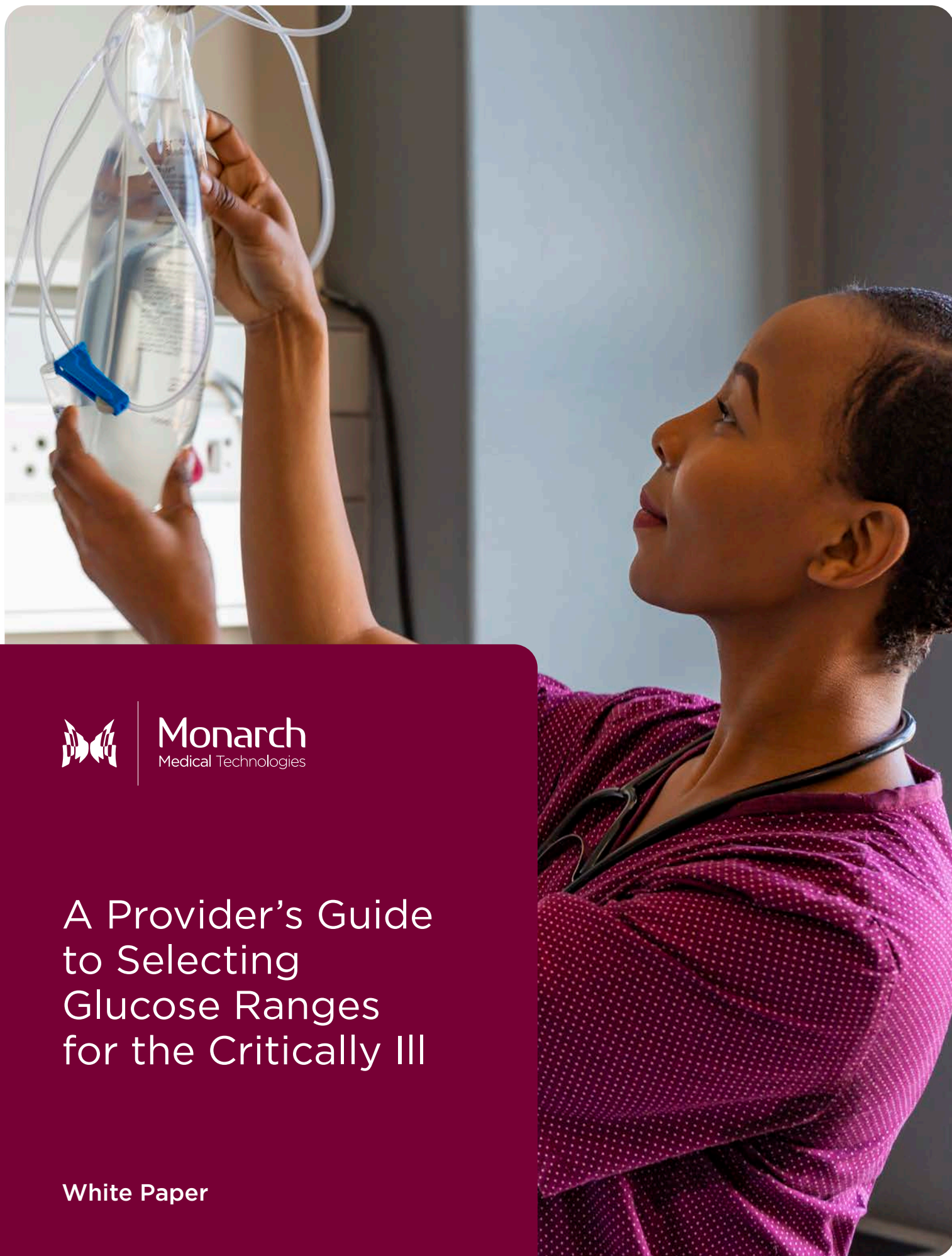




Monarch
Medical Technologies

A Provider's Guide to Selecting Glucose Ranges for the Critically Ill

White Paper

Summary

When treating hyperglycemia in critically ill patients, the desired goal range prescribed should be patient specific and not based on a patient's diagnosis or fear of hypoglycemia. Mortality is negatively impacted when desired glycemic control does not correlate with pre-hospital glycemia.

- In-patient glycemic control should be based on a patient's pre-hospital glycemic control.
- It is now recommended you have more than one glycemic goal in each critical care unit.
- Regardless of what goal is selected, there should be an extremely low level of hypoglycemia; especially for those treated to tighter goal ranges.
- EndoTool® Glucose Management System allows the clinician to customize the treatment for each patient safely and effectively with the lowest possible rates of hypoglycemia while improving nursing workflow and satisfaction.
- EndoTool allows clinicians to select one of three customizable goal ranges for each patient while minimizing the incidence of hypoglycemia ($< 70\text{mg/dl}$) to 0.6% when utilizing a goal range of 90-120mg/dl.

Introduction

Critically ill patients, whether admitted with a medical diagnosis such as sepsis or recovering from a major surgical procedure, often require an insulin infusion to maintain adequate glycemic control.

Providers usually select a specific goal range for a specific type of patient. For example, physicians will prescribe a lower goal range (90-120mg/dl) for a cardiac surgery patient to minimize the development of deep sternal wound infections but select a higher goal range (140-180mg/dl) for patients in the medical intensive care unit. Often only one goal range will be utilized in a specific critical care unit to minimize variability or because of limitations with a non-computerized dosing protocol. Recent research supports the goal range selected for a critically ill patient should now be aligned with their pre-hospital glycemic control.



Glycemic Targets

Standards of Care

Often, hospitals will be hesitant to utilize a goal range less than 140-180mg/dl based on the conclusions of the NICE SUGAR study¹ and the ADA Standards of Care 2023².

The ADA Standards of Care 2023 provides two recommendations regarding glycemic targets:

- 16.4: Insulin therapy should be initiated for the treatment of persistent hyperglycemia starting at a threshold of $\geq 180\text{mg/dl}$ (checked on two occasions). Once insulin therapy is started, a target glucose range of 140-180mg/dl is recommended for most critically ill and noncritically ill patients.
- 16.5: More stringent goals, such as 110-140mg/dl or 100-180mg/dl may be appropriate for selected patients and are acceptable if they can be achieved without significant hypoglycemia.

In the 2009 NICE SUGAR multicenter study:

- 27.5% of patients treated with intensive insulin therapy (IIT) to maintain a glucose level of 81-108mg/dl had died at 90 days.
- 24.9% of those treated with conventional therapy to maintain a blood glucose of less than 180mg/dl died at 90 days.

This difference represented an absolute difference in mortality of 2.6 percentage points (95% CI, 0.4 to 4.8), and the odds ratio for death with IIT was 1.14 (95% CI, 1.02 to 1.28; $P=0.02$).

In addition, severe hypoglycemia (blood glucose level, $\leq 40\text{mg}$ per deciliter [2.2 mmol per liter]) was reported in 206 of 3016 patients (6.8%) in the IIT group and 15 of 3014 (0.5%) in the conventional-control group ($P<0.001$).

Hypoglycemia in the intensive care unit has been associated with an increase in mortality³.

The findings from the NICE SUGAR study are in contrast with an earlier single center study by Van Den Berghe⁴, in which IIT to maintain blood glucose at or below 110mg per deciliter reduced morbidity and mortality among critically ill patients in the surgical intensive care unit.

Differences between the two studies include:

- More diabetics in the NICE SUGAR study (20% vs 13%).
- Higher percentage of surgical patients in the Van Den Berghe study (63% vs 35%).

This is consistent with other studies demonstrating that hyperglycemia in non-diabetics is associated with a higher in-hospital mortality rate than diabetics⁵.

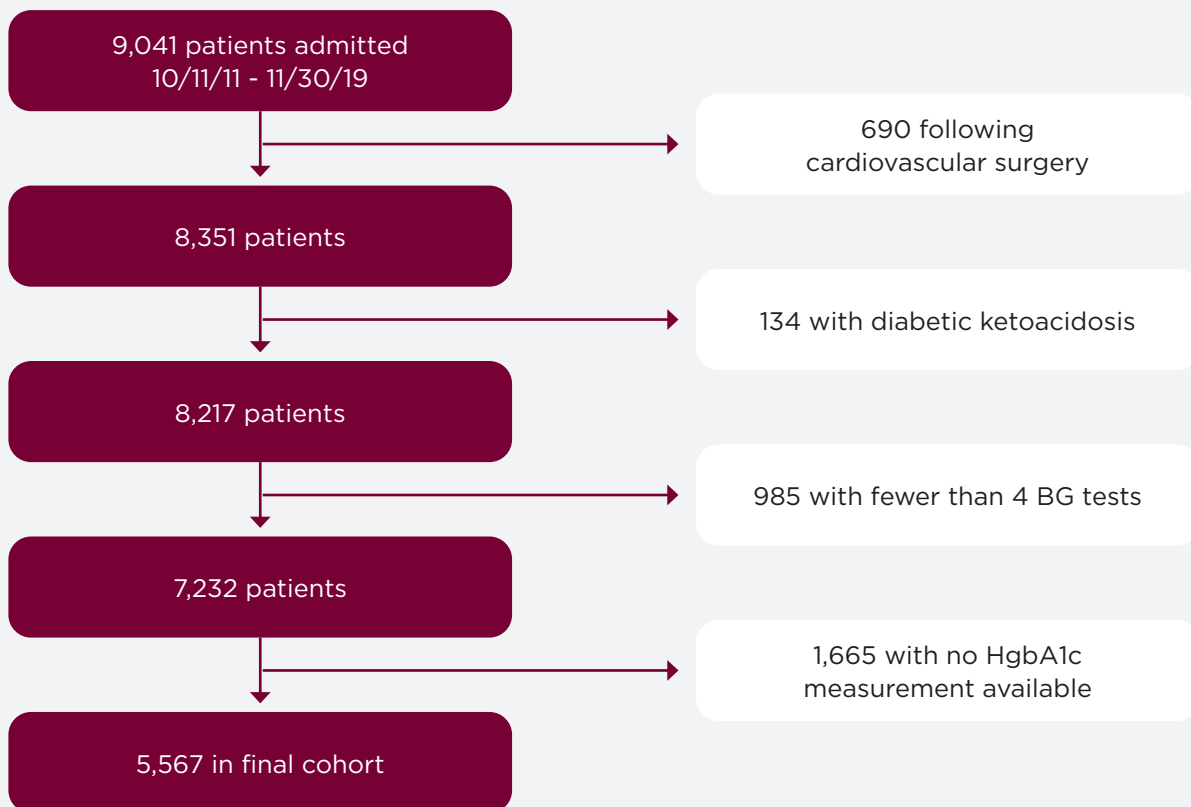
The Shift from One Size Fits All

Individualized Glycemic Targets

A recent study by Krinsley⁶ adds clarity to the above findings and defines a paradigm shift from “one size fits all” to setting a glycemic goal based on a patient’s pre-hospital glycemic status.

In this study, there were 5,567 critically ill patients analyzed who had four or more blood glucose tests and a HgbA1c level obtained and were admitted between October 11, 2011 and November 30, 2019. Patients without complete data, a diagnosis of DKA or those who were post cardiovascular surgery (due to low mortality following cardiac surgery).

Cohort Selection



The patients were treated to the following targets:

- 90-120mg/dl for patients admitted before September 14, 2014 (n = 1,614).
- One of two targets after September 14 (n= 3,953).
 - 80-140mg/dl for patients with HgbA1c less than 7%.
 - 110-160mg/dl for those with a HgbA1c greater than or equal to 7%.

The outcome of patients was stratified based on their admission HgbA1c levels; less than 6.5%, - 7.9% and equal to or greater than 8%. The primary analysis was the relationship of inpatient glucose metrics to mortality, stratified by HgbA1c bands. Among patients with HgbA1c less than 6.5%, mortality increased as mean glycemia increased; however, among patients with HgbA1c greater than or equal to 8.0%, the opposite relationship was observed.

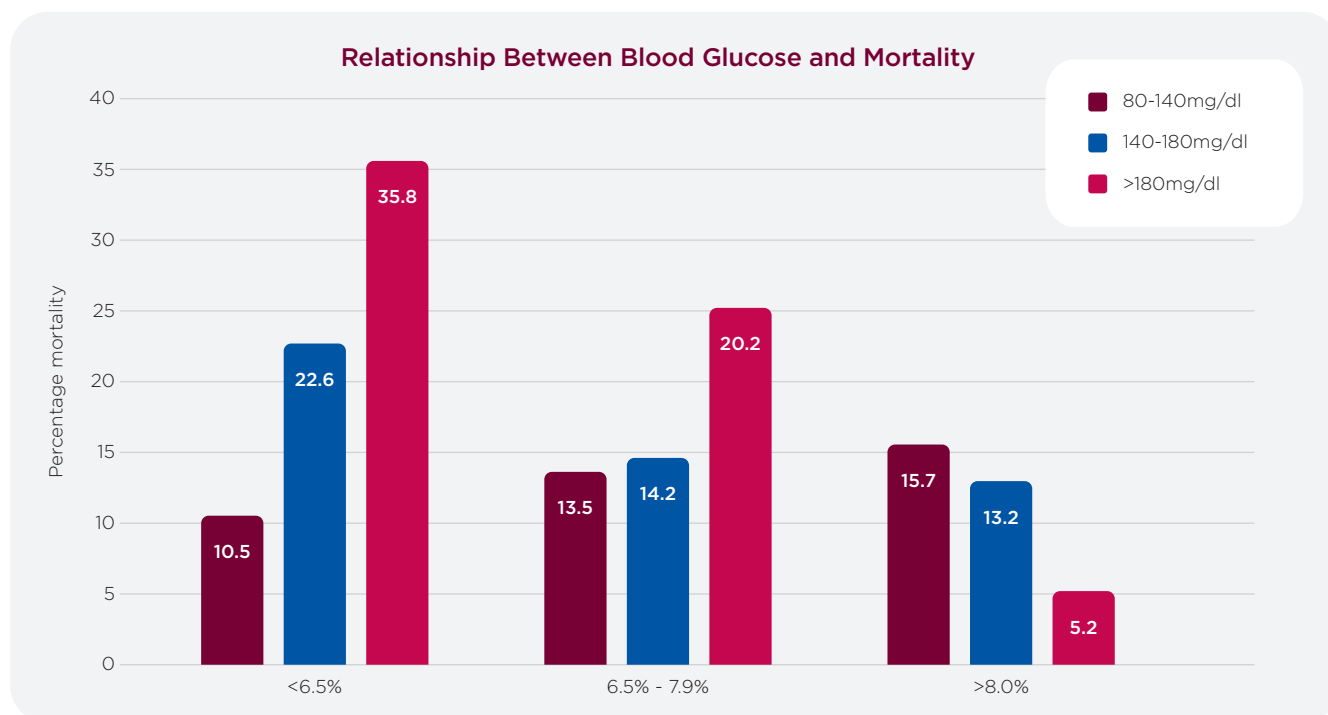


Figure 1. Relationship between mean blood glucose (BG) (mg/dl) and mortality, stratified by hemoglobin A1c (HgbA1c) level. For patients with HgbA1c less than 6.5%, higher mean BG is strongly associated with increased mortality. For patients with HgbA1c greater than or equal to 8.0%, the opposite relationship is observed.

There is a greater than a threefold increase in mortality when a non-diabetic (or HgbA1c < 6.5%) is treated with a goal of > 180mg/dl vs a goal range of 80-140mg/dl. Strictly adhering to the findings of the NICE SUGAR study.

Increasing glucose variability and hypoglycemia rates were also associated with increased mortality in patients with a HgbA1c of less than 6.5%. The rate of severe hypoglycemia, less than 40mg/dl, was 0.8% for those with a HgbA1c less than 6.5% and 1.1% for those with a value greater than 6.5%.

When comparing the NICE SUGAR with the study by Van Den Berghe, a plausible reason for the differences in mortality can be attributed to different populations in the studies which is supported by Krinsley's work demonstrating a correlation between pre-hospital glycemic status and in-hospital glycemic control.

With fewer diabetics on the Van Den Berghe study, this population would have fared better with tighter control. Whereas in the NICE SUGAR study there were more diabetics whose mortality would have been positively impacted by less intensive glucose control.

Study Conclusions

In-hospital glycemic targets in critically ill patients should be:

- 1 Patient specific; not one goal range is appropriate for all patients.
- 2 Based on a patients pre-admission HgbA1c rather than determined by the admission diagnosis or location of care.
 - Post cardiac surgery vs sepsis.
 - Medical ICU vs Surgical ICU.
- 3 Severe hypoglycemia should be avoided in all patients, especially non-diabetics.

Safe Patient Specific Treatment for Glycemic Control

The Solution

EndoTool® is clinical decision support software which provides recommendations for both intravenous and subcutaneous insulin. The nurse-driven platform is designed to help providers achieve safe, effective and patient specific glycemic control. With the ability to have up to three distinct glucose control ranges within a nursing unit, it is no longer necessary to treat all post cardiac surgery patients to the same glycemic goal. Despite what goal range is selected, the incidence of severe hypoglycemia is exceedingly low.

When utilizing a paper-based protocol, treating varying glucose goal ranges within a single nursing unit has the potential to create nursing errors and is unlikely to achieve the desired hypoglycemia rates. Paper protocols also increase nursing workflow and generally are a dissatisfier for the nursing staff when compared with a computerized dosing algorithm⁷.

EndoTool has been proven to improve nursing satisfaction and reduce dose deviation by up to ten-fold⁷.

Shown in the table is a summary of our customer database for 2022. Note the very low rates of hypoglycemia for all goal ranges. Even with the tightest goal range of 90-120mg/dl the rates are **at least five-fold lower than any rates documented in the above studies** and equate to only 13 blood glucose values less than 40mg/dl in all of 2022.

Glycemic Outcomes Based on Glucose Goal Ranges

	Glucose Goal Ranges (mg/dl)*			
	90-120	100-140	120-160	140-180
Total Readings	97474	203366	88353	274434
Hypo (< 70mg/dl)	0.60%	0.41%	0.23%	0.16%
Severe Hypo (< 40mg/dl)	0.013%	0.013%	0.014%	0.007%
Hyper (>180)	4.38%	6.93%	11.93%	23.81%
% glucoses 70-180mg/dl	94.9%	92.60%	87.80%	76.20%

*Full Year 2022

This data should allow a provider to confidently select a patient specific goal range and achieve safe glycemic control that can positively impact a patient's mortality. Given the low rates of hypoglycemia, utilizing tighter control is also within the 2023 ADA Standards of Care.

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Monarch Medical Technologies
P 877-349-4582
E info@monarchmedtech.com
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