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A Comparative Study on Continuous Glucose Monitoring Devices for Managing Diabetes Mellitus

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ABSTRACT

In recent years, the Internet of Things (IoT) has significantly influenced everyday life, extending its benefits to laypersons and experts alike. IoT-enabled devices, capable of generating periodic data from embedded sensors, have become instrumental tools for analysis, predictive modelling, and data-driven decision-making. Among the myriad applications, diabetes mellitus-- a global health burden, ranking ninth among causes of mortality-- stands as a crucial area of focus. Effective glucose monitoring is paramount in managing diabetes and mitigating its potentially life-threatening complications. This study provides an in-depth comparative analysis of three glucose monitoring techniques: electrochemical, optical, and wearable methodologies. Early intervention and effective management of diabetes can improve life expectancy and decrease the risk of associated complications such as retinopathy, neuropathy, nephropathy, cardiovascular diseases, and stroke. Top-tier wearable Continuous Glucose Monitoring (CGM) devices were evaluated based on criteria such as accuracy, cost-effectiveness, unique features, and potential limitations. The CGM device demonstrating superior accuracy, assessed via the Mean Absolute Relative Difference (MARD) value, was identified. This manuscript serves as a comprehensive guide to CGM systems, addressing their challenges and future prospects, and offering valuable insights for industry specialists and healthcare professionals striving to optimize diabetes management solutions. Furthermore, it assists Medicare beneficiaries in selecting the most suitable CGM device and provides device manufacturers with comparative data to enhance their products. Practical limitations of the devices are also discussed, providing direction for future improvements. By bridging the gap between technology and healthcare, this study contributes to the ongoing efforts to enhance the quality of life for individuals with diabetes mellitus through the adoption of advanced CGM devices.

1. INTRODUCTION

Diabetes is a chronic syndrome featured by high blood sugar (hyperglycemia) that causes deficiency in the secretion of the insulin. There is no cure for diabetes, however the disorder can be kept under control by managing glycemia, comorbid conditions, advocating healthy lifestyle, indulging in physical activities and through balanced diet. Diabetes is majorly classified into two broad categories: Type 1 Diabetes Mellitus and Type 2 Diabetes Mellitus. Other categories of Diabetes include Gestational Diabetes, Type 1.5 Diabetes, Type 3c Diabetes, prediabetes, Latent autoimmune diabetes in adults (LADA), Maturity-onset diabetes of the young (MODY), Neonatal diabetes, and Brittle Diabetes.

With the advent of technology, especially in the Medicare domain several bionic devices have been developed through the years in tracking the physiological glucose levels such as invasive methods and noninvasive methods [1]. The conventional invasive method for monitoring the glucose level includes the finger pricking process that causes harms especially in case of child, pregnant women, and physical ill patients. The majority of finger-pricking tools have a sharp, spring-loaded lancet that briefly pierces the skin and resembles ballpoint pens. There are two different kinds of finger-pricking tools made by numerous vendors. People with diabetes can use finger-pricking devices to collect a drop of blood to check their blood glucose levels on an individual basis. These single-use gadgets come with a lancet that may be thrown away. Additionally, there are finger-pricking tools designed to be used on multiple people. These have a disposable lancet as well as a disposable plastic tip that surrounds the lancet, allowing all components that come into touch with the patient's skin to be thrown away to reduce the chance of disease transmission. Further this traditional method of finger pricking might be painful especially for the children thus paving way for painless non-invasive glucose monitoring technique. To overcome such painful process, noninvasive methods were proposed as it alleviates the pain and suffering of diabetics along with continuous monitoring of the glucose levels.

A detailed summary of the report containing graphs, glucose profile and the target levels are presented in a standardized format which can be used by the medical practitioners for analysis and in rendering medications. Besides these there are glucose meters from which glucose level can be fetched only at a single point of time through a deliberate action. Recent study states that the determination of blood glucose levels is critical in the diagnosis and management of diabetes [2]. Engler et al featured the adoption barriers for continuous glucose monitoring based on the preferences from the patients survey [3]. The long-term monitoring of subcutaneous tissue glucose in a small group of diabetics is documented using a fully implanted first-generation prototype sensor/telemetry system by Lucisano et al. [4] and a wireless telemetry was developed by Gough et al. [5]. Faults in continuous glucose monitoring (CGM) of subcutaneous glucose concentration readings may impact the computation of insulin infusion rates, resulting in hypoglycemia or hyperglycemia in artificial pancreas control systems for patients with type 1 diabetes (T1D) [6]. Most of these studies targets on improving the performance and accuracy level of the CGM device whereas only limited ones focuses on the meta-analysis, type of analyte for glucose sensing, type of diabetes and the analysis of the trends and patterns of the glucose concentration. This paper provides a detailed review on the top CGM systems that are commercialized in the market for glycemic control and diabetes management.

2. METHODS FOR MONITORING GLUCOSE

Continuous Glucose Monitoring is vital for the diabetic patients to monitor their glucose level at least three times a day to maintain good health and longevity. As shown in Table 1 there are various techniques for monitoring the glucose level of the patient from which further medication can be provided. Today's technological advancement has made this monitoring process at its ease, paving way for new devices for real time monitoring and tracking. The process of glucose monitoring is broadly classified into three different categories as shown in Table 1.

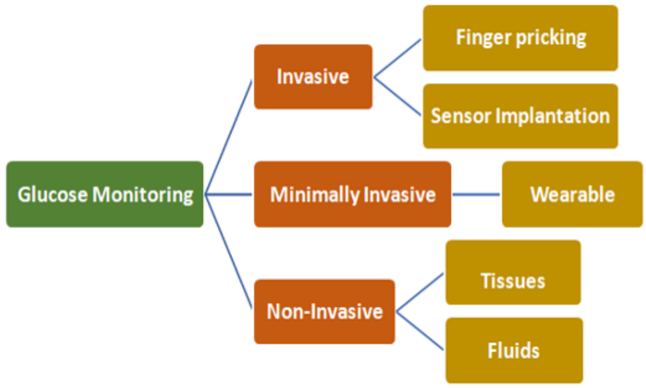

Figure 1. Methods of glucose monitoring

Table 1. Classification of glucose monitoring techniques

	Invasive	Non-Invasive	Minimally Invasive
Advantages	High accuracy Real time data Trend analysis	Painless and comfortable Reduces risk for infection Continuous monitoring Convenience Improved adherence	Accuracy Reduced discomfort Trend Analysis Real time data Reduced need for fingersticks
Disadvantages	Discomfort and pain Skin irritation Cost Need for physician	Accuracy concerns Calibration Cost Limited options Interference factors Development challenges Regulatory approval	Cost Calibration Sensor longevity Skin irritation Dependency Inference from external factors (temperature, humidity)

Invasive - This method is the traditional method of measuring the glucose level which is mostly adopted in hospitals, clinics, laboratories and households. This process involves sampling of blood in an empty stomach for accurate reading through the finger pricking process. The results of this process are more accurate as the concentration of the glucose is directly proportional to the blood sample. However, finger pricking method is not always feasible for all age groups because of its pricking nature that might cause discomfort especially for the children and pregnant women. When there is an increase in the frequency of blood collection for measuring the amount of time taken for the wound to heal also increases. This paved way for the development of non-invasive method of measuring the glucose level. The use of medical tools or procedures that need to penetrate the skin or other body tissues in order to directly access and measure blood glucose levels are known as invasive methods for glucose monitoring. People with diabetes frequently utilize these techniques to check their blood sugar levels. The most popular invasive techniques for glucose monitoring are listed below:

•Fingerstick Blood Glucose Monitoring
•Continuous Glucose Monitoring
•Implantable Glucose Monitoring
•Arterial Blood Sampling

Minimally Invasive – This technique follows an enzymatic approach, where a tiny amount of the analyte is extracted from the body for the glucose measurement. However this method is not as widely used when compared with the traditional method. A middle ground between totally invasive techniques and non-invasive approaches is provided by minimally invasive glucose monitoring techniques. In comparison to fully invasive techniques, these technologies often cause less discomfort and have a lower risk of infection while still offering a reasonable level of accuracy in glucose measurements. Following are some popular minimally invasive procedures and their guiding principles:

•Microdialysis
•Tissue Spectroscopy

For diabetics who need frequent or continuous monitoring of their blood sugar levels, minimally invasive glucose monitoring techniques provide a balance between comfort and accuracy. Individual preferences, medical requirements, and advice from healthcare professionals all go into the approach selection.

Non – Invasive – As the name implies, these methods does not cause any harm or damage to the body and are quit widely used for all age groups. The type of analyte used for measuring the glucose concentration might be based on sweat, tear, saliva, urine and Intestinal fluid (ISF). There are several non-invasive techniques such as electrochemical method, electromechanical method, optical methods and wearables. These techniques are discussed briefly in the next section. Non-invasive glucose monitoring techniques are designed to assess blood glucose levels without penetrating the skin or taking blood samples. For people with diabetes, these approaches hold enormous promise because they are less uncomfortable and more practical than invasive procedures. Numerous non-invasive strategies are being investigated and developed, however many are still in the research or testing phases. Here are a few typical non-invasive techniques and their underlying ideas:

•Spectroscopy based technique
•Optical Coherence Tomography
•Microneedles
•Saliva and Sweat analysis
•Thermal based methods

Although non-invasive glucose monitoring techniques are promising, they continue to face difficulties with regard to accuracy, calibration, and validation. As a result, numerous non-invasive glucose monitoring systems are still in the research and development stage or clinical testing. To select the best glucose monitoring method for their requirements, diabetics should speak with healthcare professionals. This study aims at reviewing the recent CGM devices currently available in the market for usage by analyzing their features and limitations providing a better suggestion for individual usage.

3. NON-INVASIVE GLUCOSE MONITORING TECHNIQUES

3.1 Electrochemical method

The electrochemical approach to monitoring blood glucose is based on the idea of electrochemical sensing, more especially the detection of glucose through redox processes. In glucose monitoring equipment like glucose meters and continuous glucose monitoring (CGM) systems, this technique is frequently utilized. An easy way to explain the sensing principle is as follows:

Enzymatic Sensing: The sensing component of the majority of electrochemical glucose sensors is an enzyme known as glucose oxidase (GOx). When oxygen is present, GOx selectively interacts with glucose molecules.

Glucose Oxidation: GOx catalyzes the oxidation of glucose into gluconic acid and hydrogen peroxide (H_2O_2) when glucose is present in the sample.

Electron Transport: The enzyme is used in this oxidation process to transport electrons from glucose to oxygen. An electrical current or charge is created as a result.

Amperometric Measurement: Glucose oxidase is coated on the working electrode in amperometric glucose sensors, which also use a reference electrode to create a steady baseline voltage. As glucose is oxidized, a current that is proportional to the amount of glucose in the sample is produced at the working electrode.

This type of glucose sensor has grabbed its attention in the recent years and is mostly commercialized in the market. The summarized study on different electro chemical method is shown in Table 2. The first generation electrochemical enzymatic biosensor was based on the oxidation of the glucose to form gluconic acid and hydrogen peroxide (H_2O_2) as shown in Eq. (1). The amount of hydrogen peroxide produced during the electrochemical reaction (Eq. (2)) is directly proportional to the current consumed for the process of conversion which in turn indicates the amount of glucose present in the blood. This method suffers from a major drawback because of its high operating potential for the conversion process that consumes high density of current. Second drawback of the first generation sensor was its inability to quickly transfer the electrons to the electrode for timely prediction. However this drawback was resolved in the second generation sensor with the introduction of redox mediator.

$$\text{Glucose} + O_2 \rightarrow \text{Gluconic Acid} + H_2O_2 \quad (1)$$

$$H_2O_2 \rightarrow 2H + O_2 + 2e^- \quad (2)$$

The major drawback faced in the enzymatic based electro chemical process is the inhibition of the enzyme and the transfer of electrons which can be overcome by replacing the enzymatic catalyst.

Table 2. Summarized study of electro chemical method

Type	Method	Merits	Demerits	Reference
Voltammetry	Voltage scan between the electrodes and sensor	Analyses 2 or more analytes at a time	Low detection	Zheng et al. [7]
Potentiometer	Voltage indicates the ion concentration	Simple	Introduce membrane layers for detection	Gao et al. [8]
Chronoamperometry	Measure the current concentration through redox mediator	Post processing	Complex	Jeong et al. [9]
Spectroscopy	Made of ultrasensitive biosensor	Covers varies frequencies	Consumes more time	Shankhala et al. [10]

3.2 Optic method

The idea behind optical approaches for glucose monitoring is to use changes in a solution's optical properties, including light absorption, scattering, or fluorescence, to infer indirectly how much glucose is present in a sample. Similar to how the electrochemical method works by detecting the electrons, this method uses photons for its detection process. Electromagnetic free, interference free, label free, internally calibrated and continuous monitoring are some of the unique features of optic method which distinguishes itself from others. This method reads the glucose concentration by emitted a light onto the tissues and the reflection of light back from the tissues is measured by appropriate detector. Spectroscopic methods such as NIR, PA sensing and Raman interacts directly with the wavelength of light and glucose molecules to measure the concentration of glucose. Likewise, fluorescence method uses fluorophores that displays the optical signal for different glucose readings by binding the glucose molecules. OCT measures the glucose concentration through the scattering characteristics changes in the skin surface. Finally the holographic sensing technique uses diffraction to stretch the substrate synthesized with the glucose sensitive agent. The summarized study of different optical methods is tabulated in Table 3 and Table 4 shows the various types of optical methods for glucose monitoring.

These optical techniques each have their own benefits and drawbacks. The approach chosen will rely on various elements, including the need for precision, the type of sample, and the particular technology employed by the glucose monitoring equipment. For non-invasive and minimally invasive glucose monitoring, researchers are still investigating and developing optical approaches to increase precision and user-friendliness in diabetes care.

Table 3. Summarized study of optical methods

Method	Wavelength	Site	Reference
Transmission NIR spectroscopy	First overtone	Aqueous solution	Ryckeboer et al. [11]
Photoacoustic spectroscopy	1220 – 1000 cm -1	Arm, skin	Pleitez et al. [12]
Fluorescence sensing	-	Arm, abdomen	Muller et al. [13]
Holographic sensing	500 – 700 nm	Blood plasma	Worsley et al. [14]
Optical Coherence Tomography	1310 nm	skin	Gabbay and Sivarajah [15]

Table 4. Types of optical methods

	Absorption Spectrum	Scattering Based Technique	Fluorescence Based Technique	Raman Spectroscopy
Principle	The basic idea behind absorption spectroscopy is that glucose molecules absorb light at particular wavelengths. Changes in the amount of light absorbed at these particular wavelengths are correlated with variations in the content of glucose in a sample.	The scattering characteristics of light, specifically their angle and intensity, can be altered by glucose molecules. The concentration of glucose can be linked to these alterations.	When stimulated by another light source, some glucose molecules can show fluorescence capabilities, emitting light at particular wavelengths. The concentration of glucose affects how intense this fluorescence is.	Raman spectroscopy involves illuminating a sample using laser light. Due to interactions with molecular vibrations, some of the scattered light experiences a wavelength shift. The wavelength shift is analyzed to ascertain the glucose content.
Method	A sample containing glucose is passed through a light source that emits light at known wavelengths. The amount of light passing through the sample is measured using a detector. The glucose concentration can be determined by comparing the transmitted light to the incident light.	The sample is illuminated by a beam of light coming from a light source. The scattering pattern or variations in the intensity of the scattered light are measured by detectors. The estimated glucose concentration obtained from these readings is then used.	The sample is mixed with a fluorescent dye or marker that binds to glucose molecules. Fluorescent molecules are excited by a light source, and detectors track the fluorescence that is released. The concentration of glucose is then estimated using the fluorescence's intensity.	The sample is illuminated with laser light, while detectors track the Raman scattered light. To determine the level of glucose, the change in wavelength is examined.
Advantages	The method's relative simplicity and ability to deliver precise measurements are advantages.	This approach can produce reliable findings and is less susceptible to interference from other substances.	Fluorescence-based techniques have the potential to be extremely sensitive and glucose-specific.	Raman spectroscopy is less prone to interference and can produce exact data.
Disadvantages	It may need correction factors because it can be sensitive to changes in other compounds in the sample. In order to take interference into consideration, different wavelengths could be necessary.	Implementing scattering-based approaches can be more difficult than absorption-based strategies.	These procedures could need the use of extra chemicals (fluorescent markers) and specific tools.	It might need expensive equipment and only have a shallow level of penetration in biological tissues.

Table 5. Summarized study of wearable methods

Wearability	Analyte	Sessor Placement	Merits	Reference
Patch	Sweat	Arm	Increased accuracy	Emaminejad et al. [16]
Tatoo	ISF	Wrist	Cheap, no skin contamination/damage	Bandodkar et al. [17]
Glucowatch	ISF	Wrist/Arm	Approved by FDA	Tierney et al. [18]
Eyeglass sensor	Sweat	Surface of eye	Integrated with wirelessly	Sempionatto et al. [19]
Patch with multimodal sensor	Sweat	Arm	Integration of iontophoresis	Lee et al. [20]

Table 6. Types of wearable methods

	Electrochemical Sensor	Optical Sensor	Sweat Bases Sensor	Impedance Sensor
Principle	Theoretically, redox processes are exploited by electrochemical sensors, like those found in conventional glucose meters and continuous glucose monitoring (CGM) systems, to assess glucose levels. They use the enzymatic conversion of glucose to produce an electric current or voltage that is detected and transformed into a glucose reading.	Using optical sensors, it is possible to determine glucose levels subtly by observing how light interacts with biological tissues. A few examples of such techniques are absorbance, fluorescence, and Raman spectroscopy.	Sweat-based sensors analyze the amount of glucose in sweat to track blood sugar levels. It is well established that blood glucose levels and sweat glucose concentrations are related.	Impedance-based sensors work on the principle that changes in glucose concentration can affect the electrical impedance of the skin, which is measured by the sensors. Skin moisture and ion concentration can be affected by glucose levels, and changes in skin impedance are related to these changes.
Method	These sensors are built into wearable gadgets, frequently in the shape of a patch or sensor that is placed on the skin's surface. The oxidation of glucose is normally catalyzed by glucose oxidase (GOx) or a related enzyme.	Light-emitting diodes (LEDs) are commonly used in wearable optical sensors to emit light into the skin, and photodetectors are used to measure the light that is reflected or transmitted. Blood glucose levels are estimated using changes in the optical characteristics of tissues brought on by variations in glucose concentration.	Wearables in this category may collect and analyze perspiration for glucose content using tiny sensors or microfluidic technologies. Some may use enzymes or chemical processes to detect glucose.	Electrodes are commonly applied to the skin's surface for wearable impedance sensors. Changes in glucose levels can be deduced by measuring the electrical impedance between these electrodes.
Advantages	Highly accurate glucose measurements can be obtained from electrochemical sensors in real-time or on a regular basis.	Since optical sensors don't need to be inserted under the skin, they have the potential to be non-invasive.	Sweat-based sensors have the benefit of being non-intrusive and offering a method for continuous monitoring. They might be appropriate for people who exercise or are active.	Impedance sensors could be non-invasive and could be incorporated into wearable technology.
Disadvantages	Even though they involve inserting a sensor beneath the skin, they may necessitate routine calibration and sensor component replacement.	They could encounter difficulties with calibration, sensitivity, and light scattering and absorption in biological tissues.	Compared to direct blood measurements, they could have accuracy and lag time issues.	They might need frequent validation and calibration to keep accuracy.

3.3 Wearable method

The major advantage of CGM system is its ability to sense the real time glucose level and transmits those data to the receiver from which glucose patterns and trends can be analyzed. CGM system is composed of 3 components:

Sensor - placed on the upper surface of the skin to measure the glucose levels.

Transmitter - transmits the glucose reading through the attached electrode and send it to the receiver.

Receiver - can be an application or a dashboard which could display the glucose level in a user-friendly manner.

CGM provides a greater benefit over invasive methods in directing the health of the patients, providing instant data, measures the variation, trends, and patterns in the glucose levels. There is substantial evidence to support CGM as a standard of care in type 1 diabetes therapy, with glycemic improvements closely related to device use time [21]. Several companies have come up with numerous intelligent sensing devices and this manuscript aims at comparing various glucose sensing device and presents a detailed study on its features and challenges in the next section. Table 5 depicts the summarized study of Wearable methods and Table 6 illustrates the various types of wearable methods.

4. COMPARATIVE STUDY ON CGM SYSTEM

4.1 Dexcom G6

Figure 2. Dexcom G6: Image taken from https://www.healthline.com/health/diabetes/dexcom-g6-cgm-product-review (accessed on June 12, 2023)

Dexcom Inc developed the world's first real time integrated CGM system in 2004 for managing Diabetes Mellitus which is available in almost 52 countries. Dexcom is a tiny, wearable device that is worn at the abdomen. Transmitter receives the wireless data from the sensor and displays the same at on the receiver. The data generated from the sensor can be shared with the family members and the healthcare professionals so that data driven decision can be made. This device is easy to use with a simple insertion process, water resistant and renders customizable alerts based on the user's preferences. This device shows an accuracy rate of 12.8% Mean Absolute Relative Difference (MARD) score. Dexcom G6 is the only device that provides accurate readings even when the patient is taking acetaminophen. Figure 2 picturises the image of Dexcom G6 device.

4.2 Eversense

Eversense was designed in 2016 by Senseonics but was fully approved in the year 2018 which can used only for people aged above 18. Eversense can be implanted for 90 days under the skin after which a replacement is required. The process of insertion, removal and reinsertion requires the attention of a physician to prevent the tissue from scar. This device comes up with an on body vibration feature that could alert the patients through vibrations according to the intensity of the glucose levels. The receiver can only be a smart phone that displays the target glucose level, achieved glucose levels, statistical report, charts, and weekly summary. The performance level of the device is measured through Mean Absolute Relative Difference (MARD) and obtains an accuracy score of 8.5% to 9.6%. Figure 3 picturises the image of Eversense device.

Figure 3. Eversense: Image taken from https://diatribe.org/180-day-implantable-cgm-eversense-e3-approved-fda (accessed on June 12, 2023)

4.3 Abbott freestyle libre

Figure 4. Abbott freestyle libre image taken from https://www.fiercebiotech.com/medtech/abbott-advises-freestyle-libre-users-potential-battery-overheating-swelling (accessed on June 12, 2023)

Compared to the CGM systems, Abbott Freestyle Libre is standalone, affordable and requires less than a minute of time to measure the glucose level and the obtained readings are displayed on the FreeStyle Libre App. The device is composed of a reader with USB cable and power adapter and a sensor kit which has a sensor applicator and a sensor pack. The devices needs 10 hours of time after the activation by the reader to produce accurate readings. The sensors embedded in this device takes 14 days of lifespan and a warmup time of 1 hour with a storage memory of 8 hours. Calibration and specific training are not required for using this device. Notifications and alarms are customized based on the user's requirements. This water-resistant device can be used during exercise, bathe, shower, and swimming up to 1 meter. The accuracy rate of Abbott FreeStyle Libre is 12.8% which is the same as that of Dexcom G5 Sensor. Figure 4 picturises the image of Abbott freestyle libre device.

4.4 Medtronic guardian connect

Guardian Connect was manufactured by Medtronic, a medical device Company in the year 2018 to measure the intestinal fluids. This device comes up with a unique feature named Sugar IQ that distinguishes itself from the other devices. This new feature analyses the glucose level, insulin of the patient and provides patterns, trends, insights to manage their glucose level on daily basis. Guardian Connect was clinically tested with the Mean Absolute Difference (MAD) of 9.0 mg/Dl. Intake of meals, insulin doses and physical exercises are continuously tracked through the Event Markers. Through Guardian Connect App the glucose reading, trends, patterns and alerts are obtained. Insulin pump can be integrated with the device which pumps the insulin out from the stored reservoir based on the basal rate or the bolus rate. A thin cannula connects the reservoir and the insulin injection site for insulin delivery. Figure 5 picturises the image of Medtronic Guardian Connect device.

Figure 5. Medtronic guardian connect: Image taken from https://www.medtronicdiabetes.com/products/guardian-connect-continuous-glucose-monitoring-system (accessed on June 12, 2023)

4.5 Medtrum A6 Touchcare

A6 Touchcare by Medtrum works without scanning and sends the glucose readings every 2 minutes. It has a small insulin patch pump made of reusable pump base and disposable reservoir patch that can last up to 3 days. The device comes up with a rechargeable transmitter, in built bolus food calculator and customizable alters on high and low readings. A6 Touchcare is calibration free and lasts for 14 days. Automatic delivery of insulin is based on the Artificial Pancreatic Algorithm (APGO) equipped with hybrid closed loop system. Built-in meal handling feature aids the patient in counting their carbs intake. Figure 6 picturises the image of Medtrum A6 Touchcare device.

Figure 6. Medtrum A6 Touchcare: Image taken from https://www.medtrum.co.uk/ (accessed on June 12, 2023)

4.6 Sugarbeat

Sugarbeat comes as a small patch which can be stuck externally either on the abdomen or at the arm. The patch is of 1mm in thickness and has an embedded tiny electronic sensor to track the glucose levels. The patch is designed based on the peel and place principle and must be replaced once in every 14 days. Patented Glucose sensing algorithm is used to detect the glucose concentration through the glucose oxidase-based sensor. Inputs such as food, exercise, and medicine are fed manually to the device to predict the impact of those inputs on the glucose levels. This device yields a MARD score of 11.92% for two fingerstick calibrations and 12.4% for single fingerstick calibration. Figure 7 picturizes the image of Sugarbeat device.

Figure 7. Sugarbeat: Image taken from https://www.healthline.com/diabetesmine/non-invasive-sugarbeat-cgm-diabetes#Accuracy-and-cost- (accessed on June 12, 2023)

4.7 Glysens ICGM

The major advantage of ICGM developed by Glysens is its long-term duration of measurement ranging up to 1 year. The device is fully interoperable where the implant has Bluetooth for seamless connectivity to the insulin pumps and other healthcare devices. ICGM uses oxygen for sensing the glucose concentration which makes it last for years and be insensitive to interferences. Accuracy of the device is improved with redundant array of detectors and resistant to noise and artifacts. Figure 8 picturises the image of Glysens ICGM device.

Figure 8. Glysens ICGM: Image taken from https://www.massdevice.com/glysens-raises-20m-for-implantable-cgm/ (accessed on June 12, 2023)

4.8 Orsense NBM 200

Figure 9. Orsense NBM 200: Image taken from https://www.orsense.com/product.php?ID=49 (accessed on June 12, 2023)

NBM 200 by Orsense is a CGM device that measures the glucose concentration by shining a light into the fingertip, along with the oxygen saturation level, hemoglobin, and pulse rate value. NBM demonstrates an overall MAD rate of 9.7mg/Dl which can be affected by the skin color, thickness and the temperature as measured by Orsense. NBM 200 has multilingual user interface feature, built in rechargeable battery and barcode reader interface that can be controlled via USB or Wi-Fi connection. This device is high stable even at ambient light environments and logs data for 300 preceding measurements. Figure 9 picturises the image of Orsense NBM 200 device.

5. MEAN ABSOLUTE RELATIVE DIFFERENCE

Mean Absolute Relative Difference (MARD)

The Mean Absolute Relative Difference (MARD) is a statistical technique used to assess measurement or forecast accuracy in relation to a reference or real value. It is often used for evaluating the amount of inaccuracy in measurements or predictions in domains such as analytical chemistry, medical diagnostics, and quality control.

Steps to calculate MARD value,

Step 1. Calculate the absolute difference between the measured/predicted value (X) and the reference or real value (Y) for each measurement or prediction.

|X - Y| is the absolute difference.

Step 2. Subtraction of the absolute difference from the reference or real value (Y).

The relative difference is defined as |X - Y| / |Y|.

Step 3. Multiply the relative difference by 100 to get the percentage.

MARD (%) = 100 / |X - Y|

Step 4. Repeat these calculations for each measurement or forecast that has to be evaluated.

Step 5. To obtain the total Mean Absolute Relative Difference, average (mean) the MARD values for all measurements or predictions.

MARD expresses how closely the measurements or forecasts fit with the reference values as a percentage. A lower MARD implies more accuracy, whereas a higher MARD indicates a greater degree of inaccuracy or divergence from the reference values. It is a useful tool for measuring the performance of measurement methods or prediction models in a variety of scientific and industrial applications.

6. DRAWBACKS OF CGM SYSTEM

From this comparative study as tabulated in Table 7, it is evident that there still exist several drawbacks with the CGM systems. The summarized drawbacks of the CGM systems are tabulated in Table 8.

•Cost
•Skin irritation/contamination and discomfort
•Certain devices cannot be used for gestational diabetes
•Less sample for prediction
•Requires physicians during insertion, removal, and reinsertion to avoid scar tissue
•Not all the devices can be integrated with the insulin pump
•Few devices require manual scanning for generating the glucose readings
•Restricted usage based on age
•Limited lifespan and continuous replacements
•Insurance coverage for CGM is limited in many regions
•Requires active user engagement
•Understanding and interpreting CGM data is challenging for new individuals
•Technical issues / connectivity issues
•Compatibility issues with the mobile device and OS
•Transmitter to be recharged
•Accuracy issue
•Secured data storage and transmission
•Authorized access

Table 7. Summarized study of CGM system

Name	Feature	Company & Year	Price	Accuracy (MARD Score)	Drawbacks
Dexcom G6	First real time integrated CGM Sharable data Water resistant Customizable alerts	Dexcom Inc 2004	$230	12.8%	Limited lifespan Skin irritation Requires calibration
Eversense	Stays for 90 days Customized alerts through on body vibration	Senseonics 2018	$400	8.5% - 9.6%	Cost of insertion, removal and reinsertion are high. Transmitter to be charged for 10mins/day. Cannot be linked with insulin pump.
Abbott FreeStyle Libre	Sharable data Water resistant No calibration	Abbott 2016	$40/month	12.8%	Sensor must be manually scanned each time to fetch the readings. Cannot be used for gestational diabetes. Compactable only with few OS and devices.
Guardian Connect	Sharable data Trend graph Alerts on predictive high and low	Medtronic 2018	$340	8.7%	Integrated with insulin pump Requires correct setting of mobile device to receive glucose readings Requires 3-4 calibrations/day
Medtrum A6 Touchcare	Touchscreen receiver Auto recovery of data Calibration free	Medtrum 2008	$150 / sensor and transmitter	9.0%	Lasts for 14 days
SugarBeat	World's first non-invasive glucose monitor Rechargable transmitter	Nemaura Medical 2016	$30/month for 8 patches	12.4%	Available only in few countries Patch needs14 days of replacement
Glysens ICGM	World's first surgically implanted cgm Worn for 1 year Fully implantable	Glysens 1998	-	9.0%	Invasiveness Not widely available Limited lifespan
Orsense NBM 200	Multilingual ui Barcode reader interface Builtin rechargeable battery	Orsense 2019	$300	8.9%	Expensive Limited availability and data Requires calibrations before use Skin variations

Table 8. Drawbacks of CGM systems

Clinical Limitations	Technical Limitations	Usability Limitations
Skin irritation/contamination and discomfort Certain devices cannot be used for gestational diabetes Requires physicians during insertion, removal, and reinsertion to avoid scar tissue Requires active user engagement Restricted usage based on age.	Authorized access Technical issues / connectivity issues Compatibility issues with the mobile device and OS Transmitter to be recharged Accuracy issue Secured data storage and transmission	Cost Not all the devices can be integrated with the insulin pump Few devices require manual scanning for generating the glucose readings Insurance coverage for CGM is limited in many regions Limited lifespan and continuous replacements

None of the CGM devices are free from inaccuracies, these might be due to calibration errors, misplacement of the sensor, tissue inflammation, glucose fluctuation, scarring, and inferences from the substances present in the intestinal fluids. Availability and the cost of the CGM device varies from vendor to vendor which makes them less affordable for the low income families for use.

All the devices majorly suffer from the calibration issue and accuracy issue in producing the right results. Some of the issues that are common among the devices are to be taken care of in the future to produce a much more efficient and potential CGM system.

7. CONCLUSION AND FUTURE WORK

Several companies have come up with innovative technologies in developing an intelligent CGM device in treating Diabetes Mellitus and its complications. As mentioned above there are several drawbacks that stills needs to be addressed for promoting India as a sugar free nation. Figure 10 represents the Mean Absolute Relative Difference Score of various CGM devices reviewed in this manuscript. Factors such as small amount of CGM data, bias, and precision of CGM measurements can affect the MARD accuracy rate. This has a clear picture that among all the CGM devices Dexcom G6 proves to be the optimal device in rendering approximately correct glucose readings. From this comparative study it is well known that Dexcom G6 outperforms the other wearable CGM devices in terms of accuracy, calibrations, compactability, customization and integration with insulin pumps.

Our future work aims at developing a non-invasive bionic device capable of sensing the glucose concentration from the sweat. The proposed method uses a novel technique named Hierarchically Recommended Clustering (HRC) Algorithm for recommending the meal plan for the diabetic patients based on their obtained glucose readings and the glycemic index of their consumed food. This device also comes up with a recommendation system that recommends food to be taken based on the glycemic index present in the food in accordance with the glucose concentration. Reports and patterns can be generated from the glucose reading stored in Cloud servers which are sharable with the authorized personnel. These data are later used by the medical professional for analysis and future medications. The proposed device is simulated using the Proteus software and the obtained results are clinical tested for its accuracy based on the Parkes Error Grid Analysis Technique. This work is a small attempt to help the Gestational Diabetes in continuous monitoring their glucose level without under painful process of finger stick so that we can reduce the mortality rate of the infant and from the passage of the disorder from the women to the infant.

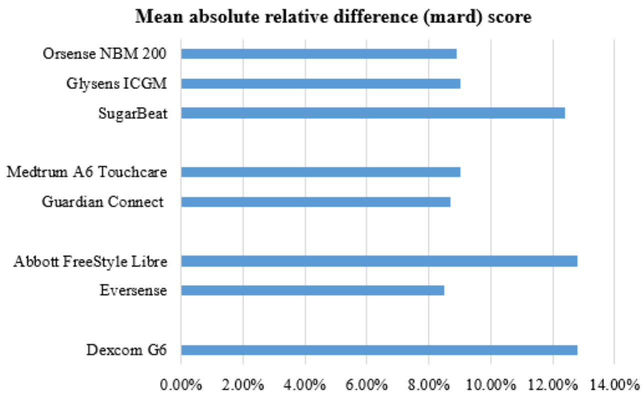

Figure 10. Mean absolute relative difference (MARD) score of CGM devices

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