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Uncertainties in radiation exposure estimates of the German uranium miners cohort

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German uranium miners cohort study

Study cohort

~59,000 male former employees of the Wismut uranium mining company (operating from 1946 to 1989 in the German Democratic Republic)

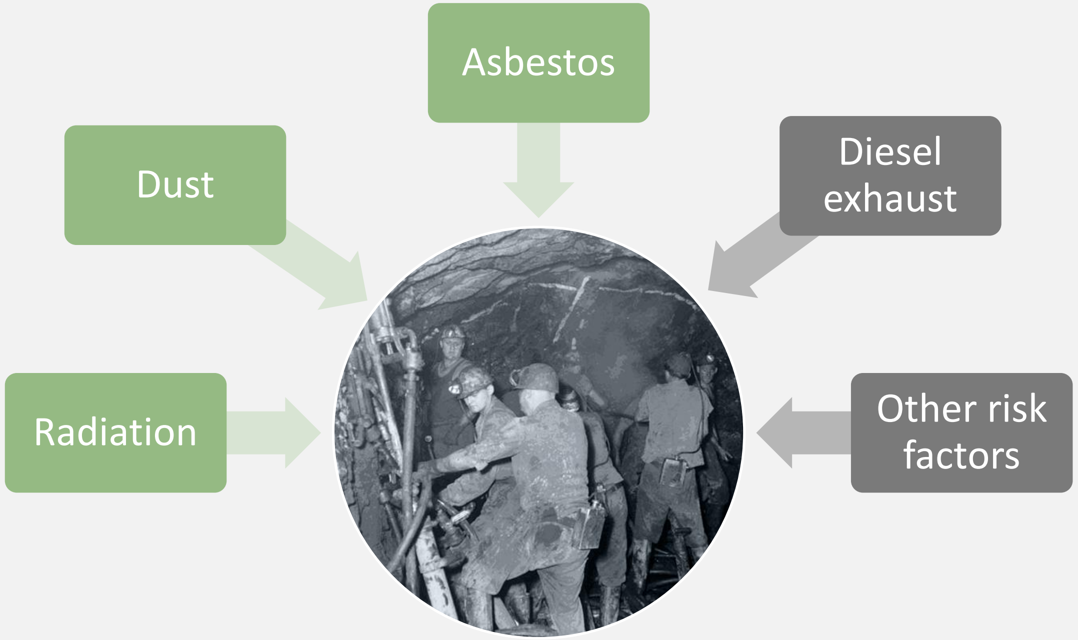
Mortality follow-ups

1998, 2003, 2008, 2013 (every 5 years)

Website

www.bfs.de/wismut-studie

Risk factors



Retrospective assessment of individual radiation exposure based on a job-exposure matrix (JEM) and individual job histories for:

- Radon and its progeny (RDP)
- External gamma radiation
- Long-lived radionuclides
- Silica dust
- Fine dust
- Arsenic dust

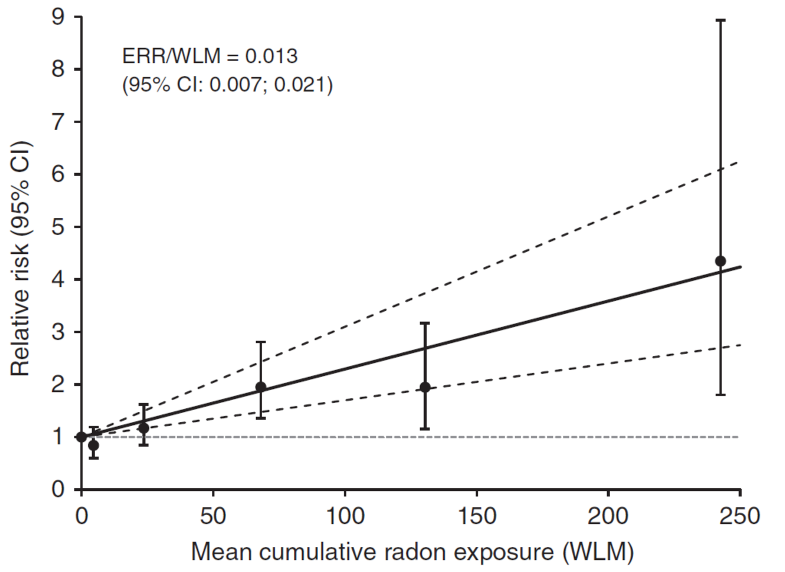
Radon-related health risks

Methods

- Internal Poisson regression
- Baseline stratification by:
  - Attained age
  - Calendar year
- Effect modifier:
  - Exposure rate
  - Time since exposure
  - Attained age

Results: lung cancer

- Former research of the German uranium miners cohort showed a **significant positive association** between exposure to radon and the risk of lung cancer.
- The relative risk of lung cancer decreases with increasing
  - exposure rate,
  - time since exposure and
  - attained age.
- For low radon exposure rates, the relative risk increases linearly with the cumulative radon exposure.



Relative risk for death from lung cancer in relation to cumulative radon exposure in the 1960+ subcohort of miners hired in 1960 or later.

Kreuzer et al. 2015

► Effects of exposure uncertainties on health risk estimation are unclear in the German uranium miners cohort study.

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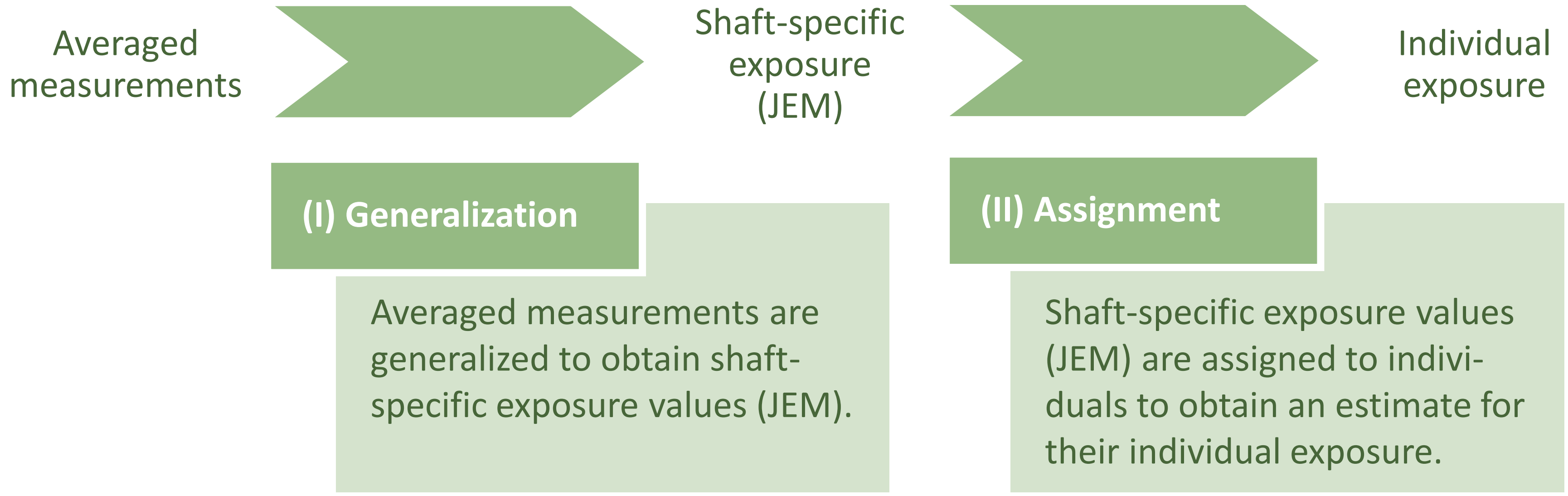
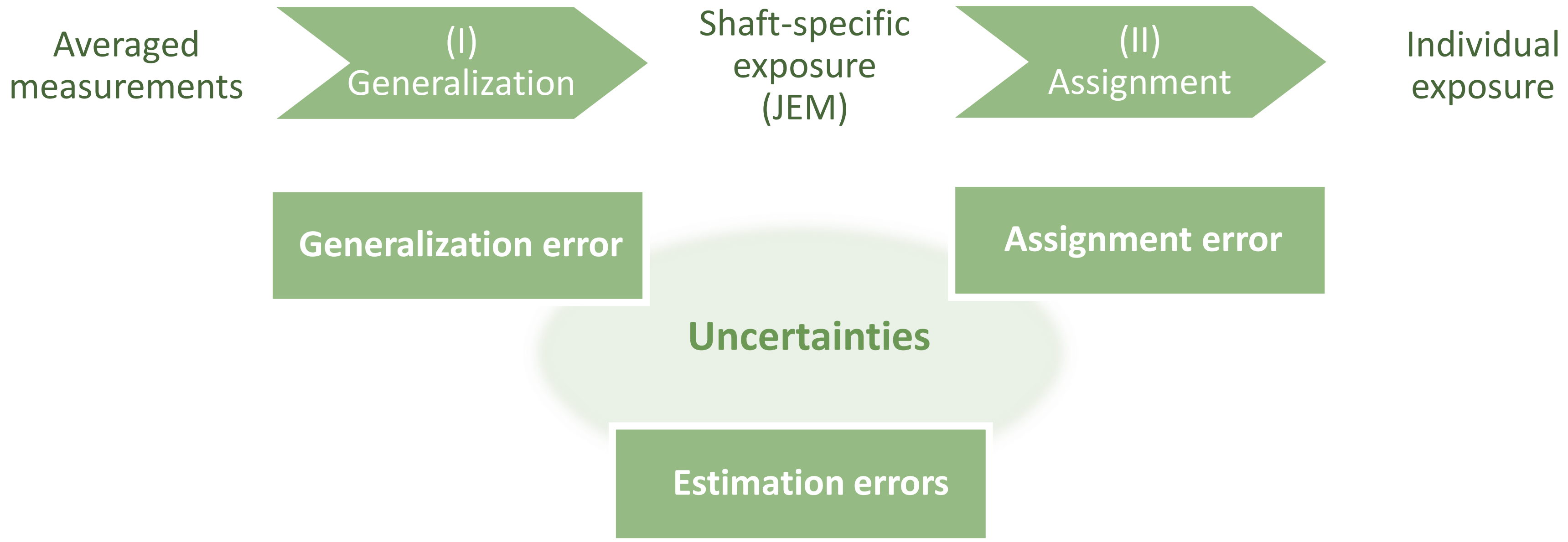
Exposure assessment with a job-exposure matrix (JEM)

- Exposure uncertainties are closely related to the approach of exposure assessment.
- Exposure to radiation and dust is assessed with a **job-exposure matrix (JEM)** in the German uranium miners cohort study.
- Exposure assessment is based on **averaged area exposure measurements**.
- Individual exposure is calculated in **two main steps**:



► This structure in general applies for exposure assessment by the use of a JEM.

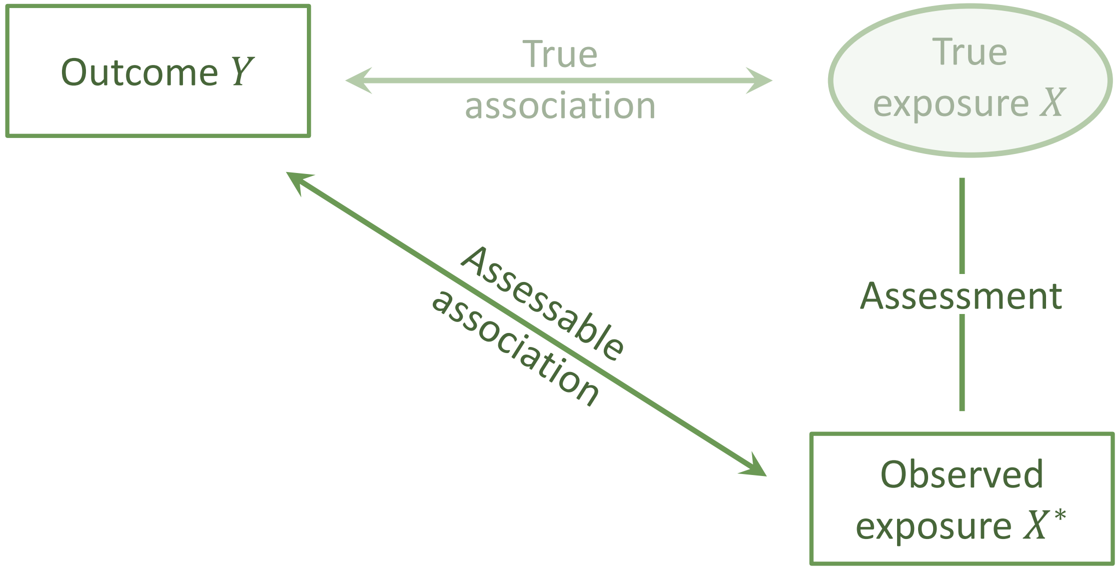
Uncertainties in exposure assessment in the German uranium miners cohort study



- The usage of a JEM involves two main sources of uncertainties: generalization error and assignment error.
- **Generalization error** occurs by using averaged measurements to assess shaft-specific exposure.
- **Assignment error** occurs by using shaft-specific exposure to assess individual exposure.
- In addition, various types of **estimation errors** occur in both steps of exposure assessment.

Health risk analysis with exposure uncertainties

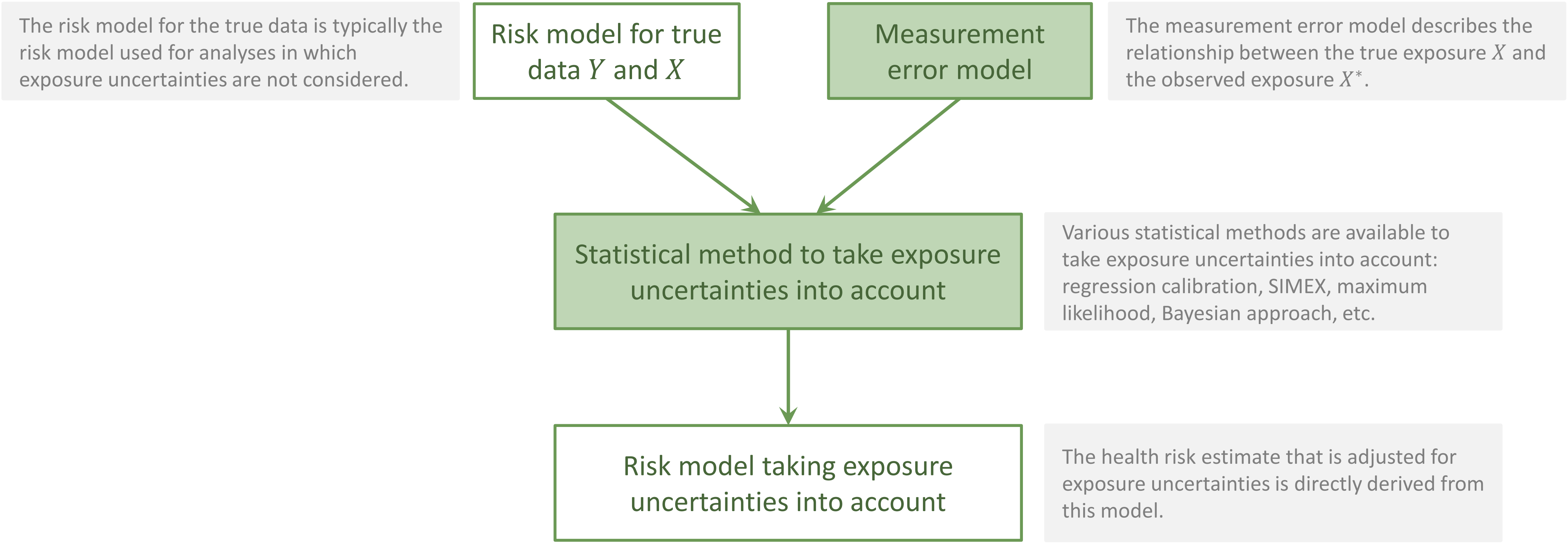
- The aim of health risk analysis is to model the association between health outcome Y and exposure X (**true health model**) in order to estimate the relative risk β_X.
- In the German uranium miners cohort study, we cannot observe the true exposure X, but we assess **exposure values X^* with uncertainties**.
- Actually only the association between health outcome Y and the observed exposure X^* is assessable (**observed health model**) with the naïve relative risk β_{X^*}.



► How can we assess the true association by using exposure data with uncertainties?

Risk model taking exposure uncertainties into account

Three components are required to assess the true association between health outcome and exposure when exposure uncertainties are present:



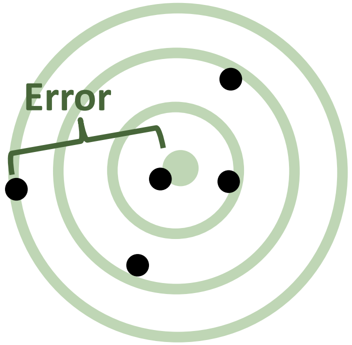
After an overview about the two main types of measurement error on the next slide, details of the measurement error model and statistical method developed for the German uranium miners cohort study are presented on the subsequent slides.

Two types of measurement error:

Classical measurement error

The observed value X^{*C} corresponds to the true value X, which is **overlaid with an error** U^C, i.e. the observed value X^{*C} varies randomly around the true value X.

$$X^{*C} = X + U^C$$



X and U^C are assumed to be independent.

Example:

X: average radon concentration in a uranium mine

X^{*C}: average of radon concentration measurements at different locations in the uranium mine

Berkson error

The observed value X^{*B} represents an **aggregated version** of the true value X, i.e. the true value X varies randomly around the observed value X^{*B}.

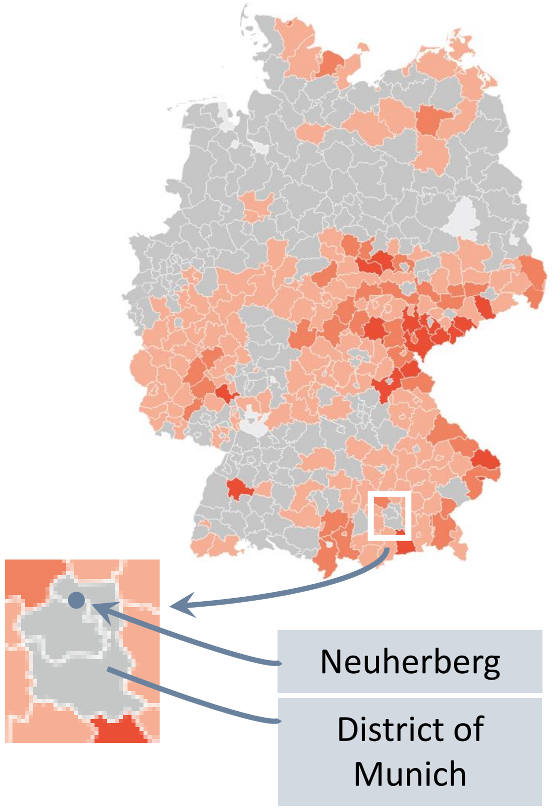
$$X = X^{*B} + U^B$$

X^{*B} and U^B are assumed to be independent.

Example:

X: radon concentration in Neuherberg

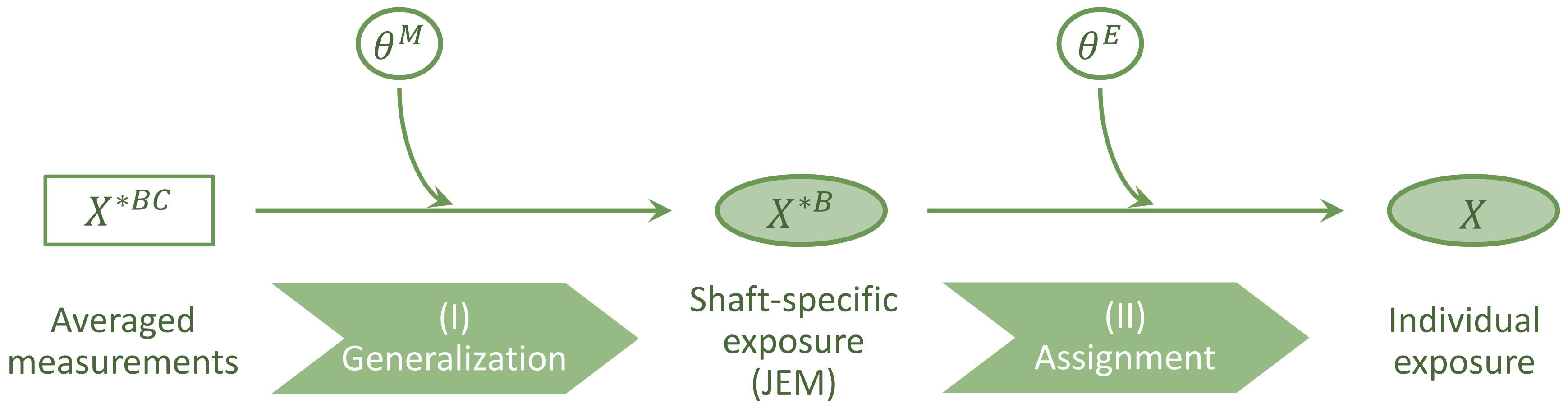
X^{*B}: radon concentration in the district of Munich



Average radon concentrations in dwellings in Germany (as of 2006)
Source: Radon-Handbuch Deutschland (BfS, 2019)

Measurement error model for the German uranium miners cohort study

- The measurement error model for the German uranium miners cohort study is directly derived form the exposure assessment procedure:



- **Individual exposure $\boldsymbol{X}$** is assessed based on Berkson error-prone **shaft-specific exposure $\boldsymbol{X^{*B}}$** and parameter values θ^E.
- Shaft-specific exposure cannot be directly observed. Therefore, X^{*B} is assessed based on classical error-prone **averaged measurements $\boldsymbol{X^{*BC}}$** and parameter values θ^M.
- The measurement error model for individual exposure X in the German uranium miners cohort study is a **complex function of the averaged measurements $\boldsymbol{X^{*BC}}$ and the parameter vectors $\boldsymbol{\theta^M}$ and $\boldsymbol{\theta^E}$**.
- The parameters θ^M and θ^E also include the magnitude of the uncertainties.

Idea of the Bayesian hierarchical approach to account for measurement error

Initial data situation: health outcome Y, exposure with classical measurement error X^{*C} or exposure with Berkson error X^{*B}, and, if any, further precisely measured covariates Z

Aim: estimate the relative risk β_X, which is adjusted for exposure uncertainties

1. Specify a parametric model for every component of the data

Classical measurement error:

$f(Y|X,Z,\cdot)$: health risk model for Y as if X were observable
$f(X^{*C}|X,Z,\cdot)$: measurement model
$f(X|Z,\cdot)$: distribution of X (exposure model)

Berkson error:

$f(Y|X,Z,\cdot)$: health risk model for Y as if X were observable
$f(X|X^{*B},Z,\cdot)$: distribution of X (exposure model)

2. Specify prior distributions for all parameters: $f(\cdot)$

3. Calculate the posterior distribution

Classical measurement error:

$f(\beta_X, X, \cdot \,|Y, X^{*C}, Z, \cdot) \propto f(Y|X,Z,\cdot) f(X^{*C}|X,Z,\cdot) f(X|Z \,\cdot) f(\cdot)$

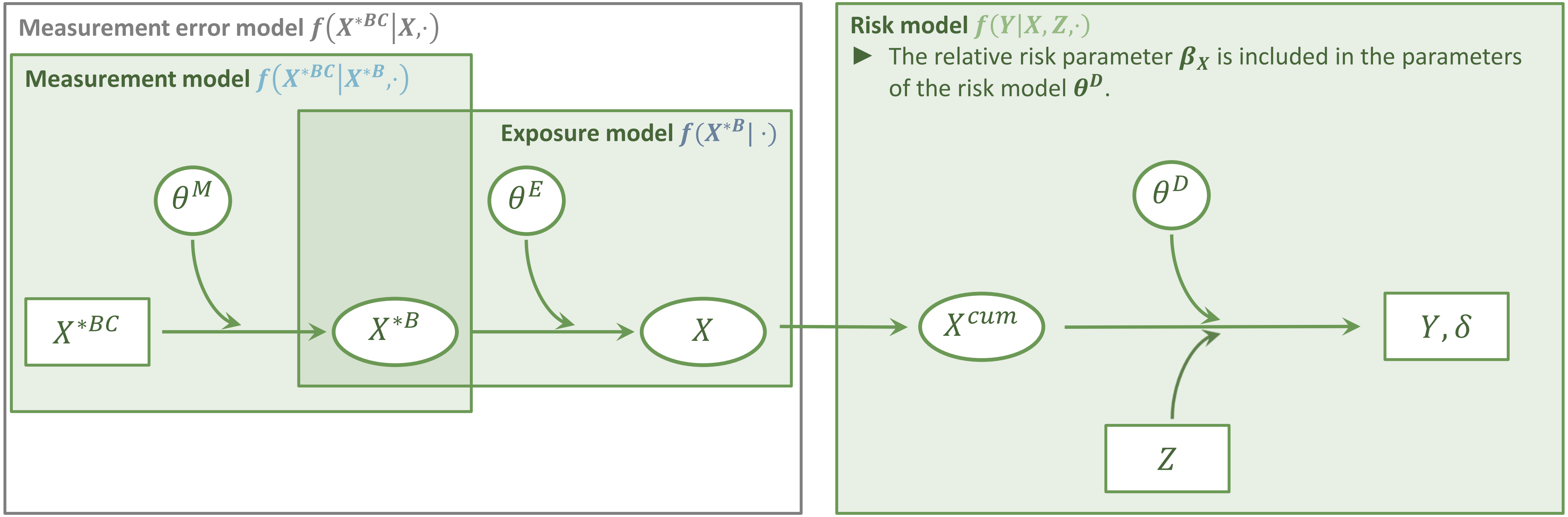
Berkson error:

$f(\beta_X, X, \cdot \,|Y, X^{*B}, Z, \cdot) \propto f(Y|X,Z,\cdot) f(X|X^{*B} \,\cdot) f(\cdot)$

Bayesian hierarchical approach for the German uranium miners cohort study

The **measurement error model** describes the relationship between the true exposure X and the observed exposure X^{*BC} and includes the measurement model and the exposure model.

The risk model describes the relationship between the health outcome Y (including the censoring indicator δ) and the true cumulative time-varying exposure X^{cum}.



The **measurement model** describes the relationship between the observed exposure X^{*BC} and the latent, shaft-specific exposure X^{*B}.

The **exposure model** describes the relationship of the latent exposure X^{*B} and the true exposure X

Summary

- Exposure assessment by a job-exposure matrix involves exposure uncertainties.
- Three major sources of exposure uncertainties were identified in the German uranium miners cohort study:

  Generalization error
  Assignment error
  Estimation error
- A Bayesian hierarchical model was developed to account for exposure uncertainties in the German uranium miners cohort study.

Outlook

- This work represents groundwork towards the estimation of lung cancer risk depending on radon exposure taking measurement error into account.
- An extension of the approach for health risk models with effect-modifying variables is currently considered.

Literature

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