This article reviews bias-correction models for measurement error of exposure variables in the field of nutritional epidemiology. Measurement error usually attenuates estimated slope towards zero. Due to the influence of measurement error, inference of parameter estimate is conservative and confidence interval of the slope parameter is too narrow. Bias-correction in estimators and confidence intervals are of primary interest. We review the following bias-correction models: regression calibration methods, likelihood based models, missing data models, simulation based methods, nonparametric models and sampling based procedures.

**Keywords** Bias-correction · Regression Calibration · Simulation Based · Food Frequency Questionnaire · Berkson model

1 Introduction

Nutritional epidemiology studies focus on unveiling the relationship between exposure factors and disease status. Researchers believe that there is a connection between dietary habits and the probability of being infected with disease or deteriorating into cancer. Typical examples of exposure variables are nutrient intake, dietary intake and total energy intake [12, 14].

Exposure factors can be investigated through a long-term survey FFQ (food frequency questionnaire) [16]. FFQ surveys the subjects on consumption frequencies and portion sizes of different primary food over a period of time usually six months or a whole year [18]. Researchers then estimate nutrient intake or energy intake from questionnaires [26]. It is relatively easy and of low cost to obtain FFQ. Sample size of FFQ is usually very large. However, FFQ is subject to a substantial possibility of being contaminated with measurement error, since there is randomness when people recall food consumption history, and different food pool included in FFQ may not be representative of everyone’s dietary habit [16, 23, 14].

In the presence of measurement error, estimated effect of exposure factors on disease status is biased [26]. Direction of bias is unknown and may be upward or downward. Bias depends on the assumptions on measurement error and the correlation structure between exposure factors. Estimated confidence interval is also biased [37, 30]. Considering bias in estimates and confidence intervals, measurement error correction models are adopted to derive unbiased point estimates, and accurate inference on unknown parameters. Researchers understand the association between nutrient intake and disease status better based upon unbiased estimation techniques.

Other methods of investigating exposure factors include 24-hour recall (24HR), food record (FR), 7-day diary (7DD) and biomarker [14]. These methods provide more accurate dietary information than FFQ but are also more expensive [15]. Due to the cost-efficiency of study design, these methods are applied on a smaller sample or a sub-sample of FFQ [27]. In real-life applications, precise records are used as validation or calibration studies to evaluate measurement
error in FFQ [38, chap. 4]. They are regarded as the “golden standards” or the reference measurements to study the relationship between unobserved true exposure and observed predictor measured with error [18, 14, 21]. “Golden standard” assumes that measurement errors are inconsequential in precise records. The premise for applying validation study is that measurement error in the validation study is independent of that in FFQ [14]. In addition, it is assumed that relationship between true and observed exposure on the precise validation data is the same as on the contaminated primary data [3].

Data collected in the nutritional epidemiology studies can be grouped into five classes, as in Carroll and Stefanski [4]. Primary data includes disease status, observed predictors measured with error and confounding predictors measured without error. Internal validation data is comprised of disease status, confounding factors, true exposure and observed covariates with measurement error. External validation data contains only the last two variables in the internal validation data. Validation data is used to estimate the relationship between observed and true exposure. Internal reliability data consists of disease status and repeated measurements on the observed predictor. External reliability data includes only the repeated measurements of observed predictor. We can estimate the variance of measurement error from the reliability data. Primary data and at least one of the validation and the reliability data must be present to correct the bias induced by measurement error [4].

1.1 Definition

Nondifferential measurement error is independent of outcome variables such as disease status. Conversely differential measurement error is dependent of outcome variable that is, the distribution of measurement error varies at different disease statuses [34]. Most statistical models assume nondifferential measurement error and that disease status D and observed predictor Z measured with error are conditionally independent given true exposure X and confounding factors W, that is $D \perp Z | (X, W)$ (conditional independence assumption).

Random measurement error is due to imprecision and fluctuates around zero [18, 34]. It can be measured by taking repeated measurements on the same individual [38, chap. 12]. Systematic measurement error leads to bias on average [18]. For instance, subjects may consistently over-recall food consumption frequency or consistently under-recall it. For different individuals, systematic measurement errors may be in different directions and of different sizes. It is generally more difficult to evaluate systematic measurement error than random measurement error, as in Willett [38] chap. 12.

Denote $\epsilon$ to be measurement error, then additive measurement error follows that $Z = \alpha' + X + \epsilon$, where $\alpha'$ is the systematic measurement error and $\epsilon$ is the random measurement error with mean zero. Multiplicative measurement error follows that $Z = X \epsilon$, where $\epsilon$ is the random measurement error with mean one [3, 10]. In most measurement error models, measurement error is assumed to be additive. By taking the logarithm transformation of all variables, multiplicative measurement error should be additive as well [16].

Willett [37] summarizes measurement error in nutritional epidemiology to be in four types: within-subject random error, within-subject systematic error, between-subject random error, and between-subject systematic error. Within-subject random error fluctuates around zero for each individual. Within-subject systematic error brings individual bias to the variable on average in different directions and of different sizes. Between-subject random error fluctuates around zero on average for each subject enrolled in the study. Between-subject systematic error brings bias to the variable on average for all subjects. Michels et al. [18] mentions that measurement error can be classified into person-specific or food-specific error. Measurement error can be between-person or within-person. It can also be within-food or between-food since every food consumption is measured with error in FFQ.

1.2 Complications

In the univariate measurement error model where measurement error is assumed to be nondifferential and where conditional independence assumption holds, measurement error attenuates the estimated parameter towards its null value [13, 16]. As the variability ratio between measurement error and true exposure increases, bias size also increases. Naive confidence interval estimate without bias correction is narrow and conservative. When measurement error is differential or depends upon true exposure, bias may be upward or downward depending upon the correlation between exposure factors. Bias size is also related to whether the study design is randomized and balanced [3].

Both correction methods in linear and nonlinear models are applicable in nutritional epidemiology. For categorical outcome variable, bias correction in nonlinear regression such as logistic regression is of particular interest [22]. For energy-adjusted model, bias correction in multiple linear regression with complex correlation structure is of concern [13].

When testing null hypothesis that the true exposure has no effect on disease status, measurement error leads to loss in testing power [3, 34]. Uncorrected power function will generally be greater and sample size required in the experimental
design is usually under-estimated [35]. For tests based upon contaminated data with measurement error, sample size required to achieve the same power is greater [13, 37, 16]. Under the framework of regression calibration model with Gaussian exposure, sample size for achieving the same statistical power is proportional to the quantity: $1/(\lambda^2 \sigma_Z^2)$, where $\lambda$ is the attenuation factor and $\sigma_Z^2$ is the variance of observed exposure [14]. If measurement error variance is large, the attenuation factor tends to be small and the required sample size is very large to achieve the same power.

Researchers in nutritional epidemiology are constantly searching for more accurate measurements of nutrient intake [38]. Statisticians are developing more measurement error models to relax assumptions and to improve the performance of bias-corrected estimators. Extensions of bias-correction models are from linear [17] to nonlinear [30] or partially linear models [25]. Bias-correction models include regression calibration method [22, 28], quasi-likelihood approximation method [4, 36], Bayesian nonparametric and semi-parametric model [2, 9, 20, 25] and simulation extrapolation method [8, 6].

Structure of our survey article is as follows. Section 2 reviews main bias-correction methods on measurement error in nutritional epidemiology. Section 2.2 presents regression calibration methods. Section 2.3 surveys likelihood-based models. Section 2.4 reviews bias-correction methods which regard measurement error as missing data. Section 2.5 summarizes simulation-based bias-correction procedure. Section 2.6 presents nonparametric and semi-parametric methods. Section 3 conducts a simulation study to compare performances of bias-correction methods. Section 4 discusses current methods and future research directions.

2 Methodology

2.1 Formulation and Assumptions

Denote $X$ to be true exposure and $Z$ to be observed exposure or surrogate, measurement error model is

$$Z_i = \alpha' + c(X_i, \eta) + \epsilon_i, \quad i = 1, \ldots, N,$$

where $\alpha'$ is an unknown parameter, $\epsilon_i$ is the measurement error, $N$ is the number of subjects enrolled in the study and $c(\cdot, \cdot)$ is a known function of $X_i$ [4]. Classical assumptions on measurement error model are as follows [13].

1. Measurement error $\epsilon_i$ is independent of true exposure.
2. Measurement errors of different exposure factors are uncorrelated.
3. Measurement error is homoscedastic.

Assumptions imposed on the conditional distributions of $\epsilon|X$ can be further relaxed.

On the other hand, Berkson measurement error model [3] is formulated as

$$X_i = \alpha' + c^*(Z_i, \eta) + \epsilon_i, \quad i = 1, \ldots, N,$$

where $c^*(\cdot, \cdot)$ is a known function of observed exposure $Z_i$. Berkson model focuses on the conditional distributions of $\epsilon|Z$ and $X|Z$ rather than $\epsilon|X$ [34].

In functional model, true exposure $X$ is regarded as fixed and nonrandom. Conversely, structural model assumes random true exposure [3, 34]. We can construct a sufficient statistic of $X$ and condition the likelihood function on the sufficient statistic, then a structural model is transformed into a functional model. After a sufficient statistic is derived, conditional maximum likelihood estimate is used as a bias-corrected estimator [31].

Confounding factors correlated with both disease status $D$ and observed exposure $Z$ are of concern in nutritional epidemiology study [18]. Furthermore, measurement errors may be correlated with true exposure and outcome variable. Measurement error in exposure factors may be correlated. Joint distribution of observed and true exposure is usually non-Gaussian and highly skewed. Random within-subject measurement error may be heteroscedastic [1]. Most statistical models only consider random within-subject error since correction of random measurement error only requires repeated measurements on the same subject, while correcting for systematic measurement error relies on replicate validation studies [38, chap. 12].

2.2 Regression Calibration Methods

Regression calibration model uses a contaminated primary dataset and a precise validation dataset. Contaminated exposure factors are precisely measured on the validation data. By calibrating contaminated exposure upon precisely measured exposure on the validation data, we can estimate a mapping between contaminated exposure and precisely
measured exposure. We assume that this mapping can be extrapolated from the small validation sample to all subjects in large primary data. Then we can use calibrated exposure factors in primary data to analyze the relation between disease and nutrition intake.

Rosner et al. [22] assumes that measurement error is nondifferential and independent of true exposure. Only random and systematic within-subject measurement errors are considered. It is common to use logistic regression to study the relation between disease status and exposure. Rosner et al. [22] proposes two bias-correction methods for slope parameter in logistic regression when exposure factors are measured with error. The model consists of two submodels: logistic regression for main data and linear regression for validation data. We denote $D$ to be the disease status, $Z$ as the observed exposure measured with error, and $X$ to be the true exposure. For simplicity, $D$ is binary. Regression calibration model is

$$
\logit\{P(D|X)\} = \alpha + \beta X,
$$

where $\epsilon \sim N(0, \sigma^2)$ is the Gaussian measurement error, $\alpha$, $\beta$, $\alpha'$, $\lambda$ and $\sigma$ are the unknown parameters. Logit function is $\logit(x) = \log(x/(1 - x))$. Parameter $\lambda$ is the attenuation factor and $\lambda$ is usually less than 1. In some cases, $\lambda$ can be greater than 1 as well [14].

Rosner et al. [22] requires that the dataset should include a contaminated primary study and a precise small-scale validation study. First, we review a regression calibration model based upon linear approximation [28]. Steps in the procedure are as follows.

1. We use ordinary least squares to regress true exposure $X$ on observed exposure $Z$ in the validation data and obtain estimates $\hat{\alpha}'$ and $\hat{\lambda}$.

2. Then we use the predicted exposure factors $\tilde{X} = \hat{\alpha}' + \hat{\lambda}Z$ in the main data and fit a logistic regression of disease status $D$ on $\tilde{X}$ to obtain a bias-corrected slope estimate $\hat{\beta}_1$.

Under the assumption that measurement error in the validation data is independent of true exposure and measurement error in primary study, bias-corrected slope estimator from regression calibration method is consistent [28].

After calibration of measurement-error-contaminated exposure factors on precise validation data, predicted exposure factors are free of measurement error. This bias-correction process extrapolates measurement error pattern on the small-scale validation data to the large primary data. For the extrapolation to hold, it is vital to assume that measurement error distribution on the small precisely calibrated sample is the same as on the large primary data.

For other more complex structural models, the idea behind regression calibration method is the same, that is, to replace the contaminated observed exposure in primary study with predicted exposure factors from a regression in precise validation data. We can fit a logistic regression of disease status $D$ on the predicted exposure $\tilde{X}$ to obtain the regression calibration estimate of slope parameter [21]. For more than one exposure factors measured with error, we can find the corresponding predicted exposures from calibration on the validation study and conduct the regression of disease status $D$ on predicted exposures.

A different perspective of regression calibration estimator is described in Rosner et al. [22]. This procedure obtains the same point estimator thus it is also a regression calibration method. Steps in the procedure are as follows.

1. We can fit a logistic regression of disease status $D$ on observed exposure $Z$ in the main data and calculate slope estimate $\hat{\beta}$.

2. We may use ordinary least squares estimation and linear regression of reference measurements $X$ on FFQ measurements $Z$ in the validation data to obtain an attenuation factor estimate $\hat{\lambda}$.

3. Regression calibration estimator for $\beta$ is $\hat{\beta}_2 = \hat{\beta}/\hat{\lambda}$.

4. The standard error of estimator is derived through Delta method assuming that $\hat{\beta}$ and $\hat{\lambda}$ are independent.

Estimation of the attenuation factor under different correlation structures between exposure factors in regression calibration measurement error model is of particular interest in nutritional epidemiology [18]. After estimating the attenuation factor, regression calibration corrected estimator is the biased naive estimator over estimated attenuation factor. Attenuation factor is usually between 0 and 1. Naive estimator is usually biased toward null value 0. Bias-corrected estimator is closer to the true value than naive estimator. Rosner et al. [23] investigates the estimation of attenuation factor when systematic bias in the primary data and the validation data are correlated. The standard error of regression calibration estimator derived with Delta method is severely under-estimated. Bootstrap scheme proposed in Haukka [11] is a better way to estimate variance in the regression calibration estimator.
Estimators proposed in Rosner et al. [22] are derived under stricter assumptions. It requires that random measurement error should be Gaussian and independent of true exposure and disease status. It also requires conditional independence assumption to be true. It does not consider the effect of confounding variable \( W \) in regression model. Kipnis et al. [13] studies energy-adjusted model in nutritional epidemiology and uses measurement error correction methods in multiple linear regression. It posits model to be

\[
E(Y|X) = \alpha + \beta_1X_1 + \beta_2X_2,
\]

where \( Y \) is the response variable and \( X_1 \) and \( X_2 \) are the true exposure factors. The observed predictors \( Z_1 \) and \( Z_2 \) are measured with error and \( X_1 \) and \( X_2 \) are true values of \( Z_1 \) and \( Z_2 \) respectively. Regression calibration model indicates that we apply a regression model to calibrate the relationship between true exposure \( X \) and observed exposure \( Z \). Kipnis et al. [13] formulates the bias-correction model as

\[
X = \alpha' + \lambda_1Z_1 + \lambda_2Z_2 + \epsilon,
\]

where \( \alpha', \lambda_1 \) and \( \lambda_2 \) are the unknown parameters and \( \epsilon \) is the measurement error. It assumes that measurement error \( \epsilon \) has a constant variance, that \( \epsilon \) is independent of \( Z_1 \) and \( Z_2 \) and that the joint distribution of \( Z_1, Z_2 \) and \( X \) is Gaussian. Kipnis et al. [13] provides an insight into bias induced by measurement error. We fit the model

\[
Y = \gamma_0 + \gamma_1Z_1 + \gamma_2Z_2 + \epsilon,
\]

where \( \gamma_0, \gamma_1 \) and \( \gamma_2 \) are the unknown parameters and \( \epsilon \) is the random error, then asymptotic expectation of ordinary least squares estimate \( \hat{\gamma}_1 \) is

\[
E(\hat{\gamma}_1) = A\beta_1 + C\beta_2,
\]

where \( A \) and \( C \) are two conformable constant matrices. Matrix \( A \) reflects the bias of \( \gamma_1 \) due to measurement error of \( Z_1 \) and \( A \) is an attenuation factor. Matrix \( C \) represents the bias of \( \gamma_1 \) caused by measurement error of \( Z_2 \). Matrices \( A \) and \( C \) are only relevant to the correlation structure between \( Z_1, Z_2, X_1 \) and \( X_2 \). That is, correlation structure between predictors in the model and measurement errors has a crucial effect on the bias caused by measurement error. Bias direction is indefinite under complex correlation structure. In a model with multiple exposures, bias on the estimated effect is subject to both attenuation effect (\( A \)) of its own measurement error and contamination effect (\( C \)) from measurement errors of other exposures in the model.

Haukka [11] describes how to use bootstrap procedures in regression calibration method. The steps are as follows.

1. Get a bootstrap sample with replacement from the validation data.
2. Estimate attenuation factor using bootstrap sample.
3. Obtain a bootstrap sample with replacement from the primary data.
4. Estimate bias-corrected estimator \( \hat{\beta} \) with disease status and predicted exposure factors in the bootstrap sample.
5. Repeat steps above for a sufficiently large number of iterations and obtain a vector of bias-corrected estimates.

Bootstrap procedure can be used to provide a better estimate of the standard error for regression calibration corrected estimator [21].

2.3 Likelihood Based Methods

Conditional independence assumption and Gaussian measurement error assumption may not hold. Quasi-likelihood approach does not require measurement error to be Gaussian. No distributional assumption is imposed upon measurement error.

Another framework for deriving bias-corrected parameter estimate for measurement error contaminated data is to apply maximum likelihood approach. Rosner et al. [22] suggests using an approximation of likelihood function \( Pr(D|\bar{Z}) \) to derive a bias-corrected estimator. Steps are as follows.

1. Fit a logistic regression of disease status \( D \) on observed exposure \( Z \) in the main data and obtain estimates \( \hat{\alpha} \) and \( \hat{\beta} \).
2. Then compute likelihood-based bias-corrected estimator of \( \beta \).
3. The standard error of corrected estimator is also derived with Delta method and explicitly expressed.

Measurement error variance is estimated from the validation study. Stefanski and Carroll [30] presents three approximate estimators in logistic regression with measurement error in exposure factors. In nutritional epidemiology, a common situation is that sample size of the validation study is much smaller than primary study. Small sample size is an obstacle in obtaining an efficient estimate of measurement error variance.
2.4 Missing Data Perspective

Conditional independence assumption and Gaussian error assumption may not hold. Quasi-likelihood approach does not require measurement error to be Gaussian. Regarding measurement error as missing data removes the conditional independence assumption. Bias-correction model proposed in Schafer [24] regards true exposure as missing data in the primary data and develops a measurement error estimation technique based on expectation-maximization algorithm (EM). It focuses only upon the main data and assumes that the magnitude of measurement error is already known. It considers including confounding covariates W which are not affected by measurement error in the model. Confounding factors W may be correlated with both disease status D and true exposure X. For confounding factors W in the model, Rosner et al. [22] recommends

1. first regressing observed exposure Z and disease status D respectively on confounding W,
2. then regressing residuals of D on residuals of Z to obtain parameter estimate.

Schafer [24] assumes that parametric distribution of disease status given true exposure D|X is in the exponential family

\[
f(d_i|x_i; \beta) = \exp\left\{ d_i(\omega_i^T \beta_1 + x_i^T \beta_2) - b(\omega_i^T \beta_1 + x_i^T \beta_2) + h(d_i) \right\}, \quad i = 1, \ldots, N,
\]

where \(d_i, x_i, \) and \(w_i\) are the realizations of \(D_i, \) \(X_i, \) and \(W_i\) respectively, and \(v'\) stands for the matrix transpose of \(v.\) It assumes that conditional independence assumption holds and that measurement error is nondifferential. Random variables \(D_i, \) \(Z_i, \) \(X_i\) of different subjects are independent. \(Z_i|X_i = x_i \sim N(x_i, \Omega_x),\) while that covariates \(W, \) \(X\) and measurement error are jointly Gaussian. It assumes that measurement error variance \(\Omega_m\) is known or has an efficient estimator \(S_m,\) so that it does not consider modeling the validation data. Unknown parameter in the model is denoted by \(z = (\beta_1, \beta_2, x, \Omega_x).\)

In Expectation-Maximization (EM) algorithm, complete data is \((D, Z, X, S_m)\) and observed data is \((D, Z, S_m)\) \(^2\)

Expectation step and maximization step are respectively

\[
Q(\xi | \xi^{(t)}) = E\{\log f(D, Z, X, S_m; \xi)|D, Z, S_m; \xi^{(t)}\},
\]

\[
\xi^{(t+1)} = \arg\max_{\xi} Q(\xi | \xi^{(t)}).
\]

Decomposition of log-likelihood is

\[
\log f(D, Z, X, S_m; \xi) = \sum_i \log f(D_i|X_i; \beta) + \sum_i \log f(X_i; x, \Omega_x) + \sum_i \log f(Z_i|X_i; \Omega_m)
\]

\[
+ \sum_i \log f(S_m; \Omega_m).
\]

Regression calibration model only considers distributions of \(D|X\) and \(Z|X\) which are the first and third items in the complete log-likelihood function. It iterates EM algorithm to estimate unknown parameters. In nutritional epidemiology study where we can estimate measurement error variance efficiently from the validation or reliability study, EM algorithm is a feasible bias-correction method.

Multiple imputation method [7] requires that a precise validation study should be conducted and that the sample in validation study should be a sub-sample of the large primary study. Similar to EM algorithm, multiple imputation method views measurement error as missing data. It assumes that the true exposure is missing at random in the primary data. For observations which lie both in the primary and the validation study, true exposure is regarded as observed exposure. But for observations which only appear in the primary study and not in the validation study, true exposure is viewed as missing data.

From validation study, the mapping between true exposure and observed exposure is estimated. Multiple imputation of true exposure is based upon the extrapolation of this estimated mapping. Each imputation produces a primary study

\(^2\)Only large contaminated primary data is considered here.
with all true exposure factors filled with imputed observations. We can fit a logistic regression of disease status on the filled true exposure \((D \sim X^*)\) factors. Rubin's estimate from multiple imputation procedure is equal to the average of all estimates. Estimate variance is the summation of between-imputation variance and within-imputation variance. Multiple imputation estimate is referred to as MIME \([7]\). MIME is approximately unbiased. The coverage of confidence interval is around the right coverage. The performance of MIME depends on the sample size of primary study and the proportion of subjects that are validated.

2.5 Simulation Based Methods

SIMEX \([8]\) is a simulation based method to correct for measurement error. The assumption is that measurement error variability is known or can be efficiently estimated from the validation or reliability study. The procedure includes the following steps.

1. Add an extra measurement error to the predictor measured with error.
2. Estimate the parameter of interest using disturbed main data.
3. Repeat steps above at different values of measurement error variance and computing the parameter estimate.
4. Calibrate the relationship between variance of extra measurement error and parameter estimate.
5. Extrapolate the relationship to cases with no measurement error and obtain a bias-corrected estimate SIMEX.

SIMEX is shown to be asymptotically unbiased and efficient in logistic regression. The statistical model of SIMEX is

\[
Z_i = X_i + \sigma \epsilon_i, i = 1, 2, \ldots, N,
\]

where \(N\) is the sample size, \(\sigma\) is known or can be efficiently estimated and measurement error \(\epsilon_i \sim N(0, 1)\). Parameter of interest is estimated by \(\hat{\theta}_T\) where \(\theta_T = f(D_i, W_i, X_i)\), a function of disease status, confounding factors and true exposure. Naive estimator \(\hat{\theta}_N = f(D_i, W_i, Z_i)\) is a function of disease status, confounding factors and FFQ measurement observations. This representation allows us to apply the simulation based method on any parameter of interest. It is free from assumptions on the joint distribution of \((X, Z)\). Extra measurement error is added through

\[
Z_{b,i}(\tau) = Z_i + \tau^{1/2} \sigma \epsilon_{b,i}, b = 1, 2, \ldots, B; i = 1, 2, \ldots, N,
\]

where \(B\) is the number of times we implement the simulation procedure, \(\tau\) is the magnitude of extra measurement error \((\tau > 0)\) and \(\epsilon_{b,i} \sim N(0, 1)\) are independent of each other and independent of data. An estimate based upon disturbed main data: \(\hat{\theta}_b(\tau) = f(D_i, W_i, Z_{b,i}(\tau))\). For each value of \(\tau\), the estimate is \(\hat{\theta}(\tau) = \frac{1}{B} \sum_{b=1}^{B} \hat{\theta}_b(\tau)\). If we vary the value of \(\tau\), we will have a set of estimates and the relationship between \(\tau\) and \(\hat{\theta}(\tau)\). By extrapolating the relation to \(\tau = -1\), the estimate \(\hat{\theta}(-1)\) is SIMEX estimator \(\hat{\theta}_{SIMEX}\).

The asymptotic bias of SIMEX estimator is \(O(\sigma^4)\) for linear extrapolation. It is better than naive estimator since the asymptotic bias is \(O(\sigma^2)\) for naive estimator. Quadratic extrapolation is preferred over linear extrapolation. SIMEX estimator \(\hat{\theta}_{SIMEX}\) is asymptotically Gaussian and approximately consistent, which implies that the estimator converges in probability to a value close to true value as sample size grows to infinity \([4]\). If the extrapolation function is exact and the variance of measurement error \(\sigma^2\) is known, SIMEX estimator is exactly consistent \([33]\).

Stefanski and Cook \([33]\) explores the asymptotic properties of SIMEX estimator \(\hat{\theta}_{SIMEX}\) by using the association between SIMEX estimator and jackknife estimator with sample size equal to one. The association is explained with jackknife extrapolation. Leave-\((-\infty)\)-out extrapolation under jackknife framework is similar to \(\tau = -1\) extrapolation in SIMEX procedure. Same as in Cook and Stefanski \([8]\), SIMEX assumes that measurement error variance is known or can be efficiently estimated. Define \(\Delta(\tau) = \hat{\theta}_b(\tau) - \hat{\theta}(\tau)\), and it reaches the conclusion that

\[
\text{Var}(\hat{\theta}_{SIMEX}) = - \lim_{\tau \rightarrow -1} \text{Var}(\Delta(\tau)).
\]

Jackknife variance estimate of SIMEX estimator includes the following steps.

1. For each value of \(\tau\), compute the sample variance \(S_A(\tau)\) of simulated data. \(\hat{\theta}_b(\tau), b = 1, 2, \ldots, B\).
2. Extrapolate the relation between \(S_A(\tau)\) and \(\tau\) to the case where \(\tau = -1\).
3. Then \(S_A(-1)\) is a variance estimate of SIMEX estimator \(\hat{\theta}_{SIMEX}\).
2.6 Nonparametric Methods

Nonparametric methods can be applied to approximate the true exposure distribution free from contamination of measurement error. For additive measurement error, \( Z = X + \epsilon \). Denote the distribution of true exposure \( X \) by \( g \), distribution of observed exposure \( Z \) by \( f \) and distribution of measurement error \( \epsilon \) by \( h \). Stefanski and Carroll [32] explains the deconvolution method to derive true exposure distribution \( g \) from \( f \) and \( h \). It is assumed that measurement error distribution \( h \) is known or can be efficiently estimated. It integrates nonparametric density estimation into deconvolution of distribution to obtain a density estimate of true exposure distribution \( g \).

Nonparametric regression may be applied to logistic regression \( D \sim X, W \), linear regression \( X \sim Z \) or both [25]. Nonparametric approximation may be used to estimate likelihood function and score function. An estimator [5] is solved iteratively from an estimating equation constructed by equaling mixed score function to zero:

\[
\sum_{j=1}^{n_1} l(d_j, x_j, \beta) + \sum_{i=n_1+1}^{n} H_n(d_i, z_i, \beta) = 0,
\]

where \( n_1 \) is the sample size of validation study and \( n - n_1 \) is the sample size of primary study. The first term is based on the score function of logistic regression in validation study and the second term is from nonparametric approximation of density \( p(D|Z) \). The advantages of nonparametric methods are as follows [5].

1. It imposes no parametric assumption on the joint distribution of \( (Z, X) \).
2. It allows nonlinear components to be included in regression.
3. It considers heteroscedasticity of measurement error.

More nonparametric or semi-parametric measurement error models are developed in recent years. A nonparametric mixture model is suggested in Roeder et al. [20]. A Bayesian regression of splines is proposed in Berry et al. [2].

2.7 Other Models

Richardson and Gilks [19] describes another approach for making bias-corrections: hierarchical model and Gibbs sampling. Measurement error model is decomposed into three sub-models: disease model of disease status conditional upon true exposure and confounding factors \((D|X, W, \beta)\), measurement model of observed exposure conditional upon true exposure \((Z|X, \lambda)\) and exposure model of true exposure conditional upon confounding factors \((X|W, \pi)\), where \( \beta, \lambda \) and \( \pi \) are unknown parameters in the sub-models. It assumes that conditional independence assumption holds so that the prior distributions of \( (\beta, \lambda, \pi) \) times the joint distribution of \((Z, X, D)|W\) can be written as

\[
f(\beta)f(\lambda)f(\pi)\Pi_1(X_i|W_i, \pi)\Pi_1(Z_i|X_i, \lambda)\Pi_1(D_i|X_i, W_i, \beta),
\]

from which we can derive the conditional distributions used in Gibbs sampling. Bias-corrected estimator can be derived based upon the posterior distribution. We require the presence of primary data, validation data and reliability data to ensure model identifiability. Hierarchical model can be applied to both measurement error model and Berkson error model [25]. In logistic regression, we impose the following assumptions.

1. \((X_i|W_i, \pi) \sim N(x, \sigma^2_x)\), where \( N(x, \sigma^2_x) \) is Gaussian distribution with mean \( x \) and variance \( \sigma^2_x \).
2. \((Z_i|X_i, \lambda) \sim N(\alpha' + \lambda X_i, \sigma^2_z)\).
3. \((D_i|X_i, W_i, \beta) \sim \text{Bernoulli}(\exp(\alpha + W_i \beta_1 + X_i \beta_2)/\{1 + \exp(\alpha + W_i \beta_1 + X_i \beta_2)\})\), where \( \text{Bernoulli}(p) \) is Bernoulli distribution with success probability \( p \).

Unknown parameters are \((\alpha', \alpha, \beta_1, \beta_2, \lambda, \sigma^2_x, \sigma^2_z, x)\). Non-informative priors may be imposed upon these unknown parameters.

Instrumental variable method is applicable in cases where there is another independent measurement \( S \) of true exposure \( X \) in the study [29]. Denote \( Z \) as the observed predictor of \( X \) in the study and \( D \) is the disease status. Instrumental variable satisfies the following conditions.

1. \( \text{Cor}(S, X) \neq 0 \), \( \text{Cor}(S, Z - X) = 0 \).
2. \( \text{Cor}(S, D - E(D|X)) = 0 \), where \( \text{Cor}(a, b) \) is the correlation between \( a \) and \( b \).
3. In addition, Stefanski and Buzas [29] assumes that \( E(S|X) = X \) and \( \text{Var}(S|X) = \text{Var}(Z|X) \).

For linear regression, bias-corrected estimator based on data \((D, Z, S)\) is represented in a nice closed form. For generalized linear regression, bias-corrected estimator is derived through linear approximations of the regression model [29]. Bias-corrected estimator is approximately consistent.
3 Simulation

In nutritional epidemiology, researchers are interested in the relation between disease status and dietary habits of people. Dietary intake measured with food frequency questionnaire (FFQ) is subject to substantial random and systematic measurement error. Measurement error introduces bias into the estimated effect of dietary intake on disease status, leads to narrow confidence interval on parameter of interest and power loss in hypothesis test. This is why we need bias-correction methods to develop better estimates in the presence of measurement error. The simulation study is conducted for the comparison of various bias-correction methods applicable in nutritional epidemiology studies.

Data in nutritional epidemiology contains FFQ, reference measurement data including 24-hour recall (24HR), 7-day dairy (7DD) and food record (FR), and biomarker measurement data [38 chap. 4]. Denote measurements in FFQ by $Z_{ij}$, reference measurements by $F_{ij}$ and biomarker measurements by $M_{ij}$, $i = 1, 2, \ldots, N$ and $j = 1, 2, \ldots, J$, where $N$ is the number of subjects enrolled and $J$ is the number of timestamps in the validation study. We also denote $X_i$ to be the true exposure of the $i$th individual. Logistic regression [22,16] is applied to model the relation between disease status $D$ and true exposure $X$:

$$P(D = 1|X) = \exp(\alpha + \beta X)/\{1 + \exp(\alpha + \beta X)\},$$

where $D$ is binary and takes values from $\{0, 1\}$, $\alpha$ is the unknown intercept parameter and $\beta$ is the unknown slope parameter of interest in nutritional epidemiology study. A typical measurement error model in nutritional epidemiology [16,23] is posited to be the following form:

$$Z_{ij} = \mu_{Zj} + \lambda_{Z0} + \lambda_{Z1}X_i + r_i + \varepsilon_{Zij},$$
$$F_{ij} = \mu_{Fj} + \lambda_{F0} + \lambda_{F1}X_i + s_i + \varepsilon_{Fij},$$
$$M_{ij} = \mu_{Mj} + X_i + \varepsilon_{Mij},$$

where $\mu_{Zj}$ is the time-specific bias of $Z_{ij}$ and $\sum_{j=1}^{J} \mu_{Zj} = 0$, $\mu_{Fj}$ is the time-specific bias of $F_{ij}$ and $\sum_{j=1}^{J} \mu_{Fj} = 0$, $\mu_{Mj}$ is the time-specific bias of $M_{ij}$ and $\sum_{j=1}^{J} \mu_{Mj} = 0$. $\lambda_{Z0}, \lambda_{Z1}, \lambda_{F0}, \lambda_{F1}$ are the unknown parameters, $r_i \sim (r, \sigma_r^2)$ is the systematic within-subject measurement error in $Z_{ij}$, $\varepsilon_{Zij} \sim (0, \sigma_{Zi}^2)$ is the random within-subject measurement error in $Z_{ij}$, $\sigma_{Zi}^2$ is simulated from uniform distribution centered at $\sigma_z^2$, $s_i \sim (s, \sigma_s^2)$ is the systematic within-subject measurement error in $F_{ij}$, $\varepsilon_{Fij} \sim (0, \sigma_{Fi}^2)$ is the random within-subject measurement error in $F_{ij}$, $\varepsilon_{Mij} \sim (0, \sigma_{M}^2)$ is the random within-subject measurement error in $M_{ij}$. True exposure $X_i$ is simulated from Gaussian distribution $N(x, \sigma_x^2)$. Kipnis et al. [16] simplifies the model to be

$$Z_{ij} = \mu_{Zj} + \lambda_{Z0} + \lambda_{Z1}X_i + r_i + \varepsilon_{Zij},$$
$$M_{ij} = \mu_{Mj} + X_i + \varepsilon_{Mij},$$

where the redundant measurement is removed. Measurement errors in the biomarker measurements are independent of those in FFQ. Performances of naive estimator (Naive), regression calibration (RC) estimator and likelihood approximation estimator (Lik) are studied in the simulation with this model.

3.1 Factors

Denote the sample size of primary study i.e. FFQ to be $n_2$ and the sample size of validation study to be $n_1$. In nutritional epidemiology, $n_2 \gg n_1$ and we set $n_2$ to be 100,000 and $n_1$ to be 1,000 in our simulation. Intuitively, as ratio $n_1/n_2$ increases, these bias-correction methods should all perform better. Two levels of slope parameter $\beta$ (related to the disease odds ratio) are considered in the simulation. Measurement error distribution is examined since estimators are derive under the normality assumption, whereas in nutritional epidemiology measurement error distribution is usually skewed. Whether measurement error variance $\sigma_{Zi}^2$ is constant across $i$ or not is pertinent because homoscedasticity of measurement error is assumed in most measurement error models.

3.2 Data Generation

There are two choices of parameter: (i) $\alpha = -1$, $\beta = 0.1$ and (ii) $\alpha = -1$, $\beta = 1$, and two different distributions of random measurement error: (i) $N(0, \sigma_r^2)$ and (ii) $\{\lognormal(0,1) - \sqrt{\varepsilon}\} \sigma_e/\sqrt{(e-1)\varepsilon}$. The second distribution is transformed from lognormal distribution. After transformation, it is a skewed distribution with mean 0 and variance $\sigma_z^2$. Taking all combinations of these two factors, we form four sets of conditions for the simulation, which are (i) $\alpha = -1, \beta = 1, N(0, \sigma_z^2)$; (ii) $\alpha = -1, \beta = 1, \{\lognormal(0,1) - \sqrt{\varepsilon}\} \sigma_e/\sqrt{(e-1)\varepsilon}$; (iii) $\alpha = -1, \beta = 0.1, N(0, \sigma_z^2)$ and (iv) $\alpha = -1, \beta = 0.1, \{\lognormal(0,1) - \sqrt{\varepsilon}\} \sigma_e/\sqrt{(e-1)\varepsilon}$.
Other relevant parameters are set as $\sigma_2^2/\sigma_1^2 = 0.3$, $\sigma_2^2 = 0.3$, $\sigma_1^2 = 1$, $n_1 = 1,000$, $n_2 = 100,000$, $\lambda_{Z0} = 0.1$, $\lambda_{Z1} = 0.5$, $r = 0.05$, $\sigma^2 = 0.05$, $x = 0$ for cases (i)(ii)(iv) and $x = 1$ for case (ii), $\sigma^2_M = 0.0001$ and $J = 2$. Simulation size is $M = 1000$. True exposure $X_i$ is generated as a random sample of size $N = n_1 + n_2$ from Gaussian distribution $N(0, 1)$.

For the main dataset of size $n_2$ with disease status and FFQ nutrient intake measurements, we use the first $n_2$ simulated true exposure. Generate a scalar from uniform distribution Uniform(0, 1). For scalar less than $\exp(\alpha + \beta X_i)/\{1 + \exp(\alpha + \beta X_i)\}$, we set disease status to be 1. Otherwise we set disease status to be 0.

For FFQ nutrient intake in the main data, first we generate individual measurement error variances $\sigma^2_{Zi}$ from uniform distribution Uniform($\sigma^2_Z - 0.05, \sigma^2_Z + 0.05$). Random measurement error in $Z_i$ is simulated from transformed lognormal distribution or normal distribution with mean 0 and variance $\sigma^2_{Zi}$. Systematic measurement error in $Z_i$ is generated from $N(r, \sigma^2_z)$. Then we add up $\lambda_{Z0} + \lambda_{Z1} X_i$, systematic measurement error and random measurement error and obtain simulated observed exposure in FFQ.

As for the validation dataset of size $n_1$ with nutrient intake from FFQ and biomarker measurements repeated at $J$ time-points, individual measurement error variance $\sigma^2_{Zi}$ is generated from uniform distribution Uniform($\sigma^2_Z - 0.05, \sigma^2_Z + 0.05$). Random measurement error $\epsilon_{Zij}$ is generated from Gaussian distribution $N(0, \sigma^2_{Zij})$ or transformed lognormal distribution with mean 0 and variance $\sigma^2_{Zij}$. Systematic measurement error $r_i$ is generated from Gaussian distribution $N(r, \sigma^2_r)$. Time-specific bias $\mu_{Zij} = 1, 2, \cdots, J - 1$ are independently generated from uniform distribution Uniform(−0.001, 0.001) and $\mu_{Zij} = -J^{-1} \sum_{j=1}^{J-1} \mu_{Zij}$. Then we add up $\lambda_{Z0} + \lambda_{Z1} X_i$, systematic measurement error, random measurement error and time-specific bias and obtain simulated observed exposure in the validation study.

As for biomarker measurements in the validation data, individual random measurement error variance $\sigma^2_{Mij}$ is generated from uniform distribution Uniform(0, 2$\sigma^2_M$). Random measurement error $\epsilon_{Mij}$ is generated from Gaussian distribution $N(0, \sigma^2_{Mij})$ or transformed lognormal distribution with mean 0 and variance $\sigma^2_{Mij}$. Time-specific bias $\mu_{Mij}, J = 1, 2, \cdots, J - 1$ are independently generated from uniform distribution Uniform(−0.001, 0.001) and $\mu_{Mij} = -J^{-1} \sum_{j=1}^{J-1} \mu_{Mij}$. Biomarker measurement is the sum of true exposure $X_i$, random measurement error and time-specific bias.

### 3.3 Estimators

Naive estimator of $\beta$ is constructed by fitting logistic regression of $D_i$ on $Z_i$ in the primary data. Slope estimate $\hat{\beta}_N$ is naive estimator. Variance of naive estimator is reported in the regression output. Fit a linear regression of $M_{ij}$ on $Z_{ij}$ and the estimated slope is $\lambda$. RC estimator of $\beta$ is $\hat{\beta}_R = \hat{\beta}_N / \lambda$. Variance of RC estimator is $\text{Var}(\hat{\beta}_R) = (1/\lambda^2) \text{Var}(\hat{\beta}_N) + (\beta_N^2/\lambda^4) \text{Var}(\lambda)$ [22]. Likelihood based estimator proposed in Rosner et al. [22] is also studied in the simulation.

### 3.4 Results and Interpretation

"Avg est" is the average of all estimates in the simulation. "Avg se" is the average of all standard error estimates in the simulation. "MC sd" is the standard deviation of all estimates in the simulation. "Coverage" is the proportion of 95% confidence intervals constructed with Gaussian approximation that cover true parameter. It indicates whether standard error estimate is reasonable.

#### 3.4.1 $\beta = 1$ and Gaussian Measurement Error

Simulation results for the case where $\beta = 1$ and measurement error distribution is Gaussian are displayed in table [I]. Likelihood based estimator contains the least bias and is closest to the true value of $\beta$. The 95% confidence intervals formed by est.± 1.96se. have coverage proportions of only 0 and 0.09 for naive and RC estimators. The standard error of likelihood based estimator is closest to the reasonable standard error. The standard errors of naive estimator and RC estimator are severely underestimated. Ratios of the average standard error to Monte Carlo standard deviation are all close to 1.

When true odds ratio ($\exp(\beta)$) is large, none of these methods shows good coverage close to 95%. Point estimates from RC and likelihood based estimation are acceptably close to the true value. Naive estimate is obviously attenuated towards 0 and is less than the average estimate of RC method and likelihood based method.
### 3.4.2 \( \beta = 1 \) and Skewed Measurement Error

Simulation results of the case where \( \beta = 1 \) and measurement error distribution is skewed are presented in table 2.

| method | Avg est | Avg se   | MC sd    | ratio of Avg se to MC sd | coverage |
|--------|---------|----------|----------|--------------------------|----------|
| Naive  | 7.61E-02 | 1.03E-02 | 1.29E-02 | 7.96E-01                 | 0.00     |
|        | (4.08E-04) | (1.77E-06) | (2.76E-04) | (1.71E-02) | (0.00)   |
| RC     | 9.11E-01 | 2.71E-02 | 1.05E-01 | 2.58E-01                 | 0.23     |
|        | (3.33E-03) | (1.82E-04) | (1.01E-02) | (2.57E-02) | (1.33E-02) |
| Lik    | 1.00E+00 | 6.31E-02 | 6.53E-01 | 9.67E-02                 | 0.42     |
|        | (2.06E-02) | (2.88E-02) | (5.16E-01) | (1.55E-01) | (1.56E-02) |

Table 2: The standard errors are in parenthesis.

The average estimate bias is comparable to table 1 for each estimator. The average standard errors and Monte Carlo standard deviations are greater than those in table 1. More outliers are present in generated exposure factors when we use shifted and scaled lognormal distribution instead of Gaussian distribution for measurement error. Ratios of the average standard error to Monte Carlo standard deviation are much less than 1 and much lower than those in table 1. This phenomenon indicates that the standard error formulas underestimate variability in this case and Monte Carlo standard deviation is a more reliable estimation of variability.

### 3.4.3 \( \beta = 0.1 \) and Gaussian Measurement Error

Simulation results when \( \beta = 0.1 \) and when measurement error distribution is skewed are given in table 3.

| method | Avg est | Avg se   | MC sd    | ratio of Avg se to MC sd | coverage |
|--------|---------|----------|----------|--------------------------|----------|
| Naive  | 8.32E-02 | 9.21E-03 | 9.46E-03 | 9.74E-01                 | 0.56     |
|        | (2.99E-04) | (7.91E-07) | (2.11E-04) | (2.18E-02) | (1.57E-02) |
| RC     | 9.98E-02 | 1.14E-02 | 1.19E-02 | 9.58E-01                 | 0.93     |
|        | (3.75E-04) | (1.27E-05) | (2.63E-04) | (2.12E-02) | (7.96E-03) |
| Lik    | 9.99E-02 | 1.14E-02 | 1.19E-02 | 9.58E-01                 | 0.93     |
|        | (3.76E-04) | (1.28E-05) | (2.64E-04) | (2.12E-02) | (8.02E-03) |

Table 3: The standard errors are in brackets.

In this case, true odds ratio of infection \( D = 1 \) versus no infection \( D = 0 \) is \( \exp(0.1) = 1.105 \), less than first two cases where true odds ratio is \( \exp(1) = 2.718 \). RC estimator and likelihood based estimator are similar. Both show little bias and standard errors are reasonable with coverage proportion close to 95%. RC estimator and likelihood based estimator both perform well for rare disease and Gaussian measurement error.
Ratios of the average standard error to Monte Carlo standard deviation are all close to 1. Coverage of naive estimate is 0.56 much smaller compared to coverage of RC estimate and likelihood based estimate. Attenuation effect is obvious here since the average of naive estimates is 0.83, farther away from true value 1 than RC estimate and likelihood based estimate. The standard error of naive estimate is still underestimated in this case, but much better than in the former two cases, where coverage is 0.

3.4.4 \( \beta = 0.1 \) and Skewed Measurement Error

Simulation results where \( \beta = 0.1 \) and measurement error distribution is skewed are summarized in table 4.

| method | Avg est | Avg se | MC sd | ratio of Avg se to MC sd | coverage |
|--------|---------|--------|-------|--------------------------|----------|
| Naive  | 8.13E-02| 9.02E-03| 8.73E-03| 1.03E+00                  | 0.46     |
|        | (2.76E-04)| (2.51E-06)| (1.97E-04)| (2.33E-02)                  | (1.58E-02)|
| RC     | 9.78E-02| 1.12E-02| 1.59E-02| 7.02E-01                   | 0.86     |
|        | (5.03E-04)| (4.57E-05)| (8.07E-04)| (3.47E-02)                  | (1.11E-02)|
| Lik    | 9.78E-02| 1.12E-02| 1.60E-02| 7.01E-01                   | 0.86     |
|        | (5.05E-04)| (4.63E-05)| (8.17E-04)| (3.50E-02)                  | (1.11E-02)|

Table 4: The standard errors are in the brackets.

Performances of RC estimator and likelihood based estimator are similar when true odds ratio is close to 1 (rare disease). For skewed measurement error distribution, more outliers are present in the simulation results and standard errors are inflated. Accordingly ratio of the average standard error to Monte Carlo standard deviation is much less than 1 both for RC estimator and for likelihood based estimator.

Coverage proportions of RC and likelihood based estimators are not as good as those in case 3 where measurement error distribution is Gaussian. The standard error is underestimated using the formula derived for skewed measurement error distribution. Naturally due to attenuation effect, the average naive estimate is less than RC estimate. The standard error of naive estimate is more severely underestimated than that of RC and likelihood based estimator.

3.4.5 Conclusions

Naive estimator is biased towards null value. The standard error of naive estimator is subject to underestimation. Regression calibration method and likelihood based model are applicable when the true disease odds ratio is small and when random measurement error is Gaussian. RC estimate and likelihood based estimate show similar performance when true odds ratio is small. For cases with large true disease odds ratio, we reach the following conclusions.

1. Estimation from likelihood based method is close to the true value but standard error is underestimated.
2. RC estimate is worse than likelihood based method and better than naive estimate.
3. Naive estimator is worse in terms of both bias and standard error of estimator.
4. Bias of RC estimate is slightly greater than likelihood based estimate.
5. Coverage proportion of RC estimate is much worse than likelihood based estimate.

For skewed measurement error distribution, we reach the following conclusions.

1. Coverage proportion of these methods are worse, which implies that standard errors face more underestimation than Gaussian cases.
2. Average estimate for these three methods are biased more towards null value than Gaussian cases.
3. Monte Carlo standard errors of RC estimate and likelihood based estimate are greater.
4. Ratio of average standard error to Monte Carlo standard deviation is much less than 1 and close to 0.
5. Monte Carlo standard deviation of the naive estimate is still close to the average standard error and is slightly less than that of the Gaussian case.

This is different from RC estimate and likelihood based estimate since the standard error formulas of RC estimate and likelihood based estimate are derived with Delta theorem but the standard error formula of naive estimate is derived from linear model.
4 Discussion

Regression calibration method is widely used for correcting bias induced by measurement error in nutritional epidemiology. Other methods are not as frequently used. Methods such as SIMEX, EM and MIME require that measurement error variance should be known or can be efficiently estimated. SIMEX and MIME measurement error models are only applicable to random measurement error and do not consider systematic measurement error. Performances of SIMEX and MIME depend upon the ratio of validation sample size to primary study sample size. As the proportion of validated individuals increases, performance of bias-correction is better.

Proper choice of measurement error bias-correction models depends upon data availability in nutritional epidemiology. Methods such as regression calibration, hierarchical models and likelihood-based methods integrate large primary study and small-scale precise validation study to conduct analysis. Bayesian methods require additionally the reliability study to ensure model identifiability. Instrumental variable method considers the situation where a second independent measurement of the same true exposure is available. This method is only applicable to this specific type of data in nutritional epidemiology. In addition, computational feasibility of bias-correction method is also of concern.

More complex correlation structure may be incorporated into measurement error models. Differential measurement error may be considered. Measurement errors in different exposure factors may be correlated. Measurement error may be correlated with disease status. Heteroscedasticity in measurement error is of interest as well.

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