An Introduction to Unit-of-Analysis Error

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KEY POINTS . . .

Unit-of-analysis (UoA) errors occur in medical and pharmaceutical intervention studies when clustering based on a unit (e.g., the provider, practice, or health care institution) to which the intervention assigned is ignored in the analysis of individual patient data.

Personal provider characteristics along with interactions between the provider and patient are very likely to influence experimental outcomes.

Studies with UoA errors run the risk of drawing artificially inflated or erroneous conclusions about the true effectiveness of the intervention.

The following article is the fourth in a series highlighting local student chapter activities and research talents. In this piece, we draw attention to an analysis design flaw known as unit-of-analysis error.

What is a Unit-of-Analysis Error?

In epidemiologic research, the unit-of-analysis (UoA) is the "what or whom" being studied. It can be an individual, group of individuals, cluster of individuals, or any aggregated grouping under investigation. For example, a recent study used contract years as the unit of analysis [1]. Growing interest in research assessing provider-level interventions on populations and cluster-randomized designs increases risk of UoA errors in pharmacoeconomic and outcomes research. This issue occurs in medical care studies when individual patient-level observations are used to make conclusions about the effectiveness of a provider's behavior [2]. Intervention studies (e.g., medication therapy management studies) examine a change in the way health care is delivered, such as implementation of patient counseling compared with standard care, with the objective of improving an individual patient's health outcomes. However, statistical analyses may treat patients' data as independent, ignoring the clustering that invariably occurs within providers, practices, or even health care institutions [2]. Personal provider characteristics, coupled with interactions between the provider and patient, are very likely to influence experimental outcomes [1]. An individual provider's ability to influence a patient's health outcomes may vary and cannot be assumed to be interchangeable when evaluating the general effectiveness of the intervention itself.

UoA errors in medical care studies can be identified using 3 criteria, originally described in 1984 by Whiting-O'Keefe [2]:

I. The study design is such that providers cannot be assumed to be interchangeable.
In general, studies test a hypothesis about a broader population in a subset of that population with the objective of drawing inferences about the larger population through statistical analysis. However, there are several assumptions that must hold. First, the subset of the population is a random and independent sample drawn from the large population upon which conclusions will be drawn. However, it is often seen in the type of studies described above that the providers selected for the study are associated with a common group practice or health system, and are treating their own patients. Consequently, these studies are not appropriate to test the hypothesis about the broader population.

> ... if meta-analyses include primary studies with unit-of-analysis, they are at a higher risk of drawing artificially inflated or erroneous conclusions about the estimation of the true effect of the intervention, as they give greater weight to the results of such studies.

II. The study results will be generalized to a larger population of providers, beyond what was actually studied.
It is understood that obtaining a random sample of the population of interest may not be feasible. Therefore, statistical approaches exist to account for this limitation. A simple technique is to modify the hypothesis and use the provider as the unit of analysis rather than the patient. In other words, the outcome for patients under each provider is averaged and applied to the provider as the statistical UoA. This approach comes at a cost since the original study hypothesis must be modified. Statistical power is dramatically decreased since patients often outnumber providers multiplicatively and generalizability may still be limited if

providers are not sampled randomly. The second approach is to retain the original hypothesis but incorporate provider effect, intervention effect, and relevant interaction effects as independent variables. These techniques, designed to control for clustering effects, include hierarchical linear modeling [3] and the use of generalized estimating equations [4]. This approach maintains the patient as the UoA, yet accounts for provider variation. These types of models still require assumptions to be made regarding the distribution, functional form, and sampling of the data; therefore, they should be used cautiously.

III. The error was not accounted for statistically using an approach that appropriately took provider effect and patient-provider interaction effects into consideration.

What are the consequences of failing to account for provider and provider-patient effects at the analysis stage? First, the study results may generate artificially low *P* values. This increases the likelihood of concluding an intervention effect when there is none (i.e., false positives). Conversely, the effect may be the opposite; the resulting *P* value is larger than expected. This can occur when the variation at the patient level is much larger than at the provider level; thus, the power to detect meaningful changes has been lost. A researcher runs the risk of drawing the wrong conclusion about the benefit of the intervention and there is a missed opportunity to estimate an accurate confidence interval (in which the true intervention effect lies).

UoA error is present when all three criteria are confirmed. When evaluating the quality of a primary study about a medical or pharmaceutical intervention for informed decision making, it is important to evaluate whether UoA error is present so that the right conclusions are drawn based on the given hypotheses. Moreover, if meta-analyses include primary studies with UoA, they are at a higher risk of drawing artificially inflated or erroneous conclusions about the estimation of the true effect of the intervention, as they give greater weight to the results of such studies [5].

References

[1] Li P, Doshi JA. Impact of Medicare Advantage Prescription Drug Plan Star Ratings on Enrollment before and after Implementation of Quality-Related Bonus Payments in 2012. PLoS One 2016;11:e0154357. [2] Whiting-O'Keefe QE, Henke C, Simborg DW. Choosing the correct unit of analysis in medical care experiments. Med Care 1984;22:1101-14. [3] Wears RL. Advanced statistics: statistical methods for analyzing cluster and cluster-randomized data. Acad Emerg Med 2002;9:330-41. [4] Hoffmann DA. An overview of the logic and rationale of hierarchical linear models. J Manag Care 1997;23:723-44. [5] Donner A, Piaggio G, Villar J. Statistical methods for the meta-analysis of cluster randomised trials. Stat Methods Med Res 2001;10:235–338. ■