Society of Critical Care Medicine Guidelines on Glycemic Control for Critically Ill Children and Adults 2024: Executive Summary

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Hyperglycemia is common in critically ill patients, is a marker for severity of illness, and may contribute directly to morbidity or mortality. Intensive insulin therapy (INT) had been shown to influence mortality and morbidity outcomes in specific research settings with early dextrose/nutritional support, but benefits are difficult to achieve in most clinical settings without significant risk of hypoglycemia and associated complications. Current consensus guidelines suggest targeting a moderate or conventional glucose control (CONV) level of glycemia to avoid extremes and minimize glycemic variability, excessive workload, and ensure consistent utilization (1, 2). This guideline addresses the clinical equipoise regarding target glucose levels for critically ill adult and pediatric (defined as ≥ 42 wk adjusted gestational age) patients, along with monitoring frequency and methods (3). Neonatal patients were excluded due to their fundamental differences in physiology, nutrition, and inadequate expertise within the guideline taskforce. This executive summary describes key points from the full guideline document. Further, this guideline is an update of the 2012 guidelines for insulin infusion therapy (4).

We convened a taskforce consisting of 22 members: 19 experts in adult and pediatric critical care, endocrinology, pharmacy, advanced practice providers, one methodologist from the Guidelines in Intensive Care Development and Evaluation group, and two patient/family members. The panel generated a series of clinical questions, identified and rated outcomes based on perceived importance to patients, performed systematic reviews of literature from January 2000 to January 2023, and generated a series of statements using The Grading of Recommendations, Assessment, Development, and Evaluation methodology. The parameters that define our comparison groups were discussed extensively, as the published range for INT insulin targets varies from 4.4 to as much as 8.3 mmol/L (80–150 mg/dL) and CONV varies from 7.8 to 12 mmol/L (140–215 mg/dL). The ranges reported were inclusive of a majority of applicable literature. Studies that did not compare these target ranges in critically ill patients were excluded.

Where evidence was inadequate, we made "in our practice" statements reflecting panel practices or "good practice" statements, which are considered equivalent to a strong recommendation. Recommendations are generally presented for adult or pediatric populations, but some were applicable to both. Subpopulations (e.g., medical, surgical, neurologic, trauma, etc.) were evaluated and analyzed when data were available.

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This executive summary provides an overview of several key recommendations, but the full document should be read for the complete recommendations and detailed evidence and justification (3). Key guideline statements for both adults and children are summarized in **Table 1** and compared with a previous related guideline on the use of an insulin infusion for management of hyperglycemia in critically ill patients (4).

KEY RECOMMENDATIONS

Adult Target

Question: Should insulin infusion therapy be titrated to achieve INT glucose levels, 4.4–7.7 mmol/L (80–139 mg/dL) or CONV glucose levels, 7.8–11.1 mmol/L (140–200 mg/dL) for unselected (mixed) critically ill adults or any patient subgroups?

Good Practice Statement: Clinicians should use glycemic management protocols and procedures that demonstrate a low risk of hypoglycemia among critically ill adults and should treat hypoglycemia without delay.

Recommendation: Based on available randomized controlled trial (RCT) data, in critically ill adults, we suggest against titrating an insulin infusion to a lower blood glucose (BG) target INT, 4.4–7.7 mmol/L (80–139 mg/dL) as compared with a higher BG target range, CONV 7.8–11.1 mmol/L (140–200 mg/dL) to reduce the risk of hypoglycemia (Conditional recommendation; moderate certainty of evidence).

Comments

- Analysis of data from neurologic or cardiac surgery ICUs yielded comparable findings and these patients should be managed like unselected patients.
- For other specific subsets of critically ill patients (e.g., cardiac, medical, surgical, trauma, etc.) data were inadequate to perform subgroup analyses and thus patients should be managed like unselected patients.
- For the subset of patients with preexisting diabetes mellitus (DM) or preadmission hyperglycemia there is insufficient evidence from RCTs to make a recommendation regarding personalized targets for glycemic control.

Research Statement: Observational data suggest a potential benefit of personalized glucose targets that more closely match chronic prehospital glycemic control. We recommend high-quality interventional trials of individualized glycemic targets in critically ill adults, stratified by prior glycemic control (such as indicated by glycosylated hemoglobin).

Rationale. Clinical benefits of INT have not been consistently demonstrated in the RCTs included in our meta-analysis; specifically no effect is shown on mortality among mixed populations of ICU patients. However, INT targets were associated with increased frequency of severe hypoglycemia, less than 2.2 mmol/L (40 mg/dL) compared with CONV targets, although there was a reduced infection risk, and lower ICU length of stay (LOS) with INT vs. CONV targets (5–42). In neurologic and cardiac surgery subsets, INT targets were associated with increased risk of severe hypoglycemia and although the cardiac surgery subset had a lower ICU mortality and lower critical illness polyneuropathy (both from a single clinical trial) there were no other outcome benefits (hospital mortality, any infection) (5, 25–31, 40–44).

A large RCT of insulin infusion targeting tight glucose control without early parenteral nutrition (TGC-Fast) comparing insulin titrated to INT vs. a higher target than the CONV range in this guideline, 10–11.9 mmol/L (180–215 mg/dL) was published after our literature review but similarly found no difference in outcomes (time to discharge alive from ICU or 90-d mortality) despite low rates of hypoglycemia in both groups (45). As a result, the upper limit for a glycemic target with insulin infusion is not well defined with current literature. Further, it appears that lower targets may be acceptable for selected patients if the risk of hypoglycemia is documented to be negligible when using a safe and effective protocol. Although observational data suggest a potential role for personalized glucose targets relative to a history of DM, the TGC-Fast trial showed no benefit of INT targets despite 80% of the patients having no history of DM (45–53). The panel recommends prospective randomized clinical trials using individualized targets for insulin titration, which will inform the need to revise this recommendation in the future.

Pediatric Target

Question: Should insulin therapy be titrated to achieve INT glucose levels, 4.4–7.7 mmol/L (80–139 mg/dL) or CONV glucose levels, 7.8–11.1 mmol/L (140–200 mg/dL) for unselected (mixed) critically ill children?

TABLE 1.
Comparison of the Current Guideline Statements With the Previously Published Guidelines (3, 4)

2012 Statements	2024 Statements
Adults	
In adult critically ill patients, we suggest that a BG ≥ 150 mg/dL should trigger initiation of insulin therapy, titrated to keep BG < 150 mg/dL for most adult ICU patients and to maintain BG values absolutely <180 mg/dL using a protocol that achieves a low rate of hypoglycemia (BG ≤ 70 mg/dL) despite limited impact on patient mortality. (Quality of evidence: very low).	Based on available randomized controlled trial data, in critically ill adults, we "suggest against" titrating an insulin infusion to a lower BG target INT: 4.4–7.7 mmol/L (80–139 mg/dL) as compared with a higher BG target range, CONV: 7.8–11.1 mmol/L (140–200 mg/dL) to reduce the risk of hypoglycemia (Conditional recommendation; moderate certainty of evidence). Observational data suggest a potential benefit of personalized glucose targets that more closely match chronic prehospital glycemic control. We recommend high-quality interventional trials of individualized glycemic targets in critically ill adults, stratified by prior glycemic control (such as indicated by glycosylated hemoglobin) (research statement).
We suggest that ICUs develop a protocolized approach to manage glucose control. Components include a validated insulin administration protocol, appropriate staffing resources, use of accurate monitoring technologies, and a robust data platform to monitor protocol performance and clinical outcome measures. A standard insulin infusion protocol should include a requirement for continuous glucose intake, standardized IV insulin infusion preparation, a dosing format requiring minimal bedside decision-making, frequent BG monitoring, provisions for dextrose replacement if feedings are interrupted, and protocolized dextrose dosing for prompt treatment of hypoglycemia (Quality of evidence: very low).	We "suggest" use of a protocol that includes explicit decision support tools (tools) over a protocol with no such tools in critically ill adults receiving IV insulin infusions for the management of hyperglycemia (conditional recommendation, moderate certainty evidence).
Pediatrics	
In the absence of compelling data, no recommendation could be made for or against the use of tight glycemic control in pediatric critical care patients.	We "recommend against" INT BG control, 4.4–7.7 mmol/L (80–139 mg/dL) as compared with CONV BG control, 7.8–11.1 mmol/L (140–200 mg/dL) in critically ill children (strong recommendation, moderate certainty evidence).
New recommendation.	We "suggest" use of explicit decision support tools over no such tools in critically ill pediatric patients receiving IV insulin infusions for the management of hyperglycemia (conditional recommendation; very low certainty evidence). We strongly recommend high-quality research on the use of explicit decision support tools for insulin infusion titration in pediatric patients (research statement).

BG = blood glucose, CONV = conventional glucose control, INT = intensive insulin therapy.
International System of Units to conventional unit conversion for glucose: 1 mmol/L × 18 = mg/dL.

Good Practice Statement: Clinicians should use glycemic management protocols and procedures that demonstrate a low risk of hypoglycemia among critically ill children and should treat hypoglycemia without delay.

Recommendation: We recommend against INT BG control, 4.4–7.7 mmol/L (80–139 mg/dL) as compared with CONV BG control, 7.8–11.1 mmol/L (140–200 mg/dL) in critically ill children (defined by

the pediatric panel as ≥ 42 wk adjusted gestational age) (strong recommendation, moderate certainty evidence).

Rationale. INT targets were associated with increased frequency of severe hypoglycemia (< 2.2 mmol/L [40 mg/dL]), shorter ICU LOS, but no effect on mortality or neurocognitive outcomes among mixed ICU and postcardiac surgery patients (54–62). The high risk of severe hypoglycemia outweighs the trivial clinical benefits of INT glucose control among critically ill children. The impact of hypoglycemia on cognitive development is a special consideration in children. While RCT data were prioritized for this guideline, observational data suggest poorer cognitive performance among children with moderate or severe hypoglycemia events, lending additional importance to hypoglycemia avoidance (54, 57, 63, 64). Like the adult population, the panel recommends prospective randomized clinical trials using individualized targets based on preexisting glycemic control to inform future practice changes.

Question: In critically ill adults and children on insulin infusion therapy, should a protocol that includes explicit decision support tools be used compared with conventional protocols for the management of hyperglycemia?

Recommendations. We suggest use of a protocol that includes explicit decision support tools (tools) over a protocol with no such tools in critically ill adults receiving IV insulin infusions for the management of hyperglycemia (conditional recommendation, moderate certainty evidence).

We suggest use of explicit decision support tools over no such tools in critically ill pediatric patients receiving IV insulin infusions for the management of hyperglycemia (conditional recommendation; very low certainty evidence).

Rationale. We defined those elements of explicit clinical decision support tools that were critical components of acceptable protocols, preferably with computerized support and interoperability of the tool with the electronic health record. While patient outcomes were prioritized for this guideline, the panel acknowledges that insulin titration protocols add to bedside caregiver cognitive burden and workload and could be minimized with a well-designed explicit decision support tool that directs treatment (65, 66). Protocols incorporating these tools were associated with reduced frequency of moderate hypoglycemia less than 3.3 mmol/L (60 mg/dL) and greater proportion of BG values within the target range (45, 50, 67–76). There were no effects on other critical outcomes such as hospital mortality or ICU LOS (moderate certainty), ICU mortality or quality of life at 90 days (low certainty). The TGC-Fast trial of INT vs. a glucose target of 10–11.9 mmol/L (180–215 mg/dL) used a computer algorithm integrated into the electronic health record with alerts to guide insulin dosing and monitoring intervals of 1–4 hours (45). With these components, a low rate of hypoglycemia was reported in this multicenter trial of adults in both INT and higher target groups. While most other studies evaluated adult protocols it was determined that the processes of glycemic management are comparable between adults and children, leading to comparable statements and endorsement of the need for high-quality interventional trials in both age groups.

CONCLUSIONS

Guidelines are limited by the quality of published data in RCTs and additional research on various aspects of glycemic control is needed. Key guideline statements are summarized in this executive summary but there is significant additional detail in the full document regarding hyperglycemic triggers, route of insulin administration, frequency of glucose monitoring, and monitoring devices (3). Clinicians should also examine the complete explanation of rationale and evidence to recommendation discussions to gain insight into strengths and weaknesses of existing data when considering how to incorporate guidelines into clinical practice.

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