132BEvidence Tables for Chapter 22. Inpatient Intensive Glucose Control Strategies To Reduce Death and Infection (NEW)

Table 1, Chapter 22. Large trials (n > 500) evaluating the health outcome effects of IIT

| **Patient population****Single or multi-center****Country** | **Implementation/ Context** | **Diabetes mellitus (%)** | **Glucose target, T v C (mg/dL)** | **Inpatient BG achieved,****T v C (mg/dL)** | **Mortality and T v C (RR, 95% CI)** | **Hypoglycemia****Definition (mg/dL), rate T v C, RR (95%CI)** | **Other reported outcomes\*****T v C** | **Quality** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| SICUSingle centerBelgium10 | Insulin protocol was developed and use overseen by study investigators.  | 13 | 80-110v 180-200 | 103 v 153†(p<0.001) | ICU mortality 4.6 v 8% (p=0.005 unadjusted)RR 0.42 (95% CI 0.22-0.62);Hospital mortality: 7.2 v 10.9% (p=0.01)RR 0.66; 95% CI 0.48-0.92 | <40, 5 v 0.76%, RR 6.65 (2.83-15.62) | Renal replacement4.8 v 8.2% (p=0.007)Sepsis4.2 v 7.8% (p=0.0003) | Fair |
| Neurosurgical ICUSingle centerItaly58 | Efforts made to limit nursing turnover. New nursing staff worked with experienced staff. | NR | 80-110 v 180-200 | 92 v 143‡ (p<0.001) | 6-month mortality: 74.0 v 72.0% (p=0.82) | <50, 93.8 v 62.8%, p<0.001 | Sepsis 2.9 v 3.3% (p=NS)Long-term disability: 40.2 v 41.1% (p=0.98) | Fair |
| MICUSingle centerBelgium59 | Study conducted in a hospital that had already conducted similar IIT study in SICU patients. Authors note the nurse:bed ratio of 2.5 was not changed for study. | 16 | 80-110 v180-200 | 111 v 153†(p<0.001) | ICU mortality: 24.2 v 26.8% (p=0.31)Hospital mortality: 37.3 v 40.0% (p=0.33) RR 0.93; 95% CI 0.81-1.0890d mortality: 35.9 v 37.7% (p=0.53) | <40, 18.7 v 3.1% | Infection 0.7 vs 0.8% (p=NS)Renal replacement 20.8 v 22.7% (p=0.50) | MICUSingle centerBelgium59 |
| MICUMulticenterGermany20 | No details provided | 30 | 80-110 v 180-200 | 112 v 151†(p<0.001) | 28d mortality: 24.7 v 26% (p=0.74)RR 0.95, 95% CI 0.70-1.2890d mortality: 39.7 v 35.4% (p=0.31) | <40, 17 v 4.1%RR 4.11 (95% CI 2.21-7.63) | Renal replacement 27.5 v 22.5% (p=0.001) | MICUMulticenterGermany20 |
| MICU/SICUMulticenterEurope60 | Characteristics from each study site were reported. Median nurse:bed ratio was 2. ICUs ranged widely in size, patient volume, and number of glucometers per ICU.  | 17 T, 22 C(p=0.031) | 80-110v 140-180 | 117 v 144‡(p<0.001) | ICU mortality: 17.2 v 15.3% (p=0.41)Hospital mortality: 23.3 v 19.4% (p=0.11)28d mortality: 18.7 v 15.3% (p=0.14) | < 40, 8.7 v 2.7% | Renal replacement (patient days) 519 v 523 (p=0.75) | Fair |
| MICU/SICUSingle centerSaudi Arabia18 | 24/7 ICU coverage by intensivists. Protocol designed by multidisciplinary team at study site. Physicians and nurses attended training sessions before and during study. | 32 T, 48 C(p<0.001) | 80-110v 180-200 | 115 v 171‡(p<0.001) | ICU mortality: 13.5 v 17.1% (p=0.70)RR□ 1.09 (0.70-1.72)Hospital mortality: 27.1 v 32.3% (p=0.19)RR□ 0.84 (0.64-1.09) | < 40, 28.6 v 3.1%, p < 0.001 | Renal replacement 11.7 v 12.1% (p=0.89)‖Sepsis 36.9 v 40.9% (p=0.35) | Fair |
| MICU/SICUSingle centerColombia53 | Three month staff training period before study.  | 13 T, 12 C(p=NS) | 80-110 v 180-200 | 120 v 149‡ (p,0.001) | ICU mortality: 33.1 v 31.2%; RR 1.06 (0.82-1.37)28d mortality: 36.6 v 32.4%;RR 1.1 (0.85-1.42) | <40, 8.3 v 0.8% | Infection 27.2 v 33.2% (p=NS)Renal replacement 10.8 v 13% (p=0.45) | Fair |
| MICU/SICUMulticenter International54 | Pre-trial pilot studies carried out to test/improve insulin protocol. Final computerized insulin protocol algorithm accessible to study sites through a central Web site. No clear explicit training prior to study.  | 20 | 80-108 v <180 | 115 v 144§ (p<0.001) | 28d mortality: 22.3 v 20.8% (p=0.17)RR 1.09 (0.96-1.23)90d mortality: 27.5 v 24.9% (p=0.02)RR 1.14 (1.02-1.28) | <40, 6.8 v 0.5%OR 14.7 (9.0-25.9) | Renal replacement15.4 v 14.5% (p=0.34)Sepsis 12.8 v 12.4% (p=0.57) | Fair |
| Acute MIMulticenter CCUSweden61  | No details provided | 39 | 126-198 v NR | 24 hours: T: 172.8 (59.4)C: 210.6 (73.8)p < .001 | 3 month mortality:12.4% v 15.6%, p = NS1 year mortality:18.6% v 26.1 %, RR 0.69; 95% CI 0.49-0.96 | <54, 15.0 v 0% (p < .001) |  | Fair |
| Acute MIMulticenter Europe62  | No details provided | 77 established DM; 23 new DM of < 1y | group 1 and 2: 126-180group 3: NR | 24 hours:group 1: 163.8 (54.0), group 2: 163.8 (50.4), group 3: 180.0 (64.8)p = .0001 | Adjusted 2-year mortality: Group 1 v 3 = 1.19 (0.86 - 1.64)Group 2 v 3 = 1.23 (0.89 - 1.69) | < 54, Gr 1 v Gr2 v Gr3: 12.7 v 9.6 v 1.0 |  | Poor |
| StrokeMutlicenter Britain63 | Conducted as a “pragmatic” trial as part of routine clinical care. No clear explicit training prior to study.  | 17 | 72-126 v <306 | 24 hour mean difference I v C (95% CI): 10.3 (4.9 - 15.5), p < .0001† | 90-day mortality:30.0% v 27.3%, OR (95% CI) = 1.14 (0.86-1.51)90 day severe disability:35.1% v 36.0%, OR (95% CI) = 0.96 (0.70-1.32) | < 72 for > 30 mins, 15.7, control group rate NR |  | Poor |

Abbreviations: BG = Blood glucose; d = day; CCU = coronary care unit ; ICU = intensive care unit; MICU = medical intensive care unit; SICU = surgical intensive care unit; C = comparator; DM = diabetes mellitus; NR = not reported; NS = not statistically significant; RR = relative risk; T = treatment
Other reported outcomes include renal replacement, infection, cardiovascular events, and long-term disability.
Quality was assessed using criteria from the US Preventive Services Task Force.
SI unit conversion for glucose: 1 mg/dL x 0.0555 = 1 mmol/L.
**\*** Infection includes wound infection, urinary tract infection, or pneumonia; or a combination of these.
† Morning blood glucose.
‡ Average of blood glucose measurements, not otherwise specified.
§ Time weighted mean blood glucose.
□Adjusted for chronic liver disease, traumatic brain injury, APACHE II and international normalized ratio.

References

1. Umpierrez GE, Isaacs SD, Bazargan N, et al. Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes.[see comment]. J Clin Endocrinol Metab. 2002;87(3):978-82.11889147

2. Levetan CS, Passaro M, Jablonski K, et al. Unrecognized diabetes among hospitalized patients. Diabetes Care. 1998;21(2):246-9.9539990

3. Furnary AP, Gao G, Grunkemeier GL, et al. Continuous insulin infusion reduces mortality in patients with diabetes undergoing coronary artery bypass grafting.[see comment]. J Thorac Cardiovasc Surg. 2003;125(5):1007-21.12771873

4. Pomposelli JJ, Baxter JK, 3rd, Babineau TJ, et al. Early postoperative glucose control predicts nosocomial infection rate in diabetic patients. JPEN J Parenter Enteral Nutr. 1998;22(2):77-81.9527963

5. Bochicchio GV, Sung J, Joshi M, et al. Persistent hyperglycemia is predictive of outcome in critically ill trauma patients.[erratum appears in J Trauma. 2005 Nov;59(5):1277-8. J Trauma. 2005;58(5):921-4.15920404

6. Capes SE, Hunt D, Malmberg K, et al. Stress hyperglycaemia and increased risk of death after myocardial infarction in patients with and without diabetes: a systematic overview. [see comment]. Lancet. 2000;355(9206):773-8.10711923

7. Capes SE, Hunt D, Malmberg K, et al. Stress hyperglycemia and prognosis of stroke in nondiabetic and diabetic patients: a systematic overview. [see comment]. Stroke. 2001;32(10):2426-32.11588337

8. Clement S, Braithwaite SS, Magee MF, et al. Management of diabetes and hyperglycemia in hospitals.[erratum appears in Diabetes Care. 2004 Mar;27(3):856 Note: Hirsh, Irl B [corrected to Hirsch, Irl B]; dosage error in text]. Diabetes Care. 2004;27(2):553-91.14747243

1. Institute for Health Care Improvement. Establish a glycemic control policy in your ICU. . 2008 [cited; Available from: www.ihi.org/IHI/Topics/CriticalCare/IntensiveCare/Changes/IndividualChanges/EstablishaGlycemicControlPolicyinYourICU.htm

10. van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in the critically ill patients. N Engl J Med. 2001;345(19):1359-67.11794168

11. Ingels C, Debaveye Y, Milants I, et al. Strict blood glucose control with insulin during intensive care after cardiac surgery: impact on 4-years survival, dependency on medical care, and quality-of-life. Eur Heart J. 2006;27(22):2716-24.16608860

12. Kansagara D, Fu R, Freeman M, et al. Intensive insulin therapy in hospitalized patients: a systematic review. Ann Intern Med. 2011;154(4):268-82.21320942

13. Green DM, O’Phelan KH, Bassin SL, et al. Intensive versus conventional insulin therapy in critically ill neurologic patients. Neurocrit Care. 2010;13(3):299-306.20697836

14. Coester A, Neumann CR, Schmidt MI. Intensive insulin therapy in severe traumatic brain injury: a randomized trial. J Trauma. 2010;68(4):904-11.20032790

15. Cao SG, Ren JA, Shen B, et al. Intensive versus conventional insulin therapy in type 2 diabetes patients undergoing D2 gastrectomy for gastric cancer: a randomized controlled trial. World J Surg. 2011;35(1):85-92.20878324

16. Umpierrez GE, Smiley D, Jacobs S, et al. Randomized study of basal-bolus insulin therapy in the inpatient management of patients with type 2 diabetes undergoing general surgery (RABBIT 2 surgery). Diabetes Care. 2011;34(2):256-61.21228246

17. Krinsley JS. Association between hyperglycemia and increased hospital mortality in a heterogeneous population of critically ill patients.[see comment]. Mayo Clin Proc. 2003;78(12):1471-8.14661676

18. Arabi YM, Dabbagh OC, Tamim HM, et al. Intensive versus conventional insulin therapy: a randomized controlled trial in medical and surgical critically ill patients. Crit Care Med. 2008;36(12):3190-7.18936702

19. Devos P, Preiser JC, Melot C. Impact of tight glucose control by intensive insulin therapy on ICU mortality and the rate of hypoglycaemia: final results of the GLUCONTROL study. Intensive Care Medicine. 2007;33(Supplement 2)(S189)

20. Brunkhorst FM, Engel C, Bloos F, et al. Intensive insulin therapy and pentastarch resuscitation in severe sepsis. N Engl J Med. 2008;358(2):125-39.18184958

21. Hermanides J, Bosman RJ, Vriesendorp TM, et al. Hypoglycemia is associated with intensive care unit mortality. Crit Care Med. 2010;38(6):1430-4.20386307

22. Dortch MJ, Mowery NT, Ozdas A, et al. A computerized insulin infusion titration protocol improves glucose control with less hypoglycemia compared to a manual titration protocol in a trauma intensive care unit. JPEN J Parenter Enteral Nutr. 2008;32(1):18-27.18165443

23. Toschlog EA, Newton C, Allen N, et al. Morbidity reduction in critically ill trauma patients through use of a computerized insulin infusion protocol: a preliminary study. J Trauma. 2007;62(6):1370-5; discussion 5-6.17563651

24. Treggiari MM, Karir V, Yanez ND, et al. Intensive insulin therapy and mortality in critically ill patients. Crit Care. 2008;12(1):R29.18312617

25. Taylor BE, Schallom ME, Sona CS, et al. Efficacy and safety of an insulin infusion protocol in a surgical ICU. J Am Coll Surg. 2006;202(1):1-9.16377491

26. Caddell KA, Komanapalli CB, Slater MS, et al. Patient-specific insulin-resistance-guided infusion improves glycemic control in cardiac surgery. Ann Thorac Surg. 2010;90(6):1818-23.21095317

27. Wilson M, Weinreb J, Hoo GW. Intensive insulin therapy in critical care: a review of 12 protocols. Diabetes Care. 2007;30(4):1005-11.17213376

28. Meijering S, Corstjens AM, Tulleken JE, et al. Towards a feasible algorithm for tight glycaemic control in critically ill patients: a systematic review of the literature. Crit Care. 2006;10(1):R19.16469124

29. Newton CA, Smiley D, Bode BW, et al. A comparison study of continuous insulin infusion protocols in the medical intensive care unit: computer-guided vs. standard column-based algorithms. J Hosp Med. 2010;5(8):432-7.20945468

30. Juneja R, Roudebush C, Kumar N, et al. Utilization of a computerized intravenous insulin infusion program to control blood glucose in the intensive care unit. Diabetes Technol Ther. 2007;9(3):232-40.17561793

31. Barletta JF, McAllen KJ, Eriksson EA, et al. The effect of a computer-assisted insulin protocol on glycemic control in a surgical intensive care unit. Diabetes Technol Ther. 2011;13(4):495-500.21355721

32. Lee A, Faddoul B, Sowan A, et al. Computerisation of a paper-based intravenous insulin protocol reduces errors in a prospective crossover simulated tight glycaemic control study. Intensive Crit Care Nurs. 2010;26(3):161-8.20430622

33. Holzinger U, Warszawska J, Kitzberger R, et al. Real-time continuous glucose monitoring in critically ill patients: a prospective randomized trial. Diabetes Care. 2010;33(3):467-72.20007948

34. Yatabe T, Yamazaki R, Kitagawa H, et al. The evaluation of the ability of closed-loop glycemic control device to maintain the blood glucose concentration in intensive care unit patients. Crit Care Med. 2011;39(3):575-8.21178768

35. Atkin SH, Dasmahapatra A, Jaker MA, et al. Fingerstick glucose determination in shock. Ann Intern Med. 1991;114(12):1020-4.2029097

36. Critchell CD, Savarese V, Callahan A, et al. Accuracy of bedside capillary blood glucose measurements in critically ill patients. Intensive Care Med. 2007;33(12):2079-84.17763842

37. Tanvetyanon T, Walkenstein MD, Marra A. Inaccurate glucose determination by fingerstick in a patient with peripheral arterial disease. Ann Intern Med. 2002;137(9):W1.12416976

38. Juneja D, Pandey R, Singh O. Comparison between arterial and capillary blood glucose monitoring in patients with shock. Eur J Intern Med. 2011;22(3):241-4.21570641

39. Kanji S, Singh A, Tierney M, et al. Standardization of intravenous insulin therapy improves the efficiency and safety of blood glucose control in critically ill adults. Intensive Care Med. 2004;30(5):804-10.15127193

40. Desachy A, Vuagnat AC, Ghazali AD, et al. Accuracy of bedside glucometry in critically ill patients: influence of clinical characteristics and perfusion index. Mayo Clin Proc. 2008;83(4):400-5.18380985

41. Pidcoke HF, Wade CE, Mann EA, et al. Anemia causes hypoglycemia in intensive care unit patients due to error in single-channel glucometers: methods of reducing patient risk. Crit Care Med. 2010;38(2):471-6.19789438

42. de Azevedo JR, de Araujo LO, da Silva WS, et al. A carbohydrate-restrictive strategy is safer and as efficient as intensive insulin therapy in critically ill patients. J Crit Care. 2010;25(1):84-9.19327317

43. Chase JG, Shaw G, Le Compte A, et al. Implementation and evaluation of the SPRINT protocol for tight glycaemic control in critically ill patients: a clinical practice change. Crit Care. 2008;12(2).18412978

44. Metchick LN, Petit WA, Jr., Inzucchi SE. Inpatient management of diabetes mellitus. Am J Med. 2002;113(4):317-23.12361818

45. Cheung NW, Chipps DR. Sliding scale insulin: will the false idol finally fall? Intern Med J. 2010;40(9):662-4.20862784

46. Umpierrez GE, Smiley D, Zisman A, et al. Randomized study of basal-bolus insulin therapy in the inpatient management of patients with type 2 diabetes (RABBIT 2 trial).[see comment]. Diabetes Care. 2007;30(9):2181-6.17513708

47. Dickerson LM, Ye X, Sack JL, et al. Glycemic control in medical inpatients with type 2 diabetes mellitus receiving sliding scale insulin regimens versus routine diabetes medications: a multicenter randomized controlled trial. Ann Fam Med. 2003;1(1):29-35.15043177

48. Korytkowski MT, Salata RJ, Koerbel GL, et al. Insulin therapy and glycemic control in hospitalized patients with diabetes during enteral nutrition therapy: a randomized controlled clinical trial. Diabetes Care. 2009;32(4):594-6.19336639

49. Datta S, Qaadir A, Villanueva G, et al. Once-daily insulin glargine versus 6-hour sliding scale regular insulin for control of hyperglycemia after a bariatric surgical procedure: a randomized clinical trial. Endocr Pract. 2007;13(3):225-31.17599852

50. Furnary AP, Wu Y, Bookin SO. Effect of hyperglycemia and continuous intravenous insulin infusions on outcomes of cardiac surgical procedures: the Portland Diabetic Project. Endocr Pract. 2004;10 Suppl 2:21-33.15251637

51. Krinsley JS. Effect of an intensive glucose management protocol on the mortality of critically ill adult patients.[see comment][erratum appears in Mayo Clin Proc. 2005 Aug;80(8):1101]. Mayo Clinic Proceedings. 2004;79(8):992-1000

52. Aragon D. Evaluation of nursing work effort and perceptions about blood glucose testing in tight glycemic control. Am J Crit Care. 2006;15(4):370-7.16823014

53. De La Rosa Gdel C, Donado JH, Restrepo AH, et al. Strict glycaemic control in patients hospitalised in a mixed medical and surgical intensive care unit: a randomised clinical trial. Crit Care. 2008;12(5):R120.18799004

54. NICE-SUGAR Study, Finfer S, Chittock DR, et al. Intensive versus conventional glucose control in critically ill patients. N Engl J Med. 2009;360(13):1283-97.19318384

55. Van den Berghe G, Schetz M, Vlasselaers D, et al. Clinical review: Intensive insulin therapy in critically ill patients: NICE-SUGAR or Leuven blood glucose target? J Clin Endocrinol Metab. 2009;94(9):3163-70.19531590

56. Furnary AP, Zerr KJ, Grunkemeier GL, et al. Continuous intravenous insulin infusion reduces the incidence of deep sternal wound infection in diabetic patients after cardiac surgical procedures. Ann Thorac Surg. 1999;67(2):352-60; discussion 60-2.10197653

57. Qaseem A, Humphrey LL, Chou R, et al. Use of intensive insulin therapy for the management of glycemic control in hospitalized patients: a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2011;154(4):260-7.21320941

58. Bilotta F, Caramia R, Paoloni FP, et al. Safety and efficacy of intensive insulin therapy in critical neurosurgical patients. Anesthesiology. 2009;110(3):611-9.19237874

59. Van den Berghe G, Wilmer A, Hermans G, et al. Intensive insulin therapy in the medical ICU. N Engl J Med. 2006;354(5):449-61.16452557

60. Preiser JC, Devos P, Ruiz-Santana S, et al. A prospective randomised multi-centre controlled trial on tight glucose control by intensive insulin therapy in adult intensive care units: the Glucontrol study. Intensive Care Med. 2009;35(10):1738-48.19636533

61. Malmberg K, Ryden L, Efendic S, et al. Randomized trial of insulin-glucose infusion followed by subcutaneous insulin treatment in diabetic patients with acute myocardial infarction (DIGAMI study): effects on mortality at 1 year. J Am Coll Cardiol. 1995;26(1):57-65.7797776

62. Malmberg K, Ryden L, Wedel H, et al. Intense metabolic control by means of insulin in patients with diabetes mellitus and acute myocardial infarction (DIGAMI 2): effects on mortality and morbidity. Eur Heart J. 2005;26(7):650-61.15728645

63. Gray CS, Hildreth AJ, Sandercock PA, et al. Glucose-potassium-insulin infusions in the management of post-stroke hyperglycaemia: the UK Glucose Insulin in Stroke Trial (GIST-UK). Lancet Neurol. 2007;6(5):397-406.17434094