



# Changing the standard of care:

Frequent insulin dose titration improves  
health outcomes and quality of life for  
those with type 2 diabetes

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## Introduction



**Insulin has been used to treat diabetes for more than 100 years. Yet over two-thirds of the 10 million people using insulin for type 2 diabetes in the United States still fail to get their blood sugar under control<sup>1</sup>. Is insulin not working? Or is it the way we use insulin that needs to change?**

Today's standard of care is to adjust insulin doses during physician office visits a few times annually. But that's not enough. The body's insulin needs change frequently, and doses need to be adjusted accordingly.

This paper will discuss why the current standard of care is failing patients who inject insulin; how frequent insulin titration will benefit patients; and how to achieve that titration frequency at the scale needed within our healthcare environment.

## A few times a year is not enough.

Today, a person with type 2 diabetes who injects insulin will typically see their doctor two to four times a year for evaluation and consultation. Insulin doses are usually adjusted during those appointments. In some practices, a nurse care manager or a pharmacist provides additional outreach and may offer coaching or other strategies for overall diabetes management.

The problem is this schedule misses the body's constant changes that occur in between insulin dose adjustments. And that is seldom safe or effective.

Insulin requirements are highly dynamic, whether or not a person has diabetes. In normal physiology, the pancreas responds to the body's constantly changing needs and modifies the amount of insulin it secretes. When diabetes is advanced and insulin injections are needed, the body's insulin requirements continue to be dynamic. However, in standard practice, the patient's insulin dose changes only when the doctor adjusts or titrates it.

But safe and effective insulin therapy requires constant titration to accommodate the body's changing insulin needs.



“Total insulin requirements per day vary considerably and constantly change without ever achieving a steady state.”

Hodish I. Insulin Therapy for Type 2 Diabetes – Are We There Yet? The d-Nav® Story. Clin Diabetes Endocrinol. 2018 Apr 10;4:8.



## Insulin therapy for patients with type 2 diabetes is a necessity, not a choice.

There are roughly 10 different classes of oral and injectable non-insulin medications available for managing type 2 diabetes.<sup>2</sup>

Typically, oral or injectable non-insulin medications are used earlier in a patient's diabetes journey. Because type 2 diabetes is a progressive condition of insulin deficiency, over time the body secretes less and less insulin. This is not the patient's fault. It is the natural trajectory of the disease. During the second decade of the disease, most patients require insulin injections because they become overtly insulin deficient and no longer respond adequately to non-insulin drugs.<sup>3</sup>

Generally, patients who progress to using insulin do not stop taking oral medications. Instead, insulin is added to their treatment regimen. This accumulation of medications can be cost prohibitive for patients, and the health system in general.<sup>4</sup>

These medications have not translated to improvements in patients' glucose levels. In a study published in *Diabetes Care*,<sup>5</sup> researchers reviewed trends in glucose-lowering drug use for 1.66 million patients for an eight-year period and found no improvement in average glycemic management.

Some non-insulin medications may offer a specific benefit to patients with diabetes with certain complications, but ultimately average glucose or HbA1c is still the most important marker of treatment success. The higher the HbA1c, the greater the chances to develop complications and unfortunately die prematurely.<sup>6</sup>



## Infrequent insulin dose adjustment leads to poor outcomes.

Insulin as a drug does not have an upper dosage limit, and there is no glucose that it cannot reduce. Yet, for the majority of patients with type 2 diabetes on insulin, adjusting insulin dosage a few times a year during office visits is not effective and the delay between titrations can even be harmful.

Not only do insulin requirements constantly change, but the total amount of insulin units required per day are unique to each individual. Some people need less than 50 units a day, while others may need more than 500.<sup>7</sup>

This does not signify that one patient is healthier than another. Rather, it's a measure of how much a person's pancreas secreted before it failed. Taking a higher number of insulin units per day may simply be what that person's body needs.

Insulin requirements change over time and never reach a steady state. This means that unless insulin doses change frequently, most of the time the patient is undertreated and suffers from high HbA1c or overtreated and suffers from hypoglycemia (when glucose is too low).

The variations in insulin needs are not trivial. It has been shown that most patients with type 2 diabetes who use insulin go through periods where insulin requirements drop considerably, almost by half, and for months at a time. It's a phenomenon that cannot be predicted. When this occurs, insulin doses must be reduced quickly, or the patient can experience hypoglycemia – which is unsafe.<sup>8</sup>

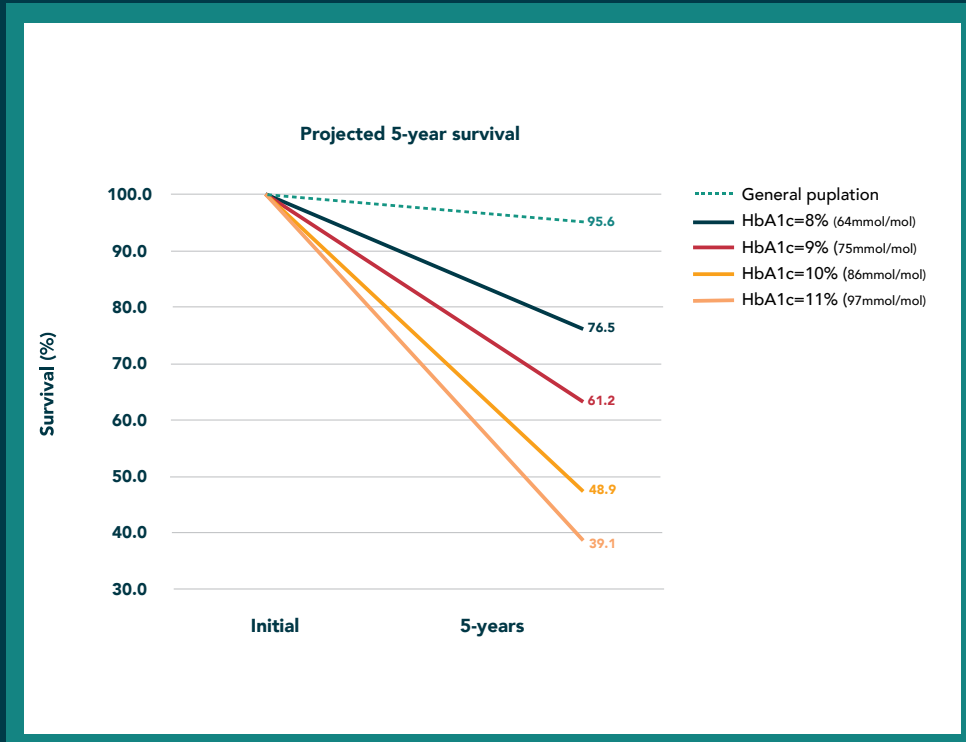
Given the limitations of the current standard of care, which does not allow insulin users to have their insulin doses optimized frequently, most patients who use insulin do not achieve target range for their HbA1c and may be exposed to unnecessary hypoglycemia. Living with elevated HbA1c presents a host of major health risks.

Research has found that every 1% HbA1c higher than 7% is associated with 15 – 45% reduced survival rates.<sup>6</sup> Using this information, Israel Hodish, MD, PhD, medical director and co-founder at Hygieia, projected the five-year survival rate for those with different HbA1c levels (Fig. 1). In his analysis, the five-year survival rate of someone living with a 10% HbA1c is less than 50%.

Furthermore, high HbA1c is associated with major complications which may become acute. For example, high HbA1c is linked to a 250% higher mortality rate from major bacterial infection in patients aged 65+<sup>9</sup>. Further, high HbA1c is linked to kidney damage, eye damage, heart attacks, heart failure, strokes, foot ulcers and more.<sup>10</sup>

Another study showed that the strongest predictor for risk of heart attack, stroke or death is elevated HbA1c. Similarly, maintaining HbA1c within the therapeutic range reduces the risks to the same level as the population without diabetes.





(Figure 1)



*Living with poorly controlled diabetes is as dangerous as living with advanced cancer.*

*- Israel Hodish, M.D., Ph.D.*



## Frequent insulin dose adjustments: the best strategy for meeting HbA1c targets.

As we've shown, maintaining HbA1c in range is singularly important for lowering the risk of complications from diabetes and increasing survival rate. The only way to achieve glycemic control in patients with advance diabetes is through frequent insulin dose adjustments.

For example, in clinical trials where insulin doses were adjusted every few days or weeks by highly funded study teams, patients achieved HbA1c goals.<sup>12, 13</sup> Yet, once those adjustments became infrequent, glycemic control worsened.<sup>14</sup>

Without the guiderails present in a controlled clinical trial environment however, it's difficult to adjust insulin doses as often as needed. First, there are limitations in time and resources. It's not practical for patients to visit their physician every week and physicians do not have the bandwidth to add weekly appointments for their patients who use insulin. Nor will insurance cover non-urgent weekly visits.

Second, insulin therapy is a complex, individualized process that needs continual oversight and modification. Most patients use more than one injection per day and each injection should be titrated independently. Any insulin titration guideline requires constant patient data review and communications, which are not feasible within the current standard of care.<sup>15</sup>



## Frequent insulin titration is possible with technology.

If frequent insulin titration is the key to reaching and maintaining glycemic control, how do we incorporate it into current healthcare practice, particularly when provider offices are stretched thin, and lack the time and resources to see patients every week for insulin adjustment?

The answer is in technology - specifically, artificial intelligence that enables patients to receive a personalized insulin dose recommendation each time they inject.

This technology currently exists in the d-Nav® Insulin Management Program, an FDA-cleared technology that uses a patient's glucose readings to autonomously calculate each dose of insulin. Patients get their dose recommendation directly without waiting for a clinician to review it. With d-Nav Technology, patients can quickly and easily receive insulin dose adjustments as often as they need it. In fact, many patients receive more than 50 insulin dose adjustments annually. The result: superior glycemic control, higher quality of life, fewer complications and less death. Studies show that nearly 90% of people using d-Nav report lower HbA1c in just three months<sup>16</sup> without increased risk of hypoglycemia<sup>17</sup>.

Looking at long-term results, patients have maintained HbA1c levels in the target range for more than seven years. (Fig. 2) This evidence was sufficient for the American Diabetes Association to recommend frequent insulin titration as a standard of care in the Standards of Medical Care in Diabetes.<sup>18</sup>



(Figure 2)

d-Nav Technology not only offers safety and effectiveness, it also provides a scalable solution. This is critical as the number of people with type 2 diabetes escalates and their demand for care outpaces the ability of physicians, and the healthcare industry, to deliver that care.

But artificial intelligence and other technologies offer medical professionals the ability to automate simpler tasks, enabling physicians to focus on the more complicated aspects of medicine that require their education, judgment, and skill.



## We must change the standard of care for insulin therapy.



Adjusting insulin doses just four times annually is failing patients. It's an expensive failure too, with an estimated \$327 billion spent on diagnosed diabetes in 2017.<sup>19</sup>

**Enabling autonomous dose adjustments is key to better outcomes.** Autonomous insulin dose titration results in superior glycemic control and treatment safety over the current standard of care. It's time to change the way we use insulin.

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