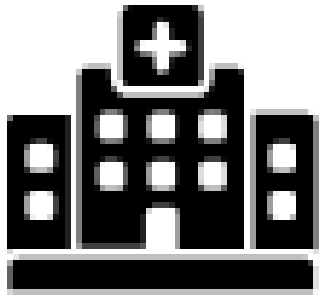
IV Insulin for Hospitalized Patients

IV Insulin for Hospitalized Patients

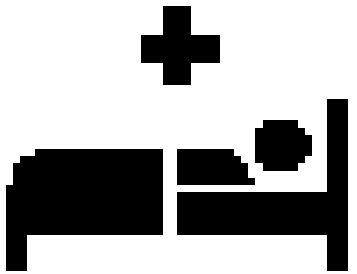
- In-Patient Hyperglycemia and Hospital-Based Outcomes Data
- Guidelines on In-Patient Glycemic Targets
- Insulin Infusion Protocol in Hospitals
- Computerized Protocol Insulin Infusion Protocol
- Paper vs. Computerized Protocol



In-Patient Hyperglycemia and Hospital-Based Outcomes Data

In-Patient Hyperglycemia

- Severe illness predisposes patients to insulin resistance and stress hyperglycemia[1]
- Elevated glucose is common in hospitalized patients, with and without diabetes[1]
- The metabolic stress of acute illness leads to worsening insulin resistance, which is associated with:[2]
  - Immune dysfunction
  - Impaired wound healing
  - Oxidative stress



1. Bogun M, et al. *Clin Ther.* 2013;35(5):724-733.
2. Kodner C, et al. *Am Fam Physician*. 2017;96(10):648-654.

Critically Ill Patients

- Critically ill patients have a different tolerance to glycemic variability and hyperglycemia, as well as a different response to insulin, than non-critically ill patients[1]
- Hyperglycemia is associated with increased mortality in critically ill, hospitalized patients[2]
  - This includes patients undergoing cardiac surgery, more than half of whom will experience hyperglycemia even without a history of diabetes[3]

1. Beesley SJ, et al. Ann Transl Med. 2016;4(18):347. 2. Falciglia M, et al. Crit Care Med. 2009;37(12):3001-3009. 3. Umpierrez G, et al. Diabetes Care. 2015;38(9):1665-1672.

Critically Ill Patients

- it is recommended that patients in the intensive care unit (ICU) receive intravenous (IV) insulin infusion when BG levels are >180 mg/dL[1,2]
  - Treatment for hyperglycemia must be individualized to avoid overly intensive management

1. Beesley SJ, et al. Ann Transl Med. 2016;4(18):347. 2. Jacobi J, et al. Crit Care Med. 2012;40(12):3251-3276.

In-Patient Hyperglycemia Management

- Prior to 2009, tight glucose control was recommended for hospitalized patients, with BG targets similar to those for non-hospitalized patients[1]
- Early clinical trial data suggested a benefit of tight glucose control in decreasing mortality and reducing hospital complications in both critically ill and non-critically ill hospitalized patients[2]
- However, glycemic variability and hypoglycemia risk are high in hospitalized patients, particularly those receiving insulin, which itself may lead to poorer outcomes[3]

1. Kelly JL. *Diabetes Spectr*. 2014;27(3):218-223.
2. Lansang MC, et al. *Cleve Clin J Med*. 2016;83(5 Suppl 1):S34-S43.
3. NICE-SUGAR Study Investigators, et al. *N Engl J Med*. 2009;360(13):1283-1297.

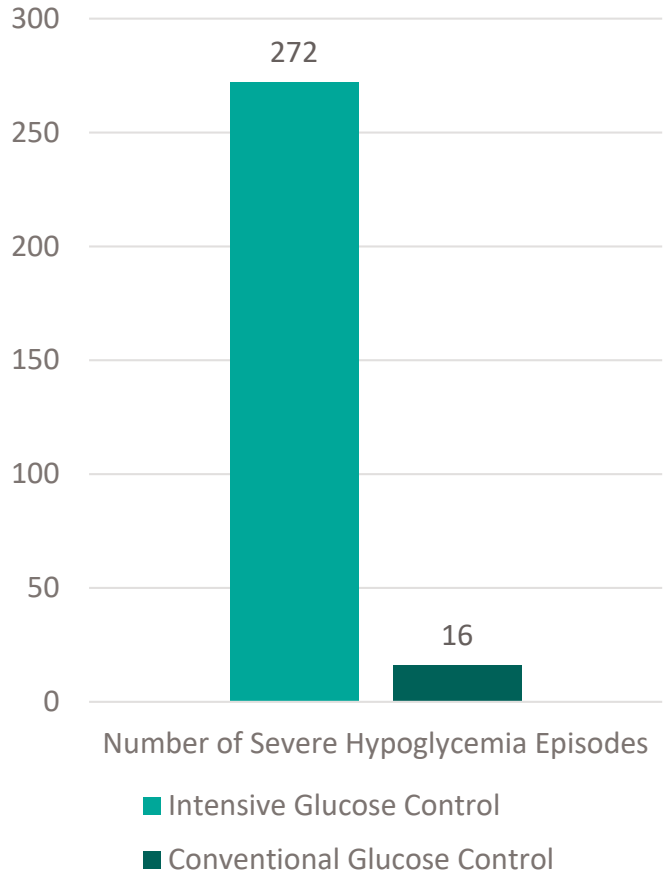
Diabetes Outcomes Studies

- Subsequent trials found conflicting results on the benefit of tight glucose control in hospitalized patients
- To determine an optimal BG target range, the Normoglycemia in Intensive Care Evaluation–Survival Using Glucose Algorithm Regulation (NICE-SUGAR) trial investigated the outcomes associated with intensive and conventional BG control in hospitalized patients in the ICU
  - This prospective study randomized over 6000 patients to intensive or conventional BG control

NICE-SUGAR Study Investigators, et al. *N Engl J Med*. 2009;360(13):1283-1297

Diabetes Outcomes Studies

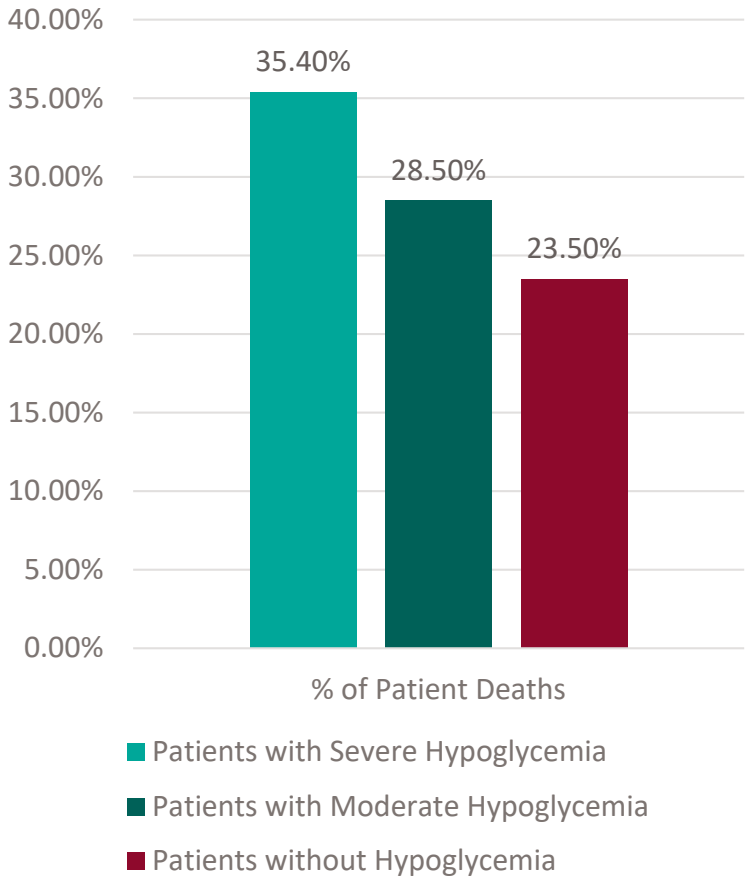
- NICE-SUGAR indicated that mortality rates were higher among ICU patients who received intensive BG control (27.5% vs 24.9%, P=0.02) and that intensive BG control was associated with significantly higher rates of severe hypoglycemia (6.8% vs 0.5%, P<0.0001)
  - A total of 272 severe hypoglycemia events were recorded in patients with intensive glucose control, compared with 16 in patients with conventional glucose control



NICE-SUGAR Study Investigators, et al. N Engl J Med. 2009;360(13):1283-1297.

Diabetes Outcomes Studies

- A post hoc analysis of NICE-SUGAR data indicated that patients with moderate or severe hypoglycemia had higher mortality rates compared with patients who did not experience hypoglycemia (28.5% and 35.4%, respectively, vs 23.5%, P<0.0001 for both)
  - These findings suggest a dose-response relationship between hypoglycemia and patient death for critically ill patients



NICE-SUGAR Study Investigators, et al. N Engl J Med. 2012;367(12):1108-1118.

Use of Insulin Infusion Protocol in the ICU

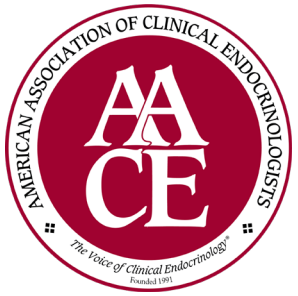
- The use of protocol in the ICU standardizes care for patients receiving IV insulin, increases adherence to evidence-based care, helps reduce variation in BG, and improves clinical outcomes.[1]
  - Many institutions have their own insulin infusion protocol, which should be validated and tailored to address the needs of the ICU patient populations being served[2]

1. Boord JB, et al. J Am Med Inform Assoc. 2007;14(3):278-287. 2. Kavanagh BP, et al. N Engl J Med. 2010;363(26):2540-2546.

Use of Insulin Infusion Protocol in the ICU cont.

- Insulin infusion protocols provide guidance on individualization of BG management, including[1]
  - Frequent monitoring and infusion rate adjustment
  - Maintaining the target BG range
  - Minimizing risk of hypoglycemia
- Nursing staff play a vital role in the coordinating of BG monitoring and insulin administration and should be implementing insulin infusion protocol in the ICU[2]
- Successful protocols incorporate data on absolute BG levels, prior BG levels, and the current insulin infusion rate to predict patient response to IV insulin to inform insulin titration[3]

1. Bogun M, et al. Clin Ther. 2013;35(5):724-733. 2. Maynard G, et al. Society of Hospital Medicine; 2015. www.hospitalmedicine.org/gc.
3. Kavanagh BP, et al. N Engl J Med. 2010;363(26):2540-2546.



Guidelines on In-Patient Glycemic Targets

ICU Targets Differ from General Floor Targets

- All hospitalized patients should be assessed for a history of diabetes and monitored for hyperglycemia[1]
- Achieving glucose targets is vital for all hospitalized patients and is considered standard of care[2]
- Hospitalized patients in the non-critical care setting are recommended a premeal glucose target of <140 mg/dL[1]
  - However, due to the risk of adverse outcomes associated with hypoglycemia, recommended targets for critically ill patients are usually between 140 mg/dL and 180 mg/dL[3-6]

1. Umpierrez GE, et al. J Clin Endocrinol Metab. 2012;97(1):16-38. 2. Wallia A, et al. J Diabetes Sci Technol. 2017;11(5):1036-1044. 3. Qaseem A, et al. Am J Med Qual. 2014;29(2):95-98. 4. American Diabetes Association. Diabetes Care. 2020;43(Suppl 1):S193-S202. 5. Moghissi ES, et al. Endocr Pract. 2009;15(4):353-369. 6. Jacobi J, et al. Crit Care Med. 2012;40(12):3251-3276.

Glycemic Targets and Recommendations

- Concerns over the deleterious effects of hypoglycemia in hospitalized patients has led to updates in clinical practice guidelines[1]
- Several published guidelines address the management of hyperglycemia in hospitalized patients, in both critical and non-critical settings[2-7]

1. Lansang MC, et al. Cleve Clin J Med. 2016;83(5 Suppl 1):S34-S43. 2. Qaseem A, et al. Am J Med Qual. 2014;29(2):95-98. 3. American Diabetes Association. Diabetes Care. 2020;43(Suppl 1):S193-S202. 4. Moghissi ES, et al. Endocr Pract. 2009;15(4):353-369. 5. Umpierrez GE, et al. J Clin Endocrinol Metab. 2012;97(1):16-38. 6. Jacobi J, et al. Crit Care Med. 2012;40(12):3251-3276. 7. Deedwania P, et al. Circulation. 2008;117(12):1610-1619.

Glycemic Targets in Hospitalized Patients

	Non-Critical Patients	Critical Patients	Notes
American College of Physicians (ACP)[1]	--	140 mg/dL to 200 mg/dL	Avoid targets <140 mg/dL
American Diabetes Association (ADA)[2]	140 mg/dL to 180 mg/dL	140 mg/dL to 180 mg/dL	110 mg/dL to 140 mg/dL for patients at low hypoglycemia risk
ADA and American Association of Clinical Endocrinologists (AACE)[3]	140 mg/dL to 180 mg/dL	140 mg/dL to 180 mg/dL	110 mg/dL to 140 mg/dL for patients at low hypoglycemia risk
Endocrine Society (ES)[4]	140 mg/dL to 180 mg/dL	--	
Society of Critical Care Medicine (SCCM)[5]	--	100 mg/dL to 150 mg/dL	< 150 mg/dL for postoperative patients following cardiac surgery
American Heart Association (AHA)[6]	< 180 mg/dL	90 mg/dL to 140 mg/dL	Guidelines for patients admitted for acute coronary syndrome (ACS)
Society of Thoracic Surgeons[7]	--	≤ 180 mg/dL ≤ 150 mg/dL for certain high-risk patients	Guidelines for patients during adult cardiac surgery

1. Qaseem A, et al. *Am J Med Qual*. 2014;29(2):95-98. 2. American Diabetes Association. *Diabetes Care*. 2020;43(Suppl 1):S193-S202. 3. Moghissi ES, et al. *Endocr Pract*. 2009;15(4):353-369. 4. Umpierrez GE, et al. *J Clin Endocrinol Metab.* 2012;97(1):16-38. 5. Jacobi J, et al. *Crit Care Med*. 2012;40(12):3251-3276. 6. Deedwania P, et al. *Circulation*. 2008;117(12):1610-1619. 7. Lazar HL, et al. *Ann Thorac Surg*. 2009;87(2):663-669.

Insulin Infusion Protocols in Hospitals

IV Insulin Infusion for Critically Ill Patients

- Over the past 20 years, hospitals have increasingly adopted insulin infusion protocols[1]
  - Insulin infusion protocol should be easy to implement and provide clear, specific directions for patient care
- A variety of insulin infusion protocols have been validated with demonstrated safety and efficacy, with low rates of hypoglycemia[2]

1. Braithwaite SS, et al. *Curr Diabetes Rev*. 2008;4(3):258-268.
2. Deedwania P, et al. *Circulation*. 2008;117(12):1610-1619.

Elements of an Insulin Infusion Protocol

- Insulin infusion protocol include algorithms that incorporate individual patient data to determine the need for titration to maintain BG targets[1]
- Frequent glucose monitoring is essential to achieve optimal glucose control while minimizing the occurrence of hypoglycemia[2]
- Safe and effective insulin infusion protocol involves the following elements:[3]
  - Includes appropriate, personalized glycemic targets and a threshold for implementation
  - Provides clear and specific directions for BG monitoring and insulin titration
  - Titration is based on current and prior BG, and rate of change
  - Effectively achieves and maintains BG targets quickly with minimal titration
  - Low risk for hypoglycemia and includes protocol to treat hypoglycemia
  - Includes transition plan from IV to subcutaneous insulin

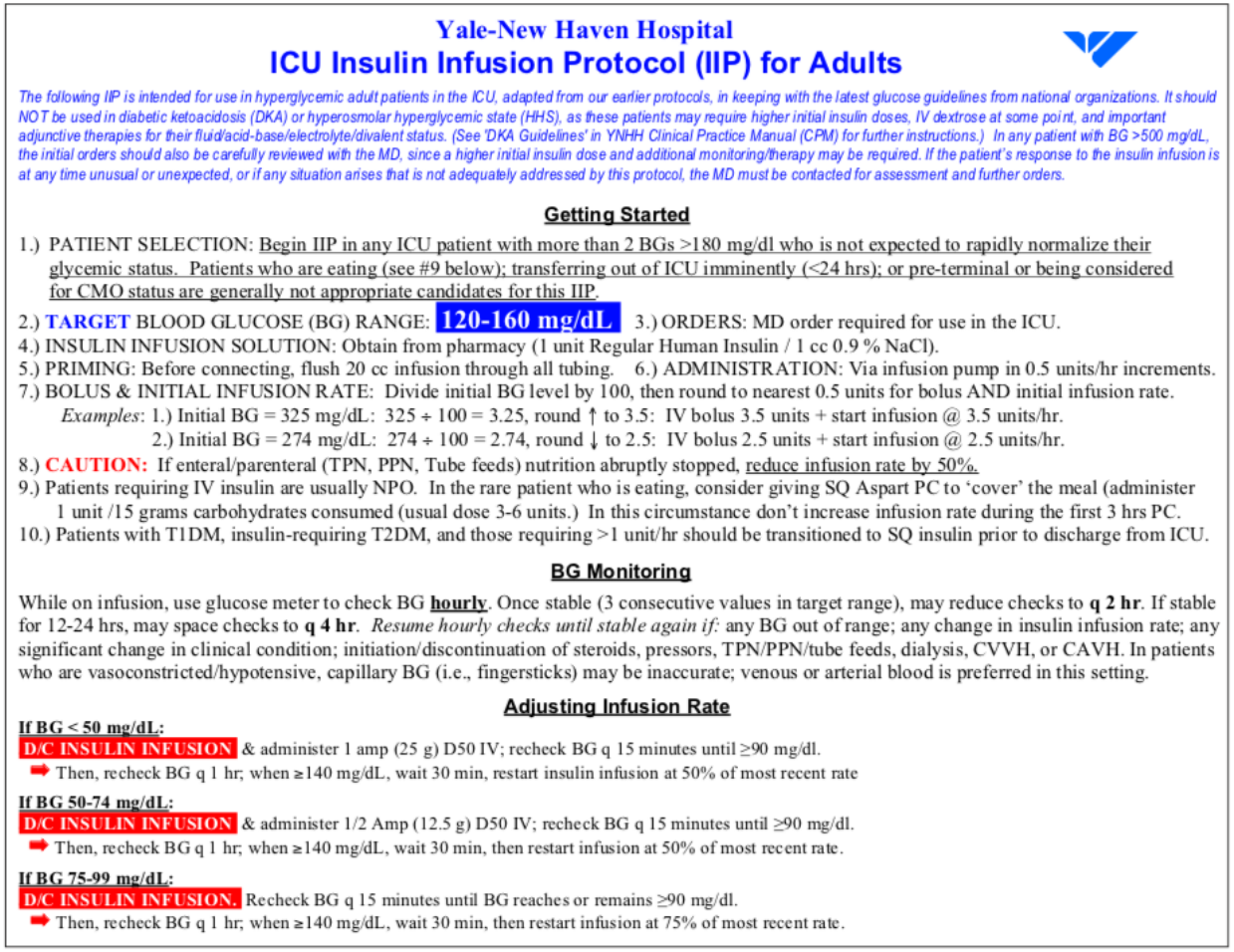
1. Braithwaite SS, et al. *Curr Diabetes Rev*. 2008;4(3):258-268. 2. Deedwania P, et al. *Circulation*. 2008;117(12):1610-1619.
2. 3. Kelly JL. *Diabetes Spectr*. 2014;27(3):218-223.

Use of Insulin Infusion Protocol in the ICU

- Insulin infusion protocol should be validated, tested, and reviewed in the ICU setting[1]
  - Protocol should include instruction for appropriate methods of blood sample collection, accurate BG measurement, and data interpretation for insulin adjustment, as necessary
- The use of protocol improves standardization of care and minimize errors in management and monitoring[2,3]
- Automated insulin adjustments can be made by nursing staff, minimizing the need for calls to physicians, for more efficient health care utilization[1]

1. Kavanagh BP, et al. N Engl J Med. 2010;363(26):2540-2546.
2. Braithwaite SS, et al. Curr Diab Rep. 2018;18(5):26.
3. Maynard G, et al. Society of Hospital Medicine; 2015. www.hospitalmedicine.org/gc.

Yale Insulin Infusion Protocol



Yale-New Haven Hospital

ICU Insulin Infusion Protocol (IIP) for Adults

The following IIP is intended for use in hyperglycemic adult patients in the ICU, adapted from our earlier protocols, in keeping with the latest glucose guidelines from national organizations. It should NOT be used in diabetic ketoacidosis (DKA) or hyperosmolar hyperglycemic state (HHS), as these patients may require higher initial insulin doses, IV dextrose at some point, and important adjunctive therapies for their fluid/acid-base/electrolyte/divalent status. (See 'DKA Guidelines' in YNHH Clinical Practice Manual (CPM) for further instructions.) In any patient with BG >500 mg/dL, the initial orders should also be carefully reviewed with the MD, since a higher initial insulin dose and additional monitoring/therapy may be required. If the patient's response to the insulin infusion is at any time unusual or unexpected, or if any situation arises that is not adequately addressed by this protocol, the MD must be contacted for assessment and further orders.

Getting Started

1.) PATIENT SELECTION: Begin IIP in any ICU patient with more than 2 BGs >180 mg/dl who is not expected to rapidly normalize their glycemic status. Patients who are eating (see #9 below); transferring out of ICU imminently (<24 hrs); or pre-terminal or being considered for CMO status are generally not appropriate candidates for this IIP.

2.) TARGET BLOOD GLUCOSE (BG) RANGE: **120-160 mg/dL** 3.) ORDERS: MD order required for use in the ICU.

4.) INSULIN INFUSION SOLUTION: Obtain from pharmacy (1 unit Regular Human Insulin / 1 cc 0.9 % NaCl).

5.) PRIMING: Before connecting, flush 20 cc infusion through all tubing. 6.) ADMINISTRATION: Via infusion pump in 0.5 units/hr increments.

7.) BOLUS & INITIAL INFUSION RATE: Divide initial BG level by 100, then round to nearest 0.5 units for bolus AND initial infusion rate.

Examples: 1.) Initial BG = 325 mg/dL: 325 ÷ 100 = 3.25, round ↑ to 3.5: IV bolus 3.5 units + start infusion @ 3.5 units/hr.

2.) Initial BG = 274 mg/dL: 274 ÷ 100 = 2.74, round ↓ to 2.5: IV bolus 2.5 units + start infusion @ 2.5 units/hr.

8.) CAUTION: If enteral/parenteral (TPN, PPN, Tube feeds) nutrition abruptly stopped, reduce infusion rate by 50%.

9.) Patients requiring IV insulin are usually NPO. In the rare patient who is eating, consider giving SQ Aspart PC to 'cover' the meal (administer 1 unit /15 grams carbohydrates consumed (usual dose 3-6 units.) In this circumstance don't increase infusion rate during the first 3 hrs PC.

10.) Patients with T1DM, insulin-requiring T2DM, and those requiring >1 unit/hr should be transitioned to SQ insulin prior to discharge from ICU.

BG Monitoring

While on infusion, use glucose meter to check BG **hourly**. Once stable (3 consecutive values in target range), may reduce checks to **q 2 hr**. If stable for 12-24 hrs, may space checks to **q 4 hr**. *Resume hourly checks until stable again if:* any BG out of range; any change in insulin infusion rate; any significant change in clinical condition; initiation/discontinuation of steroids, pressors, TPN/PPN/tube feeds, dialysis, CVVH, or CAVH. In patients who are vasoconstricted/hypotensive, capillary BG (i.e., fingersticks) may be inaccurate; venous or arterial blood is preferred in this setting.

Adjusting Infusion Rate

If BG < 50 mg/dL:

D/C INSULIN INFUSION & administer 1 amp (25 g) D50 IV; recheck BG q 15 minutes until ≥90 mg/dl.

➡ Then, recheck BG q 1 hr; when ≥140 mg/dL, wait 30 min, restart insulin infusion at 50% of most recent rate

If BG 50-74 mg/dL:

D/C INSULIN INFUSION & administer 1/2 Amp (12.5 g) D50 IV; recheck BG q 15 minutes until ≥90 mg/dl.

➡ Then, recheck BG q 1 hr; when ≥140 mg/dL, wait 30 min, then restart infusion at 50% of most recent rate.

If BG 75-99 mg/dL:

D/C INSULIN INFUSION. Recheck BG q 15 minutes until BG reaches or remains ≥90 mg/dl.

➡ Then, recheck BG q 1 hr; when ≥140 mg/dL, wait 30 min, then restart infusion at 75% of most recent rate.

- The Yale Protocol is one example of a widely used insulin infusion protocol
- The Yale Protocol adjusts the rate of insulin infusion based on current BG level, previous BG values, and current insulin infusion rate
- BG monitoring is checked hourly until stable, after which checks may be reduced to every 2 or every 4 hours

Nazer LH, et al. *Endocr Pract*. 2007;13(2):137-146.

Computerized Protocol for In-Patient IV Insulin

Electronic Glucose Management Systems (eGMS)

- Insulin infusion protocols are complex and require frequent BG monitoring and complicated calculations to titrate insulin infusion rates[1,2]
- Computer-based electronic glucose management systems (eGMS) automate the calculation steps involved in insulin infusion protocol[3]
  - Using a validated protocol is essential for successful eGMS outcomes
  - Some eGMS use existing protocol, such as the Yale protocol
- Clinical studies have demonstrated improved time to reach BG target and improved BG maintenance with eGMS, with low rates of hypoglycemia[3]
- Some eGMS integrate directly with electronic health records (EHR)

1. Boord JB, et al. J Am Med Inform Assoc. 2007;14(3):278-287.
2. Marvin MR, et al. Diabetes Technol Ther. 2013;15(3):246-252.
3. Maynard G, et al. Society of Hospital Medicine; 2015. www.hospitalmedicine.org/gc.

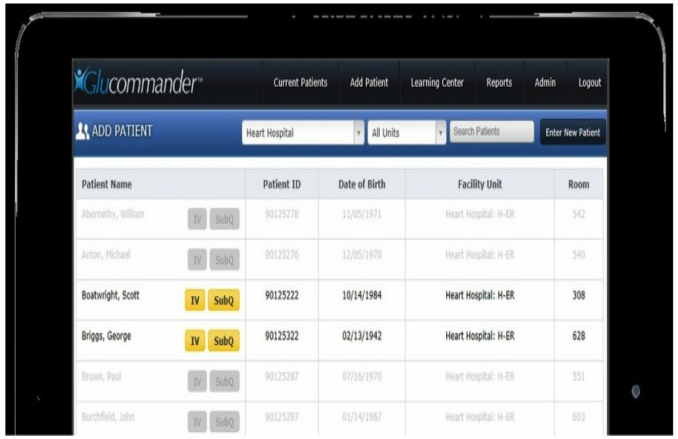
Available eGMS Technologies: EndoTool

- EndoTool IV Insulin Therapy (Monarch Medical Technologies)
- Calculates insulin dosing and timing of BG monitoring using patient-specific factors
  - Patented technology is used to model, predict, and adjust individualized insulin dosing based on 8 unique patient variables
- Rapidly achieves BG targets with minimal glucose variability or risk of hypoglycemia
- Integrates with most EHR and is available for pediatric patients

Salinas PD, et al. J Diabetes Sci Technol. 2019;13(4):682-690.

Available eGMS Technologies: Glucommander

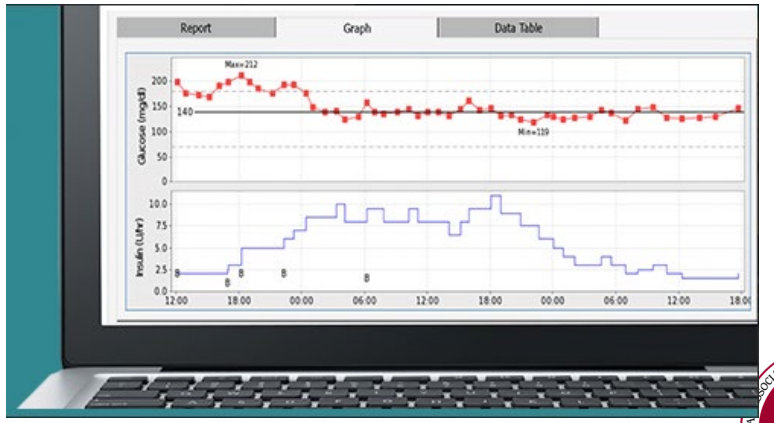
- Glucommander (Glytec Systems)
- Calculates insulin dosing based on initial glucose target ranges and patient weight
  - Adjustments are made depending on how well patient maintains BG targets
- Software recommends insulin infusion rates and suggests timing for blood glucose monitoring
- Glucommander has demonstrated safety and efficacy in the management of patients with diabetic ketoacidosis (DKA)



Salinas PD, et al. J Diabetes Sci Technol. 2019;13(4):682-690.

Available eGMS Technologies: GlucoCare 140(B)

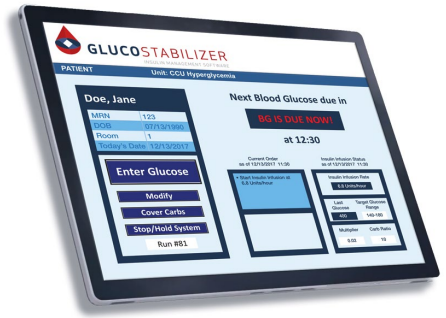
- GlucoCare 140(B) (Pronia Medical Systems)
- Uses the Yale Protocol to determine recommended insulin dosing[1]
- Targets a specific glucose level rather than a range[2]
- Calculations are made using patient current blood sugar, immediate past blood sugar, time between measurements, and current insulin infusion rate[1]
- Single-target approach results in very low hypoglycemia risk[1]
- Additional feature adds doses of bolus insulin to reduce infusion rates[1]



1. Salinas PD, et al. J Diabetes Sci Technol. 2019;13(4):682-690.
2. Pronia Medical Systems. proniamed.com/glucocare/

Available eGMS Technologies: GlucoStabilizer

- GlucoStabilizer (Medical Decision Network)
- Provides systematic and standardized insulin infusion titrations based on metabolic parameters[1,2]
- Uses an insulin sensitivity factor (ISF)
  to adjust or titrate insulin infusion rates as necessary[1]
- Can be used in adult and pediatric populations
- Recent data indicate efficacy in obstetric population, for laboring patients with diabetes, without increased maternal hypoglycemia[1]



1. Salinas PD, et al. J Diabetes Sci Technol. 2019;13(4):682-690.
2. Medical Decisions Network, Inc. glucostabilizer.net

Barriers to Implementation and Online Support for Adoption of eGMS

- The implementation of an eGMS is a large-scale undertaking[1]
  - To be successful, the use of computer-based protocol must be fully integrated into the workflow of hospital care providers
  - Training may be necessary for nurses and physicians to become comfortable with new eGMS technology
- Cost may be a barrier, including the expense of bedside computers or tablet devices and the commercial eGMS system[2]
  - While some institutions may not be in a position to integrate electronic protocol into their EHR, the use of eGMS is increasing as more options become available

1. Boord JB, et al. *J Am Med Inform Assoc.* 2007;14(3):278-287.
2. Maynard G, et al. Society of Hospital Medicine; 2015. www.hospitalmedicine.org/gc.

Barriers to Implementation and Online Support for Adoption of eGMS cont.

- To support hospitals in the adoption of eGMS, the Society of Hospital Medicine (SHM) has online, subscription-based Electronic Quality Improvement Programs (eQUIPS) resources[1]
  - Resources include an implementation guide, performance tracking, outcomes reporting, online forums, and educational webinars
- eGMS may fail under certain circumstances, including in patients who receive glucocorticoids, such as methylprednisolone, which may provoke severe hyperglycemia and therefore require increased doses of insulin [2,3]
  - It is important that clinicians be aware of specific patient situations that require deviation from the standard protocol

1. Society of Hospital Medicine. https://www.hospitalmedicine.org/clinical-topics/glycemic-control/glycemic-control-equips/
2. Korytkowski MT. Indian J Endocrinol Metab. 2013;17(Suppl 3):S630-S635.
3. Maynard G, et al. Society of Hospital Medicine; 2015. www.hospitalmedicine.org/gc.

Paper vs Computerized Protocol

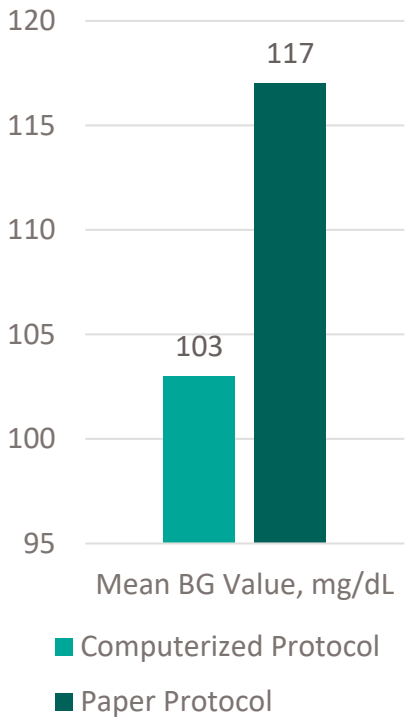
Improved Outcomes with Computerized Protocol

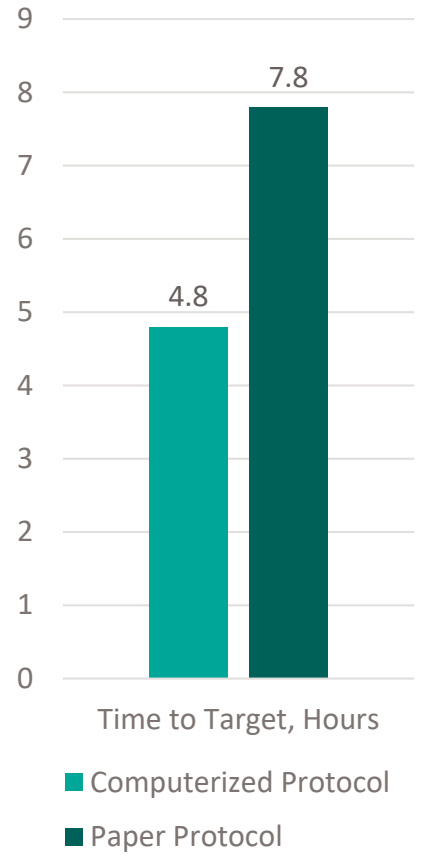
- Multiple comparative studies have shown the benefits of using a computerized protocol[1]
- A multicenter, prospective, open-label study randomized 153 ICU patients to receive insulin infusion using eGMS or paper protocol[2]
  - Data were collected for the first 10 days of ICU stay

1. Maynard G, et al. Society of Hospital Medicine; 2015. www.hospitalmedicine.org/gc.
2. Newton CA, et al. *J Hosp Med.* 2010;5(8):432-437.

Improved Outcomes with Computerized Protocol

- Compared with the use of a paper-based protocol, use of eGMS resulted in:
  - A lower mean BG value (103 ± 8.8 mg/dL vs 117 ± 16.5 mg/dL, *P*<0.001)
  - Shorter time to reach BG target (4.8 ± 2.8 hours vs 7.8 ± 9.1 hours *P*<0.01)
  - A higher percentage of BG readings falling within target BG range (71.0 ± 17.0 vs 51.3 ± 19.7, *P*<0.001)
  - Rates of hypoglycemia were similar between the 2 groups





Newton CA, et al. *J Hosp Med.* 2010;5(8):432-437.

Improved Outcomes with Computerized Protocol

- Use of eGMS may also decrease the risk of hypoglycemia
- A recent retrospective review compared hypoglycemia outcomes of 54 critically ill patients who received insulin infusions
  - Of these patients, 27 of these received care using eGMS and 27 received care using a paper-based protocol
- Compared with the use of a paper-based protocol, use of eGMS resulted in:
  - Significantly lower percentage days with hypoglycemia, defined as BG <70 mg/dL (21.5% vs 1.3%, $P<0.0001$)
  - Significantly lower frequency of severe hypoglycemia, defined as BG <40 mg/dL (5.4% vs 0.01%, $P<0.0001$)
  - Greater time spent in target BG range (31.5% vs 63.7%, $P<0.0001$)

Rabinovich M, et al. J Diabetes Sci Technol. 2018;12(1):47-52.

Conclusions

- IV insulin infusion is recommended for critically ill patients with BG levels >180 mg/dL
- The use of insulin infusion protocols standardizes care and improves clinical outcomes
- Protocol should include strict BG monitoring and personalized insulin infusion rate titration to achieve and maintain BG targets

Conclusions

- Use of a computerized eGMS minimizes clinician error and can improve time to achieve target BG and BG maintenance
- Multiple clinical studies show an advantage of computerized insulin infusion protocol, compared with paper-based
  - However, some hospitals may experience barriers to implementation, such as cost, usability, access, and understanding of protocols
- Future use of insulin infusion protocols may include use of insulin pumps and closed loop systems that may further reduce provider fatigue

Contributors

- AACE would like to thank the following endocrinologists for their contributions.

  - Dr. Georgia Davis, MD
  - Dr. Javier Morales, MD, FACE
  - Dr. Sarah Nadeem, MD, FACE

Full Reference List

American Diabetes Association. 15. Diabetes Care in the Hospital: *Standards of Medical Care in Diabetes-2020*. *Diabetes Care*. 2020;43(Suppl 1):S193-S202.

Beesley SJ, Hirshberg EL, Lanspa MJ. Glucose management in the intensive care unit: are we looking for the right sweet spot?. *Ann Transl Med*. 2016;4(18):347.

Bogun M, Inzucchi SE. Inpatient management of diabetes and hyperglycemia. *Clin Ther.* 2013;35(5):724-733.

Boord JB, Sharifi M, Greevy RA, et al. Computer-based insulin infusion protocol improves glycemia control over manual protocol. *J Am Med Inform Assoc.* 2007;14(3):278-287.

Braithwaite SS, Clement S. Algorithms for intravenous insulin delivery. *Curr Diabetes Rev*. 2008;4(3):258-268.

Braithwaite SS, Clark LP, Idrees T, Qureshi F, Soetan OT. Hypoglycemia Prevention by Algorithm Design During Intravenous Insulin Infusion. *Curr Diab Rep.* 2018;18(5):26.

Deedwania P, Kosiborod M, Barrett E, et al. Hyperglycemia and acute coronary syndrome: a scientific statement from the American Heart Association Diabetes Committee of the Council on Nutrition, Physical Activity, and Metabolism [published correction appears in Circulation. 2010 Jun 15;121(23):e444]. *Circulation*. 2008;117(12):1610-1619.

Falciglia M, Freyberg RW, Almenoff PL, D'Alessio DA, Render ML. Hyperglycemia-related mortality in critically ill patients varies with admission diagnosis. *Crit Care Med*. 2009;37(12):3001-3009.

Jacobi J, Bircher N, Krinsley J, et al. Guidelines for the use of an insulin infusion for the management of hyperglycemia in critically ill patients. *Crit Care Med*. 2012;40(12):3251-3276.

Kavanagh BP, McCowen KC. Clinical practice. Glycemic control in the ICU [published correction appears in N Engl J Med. 2011 Mar 24;364(12):1182]. *N Engl J Med*. 2010;363(26):2540-2546.

Kelly JL. Continuous Insulin Infusion: When, Where, and How?. *Diabetes Spectr*. 2014;27(3):218-223.

Kodner C, Anderson L, Pohlgeers K. Glucose Management in Hospitalized Patients. *Am Fam Physician*. 2017;96(10):648-654.

Korytkowski MT. In-patient management of diabetes: Controversies and guidelines. *Indian J Endocrinol Metab*. 2013;17(Suppl 3):S630-S635.

Lansang MC, Umpierrez GE. Inpatient hyperglycemia management: A practical review for primary medical and surgical teams. *Cleve Clin J Med*. 2016;83(5 Suppl 1):S34-S43.

Lazar HL, McDonnell M, Chipkin SR, et al. The Society of Thoracic Surgeons practice guideline series: Blood glucose management during adult cardiac surgery. *Ann Thorac Surg*. 2009;87(2):663-669.

Full Reference List

Marvin MR, Inzucchi SE, Besterman BJ. Computerization of the Yale insulin infusion protocol and potential insights into causes of hypoglycemia with intravenous insulin. *Diabetes Technol Ther*. 2013;15(3):246-252.

Maynard G, Berg K, Kulasa K, O'Malley C, Rogers K. The Glycemic Control Implementation Guide. 2nd ed. Philadelphia, PA: Society of Hospital Medicine; 2015. Accessed August 10, 2020. www.hospitalmedicine.org/gc.

Moghissi ES, Korytkowski MT, DiNardo M, et al. American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on inpatient glycemic control. *Endocr Pract*. 2009;15(4):353-369.

Nazer LH, Chow SL, Moghissi ES. Insulin infusion protocols for critically ill patients: a highlight of differences and similarities. *Endocr Pract*. 2007;13(2):137-146.

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):432-437.

NICE-SUGAR Study Investigators, Finfer S, Chittock DR, et al. Intensive versus conventional glucose control in critically ill patients. *N Engl J Med*. 2009;360(13):1283-1297.

NICE-SUGAR Study Investigators, Finfer S, Liu B, et al. Hypoglycemia and risk of death in critically ill patients. *N Engl J Med*. 2012;367(12):1108-1118.

Qaseem A, Chou R, Humphrey LL, Shekelle P; Clinical Guidelines Committee of the American College of Physicians. Inpatient glycemic control: best practice advice from the Clinical Guidelines Committee of the American College of Physicians. *Am J Med Qual*. 2014;29(2):95-98.

Rabinovich M, Grahl J, Durr E, et al. Risk of Hypoglycemia During Insulin Infusion Directed by Paper Protocol Versus Electronic Glycemic Management System in Critically Ill Patients at a Large Academic Medical Center. *J Diabetes Sci Technol*. 2018;12(1):47-52.

Salinas PD, Mendez CE. Glucose Management Technologies for the Critically Ill. *J Diabetes Sci Technol*. 2019;13(4):682-690.

Shetty S, Inzucchi SE, Goldberg PA, Cooper D, Siegel MD, Honiden S. Adapting to the new consensus guidelines for managing hyperglycemia during critical illness: the updated Yale insulin infusion protocol. *Endocr Pract*. 2012;18(3):363-370.

Umpierrez G, Cardona S, Pasquel F, et al. Randomized Controlled Trial of Intensive Versus Conservative Glucose Control in Patients Undergoing Coronary Artery Bypass Graft Surgery: GLUCO-CABG Trial. *Diabetes Care*. 2015;38(9):1665-1672.

Umpierrez GE, Hellman R, Korytkowski MT, et al. Management of hyperglycemia in hospitalized patients in non-critical care setting: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab.* 2012;97(1):16-38.

Wallia A, Umpierrez GE, Rushakoff RJ, et al. Consensus Statement on Inpatient Use of Continuous Glucose Monitoring. *J Diabetes Sci Technol.* 2017;11(5):1036-1044.