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Analysis of "Artificial Pancreas (AP) Systems for People With Type 2 Diabetes: Conception and Design of the European CLOSE Project"

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Abstract

In an article in *Journal of Diabetes Science and Technology*, Schliess and coauthors describe the conception and design of the European Automated Glu***c***ose Contro***l*** at H***o***me for People with Chronic Di***se***ase (CLOSE) initiative for the implementation of artificial pancreas (AP) systems for people with diabetes. The CLOSE consortium aims to develop integrated AP solutions (APplus) tailored to the needs of individuals with type 2 diabetes (T2D) by developing superior risk- and cost-benefit scenarios for AP operation to achieve acceptance by users and caregivers and a high likelihood for reimbursement. CLOSE is integrating the AP platform into the center of a comprehensive product and service package specifically tailored to defined T2D patient groups and care environments, leading to an interactive collaboration with users, health care providers, and other stakeholders in diabetes care. This is a very ambitious but well-conceived and delineated project which takes into consideration most of the relevant factors that may influence AP implementation in T2D care.

Keywords

type 2 diabetes, artificial pancreas, closed loop, automated management, personalized medicine, at home care

Analysis

There has been a tremendous amount of progress in the field of artificial pancreas (AP) technology and AP platforms over the past several years. The first hybrid AP system (Medtronic MimiMed 670G) was granted marketing approval for the treatment of type 1 diabetes (T1D) in the United States in September 2016 and the European Union in June 2018 based on a safety study,[1-3] and a growing number of studies have demonstrated that home use of hybrid closed-loop insulin or bi-hormonal delivery systems reduce time spent in hypoglycemia and improve time in target ranges for those with T1D. A recent systematic review and meta-analysis shows that AP systems may be efficacious and safe for the treatment of people with T1D in outpatient settings.[4] However, only few studies have evaluated hybrid AP systems in people with type 2 diabetes (T2D) and most have been performed in a hospital setting rather than under normal living conditions.[5-7] Moreover, myriad barriers still exist to the widespread implementation and commercialization of AP systems in people with diabetes, including many unanswered questions about liability, reimbursement, and quality of life/psychosocial stress. Other factors such as perceived usability, acceptability, preference, and ultimately adherence/compliance to these multicomponent systems are also of great relevance. Indeed, the uptake and use of critical components of these systems such as continuous glucose monitors (CGM) by people withT1D is still quite low (<25% in Europe and in the United States).[8]

The article by Schliess and coauthors,[9] in which the European Automated Glu***c***ose Contro***l*** at H***o***me for People with Chronic Di***se***ase (CLOSE) initiative for the implementation of artificial pancreas (AP) systems for people with diabetes is described, is to be commended for its goals and a comprehensive/scalable approach. Specifically, the primary objective of the project is to develop scenarios for AP operation in those living with T2D with the goals of achieving a positive acceptance by users and caregivers and a high likelihood for reimbursement. To meet these objectives, the CLOSE initiative is integrating the AP platform into the

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center of a comprehensive product and service package (defined as "APplus") specifically tailored to defined T2D patient groups and care environments, thereby leading to an interactive collaboration with users, health care providers, and other stakeholders in diabetes care. Importantly, the consortium is leveraging organizations with key capabilities in health care service provision as well as in the clinical development of AP systems, and are complementing these with public-private partnerships with competencies in the fields of health care research, economic modeling, quality assurance, and performance monitoring, as well as in the conceptualization and implementation of training and education. Supported by the European Institute for Innovation and Technology (EIT), CLOSE is striving to achieve EIT's "knowledge triangle" of market-oriented research, education, and business creation, and considers itself the successor of the successful AP@Home Project.[10] This comprehensive and integrated approach is also in line with the recent ADA/EASD consensus guidelines recommending a highly interactive patient-centric approach for the glycemic management of T2D.[11] However, in that consensus document,[11] the use of open- and closed-loop glucose control technologies is only marginally considered due to lack of data to inform recommendations. Thus, the implementation of the CLOSE project and its results may inform future guidance regarding the viability of AP platforms for the management of diabetes in insulin-requiring T2D individuals.

Given the heterogeneity of T2D and the current move toward "personalized" medicine, the more generalized used of AP systems in people with T2D may also offer a valuable tool for advancing individualized and more precise treatment and treatment goals. However, widespread acceptance of AP systems in people with T2D will depend on the identification of subpopulations and care settings where the use of AP could significantly improve the risk- and cost-benefit balances of T2D management compared to the current standard of care. CLOSE intends to interrogate these factors and provide more clarity. Specifically, CLOSE will apply a "top-down" approach that will, in an integrated fashion, evaluate the impact of design options on AP manufacturing and maintenance costs, time-to-market, and user acceptance. Moreover, the consortium recognizes that the heterogeneity of the T2D population and their health care environments make it unlikely that a "one-size-fits-all" solution exists for T2D management. As such, the CLOSE platform is following a co-creative approach by developing APplus in the framework of the French homecare service provision, which operates a fully integrated chronic care platform involving patients, health professionals, payers, and prescribers. The concept of a scalable co-creation process using home care service provision as an initial "learning lab" described in the article is particularly interesting and appealing as the joint creation of the model may more clearly establish the real value of the intervention with AP platforms, emphasizing the role that people with T2D and their caregivers play in the process of constructing services/management in a precision medicine context that may suit a variety of preferences of groups and/or individuals. Moreover, this is a process that is adaptable/translatable to the care of other chronic noncommunicable diseases.

Importantly, CLOSE will also enrich the current state of AP use by adding obligatory training and education models. In addition, the consortium is implementing outcome predictors to identify those people with T2D who might benefit the most from AP use as well as health- and process-related performance indicators to evaluate the impact of AP use on the quality and effectiveness of diabetes care. This is extremely important as current research identifies different subpopulations/groups given the heterogeneity of the disease. An example of a group of special interest is adolescents with T2D where the management of the disease does not seem to alter the loss of beta-cell function.[12-14] As a result, many individuals in this age-group quickly transition to insulin therapy. Early use of AP platforms in this growing population of T2D with a high risk of early disability may demonstrate significant benefit.[15] Also, the potential use of AP platforms during the prediabetes phase could be considered.

A high-arching goal of CLOSE is to optimize the sustainability of health care AP implementation in T2D care by improving the interactions of the individual patient with the health care system, the health of the respective patient population, and the per capita health care costs, thereby making AP use attractive within the scope of pay-for-performance models. By adding capabilities to capture patient-reported outcomes and behavioral data, CLOSE has the potential to converge with other health innovations in chronic care delivery to contribute to a fully integrated personalized diabetes management (iPDM) system.

Overall, the conception and design of CLOSE is very valuable as the project addresses an understudied topic, and the article by Schliess and coauthors clearly depicts the goals of the consortium. Incorporating key stakeholders, education, and health impact in the center of the APplus platform is novel and may very well be what is needed to achieve the widespread use of AP systems in people with T2D. However, although CLOSE is defined as a Consortium, it is not clearly explained what centralized entity/entities would coordinate and oversee the variety of activities, stakeholder interactions, and data collection, management, and analyses derived from the application of the complex model proposed in this article and whether some kind of hierarchical structure among the collaborating partners would be in place in order to make this more efficient from an operational point of view. One question regarding this model is why not apply it first in the T1D population in which many of these platforms have been tested and where more information is typically requested by health care payers and policy makers to evaluate their real benefit and cost-effectiveness in the wider clinical population. That would include assessing how acceptable and feasible these platforms will be in a real-world setting, particularly taking into consideration the relative low uptake of some of the main components of the systems (eg, CGM

and pumps).[8] In addition, novel open-loop/semiautomated systems of diabetes management such as sensor-augmented pumps with low glucose suspend and new technologies for MDI treatment, such as smart pens in combination with CGMs, might be equally or more efficacious and cost-effective as AP systems in T2D. As such, testing these emerging systems in an APplus-like model may also be relevant to all the stakeholders and parallel the testing of more automated systems using AP platforms.

Disclaimer

The contents of this article represent the authors' views and do not constitute an official position of the National Institutes of Health or the United States Government.

Abbreviations

ADA, American Diabetes Association; AP, artificial pancreas; CGM, continuous glucose monitor; CLOSE, Automated Glucose Control at Home for People with Chronic Disease; EASD, European Association for the Study of Diabetes; EIT, European Institute for Innovation and Technology; iPDM, integrated personalized diabetes management; T1D, type 1 diabetes; T2D, type 2 diabetes.

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