

# A new era for diabetes-specific enteral nutrition policy: A scientific update



## *Position statement from the International Special Dietary Foods Industries*

### **ISDI Policy Statement\***

Diabetes-specific formulas (DSF) are a safe, efficacious and cost-effective strategy to support the management of hospitalized patients with or at risk for poor glucose control.

Evidence shows that use of DSF helps manage blood glucose levels, aiding recovery from illness or injury, and reducing health care costs.

ISDI recommends hospital nutrition care that aims to achieve and maintain glycemic control. ISDI endorses the use of DSF, a category of foods for special medical purposes.

*\*This policy statement is intended to create awareness of the value of DSF. Since DSF may not be suitable for all hospitalized patients, their recommendation should be made by physicians and dietitians following careful consideration of each patient's medical status and dietary needs.*

## **Hospital patients are at risk for poor glucose control**

Hospitalized patients are at risk for poor glucose control — blood glucose levels that are too high, too low, or too variable. Abnormal glucose levels occur for a wide range of reasons including the presence of diabetes or pre-diabetes in admitted populations,<sup>1</sup> altered glucose metabolism due to treatment medications,<sup>2</sup> metabolic stress of critical illness,<sup>2,3</sup> or stress responses to serious injury or surgery<sup>4,5</sup> and nutrition support<sup>6-8</sup> (Figure 1). While diabetes nutrition guidelines advise how food choices can help achieve normal glucose levels,<sup>9,10</sup> patients who are hospitalized cannot always follow such diets due to illness or injury. Patients who are unable to meet

For hospitalized patients, the evidence on the importance of glycemic control is clear. Poor control leads to adverse health outcomes, while good control improves patient outcomes and cuts costs of care.

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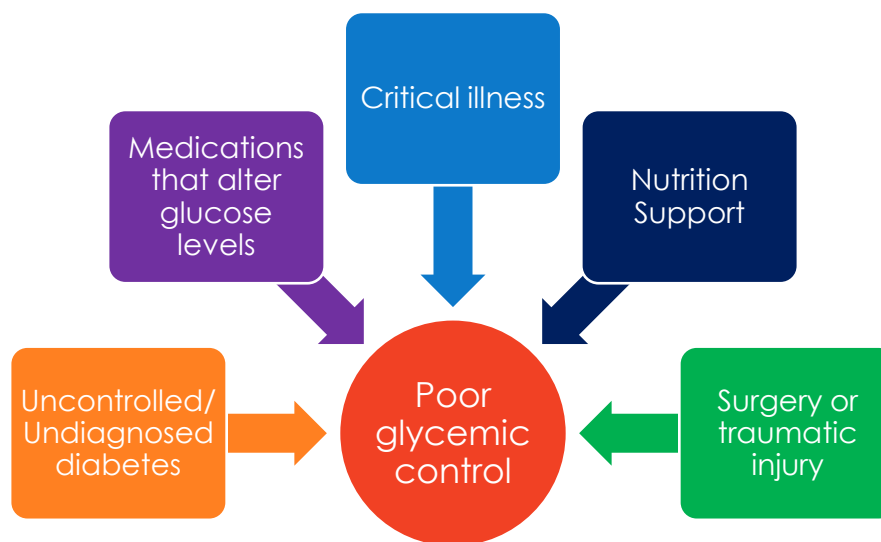
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their nutritional requirements through oral dietary intake alone often require an enteral nutrition formula to be administered via a tube to help achieve nutrition goals. In patients with or at risk of hyperglycemia, initiation of an enteral tube feeding can be challenging, since enteral tube feeding is reported to be an independent risk factor for the onset of hyperglycemia.<sup>7,8,11-13</sup> DSF are considered a safe and effective strategy to help maintain glucose control while providing essential nutrition.<sup>12,14</sup>

The evidence on the importance of glycemic control for hospitalized patients is clear. Poor glucose control leads to adverse health outcomes, while good control improves patient outcomes and cuts costs of care.<sup>14-18</sup>

*Figure 1. Factors associated with poor glucose control in hospitalized patients*



## Diabetes specific formulas improve glucose control and outcomes

According to the 2017 American Diabetes Association standard of care, two key goals for nutrition therapy of hospitalized patients are to: 1) Optimize glycemic control and 2) Provide adequate nutrients to meet metabolic demands.<sup>19</sup> Unlike standard formulas, DSF are designed specifically to help meet these goals. While both formulas are designed to provide nutrients to help meet metabolic nutrition requirements, only DSF are designed to help minimize glycemic response. DSF have some of the following features compared to standard nutritional formulas:

- Lower carbohydrate content
- Higher proportion of carbohydrates that have a low glycemic index and/or are slowly digestible, e.g. by replacement of high glycemic-index maltodextrin, starch,

and sucrose with low glycemic-index carbohydrates such as digestion-resistant maltodextrin, isomaltulose, and sucromalt, non-hydrolysed starches among others.

- Fat content enriched in unsaturated fatty acids, particularly monounsaturated fatty acids
- Higher fibre content

## Managing glycemic response

Elia et al. conducted a systematic review and meta-analysis on the impact of using DSF for nutrition (as oral nutritional supplements or as enteral tube feedings) for inpatients or outpatients with diabetes. Compared with standard formulas, DSF significantly reduced the post meal rise in blood glucose, including lower peak glucose concentration and lower glucose area under the curve. Studies within the analysis found reduced requirements for insulin (26-71% lower) and fewer complications with DSF compared with standard nutritional formulas. Elia et al. concluded that short- and long-term use of DSF as oral supplements and tube feeds are associated with improved glycemic control compared with standard formulas.<sup>20</sup>

Clinical evidence supports the use of DSF to help:

- Improve glucose levels
- Reduce hypoglycemia
- Reduce insulin requirements
- Reduced length of stay

A systematic review by Ojo and Brooke provided further evidence that DSF are effective for managing glycemic status of hospitalized patients with diabetes on enteral nutrition tube feeding by improving postprandial glucose levels, HbA1c levels and insulin responses.<sup>21</sup> In outpatients with type 2 diabetes, Huhmann et al. showed that DSF improved glucose stabilization and management compared with a standard formula.<sup>22</sup> DeLuis et al. showed reduced glycemic and insulinemic responses after administering DSF when compared to a standard formula.<sup>23</sup> In these studies, DSF were found to safely and effectively lower high blood glucose levels without increasing risk of hypoglycemia.

## Reducing glycemic variability

Glycemic variability is often used as a marker for glycemic control in clinical studies. Several studies have demonstrated the use of DSF had marked beneficial effects on reducing glycemic variability compared to the use of standard formulas.<sup>17,24,25</sup>

## Improving outcomes in acute and critical illness

Additional studies demonstrate the effectiveness of DSF for blunting hyperglycemia of stress-related metabolism in patients in acute and critical care settings. Hamdy et al. identified greater clinical benefits associated with DSF over standard formulas. The researchers conducted a retrospective analysis of 85,481 inpatients hospitalized over a 10-year period (2000-2009) and demonstrated that DSF reduced hospital length of stay by approximately one day compared to standard formulas.<sup>26</sup>

Mesejo et al. showed improved glycemic control (lowered insulin requirements, improved glycemic control and reduced the risk of acquired infections) in critically ill, mechanically ventilated patients in nine Spanish intensive care units (ICU) when patients received DSF (compared to those who received standard enteral nutrition tube feeding).<sup>17</sup>

### Reducing insulin requirements and risk of hypoglycemia

Several studies demonstrated that the use of DSF reduce insulin requirements as well as incidence of hypoglycemia.<sup>17,24,27,28</sup> de Azevedo et al. showed the use of DSF as part of a carbohydrate restrictive strategy significantly reduced insulin requirements and incidence of hypoglycemia in critically ill patients.<sup>27</sup> Han et al. conducted a retrospective analysis of clinical outcomes of patients with type 2 diabetes who were admitted to the ICU between 2009 and 2013 and were provided with DSF or non-diabetes-specific formulas (non-DSF). Results showed that the use of DSF were associated with significantly reduced insulin requirements, decreased mortality, and lower ICU costs.<sup>16</sup>

### Endorsement by the nutrition expert group

A recently published European Society for Clinical Nutrition and Metabolism (ESPEN) expert group endorses the use of DSF as part of their recommendations related to carbohydrates and insulin resistance in clinical nutrition states.<sup>12</sup>

*“Based on this available evidence, the ESPEN expert group endorses the utilization of DSFs for nutritional support of people with obesity and diabetes.”*

## Poor glycemic control is common in hospitalized patients and leads to poorer health outcomes

Patients with diabetes have a 3-fold greater chance of hospitalization than those without diabetes<sup>14</sup>. Further, in people with diabetes, hyperglycemia is often exacerbated during hospitalization due to illness or injury, treatment, and changes in eating patterns. Other hospitalized patients experiencing hyperglycemia may not have a diabetes diagnosis on admission, but the metabolic stress of illness, injury, or anesthesia and surgery can lead to insulin resistance and hyperglycemia.<sup>11,29</sup> In fact, studies suggest that approximately 80% critically ill hospitalized patients experience hyperglycemia.<sup>30,31</sup> By contrast, the incidence of hypoglycemia in hospitalized patients may seem low (8% of those with diabetes), but this condition is serious and markedly increases risk of death.<sup>32,33</sup>

Report suggests that up to 80% of critically ill patients experience hyperglycemia in the hospital

Scientific evidence demonstrates that uncontrolled glycemia predisposes hospitalized patients to adverse clinical outcomes:

- **7-times greater risk of perioperative infection** with hyperglycemia in orthopedic surgery patients (vs those with lower glycemic levels).<sup>34</sup>
- **Increased hospital length of stay (LOS)** in patients with exacerbations of chronic obstructive pulmonary disease who also had hyperglycemia; LOS was increased by 10% for each mmol/L increase in mean glucose.<sup>35</sup>
- **Greater risk for mortality** was reported for patients with penetrating-trauma injuries and hyperglycemia, i.e., patients who died were 4—8 times more likely to have experienced hyperglycemia than were those who survived.<sup>4</sup>
- **More than 2-times higher risk of mortality** among hospitalized patients with hypoglycemia; hypoglycemia can be spontaneous or can result from insulin treatment.<sup>36</sup>
- Glycemic variability in critically ill patients is recognized as a strong **predictor of mortality**.<sup>37</sup>
- **Longer LOS, more frequent 28-day readmissions, and higher mortality rates** were associated with hyperglycemia at hospital admission in acute medical patients.<sup>38</sup>

## Diabetes specific formulas provide cost benefits

Goals of nutrition therapy in healthcare include ensuring patients receive adequate energy intake and nutrients, thus improving the likelihood of better health outcomes. Recent data indicate that glycemia targeted nutrition therapy has the potential to reduce overall healthcare costs. For instance, several clinical studies using DSF demonstrate reduced LOS and lower hospital costs.

- Hamdy et al. evaluated the impact of DSF versus standard nutrition in tube-fed diabetic patients hospitalized for acute illness. The study was a 10-year, retrospective analysis of more than 85,000 hospitalized patients. Findings showed that those fed DSF had nearly a 1-day shorter stay in the hospital, reducing the total cost of care by about \$2500 US.<sup>26</sup>
- Type 2 diabetes patients hospitalized with critical illness in Taiwan received enteral feeding with either DSF or standard formula for at least 5 days. The study showed that use of DSF were associated with shorter ICU LOS significantly lowering the total ICU cost in patients fed DSF compared to those fed non-DSF (\$6700 US vs \$9200 US).<sup>16</sup>

## Summary statement

The evidence on the importance of DSF to support glycemic control for hospitalized patients is compelling. Poor glycemic control leads to adverse health outcomes, while good glycemia control improves patient outcomes and cuts total cost of care.<sup>14-18</sup> Furthermore, scientific evidence demonstrates that the use of DSF is an efficacious and cost-effective strategy to support the management of hospitalized patients at risk for poor glycemic control.

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## Appendix

### What is glycemic control?

Glycemic control refers to physiological, nutritional, and medical means of altering blood glucose levels. Normally, the pancreas releases amounts of the hormone insulin that are proportionate with levels of glucose in the blood. In turn, this circulating insulin travels to target tissues (skeletal muscle, adipose, liver), where it binds receptors on the cell surface and initiates signals to control glucose uptake, use, or storage in these cells. When insulin-mediated glucose disposal is well controlled by these normal physiological processes, blood glucose levels are normal, i.e., *euglycemia* is maintained (Table 1). However, many people, especially those who are hospitalized, experience glucose levels that are too high, too low, or too variable.

Conditions of poor glucose control can have serious adverse health consequences, thus optimal glycemic management is key to good healthcare practice.

Table 1. Blood glucose levels and glycemic status

Terms used to talk about glycemia	Definition
<b>Euglycemia</b>	<i>The prefix eu-</i> means <i>good or true</i> , so <i>euglycemia</i> refers to normal blood glucose levels or normoglycemia. The normal range for fasting blood glucose is 70—100 mg/dL (3.9—5.6 mm/L) or less than 180 mg/dL (10 mmol/L) after a meal. For individuals who are ill or injured, higher target ranges are sometimes recommended to avoid risk for abnormally low blood glucose levels.
<b>Hyperglycemia</b>	<i>Hyper-</i> means <i>over or above</i> ; <i>hyperglycemia</i> describes blood glucose levels that are above normal, as occur in people with untreated or poorly controlled diabetes mellitus.
<b>Hypoglycemia</b>	<i>Hypo-</i> refers to <i>below, beneath, or under</i> ; <i>hypoglycemia</i> , below-normal blood glucose levels, can occur when insulin or other anti-diabetic medications are given at doses that exceed what is needed for uptake of glucose by target tissues (muscle, adipose, and liver). Less frequently, hypoglycemia may occur spontaneously.