HIGH RISK RESULTS:
The Evidence for Total Serum Calcium Alert Thresholds

WILSON PUNYALACK
Pathology Update 2019, Melbourne
WHAT ARE HIGH RISK RESULTS?

• “High Risk Result” is a collective term;
  • Critical Risk Result: A test result that is life threatening, or indicates significant morbidity or irreversible harm if immediate medical action is not taken
  • Significant Risk Results: A test result that is not life threatening but requires timely medical attention and follow-up action within a medically justified timescale
  • Without timely medical attention, these results are associated with an adverse clinical outcome

• “Panic Value”, George Lundberg (1972)

• Effective communication of these results is from the laboratory to the physician is fundamental to patient safety
  – Accreditation/Regulatory bodies mandate laboratories have a HRR protocol
Is This a Critical, Panic, Alarm, Urgent, or Markedly Abnormal Result?

To the Editor:

White GH, Campbell CA, Horvath AR. Is this a critical, panic, alarm, urgent, or markedly abnormal result? Clinical Chemistry. 2014;60(12):1569-70.

Language has been historically inconsistent. 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 contexts. We 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
INTERNATIONAL SURVEYS

KEY FINDINGS

- Significant heterogeneity in all aspects of HHR reporting and communication protocols
  - Content of alert lists
  - Communication protocol
  - Escalation policies
  - Alert thresholds
  - Evidence used to derive thresholds

This variation represents a significant risk to patient safety
EVIDENCE FOR ALERT THRESHOLDS
SYSTEMATIC REVIEW

CONCLUSION:
“There is a lack of evidence and explicit reasoning in the literature to support the selection of alert thresholds for communicating critical risk laboratory results.”
HARMONISATION

INITIATIVES

AUSTRALASIAN ASSOCIATION OF CLINICAL BIOCHEMISTS INC
5/85 Bourke Rd, Alexandria NSW, 2015
Telephone: +61 2 9669 6600 Facsimile: +61 2 9669 6607 Email: office@aacb.asn.au

Guideline

Title: Consensus Statement for the Management and Communication of High Risk Laboratory Results

Document Number: 2015 GD01
Publication date: May 2015, February 2016
Next review date: May 2020
Owner: AACB/RCPA Critical results working party

• RCPA-AACB Working Party on HRR
• Harmonisation process:
  – Gather/synthesise evidence
  – Consultation with stakeholders (laborators and clinicians)
• Form Best Practice Guidelines /Recommendations to drive and support implementation of policies
  – Requires evidence based on clinical outcome studies (or strongest available evidence)
“Clinicians and laboratorians should all be concerned about the effects of that laboratory test and whether the performance of it was useful for the patient or for the public’s health”, thus stressing the need for an outcomes research agenda.

RCPA AACB HHR WORKING PARTY

- Development of best practice guidelines:

- Six step process was devised by WP for identifying and assessing the suitability of alert thresholds:

  - First step: Review the literature to identify appropriate alert thresholds

OBJECTIVE

PROJECT AIM

• To conduct a **systematic review** to determine the scope of published literature on high risk result thresholds for total serum calcium and to **identify key or seminal papers linking established alert thresholds with clinical outcomes**
  • Complete and comprehensive overview of the evidence

• It is intended the results will assist the harmonisation of calcium HRR alert thresholds by means of **informing** the AACB Working Party on High Risk Results

• Ultimately improve patient outcomes by improving diagnostic accuracy and safety – “**translatable research**”
Calcium.
### Australasian Reference Intervals - Chemical Pathology

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Age</th>
<th>Reference</th>
<th>Interpretation of age (days)</th>
<th>Interpretation of reference (units)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>0d to &lt;1w</td>
<td>(132–147) mmol/L</td>
<td>$0 \leq \delta \leq 6$</td>
<td>$0 \leq \delta \leq 6$ mmol/L</td>
</tr>
<tr>
<td></td>
<td>1w to &lt;18y</td>
<td>(133–144) mmol/L</td>
<td>$7 \leq \delta \leq 6573$</td>
<td>$33 \leq x \leq 144$ mmol/L</td>
</tr>
<tr>
<td></td>
<td>18y to &lt;120y</td>
<td>(135–145) mmol/L</td>
<td>$6574 \leq \delta \leq 43829$</td>
<td>$135 \leq x \leq 145$ mmol/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>0d to &lt;1w</td>
<td>(3.8–6.5) mmol/L</td>
<td>$0 \leq \delta \leq 6$</td>
<td>$3.8 \leq x \leq 6.5$ mmol/L</td>
</tr>
<tr>
<td></td>
<td>1w to &lt;26w</td>
<td>(4.2–6.7) mmol/L</td>
<td>$7 \leq \delta \leq 181$</td>
<td>$4.2 \leq x \leq 6.7$ mmol/L</td>
</tr>
<tr>
<td></td>
<td>26w to &lt;2y</td>
<td>(3.9–5.6) mmol/L</td>
<td>$182 \leq \delta \leq 729$</td>
<td>$3.9 \leq x \leq 5.6$ mmol/L</td>
</tr>
<tr>
<td></td>
<td>2y to &lt;18y</td>
<td>(3.6–5.3) mmol/L</td>
<td>$730 \leq \delta \leq 6573$</td>
<td>$3.6 \leq x \leq 5.3$ mmol/L</td>
</tr>
<tr>
<td></td>
<td>18y to &lt;120y</td>
<td>(3.5–5.2) mmol/L</td>
<td>$6574 \leq \delta \leq 43829$</td>
<td>$3.5 \leq x \leq 5.2$ mmol/L</td>
</tr>
<tr>
<td>Chloride</td>
<td>0d to &lt;1w</td>
<td>(98–115) mmol/L</td>
<td>$0 \leq \delta \leq 6$</td>
<td>$98 \leq x \leq 115$ mmol/L</td>
</tr>
<tr>
<td></td>
<td>1w to &lt;18y</td>
<td>(97–110) mmol/L</td>
<td>$7 \leq \delta \leq 729$</td>
<td>$97 \leq x \leq 110$ mmol/L</td>
</tr>
<tr>
<td></td>
<td>18y to &lt;120y</td>
<td>(95–110) mmol/L</td>
<td>$6574 \leq \delta \leq 43829$</td>
<td>$95 \leq x \leq 110$ mmol/L</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>0d to &lt;1w</td>
<td>(19–25) mmol/L</td>
<td>$0 \leq \delta \leq 6$</td>
<td>$15 \leq x \leq 28$ mmol/L</td>
</tr>
<tr>
<td></td>
<td>1w to &lt;2y</td>
<td>(16–29) mmol/L</td>
<td>$7 \leq \delta \leq 729$</td>
<td>$16 \leq x \leq 29$ mmol/L</td>
</tr>
<tr>
<td></td>
<td>2y to &lt;10y</td>
<td>(17–30) mmol/L</td>
<td>$730 \leq \delta \leq 3651$</td>
<td>$17 \leq x \leq 30$ mmol/L</td>
</tr>
<tr>
<td></td>
<td>10y to &lt;18y</td>
<td>(20–32) mmol/L</td>
<td>$3652 \leq \delta \leq 6573$</td>
<td>$20 \leq x \leq 32$ mmol/L</td>
</tr>
<tr>
<td></td>
<td>18y to &lt;120y</td>
<td>(22–32) mmol/L</td>
<td>$6574 \leq \delta \leq 43829$</td>
<td>$22 \leq x \leq 32$ mmol/L</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0d to &lt;1w</td>
<td>(22–53) mmol/L</td>
<td>$0 \leq \delta \leq 6$</td>
<td>$22 \leq x \leq 93$ mmol/L</td>
</tr>
<tr>
<td></td>
<td>1w to &lt;4w</td>
<td>(17–50) mmol/L</td>
<td>$7 \leq \delta \leq 27$</td>
<td>$17 \leq x \leq 50$ mmol/L</td>
</tr>
<tr>
<td></td>
<td>4w to &lt;2y</td>
<td>(11–35) mmol/L</td>
<td>$28 \leq \delta \leq 729$</td>
<td>$11 \leq x \leq 36$ mmol/L</td>
</tr>
<tr>
<td></td>
<td>2y to &lt;8y</td>
<td>(20–44) mmol/L</td>
<td>$730 \leq \delta \leq 2190$</td>
<td>$20 \leq x \leq 44$ mmol/L</td>
</tr>
<tr>
<td></td>
<td>8y to &lt;12y</td>
<td>(27–58) mmol/L</td>
<td>$2191 \leq \delta \leq 4382$</td>
<td>$27 \leq x \leq 58$ mmol/L</td>
</tr>
</tbody>
</table>

**Calcium**

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Age</th>
<th>Reference</th>
<th>Interpretation of age (days)</th>
<th>Interpretation of reference (units)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0d to &lt;1w</td>
<td>(1.85–2.60) mmol/L</td>
<td>$0 \leq \delta \leq 6$</td>
<td>$1.85 \leq x \leq 2.60$ mmol/L</td>
<td></td>
</tr>
<tr>
<td>1w to &lt;26w</td>
<td>(2.00–2.80) mmol/L</td>
<td>$7 \leq \delta \leq 181$</td>
<td>$2.00 \leq x \leq 2.80$ mmol/L</td>
<td></td>
</tr>
<tr>
<td>26w to &lt;2y</td>
<td>(2.00–2.70) mmol/L</td>
<td>$182 \leq \delta \leq 729$</td>
<td>$2.00 \leq x \leq 2.70$ mmol/L</td>
<td></td>
</tr>
<tr>
<td>2y to &lt;18y</td>
<td>(2.00–2.65) mmol/L</td>
<td>$730 \leq \delta \leq 6573$</td>
<td>$2.00 \leq x \leq 2.65$ mmol/L</td>
<td></td>
</tr>
<tr>
<td>18y to &lt;120y</td>
<td>(2.00–2.60) mmol/L</td>
<td>$6574 \leq \delta \leq 43829$</td>
<td>$2.00 \leq x \leq 2.60$ mmol/L</td>
<td></td>
</tr>
</tbody>
</table>

**Calcium corrected for albumin**

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Age</th>
<th>Reference</th>
<th>Interpretation of age (days)</th>
<th>Interpretation of reference (units)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0d to &lt;1w</td>
<td>(2.00–2.60) mmol/L</td>
<td>$0 \leq \delta \leq 6$</td>
<td>$2.00 \leq x \leq 2.60$ mmol/L</td>
<td></td>
</tr>
<tr>
<td>1w to &lt;26w</td>
<td>(2.00–2.80) mmol/L</td>
<td>$7 \leq \delta \leq 181$</td>
<td>$2.00 \leq x \leq 2.80$ mmol/L</td>
<td></td>
</tr>
<tr>
<td>26w to &lt;2y</td>
<td>(2.00–2.70) mmol/L</td>
<td>$182 \leq \delta \leq 729$</td>
<td>$2.00 \leq x \leq 2.70$ mmol/L</td>
<td></td>
</tr>
<tr>
<td>2y to &lt;18y</td>
<td>(2.00–2.65) mmol/L</td>
<td>$730 \leq \delta \leq 6573$</td>
<td>$2.00 \leq x \leq 2.65$ mmol/L</td>
<td></td>
</tr>
<tr>
<td>18y to &lt;120y</td>
<td>(2.00–2.60) mmol/L</td>
<td>$6574 \leq \delta \leq 43829$</td>
<td>$2.00 \leq x \leq 2.60$ mmol/L</td>
<td></td>
</tr>
</tbody>
</table>

- **18y to <120y:** 2.10 – 2.60 mmol/L
REFERENCE INTERVALS

2017 QAP SURVEY

Due Date: 30/09/2017

Calcium (mmol/L)

YOUR DATA

Result (\(^{\uparrow}\)) for Lower = 2.10 mmol/L
Result (\(^{\uparrow}\)) for Upper = 2.60 mmol/L

Your Method Classification: B 21L 069 A

B Cresolphthalein Complexone - no dialysis
21L Roche Diagnostics Hitachi Modular
069 Roche Diagnostics
A Serum based - analyser specific

Analytical Performance Specifications
0.10 up to 2.50: ±14% > 2.50 mmol/L

Participant No.

No. of Laboratories

<2.34 2.34 2.35 2.36 2.37 2.38 2.39 2.40 2.41 2.42 2.43 2.44 2.45 2.46 2.47 2.48 2.49 2.50 2.51 2.52 2.53 2.54 2.55 2.56 2.57 2.58 2.59 2.60 2.61 2.62 2.63 2.64 2.65 2.66 2.67 2.68 2.69 2.70 2.71 2.72 2.73 2.74 2.75 2.76 2.77 2.78 2.79 2.80 2.81 2.82 2.83 2.84 2.85 2.86

All Results (151)

Median 2.69

Your Method B 21L 069 (3)

Median 2.65

Cresolphthalein Complexone - no dialysis (22)

Median 2.55

Roche Diagnostics Hitachi Modular (5)

Median 2.60

Roche Diagnostics Reagent (54)

Median 2.60

2.10 Target Value
METHOD COMPARISON
LIQUID SERUM CHEMISTRY QAP | COMMUTABLE SAMPLE

• Arsenazo Dye
• NM-BAPTA
• Cresophthalein Complexone

calcium in calcium carbonate; pure, crystalline compound

National Institute of Standards and Technology (NIST), United States
Phone: +1 301 975 6776
Fax: +1 301 948 3730
Email: srminfo@nist.gov
Web: http://www.nist.gov/srm

<table>
<thead>
<tr>
<th>Name of the reference material</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>SRM 915b, Calcium carbonate (Clinical Standard)</td>
<td>Mass fraction</td>
</tr>
<tr>
<td></td>
<td>99.907 %</td>
</tr>
<tr>
<td></td>
<td>0.021 % relative</td>
</tr>
</tbody>
</table>

Reference(s) on commutability
Not applicable: a high-purity material used as a primary calibrator for higher order reference methods

Traceability
SI

CRM listing
List I

This (Certified) Reference Material has been reviewed for compliance with ISO 15194:2003 but not been reviewed against ISO 15194:2009

calcium in human serum

National Institute of Standards and Technology (NIST), United States
Phone: +1 301 975 6776
Fax: +1 301 948 3730
Email: srminfo@nist.gov
Web: http://www.nist.gov/srm

<table>
<thead>
<tr>
<th>Name of the reference material</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>SRM 909b, human serum</td>
<td>Amount-of-substance concentration</td>
</tr>
<tr>
<td></td>
<td>2.218 mmol/l to 3.532 mmol/l</td>
</tr>
<tr>
<td></td>
<td>0.016 mmol/l to 0.028 mmol/l</td>
</tr>
</tbody>
</table>

Traceability
SI

CRM listing
List I

This (Certified) Reference Material has been reviewed for compliance with ISO 15194:2003 but not been reviewed against ISO 15194:2009
CLINICAL UTILITY

HYPOCALCAEMIA & HYPERCALCAEMIA

• A UK survey of 94 laboratories revealed all but one lab did not report a critical limit for calcium

• HYPO Ca: Tetany, Cardiac Arrhythmia, Seizure, Renal failure, hypoparathyroidism, Vitamin D deficiency

• HYPER Ca: Malignancy, hyperparathyroidism

• Ionised Ca & Albumin Adj Ca

Short Report

A survey of laboratory ‘critical (alert) limits’ in the UK

J Tillman and JH Barth on behalf of the ACB National Audit Group

ENDOCRINOLOGY

NALHN Outpatient Service Information, Triage & Referral Guidelines

HYPOCALCAEMIA

• Corrected or ionized serum calcium should be used for accurate assessment.

Australian Clinical Practice Guidelines

Australian Institute of Health Innovation | Wilson Punyalack
Results.
• Medline: 83
• Embase: 142
• Scopus: 49
• Total: 274

• After duplicates excluded: 208

• After title and abstract screened: 48

• Final no# of papers: 5
Lum G.
Evaluation of a laboratory critical limit (alert value) policy for hypercalcemia. Archives of Pathology & Laboratory Medicine. 1996;120(7):633-6

Evaluation of a Laboratory Critical Limit (Alert Value) Policy for Hypercalcemia

Clifford Lum, MD

- **Objective:** To evaluate a laboratory critical limit policy for hypercalcemia requiring the laboratory to notify the physician for any serum calcium level higher than 2.99 mmol/L (12.0 mg/dl).

- **Design:** The protocol was assessed using the following criteria: recognition, treatment (fluids or drugs) on no treatment of hypercalcemia, and the effect of treating lower (2.64 mmol/L) or higher (3.22 mmol/L) calcium critical limits.

- **Results:** Patients were divided into four groups: group 1, 2.64 to 2.74 mmol/L (n = 131); group 2, 2.77 to 2.87 mmol/L (n = 33); group 3, 2.89 to 2.99 mmol/L (n = 16); and group 4, higher than 2.99 mmol/L (n = 11). Hypercalcemia was recognized in 48%, 55%, 56%, and 100% of patients with fluids in 0%, 0%, 1%, and 8%; treated with drugs in 0%, 0%, 0%, and 73%; and not treated in 100%, 100%, 100%, and 0% of patients in groups 1 through 4, respectively. Lower calcium critical limits of 2.64, 2.77, and 2.89 mmol/L would lead to an increase of 1571%, 443%, and 143% in telephone calls. A higher calcium critical limit of 3.22 mmol/L would have resulted in not notifying the physician of six patients (60%) who were treated for hypercalcemia.

- **Conclusions:** The present hypercalcemia policy is effective because patients with calcium levels below 2.99 mmol/L (<1%) are rarely treated for hypercalcemia and because lowering the calcium critical limit alert value would not increase physician awareness of hypercalcemic patients. It would, however, result in a significant increase in telephone calls. A higher calcium critical limit (3.22 mmol/L) would potentially result in missing a significant number of hypercalcemic patients in need of therapy.

> (Arch Pathol Lab Med. 1996;120:633-636)

Hypercalcemia is a fairly common medical problem. An increased serum calcium level may represent a medical emergency that requires immediate patient evaluation. Hypercalcemia can have potentially lethal effects, especially involving the central nervous system (e.g., altered consciousness, confusion, lethargy, stupor, and coma). Because hypercalcemia is often initially identified as a clinically unsuspected laboratory abnormality, high serum calcium levels are commonly included in a listing of laboratory critical limits for which physicians are notified of an extremely abnormal test result.

Clinical laboratories have not established a universally accepted critical limit (alert value) for hypercalcemia. Generally, the hypercalcemia critical limit for physician notification varies between 2.62 and 3.09 mmol/L (10.5-14.0 mg/dl). A national survey of 92 institutions, including 20 trauma centers, found a mean critical limit for hypercalcemia of 3.22 mmol/L (12.9 mg/dl) (standard deviation of ±0.72 mmol/L [<11]) (4). Lower calcium critical limits of 2.64, 2.77, and 2.89 mmol/L would lead to an increase of 1571%, 443%, and 143% in telephone calls. A higher calcium critical limit of 3.22 mmol/L would have resulted in not notifying the physician of six patients (60%) who were treated for hypercalcemia.

METHOD:

- Obtained list of pts w/ ↑ Ca (adults, Ca>2.62); manual comparison of high Ca result to medical records

- 1996 US Study (MA medical centre, 1 year period)

- Effectiveness of high Ca limit:
  - Recognition of hypercalcemia by physician
  - Patient treatment (administration of fluids or drugs)
  - Clinical diagnosis and outcome (mortality)
  - Workload on laboratory (no. of calls)

- Alert threshold 2.99 mmol/L (Upper RI: 2.62)
Objectives | Findings
---|---
Recognition of hypercalcaemia | • No treatment for hypercalcaemia was initiated for patients with Ca between 2.64 to 2.87  
  • 82% of pts with Ca>2.99 mmol were treated for hyperCa  
  • <1% of pts with Ca<2.99 were treated for hyperCa
Clinical Outcome | Malignancy was primary cause, majority of patients had poor outcome
Workload on laboratory | Decreasing limits by 0.10 would increase no of calls by 142%

LIMITATION: Bias, clinicians may be aware of threshold  
CONCLUSION: “adopting a lower limit for HyperCa would mean that the physician would be notified of serum calcium results in patients who may not need therapy”
Evaluation of Total Serum Calcium Critical Values

Joan H. Howanitz, MD; Peter J. Howanitz, MD

Context.—As a patient safety measure, laboratories are required by regulatory agencies to have a critical values policy. Total serum calcium commonly is included in critical values lists; however, a wide range of values are used and there is scant outcome data justifying inclusion of this analyte in these lists.

Objective.—To evaluate the appropriateness of the critical values for total serum calcium used in our institution.

Design.—We studied all critical total serum calcium results found during a 3-month period. The patients’ medical records were evaluated for the presence of documented critical results call for calcium, clinician response, and patient outcome. The patients’ outcomes were measured by time of clinical response, length of stay in the hospital, and mortality.

Results.—There were 722 (1.4%) critical results found in a total of 50,402 total serum calcium results. Using our criteria of 7 mg/dL or less as the low and 12 mg/dL or more as the high critical value, we found 171 patients with 688 critically low results and 47 patients with 114 critically high results. Eighty percent of patients with critically low results and 75% of patients with critically high results had length of stays greater than our average (3.5 days). Clinicians responded to 49% of the critical results calls within 4 hours. There was an overall mortality rate of greater than 25%, with more than half the mortality occurring in patients who had results within 0.5 mg/dL of the cutoff values used.

Conclusion.—Although broadening critical values limits would reduce required calls, this does not appear warranted. The disease severity of the patients as measured by length of stay and mortality, as well as the rapidity with which patients were treated, indicate that the current limits are appropriate and should not be widened.

(Arch Pathol Lab Med. 2006;130:828–830)

METHOD:

• Prospective study over 3 months
• Analysis of eMR for those patients with flagged results

• US study, conducted at the University Hospital of Brooklyn, NY
• Evaluate the appropriateness of critical values used for Ca at their institution
• Appropriateness defined by:
  • Diagnosis/clinical outcome
  • Clinician response
  • Patient length of stay
  • Workload on laboratories (length of call)
• Alert Thresholds (mmol/L): L-1.75 H- 3.0

N= 772 (1.4% of all reported Ca results), 608 L 114 H

<table>
<thead>
<tr>
<th>Objectives</th>
<th>Findings</th>
</tr>
</thead>
</table>
| Diagnosis/Clinical Outcome          | **Most common:**  
  • HYPO – Renal Failure (32), Trauma (27) and Gastrointestinal disorders (23)  
  • HYPER – Hyperparathyroidism (13), renal failure (12), malignancy (10)  
  **Mortality rate:** Hypo: 27% Hyper: 19% (died during stay)  |
| Clinician Response                  | (Response = Reordering Total Serum Ca, iCa or directly treating — calcaemia)  
  • Hypo: 45% treated within 4 hrs  
  • Hyper: 50% treated within 4 hrs  |
| Length of stay (>6 days)            | • Hypo: 80%  
  • Hyper: 75%  |
| Workload on laboratories (calls)    | Inpatient: 6.1 min (mean)  
  Outpatient: 13.7 min (mean) OR approx. 80hrs over a 3 month period |

**CONCLUSION:** “both high and low critical serum total calcium results were associated with prolonged LOS and high mortality…Although calling these results represents considerable work, it does not appear warranted to broaden the critical total serum calcium limits when considering the seriousness of disease in our patients”
Derivation of Outcome-Based Pediatric Critical Values

Hao Du, Corey Markus, MSc, Michael Metz, MD, Mengling Feng, PhD, and Tze Ping Loh, MBBS,BAO

From 'Saw Swee Hock School of Public Health and 1Biomedical Institute for Global Health Research and Technology, National University of Singapore, Singapore; 2Division of Chemical Pathology, SA Pathology, Women’s and Children’s Hospital, South Australia, Australia; 3School of Paediatrics and Reproductive Health, University of Adelaide, South Australia, Australia; and 4Department of Laboratory Medicine, National University Health System, Singapore.

ABSTRACT

Objectives: There is currently a lack of an outcome-based definition of critical values for the pediatric population. This has contributed to a highly heterogeneous critical value reporting practice between laboratories.

Methods: Anonymized results were extracted from a laboratory information system for 10 biochemistry tests. The probability of high-dependency/intensive care unit admission (as a proxy for adverse outcomes) for each individual lab result was calculated. A critical (or panic) laboratory value is a laboratory test result that represents a pathophysiologic state at such variance with normal as to be life-threatening if an action is not taken quickly and for which an effective action is possible. From a more operational perspective, they are also defined as laboratory results that are associated with 90% probability of death if left untreated. The laboratory practice of critical value reporting is highly heterogeneous. A Canadian survey on pediatric critical value reporting found that the thresholds differ significantly between laboratories. For example, the lower critical threshold of potassium varied from 2.4 to 3.5 mmol/L. Moreover, the cut-off of sodium was even more variable, ranging from 125.0 to 145.0 mmol/L. In the current study, we propose a novel approach to derive outcome-based pediatric critical values.

METHOD:

- Data for 10 biochemistry tests extracted (mined) for from LIS 2011-2017: 235,890 records
- Examined all patient results 24hrs prior to admission to ward
- Identified patients who were admitted to HDU/ICU vs General Paed Ward
- Bayesian theorem statistics applied

• AU/SG study, Women’s and Children’s Hospital (SA)
• Paediatric population
• Obj: Derive outcome-based critical values using probability/data science

Objectives | Findings
---|---
Probability of high dependency/ICU admission (proxy for adverse clinical outcome) | Hypocalcaemia, total calcium: 1.94 mmol/L
Thresholds determined in study agreed well with existing limits

LIMITATION: Retrospective study. The results are subject to confounders such as intervening medical treatment

CONCLUSION: Useful preliminary data that requires further validation using larger data sets

Graph used with permission

- Spanish study involving a network of laboratories part of the Catalan Health Institute (10 Hospitals and medical centres)
- Sought to establish consensual standards regarding critical results

**METHOD:**

- Delphi online methodology, “real-time Delphi”, interactive questionnaire
  - Physicians asked to select what they considered to be appropriate L and H limits from 6 options
  - Once selected, participants were able to view other participant responses
  - 2nd round of voting; physicians allowed to change vote
  - Consensus measured by size of IQR
Objectives | Findings
--- | ---
Establishing consensus for alert thresholds INPATIENTS | Inpatients limits (mmol/L): Low: 1.2-1.9, High: 3.1 – 3.5
Inpatients: A high level of consensus was achieved in the initial round. This did not change for the final round
L: 1.5 H: 3.2

Establishing consensus for alert thresholds OUTPATIENTS | Outpatient limits (mmol/L) Low: 1.5 – 1.9 High: 3.0 – 3.3
Outpatients: Upper limit only displayed medium-low level consensus. It was noted that if only GP responses where considered, there was a high degree of consensus. This variance may be due to the inclusion of physicians from a diverse range of specialities, who are more orientated to the diseases they treat in their own specialties.
L: 1.7 H: 3.1

LIMITATION: Physician demographic
CONCLUSION: “The real effectiveness of communication of critical results in terms of morbidity and mortality should be studied and could be the point of… further studies”
SUMMARY
AND FUTURE INITIATIVES

• Observations:
  • Studies revealed that existing thresholds used were appropriate
  • Use of **expert opinion** as basis of establishing limits
    • Clinician involvement important
  • Use of **data mining** techniques becoming more prevalent

• Quality appraisal of studies

• CONCLUSION:
  • Harmonisation of terminology
  • Analytical methods
  • Development of Best Practice Guideline
Thank you.