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METHODS

Exposure-measurement error is frequently ignored when interpreting epidemiologic study results

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Abstract. *Introduction:* One important source of error in study results is error in measuring exposures. When interpreting study results, one should consider the impact that exposure-measurement error (EME) might have had on study results. *Methods:* To assess how often this consideration is made and the form it takes, journal articles were randomly sampled from original articles appearing in the *American Journal of Epidemiology* and *Epidemiology* in 2001, and the *International Journal of Epidemiology* between December 2000 and October 2001. *Results:* Twenty-two (39%) of the 57 articles surveyed mentioned nothing about EME. Of the 35 articles that mentioned something about EME, 16 articles described qualitatively the effect EME could have had on study results. Only one study quantified the impact of EME on study results; the investigators used a sensitivity analysis. Few authors discussed the measurement error in their study in any detail. *Conclusions:* Overall, the potential impact of EME on error in epidemiologic study results appears to be ignored frequently in practice.

Key words: Bias, Epidemiologic methods, Measurement error

Introduction

It is a fact of epidemiologic life that all study results have some amount of error, both random and systematic. One important source of systematic error in study results is exposure-measurement error (EME) [1]. Epidemiologic textbooks teach that we should assess the impact of EME when we interpret epidemiologic study results [2–7]. How often is this done in practice? We present a survey of three epidemiologic journals over a one-year period. Our purpose is to examine how epidemiologists account for potential error in study results due to EME.

Methods

One of us (AMJ) read the titles of articles that appeared during a one-year period in the journals *Epidemiology* (2001), *American Journal of Epidemiology* (2001), and *International Journal of Epidemiology* (December 2000 through October 2001). We excluded articles that were obviously methodological, and then took a simple random sample (N = 76) from the 436 remaining articles. We wanted to include in our survey only those articles whose main intent was to examine the relationship between one or more exposures and disease or injury occurrence; 19 articles were excluded because they did not meet this criterion. Fifty-seven articles met our inclusion criteria [8–64].

Each included article was carefully read by one of the authors (AMJ) in its entirety at least three times. Some sections of some articles were read many more times depending on the article's complexity and clarity. Each article was examined for (a) statements that acknowledged the possibility of error in the measurement of any of the study exposures and (b) qualitative or quantitative evaluations of the impact of EME on study results.

Results

Fifty-seven articles were included in our analysis [8–64]. Twenty-two articles (39%, 95% confidence limits (CL): 26, 51) said nothing about EME. Only one of these studies had an exposure (gender) that, in our opinion, could have been measured with a negligible amount of EME (Table 1). The relative risks reported in these studies were not so extreme that the potential effect of EME on study results could be safely ignored with one exception: a measles vaccination study with risk ratios close to zero (Table 1).

Table 1. Study exposures and reported relative risks for articles that ignored exposure-measurement error

Study exposure	Minimum reported relative risk[a]	Geometric mean[a]	Maximum reported relative risk[a]
Race	1.30	2.09	3.10
Alcohol consumption	0.59	0.95	1.58
Husband's occupation, household income, education	0.22	0.88	3.32
Weather	1.03	1.04	1.04
Alcohol consumption	0.48	1.12	2.29
Gender	0.92	1.05	1.29
First degree relatives	1.06	2.35	5.18
Immigration status	0.45	1.03	4.11
Serum triglycerides	0.69	1.77	4.86
Sedentary hours per day, vegetarian diet[b]	–[c]	–[c]	–[c]
Air pollution	0.60[d]	–	1.80[d]
Months since last cervical smear, age (years) at first intercourse[b]	0.10	1.06	4.60
Smoking, chronic hypertension[b]	0.70	1.64	6.28
Use and duration of oral contraceptives[b]	0.41	0.85	2.06
Body mass index, physical activity[b]	0.74	1.14	1.70
Vitamin use	0.28	0.72	1.19
Maternal age at child's birth[e]	0.34	1.17	2.49
Child's birth order, cord blood immunoglobulin E	0.59	1.16	3.10
Vaccination status	0.003	0.01	0.02
Social class	1.03	1.32	1.75
Community type	0.50	1.02	2.10
Month of death[f]	0.77	1.44	2.33

[a]Minimum reported relative risk, geometric mean, and maximum reported relative risk were computed using numerical values only; results reported graphically or in a range were not used.
[b]For articles with many exposures, exposures were selected for which exposure-measurement error is plausible.
[c]Outcome variables were continuous.
[d]Results are range of values abstracted from graphs since these were the only estimates provided.
[e]Data obtained from birth certificates and then categorized.
[f]Data obtained from National Health Service Central Registry for 99.3% of men. For some analyses, death month was categorized into death during winter versus summer.

The other 35 articles (61%, 95% CL: 49, 74) said something about EME (Table 2). Eighteen of these articles (32%, 95% CL: 20, 44) acknowledged EME without discussing the influence EME could have had on study results. Sixteen other articles (28%, 95% CL: 16, 40) described qualitatively the effect EME could have had on study results. One article (2%, 95% CL: 0, 9) used a sensitivity analysis to partially quantify the impact of EME on study results.

Of the 35 articles that said something about EME, seven suggested that EME was nondifferential, although none provided any supporting evidence. Three of these seven articles concluded that, if EME were indeed nondifferential, then the bias in the study results would have been toward the null. Eight out of the 35 articles that acknowledged EME also mentioned that validation or reliability studies had been done either concurrently with the present study or in the past.

Table 2. Classification of journal articles into exposure-measurement error categories from the American Journal of Epidemiology, Epidemiology, and the International Journal of Epidemiology

Category	Journal[a]						Total	
	AJE		EPI		IJE			
	N	%	N	%	N	%	N	%
Acknowledge EME[b]	18	55	12	75	5	63	35	61
Ignore EME	15	45	4	25	3	38	22	39
Total	33	100	16	100	8	100	57	100

[a]AJE = American Journal of Epidemiology, EPI = Epidemiology, IJE = International Journal of Epidemiology.
[b]EME = exposure-measurement error.
Note: Percentages may not add to 100% due to rounding.

Only one article quantitatively evaluated the impact of EME. García Rodríguez and Hernández-Díaz viewed unreported over-the-counter drugs as an EME because only data for recorded prescription drug use was available [47]. The investigators described their sensitivity analysis results in the discussion section.

Our survey results, of course, are not immune to error caused by EME. We performed an uncertainty analysis [65–67] that examined quantitatively the error in our results that may have been caused by errors in classifying articles (Jurek et al., ''Uncertainty Analysis: An Example of its Application to Estimating a Survey Proportion,'' submitted for review). Overall, the uncertainty analysis demonstrated that our results do not change much with plausible amounts of error in classifying articles.

Discussion

In three general epidemiology journals, during 2001, EME was often mentioned but rarely accounted for when interpreting epidemiologic study results. Of the 57 articles we examined in our random survey, one-third made no mention of EME. One-third mentioned the possibility of EME but said nothing about its possible impact on study results. Slightly less than one-third described qualitatively the effect of EME on study results. Only one article out of 57 [47] quantitatively evaluated the impact of EME on study results.

Of the 16 articles that used qualitative evaluation, five did so in a thorough manner [15, 20, 34, 50, 63]: they described scenarios in which bias due to EME could have occurred. For example, one study [63] speculated that the effect of cigarette smoking could have been underestimated because pregnant women may have underreported the amount they smoked. This approach to bias evaluation is certainly worthwhile as a beginning to a quantitative evaluation. A quantitative evaluation, however, has the advantage of estimating the magnitude of the error.

Of the other 11 articles that used a qualitative evaluation, three [21, 53, 62] believed that nondifferential exposure misclassification tends to attenuate the estimate—a ''rule'' that has been common in epidemiologic texts. Three others [39, 56, 59] probably had the same rule in mind, but did not explicitly mention that EME was nondifferential in their study. There are several problems with this rule [68–81]. Five other articles qualitatively evaluated the impact of EME: for example, one [51] said to interpret the study results cautiously, and another [27] dismissed the possibility that EME affected the results.

Finally, the rest of the articles made no mention of EME. We caution against ignoring or dismissing EME, because small percentage EMEs which many authors would dismiss as quite small can have surprisingly large effects on study results. For instance, Maldonado and Greenland [1] show that an exposure measured with perfect sensitivity in cases and noncases and nearly perfect specificity (1.000 in noncases, 0.986 in cases) can make a true odds ratio of 1.03 look like an odds ratio of 1.60.

Conclusions

The fact that EME is frequently ignored when interpreting epidemiologic study results is somewhat surprising. There are alternatives to ignoring or dismissing the effect of EME on study results, or of employing a qualitative evaluation that yields neither an estimate of the magnitude of error nor can be relied on to give the correct direction of the error. These include sensitivity analysis, uncertainty analysis, and Bayesian analysis [2, 65–67, 82–86]. There are many situations in which the use of these methods can improve the informativeness and accuracy of a presentation. We hope that their use will increase as they become a part of the core training of epidemiologists, and as software tools are introduced into analysis packages [85].

Competing interests

The author(s) declare that they have no competing interests.

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