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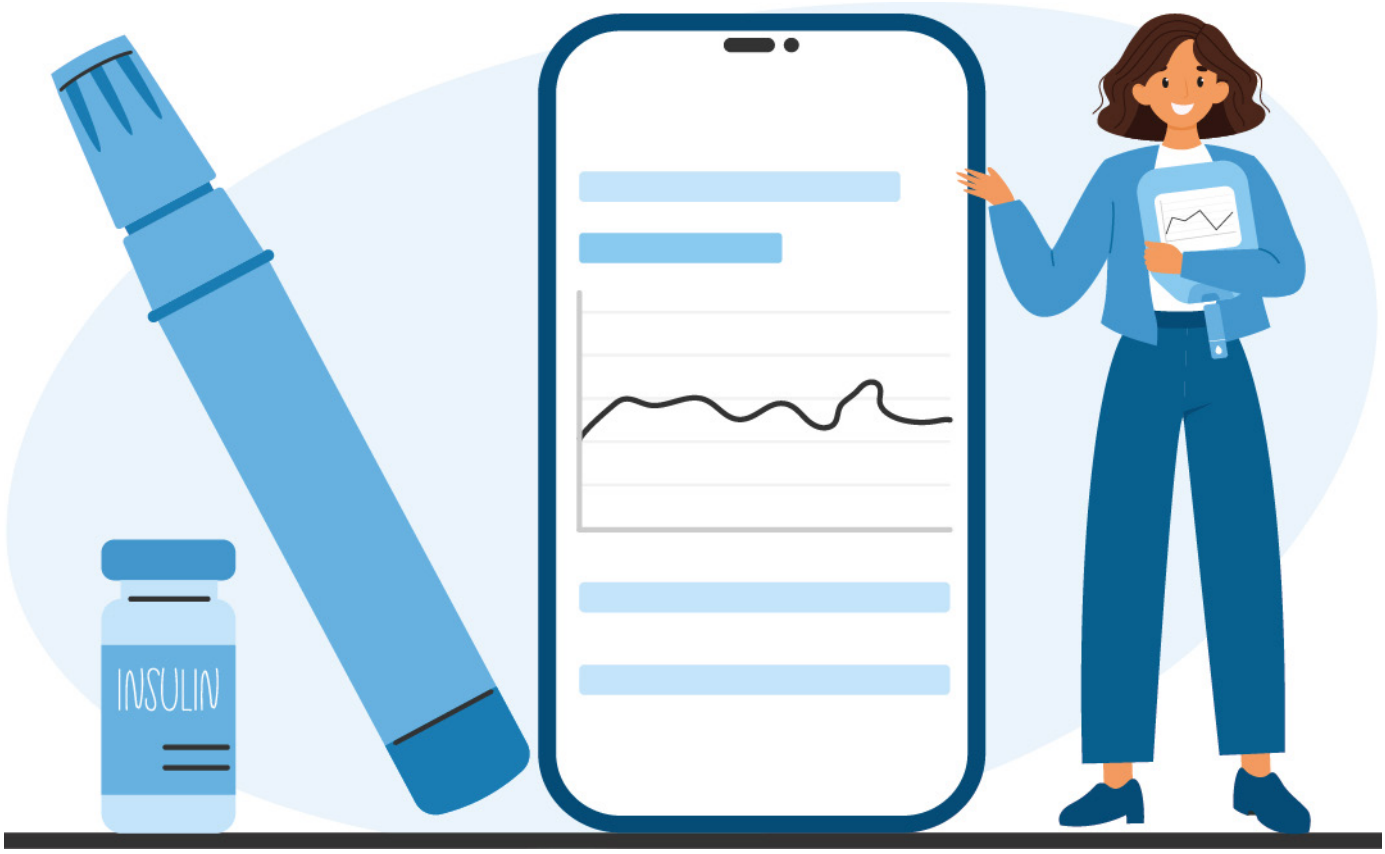


Advances in smart pens and smart caps:

What Can They Contribute to Diabetes Management?

Technological advancements have progressively reshaped the landscape of diabetes care. In recent years, we have witnessed exponential growth in the use of hybrid closed-loop insulin pumps. Data indicate that this singular advancement has translated into better glycemic control in the population with type 1 diabetes mellitus (T1DM) (1). However, the article by Ebekozien et al. showed that only 35% of people with T1DM use a hybrid closed-loop system. Additionally, this type of technology is extremely uncommon in those with type 2 diabetes mellitus (T2DM). These numbers are even lower outside developed countries. Nevertheless, the full integration of continuous glucose monitoring (CGM) and insulin therapy data is a success story that should serve as a model for other insulin delivery regimens.

Continuing with the model of integrated closed-loop systems, an important aspect is user interaction. For other individuals treated with insulin who do not use these systems, challenges include improving self-management of therapy and **enhancing information sharing with the clinical team and other caregivers**.

For many years, devices that recorded insulin dose and injection timing with pens have been available. However, only recently has the integration of CGM data and other user-assistance features been introduced. A document from the Diabetes Area of the Spanish Society of Endocrinology and Nutrition (SEEN), published recently, reviews the characteristics of marketed or soon-to-be-marketed products and the available scientific evidence. It describes various aspects, such as the profiles of users and professionals who benefit the most, barriers to widespread adoption, and changes in the care model that the implementation of these devices may bring (2).

Essentially, there are 2 approaches from the perspective of the physical device:

Some are reusable **insulin pens for use with cartridges**.

Other solutions are **caps that fit onto disposable pre-filled insulin pens**.

Regarding **insulin therapy monitoring functions, the following can be distinguished:**

Downloadable insulin pens: allow data (dose and injection timing) to be downloaded and integrated with CGM data.

Connected insulin pens and caps: can continuously share information with specific software solutions and forward it to caregivers.

Smart insulin pens and caps: some systems advise users on insulin therapy management and can therefore be aptly termed "smart."

In addition to the advantages in individual use for improving user adherence, other promising applications should be considered. The role of this technology is also to »

TECHNOLOGICAL EVOLUTION IN DIABETES AIMS AT REACHING INTEGRATED ECOSYSTEMS THAT INCORPORATE, AT A MINIMUM, ALL GLUCEMIC DATA, MEALS, AND PHYSICAL ACTIVITY. SOME OF THESE SYSTEMS HAVE SYNCHRONOUS OR ASYNCHRONOUS TELEMEDICINE INTERACTION FEATURES, SUCH AS CHAT OR VIDEOCHAT

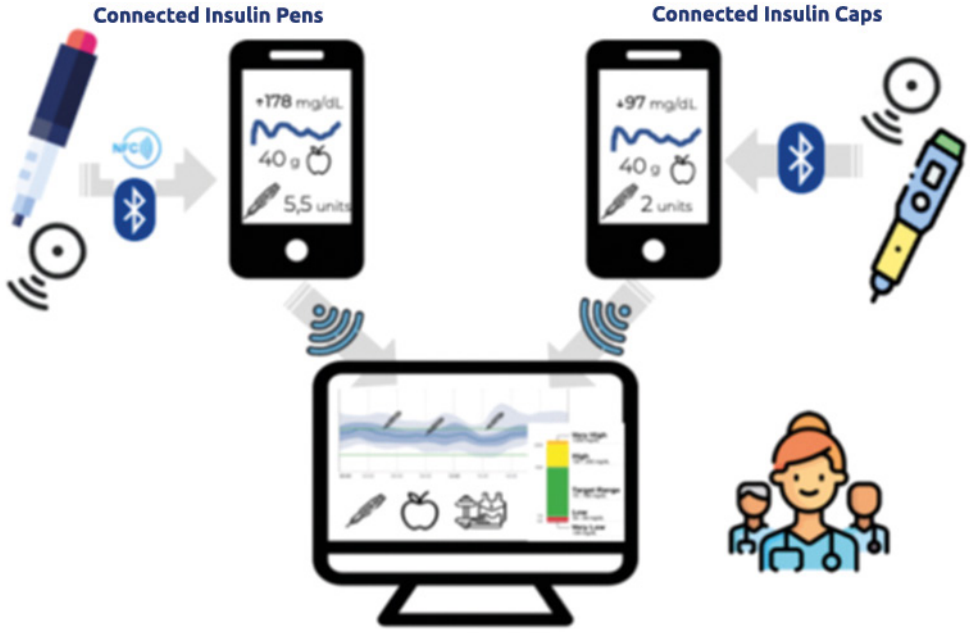
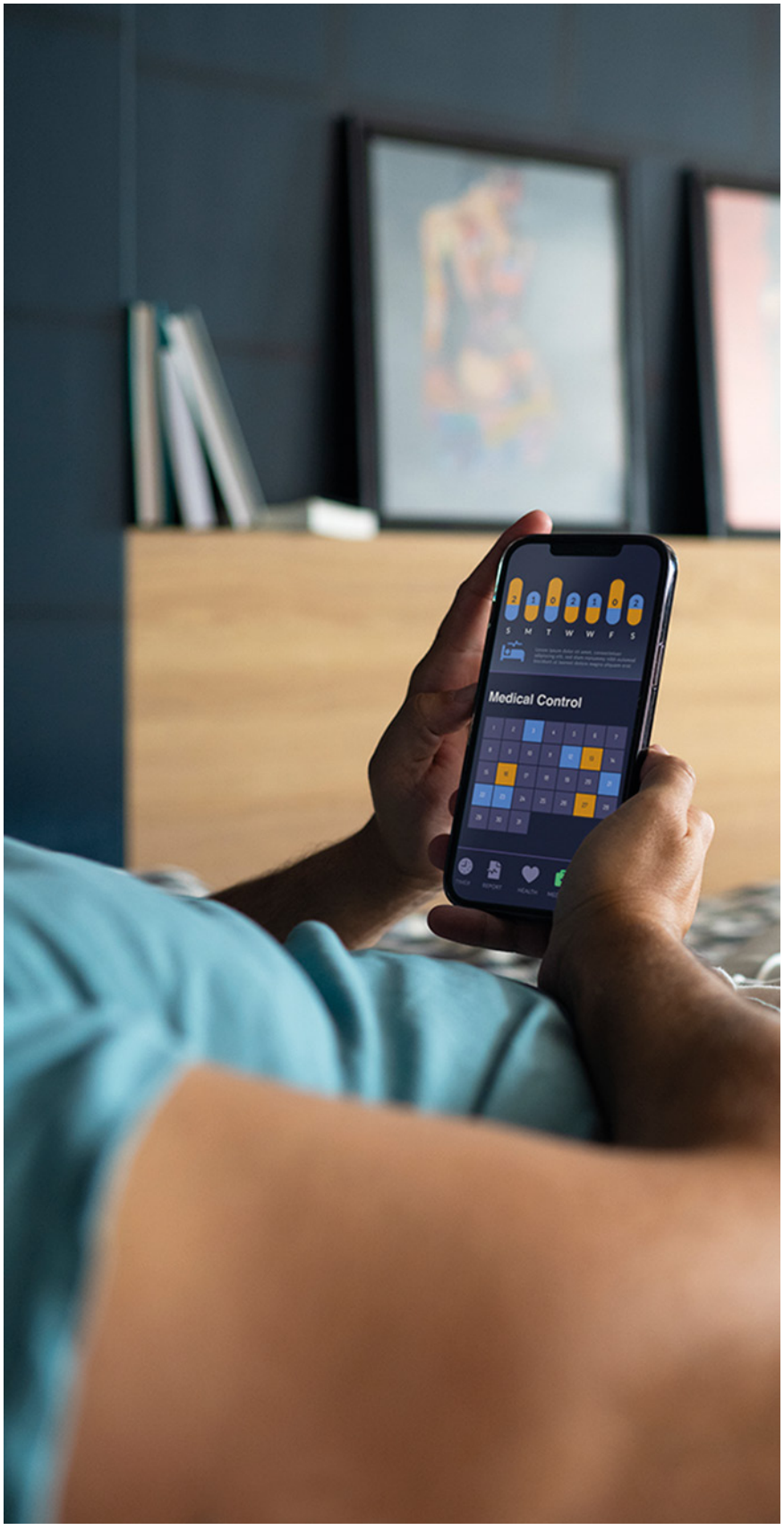


FIGURE 1. Schematic Representation of Connected Insulin Pens and Caps



close the loop with the diabetes team (including interaction through telemedicine uses), its use in institutionalized individuals treated with insulin in nursing homes or hospitals, and, finally, its utility in clinical research.

Former observational studies confirmed up to 43% missed bolus insulin doses or 11% missed basal insulin doses per week, as well as incorrect timing in insulin administration (2). Recent real-world data from users of Inpen and Novopen devices confirmed the relationship between greater punctuality or number of daily boluses with better time in range (TIR) (4,5). The first and only randomized controlled trial to test the benefits of a connected cap in people with T2DM treated with basal insulin was published by Rodolfo Galindo and the team at Emory University (6). They demonstrated that active use of the Insulclock system resulted in lower mean daily blood glucose, greater HbA1c reduction, and higher overall user satisfaction. Our group published the first randomized controlled trial of a connected cap in people with T1DM (7). Access to integrated information using the Insulclock system achieved a 6% increase in TIR and a reduction in time above 180 mg/dL (TAR180) through improved adherence to insulin doses.

The technological evolution in diabetes focuses on reaching integrated ecosystems that incorporate, at a minimum, all glycemic data, meals, and physical activity. Some of these systems have synchronous or asynchronous telemedicine interaction features, such as chat or video chat (https://www.insulcloud.com). All these features highlight the fundamental role that connected pens and caps can play in the integrated care of people with diabetes and their clinical team.

In institutional settings, such as nursing homes and hospitals, connected insulin pens and caps offer a promising solution to improve the accuracy and integration of insulin therapy data into electronic health records. By streamlining data collection and sharing processes, these devices have the potential to enhance the quality of care provided to residents, leading to safer and more efficient diabetes management practices. A good example is our Trescasas Study, a telemedicine program based on

» CGM and the Insulclock connected cap system, developed in seven nursing homes in Castile and León (Spain), including insulin-treated residents aged 68 to 102 years (8). The intervention achieved a more stable and safer glycemic profile in this complex and fragile population, reducing the rate of hypoglycemic events.

Regarding the role of connected insulin pens and caps in clinical research, some ongoing trials are already using these devices to track insulin therapy precisely and efficiently (https://www.radial.eu/en). These decentralized clinical trials (DCTs) have the potential to transform clinical trials by improving accessibility and data collection in a real-world setting while reducing the burden of participating in clinical research. Another example is how the benefits of second-generation rapid insulins ("ultra-rapid") vs first-generation analogs, which had not been systematically demonstrated in previous pivotal clinical trials, were highlighted in a recent real-world study using insulin cap technology (9).

Nevertheless, we must emphasize that further research is needed to obtain robust clinical evidence of the benefits of this technology.

The evolution of these systems from connected to smart is highly promising. Systems should be able to provide predictive advice on insulin doses and alerts to avoid hyperglycemia or hypoglycemia. With the integration of predictive algorithms and artificial intelligence-based support systems, connected insulin pens and caps are poised to offer personalized and proactive care that can bring the benefits of integrated closed-loop systems closer to the lives of people treated with insulin pens. D

CONCLUSIONS

Connected pens and caps aid in self-management of insulin therapy by integrating this data with CGM and enabling information sharing with the clinical team and other caregivers.

Observational studies and clinical trials have demonstrated that the use of these devices is associated with greater adherence to insulin therapy, better glycemic control, and higher satisfaction among people with diabetes. Their use in institutional settings such as nursing homes and hospitals can improve diabetes care in these environments.

The evolution of these systems, integrating artificial intelligence algorithms, can contribute to making insulin pen therapy as close as possible to integrated closed-loop systems.

REFERENCES

1. Ebekozien O, Mungmode A, Sanchez J, Rompicherla S, Demeterco-Berggren C, Weinstock RS, et al. Longitudinal Trends in Glycemic Outcomes and Technology Use for Over 48,000 People with Type 1 Diabetes (2016-2022) from the T1D Exchange Quality Improvement Collaborative. Diabetes Technol Ther. 2023 Nov;25(11):765–73.
2. Tejera-Pérez C, Chico A, Azriel-Mira S, Lardiés-Sánchez B, Gomez-Peralta F, Área de Diabetes-SEEN. Connected Insulin Pens and Caps: An Expert's Recommendation from the Area of Diabetes of the Spanish Endocrinology and Nutrition Society (SEEN). Diabetes Ther. 2023 May 15;
3. American Diabetes Association Professional Practice Committee. 7. Diabetes Technology: Standards of Medical Care in Diabetes-2022. Diabetes Care. 2022 Jan 1;45(Suppl 1):S97–112.
4. Adolfsson P, Hartvig NV, Kaas A, Møller JB, Hellman J. Increased Time in Range and Fewer Missed Bolus Injections After Introduction of a Smart Connected Insulin Pen. Diabetes Technology & Therapeutics. 2020 Jan 31;22(10):709–18.
5. Danne TPA, Joubert M, Hartvig NV, Kaas A, Knudsen NN, Mader JK. Association Between Treatment Adherence and Continuous Glucose Monitoring Outcomes in People With Diabetes Using Smart Insulin Pens in a Real-World Setting. Diabetes Care. 2024 Jun 1;47(6):995–1003.
6. Galindo RJ, Ramos C, Cardona S, Vellanki P, Davis GM, Oladejo O, et al. Efficacy of a Smart Insulin Pen Cap for the Management of Patients with Uncontrolled Type 2 Diabetes: A Randomized Cross-Over Trial. J Diabetes Sci Technol. 2021 Jul 22;19322968211033837.
7. Gomez-Peralta F, Abreu C, Fernández-Rubio E, Cotovad L, Pujante P, Gaztambide S, et al. Efficacy of a Connected Insulin Pen Cap in People With Noncontrolled Type 1 Diabetes: A Multicenter Randomized Clinical Trial. Diabetes Care. 2023 Jan 2;46(1):206–8.
8. Gomez-Peralta F, Abreu C, Santos E, Da Silva A, San Frutos A, Vega-Valderrama L, et al. A Telehealth Program Using Continuous Glucose Monitoring and a Connected Insulin Pen Cap in Nursing Homes for Older Adults with Insulin-Treated Diabetes: The Trescasas Study. Diabetes Technology & Therapeutics [Internet]. 2024 Nov 26 [cited 2024 Nov 26]; Available from: https://doi.org/10.1089/dia.2024.0356
9. Gómez-Peralta F, Valledor X, López-Picado A, Abreu C, Fernández-Rubio E, Cotovad L, et al. Ultrarapid Insulin Use Can Reduce Postprandial Hyperglycemia and Late Hypoglycemia, Even in Delayed Insulin Injections: A Connected Insulin Cap-Based Real-World Study. Diabetes Technol Ther. 2024 Jan;26(1):1–10.