so that the partial derivatives of r with respect to $\underset{\sim}{k}$ are as follows:

$$f_1 = \frac{1}{n}(k_3-k_4)(k_1+k_2+k_3-3k_4)^{-1} - \frac{1}{n}(k_1+k_2+k_3+k_4) \cdot (k_1+k_2+k_3-3k_4)^{-2}\,(k_3-k_4),$$

$$= \frac{4k_4(k_4-k_3)}{n(k_1+k_2+k_3-3k_4)^2}.$$

$f_2 = f_1$, since r is symmetric in k_1 and k_2.

$$f_3 = \frac{1}{n}(k_3-k_4)(k_1+k_2+k_3-3k_4)^{-1} + \frac{1}{n}(k_1+k_2+k_3+k_4) \cdot (k_1+k_2+k_3-3k_4)^{-1} - \frac{1}{n}(k_1+k_2+k_3+k_4)(k_3-k_4) \cdot (k_1+k_2+k_3-3k_4)^{-2},$$

$$= \frac{k_1+k_2+2k_3}{n(k_1+k_2+k_3-3k_4)} - \frac{(k_1+k_2+k_3+k_4)(k_3-k_4)}{n(k_1+k_2+k_3-3k_4)^2}.$$

$$f_4 = \frac{1}{n}(k_3-k_4)(k_1+k_2+k_3-3k_4)^{-1} - \frac{1}{n}(k_1+k_2+k_3+k_4) \cdot (k_1+k_2+k_3-3k_4)^{-1} + \frac{3}{n}(k_1+k_2+k_3+k_4)(k_3-k_4) \cdot (k_1+k_2+k_3-3k_4)^{-2},$$

$$= \frac{-(k_1+k_2+2k_4)}{n(k_1+k_2+k_3-3k_4)} + \frac{3(k_1+k_2+k_3+k_4)(k_3-k_4)}{n(k_1+k_2+k_3-3k_4)^2}.$$

The Use of Misclassification Models in the Evaluation of Caries Clinical Trials: Discussion of Dr. Reed's Presentation

J. D. GOLDBERG

Department of Biomathematical Sciences, Mount Sinai School of Medicine, New York, New York 10029

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I want to thank Dr. Reed for his excellent paper dealing with the use of randomization procedures to compare the incidence of caries in two groups. In the context of the dental clinical trial, Dr. Reed raises many important and interesting aspects of the effects of misclassification on data analysis and inference.

It is interesting to note that the inferences under the two models of caries misclassification studied are similar, as was the case in the earlier work of Reed and McHugh, who used a finite sampling approach for the same problem. Further, the randomization approach and the finite sampling approach yield comparable inferences (see Table). Can some practical guidelines be given for the choice of method of analysis?

I also have several questions which result from my perspective and interest in problems of misclassification. Since the effects of the two error models under study on inference are the same, can Dr. Reed add any perspective on how to choose an error model? As Dr. Reed has pointed out, the lack of "empirical research on the nature of diagnostic error provides little foundation for validating" any of the conceivable misclassification models. The example presented here suggests that both the randomization and the finite sampling procedures are robust with respect to the class of error models considered. Are there ranges of incidence rates or possible error structures which would suggest one model over another?

The example presented raises some additional issues. Each of the error models under study requires several assumptions about the nature of the diagnostic errors. These assumptions can include the requirements that the probability of a misdiagnosis is independent of the true state, and that these probabilities are equal at each time point. From the data presented, no assessment of the appropriateness of assumptions such as these is possible.

While the results of the analysis seem independent of the error model, I am puzzled by the lack of data regarding the error structure. The "false negatives" and "false positives" result from changes in classification from pre-intervention to post-intervention. Evaluation at each of the two time points is required. It is quite possible that the probabilities of false negative and false positive results prior to intervention differ from these probabilities subsequent to intervention. With some standard for evaluation and some attention to study design, error rates can be estimated prior to the study and estimated again at the conclusion of the study. The two types of errors have differing effects on inference, with the false positive rates, in general, producing more serious effects (for prevalence or incidences < 0.5). These errors may also differ among subclasses of individuals based on susceptibility to caries or with observers. Randomization to treatment and control should permit balance here; however, if the errors are different in the comparison groups as well, additional confounding could result. What effects on the randomization procedure would be expected in such circumstances?

In summary, I would reiterate Dr. Reed's conclusion that much remains to be done in the area of assessing misclassification itself in dental caries trials.

TABLE
COMPARISON OF METHODS AND MISCLASSIFICATION MODELS

Estimated Quantity	Method: Randomization		Finite Sampling*	
Model:	C-S	Lu	C-S	Lu
Treatment Incidence	0.36	0.37	0.36	0.37
Control Incidence	0.42	0.43	0.42	0.43
Difference (C-T)	0.06	0.07+	0.06	0.06
S.E. of Difference	0.099	0.100	0.099	0.092

*From Reed & McHugh, 1979.
+Rounding.