Addressing the Challenges of Invasive Glucose Monitoring

INDUSTRY PAPER
November 2019
Summary

- Diabetes is a well-recognized major disease burden worldwide that requires regular monitoring of glucose levels to help prevent serious long-term and irreversible health complications.
- Poor adherence to regular glucose monitoring with current invasive testing methods puts affected people at higher risk of these complications.
- Current available methods are painful, inconvenient, can be complex to use and costly, which deters many people from regularly testing.
- All currently available glucose test methods involve invasive penetration of the skin to:
  - Directly test blood glucose levels via finger-prick and/or
  - Insert a sensor needle under the skin.
- A high need exists for a non-invasive glucose monitoring technology to make a major improvement in the lives of millions of people around the world living with diabetes.
- The non-invasive glucose monitoring market has significant untapped potential and is considered to be the “holy grail” in the diabetes therapeutic area.
- The Saliva Glucose Biosensor is a non-invasive technology being developed that is designed to replace the need for finger-prick tests, which represents the majority of current glucose testing.
- The Saliva Glucose Biosensor accurately detects glucose in saliva with a sensing capability at concentrations 100 times less than for blood glucose testing.
- The ability of a glucose test to provide pain-free, simple, convenient and discreet, non-invasive monitoring has major potential to improve the health and well-being of millions of people living with diabetes across the globe.
Diabetes is a Global Burden

What is Diabetes?
There are two main types of diabetes:

Type 1 diabetes is a chronic autoimmune condition whereby the pancreas produces little or no insulin. Why this occurs is unknown and there is currently no way to prevent Type 1 diabetes, which requires lifelong insulin treatment to manage blood glucose levels.

Type 2 diabetes is a chronic progressive condition whereby the pancreas gradually loses the ability to produce sufficient insulin and/or the body becomes resistant to the normal effects of insulin. The condition is most often caused by lifestyle factors such as obesity and insufficient physical activity, however genetics also plays an important role, particularly in Asian populations for whom this type of diabetes is described as an “epidemic”.

Magnitude of the Disease Burden
In 2019, 463 million people globally were living with diabetes including:

- More than 1.1 million children and adolescents (0–19 years of age) with Type 1 diabetes requiring insulin.
- Approximately 90 percent of diagnosed cases with Type 2 diabetes.

In addition, an estimated 374 million people had pre-diabetes in 2019, representing 7.5 percent of the adult population aged 20-79 years.

Pre-diabetes occurs when blood glucose levels are higher than normal, but not high enough to be classified as Type 2 diabetes. Higher than normal glucose levels puts these people at greater risk of developing Type 2 diabetes and its associated complications.

The number of adults with diabetes aged 20-79 years is predicted to rise to 700 million by 2045. The economic impact of diabetes is enormous, with global health expenditure exceeding US$845 billion per year.

“The non-invasive glucose monitoring market has significant untapped potential and is considered to be the “holy grail” in the diabetes therapeutic area.”

Regular Monitoring for Long-Term Health
Regular self-monitoring of glucose levels throughout the day helps people with diabetes to understand the impact that food intake, activity, stress, illness and other factors have on their glucose levels. Self-monitoring supports people to make appropriate lifestyle changes and/or adjust medications to better control their diabetes and hence may improve long-term health outcomes. This means it reduces their risk of diabetes-related complications such as heart attack, stroke, vascular disease and irreversible damage to eyes, kidneys and nerves.

Barriers to Glucose Testing
The three major factors contributing to inadequate diabetes management are poor adherence to recommended diabetes treatment, lifestyle changes and inadequate monitoring of glucose levels which consequently may lead to long-term health complications.

Addressing the Challenges of Invasive Glucose Monitoring

Patient self-monitoring blood glucose
Devices currently available to monitor glucose levels pierce the skin and fall into three main categories:

1. **Self-monitoring blood glucose (SMBG) devices** – where people may prick their finger up to 10 times per day for testing.

2. **Continuous glucose monitoring (CGM) devices** – where glucose levels in fluid surrounding body cells (interstitial fluid) are automatically tested with a sensor inserted under the skin and accompanied by finger-pricking needed in these situations:
   - To calibrate the CGM device.
   - When glucose readings do not match symptoms.
   - When users are taking certain medications.

3. **Flash glucose monitoring (FGM) devices** – where glucose levels in interstitial fluid are monitored with a sensor inserted under the skin and finger-pricking is required to test blood glucose under these circumstances:
   - When glucose levels are rapidly changing.
   - When glucose readings do not match symptoms.
   - If the person has hypoglycemia or impending hypoglycemia.

The requirement for all three available glucose monitoring technologies to penetrate the skin creates difficulties for users and leads to people not testing as frequently as they should, as shown in Table 1.

Of the three available technologies, SMBG devices are the most affordable yet the most painful and inconvenient. While CGM and FGM offer a more convenient option, the complexity of these newer technologies can limit use, while penetration of the skin with a sensor carries a risk of pain, skin reactions, allergies and infections.4,5

There are two device systems on the market that are intended to replace finger-pricks. One is a flash glucose monitoring system and the other a specific brand of continuous glucose monitoring, however for both, finger-pricks are still required under certain clinical circumstances.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Pain</td>
<td>• Painful sensor insertion</td>
<td>• Infection</td>
</tr>
<tr>
<td>• Infection</td>
<td>• Infection</td>
<td>• Allergic reactions</td>
</tr>
<tr>
<td>• Inconvenience with bulky kit to carry around and use</td>
<td>• Skin irritation and adhesion problems</td>
<td>• Skin reactions – redness, itching and rash</td>
</tr>
<tr>
<td>• Embarrassment of testing in public</td>
<td>• Information overload</td>
<td>• Bruising and bleeding</td>
</tr>
<tr>
<td>• Fear of stigmatisation</td>
<td>• Body image concerns about the visibility of the sensor</td>
<td>• Sensor-insertion events</td>
</tr>
<tr>
<td>• Complexity of using lancet device</td>
<td>• Difficulty in placing multiple devices on small bodies</td>
<td>• Sensor adhesive or site reactions</td>
</tr>
<tr>
<td></td>
<td>• Unsettling or annoying alarms</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Annoyance issues with the sensor bumping and snagging on things</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Demanding calibration procedures using SMBG</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Lost signals resulting in data gaps</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Difficulties related to the need for additional SMBG</td>
<td></td>
</tr>
</tbody>
</table>

Table 1: Risks and Difficulties with Available Invasive Glucose Monitoring Devices for People with Diabetes

Addressing the Challenges of Invasive Glucose Monitoring
CGM and FGM are also available at a higher cost than SMBG that precludes access for many people around the world who then continue with finger-pricks despite the pain and inconvenience.

Children and adolescents with Type 1 diabetes require lifelong health management and are at higher risk of diabetes-related complications, yet adolescents in particular have known poor levels of compliance with SMBG.11,12

All these technologies require an individual to be technically competent for their successful use. Furthermore, up to 60 per cent of people with Type 1 diabetes and 67 per cent of those with Type 2 diabetes do not monitor blood glucose as often as recommended.13 Fear of needles and pain of finger-pricking are major reasons for poor adherence with blood glucose self-monitoring in people requiring insulin treatment with both Type 1 and Type 2 diabetes.14 Up to two-thirds of people consider invasiveness a barrier to SMBG and would perform glucose testing more often if there was a non-invasive technique.15 Eliminating the pain associated with current testing methods and improving the frequency of self-monitoring could have a major impact on reducing the global diabetes burden.16

Non-invasive Glucose Monitoring Meets An Unmet Need

Many, if not most, people with diabetes feel that the disadvantages of current available testing technologies outweigh the benefits, which is why the frequency of testing is less than ideal. Indeed, a recent survey found that even among people with Type 1 and Type 2 diabetes using insulin, who especially should be testing regularly, around one third said they felt like “robots”.17 Most of these people would also ideally like more freedom and flexibility from their glucose monitoring device. This research also found that 74% and 62% of people with Type 1 and Type 2 diabetes, respectively, get tired of having to check their blood glucose which is a major barrier to monitoring. Furthermore, less than half of respondents with Type 2 felt their glucose monitoring system was discreet.17

“Up to 60 per cent of people with Type 1 diabetes and 67 per cent of those with Type 2 diabetes do not monitor blood glucose as often as recommended.”13

People with diabetes need to feel confident and comfortable using a glucose monitoring device to help manage what is a chronic progressive condition. This is true for:

- **Children** – where there is a high burden on parents and caregivers to regularly monitor blood glucose levels using invasive and painful testing.11
- **Adolescents** – where embarrassment about glucose monitoring is a barrier to blood testing compliance.12
- **Adults** – where many do not adequately monitor blood glucose levels for reasons including pain associated with finger-pricking, complexity of use, inconvenience and cost.6,13

“Up to two-thirds of people consider invasiveness a barrier to SMBG and would perform glucose testing more often if there was a non-invasive technique.”15
The Saliva Glucose Biosensor

The Saliva Glucose Biosensor is a thin strip that can detect glucose levels in saliva and convert an electrical signal that displays glucose measurements in real-time on a smartphone (or another dedicated device) via a digital app.\textsuperscript{18,19}

How the Saliva Glucose Biosensor Works

1. Place the Saliva Glucose Biosensor in contact with saliva.
2. With the biosensor nearby, the digital app will display glucose levels, flagging any results that need attention.
3. The app provides real-time data and sends data to the electronic medical record or caregiver, as assigned by the user.

The Saliva Glucose Biosensor together with a smartphone app is intended to:
- Eliminate the need for needles to monitor glucose levels.
- Flag in real-time when readings are outside the recommended range.
- Enable users to access options for setting glucose testing reminders.
- Allow real-time comparisons with historical data and remote monitoring of results to identify glucose level patterns or trends.\textsuperscript{20}

The Saliva Glucose Biosensor should enable the seamless and discreet measurement of glucose, elimination of pain and so address the current major challenges with blood glucose testing, providing convenient pain-free testing, anytime and anywhere.

"Eliminating the pain associated with current testing methods and improving the frequency of self-monitoring could have a major impact on reducing the global diabetes burden."\textsuperscript{16}
Accurate Measures of Glucose

The Saliva Glucose Biosensor has high sensitivity and can detect glucose levels at much lower levels than the levels found in blood. In fact, the biosensor detects glucose in saliva at concentrations 100 times lower than levels detected in blood by other glucose monitoring devices.

A correlation between blood glucose and salivary glucose has been found in people with diabetes, with levels of glucose in saliva comparable to levels of blood glucose for the purpose of monitoring in people with diabetes.

Figures 1 and 2 show there is a high positive and statistically significant correlation between salivary glucose and blood glucose levels, both in the fasting state and post prandial (i.e. after a meal) in people with and without diabetes.

Figure 1: Correlation Between Salivary Glucose Levels and Blood Glucose Levels (Fasting)

Figure 2: Correlation Between Salivary Glucose Levels and Blood Glucose Levels (Post Prandial)

Conclusion
There is a high and urgent need for a non-invasive glucose monitoring option to improve testing adherence for millions of people worldwide living with diabetes and ultimately improve their long-term health outcomes and quality of life. None of the accepted glucose measuring devices currently on the market provide genuine non-invasive testing for people with diabetes. The newer registered technologies available are also more complex than self-monitoring blood glucose and, in addition to their much higher cost, remain out of reach for the majority of people with diabetes, particularly those who require multiple daily testing. Pain-free, simple, convenient and discreet, non-invasive testing that is cost-effective has major potential to improve the health and well-being of affected people and so make important inroads into reducing the escalating burden of diabetes across the globe.

About The iQ Group Global
The iQ Group Global is a unique enterprise that finds, funds and develops bioscience discoveries into life-changing medical innovations. The Group’s first innovation is the Saliva Glucose Biosensor, a technology intended to replace finger-prick blood testing for people living with diabetes. [www.theiqgroupglobal.com](http://www.theiqgroupglobal.com)
References