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Analysis of "Accuracy of a 14-Day Factory Calibrated Continuous Glucose Monitoring System With Advanced Algorithm in Pediatric and Adult Population With Diabetes"

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Abstract

In this study by Alva et al, accuracy of a second-generation factory calibrated continuous glucose monitoring system is evaluated. Compared to the first-generation FreeStyle Libre 14-day system (FSL), accuracy was improved throughout the 14-day wear period, including improved accuracy in hypoglycemia for adults and youth. The addition of optional real-time alerts for hypoglycemia and hyperglycemia as well as an integrated continuous glucose monitor (iCGM) designation by the FDA may further enable users to benefit from using CGM in real time, including in future automated insulin delivery systems. As CGM accuracy, affordability, and accessibility improve, we anticipate increased uptake of CGM by people on intensive insulin therapy, and also potential benefits and expansion into a broader patient population. There are growing opportunities to leverage cloud-connected CGM devices in the increasingly virtual, continuous telehealth-driven diabetes care model, which will require more focus on development and use of data interoperability standards.

Keywords

continuous glucose monitoring, diabetes mellitus, telehealth, digital health

Among many significant improvements to continuous glucose monitor (CGM) systems in the past decade, the introduction of Abbott's FreeStyle Libre 14-day system (FSL) created a paradigm shift in diabetes care. Before the FSL was introduced, the CGM was considered to be an expensive, complex medical device, restricted to select patients, prescribed by specialists, and delivered by durable medical equipment suppliers. FSL was the first system to offer users the benefits of CGM with an easy-to-use device, but with no fingerstick calibration required, at a lower cost, and with far more convenient access through traditional pharmacies. The FSL and the FreeStyle Libre 2 system (FSL2) have introduced the notion that the CGM might become sufficiently cheap, convenient, and accurate to ultimately replace fingersticks altogether and be ubiquitous in diabetes care. Introduced in Europe in 2014, and in the United States in 2018, Abbott reports that more than two million people with diabetes (PWD) are using the device across 46 countries.[1]

CGM use has been steadily increasing over the past decade. However, penetration into populations who would benefit—all patients with T1D and many patients with T2D—has remained low. Data from the T1D Exchange shows CGM use climbing from 6% in 2011 to 38% in 2018.[2] Despite myriad benefits of CGM,[3,4] barriers to use have included cost, insurance coverage, lack of awareness by providers, and perceptions of inaccuracy.[5] Recent CGM systems have overcome several of these challenges, by not requiring fingerstick calibration, and by achieving a level of data accuracy on which the FDA has approved for insulin users to make dosing decisions.

The recently released FSL2 adds several key features that improve upon the original FSL. First, it uses Bluetooth with optional alarms for hypoglycemia and hyperglycemia. It also achieved FDA designation as integrated CGM (iCGM), opening the door for partnerships with insulin delivery devices to create automated insulin dosing systems. In this article, Alva and coauthors evaluate the iterative improvements in accuracy of this second-generation FSL2, compared to the original FSL system.[6]

Accuracy was assessed by comparing sensor data to time-matched reference venous glucose values (Yellow Springs Instrument [YSI]) as well as self-monitoring of blood

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glucose (SMBG) values. Supervised in-clinic sessions were used to generate a wide spectrum of glucose values. Findings were reported as mean absolute relative difference (MARD), and proportion of the paired values within range of the reference glucose value. Compared to the original FSL (MARD 12.0%), accuracy of the FSL2 was improved (MARD 9.2% in adults, 9.7% in pediatrics). Importantly, accuracy was similar across age, type of diabetes, clinical site, mode of insulin delivery, and A1c. Of note, previously published data on the Dexcom G6 CGM showed an MARD of 9.9% in adults and 10.1% in pediatrics.[7]

Accuracy in hypoglycemia also improved in adults and children, with 94.3% and 96.1% of results, respectively, within 15% / ±15 mg/dL of the reference. Of note, however, the accuracy of FSL2 for "in range" (70-180 mg/dL) BG levels was lower than for hypoglycemia or hyperglycemia, which may have important consequences because PWD increasing rely on CGM input for automatic bolus calculators and closed loop therapy.

Time lag between reference venous value and the corresponding sensor results was nearly halved in FSL2 compared to the original FSL, now 2.4 ± 4.6 minutes down from 4.5 +/- 4.8 minutes for adult users.[6] Performance on the first day of sensor wear, which was significantly decreased in the original FSL, is improved (MARD 11.2%), meaning accuracy through the 14-day wear period of FSL2 now remains relatively consistent.

Alarms are now available with FSL2, and the authors report on true alarm rate and detection rate compared to YSI standard, both in hypoglycemia and hyperglycemia. Based on the data reported here and previously published data on Dexcom G6 on alarm accuracy, the FSL2 performs favorably.[7] For example, at a BG of 70 mg/dL, FSL2's true alarm rate and detection rate reported here were 86.0% (adults) and 80.3% (pediatrics) and 89.3% (adults) and 93.5% (pediatrics). Previously reported Dexcom data were 84.4% true alarm rate and 85.0% detection rate.[7] It should be noted that it can be difficult to compare technical outcomes between different CGMs because their protocols and patient populations are often very different. With the combination of shortened time lag and high accuracy in detection and alarm rate, FSL2 users can be alerted to make real-time management decisions. Of note, while FSL2 readers show glucose rate-of-change arrows, which are important for real-time management decisions, this analysis did not report data on their accuracy.

Optimal sensor survival and comfort for the full 14-day wear period remain areas for improvement. Of the study participants, 27.7% of the adult group and 20.9% of the pediatric group had sensors unintentionally come off during the 14-day wear period. Sensor-related cutaneous complications are common—including erythema, itching, and induration—and frequently cited as a cause for CGM discontinuation.[8,9] This evaluation would have benefited from additional information on performance metrics related to real-world sensor use, including compression artifacts, variations in adipose tissue and sensor placement, and temperature, all of which can affect the accuracy of glucose sensing.[10]

Generalizability of the results presented by Alva et al benefits from inclusion of both insulin pump users and noninsulin pump users, as well as a population with a wide spread of hemoglobin A1c. Limitations are the inclusion of few individuals with T2D and minimal ethnic diversity in the study—White participants constituted 87.0% of the adults and 78.4% of the pediatric participants.

The improvements in functionality and accuracy of the FSL2, a factory-calibrated CGM with optional real-time alerts, have the potential to continue to drive increases in CGM uptake and use. We anticipate this device will generate interest in existing populations of CGM users, including people with T1D and people with T2D using multiple daily insulin injections.

Importantly, as CGM usability, affordability, and accessibility continue to improve, FSL2 and other new CGM devices will have a role in expanding CGM technology to new patient populations and new use cases. More people experiencing dysglycemia may benefit from CGM use, including those with T2D not on insulin and people with prediabetes. Studies of people with T2D using CGM demonstrate its powerful role in facilitating behavior change. Individuals using CGM, compared to those not using CGM, more consistently adhere to exercise recommendations,[11] decrease caloric intake,[11,12] and have improved glycemic control,[12,13] in some cases without intensification of existing therapy.[14] Periodic use of CGM in T2D can also be effective, as changed behaviors persist even after CGM use.[15] Real-time CGM is modeled to be a cost-effective tool for PWD,[16] on the basis of A1c reduction and decreased complications, and will increasingly be used by health systems for population health management.[17]

Diabetes care is increasingly virtual—and in many cases, asynchronous—with CGM playing a crucial role in this transition.[18] Continuously connected and always available CGM data are necessary for effective telehealth use by patients and providers, during both synchronous and asynchronous care.[19] Tech-enabled digital diabetes coaching services, rapidly expanding in the United States, are already leveraging CGM.[20] Going forward, data-driven insights supported by machine-learning may enable a broader use of CGM by provider types beyond endocrinologists.

While the iCGM designation means fewer barriers to FSL2 integrating into a future automated insulin delivery system, it does not address the critical need for access to CGM data in other software applications for use in clinical decision-making. Diabetes device data should be accessible and easily viewed with other relevant patient data in one data visualization.[21] This will require that device makers leverage standard, open application programming interfaces (APIs) to allow this data exchange. At the moment, neither FSL nor FSL2 utilizes this important capability. Successful use of CGM within a more connected, virtual care model will optimally rely on a more connected diabetes data ecosystem with friction-free data flow.[22]

Abbreviations

API, application programming interface; CGM, continuous glucose monitor; FDA, Food and Drug Administration; FSL, FreeStyle Libre; FSL2, FreeStyle Libre 2; iCGM, integrated continuous glucose monitor; MARD, mean absolute relative difference; PWD, people with diabetes; SMBG, self-monitoring of blood glucose; T1D, Type 1 Diabetes; T2D, Type 2 Diabetes; YSI, Yellow Springs Instrument.

Declaration of Conflicting Interests

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