diuresis and is associated with dysfunction of the endothelial glycocalyx, inflammation, and possibly mortality, especially in nondiabetic patients (9–11). The American Diabetes Association (ADA) and American Association of Clinical Endocrinology (AACE) similarly recommend initiation of insulin infusion therapy for critically ill adults with persistent severe hyperglycemia (≥ 10 mmol/L on two occasions [> 180 mg/dL]) (5, 6), although no trials indicate a specific, harmful value. Patients with persistent hyperglycemia may also warrant alteration of fluids, nutrition, or medications causing hyperglycemia. The U.S. Centers for Medicare and Medicaid Services has quality measures for hospital-acquired events to measure and report the rate of adults with one BG greater than or equal to 16.7 mmol/L (300 mg/dL) or multiple BG greater than or equal to 11.1 mmol/L (200 mg/dL) also for severe hypoglycemia (< 2.2 mmol/L [40 mg/dL]) plus criteria for failure to monitor adequately (12, 13).

2. Should Insulin Infusion Therapy Be Titrated to Achieve INT BG Targets, 4.4–7.7 mmol/L (80–139 mg/dL) or CONV, 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 RCT 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).

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 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 A1c [HbA_1C]).

Rationale.

Evidence summary. Forty-four RCTs compared insulin infusion targets of INT to CONV among mixed populations of ICU patients. There was no impact on hospital mortality (23 RCTs [1, 14–35]; relative risk [RR], 0.91; 95% CI, 0.8–1.02; moderate certainty) or ICU mortality (18 RCTs [1, 2, 14–16, 18, 20–24, 27–29, 36–39]; RR, 0.97; 95% CI, 0.91–1.03; high certainty). Targeting INT was associated with lower ICU length of stay (LOS, 25 studies [1, 2, 14–16, 18–20, 23–29, 31–35, 38, 40–43]; mean difference [MD], –0.48; 95% CI, –0.82 to –0.14; low certainty), reduced infection risk (24 studies [1, 2, 14, 16, 18–20, 22, 24–27, 29–31, 37, 38, 40, 42, 44–48]; RR, 0.79; 95% CI, 0.68–0.91; moderate certainty), and increased frequency of severe hypoglycemia (< 2.2 mmol/L) (29 RCTs [1, 2, 14–28, 35–38, 40–43, 45–47, 49]; RR, 3.75; 95% CI, 2.38–5.9; high certainty). Although INT improved neurologic outcomes in six studies (26, 27, 31, 45, 50, 51) and reduced critical illness polyneuropathy in two (1, 52), all had serious risk of bias (SDC 9-2, http://links.lww.com/CCM/H476).

Two subset groups had adequate data for meta-analysis. Among neurologic ICU patients, INT increased severe hypoglycemia (six RCTs [26, 27, 38, 46, 50, 51]; RR, 2.17; 95% CI, 0.88–5.32; high certainty) but had no effect on other clinically important outcomes (SDC 9-2, http://links.lww.com/CCM/H476). In cardiac surgery patients, INT reduced ICU mortality (two RCTs [28, 52]; RR, 0.43; 95% CI, 0.21–0.87), but this finding was extensively driven by one RCT (52). Severe hypoglycemia was however increased by INT targets (five RCTs [28, 35, 42, 47, 52]; RR, 4.0; 95% CI, 1.38–11.61; high certainty). There were no effects on other clinically important outcomes (SDC 9-2, http://links.lww.com/CCM/H476).

For other specific patient subsets (medical or surgical ICU, trauma, cardiac, etc.), data were inadequate to perform subgroup analyses. INT had a potential signal for increased mortality among patients with prior DM (six RCTs [1, 2, 15, 16, 18, 22]; RR, 1.12; 95% CI, 0.97–1.29), but not in those without DM (five RCTs [1, 2, 15, 16, 22]; RR, 0.97; 95% CI, 0.79–1.18);