country dummies were introduced in the models to account for country-specific attributes. In these surveys, each sample comprises women aged 15-49 at the time of interview, and provides a complete birth history for all live births. Moreover, in-depth information on breastfeeding, ante-natal and post-natal care practices, morbidity, nutritional status and

mortality was provided for live births that occurred during a five-year period preceding the survey date. I have restricted the analyses to children born within the three-year period preceding the survey date to minimize the impact of compositional and structural changes on estimated parameters within a multilevel framework. This was necessary especially when defining communities such that they represent the most elementary real-life administrative units (districts) of residence rather than relying on clusters defined by the sampling frame for data collection purposes that are not statistically meaningful for capturing random parameter variation across individuals and their community of residence.

General Formulation of Hierarchically Clustered Survival Models

When appropriate event-duration data are available and coupled with relevant multilevel data, survival models provide the best strategy for analyzing processes of qualitative changes in states (transitions) and their multilevel determinants in terms of fixed effects and random parameter variations across individuals and groups. Since the late 1970s, various attempts have been made to formulate statistical methods for analyzing failure-time processes in the presence of multilevel correlated observations (Clayton, 1978; Vaupel et al., 1979; Heckman and Singer, 1985; Adam et al., 1990; Sastry, 1997; Kuate-Defo, 1998; Kuate-Defo, 2001).

Let there be N states an individual can occupy at any moment of time in a given context. Suppose that there are three-levels (i, j and k) of hierarchically clustered survival data for a sample of individuals (e.g., a sample of children nested within families, and families nested within area of residence or communities). Let t_{ijk} be the survival time that elapses before the i-th child (level 1) belonging to the j-th family (level 2) in the k-th area of residence or community (level 3) makes a transition from state l to state m.

In a single-level analysis, if individuals initiate the failure-time process in state l, there are (N-1) latent times with densities

$$f^{lm}(t^{lm}) = h^{lm}(t^{lm}) \exp\left[-\int_0^{t^{lm}} h^{lm}(u)du \right] \quad (m = 1, ..., N \ ; \ m \neq l) \qquad (1)$$

where $f^{lm}(.)$ is the density function of times to transition from state l to state m, and $h^{lm}(.)$ is the associated hazard function.

The joint density of the (*N*-1) latent transition times is given by

$$\prod_{\substack{m=1 \\ m \neq l}}^{N} h^{lm}(t^{lm}) \exp\left[-\int_0^t{}^{lm} h^{lm}(u)du\right] \tag{2}$$

In a three-level framework considered above, let $\varepsilon_{ijk}, \vartheta_{jk}, \theta_k$ be the random coefficients at the child-level, the family level and the community level, respectively. Ignoring the multistate situation for now, if the random effects are assumed to operate multiplicatively on the baseline hazard, they are interpreted as relative risks and the general multilevel hazard model can be written as follows

$$f_{ijk}(t_{ijk};Z_{ijk};\beta_{ijk};X_{jk};\eta_{jk};Y_k;\xi_k|\varepsilon_{ijk},\vartheta_{jk},\theta_k) =$$

$$\tag{3}$$

$$\begin{bmatrix} f_{ijk}(t_{ijk};Z_{ijk};\beta_{ijk}) + \\ f_{jk}(t_{jk};X_{jk};\eta_{jk}) + \\ f_k(t_k;Y_k;\xi_k) \end{bmatrix} f_\varepsilon(\varepsilon_{ijk})f_\vartheta(\vartheta_{jk})f_\theta(\theta_k)$$

where Z_{ijk} is a 1 x *K* vector of level-1 exogenous (time-invariant or time-varying) variables associated with survival time t_{ijk} for the *i*-th child belonging to the *j*-th family living in the *k*-th area of residence or community. β_{ijk} is a *K* x 1 vector of coefficients that may represent both fixed effects and random effects of explanatory variables. X_{jk} is a 1 x *L* vector of level-2 exogenous (time-invariant or potentially time-varying) variables associated with survival time t_{jk} for the *j*-th family living in the *k*-th community. η_{jk} is a *L* x 1 vector of associated coefficients that may represent both fixed effects and random effects of explanatory variables. Y_k is a 1 x *M* vector of level-3 exogenous (time-invariant as well as potentially time-dependent) covariates. ξ_k is a *M* x 1 vector of associated coefficients.

Following Heckman and Singer (1985), Goldstein (1999) and Kuate-Defo (2001), the multilevel hazard function can be parameterized in a general way (without level-specific or cross-level interactions) and written as

$$h_{ijk}(t_{ijk}|Z_{ijk}(t_{ijk});X_{jk}(t_{jk});Y_k(t_k);\varepsilon_{ijk};\vartheta_{jk};\theta_k) =$$

(4)

$$\exp\left\{ \begin{bmatrix} [Z_{ijk}(t_{ijk})\beta_{ijk} + X_{jk}(t_{jk})\eta_{jk} + \\ [Y_k(t_k)\xi_k &]^+ \\ \gamma_1\left[\dfrac{(t^{\lambda_1}-1)}{\lambda_1}\right] + \gamma_2\left[\dfrac{(t^{\lambda_2}-1)}{\lambda_2}\right] + \\ \varepsilon_{ijk}(t_{ijk}) + \vartheta_{jk}(t_{jk}) + \theta_k(t_k) \end{bmatrix} \right\}, \lambda_2 > \lambda_1 \geq 0$$

Duration dependence is captured by the two terms $\dfrac{t^{\lambda_1}-1}{\lambda_1}$ and $\dfrac{t^{\lambda_2}-1}{\lambda_2}$.

This general formulation allows ε_{ijk}, ϑ_{jk}, *and* θ_k to be functions of time. By exponentiating the term in brackets, equation (4) ensures that the hazard function is positive as required since it is a conditional density function. From the multilevel survival formulation in (4), the survivor function at time *t* is

$$S_{ijk}(t_{ijk};\varepsilon_{ijk};\vartheta_{jk};\theta_k) =$$
$$\exp\left\{ -\int_0^{t_{ijk}} h_{ijk}(u|Z_{ijk}(u_{ijk});X_{jk}(u_{jk});Y_k(u_k);\varepsilon_{ijk};\vartheta_{jk};\theta_k)du \right\}$$

(5)

and the likelihood is more generally:

$$L_{ijk}(\varepsilon_{ijk};\vartheta_{jk};\theta_k) =$$

(6)

$$\begin{cases} S_{ijk}(t_{ijk};\varepsilon_{ijk};\vartheta_{jk};\theta_k) & \text{if the spell is censored at } t; \\ \text{and} & \\ S_{ijk}(t_{ijk}+dt;\varepsilon_{ijk};\vartheta_{jk};\theta_k) - & \\ S(t_{ijk};\varepsilon_{ijk};\vartheta_{jk};\theta_k) & \text{if the event occurred in } (t, t+dt) \end{cases}$$

All the above formulations can be extended to multistate forms. The formulation (3) extended to the multistate multilevel hazard for the transition to state τ ($\tau = 1, 2, 3, ..., \Gamma$) would be

$$f_{ijk}^{\tau}(t_{ijk}^{\tau}; Z_{ijk}^{\tau}; \beta_{ijk}^{\tau}; X_{jk}^{\tau}; \eta_{jk}^{\tau}; Y_k^{\tau}; \xi_k^{\tau} \big| \varepsilon_{ijk}^{\tau}, \vartheta_{jk}^{\tau}, \theta_k^{\tau}) =$$

$$\begin{bmatrix} f_{ijk}^{\tau}(t_{ijk}^{\tau}; Z_{ijk}^{\tau}; \beta_{ijk}^{\tau}) + \\ f_{jk}^{\tau}(t_{jk}^{\tau}; X_{jk}^{\tau}; \eta_{jk}^{\tau}) + \\ f_k^{\tau}(t_k^{\tau}; Y_k^{\tau}; \xi_k^{\tau}) \end{bmatrix} f_{\varepsilon}^{\tau}(\varepsilon_{ijk}^{\tau}) f_{\vartheta}^{\tau}(\vartheta_{jk}^{\tau}) f_{\theta}^{\tau}(\theta_k^{\tau}) \qquad (7)$$

It follows from (4) that the multilevel multistate hazard for the transition to state τ can be parameterized in a general formulation (without level-specific or cross-level interactions) and written as

$$h_{ijk}^{\tau}(t_{ijk}^{\tau}; Z_{ijk}^{\tau}; \beta_{ijk}^{\tau}; X_{jk}^{\tau}; \eta_{jk}^{\tau}; Y_k^{\tau}; \xi_k^{\tau} \big| \varepsilon_{ijk}^{\tau}, \vartheta_{jk}^{\tau}, \theta_k^{\tau}) = \qquad (8)$$

$$\exp\left\{ \begin{bmatrix} \begin{bmatrix} Z_{ijk}^{\tau}(t_{ijk}^{\tau})\beta_{ijk}^{\tau} + X_{jk}^{\tau}(t_{jk}^{\tau})\eta_{jk}^{\tau} + \\ Y_k^{\tau}(t_k^{\tau})\xi_k^{\tau} \end{bmatrix} + \\ \gamma_1^{\tau}\left[\frac{(t^{\lambda_1^{\tau}} - 1)}{\lambda_1^{\tau}}\right] + \gamma_2^{\tau}\left[\frac{(t^{\lambda_2^{\tau}} - 1)}{\lambda_2^{\tau}}\right] + \\ \varepsilon_{ijk}^{\tau}(t_{ijk}^{\tau}) + \vartheta_{jk}^{\tau}(t_{jk}^{\tau}) + \theta_k^{\tau}(t_k^{\tau}) \end{bmatrix} \right\}, \ \lambda_2^{\tau} \succ \lambda_1^{\tau} \geq 0$$

This general parameterization allows for duration dependence, occurrence dependence, state dependence, and level dependence of parameter estimates, including random effects, that is, ε_{ijk}, ϑ_{jk}, and θ_k are functions of both time and state. The covariates are all treated as time-dependent though some of them may be time-constant. This general formulation also contains nearly all of the commonly used hazard functions as special cases.

There are several computer programs for estimating the parameters involved in the above multilevel formulations. The best known programs (and which I am

very familiar with) are: CTM (Yi et al., 1987), aML (Lillard and Panis, 2000), and MlwiN (Rasbash et al., 2000; Goldstein, 1999). These programs support multilevel (multi-process/multistate) estimation of event-duration data and follow a general rule for multilevel data organization: the data are always given at the lowest unit, that is, there is one and only one record per lowest unit. In CTM and aML, non-linear optimization routines are used to obtain maximum likelihood estimates. The MlwiN package has not yet developed such routines for non-linear and survival multilevel models.

Illustration 1: Single Spell Child-survival Model

As a first illustration, we consider a 2-level 2-state single-spell process of infant and child mortality, a non-repeatable event. The two states that a child can occupy during the follow-up are 'alive' and 'dead'. A single spell is involved since a child can exit the 'alive' state only once after a given length of exposure to the risk of death. As mentioned earlier, there are eight measurement occasions of survival status of a child (at birth and subsequently at seven follow-up interviews). I focus on a hazard process in which one or more covariates change values between intervals, but are constant within an interval (that is, one or more covariates are time-varying).

In longitudinal studies of child mortality, where there are several children per woman (family) for instance, one can envision a two-state multilevel formulation. In practical terms, at each duration of exposure d, we can define a response variable for each child i belonging to family j :

$$y_{ij}(d) = \begin{cases} 1 \; if \; i \; has \; \text{exp} erienced \; the \; event \; of \; \text{int} erest \\ 0 \; otherwise \end{cases} \qquad (9)$$

For a simple illustration, suppose we have four families (mothers). The first mother has 2 children, with the first child dying at age 6 months and the second censored at 2 months. The second mother has one child censored at 2 months. The third mother has one child censored at 12 months. The fourth mother has one child dead at 2 months. The response variable is a dichotomy coded 1 if the child dies by survival time t, and 0 otherwise. The data organization for estimating a multilevel model for these data is illustrated in Table 1.

Table 1
Data Organization for a Hierarchically Clustered Longitudinal
Single-Spell Survival Model

Level – 3 (family)	Level – 2 (child)	Level – 1 (survival times)	Response Variable
1	1	1	0
1	1	2	0
1	1	3	0
1	1	4	0
1	1	5	0
1	1	6 = death	1
1	2	1	0
1	2	2 = censored (end of survey)	0
2	1	1	0
2	1	2 = censored (end of survey)	0
3	1	1	0
3	1	2	0
3	1	3	0
3	1	4	0
3	1	5	0
3	1	6	0
3	1	7	0
3	1	8	0
3	1	9	0
3	1	10	0
3	1	11	0
3	1	12 = censored (end of survey)	0
4	1	1	0
4	1	2 = death	1

In the EMIJ mortality data used for the following illustration, there is almost one child per woman – 9774 children and 9592 mothers, such that the mother(family)-level and child-level provide the same information for estimation purposes and thus reduce the number of levels to two from three, namely child-level and wave-level. Moreover, because the number of interviews represents specific survival times for each child, there is a close correspondence between length of exposure to mortality risk and the number of waves. Thus, the wave-specific frailty (or unobserved heterogeneity) is captured by the duration structure of the baseline hazard. In previous works, such a model has been identified only under the assumption of the proportionality of hazards (Elbers and Ridder, 1982; Hoem, 1990), an assumption that cannot be assessed when unobserved variation is present (Rodriguez, 1994). We can relax the assumption of the proportionality of the hazards in order to identify the frailty component by representing the duration structure of the baseline hazard with the most familiar parametric forms such as exponential, Weibull or Gompertz.. This leads to a standard two-state random effects model that permits unobserved child-specific frailty to be correlated across waves or follow-up interviews, which can be estimated by using the algorithm developed by Heckman and Singer (1984) - an approach which has been favoured by recent studies (Petersen, 1995). Kalbfleisch and Prentice (1980), Heckman and Walker (1990) and Goldstein (1999) have shown that in general, a semi-parametric proportional hazards model does not detect some of the relationships that are apparent from fitting parametric models.

In my experience of formulating and estimating multilevel frailty models using CTM and aML, parameter estimates of regressors are not sensitive to misspecification of the baseline duration pattern. Estimation of a two-level modelling with unobserved heterogeneity in CTM is performed using a finite mixture distribution made up of support points and weights. In addition to normally distributed residuals, aML offers other finite mixture distributions as CTM does, although the former accommodates only the univariate asymmetric finite mixtures (no restriction that forces symmetry of support points or weights around zero). This implies that one of the support points (or equivalently, the intercept) is not identified and must be fixed in the estimation procedure. Only CTM and aML support finite mixture distributions and compute appropriate maximum likelihood estimates, whereas MlwiN does not.

Table 2 shows the results of the conventional parametric hazards model (without random effects) as well as those of two-level parametric hazards model (with random effects). These two-level hazard models contain both fixed and random effects. The fixed effects are in the first part of the table and the random effects in the second part. The fixed effects represent the population mean influences on infant and early child mortality specific to the measured covariates. The child-specific (or within child) random effect captured by the unobserved heterogeneity consists of two components, a measurement error plus the actual variability (heterogeneity) in the child's capacity to survive during the follow-up

Table 2
Two-Level Two-State Single-Spell Parametric Hazard Models
of Determinants of Infant and Early Childhood Mortality in Yaounde (Cameroon)

Variables	Exponential Hazards		Weibull Hazards		Gompertz Hazards	
	Single-level modelling	Two-level modelling	Single-level modelling	Two-level modelling	Single-level modelling	Two-level modelling
Part A: Fixed Effects						
Ln(duration)	--	--	-0.48 (0.05)	-0.16 (0.06)	--	--
Duration-dependence term	--	--	--	--	-11.96 (0.82)	-8.31 (0.95)
Intercept	-0.01 (0.27)	-2.42 (0.45)	-1.72 (0.30)	-3.62 (0.64)	-10.95 (0.79)	-10.6 (1.74)
Female Sex	-0.12 (0.08)	-0.12 (0.11)	-0.12 (0.08)	-0.11 (0.11)	-0.12 (0.08)	-0.13 (0.10)
Age at maternity <20 years	0.08 (0.12)	0.06 (0.16)	0.08 (0.12)	0.04 (0.16)	0.08 (0.12)	0.10 (0.15)
Age at maternity >34 years	0.25 (0.16)	0.20 (0.22)	0.24 (0.16)	0.16 (0.21)	0.25 (0.16)	0.15 (0.20)
Birth order 2-3	0.03 (0.12)	0.05 (0.17)	0.04 (0.13)	0.07 (0.16)	0.06 (0.13)	0.13 (0.15)
Birth order 4+	-0.01 (0.14)	0.03 (0.18)	0.01 (0.14)	0.06 (0.18)	0.03 (0.14)	0.14 (0.17)
Mother has some education	-0.15 (0.13)	-0.25 (0.18)	-0.14 (0.13)	-0.22 (0.17)	-0.17 (0.13)	-0.19 (0.16)
Mother is married	-0.17 (0.10)	-0.19 (0.14)	-0.18 (0.10)	-0.18 (0.13)	-0.19 (0.10)	-0.17 (0.12)
Preceding sibling deceased	0.22 (0.16)	0.23 (0.23)	0.21 (0.17)	0.14 (0.22)	0.21 (0.17)	0.12 (0.21)
Medium-level family income	-0.79 (0.11)	-0.92 (0.13)	-0.74 (0.11)	-0.91 (0.14)	-0.73 (0.11)	-0.87 (0.13)
High-level family income	-0.87 (0.17)	-1.04 (0.20)	-0.82 (0.17)	-1.03 (0.20)	-0.82 (0.17)	-0.98 (0.19)
Birth weight <2500 grams	1.55 (0.09)	2.52 (0.17)	1.52 (0.10)	2.34 (0.16)	1.52 (0.10)	2.10 (0.15)
Mother has a salaried job	-0.21 (0.13)	-0.26 (0.17)	-0.20 (0.14)	-0.22 (0.17)	-0.20 (0.14)	-0.23 (0.16)
Douala-related ethnic groups	0.22 (0.14)	0.22 (0.19)	0.23 (0.14)	0.23 (0.18)	0.22 (0.14)	0.24 (0.17)
Pahouin-Beti ethnic groups	0.08 (0.10)	0.19 (0.14)	0.10 (0.11)	0.17 (0.13)	0.11 (0.11)	0.15 (0.13)
'Others' ethnic groups	0.17 (0.18)	0.27 (0.24)	0.19 (0.18)	0.33 (0.24)	0.13 (0.18)	0.32 (0.22)
Child fully breastfed (TVC)	-0.64 (0.11)	-0.68 (0.13)	-0.71 (0.11)	-0.55 (0.12)	-1.09 (0.11)	-0.94 (0.12)
Child partially breastfed (TVC)	-0.45 (0.12)	-0.44 (0.13)	-0.57 (0.12)	-0.43 (0.13)	-0.85 (0.12)	-0.71 (0.13)
Following conception (TVC)	0.59 (0.15)	0.67 (0.15)	0.43 (0.14)	0.45 (0.15)	0.94 (0.15)	0.88 (0.16)
Has modern amenities (TVC)	-0.52 (0.17)	-0.56 (0.21)	-0.45 (0.18)	-0.54 (0.20)	-0.55 (0.17)	-0.57 (0.20)
Child fully immunized (TVC)	-1.46 (0.14)	-0.40 (0.15)	-0.37 (0.14)	-0.49 (0.15)	-0.22 (0.14)	-0.29 (0.15)
Child bedroom crowded (TVC)	0.28 (0.09)	0.22 (0.10)	0.26 (0.09)	0.20 (0.10)	0.31 (0.09)	0.25 (0.10)
Part B: Random Effects						
Child-level unobserved heterogeneity		4.34 (0.25)		4.58 (0.45)		4.32 (1.22)
Negative log-likelihood	929.30	872.25	908.00	881.41	871.10	856.06
Sample size	9774	9774	9774	9774	9774	9774

Notes: All covariates are measured as dummy variables.
  Asymptotic standard errors are in parentheses.
  (TVC): denotes time-varying covariates.

waves. Some of this variability may be genetic (Stern, 1960; Adams et al., 1990), unobservable or unmeasured by the survey.

As seen in Table 2, the general findings are consistent with evidence generated elsewhere: the protective effects of full immunization status, breastfeeding (especially full breastfeeding), possession of modern amenities and increased household income, and the deleterious effects of overcrowding, closely spaced births and low birth weight.

Note that the frailty effects are significantly different from zero. In other words, there are unmeasured child-specific randomly varying risks that affect child survival independently of measured risk factors. Failure to account for such child-specific unmeasured characteristics has several consequences. First, ignoring individual frailty leads to underestimating the standard errors of parameter estimates, creating false impression of precision. An examination of each of the parametric models (exponential, Weibull, Gompertz) under single-level and two-level specifications consistently substantiates the underestimation of all standard errors under the single-level modeling scheme, and confirms the consequences of ignoring random effects in modeling longitudinal survival data. Second, estimates of the baseline hazard duration pattern are biased in downward direction (the best way of understanding this is by imagining a process of constant hazard). Third, estimates of covariates *may* be biased. The comparative results show that while the sign of most parameters are unaffected by randomly varying risk of mortality, their magnitude and level of significance are quite affected when frailty is explicitly modeled.

Illustration 2: Multiple-spell Survival Models

For the second illustration, we consider a 2-level 2-state hazard model with unobserved frailty allowed to be correlated across spells. We use the EMIJ's repeated measurements of women's episodes of illness over the first two years following childbirth. Repeated events experienced by the same woman provide a useful way of introducing the multiple spell formulation of hazard models with correlation structure. Since the occurrence of one episode of illness does not remove a woman from the risk of experiencing another episode of illness, we have a counting (failure-time) process. A representation that takes full advantage of the prospective nature of the data is to model the episodes of illness over the entire follow-up period. Time of exposure is defined here as chronological survival time elapsed since the onset of the process at the time of childbirth. The multilevel correlation structure is that of episodes that vary and are correlated within each woman.

In longitudinal studies of maternal morbidity where there are several (wave-specific) episodes of illness per woman, we can envision a two-state multilevel formulation with the data organization as follows. At each duration *d* of

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exposure since delivery, we define a response variable for each woman j (j=1,2, …,N) with i episodes of illness (i=1,2, … n_j):

$$y_{ij}(d) = \begin{cases} 1 & \text{if } j \text{ has experienced an episode} \\ 0 & \text{otherwise} \end{cases} \qquad (10)$$

Suppose there are five women in a sample. The first woman is observed for eight survival times and has two episodes, the first episode at two months and the second at six months postpartum. The second woman has been under observation for two months, with one episode at 2 months. The third has been followed up for 12 months, with one episode at eight months. The fourth has been a sample member for three months, with one episode in the first month. The fifth woman has been in observation for 4 months without being sick. The response variable is a dichotomy coded 1 if the woman experienced an illness, and 0 otherwise. The data organization for estimating a multilevel frailty model for these data is illustrated in Table 3.

When subjects are measured repeatedly in terms of recurrent events, use of survival models that assume independence of observations is problematic since observations from the same subject are usually correlated. In the single-spell case, we had to make an assumption about individual frailty or the correlation structure of observations. In the multiple-spell case, no such assumption is needed since the data at hand has information on multiple spells for each woman, therefore specifying the correlation structure that permits woman-specific frailty across spells. Indeed, an important implication of stochastic variation at multiple levels is that repeated outcomes may not be independent, justifying the recourse to frailty models (Stiratelli et al., 1984; Vaupel, 1990; Jones, 1993). More generally, there may be multiple sources of stochastic variation, often corresponding to nested levels (Lillard and Panis, 2000).

A woman's health history is assumed to evolve from childbirth to censored time. In this study, overall morbidity is measured, without considering cause-specific morbidity. Hence, a natural extension of this application is to model multiple episodes of illness of different types, which provides a general framework for multilevel multistate hazard models.

The estimation of the model for this illustration will be done under the assumption that the morbidity function can be well represented by a Weibull hazard model. The Weibull model is used because: 1) The level of women's general morbidity decreases monotonically over the first two years of postpartum. 2) With appropriate choice of parameters, the Weibull distribution has been shown to describe adequately any bio-demographic phenomenon that declines with age (or length of exposure to the risk of experiencing the outcome) - a negative slope (Gross and Clark, 1975).

Table 3
Data Format for a Hierarchically Clustered Longitudinal
Multiple-Spell Survival Model

Level – 3 (woman)	Level – 2 (spell)	Level – 1 (survival times)	Response Variable
1	1	1	0
1	1	2	1
1	2	3	0
1	2	4	0
1	2	5	0
1	2	6	1
1	3	7	0
1	3	8 = censored (end of survey)	0
2	1	1	0
2	1	2 = censored (end of survey)	1
3	1	1	0
3	1	2	0
3	1	3	0
3	1	4	0
3	1	5	0
3	1	6	0
3	1	7	0
3	1	8	1
3	2	9	0
3	2	10	0
3	2	11	0
3	2	12 = censored (end of survey)	0
4	1	1	1
4	2	2	0
4	2	3 = censored (end of survey)	0
5	1	1	0
5	1	2	0
5	1	3	0
5	1	4	0

In the illustration, a 2-level Weibull hazard model with nested frailty effects is fitted to the maternal health data, by incorporating a heterogeneity component using the Heckman-Singer procedure as in the previous illustration. As regards distributional assumptions, models of repeated measures data have usually assumed that the errors have Gaussian distributions, while other studies of frailty models have used log-gamma or gamma distributions which lead to a closed form solution. These assumptions are often strong and there has been much work in recent years on models with non-Gaussian distributions of longitudinal data especially in the context of serial observations with binary response (Stiratelli et al., 1984; Rodriguez, 1994; Kuate-Defo, 1998). Although the closed-form solution is mathematically appealing, the mixture of distributions allows consideration of multiple random effects as well as various distributional forms for the random effects., including normally-distributed random effects. I use a mixture distribution to numerically integrate the distribution of random effects.

Sensitivity analysis

One of the most serious problems in prospective surveys is the selective loss to follow-up. The extent to which these losses may create bias depends on the nature of the mechanisms engendering the loss. If the reason that a woman is lost to follow-up is related to her health status, then the analysis will be biased unless losses are properly accounted for (Lillard and Panis, 1998). In the illustration at hand, three mechanisms are relevant. The first involves losses attributable to factors unrelated to the phenomenon under study (women's health) and hence constitutes a nuisance that does not threaten statistical inferences. The second concerns losses ascribed to factors related to the phenomenon under investigation; if these factors are well measured and taken into account in the models, the bias can be minimized or eliminated. The third mechanism corresponds to losses that are triggered by the occurrence of the outcome of interest; this is less tractable and requires special estimation procedures. If this mechanism operates, a woman is exposed to two types of censoring. The first type is non-informative and independent censoring. The second type is censoring that occurs with some probability as a result of ill-health of the woman. In this case, a random mechanism can be posited that assigns women into two groups: those that are identified as unhealthy and those that are confused with censored cases. The likelihood of the sample will then be composed of the product of three components: the likelihood for true censored cases, the likelihood for those identified unhealthy, and the likelihood of those unhealthy women who are confused with censored cases. More formally, conditional on random effects ϑ_j and ε_{ij}, a general formulation of the likelihood for a case j with i episodes of illnesses is given by:

$$L_{ij}(\varepsilon_{ij}; \vartheta_j) =$$

$$\left[h_{ij}(t_{ij} | Z_{ij}(t_{ij}); X_j(t_j); \varepsilon_{ij}; \vartheta_j) \rho_{ij} \right]^{C_{1_{ij}}} \tag{11}$$

$$\left[h_{ij}(t_{ij} | Z_{ij}(t_{ij}); X_j(t_j); \varepsilon_{ij}; \vartheta_j)(1 - \rho_{ij}) \right]^{C_{2_{ij}}} e^{(-\int_0^t h(u)\,du)}$$

where $C_{1_{ij}}$ is 1 if the *j*-th woman under study belongs to the class of well identified unhealthy women, $C_{2_{ij}}$ is 1 if that *j*-th woman belongs to the class of unhealthy women confused with censored cases, and ρ_{ij} is the probability that the random procedure assigns unhealthy women to the class of unhealthy women. The practical problem faced here is the lack of observation on which women belong to which class. Thus, the likelihood is undefined, even if assuming that ρ_{ij} is unity restores the tractability of the problem, yet under the assumption of independent and non-informative censoring.

I suggest estimating the model parameters by formulating two hypothetical constructs within which true estimated effects must lie. First, I construct a multilevel event-duration model under the assumption of independent censoring between dropouts and "normal" end of follow-up interviews, that is, due to child's death or end of follow-up period (Model 1). Second, I estimate another multilevel model assuming that all dropouts were healthy (Model 2) or unhealthy (Model 3). These limits give us an interval that contains the true effect. When the data provide good estimates of the true effect, the interval will be relatively narrow and there will be little uncertainty about its true size. Conversely, when the data provide poor estimates, the interval will be relatively wide and there will be much uncertainty. With longitudinal studies, it is more appropriate to provide an interval estimate than only a point estimate when uncertainty about the proper model specification exists. In the face of such uncertainty, a single point estimate is simply misleading in its apparent precision (Little and Schenker, 1995; Murray and Findlay, 1988).

Based on the above argument, Table 4 presents the results on the determinants of Yaounde women's health status for the three models. According to Model 1, women who are employed, have clean water at home, women whose partner is employed, and younger women are significantly less likely to be unhealthy over time. In contrast, women from the Pahouin-Beti ethnic groups, with poor obstetric history, who are older than 34 years, and who have more than three children, are more likely be unhealthy following childbirth.

We also assess the sensitivity of estimated parameters to various assumptions about sample attrition through dropouts inherent in observational studies. In doing so, the illustration points to the usefulness of multilevel analysis for correlated survival data, particularly in accounting for variability attributable to

Table 4
Two-level Two-state Multiple-spell Weibull Hazard Models
of Determinants of Women's Health in the Presence of Sample-Attrition
through Dropouts in Yaounde (Cameroon)

Variables	Simulations about sample-attrition through dropouts:		
	Model 1: Dropout process is governed by a random mechanism throughout the follow-up period	**Model 2:** All dropouts are healthy	**Model 3:** All dropouts are unhealthy
Part A: Fixed Effects			
Ln(duration)	-0.15 (0.01)	-0.28 (0.01)	-0.56 (0.02)
Intercept	-2.84 (0.46)	-3.32 (0.21)	-1.37 (0.26)
Woman is unmarried	0.04 (0.08)	0.05 (0.06)	-0.27 (0.08)
Woman has some education	0.07 (0.05)	0.09 (0.03)	-0.07 (0.06)
Woman has a salaried job	-0.18 (0.04)	-0.14 (0.03)	-0.16 (0.05)
Household has clean water (TVC)	-0.10 (0.04)	-0.10 (0.03)	-0.07 (0.07)
Household has electricity (TVC)	-0.01 (0.04)	-0.01 (0.03)	-0.20 (0.06)
Woman belongs to Pahouin-Beti ethnic groups	0.21 (0.05)	0.18 (0.04)	-0.27 (0.05)
Woman belongs to Douala-related ethnic groups	0.04 (0.06)	0.05 (0.04)	-0.03 (0.07)
Woman belongs to Bamileke-related ethnic groups	0.08 (0.05)	0.10 (0.04)	-0.22 (0.05)
Woman's partner has some education	0.07 (0.04)	0.07 (0.03)	-0.04 (0.05)
Woman's partner has a salaried job	-0.03 (0.07)	-0.02 (0.05)	-0.53 (0.07)
Woman has a history of stillbirths	0.10 (0.07)	0.07 (0.05)	-0.06 (0.09)
Woman has a history of abortions	0.08 (0.04)	0.06 (0.03)	-0.04 (0.05)
Woman's age at the index maternity <20 years	-0.17 (0.05)	-0.17 (0.04)	0.12 (0.05)
Woman's age at the index maternity is >34 years	0.15 (0.05)	0.15 (0.04)	-0.10 (0.08)
Woman's parity is 2-3	0.08 (0.05)	0.07 (0.04)	-0.10 (0.05)
Woman's parity is 4+	0.26 (0.05)	0.27 (0.04)	-0.38 (0.06)
Mother has received no prenatal care	0.14 (0.09)	0.17 (0.07)	-0.19 (0.10)
Mother is breastfeeding (TVC)	-0.09 (0.24)	0.01 (0.19)	-0.15 (0.21)
Part B: Random Effects			
Multiple-spell clustering effects	-1.35 (0.06)	-1.54 (0.03)	-0.96 (0.34)
Negative log-likelihood	29 377.27	29 798.73	15 153.30
Sample size	9 592	9 592	9 592

Notes: All covariates are measured as dummy variables.
 Asymptotic standard errors are in parentheses.
 (TVC): denotes time-varying covariates.

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data clustering. The estimate of random effects shows the degree of data clustering in longitudinal surveys.

For models 2 and 3, most results are in the expected directions given the literature on women's reproductive health (Institute of Medicine, 1996). These Models also assess the impact of distributional assumptions about sample attrition through dropouts in longitudinal surveys on parameter estimates of multilevel hazard models. First, a comparison of the three models shows that the covariate estimates of Model 1 are indeed contained within the interval delimited by the upper and lower values obtained from Models 2 and 3. For all the three models, women with paid employment and women with modern amenities in the home, are less likely to be unhealthy compared to other women. Second, the estimates in Models 1 and 2 are quite close (both in terms of significance level and size of the estimates), unlike estimates from Model 3 which stand rather sharply apart. The estimated random parameters are large in all the models and significantly different from zero. This result confirms the conjecture that the multiple-spell data are highly correlated within women in the presence of unobserved woman-specific heterogeneity.

Multilevel Discrete-time Hazard Model

In practice, a discrete-time model specification is useful because of the problem of ties. In continuous-time models, it is usually assumed that each failure time is associated with a single failure. For lack of accuracy in measurement, many failures will often be recorded to occur at the same time or the time data may also be deliberately grouped. In such cases, instead of defining the risks as in models formulated so far, we can define the odds of failure as if they followed a multilevel logistic pattern for an age interval α, conditional on child-specific (ε_{ijk}), family-specific (ϑ_{jk}) and community-specific (θ_k) random effects assumed to operate multiplicatively on the baseline hazard. In a study of infant mortality, for example,

$$
\frac{q_{ijk}(\alpha)}{1-q_{ijk}(\alpha)} =
$$

$$
\exp\left\{-\left(\left[\beta_{ijk} * Z_{ijk}(\alpha)\right]\left[\eta_{jk} * X_{jk}(\alpha)\right]\left[\xi_k * Y_k(\alpha)\right]\right)\varepsilon_{ijk}\vartheta_{jk}\theta_k\right\}
$$

$$(12)$$

where $q_{ijk}(\alpha)$ is the probability of dying during the first year of life in the interval α for the *i*-th child born to the *j*-th mother (family/couple) residing in the *k*-th community (district or area of residence). As mentioned earlier, with the

DHS data, we consider only children born within the last three years preceding the survey. It is assumed that the place of residence and family in which children are born within the last three years preceding the survey have not changed within that three-year period.

Including a unit variable in the vector Z leads to a model in which the odds are proportional to each other. The estimate of the constant is an estimate of the baseline for the odds. Thus, the parameters that one retrieves do not correspond to estimates of influences on the hazards. Nonetheless, the discrepancies are minor when the intervals are small or when the underlying risks are low.

The above formulation has the advantage of being estimated with standard multilevel programs that have been designed to perform analysis with discrete data. The estimation is done jointly across time intervals, and this feature allows testing of multilevel survival models that are more general than the ones included in the proportional hazards model. In fact, one can test the hypothesis that the causal process may be different across time intervals to the extent that the values of covariates or of the estimated parameters differ by time interval (violation of the proportionality assumption).

It is also worth noting that most computer programs used for estimating a logistic hazard model do not provide correct estimates of the baseline odds, because the procedures usually assume that if the individuals are censored within an interval, they are censored right before the end of the interval. Other estimation procedures for discrete versions of a proportional hazards model suggested by, for example, Cox (1972) and Kalbfleisch and Prentice (1980) unfortunately involve likelihood functions that cannot be easily maximized with standard software. In order to produce more accurate estimates, we can incorporate a series of dummies capturing the duration structure of the hazard function during the first year of life while monitoring closely the full survival time of both censored and uncensored cases, following the well-known age-specific structure of infant mortality (Pressat, 1985).

With these methodological precautions taken into account, we have survival times grouped into predetermined categories (like 0-1, 1-3, 4-7, and 8-11 months in the application below) and specify the survivor function at time interval α as S_α. Denoting the corresponding density by $g(\alpha)$ and hazard by $h(\alpha)$, we have

$$g_\alpha = S_{\alpha-1} - S_\alpha, \qquad h_\alpha = \frac{g_\alpha}{S_{\alpha-1}},$$

$$S_\alpha = \prod_{\alpha=1}^{\Omega} \left(1 - h_\alpha\right), \quad with \ \ S_0 = 1$$

(13)

which can be used to estimate the survivor function from the set of estimated hazards. For the three-level logit-hazard model formulated here, the expected hazard is given by

$$
\begin{cases}
h_{ijk}(t_{ijk}|Z_{ijk}(t_{ijk}); X_{jk}(t_{jk}); Y_k(t_k); \varepsilon_{ijk}; \vartheta_{jk}; \theta_k) \\
= 1 - \exp\left\{-e^{\alpha_{t_{ijk}} + Z_{ijk}(t_{ijk})\beta_{ijk} + X_{jk}(t_{jk})\eta_{jk} + Y_k(t_k)\xi_k + \varepsilon_{ijk}(t_{ijk}) + \vartheta_{jk}(t_{jk}) + \theta_k(t_k)}\right\} \\
and \\
\log\left(-\log\left[1 - h_{ijk}(t_{ijk}|Z_{ijk}(t_{ijk}); X_{jk}(t_{jk}); Y_k(t_k); \varepsilon_{ijk}; \vartheta_{jk}; \theta_k)\right]\right) \\
= \alpha_{t_{ijk}} + Z_{ijk}(t_{ijk})\beta_{ijk} + X_{jk}(t_{jk})\eta_{jk} + \\
Y_k(t_k)\xi_k + \varepsilon_{ijk}(t_{ijk}) + \vartheta_{jk}(t_{jk}) + \theta_k(t_k)
\end{cases} \tag{14}
$$

where the $\alpha_{t_{ijk}}$ are the age effects to be estimated, one for each time interval.

A frequent question in epidemiological studies is whether change in some variable during the course of the study varies according to its value at the beginning of the study. It has been recognized even from the 1950s that the association between change in a variable and its initial value is complicated by the presence of measurement errors and intrinsic within-subject variability (Garside, 1956; Oldham, 1962; Lindsey, 1999). Because of the presence of such variations, children whose initial risks of mortality are high (e.g., measured by health conditions at birth) will on average be found to have lower mortality risks at the end of the observation period even in the absence of any treatment. This artificial reduction, an example of 'regression to the mean', will be greatest in those with the highest recorded values, and will therefore induce a spurious association between change and initial value. Child-specific random effects should therefore be used to capture these unmeasured risks and other unobservables at the child-level.

Parameters in (14) can be estimated using the MlWin package, which employs an Iterative Generalized Least Squares (IGLS) procedure or the second order predictive quasi-likelihood (PQL) approximation that have been shown to be both efficient and to provide greater accuracy of estimates of both the fixed and random parameters in multilevel models for binary response data in general (Rodriguez and Goldman, 1995; Yang et al., 2000; Goldstein, 1999). The general strategy for the data arrangement is similar to the one presented in Table 3 above, with a level-4 unit being the district, the level-3 unit being the families, level-2 unit being the children and level-1 unit being the survival times.

The results from the fitted multilevel discrete-time failure-time models are presented in Table 5 including the fixed and random effects for each geographic region in Africa. In all these models, the estimated duration effects are properly signed and follow a declining mortality schedule consistent with expected declining mortality risks as the child ages. Notwithstanding regional differences

Table 5
Multilevel Discrete-Time Hazards Models of Infant Mortality
in Africa by Geographic Regions

Variables	NORTH	CENTRAL	EAST & SOUTHERN	WEST
Part A: Fixed Effects				
Duration 1-3 months (baseline duration is 0-1)	-0.24 (0.10)	-0.51 (0.14)	0.06 (0.14)	-0.24 (0.10)
Duration 4-7 months (baseline duration is 0-1)	-1.06 (0.13)	-1.55 (0.21)	-0.95 (0.17)	-1.05 (0.13)
Duration 8-11 months (baseline duration is 0-1)	-1.88 (0.16)	-2.34 (0.24)	-1.67 (0.19)	-1.86 (0.16)
Intercept	-3.44 (0.09)	-6.83 (2.89)	-3.52 (0.21)	-3.34 (0.09)
Preceding sibling deceased	0.21 (0.10)	0.36 (0.16)	0.49 (0.12)	0.20 (0.10)
before the conception of the index child				
Index child is breastfed (TVC)	-0.10 (0.08)	-0.60 (0.13)	0.45 (0.08)	-0.03 (0.08)
Index child is followed by a conception (TVC)	1.15 (0.12)	1.29 (0.19)	1.01 (0.12)	1.14 (0.12)
Index child is fully immunized for its age (TVC)	-1.36 (0.11)	-1.89 (0.24)	-1.09 (0.08)	-1.34 (0.11)
Part B: Random Effects				
At the district-level (within country)				
(between-district variance)	0.05 (0.07)	0	0.52 (0.08)	0.03 (0.06)
(between-district variance in the deleterious effects of preceding sibling' death)	0.12 (0.42)		0.67 (0.28)	0.33 (0.12)
(covariance between districts and preceding sibling's death)	0.28 (0.13)		-0.28 (01.2)	0.14 (0.41)
At the family-level (within district)				
(between-family variance)	0	0	0	0
At the child-level (within family)				
(between-children variance)	1.15 (0.01)	1.31 (0.01)	1.00 (0.01)	1.15 (0.01)
Hierarchical organization of the data				
Number of districts	105	150	448	600
Number of families	3412	4 922	20864	25554
Number of children	16049	21743	95327	122730

Notes:

1. North Africa comprises only Morocco, the only country of the region having accessible, pertinent and comparable data
   for this study. Central Africa comprises only Cameroon and Central African Republic. East and Southern Africa includes
   Kenya, Malawi, Uganda, Tanzania, Madagascar and Zimbabwe. West Africa includes Cote d'Ivoire, Burkina Faso,
   Mali, Senegal, Niger and Nigeria. The estimated effects of country-dummy variables are not shown.
2. All covariates are measured as dummy variables. Asymptotic standard errors are in parentheses.
3. TVC denotes time-varying covariates.

within the continent found in Table 5, there are significant deleterious effects of death of the preceding child and the short next birth interval on the index child's survival. In contrast, breastfeeding and full immunization status provide protection to children during infancy (except for Southern Africa). Compared to the models without random effects (not shown here), those that incorporate random effects show differences in the estimates in various degrees by region, even though they remain for the most part quite robust.

The importance of random effects varies by region. Observations show strong correlation so that the between-children variance is significant in all models. District-level random effects are non negligible as well in all regions, but much of the random variation in child mortality risks at the district level seems to be attributable to differential access and utilisation of immunization services (after comparison with step-wise models that are not shown here). In particular, in Central Africa, the between-district variance is eliminated when the immunization variable is taken into account in the model. This suggests that some randomly varying mortality risk at the district level in Central Africa is due to differences in the extent to which children have received all their immunizations for their age.

It is also important to underline that the variable 'survival status of the preceding sibling' has both fixed and random effects (both variance and covariance) that are significantly different from zero in most regions, implying significant child mortality concentration within certain families and districts (communities) in Africa. Within districts, there are generally no family-level random variations. Overall, the fixed and random parts of the three-level frailty model presented here show significant and net random within-family and between-district effects on child survival.

Conclusions

In this paper, I have shown how conventional hazard models can be extended to handle multilevel data structures. We need to collect longitudinal data that are suited to benefit from the new tools of analysis, which are outpacing most available longitudinal data. Contextual longitudinal studies where observations are fully crossed (over time and context by multiple levels of observation units) and nested within larger clusters appear to be the proper venue. The observations within those clusters tend to be more similar than those in different clusters, and this paper shows how to estimate hazard models that take the clustering into account and model the various random parameters across individuals and groups.

This paper has shown through a few illustrations that individual-level, family-level, community-level and area-level influences have independent effects on mortality and health processes, especially in the case of infant mortality and women's reproductive health after childbirth. It should be admitted, however, multilevel failure-time models can become quite complex and there may be limitations of most computer programs for estimating such complex hierarchically clustered survival models, especially if some or all variables are time-dependent and context-dependent.

References:

Adams J., A. Hermalin, D. Lam and P. Smouse. 1990. *Convergent Issues in Genetics and Demography.* New York: Oxford University Press.

Baltagi B. 1995. *Econometric Analysis of Panel Data.* Chichester: John Wiley & Sons Ltd.

Bryk A.S. and S.W. Raudenbush. 1992. *Hierarchical Linear Models.* New York: Sage Publications.

Choi S.C. and D.M. Stablein. 1988. "Comparing incomplete paired binomial data under non-random mechanisms," *Statistics in Medicine* 7: 929-939.

Clayton D. 1978. "A model for association in bivariate life tables and its application in epidemiological studies of familial tendency in chronic disease incidence," *Biometrika* 65: 141-151.

Cox D.R. 1972. "Regression Models and Life Tables," (with discussion), *Journal of the Royal Statistical Society* 34: 187-220.

Elbers C. and G. Ridder. 1982. "True and spurious duration dependence: the identifiability of the proportional hazards model," *Review of Economic Studies* 49: 403-409.

Goldstein H. 1999. *Multilevel Statistical Models, Internet Edition*. London: Arnold.

Gross A. and Clark V. 1975. *Survival Distributions: Reliability Applications in the Biomedical Sciences.* New York: Wiley.

Halabi S., H. Zurayk, R. Awaida, R. Darwish and B. Saab. 1992. "Reliability and validity of self and proxy reporting of morbidity data: a case study from Beirut, Lebanon," *International Journal of Epidemiology* 21: 607-612.

Heck R.H. and S.L. Thomas. 2000. *An Introduction to Multilevel Modeling Techniques*. New Jersey: Lawrence Erlbaum Associates Publishers.

Heckman J.J. and B. Singer (eds.). 1985. *Longitudinal Analysis of Labor Market Data*. Cambridge: Cambridge University Press.

Heckman J.J. and B. Singer. 1984. "A method for minimizing the impact of distributional assumptions in econometric models for duration data," *Econometrica* 52: 271-320.

Heckman J.J. and Walker J. 1990. "The relationship between wages and income and the timing and spacing of births: evidence from Swedish longitudinal data," *Econometrica* 58: 411-441.

Hoem J. 1990. "Identifiability in hazard models with unobserved heterogeneity: the comparability of two apparently contradictory results," *Theoretical Population Biology* 37: 124-128.

Institute of Medicine. 1996. *In Her Lifetime: Female Morbidity and Mortality in Sub-Saharan Africa*. Washington DC: National Academy Press.

Jones R.H. 1993. *Longitudinal Data with Serial Correlation: A State-Space Approach*. London: Chapman & Hall.

Kalbfleisch D.J. and Prentice R.L. 1980. *The Statistical Analysis of Failure Time Data*. New York: Wiley.

Kuate-Defo, B. 2001. *Méthodes Multi-États et Multi-Niveaux d'Analyse des Biographies.* Montreal : PRONUSTIC Research Laboratory, University of Montreal.

Kuate-Defo, B. 1998. "Fertility Response to Infant and Child Mortality in Africa with Special Reference to Cameroon," in Montgomery M. and B. Cohen (eds.), From Death to Birth: Mortality Decline and Reproductive Change. Washington DC: National Academy Press. Pp. 254-315.

Kuate-Defo, B. 1997. "Effects of Socioeconomic Disadvantage and Women's Status on Women's Health in Cameroon," *Social Science and Medicine* 44: 1023-1042.

Kuate-Defo B. 1992. "Mortality and attrition processes in longitudinal studies in Africa: An appraisal of the IFORD Surveys," *Population Studies* 46: 327-348.

Lillard L. and C. Panis. 2000. *aML Multilevel Multiprocess Statistical Software: User's Guide and Reference Manual, Release 1.0.* Los Angeles: EconWare.

Lillard L. and C. Panis. 1998. "Panel Attrition from the Panel Study of Income Dynamics: Marital Status, Income, and Mortality," *Journal of Human Resources* 33(2): 437-457.

Little R. and N. Schenker. 1995. "Missing data," in: Arminger G., Clogg C. and Sobel M. (eds.), *Handbook of Statistical Modeling for the Social and Behavioral Sciences*. Pp. 39-75.

Mason W.M., G.M. Wong and B. Entwistle. 1983. Contextual analysis through the multilevel linear model, in Leinhardt S. (ed.), *Sociological Methodology*. San Francisco: Jossey-Bass. Pp. 72-103.

Murray G.D. and J.G. Findlay. 1988. "Correcting for the Bias caused by Drop-outs in Hypertension Trials," *Statistics in Medicine* 7: 941-946.

Oldham P.D. 1962. "A Note on the Analysis of Repeated Measurements of the Same Subjects," *Journal of Chronic Diseases* 15: 969-972.

Petersen T. 1995. "Analysis of Event Histories," in: Arminger G., Clogg C. and Sobel M. (eds.), *Handbook of Statistical Modeling for the Social and Behavioral Sciences*. New York: Plenum Press. Pp. 453-517.

Rasbash J., W. Browne, H. Goldstein et al. 2000. *A User's Guide to MlwiN version 2.1*. London: Institute of Education.

Rodriguez G. 1994. "Statistical Issues in the Analysis of Reproductive Histories using Hazard Models," *Annals of the New York Academy of Sciences* 709: 266-279.

Sastry N. 1997. "A nested frailty model for survival data, with an application to the study of child survival in Northeast Brazil," *Journal of the American Statistical Association* 92: 426-435.

Snijders T. and R. Bosker. 1999. *Multilevel Analysis: An Introduction to Basic and Advanced Multilevel Modeling.* Thousand Oaks: SAGE Publications.

Stern C. 1960. *Principles of Human Genetics*. San Francisco : W.H. Freeman and Company.

Stiratelli R., N. Laird and J.W. Ware. 1984. "Random-effects models for serial observations with binary response," *Biometrics* 40: 961-971.

Terman L.M. 1925. *Genetic Studies of Genius. Vol 1 : Mental and Physical Traits of a Thousand of Gifted Children*. Stanford: Stanford University Press.

Vaupel, J. 1990. "Relatives' Risk: Frailty Models of Life History Data," *Theoretical Population Biology* 37: 220-234.

Vaupel J., K. Manton and E. Stallard. 1979. "The impact of heterogeneity in individual frailty on the dynamics of mortality," *Demography* 16: 439-454.

Yang M. and H. Goldstein. 1996. "Multilevel models for longitudinal data," in: Engel U. and Reinecke J. (eds.), *Analysis of Change: Advanced Techniques in Panel Data Analysis*. New York: Walter de Gruyter. Pp. 191-220.

Yi K.M., J. Walker and B. Honore. 1987. *CTM: A User's Guide*. Unpublished manuscript. NORC, University of Chicago.