Undergraduate Thesis Prospectus

Comprehensive meal record reconstruction and meal detection for patients with T1D

(technical research project in Biomedical Engineering)

Access to Diabetes Treatment: Survival of Low-Income T1D Patients

(STS research project)

by

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On my honor as a University student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments.

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General Research Problem

How may the quality of life for patients with type I diabetes be improved?

In 2015, 30.3 million people were diagnosed with diabetes, of whom 5% were diagnosed with type 1 diabetes (T1D). Type I diabetes is an autoimmune disorder in which beta cells in the pancreas are destroyed, impairing insulin production. Insulin brings glucose into cells from the blood stream; without adequate pancreatic function, glucose levels can fluctuate immensely, and can cause dangerous hyperglycemia or hypoglycemia. T1D patients constantly rely on insulin, insulin pumps, glucose level monitoring, and thorough medical care, indicating a need for improvement in all aspects.

Comprehensive meal record reconstruction and meal detection for patients with T1D

How can meal consumption be tracked and modeled in patients with type I diabetes?

Physicians need patients' meal records, but such records are often incomplete, either lacking in correct time stamps or missing meals altogether. A system that retrospectively reviews a patient's continued glucose monitoring (CGM) data and reconstructs the meal record would offer more complete data. An artificial pancreas (AP) system can counteract large spikes in glucose automatically, whereas currently the system is reliant on patient input to bolus properly. A meal detection algorithm that can operate in real time will help reduce the need of patient input into the AP system. I aim to accurately develop a retrospective meal record reconstruction system that identifies meal times and meal types, for later development into a real-time tool for meal detection. I am completing my capstone project alongside Saurav Pandey in the Biomedical Engineering Department under the advisement of Dr. Chiara Fabris Ph.D. at the Center for Diabetes Technology.

Meal Record Clinical Usage

In order for T1D patients to maintain proper nutrition, professional help is often recommended. Each nutrition plan should be customized to meet individuals' needs, which may require major lifestyle changes. This is typically with aid from registered dieticians and registered dietician nutritionists, as well as referrals to diabetes self-management education program. A robust retrospective meal record reconstruction system that details both the time of meal occurrence as well as meal content would be beneficial to each agent involved in the care management process. By providing relevant information to professionals aiding the T1D patients, they are enabled to adjust specific components of the nutrition plan to account for individualized patient responses (Gray & Threlkeld, 2000).

Meal Detection in the Artificial Pancreas

The artificial pancreas system strives to closely mimic the regulatory function of the pancreas in blood glucose management. In an idealized model, AP systems utilize closed-loop control, which enables the designed algorithm to automatically adjust insulin delivery based on continuous glucose monitoring (CGM) trends. (Forlenza et al., 2018) Due to limitations in design, current AP systems primarily utilize hybrid closed-loop systems, which require users to check glucose values at least twice daily to calibrate the CGM device (Allen and Gupta, 2019). Users of hybrid systems are able to self-dispense pre-meal boluses aided by inter-prandial insulin injections or manually indicate a meal flag while consuming food, enabling the controller system to adjust BG levels accordingly.

The transition from hybrid closed-loop systems to fully closed-loop systems is contingent on a well-tested meal detection tool. The consequences of unannounced meals being missed must certainly be considered as studies have shown missed bolus resulting in increased glycated hemoglobin (HbA1c) levels for patients. Higher levels of HbA1c has many long-term effects such as retinopathy, nephropathy, neuropathy, heart disease, and stroke, and highlights the need to reduce poor detection outcomes in instances of unannounced meals. (Bergenstal et al., 2016)

Various meal detection algorithms for AP systems have been proposed in order to accurately determine identify meals from CGM data (Samadi et al., 2017). Model predictive control algorithms attempt to predict glucose levels in the near future and attempt to adjust insulin delivery accordingly. Fuzzy logic algorithms determine insulin doses based on various parameters to mimic a clinician making real-time adjustments based on the CGM data (Allen & Gupta, 2019). These models have varying degree of successes, typically able to detect a meal with around a 90% level of accuracy. However, these models tend to fail in instances of small meals and often have high false positive rates, which would lead to insulin dosing despite no spikes in BG levels, which can lead to hypoglycemia. (Weaver & Hirsch, 2018)

Our project integrates these existing methods into our meal detection algorithm as well as new concepts such as a voting scheme algorithm that depends on monitoring the rate of change in glucose levels and utilizing first and second derivative curves to reach the decision of whether a meal has occurred (Dassau, Bequette, Buckingham, & Doyle, 2008). Preliminary studies seem promising with a meal detection accuracy of about 75 percent. Further tweaking the currently designed algorithm in conjunction with novel filtering techniques will hopefully increase the model’s ability to accurately predict meal occurrence. Combining these meal detection techniques alongside meal content analysis will provide a robust framework will eventually pave the way for a fully closed-loop AP system.

Modeling Glucose Appearance During a Meal

Modeling the glucose appearance in the bloodstream following a meal can be completed using various different models that mimics different elements of physiological processes. The model selected for our study is known as the double triangular minimal model (dTMM), which contains nine equations to model glucose appearance in the bloodstream following a glucose input through consumption of a meal. This model is based on the classic glucose kinetics model, which is used to determine the rate of glucose disappearance in the bloodstream following a glucose input, using insulin over time as an input. Optimized parameters from this model can be used to quantify an insulin sensitivity parameter that is specific to each individual (Dalla Man, Rizza, & Cobelli, 2007). Model parameters can also be compared with the meal's content to establish overall trends and correlations between them. This is especially crucial given that meal content studies are only now beginning to relate glycemic index (GI), fat, and protein to glucose appearance and insulin actions for each meal type. (Bell et al., 2015) However, no other study has been performed successfully to our knowledge using to model parameters in order to identify meal content and meal type when provided with only glucose, time, and insulin data for a meal.

Access to Diabetes Treatment: Survival of Low-Income T1D Patients

How do diabetics in low-income communities manage despite deficient clinical care and rising treatment costs?

According to the American Diabetes Association, diabetes-afflicted patients in 2017 "incur[red] average medical expenditures of ~$16,750 per year, of which ~$9,600 [was] attributed to diabetes" (ADA, 2018). In 2016, individuals with type I diabetes spent approximately $5,705 on insulin alone due to rising insulin prices (Biniek & Johnson, 2019).

Rising medical costs are prohibitive, especially in developing communities and low-income households. According to the Canadian National Diabetes Surveillance System (CNDSS), low-income people have a higher rate of diabetes prevalence. (Rabi et al., 2006) Diabetes is one of the leading risk factors of cardiovascular disease (CVD), along with smoking, hypertension, and elevated cholesterol levels. Diabetes is highest among individuals whose income is at or below the poverty line (Odutayo et al., 2017). Higher prevalence of diabetes in low income communities indicates poor communities warrant greater attention due to large income disparities in healthcare.

The Diabetes Patient Advocacy Coalition (DPAC) is an advocacy striving to increase "affordable access to all medications, devices, and services to ensure healthy daily diabetes management." DPAC calls for lower insurance and out-of-pocket expenses for patients with T1D. It also funds a variety of programs to alleviate the financial burden of diabetes on families, such as the Affordable Insulin Project, which provides a plethora of resources for T1D families can use to access insurance coverage for insulin (DPAC, n.d.). This coalition works with the Congressional Diabetes Caucus (CDC), led by Diana DeGette, Democrat from Colorado, and Tom Reed, Republican from New York. The bipartisan effort aims to reduce the cost of diabetes management by reducing the cost of insulin. The CDC proposes to increase price transparency, promote competition between insulin makers, develop patent reforms, and streamline the process of FDA approval for biosimilar insulins. Caucus leadership introduced the "Eliminating Disparities in Diabetes Prevention, Access, and Care Act" to increase research on diabetes in minority communities and increase federal efforts to address disparities in minority populations with respect to minimizing the growth of this disease. (Congressional Diabetes Caucus, n.d.) Federal initiatives such as legislature introduced by the CDC have the potential to bring about effective change and make a positive impact on the T1D community as a whole. Shortcomings of related legislature can be identified through further research on the execution of these federal initiatives as well as research on opponents of this caucus.

Vest et al. 2013 investigated diabetes management in high-poverty settings, finding inadequate insurance and mistrust of the medical system impedes self-management of diabetes. The Diabetes Technology Society (DTS) is a nonprofit organization striving to deploy technology in the fight against T1D. DTS does not favor controlling of patient expenses and does not work to improve access to low-income communities (Society, n.d.). Centers that conduct clinical trials incentivize studies by offering high-end technology to diabetic patients through the study's duration, offering only temporary relief. For instance, a clinical trial Trial Net was conducted on young children to screen for them antibodies that "help predict whether their immune system has begun to recognize the pancreas as foreign." (Madhusoodanan, 2019). Children whose parents are diabetic have a higher genetic risk of developing T1D, so these family used this trial as a preventative measure. However, the National Institute of Diabetes and Digestive and Kidney Diseases scaled back support for Trialnet, even though many parents relied on it. Families that substitute clinical trials for expensive proper clinical care, especially in low-income communities, suffer when the study is no longer active or available.

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