# ACP Releases Guideline on Intensive Insulin Therapy in Hospitalized Patients

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**Guideline source:** American College of Physicians

**Evidence rating system used?** Yes

**Literature search described?** Yes

**Guideline developed by participants without relevant financial ties to industry?** Yes

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Hyperglycemia is a common condition in medical and surgical patients during hospital admission, with a prevalence of approximately 40 percent. It is linked to poor immune response, increased cardiovascular events, and thrombosis, among other problems. Uncontrolled hyperglycemia is associated with increased morbidity, mortality, and costs. Achieving tight glycemic control in hospitalized patients often involves intensive insulin protocols. Intensive insulin therapy is defined as the use of intravenous insulin to meet target blood glucose levels with frequent glucose testing and adjustment of insulin doses. In the intensive care unit (ICU) setting, the usual target range for blood glucose (normoglycemia) is 80 to 110 mg per dL (4.4 to 6.1 mmol per L). In non-ICU settings, target glucose levels vary, ranging from 80 to 110 mg per dL to less than 200 mg per dL (11.1 mmol per L).

The American College of Physicians (ACP) has issued a clinical guideline on the use of intensive insulin therapy in hospitalized patients with or without diabetes mellitus to achieve glycemic control and improve health outcomes. Most of the studies evaluated in the literature search focused on patients in the medical intensive care unit (MICU) and surgical intensive care unit (SICU).

*Recommendation 1: Intensive insulin therapy should not be used to strictly control blood glucose in non-SICU/MICU patients with or without diabetes (strong recommendation; moderate-quality evidence).* Available evidence showed no reduction in mortality with a target blood glucose level of 80 to 180 mg per dL (4.4 to 10.0 mmol per L) compared with a higher or unspecified target. Studies found in the literature review used a variety of intensive insulin therapy regimens in patients with myocardial infarction, stroke, or acute brain injury, or in patients under perioperative care. Harms were more likely to occur at lower target levels; therefore, target levels less than 140 mg per dL (7.8 mmol per L) should be avoided. The effects of hypoglycemia in hospitalized patients are unclear, although there is some evidence for increased mortality or extended length of stay in patients who have one or more episode of hypoglycemia. Some studies found that hypoglycemia is associated with an increased risk of dementia in patients with type 2 diabetes, and that hypoglycemia may induce transient ischemia and catecholamine surges. There is no optimal target blood glucose level in non-SICU/MICU patients because studies found that intensive insulin therapy was associated with an increased risk of hypoglycemia, with no differences in mortality at any specific target level.

*Recommendation 2: Intensive insulin therapy should not be used to normalize blood glucose in SICU/MICU patients with or without diabetes (strong recommendation; high-quality evidence).* No mortality benefit was found using intensive insulin therapy to achieve normoglycemia. Some studies showed an increase in mortality associated with intensive insulin therapy and ▶

hypoglycemia. Data were inconclusive on the association between intensive insulin therapy targeted to normoglycemia and the length of stay in the ICU.

*Recommendation 3: A target blood glucose level of 140 to 200 mg per dL (7.8 to 11.1 mmol per L) is recommended if insulin therapy is used in SICU/MICU patients (weak recommendation; moderate-quality evidence).* Because poorly controlled hyperglycemia is associated with increased morbidity and mortality, and worse health outcomes in ICU patients, a target blood glucose level of 140 to 200 mg per dL is appropriate. Insulin therapy targeted to this range is associated with similar mortality outcomes and a lower risk of hypoglycemia compared with therapy targeted to 80 to 110 mg per dL. There is not enough evidence to determine whether blood glucose levels of 180 to 200 mg per dL (10.0 to 11.1 mmol per L) are associated with outcomes similar to those of lower target levels. Hypoglycemia was observed in studies using a range of target levels, although the risk was higher when lower target values were used. Achieving glucose targets with low rates of hypoglycemia may be associated with titration characteristics of the protocol, patient characteristics, staffing ratios, and physician acceptance. Quality improvement and training initiatives should be incorporated in hospitals to achieve target glucose levels while minimizing rates of hypoglycemia in ICU patients. ■

### Answers to This Issue's CME Quiz

**Q1.** E
**Q2.** A, B, D
**Q3.** A
**Q4.** A, B, C
**Q5.** A, C
**Q6.** B
**Q7.** C
**Q8.** A, B, C
**Q9.** C
**Q10.** B
**Q11.** A, B, C, D
**Q12.** A, B, C

### GLOSSARY OF EVIDENCE-BASED MEDICINE AND STATISTICAL TERMS

| *Term* | *Abbreviation* | *Definition* |
|---|---|---|
| Sensitivity | Sn | Percentage of patients with disease who have a positive test for the disease in question |
| Specificity | Sp | Percentage of patients without disease who have a negative test for the disease in question |
| Predictive value (positive and negative) | PV+<br>PV- | Percentage of patients with a positive or negative test for a disease who do or do not have the disease in question |
| Pretest probability | | Probability of disease before a test is performed |
| Post-test probability | | Probability of disease after a test is performed |
| Likelihood ratio | LR | LR >1 indicates an increased likelihood of disease, LR <1 indicates a decreased likelihood of disease. The most helpful tests generally have a ratio of less than 0.2 or greater than 5. |
| Relative risk reduction | RRR | The percentage difference in risk or outcomes between treatment and control groups. Example: if mortality is 30 percent in controls and 20 percent with treatment, RRR is (30 - 20)/30 = 33 percent. |
| Absolute risk reduction | ARR | The arithmetic difference in risk or outcomes between treatment and control groups. Example: if mortality is 30 percent in controls and 20 percent with treatment, ARR is 30 - 20 = 10 percent. |
| Number needed to treat | NNT | The number of patients who need to receive an intervention instead of the alternative in order for one additional patient to benefit. The NNT is calculated as: 1/ARR. Example: if the ARR is 4 percent, the NNT = 1/4 percent = 1/0.04 = 25. |
| Number needed to harm | NNH | The number of patients who need to receive an intervention instead of the alternative in order for one additional patient to experience an adverse event. |
| 95 percent confidence interval | 95% CI | An estimate of certainty. It is 95% certain that the true value lies within the given range. A narrow CI is good. A CI that spans 1.0 calls into question the validity of the result. |
| Systematic review | | A type of review article that uses explicit methods to comprehensively analyze and qualitatively synthesize information from multiple studies |
| Meta-analysis | | A type of systematic review that uses rigorous statistical methods to quantitatively synthesize the results of multiple similar studies |