Is This a Critical, Panic, Alarm, Urgent, or Markedly Abnormal Result?

To the Editor:

Medical laboratories often produce clinically unexpected results that require timely clinical evaluation because they herald an imminent life-threatening condition or major clinical deterioration. Laboratories therefore need to proactively identify and report such results sooner than would routinely occur, and have policies and procedures that minimize the possibility of patient harm due to delayed clinical awareness.

Since Lundberg’s first description of so-called panic values (1), a variety of other terms have appeared in the literature, for example: urgent, critical, acute, alert, emergent, abnormal, markedly or significantly abnormal, clinically significant, vital, red-orange-yellow zone values, and various combinations thereof. Most of these definitions are reworded alternatives of Lundberg’s original description (2, 3). Two recent literature reviews emphasize the need for an agreed terminology to assist global harmonization of the laboratory management of such test results (4, 5).

Current definitions focus on the degree of result abnormality, timeliness of communication, and likely patient outcomes (e.g., mortality, morbidity) rather than on the risk to patient safety. Although it is true that unexpected results requiring urgent reporting are often very abnormal, it is not always true that such results represent imminent high risk to patient safety and well-being; examples include high creatinine and chronic elevation of troponin concentrations in stable chronic renal failure and long-term hemodialysis patients, respectively. In our view, categorizing unexpected urgent results on the basis of the magnitude of their abnormality does not allow for individual patients in specific clinical circumstances for whom slightly or moderately abnormal results, or too-rapid normalization of results, suggest impending high risk to their well-being, or for those patients with stable chronic conditions in whom very abnormal results do not pose imminent risk of significant clinical deterioration. Another shortcoming of existing terms is that they often combine results that represent different degrees of risk to patient safety and thus may lead to patient harm due to alert fatigue.

From these considerations, it is clear that none of the currently used terms adequately reflect the core attribute of such results. For example, the most common term, “critical result,” does not identify the characteristic that is critical. In our view, the primary attribute of such results is that they represent high and imminent risk to patient safety and well-being. Therefore we propose a clinically more appropriate terminology that emphasizes the degree of risk to patients.

We propose to differentiate two risk categories. Critical-risk result is defined as results requiring immediate medical attention and action because they indicate a high risk of imminent death or major patient harm (e.g., neonatal hypoglycemia). The other risk category, significant-risk results, labels test results that are less urgent but need to be reported within a shorter timeframe than that for routine results (e.g., positive blood cultures). Significant risk results are defined as results that are not imminently life-threatening, but signify significant risk to patient well-being and therefore require medical attention and follow-up action within a clinically justified time limit. We also propose high-risk results as an appropriate umbrella term for critical and significant risk results.

Introduction of the concept of patient-focused risk in the proposed terminology should encourage laboratories to fundamentally review their criteria for identifying high-risk results, so that alert thresholds are not defined simply by magnitude of abnormality but are set more flexibly and by consideration of relevant patient characteristics, clinical conditions, and the needs of clinical staff. By focusing on patient risk, the proposed terms highlight that the management of such results should be informed by risk assessment processes.

Risk-based definition of results is also expected to reduce alert fatigue and may encourage the development of more flexible and user-friendly automated alert systems. Such an approach will require close consultation with clinical users to identify specific high-risk parameters for specific clinical conditions, patient subgroups, and individual patients. To assist laboratories, a guideline for managing high-risk results is currently being developed by the CLSI. Establishing the criteria for these risk-based and more personalized categories will require close interactions between laboratories and key clinicians as well as future studies to determine their impact on response times and organizational, economic, and patient outcomes.

In summary:

• Immediate high risk to patient well-being is the defining attribute of unexpected test results requiring urgent reporting.
• The level of patient risk determines whether results require immediate or less rapid reporting.
• The proposed terms critical-risk results, significant-risk results, and the umbrella term high-risk...
results provide a harmonized terminology that addresses the shortcomings of currently used terms.

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Biological Variation of Hemoglobin A1c: Consequences for Diagnosing Diabetes Mellitus

To the Editor:

For optimal monitoring and diagnosing of patients with diabetes by use of glycated hemoglobin (Hb A1c) measurements, the analytical CV (CVa) of the Hb A1c assay and the within-person biological variation (CVwp) are of relevance. CVwp refers to an inherent biological variation around an individual patient’s set point of a biological parameter. Several studies have been published assessing the CVwp of Hb A1c (1–3). However, none of those studies used >1 Hb A1c method to determine the CVwp. The aim of this study was to apply 4 different IFCC and National Glycohemoglobin Standardization Program (NGSP) certified secondary reference measurement procedures (SRMPs) using different assay principles and calibrated in SI units (mmol/mol) and Diabetes Control and Complications Trial (DCCT) units (% Hb A1c) to see whether there were differences in the CVwp obtained. In addition, we addressed the consequences for diagnosing diabetes mellitus of the CVwp found.

We recruited 21 presumed healthy hospital employees to participate in the study (11 men and 10 women). Five K3EDTA-treated whole blood samples were collected from each individual every 2 weeks for 2 months. On collection, aliquots of each sample were immediately stored at ~80 °C. Full analysis was performed at the end of the 2-month collection period. The samples were analyzed in a single run in duplicate using the following 4 SRMPs:

• Tina-quant Gen.2 HbA1c on Integra 800, immunoassay, IFCC and NGSP certified (Roche Diagnostics);
• Premier Hb9210, boronate affinity chromatography HPLC, at the time not yet officially certified (Trinity Biotech);
• Tosoh G8, Cation-Exchange HPLC, IFCC certified (Tosoh Bioscience); and
• Ultra2, boronate affinity chromatography HPLC, IFCC and NGSP certified (Trinity Biotech).

All 4 SRMPs have documented good results in the IFCC and NGSP monitoring programs [CV <3.0% in SI units, <2.0% in DCCT units, no bias or a very small bias (±1 mmol/mol) compared to the IFCC primary reference measurement procedure (PRMP)] and were calibrated using the IFCC secondary reference material with assigned IFCC and derived DCCT values.

The data were analyzed using a 2-level nested ANOVA model.