Approche hiérarchique bayésienne pour la prise en compte d’erreurs de mesure d’exposition complexes dans les études de cohortes professionnelles. Application en épidémiologie des rayonnements ionisants.

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Journées GDR "Statistique et Santé" /SFB, Nantes, 27/09/2018
Context & Objectives

Measurement error characteristics in occupational cohort studies

Simulation studies: the effects of different error structures on statistical inference

Motivating study: Accounting for exposure uncertainty in risk estimation in the French cohort of uranium miners

Conclusion
Exposure measurement error in epidemiological studies

○ Exposure measurement error is
  - ubiquitous
  - one of the most important source of uncertainty

  in epidemiological studies

○ If not or only poorly accounted for, exposure measurement error may cause:
  - bias in risk estimates
  - a distortion of the exposure-risk relationship
  - a loss in power

○ In occupational cohort studies:
  - complex patterns of exposure measurement error
  - attenuation of the exposure-risk relationship for high exposure values
    [HertzPicciotto (1993), Stayner (2003)]

→ Suggested to be explained by the effect of measurement error
Methods to account for measurement error

- Many methods for the correction of measurement error, like regression calibration and simulation extrapolation (SIMEX)
  - Lack of flexibility to account for complex error structures
  - Disjoint steps to estimate true exposure and risk parameters
  - Difficult to obtain confidence intervals

- The Bayesian hierarchical approach
  - Provides a natural way of combining exposure and parameter uncertainty in a coherent framework
  - Flexible approach to describe and account for complex measurement error:
    - Measurement error in time-varying exposures
    - Different types of measurement error simultaneously
    - Heteroscedastic measurement error variances
    - Uncertainty in measurement error variance parameters
  - Allows for the joint estimation of true exposure and risk parameters
  - Allows to integrate external information through the specification of informative prior distributions to obtain more precise estimates
Latent random variables $Z$ describe an *unobserved internal random process* $\Rightarrow$ Out-of-control internal fluctuations (variability)

- Ex: "true" exposure, organ-specific dose, inter-individual variability

Complex models to infer...

Under the Bayesian paradigm: one additional level of modelling: assigning a prior probability distribution to $\theta$ to describe epistemic uncertainty.
Motivating study

The French cohort of uranium miners allows to estimate the health effects associated with radon exposure.

- Radon is a radioactive gas which presents the primary source of background radiation.
- Radon is the second cause of lung cancer [Samet and Eradze, 2000].
The French cohort of uranium miners

5086 uranium miners employed for at least one year at CEA-COGEMA

- deceased: n = 1935
- deceased by lung cancer: n = 211 (11%)
- alive: n = 2924

mean cumulated exposure: 36.61 WLM$^1$ (0.003 - 960.11)

mean follow-up: 35 years (0.1-60)

$^1$Working Level Months (WLM)
Challenge: accounting for exposure measurement error

Measurement error

Obtain a measurement corrected estimate of the lung cancer risk associated with cumulative exposure to Radon
Objectives

Promote the use of the **Bayesian hierarchical approach** to account for exposure measurement error in risk estimates in epidemiology

1. Study the **impact** of different error structures on statistical inference on simulated data
2. Propose different **hierarchical models** to account for exposure uncertainty in risk estimation
3. Implement **Bayesian inference** for the proposed hierarchical models in the French cohort of uranium miners
1 Context & Objectives

2 Measurement error characteristics in occupational cohort studies

3 Simulation studies: the effects of different error structures on statistical inference

4 Motivating study: Accounting for exposure uncertainty in risk estimation in the French cohort of uranium miners

5 Conclusion
Different types of measurement error

Classical measurement error

$$Z_i(t) = X_i(t) \cdot U_i(t)$$

- $U_i(t) \perp X_i(t)$
- $\text{Var}(Z_i(t)) > \text{Var}(X_i(t))$

$Z_i(t)$: observed exposure  
$X_i(t)$: true exposure
**Different types of measurement error**

### Classical measurement error

\[ Z_i(t) = X_i(t) \cdot U_i(t) \]
- \( U_i(t) \perp X_i(t) \)
- \( \text{Var}(Z_i(t)) > \text{Var}(X_i(t)) \)

**Berkson error**

\[ X_{ji}(t) = Z_j(t) \cdot U_{ji}(t) \]
- \( U_i(t) \perp Z(t) \)
- \( \text{Var}(X_{ij}(t)) > \text{Var}(Z(t)) \)
Radon exposure in the French cohort of uranium miners

- Context
- Measurement error characteristics
- The effects of measurement error
- Accounting for exposure uncertainty
- Conclusion

Graph showing annual mean exposure to Radon (WLM) from 1956 to 2000 with data points from 1947 to 1955.
Unshared classical measurement error
Period 2 - Prospective group exposure assessment
Classical measurement error shared between miners

\[ Z_j(t) = \xi_j(t) \cdot U_j(t) \]

- \( Z_j(t) \): measurement
- \( \xi_j(t) \): true mean exposure
- \( U_j(t) \): random variable

Period 2 - Prospective group exposure assessment
Period 2 - Prospective group exposure assessment

\[ X_{j1}(t) \rightarrow \xi_j(t) \rightarrow X_{j2}(t) \]

true mean exposure

Berkson error

\[ Z_j(t): \]

\[ \text{Berkson error} \]

Context Measurement error characteristics The effects of measurement error Accounting for exposure uncertainty Conclusion
Period 2 - Prospective group exposure assessment

**Timepoint 1**

\[ X_{j2}(t_1) \]

\[ \xi_{j1}(t_1) \text{ true mean exposure} \]

\[ X_{j1}(t_1) \]

**Timepoint 2**

\[ X_{j2}(t_2) \]

Berkson error shared within miners

\[ X_{j}(t) = \xi(t) \cdot U_i \]

\[ \xi_{j2}(t_2) \text{ true mean exposure} \]

\[ X_{j1}(t_2) \]
Period 1 - Retrospective group exposure assessment

Timepoint 1

- $X_{j1}(t_1)$
- $X_{j2}(t_1)$
- $X_{j1}(t_2)$
- $X_{j2}(t_2)$

Timepoint 2

- $Z_j$: true mean exposure

$\xi_j$: true mean exposure

- $\xi_j$: true mean exposure
Period 1 - Retrospective group exposure assessment

**Timepoint 1**

\[ X_{j_2}(1) \]

**Timepoint 2**

\[ X_{j_1}(1) \]

\[ Z_j: \text{true mean exposure} \]

Classical measurement error shared both between and within miners

\[ Z_j = \xi_j \cdot U_j \]
Period 1 - Retrospective group exposure assessment

Timepoint 1

\[ X_{j_2}(1) \]

\[ X_{j_1}(1) \]

\[ \xi_j : \text{true mean exposure} \]

Berkson error shared within miners

\[ X_{j_2}(t) = \xi_j \cdot T_j(t) \cdot U_i \]

Timepoint 2

\[ X_{j_2}(2) \]

\[ X_{j_1}(2) \]

Context  Measurement error characteristics  The effects of measurement error  Accounting for exposure uncertainty  Conclusion
Summary of measurement error characteristics in the cohort

Reconstructed retrospectively

1956
Ambient measurements

1983
Individual dosimetry

**Precision of the measurement device:**
- Classical measurement error shared both between and within miners
- Unshared classical measurement error

**Individual worker practices:**
- Berkson error shared within miners
- Berkson error shared within miners

Summary of measurement error characteristics in the cohort

Context  | Measurement error characteristics | The effects of measurement error | Accounting for exposure uncertainty | Conclusion
Summary of measurement error characteristics in the cohort

Precision of the measurement devices:

Classical measurement error: shared between miners

Individual worker practices:

Berkson error: shared within miners

Reconstructed retrospectively

1956
Ambient measurements

1983
Individual dosimetry

Unshared Berkson error

Unshared classical measurement error
Context & Objectives

Measurement error characteristics in occupational cohort studies

Simulation studies: the effects of different error structures on statistical inference

Motivating study: Accounting for exposure uncertainty in risk estimation in the French cohort of uranium miners

Conclusion
The effects of different structures of measurement error

- In simulation studies that assume unshared heteroscedastic error, only a mild attenuation of the exposure-response relationship is observed [Stayner et al. 2003, Steenland et al. 2015]
- Error components that are shared between individuals or for several years of the same individual could have more impact on risk estimation than unshared error components [Kipnis et al. 2001, Simon et al. 2015]

1. Do shared and unshared error components have the same impact on risk estimation?
   ⇒ Simulation study 1

2. Can error structures which are typical for an occupational cohort study cause an attenuation of the exposure-risk relationship?
   ⇒ Simulation study 2
Design of the simulation study

- Use exposure data of the French cohort of uranium miners
Design of the simulation study

- Use exposure data of the French cohort of uranium miners
- Generate
  1. Measurement error assuming one period of exposure with measurement error that is unshared, shared between workers or within workers
  2. Measurement error assuming 3 periods of exposure with changes in the type of measurement error that reflect the exposure conditions of an occupational cohort
Use exposure data of the French cohort of uranium miners

Generate

1. Measurement error assuming one period of exposure with measurement error that is unshared, shared between workers or within workers
2. Measurement error assuming 3 periods of exposure with changes in the type of measurement error that reflect the exposure conditions of an occupational cohort

Compare the effects when data are generated according to the

- Cox model: \( h_i(t) = h_0(t) \cdot \exp(\beta X_{i,cum}(t)) \)
- Excess Hazard Ratio model: \( h_i(t) = h_0(t) \cdot (1 + \beta X_{i,cum}(t)) \)

where \( h_0(t) \) is described by a piecewise-constant model
Design of the simulation study

- Generate
  1. Measurement error assuming one period of exposure with measurement error that is unshared, shared between workers or within workers
  2. Measurement error assuming 3 periods of exposure with changes in the type of measurement error that reflect the exposure conditions of an occupational cohort
- Compare the effects when data are generated according to the
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where \( h_0(t) \) is described by a piecewise-constant model
- Generate failure times as a function of time-varying covariates using a method based on piecewise-exponential variables proposed by [Hendry, 2014]
Design of the simulation study

- Generate
  1. Measurement error assuming **one period of exposure** with measurement error that is unshared, shared between workers or within workers
  2. Measurement error assuming **3 periods of exposure** with changes in the type of measurement error that reflect the exposure conditions of an occupational cohort

- Compare the effects when data are generated according to the
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  where \( h_0(t) \) is described by a piecewise-constant model

- Generate failure times as a function of time-varying covariates using a method based on piecewise-exponential variables proposed by [Hendry, 2014]

- Conduct statistical inference without accounting for measurement error
Simulation study 1: One period of exposure

**Aim:** Compare the impact of shared and unshared error on risk estimation

Berkson error:

\[ X_{ij}(t) = Z_{j}(t) \cdot U_{ij}(t) \]

Classical measurement error:

\[ Z_{ij}(t) = X_{ij}(t) \cdot U_{ij}(t) \]

where:
- \( U_{ij}(t) \perp Z_{j}(t) \) for Berkson error and \( U_{ij}(t) \perp X_{ij}(t) \) for classical error
- \( U_{ij}(t) = U_{j}(t) \) for error shared between workers,
- \( U_{ij}(t) = U_{i} \) for error shared within workers
- \( U_{ij}(t), U_{j}(t), U_{i} \sim \mathcal{LN}(−\frac{\sigma^2}{2}, \sigma) \)
Results: The impact of measurement error on risk estimation

Impact of measurement error for $\beta = 5$ (EHR), $\beta = 2$ (Cox) and $\sigma = 0.9$

<table>
<thead>
<tr>
<th>Type of error</th>
<th>EHR</th>
<th>Cox</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\hat{\beta}$</td>
<td>Relative bias</td>
</tr>
<tr>
<td>unshared</td>
<td>Berkson</td>
<td>4.65</td>
</tr>
<tr>
<td></td>
<td>classical</td>
<td>4.34</td>
</tr>
<tr>
<td>between</td>
<td>Berkson</td>
<td>4.69</td>
</tr>
<tr>
<td></td>
<td>classical</td>
<td>4.44</td>
</tr>
<tr>
<td>within</td>
<td>Berkson</td>
<td>3.98</td>
</tr>
<tr>
<td></td>
<td>classical</td>
<td>3.03</td>
</tr>
<tr>
<td>none</td>
<td></td>
<td>4.90</td>
</tr>
</tbody>
</table>
Aim: Compare the effects of shared and unshared components of error on the
shape of the exposure-risk relationship

- Introduce different types of measurement error for the three exposure periods
- Study the shape of the exposure-response relationship via natural cubic splines
Results: Effects of error structures on the exposure-risk relationship

EHR with $\beta = 5$

Cox with $\beta = 2$
Summary of results on simulated data

- **Simulation study 1:**
  - More bias in risk estimation caused by measurement error shared within workers than shared between workers or unshared

- **Simulation study 2:**
  - The attenuation of the exposure-risk relationship observed in many occupational cohorts could be caused by components of shared exposure uncertainty that occur in a retrospective exposure estimation

⇒ Important to account for measurement error in occupational cohort studies and to distinguish shared and unshared error components
1. Context & Objectives

2. Measurement error characteristics in occupational cohort studies

3. Simulation studies: the effects of different error structures on statistical inference

4. Motivating study: Accounting for exposure uncertainty in risk estimation in the French cohort of uranium miners

5. Conclusion
Challenge: accounting for exposure measurement error

Measurement error

Obtain a measurement corrected estimate of the lung cancer risk associated with cumulative exposure to Radon
Accounting for measurement error in a hierarchical model

In a hierarchical framework, one can account for measurement error combining the following submodels:

- Disease model
- Measurement model
- Exposure model

⇒ Joint modelling of all sub-models using conditional independence assumptions [Richardson and Gilks, 1993]
⇒ Joint estimation of all unknown quantities
The disease model

Modelling failure times

- $Y_i = \min(T_i, C_i)$ is right-censored age at death by lung cancer
- $h_i(t) = h_0(t)(1 + \beta X_i^{cum}(t))$
- Suppose a piecewise constant model for $h_0(t)$ with $\lambda = (\lambda_1, \lambda_2, \lambda_3, \lambda_4)$

Effect modifying variables

- Test the linearity of the exposure-risk relationship via piecewise linear models
Measurement and exposure model: $\mathcal{M}_1$

**The measurement model**

- **Berkson error 1946 -1982:**
  \[ X_i(t) = Z_i(t) \cdot U_i(t) \]
  where \( \mathbb{E}(U_i(t) | Z_i(t)) = 1 \)

- **Classical error after 1983:**
  \[ Z_i(t) = X_i(t) \cdot U_i(t) \]
  where \( \mathbb{E}(U_i(t) | X_i(t)) = 1 \)

- \( U_i(t) \sim \mathcal{LN} \left( -\frac{\sigma^2_{p_i(t)}}{2}, \sigma^2_{p_i(t)} \right) \) [Darby, 1998]


**The exposure model for classical measurement error**

- \( X_{iq} \sim \mathcal{LN} \left( \mu_x, \sigma_x^2 \right) \) [Lubin et al. 1995, Heid et al. 2002]

Accounting for unshared measurement error

\[ \lambda \]
\[ \beta \]
\[ \mu_x \]
\[ \sigma^2_x \]
\[ \sigma^2_{U,B} \]
\[ \sigma^2_{U,2} \]

\[ V_{1i}(t), \ldots, V_{pi}(t) \]

effect modifying variables

\[ Y_i, \delta_i \]

time until death by lung cancer

\[ \chi_{i\text{cum}}(t) \rightarrow \chi_{i\text{q}}(t) \]

true cumulated exposure

\[ \chi_{i\text{q}}(t) \]

true annual exposure

\[ U_{iB}(t) \rightarrow Z_{iB}(t) \rightarrow U_{i5}(t) \]

observed annual exposure (Berkson period)

\[ \sigma^2 x \mu x \sigma^2_{U,B} \sigma^2_{U,2} \]

\[ Z_{i5}(t) \]
Measurement model $M_2$

- **Reconstructed retrospectively**
  - 1956: Ambient measurements
  - 1983: Individual dosimetry

**Precision of the measurement device:**

- Classical measurement error shared both between and within miners
  - Individual worker practices
  - Berkson error shared within miners

- Classical measurement error shared between miners
  - Individual worker practices
  - Berkson error shared within miners

- Unshared classical measurement error

Context | Measurement error characteristics | The effects of measurement error | Accounting for exposure uncertainty | Conclusion
Measurement model $M_2$

**First period 1946 -1955:**
- Berkson error shared within miners:
  - $X_i^1(t) = Z_i^1(t) \cdot U_i^1$
  - $U_i^1 \sim \mathcal{LN} \left( -\frac{\sigma_{U_1}^2}{2}, \sigma_{U_1}^2 \right)$

**Second period 1956 -1982:**
- Berkson error shared within miners:
  - $X_i^2(t) = Z_i^2(t) \cdot U_i^2$
  - $U_i^2 \sim \mathcal{LN} \left( -\frac{\sigma_{U_2}^2}{2}, \sigma_{U_2}^2 \right)$

![Diagram showing the measurement model with observed annual exposure before 1956 and between 1956 and 1982]
Accounting for measurement model $\mathcal{M}_2$

- $\lambda$
- $\beta$
- $V_{1i}(t), \ldots, V_{pi}(t)$
  - effect modifying variables
- $Y_i, \delta_i$
  - time until death by lung cancer
- $X_{i\text{cum}}(t)$
- $X_{iB}(t)$
  - observed annual exposure between 1956 and 1983
- $Z_{iB}(t)$
  - annual exposure after 1983
- $\sigma_{U,B}^2$
- $\sigma_{U,B}^2$
- $U_{iB}$
Measurement model $\mathcal{M}_3$

- **Reconstructed retrospectively**

- **1956**: Ambient measurements
  - **Precision of the measurement device:** Classical measurement error shared between miners
  - **Individual worker practices:** Berkson error shared within miners

- **1983**: Individual dosimetry
  - **Precision of the measurement device:** Classical measurement error shared between miners
  - **Individual worker practices:** Berkson error shared within miners

- **Accounting for exposure uncertainty**
**Measurement model** $M_3$

**First period 1946 -1955:**
- Classical measurement error shared both within and between miners:
  - $Z_j^1 = \xi_j \cdot U_j^1$
  - $U_j^1 \sim \mathcal{LN}\left(-\frac{\sigma_{U^*}^2}{2}, \sigma_{U^*}^2\right)$

- Berksom error shared within miners:
  - $X_{ij}^1(t) = \xi_j \cdot T_{ij}(t) \cdot U_i^1$
  - $U_i^1 \sim \mathcal{LN}\left(-\frac{\sigma_{U^1}^2}{2}, \sigma_{U^1}^2\right)$

- The exposure model:
  - $\xi_j \sim \mathcal{LN}(\mu_{\xi}, \sigma_{\xi})$
Accounting for measurement model $\mathcal{M}_3$

Variables and parameters:
- $\lambda$, $\beta$
- $\sigma_{U^*}^2$
- $\mu_\xi$
- $\sigma_\xi$
- $\sigma_{U,B}^2$
- $V_{1i}(t), \ldots, V_{pi}(t)$
- $X_{i\text{cum}}(t)$
- $Y_i, \delta_i$
- $Z_{i1}(t)$
- $Z_{i2}(t)$
- $Z_{i3}(t)$
- $T_{ij}(t)$
- $X_{ijB}(t)$
- $U_j^1$
- $\xi_j$
- $U_i^B$
- $\nu$.

Equations:
- $\text{time until death by lung cancer}$
- $\text{annual exposure after 1983}$
- $\text{observed annual exposure between 1956 and 1983}$
Prior distributions

- **[\[β\]]**: $β \sim \mathcal{N}(0, 10^4)$
  truncated to guarantee $h_i > 0$

- **[\[λ\]]**: $λ_j \sim \mathcal{G}(\alpha_{0j}, \lambda_{0j})$ for each component $j$, $j = 1, \ldots, 4$ based on the lung cancer mortality in the general French male population between 1968 and 2005

- **[\[μX\]]**: $μ_X \sim \mathcal{N}(-1.44, 10.24)$

- **[\[σ^2_X\]]**: $σ^2_X \sim \mathcal{IG}(1.75, 0.88)$

- **[\[σ_U\]]**: Normal distributions with small variances, centered around ”guess estimates”: $\hat{σ}_{U,B_1} = 0.94$, $\hat{σ}_{U,B_2} = 0.47$, $\hat{σ}_{U,B_3} = 0.42$, $\hat{σ}_{U,B_4} = 0.33$, $\hat{σ}_{U,C_5} = 0.10$
Bayesian inference - Model $\mathcal{M}_3$

Target: Joint posterior distribution of $\theta = (\beta, \lambda, X, \xi, \mu_\xi, \sigma_\xi)$

\[
[\theta | y, Z] \propto [\beta][\lambda] \prod_{i=1}^{n} \left[ y_i \sum_{q=1}^{Q_i} X_{iq} \beta, \lambda \right] \\
\cdot \prod_{i=1}^{n} \prod_{q=1}^{Q_2} \left[ X_{iq}^2 | Z_{iq}^2, \sigma_{U2}^2 \right] \\
\cdot \prod_{i=1}^{n} \prod_{q=1}^{Q_1} \left[ X_{iq}^1 | \xi_j, T_{ij}(t), \sigma_{U1}^2 \right] \\
\cdot [\mu_\xi][\sigma_\xi] \cdot [Z_j | \xi_j, \sigma_{U*}^2] \left[ \xi_j | \mu_\xi, \sigma_\xi \right]
\]

⇒ Adaptive Metropolis-Within-Gibbs algorithm developed and tested in Python

- Complex
- No analytical solution
- High-dimensional
Main difficulty: Updating latent exposures

- In total 49 000 exposure values to update at each iteration
- Create homogeneous groups of miners based on information on:
  - Mine location
  - Type of mine
  - Type of work
- Multiple correspondance analysis $\Rightarrow$ hierarchical clustering
- Result: 239 groups with no more than 150 values to update
- Update $\log(X)$ instead of $X$ in order to respect the constraint $X > 0$ and to improve convergence
### Results when accounting for unshared measurement error ($M_1$)

<table>
<thead>
<tr>
<th>Model</th>
<th>Uncorrected</th>
<th>Corrected</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EHR per 100 WLM</td>
<td>DIC</td>
</tr>
<tr>
<td>Linear</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.87 [0.42;1.50]</td>
<td>5435.08</td>
</tr>
<tr>
<td>Period of exposure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>until 1955</td>
<td>0.31 [-0.01;0.80]</td>
<td>5428.12</td>
</tr>
<tr>
<td>after 1955</td>
<td>1.94 [1.15;2.96]</td>
<td></td>
</tr>
<tr>
<td>Piecewise linear</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$&lt;50$ WLM</td>
<td>2.57 [1.18;4.57]</td>
<td>5429.31</td>
</tr>
<tr>
<td>$\geq50$ WLM</td>
<td>0.30 [-0.15;0.98]</td>
<td></td>
</tr>
</tbody>
</table>
# Results when accounting for shared measurement error ($M_2$ & $M_3$)

| Model          | Uncorrected  | Measurement model $M_2$ | Measurement model $M_3$ | Uncorrected  
|----------------|--------------|------------------------|------------------------|--------------
|                | Full cohort  | Full cohort            | Full cohort            | Post-55      
| EHR per 100 WLM|              |                        |                        |              
| Linear         | 0.87         | 0.99                   | 1.44                   | 2.75         
|                | [0.42;1.50]  | [0.49;1.71]            | [0.66;2.69]            | [1.18;5.32]  
| Piecewise linear | 2.57     | 3.05                   | 2.70                   | 3.20         
| <50 WLM        | [1.18;4.57]  | [1.10;3.54]            | [0.95;5.11]            | [0.80;7.03]  
| ≥50 WLM        | 0.30         | 0.44                   | 1.00                   | 2.82         
|                | [-0.15;0.98] | [-0.13;1.11]           | [-0.04;2.95]           | [0.19;8.14]  |
Results: comparing the posterior distributions for $\beta$

**Posterior distribution for $\beta$**

Uncorrected

Measurement model $\mathcal{M}_2$

Measurement model $\mathcal{M}_3$

- with $\sigma U^* = 0.93$, $\sigma U_1 = 0.93$
- with $\sigma U^* = 0.93$, $\sigma U_1 = 0.39$
- with $\sigma U^* = 0.63$, $\sigma U_1 = 0.63$
Convergence diagnostics: Trace plots

Trace of beta1

Trace of lambda2

Trace of sigma_ksi

Trace of ksi_FOR
Convergence diagnostics: Intra-Chain autocorrelation
When accounting for a combination of shared Berkson and classical measurement error
- We observe a **marked increase** in the risk coefficient estimated in the linear EHR model
- There is a **less pronounced attenuation** of the exposure-risk relationship

When accounting for unshared measurement error, we **do not observe a substantial difference** between corrected and uncorrected risk estimates
1 Context & Objectives

2 Measurement error characteristics in occupational cohort studies

3 Simulation studies: the effects of different error structures on statistical inference

4 Motivating study: Accounting for exposure uncertainty in risk estimation in the French cohort of uranium miners

5 Conclusion
Conclusion

1. The Bayesian hierarchical approach allows to account for complex structures of exposure measurement error in risk estimation.

2. Results on simulated data
   - Measurement error shared within miners can cause more bias in risk estimation than unshared measurement error (for the considered disease models!)
   - Error structures in an occupational cohort study can lead to an attenuation of the exposure-risk relationship.

3. In the French cohort of uranium miners
   - We observe a marked increase in the risk coefficient in the linear EHR model when accounting for shared Berkson and classical measurement error.
Limitations

- It was not possible to adjust for tobacco consumption, exposure to diesel exhaust, arsenic, asbestos and silica quartz.
- The estimated risk coefficients which are corrected for measurement error are sensitive to the chosen values for the measurement error variance parameters.
- The random walk Metropolis-Hastings algorithm is quite inefficient when exploring high-dimensional posterior distributions.
- Use of the DIC for model comparison...
References


Thank you for your attention!
Design of the simulation study: Generate failure times with time-varying covariates

- Hendry (2014) proposes to write the hazard of individual $j$ at time $t$ as
  \[ h_i(t) = h_0(t) \cdot \lambda_i(t) = \left[ \frac{\partial g^{-1}(t)}{\partial t} \right] \cdot \exp(X_i(t) \cdot \beta) \]

- Choose baseline hazard $h_0(t) = \frac{\partial [g^{-1}(t)]}{\partial t}$ with $g(0) = 0$, $g(t) \nearrow$ and $g^{-1}(t)$ differentiable

- Calculate $\{\lambda_{ij}\}_{j=1}^{t}$ for every subject $i$ at time $j$ and generate $V_i$ as truncated piecewise exponential with rates $\lambda_{i1}, \ldots, \lambda_{iJ}$

- Calculate $T_i = g(V_i)$
Regression calibration

**Basic idea:** Replace $X$ by the regression of $X$ on $(Z, W)$ where $W$ are predictors measured without error

**Algorithm:**

- Using replication, validation or instrumental data, estimate the regression of $X$ on $(Z,W)$
- Replace the unobserved $X$ by its estimate and run a standard analysis to obtain parameter estimates
- Adjust the resulting standard errors to account for exposure uncertainty using either the bootstrap or a sandwich method
**Effect of calendar period on baseline hazard**

**Figure:** Hazard of lung cancer mortality in French males for the following periods: 1968-1977 (red), 1978-1987 (orange), 1988-1997 (blue), 1998-2005 (lightblue)

**Resulting priors:**

\[
\begin{align*}
\lambda_1 & \sim \mathcal{G}(23.6, 4.90 \cdot 10^8), \\
\lambda_2 & \sim \mathcal{G}(35.5, 2.58 \cdot 10^7), \\
\lambda_3 & \sim \mathcal{G}(88.1, 1.61 \cdot 10^7), \\
\lambda_4 & \sim \mathcal{G}(29.7, 3.25 \cdot 10^6),
\end{align*}
\]