Innovative Medical Devices in Diabetes Management: FDA Device Classification, Current Status and Future Directions

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ABSTRACT

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by high blood glucose levels due to insufficient insulin secretion, impaired insulin action, or both. This review explores recent advancements in diabetes management, focusing on medical devices for glucose monitoring and insulin delivery. Emerging technologies, such as wearable devices and artificial intelligence (AI), are revolutionizing diabetes care. The review analyzed current literature on blood glucose monitoring devices, including blood glucose meters and continuous glucose monitors (CGMs), as well as insulin delivery systems, from syringes to closed-loop systems. Emphasis was placed on traditional and advanced devices, including AI-integrated wearables, with attention to FDA regulations ensuring safety and efficacy. CGMs provide real-time glucose data, optimizing blood sugar control and reducing complications, while advanced insulin delivery methods improve precision and convenience. Innovations like wearable technologies and AI enable predictive analytics and automated insulin management, leading to better outcomes and empowering self-management for patients. These advancements represent significant progress toward a technology-driven, patient-centered approach to diabetes care, enhancing quality of life and clinical outcomes. Continued research into these technologies is essential to further improve diabetes management and achieve more effective, personalized treatments for individuals with diabetes.

KEYWORDS: Diabetes mellitus (DM), Blood glucose monitoring, Insulin delivery systems, Wearable devices, FDA device classification.

INTRODUCTION

Chronic hyperglycemia occurs due to inadequate insulin secretion, impaired insulin function, and disruptions in the body's metabolism of carbohydrates, fats, and proteins. Insulin, a key anabolic hormone, regulates these metabolic processes, and its dysfunction can result in various metabolic complications. The type of diabetes and how long it lasts affect the severity of the symptoms. Like children with type 1 diabetes, people with severe insulin shortage may experience symptoms like increased appetite, excessive thirst, frequent urination, weight loss, and eyesight issues. However, many people with type 2 diabetes may not show any symptoms, especially if the disease is still in its early stages. [1]

About 537 million adults between the ages of 20 and 79 worldwide have diabetes, accounting for 10.5% of the total population. The number of individuals with diabetes is expected to climb to 643 million by 2030 and 783 million by 2045. Over the past 20 years, the incidence of diabetes in Southeast Asia has significantly increased, exceeding previous projections.[2]

Classification of Diabetic Mellitus

Diabetes is characterized by high blood glucose levels resulting from the body's ineffective production or use of insulin (a hormone essential for controlling blood sugar levels) known as diabetes mellitus. It is a complicated and chronic metabolic disease composed of 3 major types: Type 1, type 2, and gestational diabetes are the three main forms of this illness, and each has unique symptoms and start patterns. [3]

- **Type I Diabetic Mellitus:** Type 1 diabetes mellitus (T1DM), is typically identified early in life due to insulin insufficiency. Because exogenous insulin is now widely available, the life expectancy of people with type 1 diabetes has significantly increased compared to thirty years ago, but it is still lower than that of healthy individuals. [4]
- **Type II Diabetic Mellitus:** Defective insulin production is a major factor in the pathophysiology of type 2 diabetes (T2D). To maintain appropriate glucose levels, insulin sensitivity causes a wide range of variations in insulin output. Additionally, people with

type 2 diabetes cannot effectively increase their insulin production to fight insulin resistance since they have a low disposition index. [5]

- **Gestational Diabetes:** The risk of adverse consequences for the mother, fetus, and infant is increased when hyperglycemia occurs during pregnancy. Whether the hyperglycemia takes on the T2D form identified before or during pregnancy, this risk exists. The risk of getting diabetes as an adult is higher for newborns whose mothers have gestational diabetes. [6]

Challenges of Diabetes Mellitus

Diabetes mellitus presents several challenges, including long-term complications like cardiovascular disease, kidney damage, and neuropathy. Effective management requires strict blood sugar control, which can be difficult for many patients due to lifestyle factors, medication adherence, and diet restrictions. Psychological issues such as stress, depression, and anxiety can further hinder management. [7,8]

Medical Device

Per Section 201(h)(1) of the Food, Drug, and Cosmetic Act, a device is:
An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a part, or accessory which is:

- Included in the official National Formulary, the United States Pharmacopeia, or any of their supplements, designed for diagnosing diseases or conditions, or for curing, alleviating, treating, or preventing diseases in humans or animals, or intended to influence the structure or function of the human or animal body, without achieving its primary purpose through chemical action within or on the body, and without relying on metabolism to achieve its primary purpose. The term "device" excludes software functions specified under section 520(o).[9]
- Medical devices are classified into 3 classes based on the risk of the device. They are, [10]
    - Class I:
        - Risk Level: Low risk; general controls are sufficient.
        - Examples: Manual wheelchairs, bandages.

        - Regulatory Requirements: 95% are exempt from premarket notification.
    - Class II:
        - Risk Level: Moderate risk; general controls are insufficient alone.
        - Examples: Blood pressure cuffs, syringes.
        - Regulatory Requirements: Typically requires a 510(k) premarket notification demonstrating substantial equivalence to a predicate device.
    - Class III:
        - Risk Level: High risk; usually sustain or support life.
        - Examples: Pacemakers, breast implants.
        - Regulatory Requirements: Must undergo rigorous premarket approval (PMA) process. [11,12]

METHOD

This review was conducted through an extensive analysis of the current literature on diabetes-related medical devices, regulatory frameworks, and emerging technologies. The methodology includes:

- Reviewing peer-reviewed journal articles, regulatory documents, and clinical trial reports.
- Analyzing the classification and approval process for blood glucose monitoring and insulin delivery devices under FDA regulations.
- Comparing traditional and modern approaches in diabetes management based on effectiveness, patient adherence, and clinical outcomes.
- Evaluating advancements in wearable technology and AI-based systems in diabetes care.

RESULTS

Blood Glucose Monitoring Devices

Blood glucose monitoring devices are fundamental tools in diabetes management, providing crucial data to guide treatment decisions and prevent complications. There are two primary types: blood glucose meters (BGMs) and continuous glucose monitoring (CGM) systems.

1. **Blood Glucose Meters (BGMs)**
    - Blood Glucose Meters (BGM) are the most widely used devices for blood glucose monitoring. They require a small blood sample (from 0.3 to 1 microL), usually obtained by pricking the finger, which is placed on a disposable test strip that the meter reads. BGMs are affordable and easy to use, making them accessible to many patients. However, they provide only intermittent glucose readings, which may limit the ability to detect trends or fluctuations throughout the day. A glucometer, test strips, and a lancet for skin pricking are the equipment needed for capillary blood glucose testing. [13]
    - Blood glucose meters are classified as Class II medical devices. This classification is defined under the U.S. Food and Drug Administration (FDA) regulations, specifically in 21 CFR Section 862.1345, which pertains to glucose monitoring systems [14]. To ensure safety and efficacy, Class II devices must adhere to specific regulations, such as performance criteria, postmarket surveillance, and patient registries. [15,16]
2. **Continuous Glucose Monitoring (CGM) systems**,
    - CGMs detect the amount of glucose in the interstitial fluid constantly using a tiny sensor that is placed beneath the skin. These systems provide valuable information on glucose trends and fluctuations, helping patients avoid episodes of hyperglycemia and hypoglycemia. The three components of a CGM system are a sensor that measures the amount of glucose in the interstitial fluid at intervals of one to five minutes and a transmitter that gathers and sends the glucose values to the third part (a receiver) that shows the data. [17] Using CGM can lower glycated hemoglobin (HbA1c) readings by 0·17 to 0·70%. It is significant for CGM found in meta-analyses, which range from 0·20 to 0·48% for Type 2 diabetes and from 0·23 to 0·37% for Type 1 diabetic patients.[18] Depending on the product, the sensor may stay on the patient for three to fourteen days. A reader that scans the

sensor can show the interstitial fluid glucose level as well as trends over the last eight hours. CGM devices have a 90-day glucose data storage capacity. [19]

- The U.S. Food and Drug Administration (FDA) has designated Continuous Glucose Monitoring (CGM) devices as Class II medical devices. According to this classification, CGM devices are deemed to be moderately risky must show substantial equivalence to existing devices and require a premarket notification (510(k) submission). [20] The regulation number for CGM systems is 21 CFR 862.1355, which pertains to integrated continuous glucose monitoring systems.[14] The product code assigned to CGM devices is QII. [21]

Insulin Delivery Systems

Insulin Delivery Systems for delivering insulin are essential for managing diabetes, particularly for those who need insulin therapy to control their blood sugar levels. These systems ensure accurate and timely delivery of insulin to mimic the body's natural insulin response. The most common insulin delivery methods include syringes, insulin pens, insulin pumps, and newer innovations like artificial pancreas systems and smart insulin pens.

1. **Syringes**:
    - Insulin syringes are essential tools for administering insulin to individuals with diabetes, particularly those with Type 1 diabetes who require regular insulin injections. These syringes are specifically designed for subcutaneous use, mimicking the natural secretion of insulin by the pancreas. An insulin syringe typically consists of three main components: the needle, barrel, and plunger. The needle is usually thin and short, designed to minimize pain during injection. Insulin syringes are disposable, and intended for single use to maintain sterility and reduce infection risks. Insulin syringes come in various sizes to accommodate different dosages of insulin. Common barrel sizes include 0.3ML, 0.5ML, and 1.0ML The needle gauge also varies, affecting thickness; a higher gauge indicates a thinner needle, which may be more comfortable for some users. [22]
    - The U.S. Food and Drug Administration (FDA) has designated Insulin syringes as Class II medical devices. According to this classification, Insulin syringes are

subject to specific regulatory controls that require 510(k) clearance to ensure safety and effectiveness. To ensure the safety and efficacy of insulin syringes, manufacturers must show that it is substantially equivalent to a legally marketed predicate device. The FDA requires evidence of satisfactory performance, including accuracy in dosage measurement and safety in design to minimize risks such as needle stick injuries. [23]

2. **Insulin Pens**:
    - Insulin pens are more convenient and user-friendly than syringes. These devices resemble a pen and come either as disposable or reusable versions. An insulin cartridge is placed into the delivery chamber of reusable pens. In addition to offering patients greater flexibility (i.e., If their prescription changes, they can switch insulin pens without purchasing a new pen.), this may be less expensive than utilizing prefilled pens. The reusable pens are made to last longer and are simple to use and long-lasting. Prefilled pens: Pens that come prefilled, these pens come with an integrated single-use insulin cartridge. This device is highly comfortable and simple to use because the patient does not need to load it. These are lightweight, portable, and simple to use for patients who have problems handling the cartridges in reusable pens or for people who would prefer not to refill the cartridges. [24]
    - Smart insulin pens are digital, networked insulin pens that wirelessly send clinical data to a mobile application (app) using Bluetooth® technology. [25] Pens provide greater flexibility, precision, discretion, and long-term cost-effectiveness than syringes, which enhances treatment adherence and persistence. [26]
    - The U.S. Food and Drug Administration (FDA) has designated Insulin Pens as Class II medical devices, particularly those used to inject insulin for the treatment of diabetes. Class II devices need particular controls, such as performance benchmarks and post-market monitoring, to guarantee their efficacy and safety.
    - Insulin pens are subject to the 510(k) premarket notification process regulated by the U.S. Food and Drug Administration (FDA). To ensure the safety and efficacy of insulin syringes, manufacturers must show that it is substantially equivalent to a legally marketed predicate device.

- For instance, the FDA has granted 510(k) clearance for various insulin pen-related devices, including smart insulin pen caps that enhance diabetes management by providing real-time alerts and dose recommendations based on continuous glucose monitoring data. [27]

3. **Insulin Pumps**:
   - Insulin pumps are small, computerized devices that continuously deliver a steady amount of rapid-acting insulin via a catheter placed under the skin. The pump can be programmed to give patients bolus doses of insulin at mealtimes to cover carbohydrate intake and basal (background) insulin throughout the day. Insulin pumps provide better glucose control and flexibility in lifestyle compared to syringes and pens. Studies have shown that pump therapy can reduce HbA1c levels and minimize the risk of hypoglycemia. [28,29]
   - The U.S. Food and Drug Administration (FDA) has designated Insulin Pumps as Class II medical devices, particularly those used to inject insulin for the treatment of diabetes. This classification of the device indicates that they are considered to pose a moderate risk to patients and require a premarket notification, commonly referred to as a 510(k) submission. [30,31]
4. **Artificial Pancreas (Closed-Loop Systems)**:
   - These systems automate insulin delivery by combining an insulin pump, an algorithm, and Continuous Glucose Monitoring (CGM). The technology reduces the need for manual intervention by continually monitoring glucose levels and adjusting insulin supply accordingly. [32] The artificial pancreas offers a promising future for diabetes management by mimicking the body’s natural insulin regulation and improving overall glycemic control. DIY systems link commercially available insulin pumps and CGMS to an open-source algorithm that analyzes glucose data from the sensor and remotely modifies the pump's insulin delivery. The algorithm can be stored in custom hardware or a smartphone application. [33]
   - Closed-loop systems for diabetes management are classified as Class III medical devices due to their high-risk nature and the critical need for accurate performance in managing blood glucose levels. This classification is due to their complexity and the significant risks associated with their use. It ensures that these advanced

technologies undergo thorough evaluation before they can be marketed for patient use. [34]

- These devices are considered high-risk and typically require a more rigorous Premarket Approval (PMA) process, which involves extensive clinical data to demonstrate safety and effectiveness. [20]
- Closed-loop systems with continuous glucose monitoring (CGM), insulin delivery systems necessitating precise control to avoid potential health risks such as severe hypoglycemia or hyperglycemia. The FDA oversees the approval process for closed-loop systems under specific regulations that ensure they meet stringent safety and efficacy standards. [35]

Wearable Devices And Smart Technology

1. **Wearable Monitors**: Due to the extensive usage of wearable technology and other systems, a large amount of information is now accessible to the general population. A fresh approach to algorithm construction has been made possible by the availability of many CGM data sources and recent advances in artificial intelligence (AI) approaches. As a result, it can more effectively personalize blood glucose prediction. [36]
2. **Smartwatches**: One of the most significant side effects of diabetes is hypoglycemia, which causes changes in physiological parameters that can be recorded by smartwatches and identified by machine learning (ML). It is unknown how well these algorithms work in scenarios involving cognitive and psychomotor stress or in various hypoglycemic ranges. [37]

Future Directions and Innovations in Diabetes Management

- **Fully Closed-Loop Systems**: Although there are now hybrid closed-loop systems in operation, research is being done to create fully automated systems that do not need patient input. By managing insulin supply on their own, these systems hope to increase user convenience and efficacy. [38]
- **Artificial Intelligence (AI)**: By utilizing vast amounts of structured data and a wealth of computer resources, ongoing machine learning research and attempts at real-world

implementation will optimize AI's predictive performance and significantly raise the prediction accuracy of diabetes diagnosis, prevention, and treatment. [39]

DISCUSSION

The landscape of diabetes management has evolved significantly with the integration of advanced medical devices and digital health solutions, offering more precise and efficient ways to monitor blood glucose levels and administer insulin. Traditional blood glucose meters (BGMs) and insulin syringes, though widely used, present limitations such as the inability to provide continuous glucose readings and the need for frequent manual intervention. Continuous Glucose Monitoring (CGM) systems have emerged as a transformative technology, enabling real-time glucose tracking and reducing the risks of hypoglycemia and hyperglycemia. Studies have demonstrated that CGMs contribute to improved glycemic control by providing patients and healthcare providers with continuous data, allowing timely adjustments in insulin therapy. However, challenges such as sensor accuracy, high costs, and accessibility continue to affect their widespread adoption, particularly in low-resource settings.

Insulin delivery methods have also progressed from conventional syringes and pens to more sophisticated solutions such as insulin pumps and closed-loop artificial pancreas systems. Insulin pens offer better dose accuracy and convenience, while insulin pumps provide continuous subcutaneous insulin infusion, closely mimicking the body's natural insulin secretion. The development of artificial pancreas systems, which integrate CGMs with automated insulin delivery, marks a significant advancement in diabetes care by reducing the burden of manual insulin administration and improving glycemic outcomes. Despite these benefits, the cost of insulin pumps and closed-loop systems, along with regulatory barriers, poses challenges for widespread implementation.

Regulatory frameworks play a crucial role in ensuring the safety and efficacy of diabetes-related medical devices. Under the U.S. Food and Drug Administration (FDA) classification system, CGMs and insulin pumps are categorized as Class II medical devices, requiring a 510(k) premarket notification to demonstrate substantial equivalence to an existing device. Artificial pancreas systems, given their complexity and higher risk, fall under Class III, necessitating rigorous

Premarket Approval (PMA). These regulatory processes ensure that new medical technologies meet strict safety standards before being made available to patients. However, the time-consuming approval procedures and compliance requirements can delay the introduction of innovative devices into the market.

The integration of artificial intelligence (AI) and wearable technology is revolutionizing diabetes management by enabling predictive analytics, personalized insulin recommendations, and automated glucose monitoring. AI-driven systems analyze vast amounts of glucose data to predict fluctuations, allowing for proactive insulin adjustments. Smartwatches and non-invasive glucose monitoring devices are being explored as potential alternatives to traditional CGMs, although their accuracy and reliability remain areas of active research. While these innovations hold promise, issues such as data privacy, cybersecurity, and patient adoption must be addressed to ensure seamless integration into diabetes care.

Despite the significant progress in diabetes technology, challenges related to affordability, accessibility, and patient education persist. Future research should focus on improving device affordability, enhancing accuracy, and expanding access to advanced diabetes management tools. By overcoming these challenges, the healthcare industry can move toward a more patient-centered, technology-driven approach that enhances clinical outcomes and improves the quality of life for individuals with diabetes.

CONCLUSION

Diabetes Mellitus (DM) a complex and multifaceted metabolic disorder, requires a comprehensive approach to management that integrates advanced technology with conventional treatment methods. Medical devices, including blood glucose monitoring systems, insulin delivery systems, and wearable technology, play a critical role in enhancing diabetes care by offering accurate and real-time data for effective blood sugar management. The classification and regulatory pathways for these devices, particularly to ensure safety and efficacy through the U.S. Food and Drug Administration (FDA), support patients in navigating diabetes-related challenges and improving their quality of life. Innovations like continuous glucose monitors, insulin pumps, and emerging closed-loop systems are revolutionizing the field, offering more personalized and less invasive management options. The combination of AI and machine learning offers a bright future for

predictive analytics in diabetes treatment as research progresses, eventually leading to better patient outcomes and simpler disease management.

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