**The Clinical Laboratory Data Warehouse**

An Overlooked Diamond Mine

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Elevitch and Aller\(^1\) have long emphasized the value of permanently saving an electronic image of clinical laboratory data, and others have illustrated the valuable clinical, operational, and management information that can be derived from these data.\(^2,3\)

It is important to recognize the distinction between a data warehouse and a clinical repository (or electronic medical record). The data warehouse is constituted primarily for retrospective data analysis and contains sophisticated analytic tools, and a response time of 1 to 2 minutes is quite acceptable. The data repository\(^4\) might contain data of an equal volume, variety, and longevity, but it is organized and optimized for pulling together all clinical observations on a patient. Because the data repository is constituted to support patient care, subsecond response time is required. Despite the clinical benefits already obvious a decade ago, health care institutions have been slow to implement repositories.

Altshuler\(^5,6\) emphasized and illustrated the importance of saving and using the data generated from the laboratory database. Regrettably, far too few laboratorians have taken this pioneering work to heart. One encouraging exception has been the laboratory directed by C. Terrance Dolan, MD, in Tulsa, OK. The staff of this laboratory has been building this data warehouse for a decade, and it has been put to several useful applications, which Dr. Dolan has presented at a number of professional meetings. In last month’s *Journal*, Bock et al\(^7\) illustrated yet another valuable by-product of saving your data.

Reference range studies done by more traditional methods include, at most, only a few hundred subjects and typically do not represent well the changing demographics of our patient population. Recruiting “normal” people is only a small part of the problem—a much larger one is the cost of performing all those assays. The days are long past when a laboratory had the “spare” resources to perform hundreds of nonreimbursed assays to establish (or validate) a new reference range.

Transferring reference ranges from one laboratory to another—as most laboratories are forced to do by subject availability and simple economics—runs the risk not only of nonrepresentative demographics but also of clinically different results owing to different methods used by different laboratories.

Interestingly, I have been using a similar (although less elegant) procedure to establish reference ranges in virtually every laboratory I have directed since 1984. Although we did not have as large a warehouse and, therefore, could not establish detailed ranges with specificity equal to that established by Bock et al,\(^7\) we established reference ranges for our 24-test chemistry panels in a community-based laboratory during the late 1980s and for our 25-test chemistry panels in a hospital and community setting during the early 1990s using the “warehouse” patient data accumulated during 2 to 3 years of chemistry panels.

This exercise was simpler in a time when we routinely run much larger numbers (23 or 25) of analytes in a panel. We took a simplistic histogram approach, but the results performed well clinically in both settings. In brief, we selected all panels in the database that were within previously defined reference intervals for all other analytes. We then prepared a histogram for the analyte of interest. Visual examination of this histogram (rather than calculation of 2.5 and 97.5 percentiles) usually made clear the appropriate range. Age- and sex-specific ranges could be derived by preparing the histogram for a subset of the data, but only fairly broad age

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ranges could be studied, because the data set was considerably smaller than that used by Bock et al. Subsequently, we used a similar approach in a university hospital (with a large clinic population) during the mid 1990s and a statewide core laboratory at the turn of the century. I had never published this approach, as I assumed it to be widespread. Therefore, I am delighted to comment on the study by Bock et al, which provided a more rigorous description and evaluation of population-based reference ranges.

In some cases, the article overstates the case for population-based reference values. For example, it is well recognized that alkaline phosphatase values are much higher in teenagers owing to bone growth. Their “historic” values do not show even this rudimentary age correction. Nevertheless, the article represents an important contribution to laboratory practice and should be considered seriously by all with a responsibility for establishing laboratory reference ranges.

An important aspect of the system described by Bock et al is that it defines unique patients. Thus, the particular analyte values for a patient who happened to have a number of chemistry panels within the period of study would not overload the data set. In particular, patients who had more than 3 panels during the period of study were probably clinically ill and would not be a valid choice for a reference specimen.

Bock et al not only describe the definition of a reference range but also validate it by evaluating patient results correlated with physician-supplied diagnosis codes.

There is no shortage of patients capable of serving as reference subjects: in the study by Bock et al, more than 64,000 patients had normal results for all analytes other than glucose and could, therefore, serve as reference subjects.

The omission of glucose for excluding patients from the reference group is an important innovation. I suspect we missed using many validly healthy people in our previous reference range studies because we excluded those with “abnormal” glucose levels.

Detailed quantitative data on many tightly focused age groups have enabled discernment of important age- and sex-related trends (eg, that young males have typically “high” alanine aminotransferase levels and that a “normal” bilirubin level in a woman actually might be pathologically elevated), which have been lost in previous reference range studies that studied a total of only a few hundred people. The new reference ranges will permit dramatic increases in women’s rates (and substantial decreases in men’s rates) of recognized abnormalities in aspartate aminotransferase levels (suggesting that we previously missed some disease in women and overcalled abnormality in men).

Elevated alkaline phosphatase values are expected in teenagers with active bone growth and are appropriately found in the study by Bock et al. On the other end of the age spectrum, I was surprised that they did not find elevations in elderly people. This was a consistent finding in reference ranges we established by such methods during the late 1980s and early 1990s. Were the demographics of southern California that much different from those of Oklahoma?

One perhaps could argue that any one of a number of different statistical methods should have been used. The real take-home message of the article by Bock et al, though, is the use of a large population to establish the reference range, rather than a few dozen or a few hundred healthy people.

Data warehouse-based methods for establishing reference ranges overcome many difficulties. I commend this approach to reference-range establishment to the reader. It is far less expensive than the traditional recruit-volunteers-and-test-them approaches. At the same time, it derives the reference range from a much larger population than would be feasible by traditional methods. It avoids the pitfalls inherent in transferring reference ranges from one laboratory to another with questionably comparable methods and divergent patient populations. It fashions ranges that are better suited to the age and sex of the patient, avoiding false-positive and false-negative results, the latter especially true for women who had reference ranges far lower than “traditional” values. This approach is more cost-effective than traditional “purist” methods—it is both less costly and more effective.

The concept of measuring analytes on a handful of healthy people and then statistically extrapolating to a large patient population should be reserved for only relatively new or rarely performed analytes, for which there has not been time to establish a population-based reference study such as that performed by Bock et al.

The bottom line:
1. All laboratories should ensure that records of all patient testing are preserved in a permanent, machine-readable form—preferably online on an analysis engine. Disk and machine capacities are now so large that insufficient disk space is no longer an acceptable excuse. Of course, if your laboratory information system requires 5,000 bytes to store a single potassium result, it will be necessary to copy all data to a more modern computer (such as a PC) where it can be stored long-term and analyzed. If you have not saved your data, you cannot mine it for outcome studies or for clinical and management applications.
2. Every well-established outpatient-oriented laboratory should pursue the approach used by Bock et al (or a similar population-based method) for defining its reference ranges for common chemistry analytes.

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References