

Globalizing Continuous Glucose Monitoring Systems: A Paradigm Shift from Traditional Self-Monitoring Blood Glucose Devices

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Continuous glucose monitoring (CGM) systems symbolize a major advancement in diabetes management, especially for patients requiring intensive, accessible and convenient insulin therapy. In contrast to traditional self-monitoring blood glucose (SMBG) devices, CGMs leverage technology to facilitate real-time glucose monitoring. This enables dynamic and data-driven clinical decisions to provide personalized and precise lifestyle and medication adjustments. This paper conducts a comprehensive analysis of the global feasibility of CGM technology adoption and its superiority as an alternative to SMBG. Key metrics such as device reliability, user accessibility, cost-effectiveness, accuracy and socio-economic barriers to large scale deployment, especially in low- and middle-income countries, form the basis of the review. In the long term, CGMs offer significant advancement in glycemic control and quality of life by leveraging predictive analytics. However, opportunity costs, financial burdens, and technological infrastructure pose obstacles to widespread adoption. Therefore, the study also covers scalability, targeted intervention and the strategic implementation of CGMs to facilitate its globalization.

Introduction

Diabetes is one of the most widespread chronic diseases globally. According to recent statistics from the International Diabetes Federation (IDF), 537 million adults are suffering from diabetes, and this figure is projected to escalate to an astonishing 643 million by 2030¹. Additionally, an estimated 1.5 million children and adolescents under the age of 20 suffer from type 1 diabetes (T1D)².

Therefore, effective management of diabetes necessitates rigorous, regular and continuous monitoring of blood glucose levels. Traditionally, this was conducted using self-monitoring blood glucose (SMBG) devices such as the traditional finger-stick blood glucose meters (glucometers), which required multiple daily measurements in order to adjust the individuals insulin (hypoglycemic hormone) levels by subcutaneous injections. The prevalent adoption of SMBG was because insulin therapy was the only therapeutic strategy to treat both T1D and T2D. For that very reason, more than 15 years ago, continuous glucose monitoring (CGM) devices were introduced to the scientific and commercial market, emerging as a pivotal innovation that transformed SMBG methodologies.

Our paper focuses more on type 1 diabetes, as individuals with T1D are completely dependent on exogenous insulin and need meticulous glucose regulation to prevent severe complications such as diabetic ketoacidosis (DKA) and hypoglycemia. T1D requires lifelong insulin therapy compared to type 2 diabetes (T2D), which can generally be managed through lifestyle modifications and oral medications. Essentially, T1D management,

in comparison to T2D, involves multiple daily insulin doses or continuous delivery via pumps, requiring frequent adjustments to match carbohydrate intake and activity levels - CGM can make these adjustments more accurate. Finally, T1D patients are more prone to developing hypoglycemia unawareness, a condition where they cannot detect low blood sugar symptoms. Therefore, while CGMs are also effective in T2D management, particularly for insulin-dependent patients, their impact is most pronounced in T1D due to the absolute necessity of long-term frequent glucose control.

As stated, in comparison to SMBGs intermittent data, CGM allows for continuous real-time monitoring (1-15 min)³ and enhanced glycemic control and clinical data. However, the high financial cost per patient of 10,536, nearly 200x the price of SMBGS (4,971), severely constrained their widespread adoption⁴. Despite this barrier, the health benefits justify this trade-off: many studies showed that real-time CGM (RT-CGM) revealed a superior effect in lowering HbA1c (Glycated Hemoglobin) levels compared to SMBG [mean difference -0.18% (95% CI -0.35% to -0.02%, p = 0.02)]. Furthermore, in adults with T2DM, a significant reduction in HbA1c levels was detected with CGM compared to SMBG [mean difference -0.31% (95% CI -0.6% to -0.02%, p = 0.04)]⁵.

In addition to the continuous tracking mechanism, CGMS can also provide various granular insights about the body's response to exogenous stimuli such as dietary intake, physical exercise, environmental factors affecting glycemic modulation. Furthermore, CGMs deliver nearly instantaneous feedback on acute fluctuations, i.e. elevated or lowered blood glucose levels, which

offers critical indications of hyperglycemia or hypoglycemia. Thereby mitigating, to an extent, the risk of diabetes-related macrovascular and microvascular issues such as myocardial infarctions, nephropathy, peripheral neuropathy and kidney damage. Glycated hemoglobin levels are also known to decrease in response to CGMs, indicating a reduction in both the frequency and severity of hyperglycemic events. Moreover, CGMs are especially helpful in cases of children or in inaccessible scenarios such as sleeping, driving, or during pandemics³.

Due to their demonstrated effectiveness, CGM systems (CGMSs) are increasingly considered the quintessential standard for ideal diabetic glucose control monitoring mechanisms. Recent integration of modern technology, particularly the incorporation of machine learning and real-time data analysis, has improved measurement precision and patient compliance compared to SMBG systems (SMBGSs). This not only facilitates in vivo, real-time, continuous glucose monitoring but also allows future glucose prediction through trend and temporal analysis. The prediction of future glucose concentrations by analyzing glucose changes over time⁶. Furthermore, owing to their reliable accuracy, certain CGM devices are now sanctioned for therapeutic decision-making: this means that. These diabetes treatment plans can be changed solely based on CGMS results. This new horizon of fully integrated hybrid closed-loop systems that meld CGMs with insulin pumps can herald a novel possibility of automated insulin delivery systems, which will approximate the function of a bioengineered artificial pancreas.

In a nutshell, this paper will establish and explore the following domains:

1. A comparative review of CGM and SMBG on essential attributes and metrics such as cost, accuracy, reliability, and user convenience.
2. Feasibility of globalizing CGMs and their evaluation as an alternative to SMBGs through economic, technological, legal, operational and other lenses

Results

Establishing Context on Diabetes and Glucose Monitoring Devices

1. Diabetes Pathophysiology : Classification and Etiology

Diabetes is a chronic metabolic disorder characterized by persistent hyperglycemia, which arises from either impaired insulin secretion, irregular insulin action or both and leads to a significant increase in blood glucose, also called blood sugar. Glucose, the primary energy substrate for cellular processes, is the main source of energy in your body. Although your body can synthesize glucose, it is often derived from dietary intake. The hormone insulin, synthesized and secreted by pancreatic β -cells, enables

glucose intake and thus its energy utilization. In individuals with diabetes, this finely tuned mechanism is disrupted, due to insufficient production or inefficient utilization of insulin, leading to glucose persisting in your bloodstream and unable to be transported to cells for metabolism⁷.

The two predominant types of diabetes are type 1 diabetes (T1D) and type 2 diabetes (T2D). T1D, an autoimmune disorder, occurs when the immune system aberrantly targets and destroys insulin-producing pancreatic cells, resulting in deficient or negligible insulin. T1D is typically diagnosed in childhood or adolescent phases but can manifest at any age. Conversely, T2D is characterized by insulin resistance. Although the cells consume insulin produced and the pancreas continues production, it is insufficient to maintain blood glucose level in the normal range. T2D is commonly diagnosed in adults, though in general it can be prevalent in any age as it is highly correlated by causation or risk factors such as obesity, sedentary lifestyles or having a family history of the disease.

2. Global and Demographic Insights

As per the latest statistics from the International Diabetes Federation (IDF)¹, an estimated 537 million adults aged 20-79 years are currently living with diabetes : this represents a substantial 10.5% of the world's population within this age demographic. Furthermore, projections indicate that this figure will rapidly escalate to 643 million by 2030 (11.3% of population) and further soar to 783 million by 2045, eventually encompassing 12.2% of population. Additionally, over 1.2 million children and adolescents are affected by type 1 diabetes, with 54% of cases occurring in individuals under the age of 15. These statistics underscore the truly alarming and growing prevalence of diabetes, particularly within younger populations. This reflects an urgent need for improved therapeutic measures and enhanced preventive measures.

Design and Functionality of SMBG and CGM

Glucose monitoring plays a critical role in identifying individual blood glucose patterns, which is essential for optimizing meal planning, activity scheduling, and determining the optimal times for medication administration. Regular testing facilitates prompt responses to abnormal fluctuations in blood glucose levels: high blood sugar (hyperglycemia) or low blood sugar (hypoglycemia). This assists us with decision making for timely adjustments in dietary choices, exercise regimens and insulin management as directed by the healthcare provider⁸.

1. Self Monitoring of Blood Glucose (SMBG)

Self-monitoring of blood glucose involves the use of a glucose meter, also known as a glucometer, to assess the

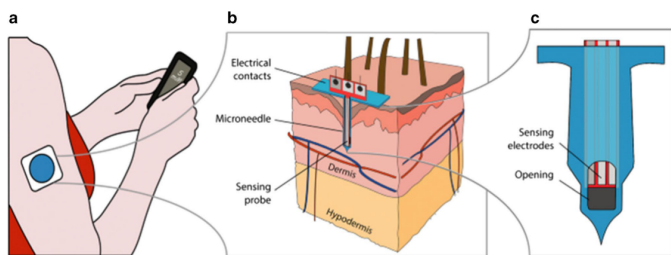


Fig. 1 Illustration of the typical implementation of a commercial CGM system¹⁰

concentration of glucose in the blood. The procedure typically requires a skin prick, usually on the fingertip, to obtain a small blood sample that is applied to a disposable test strip. To determine the glucose level in the blood different manufacturers use a plethora of techniques, but most systems rely on measuring electrical properties to determine blood glucose level. SMBG primarily assesses capillary blood glucose, which reflects the glucose concentration in capillary blood. Testing may be performed after fasting or at random non-fasting intervals (random glucose tests), with each approach providing distinct insights for diagnosis or monitoring⁸.

A glucometer is an electronic device used designed to measure blood glucose levels. This device is greatly advantageous as it only requires a relatively small drop of blood for the blood sample and digitally displaces blood glucose, in various units such as milligrams per deciliter (mg/dL) and millimoles per liter (mmol/L), within a few seconds. The minimum blood sample and the rapid result generation contribute to reduced testing time and effort. This significantly improves the compliance of diabetics to their testing regimens, by improving accessibility and user convenience, which leads to an overall better lifestyle⁹.

2. Continuous Glucose Monitoring (CGM)

Continuous glucose monitoring systems provide a more advanced and dynamic mechanism of tracking blood glucose levels. A significant advantage is the fact that they offer continuous monitoring in contrast to intermittent or periodic measurements by SMBGs. CGMs are predominantly utilized by individuals who treat their diabetes with insulin therapy: this includes people with T1D, T2D, or other types of diabetes, such as gestational diabetes¹¹.

A typical CGM device comprises three key components: a sensor, transmitter, and a receiver. The sensor, inserted subcutaneously into the adipose tissue (fatty layer of skin immersed in interstitial glucose (Fig 1) using an automatic device, continuously detects glucose concentrations in the interstitial fluid. The transmitter, which is either rechargeable or battery powered, communicates glucose readings

to the receiver at regular intervals such as 1 or 15 minutes. Some receivers are even integrated with insulin pumps to create hybrid automated insulin delivery mechanisms¹¹. Compared to SMBG, which are based on capillary blood glucose measurements, CGMs leverage enzymatic technology that reacts with glucose molecules in the body's interstitial fluid¹². This generates a minor electric current, proportional to glucose concentration, which is transmitted via short-range radio frequencies to the receiver¹³. This is eventually digitally displayed for user interpretation. CGM technology has evolved into various categories based on recording and communication mechanisms for glucose data.

Retrospective CGM.

These systems are continuous but do not provide real-time feedback. Rather, healthcare professionals retrospectively analyze data, which has been stored for typically 3 to 7 days. This mechanism provides insights into glycaemic trends and variability for pattern identification and therapeutic adjustments. Examples include the older Medtronic iPro2 system, which helped inform long-term treatment strategies, though it lacked immediate intervention capabilities¹⁴.

Real Time CGM (rtCGM).

rtCGM devices provide continuous data with spontaneous alerts for conditions such as hyperglycaemia or hypoglycaemia. These are typically worn for 10 to 14 days and transmit data wireless to dedicated receivers. This mechanism offers tight control and rapid response especially for patients with labile glucose levels. A meta-analysis by Wojciechowski et al. (2021) demonstrated that rtCGMs were associated with a 70% reduction in HbA1c and 40% in Type 1 diabetes hypoglycemic episodes¹⁵.

Non-Invasive CGM.

These technologies aim to eliminate the requirement for sensor insertion by using optical, electromagnetic, or ultrasound-based techniques: modern examples like GlucoTrack and SugarBEAT utilize electromagnetic and transdermal methods to evaluate glucose levels. By integrating with real-time feedback systems, they can increase patient comfort and adherence. However, these mechanisms are susceptible to external factors such as temperature, skin hydration, and pressure¹⁶.

Invasive CGM.

Although these are relatively accurate and reliable, their benefits are undermined by limitations such as sensor-induced irritation, risk of infection, and the need for sensor replacement every 10 to 14 days. Therefore, recent advancements are working on longevity of sensor wear and ameliorating biocompatibility: Eversense is an implantable CGM device with a 180-day sensor lifespan¹⁷, thus reducing replacement frequency and associated discomfort.

Comparative Analysis between CGMs and SMBGs in Glycemic Control

CGMs have proven better than SMBG in glucose monitoring and diabetes management, specially in monitoring HbA1c and detecting hyperglycemia and hypoglycemia episodes that originally went undetected by SMBG. This section explores the comparative effectiveness of CGMs versus SMBG in metrics such as accuracy, reliability, and cost-effectiveness.

1. Accuracy and Reliability of Glucose Monitoring Methods

The accuracy and reliability of glucose monitoring methods are crucial for effective diabetes management. This sub-section compares CGM to SMBG in key benchmarks like Glycated Hemoglobin (HbA1c) and the detection of glycemic excursions, which includes hypoglycemic and hyperglycemic events.

Glycated Hemoglobin (HbA1c)

HbA1C is a crucial marker for evaluating long-term glycemic control. In line with the hypothesis, a significant reduction in HbA1c was the primary outcome in studies evaluating the usage of CGMs in T2D¹⁸. This is further substantiated by multiple studies, which consistently demonstrate that CGM adoption is more effective in HbA1c reduction than SMBG¹⁹.

CGMs are extremely adept at reducing glycated hemoglobin (HbA1c) levels. Their continuous real-time glucose data encourages patients to make immediate and long-term adjustments to their lifestyle and treatment plans. Unlike the intermittent readings of SMBG, CGMs provide dynamic glucose trend data, facilitating timely interventions to prevent prolonged hyperglycemia. Real-time alerts on glucose fluctuations further encourage users to take corrective actions, such as modifying insulin dosages, adjusting carbohydrate intake, or engaging in physical activity to minimize the frequency and duration of hyperglycemic episodes. Additionally, the continuous stream of data enables patients to identify recurring patterns and triggers that contribute to poor glycemic control, fostering more informed decision-making about their diet, exercise, and medication adherence. In the long run, this also develops behavioural adaptation which leads to a higher percentage of time spent within the target glucose range. In fact, the psychological impact of having immediate feedback also increases patient engagement and adherence to therapeutic regimes. Finally, CGMs provide healthcare providers with precise glucose metrics, such as time-in-range and glycemic variability, which allow for more precise and personalised treatment modifications.

In an analysis conducted in 2019 that analyzed data from five randomized controlled trials, the initial cumulative

mean baseline HbA1C of $8.53 \pm 0.91\%$ indicated suboptimal glycemic control among participants²⁰. However, the pooled results revealed that CGM was strongly associated with a reduction in HbA1c, with a mean difference of -0.25 and 95% confidence interval between -0.06 and -0.45) compared to SMBG, which is conducted with a statistical significance of more than 95% ($p = 0.01$)²¹. The reliability of results is further underscored by the fact that on average participants initially have elevated levels indicative of poorly controlled diabetes.

The periodic usage of RT-CGM over a twelve-week period not only resulted in a reduction in HbA1c but also demonstrated a sustained effect at week 40, despite the discontinuation of CGM at week 12¹⁷. It was additionally observed that CGM usage for a duration of just 14 days yielded a robust approximation of key metrics like average glucose levels, time in range, and hyperglycemia indicators for an average period of three months. However, extending data collection for further duration did not demonstrate any additional improvement in correlation to standard glucose metrics like HbA1c and mean glucose²². These observations demonstrate that even short-term usage of CGM is highly beneficial and equivalent.

Performance Comparison on Hypoglycemia and Hyperglycemia

Long-standing diabetes can lead to peripheral neuropathy and diminished hypoglycemia awareness, particularly among the elderly. In fact, hypoglycemia is a more frequent cause of hospitalization in elderly patients with diabetes compared to hyperglycemia²³. This highlights the importance of detecting hypoglycemic episodes, making CGM a preferable choice for diabetes management by healthcare providers²⁴.

Multiple studies have demonstrated that CGMs are significantly more effective in detecting hypoglycemic episodes compared to SMBGs or symptom-based assessments (symptomatic hypoglycemia)²⁵. For example, while SMBG detected hypoglycemia in 50% of the patients, CGM was able to detect hypoglycemia in 59% of patients²⁶. This means that CGM detected hypoglycemia in 9% more patients who originally went undetected by SMBGs. On an episode-level detection, CGM identified far higher percentages of hyperglycemic and hypoglycemic episodes compared to SMBG (61.1% vs. 50.8%; $p = 0.047$) and (3.8% vs. 1.7%; $p = 0.016$). For hyperglycemia, the p-value (probability that the observed results occurred by chance rather than due to a real effect) is close to 0.05, indicating that the differences are statistically significant but marginally so. However, the difference in hypoglycemic episodes is more statistically significant, indicating a stronger likelihood that the reduction was due to

the intervention rather than random variation. Additionally, 19% of patients who had no data concerning hypoglycemia recorded by SMBGs had detected hypoglycemia with CGM usage. Notably, 33% of patients experienced nocturnal hypoglycemia²⁵. This naturally goes unnoticed, which makes the timely intervention very challenging and increases the risk of mortality. However, CGMs with integrated alarms for extreme glycemic excursions help detect imminent severe hypoglycemic episodes and take immediate action. Additionally, recent research has demonstrated that CGM was shown to be a good method to identify postprandial hyperglycemia, which improves therapeutic management. The research validated the low sensitivity of CGMS to detect undetected hypoglycemia in T1D patients, where the mean values were 191.8 46.2 mg/dl by SMBG versus 190.9 42.1 mg/dl by the CGMS sensor²⁷.

Despite the promising results, the effectiveness of CGMs in detecting hypoglycemic episodes compared to SMBGs must be analyzed through multiple effect size measures. The Cohens h value for hypoglycemia detection (CGMs: 59%, SMBGs: 50%) is 0.18, indicating a modest yet meaningful effect. However, relative measures highlight this impact more strongly. Relative risk (RR) shows that CGMs detected hypoglycemia in 18% more patients than SMBGs (RR = 1.18), and for hypoglycemic episode-level detection, CGMs were 2.24 times more likely to detect hypoglycemia compared to SMBGs (RR = 2.24). Similarly, the odds ratio (OR) for hypoglycemic episodes is 2.29, meaning CGMs more than doubled the likelihood of detecting hypoglycemia compared to SMBGs. These statistics suggest that while absolute differences appear modest, CGMs significantly enhance hypoglycemia detection, particularly in episodes that might go unnoticed by traditional methods.

Having said this, some studies have also revealed that CGM data reported no significant difference from the controls, possibly due to relatively healthier populations studied who experienced fewer glycemic excursions than other regions²⁸. It is also crucial to note that confounding factors often influence experiment findings. Factors such as device calibration errors, sensor accuracy variability, and individual differences in glucose fluctuation could lead to variation in detection rates. Secondly, inconsistent patient behaviour with SMBG - such as poor adherence to testing schedules or selective monitoring during symptomatic episodes - could lead to an underestimation of hypoglycemic and hyperglycemic events.

2. Cost Effectiveness and Utility

According to a 2023 study in Denmark, RT-CGM usage was associated with an incremental gain of 1.37 quality-adjusted life years (QALYs) over SMBG²⁹. Total mean

lifetime costs were 894,535 (\$130,870 in 2023) Danish Krone (DKK) for RT-CGM and DKK 823,474 (\$120,474 in 2023) for SMBG, yielding an incremental cost-utility ratio of DKK 51,918 (\$7,595 in 2023) per QALY gained versus SMBG. This study concludes that in Denmark, RT-CGM is a highly cost-effective methodology compared with SMBG, using a willingness-to-pay threshold of 1 per capita gross domestic product (GDP) per QALY gained²⁹.

In another 2023 study conducted in Canada, the projected total mean lifetime costs were 207,466 (\$152,694 in 2023) Canadian Dollar (CAD) for RT-CGM versus CAD 189,863 (\$139,739 in 2023) for SMBG, which projected a price difference of CAD 17,602 (\$12,955 in 2023). Additionally, it estimated a mean quality-adjusted life expectancy of 9.97 QALYs for RT-CGM versus 9.02 QALYs for SMBG (difference: 0.95 QALYs), resulting in an incremental ICUR (Incremental Cost-Utility Ratio) of CAD 18,523 (\$13,632 in 2023) per QALY gained for RT-CGM versus SMBG³⁰. Its important to note that findings were sensitive to changes in the HbA1c treatment effect, annual cost, and quality of life benefit associated with using RT-CGM, SMBG frequency, and baseline age, but ICURs remained below CAD 50,000 (\$36,800 in 2023) per QALY in all analyses³¹. Additionally, besides individual cost analysis, the broader economic impact on healthcare systems is also essential. Our analysis shows that RT-CGM can yield substantial long-term savings by reducing hospitalizations and emergency interventions due to severe hypoglycemia and hyperglycemia - by effectively reducing diabetes-related complications, RT-CGM can thus offset its higher upfront costs. Moreover, effective glucose monitoring can delay or prevent costly long-term complications such as neuropathy, nephropathy, and cardiovascular disease, reducing long-term financial strain on healthcare systems globally.

To conclude, it is crucial to analyze the applicability of RT-CGM cost-effectiveness across diverse healthcare systems. In countries with universal healthcare, such as Denmark and Canada, government funding and insurance coverage substantially reduce the direct costs for patients, making RT-CGM more accessible and enhancing its cost-effectiveness. In contrast, in privatized systems like the United States, where coverage varies by insurer, high upfront costs, co-pays, and limited insurance coverage often limit adoption. Furthermore, patients may face significant out-of-pocket expenses as private insurers may not prioritize reimbursement for RT-CGM. Affordability also remains a critical challenge in middle- and low-income countries, where limited insurance coverage and high out-of-pocket expenses prevent the widespread implementation of RT-CGM. Additionally, different reimbursement models, such as pay-for-performance systems, could im-

prove RT-CGMs cost-effectiveness by incentivizing better disease management and preventive care. On the other hand, if reimbursement is tied to a fixed budget or capped amount, as seen in some national health insurance models, the cost-effectiveness could be constrained, particularly in countries with tight healthcare budgets. Therefore, strategies like national reimbursement programs, cost-sharing policies, subsidy models, and public-private partnerships are essential to realizing the economic and clinical benefits of RT-CGM.

Technological Integration and Modern Advancements in Device Technology

1. Sensors

Many devices utilize enzyme-based electrochemical sensors to measure interstitial glucose levels. For instance, the Dexcom G7s provides a 10-day wear period, rapid warm-up times, and reduces the need for fingerstick calibrations. Freestyle Libre 3 is pioneering advancements in sensor miniaturization³² while balancing real time glucose readings. In addition, the Medtronic Guardian Sensor 4 also employs enzyme-based electrochemical sensors that react with glucose in interstitial fluid to generate an electrical current proportional to glucose concentration. However, the precision of these devices can be impacted because of environmental factors such as temperature, humidity, and pressure. While electrochemical glucose sensing is a key component of CGM, no FDA-approved pharmacological agents function as direct electrochemical glucose sensors as electrochemical sensing is the result of improvements in sensor technology and detection mechanisms instead. However, in general, several drugs rely on CGM data for optimizing glucose control. Dapagliflozin (Farxiga), an SGLT2 inhibitor, reduces blood glucose by preventing renal glucose reabsorption, with CGMs assisting in tracking glycemic response. Similarly, Exenatide (Byetta, Bydureon) and Pramlintide (Symlin) aid in postprandial glucose regulation, where CGMs help prevent hypoglycemia and assess glycemic variability.

A newer evolution in modern systems is the use of micro-electromechanical systems (MEMS) and advanced enzyme chemistries. MEMS technology improves sensor performance by enabling the fabrication of miniaturized, highly sensitive biosensors with increased surface area for enzymatic reactions, leading to greater glucose detection precision. These microscale components reduce signal noise caused by environmental factors such as temperature fluctuations, humidity, and pressure variations, ensuring more consistent readings. Additionally, they enhance durability, flexibility, and user comfort by enabling thinner, more biocompatible designs, which support extended wear periods.

Advanced enzyme chemistries further refine glucose sensing by incorporating engineered glucose oxidase variants with improved stability, reducing enzyme degradation over time. Traditional sensors require frequent recalibrations due to enzyme denaturation, which often lead to fluctuating readings. Modern CGMs utilize stabilized enzyme formulations that resist oxidative damage and metabolic byproducts, ensuring sustained accuracy. Furthermore, the integration of cofactors and mediator molecules enhances electron transfer efficiency, thereby reducing signal drift and improving response times in glucose detection.

2. Accuracy and Reliability

Early devices had MARD (Mean Absolute Relative Difference) values in the 15-20% range, leading to unreliable data. In comparison, neo-generation CGMs boast MARD scores in the range of 8-9%³³, reducing the accuracy gap from traditional blood glucose monitoring methods. In addition, improvements in calibration algorithms, such as self-calibrating mechanisms and adaptive filtering algorithms, have reduced the frequency of manual calibrations, thereby decreasing human error.

3. Accessibility and Increased Digital Integration

Integration of CGM systems with smart devices/wearables has opened new avenues for in real-time health monitoring, data analysis, and personalized diabetes management. For example, through wearable watches, users can conveniently manage glucose levels. This can be promoted through collaborations with fitness tracking platforms like Apple and Fitbit : glucose can be analyzed for exercise routines, offering insights into how activities affect blood sugar levels. The digital integration has various advantages: instant data access, enabling quick decisions to adjust and modify dietary intake³⁴; predictive alerts, warnings on impending hypo- or hyperglycemia allow for preventive action; trend analysis, glucose temporal analysis patterns over various timeframes; and notification remote sharing capability with concerned stakeholders such as caregivers, pediatric patients or individuals with disabilities.

Significant empirical research has been done to validate the efficacy of digital integration for CGM. A 2023 study published in *Diabetes Technology & Therapeutics* investigated the Dexcom G6s integration with Apple Health and Fitbit, revealing a 32% reduction in post-exercise hypoglycemia and a 26% increase in time-in-range (TIR) ($p < 0.001$) compared to non-integrated CGM users. Similarly, a 2022 clinical trial by Massachusetts General Hospital assessed the impact of CGM-enabled Apple Watch alerts on type 1 diabetes patients, showing that 80% of participants reported improved glucose control, with a 19% reduction

in glucose variability ($p = 0.004$) due to more precise insulin adjustments based on wearable-tracked activity data. Additionally, a Stanford University study (2022) found that Fitbit users with CGM integration (via LibreView) exhibited a 24% improvement in overnight glucose stability ($p < 0.005$), demonstrating the utility of real-time alerts in mitigating nocturnal hypoglycemia. Finally, a clinical trial published in *Diabetes Technology & Therapeutics* conducted by Harvard Medical School and Brigham and Women's Hospital demonstrated that patients using the Dexcom G6 CGM integrated with Apple Watch showed a 24% reduction in hypoglycemic episodes, 19% improvement in time-in-range ($p < 0.001$), and significant improvement in insulin delivery adjustments based on real-time CGM data.

If CGM is commercially integrated into wearable devices, these devices would need to comply with stringent medical device regulations, as they transition from general wellness tracking to clinical glucose monitoring. In the United States, the Food and Drug Administration (FDA) categorizes CGMs as Class II or Class III medical devices, requiring rigorous premarket review, clinical validation, and adherence to accuracy and reliability standards. Manufacturers of CGM-enabled wearables would need to obtain FDA clearance or approval, similar to standalone CGMs like Dexcom G7 and FreeStyle Libre. In the European Union, such integrations must comply with the Medical Device Regulation (MDR) (EU 2017/745), which enforces strict performance, safety, and cybersecurity requirements for health-monitoring devices. Unlike traditional smartwatches, CGM-integrated wearables must meet ISO 15197 standards for blood glucose monitoring, ensuring clinical-grade precision. Additionally, regulatory frameworks such as HIPAA (Health Insurance Portability and Accountability Act) in the U.S. and GDPR (General Data Protection Regulation) in the EU mandate strict controls over health data storage, transmission, and third-party sharing. Compliance will be essential to protect users' medical information, especially since CGM wearables sync data across cloud servers, healthcare providers, and mobile applications.

4. Predictive Analytics

CGMs can leverage machine learning algorithms to predict glucose levels based on real-time and historical data. These algorithms use personalized variables such as meal intake, insulin dosage, physical activity, and stress levels. This allows consumers to anticipate fluctuations and adjust their treatment accordingly. Predictive analysis also allows personalized diabetes management by analyzing vast quantities of user-specific data points. Recently, AI-driven deep learning virtual assistants such as mySugr and Sugarmate, have also been able to integrate with CGM systems

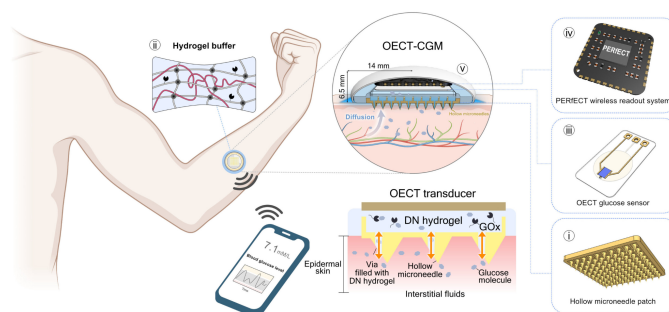


Fig. 2 Visual depiction of next generation CGM wearables equipped with advanced wireless systems and transducers³⁶

to provide real-time advice based on glucose trends, meal patterns, and activity levels. On a technical perspective, advanced insulin titration algorithms utilize regression models and Markov decision processes (MDPs) to calculate precise insulin dosages based on glucose readings.

Studies from journals like *Nature Medicine* have assessed deep learning-based glucose prediction models, showing that long short-term memory (LSTM) networks achieved a Mean Absolute Error (MAE) of 10.8 mg/dL for 30-minute forecasts, outperforming traditional autoregressive models (MAE = 14.2 mg/dL, $p < 0.001$). Another 2022 study in *Diabetes Technology & Therapeutics* compared gradient boosting machines (GBMs) and reinforcement learning-based Markov decision processes (MDPs) for insulin titration, finding that MDP-based dosing improved time-in-range (TIR) by 21% ($p = 0.003$) and reduced nocturnal hypoglycemia incidence by 17% ($p = 0.005$) over standard physician-guided adjustments. Furthermore, meta-analysis published in the *IEEE Journal of Biomedical and Health Informatics* found that hybrid AI models combining convolutional neural networks (CNNs) and attention mechanisms reduced hypoglycemia prediction errors by 18.5% ($p < 0.01$) and achieved an F1-score of 0.89 for hypoglycemia event detection. Finally, clinical validation studies by Duke University on CGM-integrated AI models reported that patients using ML-driven glucose prediction tools spent an average of 5.6 more hours per day in the optimal glucose range ($p < 0.001$) compared to those relying on standard CGM alerts. While these results are promising, accuracy still varies based on dataset size, patient variability, and external factors such as meal composition and stress levels. Future research must focus on standardizing performance benchmarks across different ML models and improving explainability using techniques like SHAP (Shapley Additive Explanations) and LIME (Local Interpretable Model-Agnostic Explanations)³⁵, ensuring that predictions are clinically interpretable and actionable for diabetes management.

There have also been several advancements in the devices themselves that have improved their accuracy and optimized their user experience.

1. Non-Invasive and Minimally Invasive Sensors

Modern researchers are focusing on developing sensors that use light-based techniques, Raman spectroscopy or near-infrared spectroscopy, to measure glucose without piercing the skin. These work by detecting glucose molecules in interstitial fluid beneath the skin. Secondly, electromagnetic and radiofrequency sensors also have immense potential by detecting impedance changes caused by tissue glucose concentration³⁷. These sensors will be non-invasive, small and can integrate with wearable devices and provide the needle free experience. Thirdly, microneedle patches are another alternative for minimal discomfort.

In this microscopic needles can penetrate just the outer layer of the skin, without reaching nerve endings. Fourthly, ultrasound transducers offer immense potential to detect glucose by measuring acoustic properties of blood and interstitial fluid. - these are still in experimental phases. Finally, modern research is also focusing on photoacoustic imaging for non-invasive monitoring. By applying short pulses of laser light to the skin, sensors can measure glucose levels based on the specific way glucose molecules absorb and release energy.

2. Real-Time Sweat Analyte Detection with Flexible Bioelectronics

Recent advancements in nanotechnology have enabled the creation of electrochemical sensors within flexible materials, such as graphene-based bioelectronic skin patches. These can adhere to the skin to measure glucose levels through sweat : they can monitor glucose and assess biomarkers like lactate, pH, and dehydration levels³⁶, offering a broader understanding of the users health. To complement this effort, wearable patches are now being developed with self-healing materials, allowing them to be worn for extended periods with minimal wear and tear.

Despite these advancements, there are no commercially available devices based on sweat detection. Companies like Abbott and Evolv Technology are developing prototypes, such as the Abbott Libre Sense, which integrates sweat sensors to track glucose trends. However, these devices are still in experimental or limited-release phases and are not widely available for mainstream use. The primary obstacle to sweat-based glucose monitoring lies in sensor accuracy and reliability since sweat glucose concentrations are 1001000 times lower than blood glucose. Furthermore, sweat secretion rates fluctuate based on external factors like hydration, temperature, and physical activity, leading

to unreliable readings. Additionally, environmental factors such as humidity, skin contamination, and interference from other sweat analytes like lactate and sodium complicate glucose detection, making it difficult to isolate an accurate glucose signal. Although researchers are working on overcoming these obstacles through advanced nanomaterial coatings, AI-driven correction algorithms, and hybrid sensor integration, significant breakthroughs are still necessary before sweat-based glucose monitoring can become a reliable, clinically viable alternative to current methods.

3. Implantable Nanotube Sensors for Long-Term Monitoring

A cutting-edge advancement is the development of micro carbon nanotube based sensors³⁸. Once inserted into the skin, they can provide continuous readings for up to a year, providing a stable and long term alternative. However, there is a possibility of lack of biocompatibility and inflammatory responses. Sensors can be coated with advanced polymers to prevent immune reactions : some models even use coatings that release inflammatory agents.

4. Conformal and Ultra-Thin CGM Patches for Non-Invasive Wear

Discomfort has always been a major issue with CGMs. Thus, new ultra-thin CGM patches are being designed to move with the skin without causing irritation or discomfort. Flexible and stretchable materials can adhere snugly to the skin : this is especially beneficial for children or people with sensory sensitivities³⁹. Another exciting field is the integration of CGM sensors into clothing. These textiles use flexible fibers with conductive properties that can measure glucose in sweat or interstitial fluids - however this is still under development. They could potentially also include haptic feedback such as gentle vibrations when glucose levels are out of range.

Areas of Work and Emerging Trends

1. Challenges and Limitations of CGMs

Technical Limitations and Potential Overreliance
Sensor accuracy is critical for effective diabetes management : sensor lag, sensor drift and calibration issues, especially postprandial glucose spikes during intense physical activity, can cause result discrepancies. Moreover, environmental factors such as temperature extremes and humidity fluctuations can impact CGM sensor performance. Even internal physiological elements like skin conditions or hydration levels affect CGM longevity.

Therefore, predictive analytics does not always account for individual physiological variations, sensor inaccuracies, or unanticipated external factors. Inaccuracies in sensor

readings due to delayed interstitial glucose response, dehydration, or compression artifacts (e.g. "compression lows" when a user sleeps on the sensor site) can lead to false alarms or misleading predictions. This can cause unnecessary insulin adjustments or user anxiety, which may increase the risk of hypoglycemia or hyperglycemia, contributing to glycemic instability. Studies show that predictive alerts can have false-positive rates of up to 14% for hypoglycemia warnings, leading users to overcorrect glucose levels ($p < 0.01$), causing more harm than good. Furthermore, there can be inherent data bias : algorithms trained on population-level data, may not reflect metabolic variations in diverse user groups (e.g. age, ethnicity, comorbidities). Additionally, over-reliance on these predictions without proper clinical oversight can further exacerbate the risks, especially when users make decisions based solely on CGM data rather than a more holistic contextual view of their health. Moreover, if healthcare professionals rely heavily on CGM predictions for insulin dosing, serious legal liability questions arise. Lastly, users can develop an overdependence on CGM insights, leading to a diminished ability to recognize their own glucose fluctuations. Over-reliance also leads to increased anxiety and obsessive tracking behavior

Data Privacy Issues

Many CGM systems integrate with cloud-based platforms, electronic health records (EHRs), and third-party applications, enabling real-time glucose monitoring by caregivers and physicians, etc. However, personal health information (PHI) may be vulnerable to breaches, unauthorized access, or potential misuse. For example, employers or insurance providers may use this data for discriminatory purposes, such as adjusting premiums or denying coverage. Additionally, it can lead to third-party data monetization by enabling companies to target advertisements based on the user's health profile. Despite stringent regulations such as the Health Insurance Portability and Accountability Act (HIPAA) in the U.S. and the General Data Protection Regulation (GDPR) in the EU, studies indicate that CGM-related health apps often have ambiguous privacy policies. An investigation by the Journal of Medical Internet Research found that nearly 30% of diabetes-related mobile health apps shared user data with third parties without explicit consent ($p < 0.001$). In fact, many CGM apps do not fall under strict HIPAA regulations. Addressing these challenges requires stricter regulatory oversight, end-to-end encryption protocols like Zero-Knowledge-Encryption (to prevent cyber-attacks), and enhanced user control (explicitly opt-in mechanisms) over data sharing preferences to balance the benefits of CGM connectivity with the need for data security.

Cost Barriers

CGM systems require significant financial investment : the cost structure includes upfront device outlay, recurring sensor expenses and transmitters/receiver costs. For example, the Dexcom G7, with an average cost of 377 per sensor, is more expensive than SMBG systems like the 30 Contour Next EZ⁴⁰. However, cost-effectiveness analysis (CEA) studies demonstrate that while the opportunity cost is higher, the long-term savings and reduced hypoglycaemic severity compensate for this. This incremental-effectiveness ratio (ICER) is significantly better for CGMs⁴¹ Long term economics models also substantiate that broad adoption can reduce the cost burdens by up to 15%. Secondly, a variance in reimbursement policies affects CGM adoption : Medicare and private insurers in the United States provide partial reimbursement, typically for patients with Type 1 Diabetes or Type 2 Diabetes.

User Compliance

Reports show that 25% of CGM users can feel discomfort related to sensor insertion and long-term wear. Emergingly, smaller and less intrusive sensors are being developed to address this. On an alternative lens, more than 30% of patients with T1D experienced anxiety⁴², including psychological barriers to perceived invasiveness, which affected treatment satisfaction and adherence. This is particularly prevalent among older adults and lower-income populations due to factors like technological unfamiliarity, cost concerns, self-consciousness and lack of immediate benefits.

2. CGMs in Special and Target Populations

Pregnant Women with Gestational Diabetes

CGMs are crucial in managing blood glucose levels throughout pregnancy. This can reduce incidences of adverse pregnancy outcomes such as preeclampsia and fetal macrosomia⁴³. Moreover, pregnancy can increase skin sensitivity, necessitating the development of hypoallergenic CGM sensors. Thus, effective use of CGMs requires coordination with prenatal care providers and could be integrated into overall care plans.

General Consumer Base

In addition to this, CGM technology is highly advantageous for a variety of patient segments : children and adolescents who lack better self-management skills during this critical period of growth; elderly adults, who may struggle due to physical or cognitive limitations, or respective care facilities; individuals with hypoglycemia unawareness, wherein early warning signs and symptoms are too subtle to be notices; athletes and active individuals effects of exercise on their blood glucose levels in real-time, patients with

unstable/brittle diabetes as CGM allows more precise and accurate episodic management; and high risk patients on intensive insulin therapy.

3. Integration with Hybrid Closed Loop Systems

Artificial Pancreas Mechanism

These systems aim to emulate the endogenous functions of the pancreas by automating insulin delivery, using real-time glucose data. This mechanism combined insulin pumps and a control algorithm to maintain normal glucose levels without frequent user input. The hybrid closed-loop (HCL) still requires user intervention for meal-time boluses but automatically adjusts basal insulin delivery based on CGM readings. These systems improved time-in-range by 12-20% compared to open-loop systems⁴⁴: systems such as Medtronic MiniMed 670G and Tandem Control-IQ employ hybrid algorithms to maintain optimal glucose levels.

Automation and Impact

The bionic pancreas” represents the ultimate goal of eliminating manual intervention completely: systems like Beta Bionics’ iLet show promising results in clinical trials⁴⁵. Their CGM systems leverage machine learning models to predict glucose trends and optimize insulin delivery. This allows preemptive insulin adjustments before glucose excursions occur, enabling for more consistent glycaemic control and reduces patient burdens.

Multi-Molecular Sensing

A recent trend in CGM development is the integration of multi-molecular sensing capabilities. Future technologies will also monitor key metabolic markers such as lactate, ketones, and cortisol levels. This multi-analyte monitoring would offer a more comprehensive view of a patient’s metabolic health⁴⁶: this would enable detection of diabetic ketoacidosis or metabolic distress. This has been facilitated by biosensor technology which enabled the creation of multi-purpose electrochemical sensors. Hence, this neo-generation approach promises to elevate the utility of CGMs from a single-purpose glucose monitor to a holistic metabolic health tool.

Overall Evaluation

To comprehensively compare Continuous Glucose Monitoring (CGM) systems with Self-Monitoring Blood Glucose (SMBG) devices, we have developed a systematic scoring framework on a scale of 1 - 10.

1. Metrics and Weights

1. Accuracy (30%) Measures the precision and reliability of glucose readings, essential for effective diabetes management. This includes detection of glycemic excursions

and the Mean Absolute Relative Difference (MARD) of the system.

2. Cost-Effectiveness (20%) Evaluates the balance between initial costs and long-term economic benefits, considering factors such as reduction in complications and overall healthcare savings.

3. Usability (15%) Assesses ease of use, including user experience, real-time feedback, trend analysis, and integration with other health-monitoring devices.

4. Accessibility (15%) Considers the affordability and availability of the system across different regions, particularly in low- and middle-income countries (LMICs).

5. Reliability (10%) Examines sensor calibration requirements, durability, and the consistency of glucose readings over time.

6. User Satisfaction (10%) Evaluates psychological comfort, adherence, and the overall experience of users, including convenience and reduction in monitoring-related distress.

Each metric is scored and the weighted total is calculated as: $\text{Weighted Score} = \text{Metric Score} \times \text{Weight}$. The composite score is the $\sum(\text{Weighted Scores})$.

2. Evaluation and Results

Table 1 Absolute and weighted scores comparing CGM and SMBG over chosen criteria

Metric	CGM Score	CGM Weighted Score	SMBG Score	SMBG Weighted Score
Accuracy	9	2.7	7	2.1
Cost-Effectiveness	7	1.4	6	1.2
Usability	9	1.35	6	0.9
Accessibility	6	0.9	9	1.35
Reliability	8	0.8	8	0.8
User-Satisfaction	9	0.9	6	0.6

Continuous Glucose Monitoring - (Total Score: 8.05/10): CGMs continuously monitor glucose levels, reducing undetected glycemic excursions by 19% and providing more precise and accurate insulin adjustments. They integrate with digital tools, offering real-time alerts and automatic trend analysis, making glucose management seamless. CGMs also reduce finger pricks, improve confidence in glucose control, and lower anxiety among users. Modern CGMs are highly accurate, though sensor calibration and wear duration still pose minor challenges. Additionally, while they

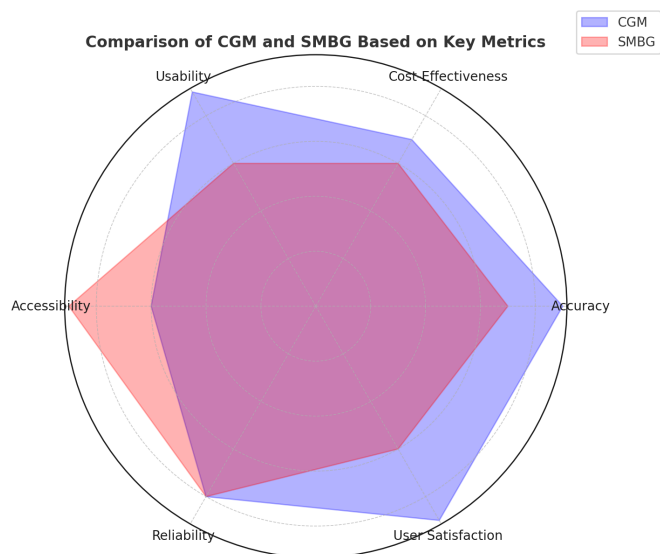


Fig. 3 Radar chart visualization comparing absolute scores of CGM vs SMBG

have a higher upfront cost, they significantly lower long-term complications, reducing emergency hospitalizations. However, in terms of accessibility, CGMs are still expensive and less available in lower-income regions, limiting their widespread adoption.

Self Monitoring of Blood Glucose - (Total Score: 7/10): SMBGs are widely available and affordable, making them the preferred choice in LMICs (Low- or Middle-Income Country). However, SMBGs provide accurate but intermittent data, missing glucose fluctuations that CGMs detect. Though it is mechanically simple and reliable, SMBG is often subject to human error. Frequent finger pricks and manual record-keeping also make SMBGs less convenient. In fact, finger pricks and lack of continuous data lower patient comfort and adherence. Thus, although they have a lower initial cost, long-term expenses from undetected complications often accumulate.

This structured analysis confirms CGMs' superiority over SMBGs, particularly in accuracy, usability, and long-term effectiveness. CGMs significantly reduce HbA1c levels, improve user adherence, and provide real-time trend analysis, unlike SMBGs, which rely on intermittent readings. However, SMBGs remain more accessible in LMICs due to significantly lower initial costs and lower infrastructural requirements. Despite these barriers, the composite score (8.05 vs. 7.00) clearly demonstrates CGMs advantages, making it the superior choice for diabetes management in the long-run provided limitations are addressed.

Pathway to Globalization

1. Telemedicine and Remote Monitoring

CGMs are emerging being integrated with digital health platforms, especially in regions where healthcare is inaccessible. The data can be transmitted to healthcare providers through telehealth systems, reducing the need for in-person visits in rural and underserved areas. A study in the United States demonstrated that integrating CGMs with telemedicine for rural populations improved HbA1c levels by an average of 0.6% over six months, a notable improvement compared to traditional care methods. This is facilitated by innovative platforms such as Medtronic CareLink, which is equipped with predictive analytics that notify healthcare providers of impending scenarios⁴⁷. To combat obstacles with digital infrastructure, mobile health (mHealth) solutions, such as SMS-based CGM alerts are emerging : a pilot study in Tanzania, demonstrated a 20% reduction in severe hypoglycaemia episodes, highlighting the potential of low-tech solutions to extend CGM benefits in areas with limited connectivity.

Cloud-Based Platforms.

It is important to consider that this will require robust cloud-based platforms capable of amalgamating data from multi-modal devices to enable remote monitoring for healthcare providers. Therefore, innovations in mobile health (mHealth) infrastructure, leveraging 4G/5G networks, will be critical in ensuring transmission of real-time data across geographic locations.

2. Country Specific Approaches to Collaborative Models

To deal with financial constraints, Cubas healthcare model promotes preventive care and government-sponsored chronic disease management. Therefore, it has launched community-based glucose monitoring programs where local clinics distribute CGMs, specially for patients with Type 1 diabetes. Studies reveal that 72% of Cuban patients using government-distributed CGMs achieved target glucose levels compared to only 38% under conventional care⁴⁸. Moreover, the costs of these programs are reduced through bulk purchasing and domestic production.

On the other hand, India has embraced rural healthcare innovations. Low-cost CGM devices, such as the HealthCube system, are being deployed in rural areas. Healthcare workers are also trained to operate the devices, overcoming the limitations of physician availability. Additionally, the implementation of Ayushman Bharat, a public health insurance scheme, has subsidized CGMs to increase their affordability for low-income populations. Reports demonstrate that the increased adoption of CGMs in rural districts of Karnataka led to a 15% improvement in patient compliance with diabetes care protocols⁴⁹.

In Scandinavia and Denmark, government-subsidized CGMs are integrated into national diabetes care programs. In fact, 89% of adults with Type 1 diabetes have access to free CGMs as part of the public health care system. The integration of CGMs has led to a 1.1% reduction in average HbA1c levels among Type 1 diabetes patients. In addition, globally, collaborative public-private partnerships have been critical to scaling CGM adoption in low-income areas. In Kenya, Abbott and the Kenyan Ministry of Health have partnered to introduce the FreeStyle Libre CGMs at a reduced cost through bulk purchasing. After complementing this with educational workshops, the program led to a 27% increase in CGM adoption among patients with Type 1 diabetes in the first year⁵⁰. Such models highlight the importance of coordinated efforts between the private sector, governments, and NGOs in expanding CGM access globally.

3. Sustainability in Production and Widespread Adoption

Eco-Friendly Production Methods

Manufacturers are increasingly focusing on being environmentally friendly during the production lifecycle. Models, like the Dexcom G6 and Abbott FreeStyle Libre, rely on non-recyclable plastic components and lithium-ion batteries, contributing to electronic waste. However, a major transition to biodegradable materials for sensor patches, as proposed in various pilot studies, could reduce plastic waste by up to 40% per device without compromising efficacy⁵¹. In low-income and middle-income countries (LMICs), there is a growing trend of leveraging scalable and affordable materials such as paper-based sensors or organic electronics, to reduce production costs. Moreover, rechargeable sensor batteries could extend the lifespan of devices and reduce toxic battery waste. For instance, a prototype CGM developed by the University of Cambridge integrates a micro-energy harvester, which utilizes the patients kinetic energy to power the device.

Localized Production and Government Policies

Localization of production in many regions such as Southeast Asia and sub-Saharan Africa can greatly reduce transportation emissions and lower costs. Empirical studies demonstrate that LMICs could reduce CGM production costs by up to 25%, making the technology more accessible to underserved populations⁵². There is also an industry shift toward modular CGM designs that could allow for easier repairs and component replacement. Moreover, governments can incentivize CGM use through various public health initiatives and reimbursement policies : programs such as national diabetes prevention programs (DPPs) or universal health coverage (UHC) frameworks could prioritize CGM technologies as part of routine diabetes care.

Partnerships with Global Health Organizations

These partnerships can include subsidized pricing, bulk purchasing, and training programs for healthcare workers in underserved regions. A promising avenue is to scale the adoption through global health organizations like the World Health Organization (WHO), which could facilitate bulk purchasing agreements similar to the Global Fund model used for vaccines. For example, in countries like Nigeria, a partnership between local manufacturers and global donors has successfully produced low-cost glucometers; regions like sub-Saharan Africa and South Asia have also actively partnered with local governments and health ministries to introduce CGM donation programs⁵³. Finally, education campaigns focusing on the benefits of CGMs would strongly promote both the technological and social acceptance of glucose monitoring.

Discussion

This study highlights the critical role of CMGSs and the feasibility of globalizing their adoption for medical and commercial use. Our research indicates that in the long term, CGMs are significantly more reliable and accurate. This is because in the experimental studies, CGM was significantly more effective in reducing HbA1c (mean difference of -0.25 and 95% confidence interval between -0.06 and -0.45) than SMBG, conducted with a statistical significance of more than 95% ($p = 0.01$). Also, CGM detected significantly higher percentages of hyperglycemic and hypoglycemic episodes than SMBG (61.1% vs. 50.8%; $p=0.047$) and (3.8% vs. 1.7%; $p=0.016$). In addition, its also more cost-effective with the willingness-to-pay threshold of 1 per capita gross domestic product per QALY gained. These results highlight the potential of CGM globalization as the main method for glucose monitoring worldwide, especially in high and upper-middle-income countries, leading to a more convenient and less painful way for blood glucose management.

Although CGMs are more cost-effective in the long term, they have a significantly higher price. For example, the Dexcom G7 is priced at \$377 (Aug 2024), whereas many SMBG devices like the Contour Net EZ are priced at \$30 or less (Aug 2024). This huge price difference is the main barrier that limits the global adaptation of CGM as the main glucose monitoring system, especially in low and middle-income countries. Despite these limitations, CGM is the fastest-growing technology in glucose monitoring, with a market size of \$8.8 billion in 2023 and projected to be \$25.8 billion by 2032³¹. Additionally, many researchers believe that CGM will become the primary choice for glucose monitoring and replace SMBG in clinical practice over the next 510 years in insulin-requiring patients with diabetes³².

Moreover, emerging trends, such as non-invasive CGMs, enhanced wearable integration, and advanced machine-learning-based predictive analytics, multi-molecular sensing all point to the true potential of CGMs. Their scientific and medical poten-

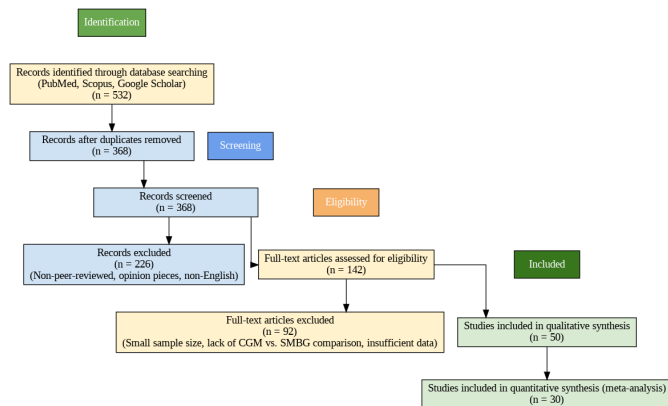


Fig. 4 PRISMA flow diagram demonstrating stages of the study selection process

tial has no limits and the impact they can have on diabetes care is truly profound. Equipped with these advancements, they are positioned to become the standard glucose monitoring device in the coming years. Additionally, through partnerships and collaborations, stakeholders can build awareness and alleviate cost issues - thus combatting obstacles to widespread adoption.

In a nutshell, it is suggested that future research focuses on developing CGM devices that are both affordable and durable for widespread commercial use. If achieved successfully, this would revolutionize how CGM technology is perceived, making SMBG devices seem outdated and less appealing. Current partnerships in countries like India and Cuba, where subsidized and government-distributed CGMs have shown improved patient outcomes, exemplify scalable models for CGM adoption in underserved regions. The healthcare trend is shifting towards CGMs and its globalization is a feasible reality for patients and clinics across the world.

Methodology

Search strategy: Our review utilized various credible information databases such as PubMed, Scopus, and Google Scholar to identify all relevant studies published between 2019 and 2024. Our search queries were tailored to identify specific studies by using boolean search to emphasize keywords such as Continuous Glucose Monitoring (CGM), Self-Monitoring Blood Glucose (SMBG), Comparison of CGM and SMBG, HbA1c, hypoglycemia, hyperglycemia, CGM Globalization and Partnerships, CGM Technological Device Advancements, QALY, (Quality Adjusted Life-Year), and CGM Cost-Effectiveness were utilized. We further applied filters to focus on peer-reviewed articles, randomized controlled trials (RCTs), cohort studies, and meta-analyses. The search process was systematically documented to allow for replication.

Study Selection Design: To enhance transparency and re-

producibility, we followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines for study selection.

- **Identification:** The initial database search yielded a total of 532 studies, distributed as follows: PubMed (210 studies), Scopus (160 studies), and Google Scholar (162 studies). After removing 164 duplicate studies, a total of 368 unique studies remained.
- **Screening:** Titles and abstracts were reviewed for relevance, and non-peer-reviewed articles, opinion pieces, and non-English publications were excluded. After this stage, 142 studies remained for full-text review.
- **Eligibility:** Full-text assessment was conducted on 142 studies to determine their suitability based on predefined criteria. Studies were excluded if they had a small sample size ($n < 30$ participants), lacked a direct CGM vs. SMBG comparison, or did not report sufficient quantitative results. A secondary reviewer verified the eligibility of the articles to ensure reliability in the selection process.
- **Inclusion:** A total of 50 high-quality studies met all inclusion criteria and were incorporated into the final analysis. These studies provided quantitative metrics on HbA1c reduction, hypoglycemia detection, cost-effectiveness, and accuracy of CGM compared to SMBG.

Inclusion Criteria: Our review studies met the following criteria: (i) Published between 2019 and 2024, (ii) Involve adult participants with diabetes (Type 1 or Type 2), (iii) Provided direct comparison between CGM and SMBG, (iv) Report fundamental outcomes such as changes in HbA1c levels, hypoglycemic event rates, accuracy and cost-effectiveness, (v) Utilized randomized controlled trials (RCTs), cohort studies, or meta-analyses, (vi) Analyzing device, IoT, ML algorithm enhancements or ongoing experiments in the same, (vii) Discussing partnerships, globalization and adoption case-studies.

Exclusion Criteria: Besides the above criteria, studies were excluded if they had a small sample size ($n < 30$ participants), lacked direct CGM vs. SMBG comparison, did not report quantitative results relevant to this study, were non-peer-reviewed sources (e.g., conference abstracts, editorial opinions).

Data extraction: This was performed systematically by recording key study characteristics, including author information, publication date, study design, sample size, participant demographics (e.g., age, gender). Then we leveraged descriptive statistical techniques to aggregate data from selected studies: this includes baseline characteristics (e.g., baseline HbA1c levels), intervention duration, participant demographics (e.g. mean age) and outcomes such as HbA1c reduction and the incidence rates of hypoglycemic events. These metric summaries laid the foundational groundwork for understanding the relative performance

and clinical consequences of using CGM and SMBG. Both qualitative and quantitative metrics were leveraged. For the narrative aspect, structured summaries and analysis of studies were conducted to highlight the key advancements and record novel insights.

Quality Assessment: All studies are taken from reputable and credible academic journals and webpages. For studies referenced from other sources, verification of information has been conducted thoroughly. We further checked for criteria such as selection bias, performance bias, and attrition bias. Referencing the GRADE approach, we considered factors like study limitations, inconsistency, and imprecision. Quality assessment of studies can be performed by using the Cochrane Risk of Bias tool for RCTs and the Newcastle-Ottawa Scale for cohort studies.

Potential Limitations: The paper was partially constrained by notable heterogeneity in study populations, sample sizes, and duration of trial interventions. Additionally, spikes in CGM technological advancements introduced potential temporal inconsistencies in outcome comparisons. Although this posed obstacles in standardizing results across different technological iterations, the review accommodates these biases and variance to a fair extent.

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