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Understanding the Impact of Design and Analytical Errors in POCT Research

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Errors in POCT Research

Abstract

The purpose of this review is to address the numerous issues surrounding the qualitative and quantitative research designs centered upon point-of-care diagnostic laboratory equipment. In particular, this review will address common errors associated with such research utilizing an existing research publication examining the accuracy of 3 point-of-care devices designed for lipid testing. The article chosen (Gonzales et. al. 2009) has typical common mistakes involving collection, sampling and analysis, which can cause a misleading conclusion.

Introduction

As point-of-care testing (POCT) has become more common in the clinical environment, the number of comparative studies in publication has increased. While POCT comparisons to recognized reference standards are best practice, many authors also have undertaken POCT system comparisons. Such comparisons must be scrutinized for accuracy of both data as well as study design. Additionally, the key reason for ensuring POCT method comparisons are accurately performed is one of validity— the extent to which the interpretations of the results of the study follow from the study itself and the extent to which results may be generalized to other situations with other devices (Ying, 2007). Proper design is critical to external validity—the extent to which findings of a study can be generalized to devices or applications other than those observed in the study (Ying, 2007). To generalize validity, the findings from a sample to a defined reference requires that the sample was drawn according to one of several legitimate probability sampling plans and these plans are applied equivalently throughout each comparative device.

Method Comparison Design

Sampling

As with any diagnostic laboratory device, the adherence to manufacturer collection and sample processing guidelines is paramount to ensure accurate and precise results. Deviating from said guidelines during a research method comparison cannot only result in erroneous results but also be seen as incorporating bias pre-analytically to influence outcome results (Creswell, 2009). Focusing on the lipid comparison article by Gonzales et. al., one can note various and significant deviations from a specified manufacturer's recommendation.

This analysis involved two Accutrend® models manufactured by Roche Diagnostics and one instrument model, the CardioChek® PA, manufactured by Polymer Technology Systems, Inc. Each instrument is designed to measure a patient's fractionated cholesterol via capillary whole blood. Based upon good research design, the samples utilized for POCT instrument to POCT instrument comparison and to the reference method should have uniformly used whole capillary blood.

However, capillary blood was utilized in the two Roche models, while EDTA venous blood, not freshly drawn, was utilized on the CardioChek PA (Gonzales, Marques, & Llanos, 2009). While it was noted that the EDTA venous blood was stored refrigerated, it does not denote if it was stored beyond the 48-hour validity period based upon CLSI guidelines for the storage and testing of EDTA samples for clinical chemistry samples (Gonzales, Marques, & Llanos, 2009).

This is a crucial design flaw as it not only introduces bias, but it also removes the qualitative context of the POCT comparison. As POCT devices are designed for near patient care it is critical that researchers utilize sampling methods that most mimic the device application within the intended healthcare setting (Sittig, 2008). By not utilizing contextual design within the comparison, they reduced the overall generalization of the research, meaning that the conclusions found do not apply to the designed applications of each device. This not only reduces the external validity of the research, but also eliminates internal validity and the validity of the research constructs themselves.

Issues surrounding sampling were further enhanced by the amount of instruments included within the research evaluation. For both models of the Accutrend, two instruments were utilized for testing, while only one instrument was utilized for the CardioChek PA (Gonzales, Marques, & Llanos, 2009). This is important to note, as the article does not mention if data inclusion or exclusion was utilized for the Accutrend models to reach the (n) of 101 and 102. This type of vague sampling disclosure is not discrediting, however it brings about strong questions surrounding the validity of the overall comparison (Bryman, 2006).

Data Exclusion

In general, the majority of researchers base the sample size on the margin of error that can be tolerated or the precision required for estimates (Creswell, 2009). Nevertheless, most survey studies are designed to make a variety of estimates, not just a single estimate. It is also highly improbable that a researcher can specify the acceptable margin of error in advance, but must anticipate a given level of error (Creswell, 2009). To surmise, the sample size decision must be made on a case-by-case basis, considering the variety of goals to be achieved by a particular study and taking into account numerous other aspects of the research design, including data exclusion. To address the exclusion criteria exhibited in Gonzales, Marques and Llanos, 2009), it is apparent that there are gross deviations in these criteria.

The article states that eight specimens were excluded for the Accutrend models comparison to reference serum sample due to hemolysis (Gonzales, Marques, & Llanos, 2009). Being that a cohesive and properly performed method comparison should utilize the same participants and samples, this same exclusion for sample hemolysis was not afforded to the CardioChek PA. Should any gross deviations be isolated to these specified samples, the data reduction obtained would be erroneous and once again, the lack of uniformity in design criteria introduces potential bias. In designing a method comparison for research, inclusion or exclusion criteria can be slanted to induce a particular result even though it is inaccurate based upon the biased sampling methods (Ying, 2007). Should this occur, any presented information for publication could be damaging, even discrediting, to the manufacturer and researcher in addition to rendering the findings non-applicable to the product's intended use.

Accuracy and Precision

The overall goal for method comparisons such as the one being discussed is such that a clear determination can be made as to the overall performance of each device.

This is a key point to address as consumers may base their decision for choosing a POCT platform based upon researcher performed method comparison. Should the study design or the researchers' bias be introduced into the study, the overall findings may be erroneous and can result in the consumer opting for a device that does not meet their overall healthcare application needs (Sittig, 2008). Gonzales, Marques, Llanos et. al., once again exhibits poor study design in this element.

A critical observation is that the study conducted accuracy and precision comparisons using unassayed control material. Unassayed control materials can be used to measure imprecision, but not accuracy. In order to conduct an accuracy study using controls, they must first be assayed to produce instrument specific values. Once these instrument specific values are obtained and a statistically relevant number of runs are performed, then can valid precision and accuracy information be obtained. To delve deeper into precision and accuracy surrounding POCT devices, their application must also be examined to understand the intended clinical value (Sittig, 2008).

The overall healthcare application of point-of-care testing is to provide accurate and reliable results quickly for front line healthcare workers. With this being said, the basis of classification accuracy versus imprecision would have been the most logical choice for statistical evaluation. This is done utilizing a receiver operator curve or, ROC. This method depicts the data in terms relative to risk classification or in this case, comparison based upon reference method results as true/false positives and negatives based upon risk classification. Utilizing this approach based upon obtained patient data, the CardioChek PA was able to stratify patient risk more aptly than both Accutrend models.

Discrepancy Overview

Device	Mfg. Instructions Adhered To	Data Exclusion Performed	Recommended Patient Sample Used for Testing
Accutrend® Plus	Yes	Yes	Yes
Accutrend® GCT	Yes	Yes	Yes
CardioChek® PA	No	No	No

Conclusion

In objective medical device comparison design, the device should be judged based on the purpose and rationale for each application and the sampling strategy used to achieve the study's stated objectives. The validity, meaningfulness, and insights generated from comparison inquiry have more to do with the information richness of the overall design selected and the observational/analytical capabilities of the researcher than with the device itself. That is to say, if the researcher makes no attempt, or only a limited attempt, to ensure that the design is an accurate reflection of the device's application in addition to its proper use. The research introduces bias and potential consumer confusion surrounding performance and application of the devices examined. In conclusion, the article titled "Lipid Profile Ambulatory Patients Using 3 Point-of-Care Devices and Comparison With Reference Methods" exhibits several flaws in design, sampling and excluding factors that could create a biased statistical evaluation favoring the Accutrend systems.

References

1. Bryman, A. (2006). Integrating qualitative and quantitative research: how is it done? Qualitative Research, 24-32.

2. Creswell, J. (2009). Research Design: Qualitative, quantitative and mixed methods approaches. Thousand Oaks, Ca: Sage.

3. Gonzales, Marques, & Llanos. (2009). Lipid Profile in ambulatory Patients Utilizing 3 Point-of-Care Devices and Comparison With Reference Method. Journal of Point of Care Testing, 110-116.

4. Sittig, D. (2008). Grand challenges in clinical decision support. Journal of Biomedical Science, 23-36.

5. Ying, R. (2007). Case study research: Design and methods. New York City: Clearing House.