Exposure Prediction and Measurement Error in Air Pollution and Health Studies

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Introduction

- Most epidemiological studies assess associations between air pollutants and a disease outcome by estimating a health effect (e.g. regression parameter such as a relative risk):
  - A complete set of pertinent exposure measurements is typically not available

  ➔Need to use an approach to assign (e.g. predict) exposure
- It is important to account for the quality of the exposure estimates in the health analysis

  ➔*Exposure assessment for epidemiology should be evaluated in the context of the health effect estimation goal*
- Focus of this talk: Exposure measurement error in cohort studies

Typical Approach for Air Pollution Epidemiology Studies

1. Assign (or predict, estimate) exposure as accurately as possible
2. Plug in exposure estimates into the disease model; estimate health effects

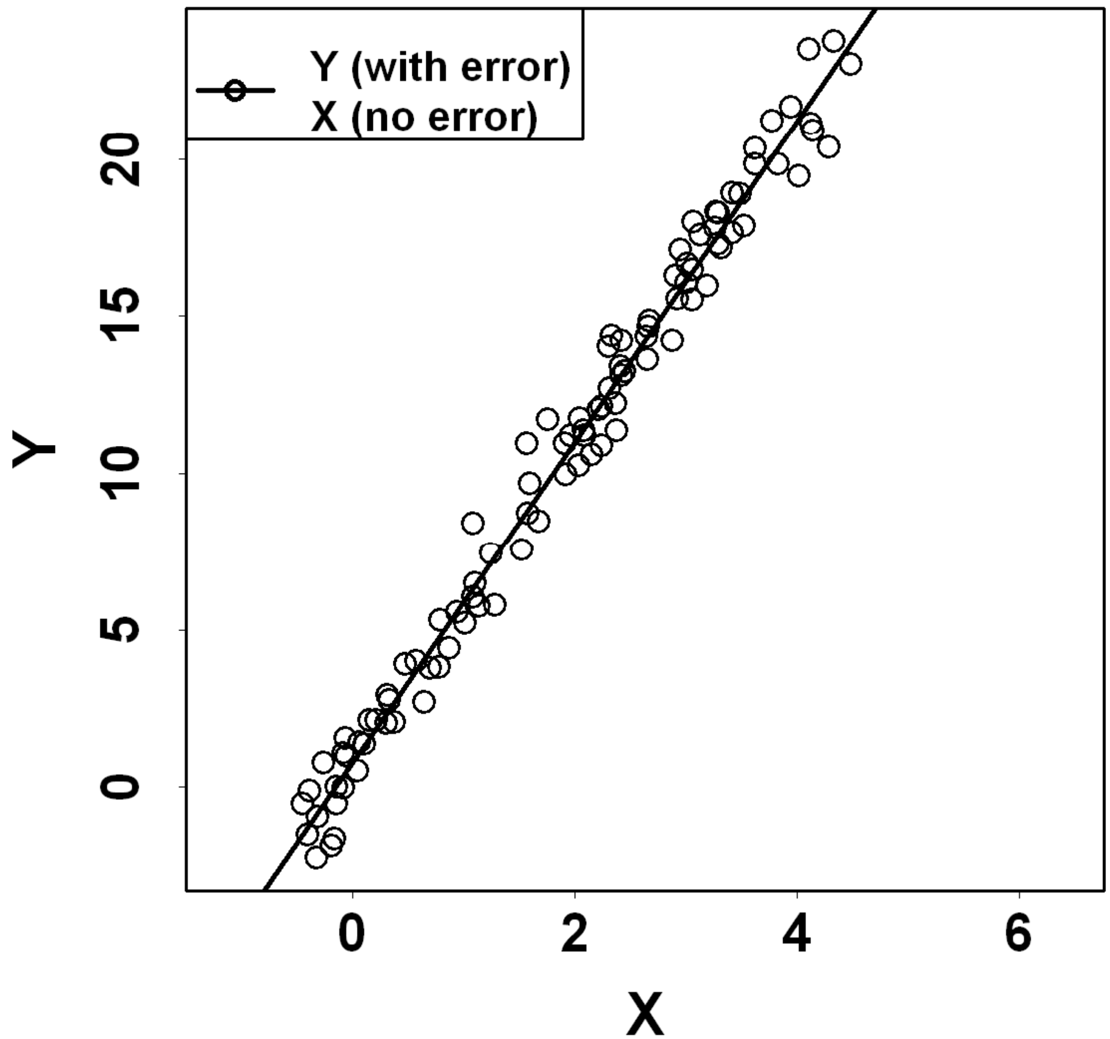
- Challenge – exposure measurement error
  - Health effect estimate is affected by the nature and quality of the exposure assessment approach
  - Health effect estimate may be
    - Biased
    - More (or less) variable
  - Typical analysis does not account for uncertainty in exposure prediction ➔ inference not correct

Measurement Error

- Error in the outcome
  - Standard part of regression
    - Models don't explain all the variation in health outcomes
  - Explicitly incorporated: $Y = \beta_0 + X\beta_X + \varepsilon$
- Measurement error in the exposure
  - Not a routine part of regression
  - Two general classes:
    - Berkson – "measure part of the true exposure"
    - Classical – "measure the true exposure plus noise"
  - Has an impact on health effect estimates, typically:
    - Berkson – unbiased but more variable
    - Classical – biased and (more or) less variable
    - Often the exposure measurement error structure will have features of both types

Outcome Error Only

“true outcome is model + error”



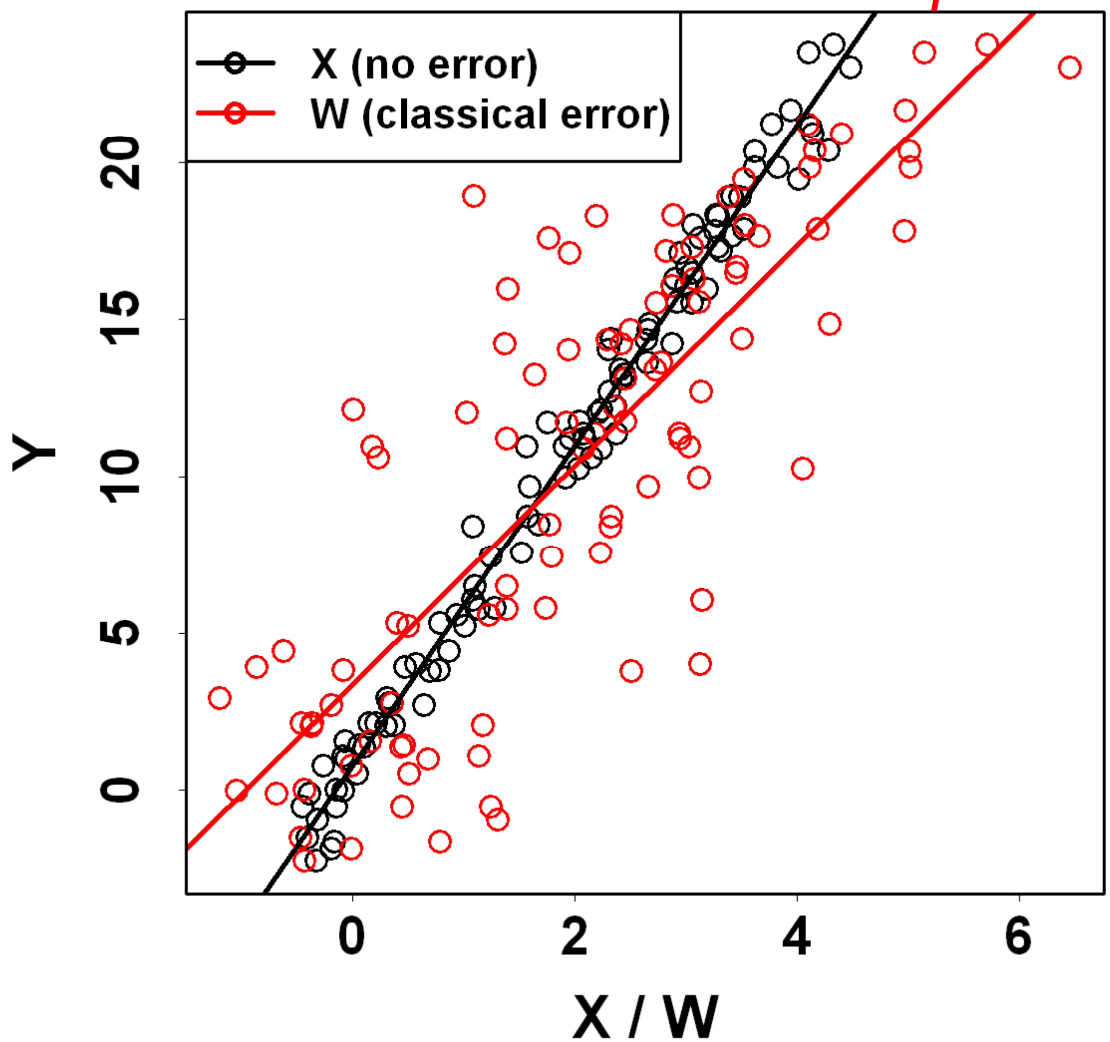
Outcome error;

No measurement error

$\hat{\beta}_X = \mathbf{5.11},\ \hat{\sigma}_X = \mathbf{0.066}$

Classical Measurement Error

“measure true exposure + noise”



No measurement error

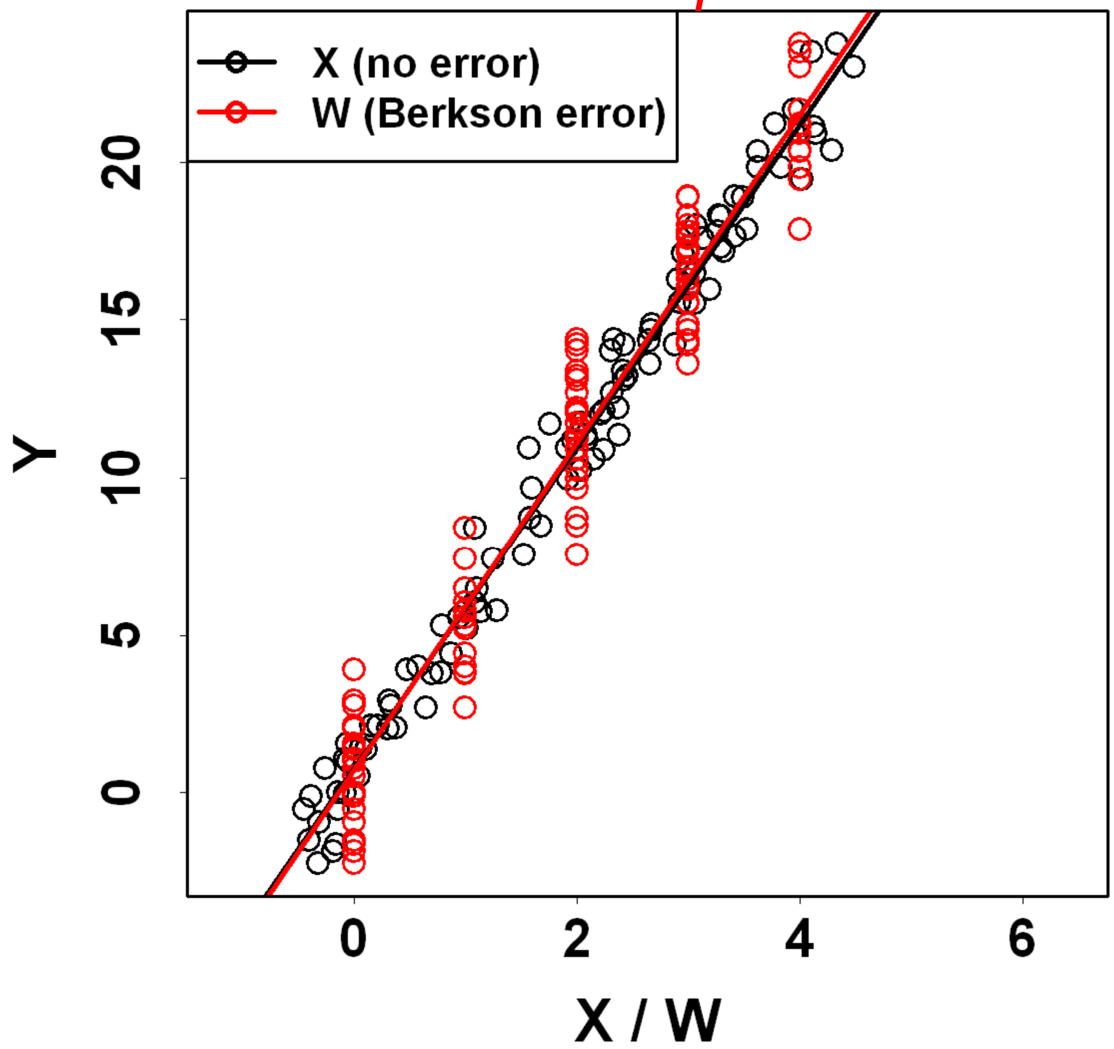
$\hat{\beta}_X = 5.11, \ \hat{\sigma}_X = 0.066$

Classical measurement error

$\hat{\beta}_X = 3.50, \ \hat{\sigma}_X = 0.256$

Berkson Measurement Error

"measure part of the true exposure"



No measurement error

$\hat{\beta}_X = 5.11, \ \hat{\sigma}_X = 0.066$

Berkson measurement error

$\hat{\beta}_X = 5.21, \ \hat{\sigma}_X = 0.122$

“Plug-in Exposure” Health Effect Estimates

- Typical exposure assignment approaches
  - Time series studies: Daily average of all regulatory monitor measurements in a geographic area
  - Cohort studies: Predicted long-term average concentration for each subject based on a model (kriging, land use regression) or the nearest monitor
- Health effect regression models that ignore exposure assignment approach can be (but aren’t always) misleading. Impact depends on
  - Study design
    - Type of study – focus on temporal or spatial variability?
    - Alignment of monitoring and subject networks?
    - Sample sizes
  - Underlying exposure distribution
  - Exposure assignment approach and quality
    - Research is needed to define the best criteria

Impact on Time Series Study Results:
Average Concentration vs. Personal Exposure

- Measurement error comes from a mixture of sources; some are Berkson and unlikely to cause bias
  - Berkson: Non-ambient source exposure doesn't affect estimates when it is independent of ambient concentration;
  - Classical: Average concentration from multiple representative monitors gives better results (reduction in classical measurement error)
  - Unknown impact: Siting of regulatory monitors, particularly for pollutants with strong spatio-temporal structure
- Differences between health effect estimates in different studies may be driven by variations in population exposures
  - Parameter misalignment: Different health parameter due to replacing exposure with concentration
    - Behaviors affecting population exposure vary by metropolitan areas
- Impact of monitor siting: Spatially homogeneous pollutants are not as sensitive to monitor locations

  ➔ Some components may be very sensitive to monitor siting

References: Zeger et al 2000; Sheppard et al 2005; Sarnat et al 2010

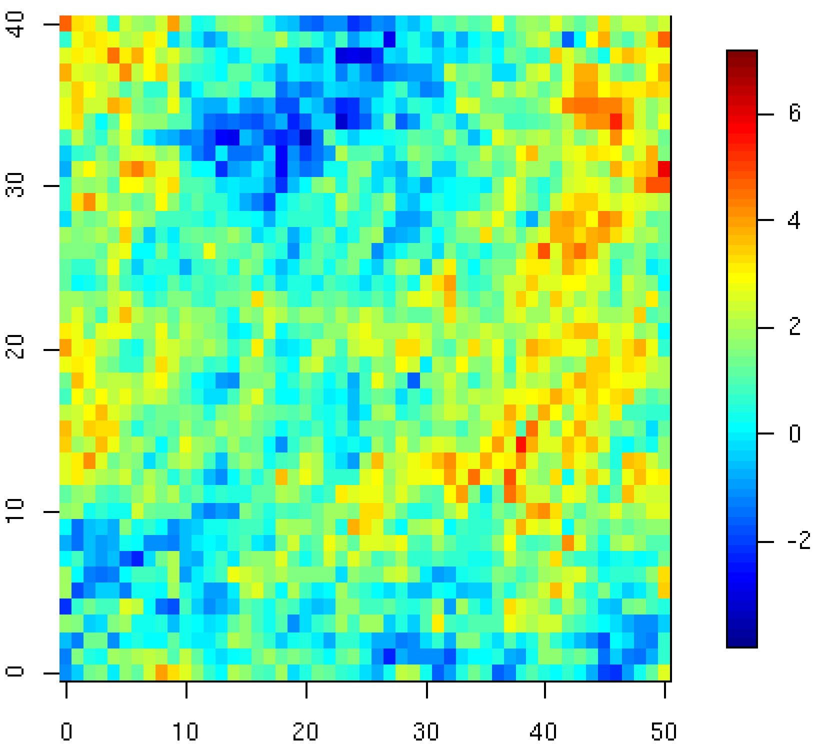
Impact on Cohort Study Results:

Individual Exposure Predictions with Spatially Misaligned Data

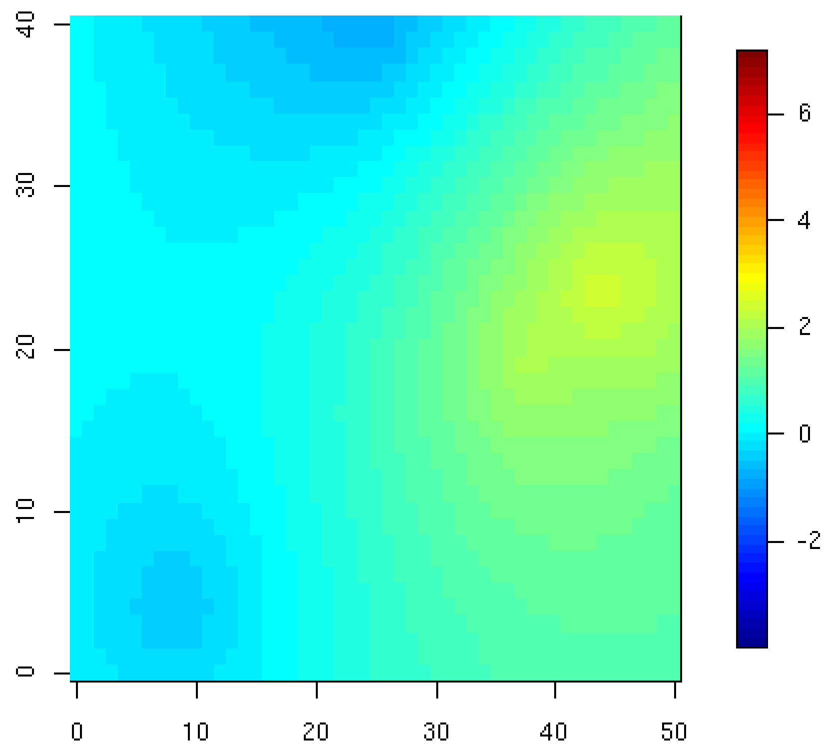
- Cohort study disease model relates individual exposure to individual disease outcomes
- Exposure data are “spatially misaligned” in the cohort study setting
  - Spatial misalignment occurs when exposure data are not available at the locations of interest for epidemiology
- Air pollution exposures are typically predicted from misaligned data using
  - Nearest monitor interpolation
  - GIS covariate regression (land use regression)
  - Interpolation by geostatistical methods (kriging)
  - Semi-parametric smoothing
- Measurement error from predicted exposures can be decomposed into two parts:
  - Berkson-like
  - Classical-like

Exposure Surface Prediction

True Exposure: X



Predicted Exposure: W



Impact on Cohort Study Results:

Measurement Error from Spatially Misaligned Predictions

- Measurement error structure is complex
  - Not purely classical or Berkson
    - Berkson-like component results from information lost in smoothing (i.e. predictions are smoother than data)
    - Classical-like component is related to uncertainty in estimating the exposure model parameters
    - Reference: Szpiro, Sheppard, Lumley (2010). *Efficient measurement error correction with spatially misaligned data*. http://www.bepress.com/uwbiostat/paper350/

    ➔ Standard correction approaches are not appropriate

- Measurement error *might be* less of a problem when the exposure is more predictable. Depends on:
  - Good spatial structure in the underlying exposure surface
    - Spatially varying mean structure
    - Longer range (i.e. large scale spatial correlation)
    - Small nugget (not much local variation left over)
  - The availability of data to capture this structure
    - Measurements that represent the exposure variability
    - Comparability of the subject and monitor locations

Health Effect Estimates Example –
The Longer the Range the Better the Performance

True exposure	Fitted exposure (R^2)	$Bias^2$	Variance	Mean square error	Coverage probability of 95% confidence interval
Least predictable (shortest range)	True	0	9	9	0.95
	Nearest	327	23	350	0.03
	Kriging (0)	342	778	1120	0.58
	True	0	31	31	0.95
	Nearest	33	58	91	0.76
	Kriging (.20)	1	734	735	0.74
	True	0	69	69	0.95
	Nearest	30	125	155	0.87
	Kriging (.40)	1	426	427	0.89
Most Predictable (longest range)	True	0	56	56	0.96
	Nearest	34	105	139	0.85
	Kriging (.47)	0	153	153	0.92

Note: Exposure models based on a constant mean model and dependence characterized by a spherical variogram with fixed partial sill (45), no nugget, and varying range (1-500 km)

Reference: Kim, Sheppard, Kim (2009) *Epidemiology*

Exposure Measurement Error –

Correction Approaches for Spatially Misaligned Data

Exposure Simulation

- Use simulated exposure in the health analysis:
  - Generate multiple samples from the estimated exposure distribution
  - Plug into disease model and estimate parameters
  - Average estimates and fix the variance
- Gives biased estimates (Gryparis et al, 2009; Little 1992)
- Reasonable to simulate exposure for risk assessment

Joint Model

- Estimate exposure and disease models jointly
  - Asymptotically optimal
- Practical problems
  - Computationally intensive
  - Published simulation examples haven't worked (Gryparis et al, 2009; Madsen et al 2008)
  - Feedback between exposure and health models can lead to bias
    - Particularly with sparse exposure and rich health data (Wakefield & Shaddick, 2006)

2-Stage Approach

- Predict exposure at subject locations in the first stage
- Correct the disease model estimates for the predicted exposure in the second stage.
  - Parametric bootstrap
  - Parameter bootstrap
  - Szpiro, Sheppard, Lumley (2010). *Efficient measurement error correction with spatially misaligned data*. Available online.

Exposure Measurement Error Correction – Simulation Results

	Bias	SD	E(SE)	Mode(SE)	Coverage
No correction	-0.002	0.027	0.016	0.016	78%
Partial parametric bootstrap[1]	-0.002	0.027	0.023	0.023	91%
Parameter bootstrap	0.001	0.027	0.028	0.027	96%
Parametric bootstrap[2]	-0.002	0.027	0.029	0.027	97%

True health effect coefficient: $\beta_X = -0.322$
[1]Partial parametric bootstrap only corrects for the Berkson-like error component
[2]Parametric bootstrap based on 100 simulations; all others based on 2,000

Reference: Szpiro, Sheppard, Lumley (2010)

Exposure Measurement Error – Discussion

- The quality of exposure estimates affects health results
  - Assess:
    - Bias
    - Variance
    - Coverage
  - Also relevant
    - Study design and data structure
      - Monitoring network vs. subject locations
    - Features of the underlying exposure
    - Exposure prediction approach and estimation results
- Measurement error structure is complex and not purely classical or Berkson
- Emerging research findings suggest exposure prediction and health effect estimation should be treated as one problem