Novel Mathematical Models for Investigating Topics in Obesity[1–3]

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ABSTRACT

There is limited insight into the mechanisms, progression, and related comorbidities of obesity through simple modeling tools such as linear regression. Keeping in mind the words of the late George E. P. Box that "all models are wrong, some are useful," this symposium presented 4 useful mathematical models or methodologic refinements. Presenters placed specific emphasis on how these novel models and methodologies can be applied to further our knowledge of the etiology of obesity. *Adv. Nutr. 5: 561–562, 2014.*

Empirical Simulation

The symposium began with a discussion of modeling through empirical simulation of factors that cannot practically or ethically be examined in an experimental setting. Two such factors are assortative mating by BMI, wherein individuals are more likely to couple with an individual with a similar BMI, and differential realized fertility, where the number of children born to women over their lifetime differs by BMI. Because experimental investigation of such topics is not feasible, inference must proceed via building models informed by observational survey data, such as those from the National Longitudinal Survey of Youth. By informing model parameters with and without factors of interest (e.g., a model for birth events that does and does not depend on maternal BMI), instantiations of those models through simulation can be compared to estimate the effect that a given factor may have on an outcome, such as the prevalence of obesity or mean BMI among offspring in the next generation, under a causal model. A more detailed application of this methodology in predicting the propagation of obesity across generations was published by some of the presenters (1).

Predicting Long-term Weight Loss

The forum transitioned to a discussion of prediction of long-term weight loss. It has long been known that individual characteristics such as age, sex, height, initial weight, energy intake, and energy expenditure are crucial components of any weight-loss prediction model. Furthermore, these models need to take into account the continuous changes in energy expenditure in response to weight loss. Dynamic models capture both the individual characteristics and the continual changes in energy expenditure during weight loss. Although the models described by Hall et al. (2) and Thomas et al. (3) differ in their development and term formulation, it was noted that in practice their predictions are generally in agreement. In fact, the model predictions even agree with the first dynamic models developed several decades ago. This convergence of model predictions adds credibility to the use of such methodology as well as a boost to its practical usage. Such models have practical utility for weight-loss goal-setting and monitoring adherence to clinical interventions, and examples were provided to highlight these applications using both diet interventions (4) and obesity pharmacotherapy (5).

A novel application of dynamic models was predicting long-term weight-loss success from observations of short-

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term weight loss. To determine which subjects would be "responders" and lose at least 5% of initial weight within a year, personalized cutoff values of early weight loss that identified responders were computed on the basis of comparison to weight-loss data. Timely identification of individuals not responding to dietary interventions may allow alternate weight-loss strategies to be pursued earlier, reducing participant and health care provider costs and effort.

Separating Out Direct Effects in Nonlinear Regression Models

The symposium concluded with a presentation of how the KHB method, named for Karlson, Holm, and Breen (6), can separate the direct effect from the total effect in mediation in nonlinear regression models. This specific issue is important in the study of observational data with obesity-related outcomes, because epidemiologic work in this area is often focused on teasing apart potential causal roles of measured characteristics in models of whether persons are obese. The method also includes methodology for testing whether the mediation is significantly different from zero. The separation of effects and testing can be constructed for multiple predictors of interest as well as for multiple mediators (confounders), and furthermore, models can incorporate additional concomitant explanatory variables. By using the KHB methodology, researchers interested in mediation analysis can investigate outcome variables that have limited outcomes.

The presentation demonstrated the application and properties of estimators in the usual linear regression setting, and then extended the examples in the logistic regression setting. Mediators and covariates of interest could be continuous or binary: when they are binary, the estimation of the total effect of the variable of interest in a logistic regression setting requires fitting 2 logistic regression models. The initial model from which the direct estimate is obtained adjusts for the covariates of interest, the mediators, and the concomitant variables. This is in comparison to the reduced model, from which the total estimate is obtained, which substitutes residuals for the mediators. Specifically, the residuals are obtained from a linear regression of the mediator on the covariates of interest; note that this is a linear regression even if the mediator is a binary variable. Once the direct and total effect estimates are obtained from the logistic regressions, methods for assessing the difference or ratio were discussed as well as interpretation of the total, direct, and indirect effects. Finally, it was shown how to apportion the indirect effect of a given covariate of interest among the mediators in the model.

Concluding Thoughts

This symposium presented 4 novel mathematical models or methodologic refinements that further our knowledge of the etiology of obesity. Although the applications herein are specific to certain facets of obesity research, other research topics can benefit from similar collaborations between researchers from the mathematical and nutritional communities.

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