The Relationship between Diabetes Self-Management and Individual and Family Factors with Glycemic Outcomes in Adolescents with Type 1 Diabetes

by
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Dedication

My Parents

For your sacrifice and giving up the comfort of your motherland that I may have the

opportunity to dream and be who I am today.

My Husband, Steve

You were there for me from day one of this journey towards my dissertation.

This dissertation literally would not have been possible without your support and encouragement!

I love you and I am so grateful to have you as my partner.

My Baby, Claire

You are the reason why I get up each day to work hard, so that I can be someone you will be proud of.

I love you more than you will ever know!

Lastly,

The enclosed dissertation chapters are dedicated to all the patients with T1D and their families!

This work would not have been possible without your altruism! Thank you!

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with Glycemic Outcomes in Adolescents with Type 1 Diabetes

Hyojin Jennifer Min

Abstract

Type 1 diabetes (T1D) is one of the most common pediatric chronic conditions, where the risk of developing future complications is closely related to the tight surveillance of daily glycemic control. The majority of adolescents with T1D are unable to meet the target glycemic outcomes.

In this cross-sectional study, adolescents with T1D and one caregiver were recruited from telehealth visits at a tertiary, multidisciplinary pediatric diabetes center to complete a self-report survey. Factors included in the self-report surveys include diabetes self-management, diabetes technology use, diabetes distress, parenting stress, and family functioning from the individual and family domains. Age, gender, BMI, insurance type, daily insulin dose, insulin regimen, and A1C were collected by medical chart review. Continuous glucose monitor (CGM) data were collected from device software. Univariate and multivariable regression models were conducted for association with outcomes of interest.

The variables in the family domain, particularly the parent diabetes-related distress, is a crucial, modifiable factor associated with the adolescent's glycemic outcome. There is also an association between parent's diabetes-related distress and the adolescent's diabetes technology satisfaction. In summary, high satisfaction of diabetes technology by the adolescent was associated with lower level of diabetes related distress among parents, which was ultimately

associated with optimal glycemic outcome, as evidenced by hemoglobin A1C (A1C) and higher time in range (TIR).

The relationship between diabetes self-management, and individual and family factors with glycemic outcomes is complex. Future higher-powered studies are needed to include all four domains (individual, family, community, and health care systems), particularly variables in the family domain should be targeted to design interventions optimizing glycemic control of adolescents with T1D. Lastly, disparity in diabetes technology use should be explored.

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CHAPTER ONE

Introduction to the Problem

Type 1 diabetes (T1D) prevalence and incidence are on the rise globally.[1] T1D affects about 1.9 million people in the United States (U.S.), where 244,000 cases are children and adolescents.[2] Researchers have also predicted that the number of T1D cases in pediatric population will increase to 600,000 by 2050.[3] Optimal glycemic outcomes in adolescence, particularly in mid-adolescence, have been a challenge, and the majority of the youths with T1D had hemoglobin A1c (A1C) values above the recommended target level.[4] T1D management for children and youth is time-consuming, requiring never-ending monitoring of blood glucose (BG) levels in order to remain in the optimal glucose range.[5] The recent advancement of diabetes technologies has provided better glycemic control outcomes and quality of life,. However, these technologies have become more complex with the advent of the hybrid closed loop technology.[6]

Theoretical Framework

The theoretical framework for this dissertation is based on the Pediatric Self-Management Model (PSMM).[7] PSMM is a comprehensive model comprised of the individual, family, community, and the health care system domains, each with modifiable and non-modifiable variables ultimately impacting self-management behavior through cognitive, emotional, and social processes.   Ongoing self-management is an essential component of T1D glycemic control. The model highlights the importance of taking into the consideration a whole-person approach when analyzing variables associated with an outcome or for designing interventions and proposing a policy change.

Dissertation Outline

This dissertation is organized into three papers aiming to expand upon the knowledge of variables in the individual, family, community and health care systems domains and their association to glycemic outcomes in adolescents with T1D. It also aims to understand the underlying relationship between glycemic outcomes and variables in the PSMM domains and diabetes technology for adolescents with T1D.

Paper One: A Systematic Review of Pump Discontinuation in Pediatric Patients with T1D

The purpose of this systematic review:

1) To describe the frequency of insulin pump discontinuation amongst pediatric patients with T1D in the past two decades.

2) To systematically categorize modifiable and non-modifiable variables reported by the studies included in the review according to the PSMM.

2) To summarize the findings of variables associated with insulin pump discontinuation.

Paper Two: Diabetes-Related Distress for Parents and its Association to Glycemic Outcome in Adolescents with Type 1 Diabetes

The purpose of this study:

1) To perform a theory-based analysis to determine the factors associated with individual and family domains with glycemic outcomes (A1C and CGM sensor data TIR from 70-180 mg/dL) in adolescents with T1D.

2) To compare and contrast the multivariable models associated with A1C and TIR.

Paper Three: Diabetes Technology Use and Its Relationship with Parental Stress in Caring for Adolescents with Type 1 Diabetes

The purpose of this study:

1) To determine the factors associated with diabetes-related distress in parents caring for adolescents with T1D.

2) To describe diabetes-related distress in parents as it related to diabetes technology use.

Study Objectives

Measure for Effective Control of Blood Sugar

Pediatric Self-Management (PSMM) Framework

Augmented Ability to Monitor & Respond

Glycemic Outcomes

Individual | Family

Community | Healthcare System

Diabetes Technology

A1C*

Time in Range (TIR)
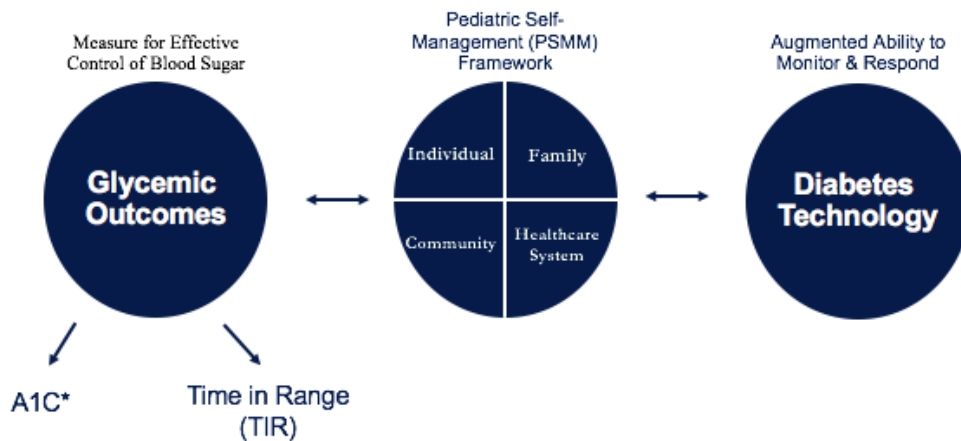
Understand the underlying relationship between glycemic outcomes and variables in Pediatric Self-management (PSMM) domains and diabetes technology for adolescents with T1D

* A1C measures the percentage of your red blood cells that have sugar-coated hemoglobin

Figure 1.1 Dissertation Study Objectives

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CHAPTER TWO

Systematic Review of Insulin Pump Discontinuation and Associated Factors in

Pediatric Patients with Type 1 Diabetes

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Abstract

Purpose: The purpose of this study is to ascertain the trend of insulin pump discontinuation amongst pediatric patients with type 1 diabetes (T1D), and to systematically assess factors that are associated with insulin pump discontinuation.

Methods: A systematic literature search was performed according to the 2009 PRISMA guidelines on five major electronic databases. Studies published after 2000 were included using the search terms 'type 1 diabetes', 'insulin pump', and 'discontinuation'. Covidence was used for screening full text for review. The Pediatric Self-Management Model (PSMM)[1, 2] was used as the theoretical framework to guide this systematic review.

Result: 82 articles were screened, and final 10 studies met the inclusion criteria to be analyzed. All but one of the studies were retrospective, observational studies using medical chart review. None of the studies reported conceptual or theoretical frameworks. Overall, there was a decreasing trend in insulin pump discontinuation amongst pediatric patients with TID. All studies examined variables in the individual domain, but there was a lack of studies exploring variables in the family, community, and health care systems domains. Higher hemoglobin A1C (A1C), older age, and female gender were frequently reported to be significantly associated with insulin pump discontinuation.

Conclusion: Insulin pump discontinuation in pediatric patients with T1D has declined in the past 20 years. A theory-guided prospective study including variables in the family, community, and health care system domains may help further elucidate variables associated with insulin pump discontinuation. Furthermore, the rapid innovation in the diabetes technology, including the use of continuous glucose monitors and the use of hybrid-closed loop systems must be considered for future studies.

Background

Approximately 1.25 million Americans live with type 1 diabetes mellitus (T1D), including about 200,000 pediatric patients who are less than 20 years of age.[3] Three-quarters of all people diagnosed with T1D are less than 18 years of age, making it one of the most common pediatric chronic conditions in the United States (U.S.).[4] The American Diabetes Association (ADA), and the International Society for Pediatric Adolescent Diabetes (ISPAD) recommend that pediatric patients under 19 years of age should aim for a hemoglobin A1C (A1C) value of less than 7.0 percent. [5] This goal A1C was recently lowered from 7.5% to 7.0% by the ADA based on a review paper showing elevated blood glucose levels associated with significant complications during child development, including abnormalities in the brain, the heart and the eyes[2]. This A1C goal is only met by one in five adolescents with T1D.[6] In addition, from 2002 to 2012, there was a significant linear increase in the prevalence of T1D in the pediatric population, with no clear etiology for this surge.[7] Moreover, the increase in disease burden is also disproportionately affecting youths from historically marginalized racial and ethnic backgrounds with T1D[7].

There are many studies demonstrating suboptimal glycemic control associated with physiological and psychological complications [2, 8-10]. Micro- and macro-vascular complications such as retinopathy, neuropathy or cardiovascular disease risks are associated with suboptimal glycemic outcomes.[11-13] Moreover, chronically elevated or widely fluctuating blood glucose levels, particularly in the developing brain in young children with T1D, may result in alterations in the white matter and cognitive ability.[14] Diabetes-related stress is described to be difficult, demanding, and never-ending, and often negatively impacts glycemic control[15, 16]. Maintaining optimal glycemic control is imperative in prevention of complications for pediatric patients living with T1D.

The landmark Diabetes Control and Complications Trial (DCCT) demonstrated that intensive insulin therapy administration reduced long term complications compared to a control group receiving conventional therapy.[10] Furthermore, in 2007, multiple academic societies released a consensus statement

stating insulin pump use in pediatric populations is associated with improved glycemic control and quality of life, and poses no greater, and possibly less, risk than multiple daily injections (MDI).[17] Finally, a systematic review and meta-analysis showed that CSII in the pediatric T1DM population was associated with small mean reduction in A1C, and decreased risk of severe hypoglycemia in comparison to MDI treatment.[18]

Diabetes Technology Progression

Since its inception in the 1960s, insulin pumps advanced tremendously, and have become readily acceptable as a preferred method of managing T1D in the pediatric population.[17] Current insulin pumps are more discreet in size, less fragile (water-resistant), and "smarter" than the older generations of insulin pumps with ability to calculate boluses and administer varying levels of basal or bolus insulin depending on the data received from the continuous glucose monitoring (CGM) system. The T1D Exchange (T1Dx) Clinic Registry in the U.S. is one of the most comprehensive clinic-based databases in the U.S. comprised of approximately 25,000 participants from 67 pediatric and adult endocrinology clinics.[19] According to this registry, continuous subcutaneous insulin infusion (CSII) or insulin pump uptake and usage did not vary across the different age groups, averaging about 60% of registry participants with T1DM.[20]

Selection of the optimal insulin delivery method can be a difficult decision, especially for newly diagnosed pediatric patients with T1D. Currently, prescription of insulin pump therapy for patients diagnosed with T1D is common for adolescents with adequate support and encouragement. The general acceptance of medical devices by adolescents and young adults may influence the wider use of insulin pump technology in youth with T1D.[21] Many adolescents with T1D incorporate diabetes technology for daily self-management. Many choose to deliver insulin or keep track of their glucose level to make real-time informed decisions by leveraging diabetes technology. For example, an insulin pump reduces the burden of giving multiple subcutaneous insulin injections per day. Moreover, the pump has helpful features to help calculate the correct dose of insulin bolus depending on carbohydrate consumption. CGM is a powerful tool which allows for accurate "sensor glucose" readings every 5 minutes. This real-time

reflection of glucose levels can inform the adolescent to self-manage accordingly in order to optimize time spent in target range. More recently, the advent of the hybrid closed-loop systems allows for the insulin pump to provide basal rate changes based on the CGM readings.

Current Gap

Even with the advent of novel diabetes technologies becoming more available for the pediatric population, there exists a subset of the patients who do not successfully adapt to diabetes technology use or who never initiate diabetes technology. There is a need for more evidence in the literature describing factors associated with the successful adoption or the lack of successful adoption of diabetes technology. Moreover, factors associated with discontinuation and sustained use must be explored.

Research Question

Our research question is, amongst (P) pediatric patients with T1D who are prescribed (I) insulin pumps as the primary treatment plan, (O) how often is insulin pump use discontinued? Additionally, what are characteristics associated with discontinuation of insulin pump use?

Review Aim

The aims of this systematic review are to 1) describe the frequency of insulin pump discontinuation amongst pediatric patients with T1D in the past two decades, and to 2) describe the characteristics associated with insulin pump discontinuation. The findings from this systematic review will provide directions for designing interventions to prevent insulin pump discontinuation in pediatric patients with T1D.

Methods

Search Strategy

PRISMA 2009 guidelines were used for this systematic review. In collaboration with a librarian, we developed individualized search strategies for five electronic databases: EMBASE, PubMed,

CINAHL, Web of Science, and the Cochrane Library (see Supplement 1). Prior to 1999, less than 10% of T1D pediatric patients were offered an insulin pump as a treatment option.[22] Therefore, studies published prior to January of 2000 were excluded. The search terms utilized were 'insulin pump', 'discontinuation', and 'type 1 diabetes'. The final search date was performed on February 15, 2021.

The inclusion criteria to be included for review were peer-reviewed journal articles published in English, between January 1, 2000, and February 15, 2021. Studies were included for review only if it reported insulin pump discontinuation as one of its quantitative outcomes. For example, qualitative studies without rate or frequency reporting were excluded. Studies were excluded if their sample was exclusively adult, and if only abstract or poster information were available.

Study Selection

The librarian and reviewer (H. M.) decided on the search terms based on exploring MeSH terms, as well as synonyms for the respective databases. Then two reviewers (H.M. and Y. F.) utilized Covidence©, an online software program designed to organize and streamline systematic review article selection process. Covidence© was endorsed as a standard production platform in production of systematic reviews per the Cochrane as of 2015. All studies passing the initial screening per the title were uploaded into Covidence© by one reviewer, at which point the software identified and removed duplicates. Abstracts were screened, and studies that were deemed ineligible due to irrelevance were further removed manually. If there were inconsistencies, both reviewers conducted a full article review, and came to a consensus decision.

Theoretical Framework

The Pediatric Self-Management Model (PSMM) was used as a framework to guide this systematic review and to determine domains examined in the studies reviewed (See Supplement 2). The PSMM is a conceptual framework developed to guide researchers and clinicians in developing evidence-based interventions to improve adherence in pediatric chronic disease management, and to inform health

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care policy processes that can improve the future of children living with chronic conditions.[1]   The PSMM

places emphasis on approaching the *individual* with the chronic condition with the *family*, the *community*,

as well as the *health care system* in mind. Each of the domains has dichotomized influences to be

modifiable or non-modifiable. The PSMM also stipulates that self-management behaviors manifest

through cognitive, emotional, and social processes.

Data Extraction

Data across the ten articles were organized into three tables including: 1) study characteristics, 2)

summary of discontinuation frequencies and associated variables, and 3) theory-based quality assessment.

The data extraction was performed by the first reviewer (H.M.) and verified by the second reviewer (Y.F).

The following data were extracted: 1) author, publication year, location, setting, research question or

aims, theoretical framework, study design, sample characteristics, data source, measurement methods, and

duration of follow-up; 2) summary of discontinuation frequency or rate, reported in a chronological

manner to demonstrate the trend according to time, and variables associated with discontinuation, and 3)

theory-based quality assessment of the studies.

The variables of interest were categorized by modifiable (e.g., knowledge level, anxiety, or

depression levels) versus non-modifiable variables (e.g., age, gender, SES, duration of diabetes, or

comorbidities). Studies were also evaluated in terms of how many of the four domains were explored as

part of the study. For instance, outcomes reported were categorized into one of four domains: 1)

individual, 2) family, 3) community, and 4) health care system.

Quality Assessment of Observational Studies

The Quality Assessment Tool for Systematic Reviews for Observational Studies (QATSO) Score

is a parsimonious tool consisting of four domains, with a total score of five.[23]   The score results are based

on each of the following domains: one-point for *external validity*, two-points for sufficient *reporting*

allowing for the consumer of the article to be able to come to an unbiased conclusion, one-point for

acknowledgement of bias present in the study, and another one-point for any attempts made to adjust for *confounding factors* in the analysis, for a total of five. The second domain "reporting" has the greatest weight of two-points, where all the other domains are designated with one-points each. Scores are transcribed into percentage by dividing the numerator study score by total score of five as the denominator. Scores greater than 67% are regarded "good" quality, 34%-66% are regarded "fair", and less than 33% are regarded "poor". [23]

*Result*s

The study selection process is illustrated in Figure 1 according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines[24]. The earliest publication year included in the final selection was from November 2006, even though we started the search year as of 2000. We initially identified a total of 148 abstracts to screen from across the five databases. Sixty-six studies were removed as duplicates. Eighty-two studies were screened by title and abstract, and forty-nine studies were removed as irrelevant. Thirty-three full-text articles were assessed for eligibility, and twenty-three studies were excluded. Irrelevant topics included adherence issues related to continuous glucose monitoring (CGM), T1D patients with co-morbidities, such as cystic fibrosis, pharmacodynamics of fast acting insulin, protocols on how to manage admitted inpatients on pumps, and temporarily removing the pump during sports or physical activities. Nine abstract or poster submissions to conferences were excluded, and three articles were not available in English language. Two articles were excluded for reported findings on adult population and two more articles were excluded for not having a quantitative outcome for insulin discontinuation. Ultimately, a total of ten articles were included in the final analysis.[25-33]

Study Characteristics

Table 2.1 summarizes the characteristics of the ten articles. The included studies were published between November of 2006 and May 2020. Seven different countries were represented in the final

selection of studies including: Germany, Austria, Israel, Italy, Canada, South Korea, and the U.S., though

four out of ten studies were studies from the U.S. All but one of the studies were retrospective,

observational studies, using medical chart or data base review for secondary analysis. The sample size

ranged from 46 from a single children's hospital in Milwaukee, Wisconsin to 11,710 from a multinational

data base, Diabetes Patienten Verlausdokumentation (DPV), in Germany and Austria, established in

1990s.[34] Objective measurements relating to diabetes management most often included A1C, frequency of

self-monitoring of blood glucose (SMBG), anthropomorphic measurements, and insulin requirements.

Since the data were limited to retrospective, secondary analysis, subjective measures relied on medical

chart documentations of reasons for starting or stopping insulin pump use by the provider. The single

prospective cohort study utilized Pediatric Quality of Life Inventory (PedsQL), and Children's

Depression Inventory (CDI) as variables of interest to investigate insulin pump discontinuation. The

duration of follow-up to capture insulin pump discontinuation ranged on from one year to seven years.

Lastly, none of the studies reported theoretical or conceptual framework as part of the study design.

Insulin Pump Discontinuation

Table 2.2 summarizes the reported outcomes of insulin pump discontinuation chronologically in

percentage (except for one study reporting as person per year rate). It also summarizes the variables

reported to be statistically significant ($p<0.05$) in its association with insulin pump discontinuation.

Overall, there is a decrease in the reported percentages of insulin pump discontinuation, from of 18.0% in

2006 to 4.2% (0.42/100 person-yr) by the year 2017. The last study from South Korea is an outlier,

reporting ten out of fifty-four patients discontinuing insulin pump, resulting in 18.5%. To note, the South

Korea is the only Asian country represented in this study. The four studies conducted in the U.S.

demonstrate a linear decrease over time from 18% in Boston from 2006, 15% in Milwaukee from 2009,

6% in Cincinnati from 2016, and 3% from the multisite study in 2016. The outcome variables reported

were grouped as clinical (e.g., A1C, SMBG or duration of T1D) or demographic (e.g., gender, age, or

parental supervision).

The most frequently reported factor associated with insulin pump discontinuation was less optimal diabetes management, as defined by higher A1C either at the pump initiation, or worsening during the follow-up period, and less frequent SMBG in comparison to those who remained on insulin pump therapy.[25-29, 31, 33] Female gender[25-28, 30, 33], and adolescence [25, 27-30], or older age at time of insulin pump initiation were reported to be associated with discontinuation.

Sub-optimal A1C at the time of follow-up (e.g. 1 year) was associated with insulin pump discontinuation (Wood: $8.6\% \pm 1.3\%$ $vs.$ 8.0% $\pm$ $1.3\%, p = 0.04$ and Babar: $8.6\% \pm 0.7\%$ vs $7.6\% \pm 0.7\%, p < 0.0001$).[25, 26] Similarly, de Vries and Wong reported elevated A1C at the time of insulin pump initiation as a potential risk factor related to insulin pump discontinuation (de Vries: $8.6\% \pm 1.27\%$ vs $8.1\% \pm 1.04\%, p = 0.02$) and Wong: $9.5\% \pm 1.4\%$ vs $8.4\$ \pm 1.4\%, p = 0.0005$).[28, 31, 33] Hofer suggested insulin pump use without reduction in A1C may also be a predictor of pump discontinuation (8.41% vs $9.3\%,$), but no p-values were reported.[27]

Five studies reported female pediatric patients with T1D were more likely to discontinue insulin pump (female vs. male: 90% vs. $67\%, p = 0.02$; 71.4% vs $58.9\%, p < 0.0001$; 75% vs $46\%, p = 0.001$; 65% vs. $55\%, p = 0.017$; 88.9% vs. 48.2%, p=0.02, respectively).[25, 26, 28, 30, 33] Older age at diagnosis (8.2 ± 3.2 $vs.$ 6.7 ± 3.5 $years$ of age at $diagnosis, p = 0.04$) were found to be related to insulin pump discontinuation.[25] De Vries reported that patients who were greater than 10 years of age at pump initiation were more likely to discontinue insulin pump use as compared to those younger than 10 years of age (OR =2.55, $p = 0.03$)[28], and similarly Lombardo reported older age at pump initiation related to higher chances of insulin pump discontinuation (12.1 ± 3.2 $years$ at $pump$ $initiation$ vs $10.3 \pm 3.8, p = 0.0001$).[29] Lee also reported similar findings in that patients who stopped using insulin pump were more likely older (≥ 10 years of age; 100% vs. 63.6%, p =0.024) and have longer diabetes duration (≥ 2 years; 100% vs. 54.5%, P=0.020) when compared to those who remained on insulin pump therapy. Lastly, age at insulin pump discontinuation was older and closer to adolescence or puberty compared to pre-pubescent patients with T1D (14.7 ± 5.3 $vs.$ $13.0 \pm 6.1, p = 0.001$).[30]

Variables Associated with Insulin Pump Discontinuation based on PSMM

Table 2.3 shows variables associated with insulin pump discontinuation categorized according to the Pediatric Self-Management Model (PSMM).[1] The insulin pump durability is ultimately related to the daily self-management tasks and influenced by variables from the four domains (individual, family, community, and health care systems). The four domains are further categorized into modifiable versus non-modifiable variables. Examples of non-modifiable individual variables are age, duration of T1D, pubertal staging, and other comorbidities.[25-33] Alternatively, examples of modifiable individual variables are A1C, frequency of SMBG and BMI. There was only one study which reported the non-physiological clinical factor of depression, as measured by the Children's Depression Index (CDI).[33]

The extracted data across the ten articles were categorized according to the PSMM. The overwhelming majority of the variables were categorized into the individual domain. There was paucity of variables reported overall in the family, community and health care system domains. Studies published after 2016 included few non-modifiable variables such as the primary caretaker's educational level, family status, and household income.[31-33] Significantly higher proportions of T1D patients from a single parent families (29% vs 4%, $p = 0.0002$)[25], and with less than high school/GED parental education level (4% vs 2%, $p = 0.02$)[33] were found to discontinue pump use. None of the studies reported on modifiable variables in the family domain, such as parental stress level, or level of parental knowledge in daily management with hyper-or hypoglycemia. The least number of overall variables reported was in the community domain. One study looked at whether or not the patient was keeping his or her T1D diagnosis a secret from peers[28], and another explored at the rurality index, in which those patients seen at a small community center demonstrated higher risk for pump discontinuation (HR=2.23, $p = 0.036$).[32] Lastly, in the health care systems domain, the presence of multi-disciplinary team screening prior to initiating pump therapy[26], and a greater number of clinic visits per year ($3.4 \pm 1, vs\ 4.4 \pm 1.0, p = 0.004$),[28] were found to be related to lower rates of insulin pump discontinuation. In the non-modifiable health care systems

domain, any change in insurance status in general (8% vs 2%, p=0.008) was related to higher insulin pump discontinuation.[31]

Quality Assessment According to QATSO Scores

The Qualitative Assessment Tool for Systematic Review of Observational Studies (QATSO) scores ranged from "fair" to "good", with which four of the studies scored 3/5 [27, 29, 30], five of the studies scored 4/5 [25, 26, 28, 31, 32], and just one study scored 5/5.[33] Table 2.4 summarizes and tabulates the results of the quality assessment according to the five items: external validity, reporting, bias, and confounding. The single prospective, observational cohort study scored 5/5, and the rest of the studies were all retrospective observational studies. The criteria for external validity or generalizability of the findings were all systematically done, and majority of the studies utilized a medical chart review, without solely relying on a self-reported measure. Moreover, the majority of the studies were descriptive in nature, which meant confounding variables had to be adjusted for in a non-a priori manner.

Discussions

We systematically reviewed and synthesized the modifiable and non-modifiable variables related to insulin pump discontinuation in pediatric patients with T1D from 2000 to 2020 based on PSMM. To the best of our knowledge, this is the first systematic review to investigate insulin pump discontinuation and its related factors. One of the major findings was a generalized pattern of decrease in insulin pump discontinuation among the pediatric T1D population since 2000. This pattern may be due to the technological advancement of the insulin devices leading to more optimal glycemic control, and improvements on usability of the devices compared to the MDI.[35] A historical account of insulin pump milestones in the U.S. is highlighted in Supplement 3. A major advantage of insulin pumps over MDI includes a reduced number of needle sticks, ability to deliver more accurate and precise amounts of insulin, and the ability to adjust continuous (basal) insulin delivery throughout the day, leading to fewer episodes of extreme highs or lows of blood glucose levels.[36, 37] Alternatively, disadvantages of using

insulin pumps are associated with higher risk of DKA from infusion set failures[38], and higher financial cost of supplies[39], and requirement of having a medical device attached to one's body, which may serve as a constant reminder of living with T1D. Additional potential factors related to the decline in insulin pump discontinuation may be attributed to an increase in the health care providers' growing experience and knowledge of management of T1D using new technology, and the increase in availability of educational resources designed to help health care providers manage insulin pumps.[40]

Our analysis highlights that suboptimal A1C at the time of insulin pump initiation, or at the time of follow-up is associated with insulin pump discontinuation.[25, 26, 28, 33] This means those with less optimal glycemic control, who would benefit most from remaining on insulin pump therapy, are most likely the ones failing to remain on it. From this analysis, it is unclear whether the insulin pump discontinuation precedes an increase in A1C or vice versa.

There is a growing body of evidence in support of the efficacy of insulin pumps over MDI in improving A1C in children with T1D, hence decreasing the risk of future complications related to diabetes.[41] Moreover, insulin pump use is related to fewer severe hypoglycemic episodes, and potential improvement in quality of life.[41-43] However, it is difficult to fully comprehend the reasons behind insulin pump discontinuation from a retrospective medical chart review alone. Future studies with emphasis on the qualitative user experience are necessary to draw a conclusion about the relationship between insulin pump discontinuation and A1C.

We also found that girls were more likely to discontinue insulin pumps as compared to boys, and older age closer to adolescence, at T1D diagnosis or age of insulin pump initiation was also related to pump discontinuation.[25, 26, 28, 30, 33] Adolescence is marked by the struggle in developing sense of self-identity, and friends and peers becoming a major priority in one's life.[44] Embarrassment related to diabetes management, and potentially negative perception of self by others are common are significant psychosocial and emotional barriers mentioned by several authors included in this review. Furthermore, adolescents in puberty undergo tremendous biological changes, which may impact young women more

17

than men. In a systematic review and meta-analysis of self-esteem levels in Western cultures, women's self-esteem levels were significantly lower than those in male participants, and the gender difference was greatest in the middle adolescence.[45] The close relationship between one's perception of body image and self-esteem can then have a direct impact on diabetes relates self-management behaviors, including the ability to maintain insulin pump therapy. Insulin pumps are difficult to keep discreet and can become a source of perceived negative stigma, which may discourage use disproportionately in the adolescent female patients.

The nature of the T1D management is an intricate and constant demand to perform daily tasks in order to maintain optimal glycemic control, and can create an enormous amount of emotional and psychological stress and burden.[43, 46] Self-management behaviors are crucial maintaining optimal glycemic control in T1D. However, our systematic review found that although all of the studies examined modifiable and non-modifiable variables in the individual domain in the PSMM, there was a lack of variables explored in the family, community, and health care system domains. While the ability to perform and keep track of the daily self-management behaviors on the individual level is critical for successful T1D management, the ability to carry out self-management behaviors is heavily influenced by family, friends, the surrounding environment, and health care access. Identifying variables in these domains beyond the individual as risk factors for insulin pump use and discontinuation is important to target as novel interventions for future studies.

Study Limitation

Several limitations need to be acknowledged. First, there are major study design differences among the included studies. For example, while some studies used large registry data bases, such as the DPV and T1Dx, some were based solely on medical chart review. The studies also had a wide range of follow-up durations in years. There is also heterogeneity amongst the different medical centers, especially when considering centers in different countries. The support offered to patients, and the level

of service available by the medical team are not reported in detail in these studies. In addition, only studies published in English that targeted pediatric patients with T1D were included in this systematic review. Therefore, the findings of this systematic review cannot be generalized to adults and non-selected geographical regions included in the review due to the different health care systems. Because all but one of the studies included in the review are retrospective observational studies using medical chart reviews, any causal inferences cannot be established. Lastly, the actual prevalence of insulin pump discontinuation in the pediatric population could be greater than the findings of this review since the studies do not include those patients who never got a chance to be started on an insulin pump. Lost to follow-up or uninsured children might not be fully represented.

Conclusions

Rates of insulin pump discontinuation are declining due to the improvement of diabetes technology augmenting T1D management. In most studies, only variables in the individual domain were examined. In the pediatric T1D population, those with less optimal A1C, older age, and female gender discontinued insulin pump use and reverted back to MDI. The findings from this study emphasize the need for clinicians and researchers to be aware of the potential that those who start using insulin pumps with poor glycemic control, with longer T1D duration, who are female, and who are entering mid to late adolescence, are at increased risk of discontinuing insulin pump therapy. A theory-guided study design with a comprehensive approach including measures in not only at the individual level, but at the family, community, and health care system levels may help improve insulin pump discontinuation in the high-risk population.

Table 2.1 Study Characteristics

	Authors, Publication year, Location, # of sites if applicable	Research Aim/ Question[1]	Study Design	Sample Characteristics		Eligibility Criteria	Data Sources	Measurement		Duration of Follow Up
				Overall Sample Size	Mean Age (SD)/ Range			Glycaemia Related (Objective)	Barriers (Subjective)	
1	Wood et al., 2006 Boston, MA, USA	-To examine reasons, and rate of pump discontinuation. -To identify characteristics of those who remain on pumps	Retrospective observational study	n=161	Mean age: 14±3.7 Range: 3.7-21.7	Youth with T1D less than 18 y/o, who began pump therapy between January 1st, 1998 to December 31st, 2001	Medical chart review	-HbA1c -# of SMBG3 -Height -Weight -BMI -Tanner Staging	-Reasons for starting pump -Reasons for discontinuation -Insulin regimen at discontinuation, and at most recent visit	Average of 3.8±1.1 yrs Range: 0.6-8.8 yrs
2	Babar et al., 2009 Milwaukee, WI, USA	To assess predictors associated with nonadherence to insulin pump therapy	Retrospective observational study	n=46	Mean age: 9.9±3.4 Range: Not specified	Pediatric patients with T1D, who initiated insulin pump therapy between July 1999 to June 2003	-Medical chart review	-HbA1c -BMI -Daily insulin requirement -Bolus: Basal ratio -# of SMBG -Pubertal status -Adverse events4 -Lipohypertrophy	-Diabetes pump readiness screening form -Reasons for starting pump	2-7 years
3	Hofer et al., 2010 Austria and Germany (Multi-site), 202 pediatric sites	To characterize those who discontinue pump therapy from different pediatric age groups	Retrospective observational study	n=11,710	Mean age: 19.2, no SD reported Range: Not specified	Patients with T1D < 20 y/o documented as pump users since 1995	-Medical chart review of electronic diabetes documentation database (DPV)	-HbA1c -BMI -Time on pump	-Reasons for starting pump	Not specified
4	deVries et al., 2011 Tel Aviv, Israel	To study the rate and predictors of insulin pump discontinuation	Retrospective observational study	n=530	Mean age: 15.2±6.3 Range: 3.5-24	Pediatric patients with T1D who started pump between January 2000 to December 2008	-Medical chart review	-HbA1c -BMI -# of SMBG -Pubertal stages -Adverse events -Daily insulin requirement -T1D duration -Pump model -Family history of T1D	-Reasons for starting pump -Reasons for stopping pump	-3 days to 5 years in duration -Mean f/u time was 5.6±1.6yr
5	Lombardo et al., 2011 Messina, Italy (Multi-site), 28 sites	To evaluate discontinuation rate of insulin pump and its related factors	Retrospective observational study	n=985	Non-DIscont. Mean Age: 10.3±3.8 Range: 0.4-17.7 Discont. Mean Age: 12.1±3.2 Range: 6.4-15.8	Pediatric patients with T1D < 18 y/o, who completed the survey from December 1998 to December 2007 identified as pump users	-Medical chart review -Survey taken during 9-yr period (December 1998-December 2007)	-HbA1c -DM duration -Type of insulin therapy -Daily insulin requirement -Age at pump initiation -Age at pump discontinuation -Height -Weight -BMI -Adverse events	-Reason for stopping pump when possible	Baseline, yr1, yr4

	Authors, Publication year, Location, of sites if applicable	Research Aim/ Question[1]	Study Design	Overall Sample	Mean Age (SD)/ Range	Eligibility Criteria	Data Source	Objective	Subjective	Duration of Follow Up
6	Kostev et al., 2014 Frankfurt, Germany (Multi-site)	To identify characteristics of patients who discontinue insulin pump therapy	Retrospective observational study	n=2,452	Non-DIscont. Mean Age:: 13.0±6.1 Discont. Mean Age:: 14.7±5.3 Range: Not specified	Patients with T1D < 25y/o who received prescription for pump from 2009 to 2010	-Review of nationwide database covering prescriptions of insulin pumps	-Insulin pump prescription -Insulin or needle prescription -Daily insulin requirement -No HbA1c, BMI	-None	1-yr follow up
7	Wong et al., 2016 Cincinnati, OH, USA	To examine relationship between depressive symptoms and method of insulin delivery	Prospective, observational cohort study	n=95	Mean age: 15.4±1.4 Range: Not specified	Pediatric patients with T1D, 13-18 y/o	-Medical chart review	-HbA1c -# of SMBG	-Pediatric Quality of Life Index (PedsQL) -Children's Depression Inventory (CDI)	2yr f/u
8	Wong et al., 2016 Multisite, USA	To provide participant reported reasons for stopping pump therapy	Retrospective analysis of longitudinal cohort study	n=8,935 <6, n=322 6 to <13, n=2,542 13 to <18, n=2,173 18 to <26, n=1,145 >26, n=2,752	Mean age: 23.3±17.4 Range: Not specified	Patients with T1D 2-26 y/o enrolled in T1DX Registry between September 2010 – July 2012	-Secondary data analysis of T1DX database	-HbA1c -Adverse events	-None	1 yr f/u
9	Shulman et al., 2017 Ontario, Canada, 33 sites	To describe insulin pump use	Observational cohort study	n=3,193	Age group: -< 6y/o -6-13y/o ->13y/o Mean/ Range: not specified	Youth with T1D < 19 y/o who received pump funding from 2006 to 2013 according to Ontario Pediatric Diabetes Network	-Health administrative database review	-HbA1c -Adverse events	-None	f/u from 2012, 5 yrs
10	Lee et al., 2020 Seoul, South Korea	Investigate durability and effectiveness of insulin pump therapy among Korean pediatric T1D patients	Retrospective, Medical chart review	n=54	Mean Age: 7.4 y/o Range: 1.1-14.1 y/o	Initiated insulin pump between Aug 2016 – Nov 2019	-Medical chart review	-Anthropometric (Height, Weight, BMI, Tanner Staging) -HbA1c -DM Duration -Age at Pump Initiation -Health Insurance Type	-Reasons for stopping pump	3 yrs and 4 months

1. Theoretical frameworks were not reported in the above studies.
2. HbA1c = hemoglobin A1c
3. SMBG = self-monitoring of blood glucose
4. Adverse events = episodes of severe hypoglycemia or diabetic ketoacidosis (DKA)

	Authors, Publication year, Location	Discontinuation Frequency or Rate (% / person-year)		Glycemic Outcomes Associated with Discontinuation	Non-Glycemic Outcomes Associated with Discontinuation
		Author Reported	Actual Numbers		
1	Wood et al., 2006 Boston, MA, USA	18%	(29/161)	-**Monitor BG less** often at both baseline (3.6±0.6 vs. 4.1±1.3, $P = 0.002$), and yr-1 (4.0±1.2 vs. 4.7±1.7, $P = 0.05$ -**Worsening HbA1c** by year-1 (8.6%±1.3% vs. 8.0%±1.3%, P=0.04), and at most recent clinic visit (9.4%±2% vs. 8.4%±1.2%, P=0.01) compared to those who remained on pump	-More commonly **female** (90 vs. 67%, P=0.02) -**Older** at age of diagnosis (8.2±3.2 vs. 6.7±3.5 yrs, P = 0.04) -Significantly higher proportion of **single parent family** (29 vs 4%, P=0.0002)
2	Babar et al., 2009 Milwaukee, WI, USA	15%	(7/46)	-**Worsening HbA1c** by yr-1 (7.6%±0.7% vs. 8.6%±0.7%, P<0.0001; hazard ratio, 3.9, 95% CI 1.49, 10.22, P =0.0001 -**Higher fasting BG** (160±37 vs. 219.2±49.1, $p < 0.002$), and episode of severe **lipohypertrophy** (1.2±0.7 vs. 2.21±0.9, $p < 0.002$) by yr-2	-More commonly **female** (71.4% vs. 58.9%, P<0.0001) - **Screening** by multi-disciplinary team prior to pump start results in lower discontinuation rates
3	Hofer et al., 2010 Austria and Germany	4.0%	(463/11,710)	-**Worsening A1c** when comparing baseline to end of pump (8.41% vs. 9.32% for 10-15 y/o, no P-values reported). -Pump use w/o success in HbA1c reduction is strong indicator of pump discontinuation	-Discontinuation frequency was highest in the **10-15 years** cohort (2%), and lowest in the <5 years cohort (0.1%). No p-values reported -**Girls** more often than boys (60.5% vs. 39.5%, no P-values reported) -**Decreasing parental supervision** during puberty -**Longer time on pump** related to less discontinuation. Patients on pump for more than 2-3yrs rarely discontinued pump
4	deVries et al., 2011 Tel Aviv, Israel	11.3%	(60/530)	-**Higher A1c at pump initiation** (8.1%±1.04% vs. 8.6%±1.27%, P=0.02) -**Higher A1c at the most recent visit** (7.6%±1.0% vs. 8.8%±1.8%, P<0.001, OR=1.52) -Higher proportion of v**ery poorly controlled patients,** indicated HbA1c >10% was higher (25% vs. 4%, p<0.001)	-**Inadequate control/compliance** such as DKA, worsening of HbA1c, missed insulin dosing (35%) -Psychological issues such as **body image concerns** (31%) -**Technical issues** such as recurrent catheter obstruction, insulin infusion site failures, technical difficulty (25%) -**Incongruent lifestyle** such as competitive sport (8%) -**More females** (75% vs. 46%, p=0.001, OR=3.54) -**Age at pump initiation** was > 10 y/o (94% vs. 80%, p=0.03, OR=2.55) -**Higher number of visits**/yr (3.4±1 vs. 4.4±2.1, p=0.004)

Table 2.2 Insulin Pump Discontinuation Trends in Pediatric T1D Population and Associated Factors

	Authors, Publication year, Location	Discontinuation Frequency or Rate (% / person-year)		Glycemic Outcomes associated with Discontinuation	Non-Glycemic Outcomes associated with Discontinuation
5	Lombardo et al., 2011 Messina, Italy	6.1%	(60/985)	-**Shorter DM duration** 8.6 ± 2.7 vs 10.2 ± 3.7) $p=0.0001$ -**Worsening A1c** over time at 6 months (8.5%±1.5% vs. 7.2%±1.1%, P=0.0001), at 12 months (8.5%±1.5% vs. 7.2%±1.1%, P=0.0001), at 18 months (8.6%±1.6% vs. 7.7%±1.3%, P=0.0001), and at 24 months (8.9%±1.9% vs. 7.4%±1.0%, P=0.0001)	-**Older age** at pump initiation $(12.1\pm3.2$ $vs.10.3\pm3.8, p=0.0001)$ -**Increasing age cohort, increase in frequency**: 0-6yrs, 1.2%; 7-11yrs, 3.1%; 12-18yrs, 8.8%, P=0.002 -Highest discontinuation **between yr1-yr2** (28.3%), then at 6-12months (25%), and over yr3 (18.3%).
6	Kostev et al., 2014 Frankfurt, Germany	7.2%	(177/2,452)	-**Not using Teflon** needles (steel needles reference, 70.6% vs. 80%, p=0.003) -Discontinuation lowest in < 6y/o cohort, since pump allows for more accurate insulin dosage delivery at lower doses	-**Older age** $(14.7\pm5.3$ $vs.13.0\pm6.1, p=0.001$ -**More Females** (65% vs. 55%, p=0.017) -Discontinuation lowest in < 6y/o cohort, since pump allows for more accurate insulin dosage delivery at lower doses -Taking **prescription medications**: thyroid (27.1%) antiepileptic (8.5%), antidepressant (7.9%), antihypertensive (13%), lipid-lowering agent (5.7%), all p-Values <0.001
7	Wong et al., 2016 Cincinnati, OH, USA	6.0%	(9/150)	-**Higher HbA1c** at baseline (9.5%±1.4% vs. 8.4%±1.4%, P=0.0005) -**Less BG checks** at baseline (3.8±1.5 vs. 4.6±1.8; $P=0.0004$) -Mean A1c was 1.38% higher for those who discontinued pump and resumed MDI (95% CI 0.68,2.08; p<0.001)	-**Every 10-point increase on CDI[2]** related to **0.39% increase in HbA1c** (95% CI 0.16, 0.61; p=0.001) -More **females** (88.9% vs. 48.2%; p=0.02)
8	Wong et al., 2016 Multisite (how many states, site), USA	3%	(240/8,935)	-**Higher HbA1c** at baseline for 6 to <13 y/o, and 13 to <18 y/o (p<=0.01) -Prior episodes of **DKA**, particularly in 13 to <18 y/o (p<0.001)	-**Change in insurance status** in 6-13y/o cohort (8% vs. 2%, P=0.008) -**Parental education level** with less than high school/GED education (4% vs 2%, P=0.03) -Majority reported issues with wearability (57%), feeling anxious (44%), poor glycemic control (30%), recommendation per provider (20%), not finding pump helpful (19%), and technical pump difficulty (19%).
9	Shulman et al., 2017 Ontario, Canada	0.42/100 person/yr	(51/3,193) 2%	-No statistical difference in HbA1c reported	-**Younger age** (6-13y/o) at pump initiation (compared to 13-19y/o), HR=0.31 (0.14,0.66; p=0.0024) -Seen at **small community center**, HR=2.24 (1.05,4.76; p=0.0360)
10	Lee et al., 2020 Seoul, South Korea	18.52%	(10/54) or 81.5% continued pump	-**Longer diabetes duration** at initiation of pump p<0.05	-**Older age at pump initiation** > 10 y/o p<0.05

Table 2.3 Variables Associated with Pump Discontinuation Organized According to Pediatric Self-Management Framework[1]

		Individual		Family		Community		Healthcare System	
		Modifiable	Non-Modifiable	Modifiable	Non-Modifiable	Modifiable	Non-Modifiable	Modifiable	Non-Modifiable
1	Wood et al., 2006 Boston, MA, USA	-Insulin requirement -Daily BGM frequency* -HbA1c* -BMI	-T1D Duration -Age -Sex* -Pubertal Stage	-NR[2]	-Single parent family	-NR	-NR	-NR	-NR
2	Babar et al., 2009 Milwaukee, WI, USA	-BMI -HbA1c* -Insulin requirement -Bolus:Basal ratio -Hypoglycemic episodes -Fasting BG* -Lipohypertrophy* -Pump start age	-Sex* -Pubertal Stage -T1D Duration	-NR	-NR	-NR	-NR	-Multi-disciplinary team screening	-NR
3	Hofer et al., 2010 Austria and Germany	-HbA1c* -Pump Usage Duration* -BMI	-Age* -Sex -T1D Duration	-NR	-NR	-NR	-NR	-NR	-NR
4	deVries et al., 2011 Tel Aviv, Israel	-Pump Usage Duration -BMI -HbA1c* -Insulin requirement -Daily BGM frequency -Episodes of hypoglycemia/week* -Episodes of DKA	-Sex* -Age* -T1D Duration -Pump start age -Pubertal stage	-NR	-NR	-Keeping diabetes secret	-NR	-Number of visits/yr*	-NR
5	Lombardo et al., 2011 Messina, Italy	-HbA1c -Insulin requirement -BMI -Episodes of hypoglycemia -Episodes of DKA	-Age* -T1D Duration*	-NR	-NR	-NR	-NR	-NR	-NR

		Individual		Family		Community		Healthcare System	
		Modifiable	Non-Modifiable	Modifiable	Non-Modifiable	Modifiable	Non-Modifiable	Modifiable	Non-Modifiable
6	Kostev et al., 2014 Frankfurt, Germany	-Type of needle* -Insulin requirement -Prescriptions*	-Age* -Sex	-NR	-NR	-NR	-NR	-NR	-NR
7	Wong et al., 2016 Cincinnati, OH, USA	-HbA1c* -Daily BGM frequency* -CDI*	-Age -Sex* -Ethnicity* -T1D Duration	-NR	-Education level of primary caregiver* -Family status*	-NR	-NR	-NR	-Insurance status*
8	Wong et al., 2016 Multisite (how many states, site), USA	-HbA1c* -Episodes of DKA* -BMI -Pump usage duration -Episodes of hypoglycemia -Daily BGM frequency	-Sex -Race/Ethnicity -T1D Duration -Pump manufacturer	-NR	-Education level of primary caregiver* -Household income*	-NR	-NR	-NR	-Insurance status*
9	Shulman et al., 2017 Ontario, Canada	-HbA1c -Episodes of DKA -T1D related hospital admissions/ ED visits	-Age* -Sex -T1D Duration -Other chronic comorbidities	-NR	Neighborhood income quartile*	-NR	-Rurality index	-NR	- Center type*
10	Lee et al., 2020 Seoul, South Korea	-HbA1c -BMI -Episodes of DKA	-Age -Sex -T1D Duration	-NR	-NR	-NR	-NR	-NR	-Insurance status

1) Pediatric Self-Management Framework by Modi et al.

	Table 2.4 Quality Assessment According to the QATSO[1]			
	Authors, Publication year, Location	**Study Design**	**Quality Assessment of the Study**	**Final Ratings**
1	Wood et al., 2006 Boston, MA, USA	Retrospective observational study	External Validity: 1 systematic sampling vs convenient sampling Reporting: 2 medical chart review vs self-report Bias: 1 Confounding: NA descriptive study	4/5 Good
2	Babar et al., 2009 Milwaukee, WI, USA	Retrospective observational study	External Validity:1 systematic sampling vs convenient sampling Reporting: 2 medical chart review vs self-report Bias: 1 Confounding: NA descriptive study	4/5 Good
3	Hofer et al., 2010 Austria and Germany (Multi-site)	Retrospective observational study	External Validity:1 systematic sampling vs convenient sampling Reporting: 1 electronic database of self-reports vs. medical chart review Bias: 0 Confounding: 1 adjusted for HbA1c values, and age	3/5 Fair
4	deVries et al., 2011 Tel Aviv, Israel	Retrospective observational study	External Validity:1 systematic sampling vs convenient sampling Reporting: 2 medical chart review vs self-report Bias: 1 Confounding: NA descriptive study	4/5 Good
5	Lombardo et al., 2011 Messina, Italy (Multi-site), 28 sites	Retrospective observational study	External Validity:1 systematic sampling vs convenient sampling Reporting: 1 prescription index Bias: 1 Confounding: NA descriptive study	3/5 Fair
6	Kostev et al., 2014 Frankfurt, Germany (Multi-site)	Retrospective observational study	External Validity: 0 convenient sampling Reporting: 2 medical chart review vs self-report Bias: 1 Confounding: NA descriptive study	3/5 Good
7	Wong et al., 2016 Cincinnati, OH, USA	Prospective, observational cohort study	External Validity: 1 systematic sampling Reporting: 1 self-report instruments, and medical chart review Bias: 1 Confounding: NA descriptive study	5/5 Good
8	Wong et al., 2016 Multisite, USA	Retrospective analysis of longitudinal cohort study	External Validity: 1 systematic sampling Reporting: 2 electronic database of self-reports vs. medical chart review Bias: 1 Confounding: 1 adjusted for HbA1c, age, duration of diagnoses etc	4/5 Good
9	Shulman et al., 2017 Ontario, Canada	Observational cohort study	External Validity: 1 systematic sampling Reporting: 2 electronic database of self-reports vs. medical chart review Bias: 1 Confounding: NA descriptive study	4/5 Good
10	Lee et al., 2020 Seoul, South Korea	Retrospective observational study	External Validity: 2 convenient sampling at single institution (2 sites) Reporting: 1 self-report instruments, and medical chart review Bias: 0 Confounding: NA descriptive study	3/5 Fair

Identification

Articles identified through database search: N=148
PubMed (n=47) CINAHL (n=25)
EMBASE (n=32) WoS (n=40)
Cochrane Library (n=4)

Initial duplicates removed
n=66

Screening

Articles after duplicates removed and screened
n=82

Articles excluded
As irrelevant by abstract
n = 49
Irrelevant topics addressing:
- CGM
- Comorbidities e.g. CF
- Pharmacodynamics
- RCT of pump feasibility
- Outpatient pump transition
- Temporarily taking off pump during sports

Eligibility

Full-text articles assessed for eligibility
n=33

Full-text articles excluded, with reasons
n = 23
- Poster submissions to conferences (n=9)
- Duplicate (n=3)
- Not English (n=3)
- Adult (n=2)
- Does not report IP discontinuation as outcome (n=1)
- Irrelevant – describing IP use in general, assessment of screening tool for pump start, overview of diabetes tech management (n=4)
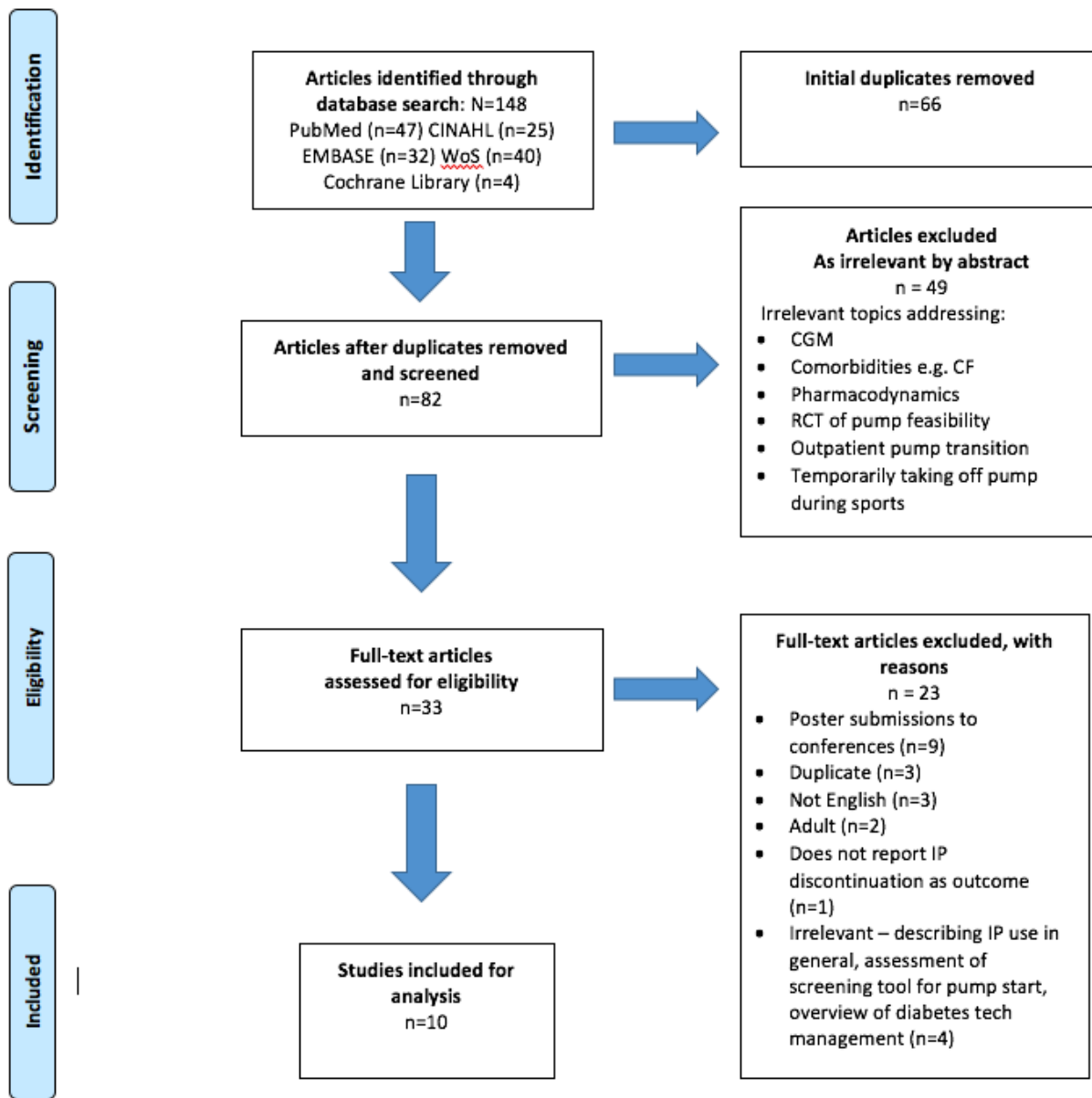
Included

Studies included for analysis
n=10

Figure 2.1 Flow Diagram of Study Selection Process in Identifying Insulin Pump Discontinuation Prevalence in Pediatric Patients with Type 1 Diabetes
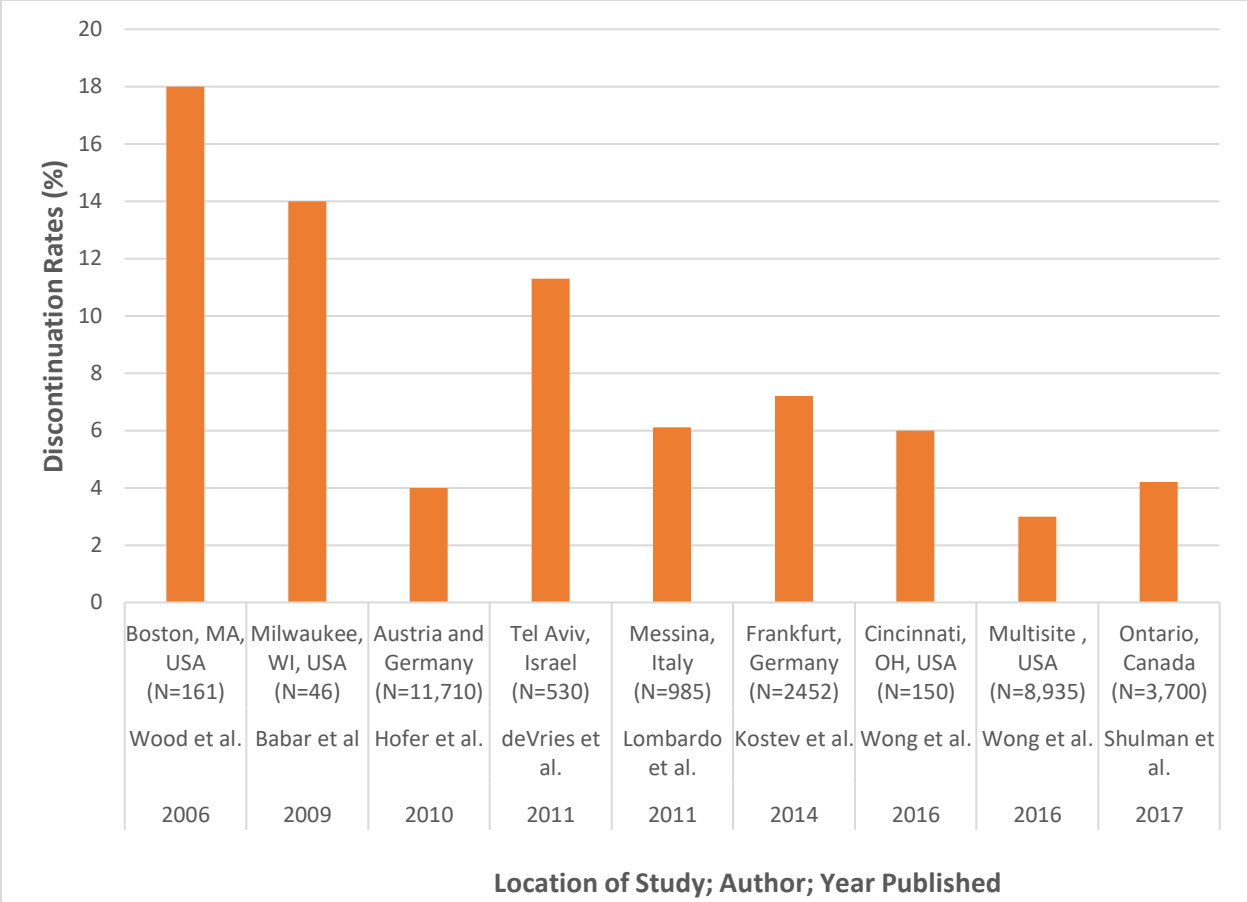
27

Figure 2.2 Chronological Display of Insulin Pump Discontinuation Prevalence Amongst Pediatric Type 1 Diabetes Patients

Supplement 2.1 Search Term and Strategy List

Date of Search: February 15, 2021

PubMed

#	Searches Publication Date From 2000	Results
1	"diabetes mellitus, type 1"[MeSH Terms] OR "type 1 diabetes" OR "insulin–dependent diabetes" OR IDDM OR "juvenile onset diabetes" OR "juvenile diabetes"	61,809
2	(Insulin infusion systems [mh] OR "insulin pump" OR "insulin pumps" OR pump OR pumps OR "insulin infusion" OR ((insulin [mh] OR insulin) AND pump OR pumps)) AND (discontinued OR discontinuation OR discontinuing)	1,159
3	Adolescent [mh] OR adolescents OR adolescence OR teens OR teen OR teenagers OR teenage OR youth OR youths OR child [mh] OR child OR children OR infant [mh] OR infant OR infants OR pediatric OR pediatrics	2,684,905
4	#1 AND #2 AND #3	47

EMBASE

#	Searches	Results
1	'insulin dependent diabetes mellitus' OR 'type 1 diabetes' OR 'type i diabetes' OR 'iddm' OR 'juvenile onset diabetes'	325,502
2	'insulin pump' OR 'insulin infusion pump' OR 'insulin infusion systems' OR AND 'continuous subcutaneous infusion'	8,556
3	'Discontinued' OR 'discontinuing' OR 'discontinuation'	138,112
4	'adolescent'/exp OR 'adolescent' OR teen OR teens OR teenager OR teenagers OR 'juvenile' OR 'pediatrics' OR 'pediatric' OR 'child'/exp OR child OR children	5,138,882
5	1# AND #2 AND #3 AND #4 (('insulin dependent diabetes mellitus'/exp OR 'insulin dependent diabetes mellitus') AND ('insulin pump'/exp OR 'insulin pump') OR 'continuous subcutaneous insulin infusion'/exp OR 'continuous subcutaneous insulin infusion') AND discontinuation AND ('pediatric'/exp OR pediatric) AND ('adolescent'/exp OR adolescent) AND ('child'/exp OR child) AND [2000-2021]/py	32

CINAHL

#	Searches	Results
1	((MH "Diabetes Mellitus, Type 1") OR "type 1 diabetes" OR "juvenile diabetes" OR "juvenile onset diabetes" OR IDDM OR "insulin dependent diabetes")	80,458
2	((MH "Insulin") OR insulin) AND (pump OR pumps) OR (MH "Insulin Infusion Systems") OR "insulin pump" OR "insulin pumps"	3,953
3	discontinuing OR discontinuation OR discontinued	26,133
4	(MH "Child+") OR (MH "Adolescence+") OR child OR children OR adolescent OR adolescents OR teen OR teens OR youth OR teenager OR teenagers OR pediatric	1,227,272
5	#1 AND #2 AND #3 AND #4 ((MH "Child+") OR (MH "Adolescence+") OR child OR children OR adolescent OR adolescents OR teen OR teens OR youth OR teenager OR teenagers OR pediatric) AND (((MH "Diabetes Mellitus, Type 1") OR "type 1 diabetes" OR "juvenile diabetes" OR "juvenile onset diabetes" OR IDDM OR "insulin dependent diabetes")) AND (((MH "Insulin") OR insulin) AND (pump OR pumps) OR (MH "Insulin Infusion Systems") OR "insulin pump" OR "insulin pumps") AND (discontinuing OR discontinuation OR discontinued)	25

Web of Science

#	Searches
1	"diabetes mellitus, type 1"[MeSH Terms] OR "type 1 diabetes" OR "insulin-dependent diabetes" OR IDDM OR "juvenile onset diabetes" OR "juvenile diabetes"
2	(Insulin infusion systems [mh] OR "insulin pump" OR "insulin pumps" OR pump OR pumps OR "insulin infusion" OR ((insulin [mh] OR insulin) AND pump OR pumps)) AND (discontinued OR discontinuation OR discontinuing)
3	Adolescent [mh] OR adolescents OR adolescence OR teens OR teen OR teenagers OR teenage OR youth OR youths OR child [mh] OR child OR children OR infant [mh] OR infant OR infants OR pediatric OR pediatrics
4	#1 AND #2 AND #3 Results: 40

From: **Pediatric Self-management: A Framework for Research, Practice, and Policy**

Figure Legend:

In the Pediatric Self-management Model, self-management behaviors (pictured left) operate within individual, family, community, and health care system domains. Modifiable and nonmodifiable domain-specific influences impact self-management through underlying cognitive, emotional, and social processes. The degree to which self-management behaviors affect adherence, and ultimately outcomes, may result in changes in self-management behaviors.

Supplement 2.2 Pediatric Self-Management Model

1963 - First prototype of pump, which actually delivered both insulin and glucagon developed by Dr. Arnold Kadish of Los Angeles, CA.

1978 – First portable pump, but not user-friendly. Some even requiring use of screwdriver to adjust insulin dosing.

1990s – Major technological advances allowing for smaller, and more efficacious pumps.

2000s - Continued advancements of more user friendly, and durable pumps (e.g. water resistant → proof), with ability to administer insulin more accurately.

2003 – First "intelligent" insulin pump, beaming over blood glucose (BG) values from meter to pump. Bolus Wizard® calculator recommending insulin bolus according to the programmed ratios.

2004 - Launch of software system, which allows patients to share information on the devices with providers for care management.

2007 – Food and Drug Administration (FDA) approval of continuous glucose monitor (CGM) system for children and teenagers.

2010 – FDA approval of insulin pump that combines CGM data to provide predictive alerts.

2011 – First tubeless insulin pump released.

2013 – Insulin pump with ability to stop insulin delivery once BG reaches a low set point.

2015 – First touch screen, slim pump released.

2017 – First hybrid closed loop approved for use for children over the age of 14 by the FDA.

Future – Artificial Pancreas: towards fully automated insulin/glucagon delivery

https://www.medtronicdiabetes.com/about-medtronic-innovation/milestone-timeline
https://www.medscape.org/viewarticle/460365_2

Supplement 2.3 Historical Accounts of Insulin Pump Milestones in United States

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CHAPTER THREE

Diabetes-Related Distress for Parents and its association with Glycemic Outcomes in Adolescents with Type 1 Diabetes

Introduction: This study aims to determine the glycemic outcomes in relation to the individual and family, community, and healthcare systems factors in adolescents with type 1 diabetes (T1D). The current gap in the literature is the lack of best practices in screening for psychosocial factors across the aforementioned four domains.

Methods: In this cross-sectional study, adolescents with T1D and one caregiver were recruited from telehealth visits at a tertiary, multidisciplinary pediatric diabetes center. Glycemic outcomes, hemoglobin A1c (A1C) and time in range (TIR) from 70-180mg/dL based on continuous glucose monitoring (CGM) data, were collected by medical chart review. Participants were asked to fill out the self-report survey, including diabetes self-management, diabetes technology use, diabetes distress, parenting stress, and family functioning from the individual and family domains. Age, gender, BMI, insurance type, daily insulin dose, insulin regimen, and A1C were collected by medical chart review. CGM data were collected from device software. Univariate and multivariable regression models were conducted for association with glycemic outcomes (A1C and TIR).

Results: Thirty-five adolescents with T1D (14.9±1.7 years old) and their caregivers (46±6 years old) participated in this study. The mean (SD) A1C was 8.48±(2.6%) and the mean (SD) TIR was 60.5%±(19.5%). Multivariable analysis showed higher parent diabetes-related distress was associated with higher A1C, and family income greater than U.S. $100,000/year was associated with lower A1C. Similarly, multivariable analysis showed higher parent diabetes-related distress

was associated with lower TIR, and parent education higher than a bachelor's degree was associated with higher TIR.

Conclusion/Implications: Only the association of variables in the family domain with glycemic outcomes was statistically significant. Future interventions aiming to optimize glycemic control of adolescents with T1D must consider the family domain.

Keywords*: Type 1 diabetes mellitus, Insulin pumps, Continuous glucose monitoring, Diabetes data, Self-Management, Pediatric Self-Management Model

Introduction

The Rise of T1D Incidences

Type 1 diabetes (T1D) is a common chronic childhood condition impacting approximately 1.25 million American children and adults, with evidence of rising incidences, particularly among youths.[1-3] T1D is inherently a pediatric disease, whereas type 2 diabetes (T2D) only recently emerged as a phenomenon amongst the younger population as a consequence of the obesity epidemic. The SEARCH for Diabetes in Youth (SEARCH) estimated incidences of diabetes in youths less than 20 years of age in the U.S from 2002 to 2015, indicating a 4.8% increase per year for T2D and 1.9% increase per year for T1D.[4-6] The incidences of both types of diabetes are on the rise worldwide from 2% to 4% every year, where the prevalence of T1D in the US is projected to triple by 2050.[4, 7]

Economic Costs of T1D

The economic burden of T1D is significant to the individual and society. A recent study created a model to compare an estimated lifetime economic burden for those living with T1D versus those without. The study consisted of 1,630,217 individuals with T1D, and a comparator group equal in size without T1D, and showed that the difference in the health care cost over 100 years (person's lifespan) was $813 billion.[8] Another study found that, the mean hospital charge per admission for diabetes ketoacidosis (DKA) was $26,566.[9] Lastly, the high cost of insulin in the U.S. has been scrutinized for going from costing $21 for one vial to $199 to $332 in 2019, indicative of more than 1000% increase in the price.[10]

The Burdens of Living with T1D

It takes meticulous planning and diligence in order for an adolescent with T1D to remain in the optimal glycemic range.[3] The never-ending hour-by-hour (or minute-by-minute) monitoring and adjusting blood glucose (BG) to be "in range" can be overwhelming, especially given adolescence is already a stressful time even for healthy individuals while learning to balance school, work and family obligations. Moreover, adolescents with T1D face burdens at school relating to the lack of appropriately trained staff, policies that prohibit non-nurse assistance, and limitations on the participation of school-sponsored events.[11, 12] Lastly, adolescents with T1D are twice as more likely to develop psychological conditions including depression, anxiety, eating disorders and family conflict related to diabetes management[13, 14].

Maintaining blood glucose (BG) levels within the recommended parameters is necessary to prevent future micro- and macro-vascular complications.[15, 16] The Diabetes Control and Complications Trial (DCCT) is a landmark trial, which demonstrated intensive insulin therapy (multiple injections per day or insulin pump) to reduce long-term complications when compared to the control group receiving conventional therapy (twice daily injections).[17] Inadequate glycemic control can manifest itself in acute diabetes complications warranting emergency room visits and hospitalization related to severe hypoglycemic episodes or diabetes ketoacidosis (DKA).[18]

Theoretical Framework

The Pediatric Self-Management Model (PSMM) is the framework used to guide and organize the variables of interest in this study.[19] The PSMM emphasizes the importance of approaching the *individual* as a whole, being mindful of the factors in the surrounding *family*,

community, and the *health care system*. In each of the four domains, there are modifiable and non-modifiable influences leading to the individual's self-management behaviors (Figure -1). Distinguishing modifiable versus non-modifiable variables is a helpful process in the development of future interventions. The PSMM also stipulates that self-management behaviors manifest via cognitive, emotional, and social processes. There has been a large body of work that has already explored factors influencing glycemic outcomes. However, there is a lack of studies examining factors spanning across the multi-domains associated with the glycemic outcomes in adolescents with T1D based on the PSMM.

Operational Definitions

Hemoglobin A1C (A1C) is a measure that reflects a person's average BG level over the past two to three months. The A1C result shows the amount of glucose that appears on the surface of the red blood cell, which is proportional to the amount of glucose in the blood and is reported in percentage (%). Time in Range (TIR) is a target range of blood glucose values collected by the continuous glucose monitor (CGM), and is the time spent in 70 to 180mg/dL and is also reported in percentage (%).

Aims

The purpose of this study is to identify factors in the individual, family, community, and healthcare systems and their association with glycemic outcomes in adolescents with type 1 diabetes (T1D) as defined by hemoglobin A1C (A1C) and time in range (TIR) from 70-180 mg/dL.

The research question is: for adolescents 12 to 17 years of age with T1D, what are the variables associated with glycemic outcomes, A1C and TIR? The hypothesis of this study is that the factors associated with glycemic outcomes by A1C and TIR will be similar.

Methods

Study Design, Population, Setting

This study is an observational, cross-sectional study. A one-time self-report survey was administered to the adolescent and the parent, or the primary caregiver seen at a tertiary, multidisciplinary pediatric diabetes center. Inclusion criteria were adolescents with T1D 12 to 17 years of age, with a parent or caregiver willing to provide consent, and able to read and understand English. Patients with any other significant co-morbid conditions, or less than `12 months of T1D diagnosis were excluded. Additional data was extracted via electronic medical chart review, along with diabetes technology data cross-referenced from Tidepool.[20] Tidepool is an open-source platform for diabetes data, which consolidates data across multiple diabetes devices onto a single platform and makes diabetes data and pattern recognition for both clinicians and patients. The study was approved by the University of California, San Francisco institutional review board before the subject enrollment began. Due to the COVID-19 pandemic, the initial plan for patient recruitment onsite at the multidisciplinary diabetes clinic was shifted to a virtual recruitment using a video platform (Zoom). An email permission from the patient care team was obtained prior to joining the telehealth visits, and once a verbal consent was obtained, a REDCap link with a series of self-report surveys was distributed. The parent or the primary caregiver completed 4 surveys (P-PAID-T, PIP, FAD-GF, and demographic questionnaire), and

the adolescent completed 3 surveys (SMOD-A, PAID-T, DTQ). The online survey data collection occurred from April of 2020 to August 2021.

Measures Used for Adolescent Participants

Self-Management of Diabetes-Adolescents (SMOD-A)

The SMOD-A is a self-report survey developed by a team of nurse scholars to measure self-management in adolescents with T1D. It is a 52-item self-report questionnaire, with five subscales: 1) Collaboration with Parents -13q, 2) Diabetes Care Activities -15q, 3) Diabetes Problem Solving – 7q, 4) Diabetes Communication -10q and 5) Goals 7q.[21] SMOD-A differentiates itself from the other measures by focusing specifically on self-management. The internal consistency, or the Cronbach's alphas for the five ranged from 0.71 to 0.85.[21] It has a very strong content validity (0.93), and strong subscale reliability (0.71-0.85). It is scored on a four-point Likert scale where (0=Never, 3 = Always). For each of the five subscales, the minimum possible score is 0. Maximum possible scores are 39 (Collaboration with Parents), 45 (Diabetes Care Activities), 21 (Diabetes Problem-Solving), 30 (Diabetes Communication), and 21 (Goals). Higher scores indicate more collaboration with parents, higher diabetes care activities by the teen, higher problem-solving skills, better communication, and goals, respectively[5].

Problem Areas in Diabetes Teen Version (PAID-T)

PAID-T is a self-report survey developed to measure diabetes-specific emotional distress.[22] It is a measure used in a clinical setting to screen for diabetes-related distress. Problem Areas in Diabetes (PAID) has two corresponding surveys, one for the adolescent with T1D (PAID-T) and one for parents (P-PAID-T).[23] It is 14-item survey scored in a six-point Likert

scale (1=Not a problem, 6 = Serious problem), where the scores range from 14-84. Higher total score is indicative of higher diabetes-related emotional distress. Cronbach's alpha (α) for the resulting 26 item measure was strong α =0.96.[21] The distress cutoff scores for PAID-T and were determined ≥54. Those who score on the high stress side of the cutoff point warrant closer follow-up for depression and anxiety screening the adolescent.

Measures used by Parent or Primary Caregiver

Family Assessment Device (FAD) – General Functioning (GF12)

The McMaster FAD is originally a 60-item questionnaire designed to measure individual's perceptions of the family.[24] This study utilized the general function (GF12) subscale that consists of 12 items. The GF12 subscale of the FAD has also been validated as a single index for characterizing overall family functioning, with good psychometric properties (α =0.71).[25-27] The brevity and ease of administration of the GF12 have enabled several studies, including an assessment of the health of families in large population-based samples.[28, 29]

It is scored on a four-point Likert scale (1=strongly agree to 4=strongly disagree), and the final score is a sum of the items divided by the total item. Higher scores indicate worse levels of family functioning, and a score greater than 2.0 is indicates problematic family functioning.

Pediatric Inventory for Parents (PIP)

PIP is a reliable and valid measure (α =0.80 to 0.96) for parenting stress related to caring for a child with a chronic condition.[30] It was initially designed to study parents caring for children with cancer, and then was validated for parents caring for children with T1D.[31]

It is comprised of 42 items, and categorized into four subscales: 1) Communication, 2)

Emotional Functioning, 3) Medical Care, and 4) Role Function. Moreover, lower parental self-

efficacy, greater responsibility in T1D management, and greater fear of hypoglycemia were more

frequently associated with higher stress.[31] Parents rate each item along a five-point Likert scale

(1 = Not at all, 5 = Extremely) on item's frequency and its difficulty. Then, the frequency (PIP-F)

and difficulty (PIP-D) scores are summed separately for each of the four domain scales. Higher

scores indicate the greater frequency and difficulty. The range of possible scores on the PIP

scales is 42 to 210.

Diabetes Related Measures/Sociodemographic Data

Data collected from the electronic medical record included A1C, and continuous glucose

monitoring (CGM) metrics were collected from Tidepool. Glycemic outcomes included A1C and

continuous glucose monitor (CGM) sensor data time in range (TIR) based on CGM data. Parents

completed the demographic questionnaire to report the race and ethnicity of the child, parent's

marital status, household income, and parent's education level. This survey also included some

diabetes-related data including missed number of school days due to T1D, diabetes camp

attendance, data on who initiated diabetes technology, and open text on barriers and facilitators

of using diabetes technology.

Data Analysis

Descriptive analyses were conducted using mean and standard deviation (SD) and 95%

confidence intervals for standardized continuous variables, and median and interquartile range

for skewed variables. To assess individual factors associated with A1C and TIR, univariate

regression analyses were performed using a significance level of $\alpha < 0.05$.

Data was missing sporadically throughout the dataset, such that a complete case analysis under the usual stepwise regression would have removed over half of the data. Thus we conducted stepwise regression under multiple imputations, as has been described and shown to work well.[32] The method was implemented by generating 50 multiple imputations. Forward stepwise regression was performed in the usual way, but every variable was tested under the usual pooled (over multiple imputations) test statistic, and was included if $p < 0.05$. The backward stepwise regression model resulted in the same approach. STATA (StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC.) was used to perform statistical analysis. A priori value p-value of less than 0.05 was set.

Results

Characteristics of the Participants

A total of 35 adolescents and corresponding primary caregivers participated in this study. The age range was 12-17 (mean= 14.9±1.7 years), with the majority being female (63.6%). Participants had a mean BMI of 24.8±5.8kg/m$^{2.}$ The age range for parents was 35 to 52 (mean= 46±6), with 82.9% of the survey completed by mothers. About 68.8% of the adolescents identified as non-Hispanic White, 63.6% of the parents reported education level of bachelor's degree and above, 81.3% reported married and living together with a partner, 62.5% had reported family income of greater than $100,000/year, and 71% of the participants reported having private insurance.

Younger parent's age, higher annual household income, and reporting private insurance were associated with lower A1C (parent's age (p=0.018, beta coefficient of -0.184), family income of less than U.S. $100,000 per year (p<0.001, β coefficient= -3.60), and having a private

insurance as opposed to public (p=0.041, β coefficient = -2.104). Non-Hispanic, white race, and education level of greater than bachelor's level were associated with higher TIR (p <0.001, β coefficient = -0.223), parent's level of education greater than bachelor's degree (p=0.007, β coefficient = 0.245) were statistically significant).

Table 3.1 Participant Characteristics and A1C Association by Univariate Linear Regression Analysis (N=35)

Variable	M±SD or Percentage (%)	Coef.	CI		*P-Value*
Adolescent Age, years	14.9±1.7	0.233	-0.317	0.784	0.394
BMI, kg/m^2	24.8± 5.8	0.060	-0.100	0.220	0.452
Gender, Female, %	63.6	1.613	-0.264	3.491	0.089
Race, Non-White, %	31.2	1.561	-0.456	3.580	0.124
Parent Age, years	46±6.0	-0.184	-0.334	-0.033	**0.018**
Parent Highest Level of Education: Bachelor's Degree and above, %	63.6	-1.710	-3.804	0.404	0.108
Marital Status: Parent Married/Living Together, %	81.3	0.749	-0.544	2.043	0.246
Survey Completed by, % Mother	82.9	0.919	-1.453	3.290	0.436
Family Income: Less than US$100,000/year, %	31.0	-3.590	1.780	5.401	**<0.001**
Insurance: Private, %	71.0	-2.104	-4.120	-0.088	**0.041**

Table 3.2 Participant Characteristics and TIR Association by Univariate Linear Regression Analysis (N=26)

Variable	Coef.	CI		*P-Value*
Adolescent Age, years	0.010	-0.037	0.057	0.680
BMI, kg/m^2	-0.012	-0.026	0.002	0.093
Gender, Female, %	-0.100	-0.259	0.060	0.211
Race, Non-white, %	-0.223	-0.380	-0.065	**<0.001**
Parent Age, years	0.012	-0.001	0.025	0.071
Parent Highest Level of Education: Bachelor's Degree and above, %	0.245	0.075	0.416	**0.007**
Marital Status: Parent Married/Living Together, %	-0.025	-0.144	0.094	0.673
Parent Married/Living Together, %	-0.025	-0.144	0.094	0.673
Survey Completed by, % Mother	0.018	-0.185	0.221	0.855
Family Income: Less than US $100,000/year, %	-0.138	-0.296	0.020	0.083
Insurance: Private, %	0.054	-0.153	0.261	0.598

Diabetes-Related Characteristics

About 91.4% of the participants were using an insulin pump (Tandem, Medtronic or Omnipod), and 9.1% are using MDI as mode of insulin delivery regimen. Of those using insulin pump, 51.5% reported using a hybrid closed loop (Control IQ, Medtronic 670G, or Omnipod with DIY loop), 82.1% of the participants reported that the insulin pump was initiated by a healthcare provider, and 10.7% initiated from a T1D family friend's recommendation. All but one participant reported using CGM (Dexcom G6, Freestyle Libre, and Guardian) and 78.8% of

the adolescents attended diabetes camp. The age at T1D diagnosis ranged from 6 months to 16 years of age, and the mean age at diagnosis was 7.6±4.2 years of age. The mean diabetes duration was 7.2±4.0 years for our sample ranging from 12 to 17 years of age. A1C ranged from 5.5 to 16 (8.48±2.6%), and the average daily insulin dose was 0.89±0.3 units/kg.

Table 3.3 Diabetes Related Variables and A1C Association by Univariate Linear Regression Analysis (N=35)

Variables	M±SD or Percentage (%)	Coef	CI		P-Value
Age at Diagnosis, years	7.6±4.2	-0.067	-0.294	0.160	0.550
Diabetes Duration, years	7.2±4.0	0.115	-0.118	0.348	0.322
Attended Diabetes Camp: Yes, %	78.8	0.914	-1.369	3.198	0.420
Daily Insulin Dose, Units/kg	0.890±0.3	2.767	-0.294	5.829	0.075
Regimen, %		-0.124	-0.453	0.206	0.450
Pump	91.43				
Injections	8.57				
Using hybrid closed loop, Yes, %	51.5	-0.903	-2.722	0.916	0.319
Pump Initiation: By Healthcare Provider, %	82.1	-0.020	-1.195	1.154	0.972
Sensor Usage, %	73.4±29.9	-0.958	-4.120	2.284	0.548
Time in Range 70-180 mg/dL, %	60.5±19.5	-5.618	-9.834	-1.401	**0.011**
Glucose CV[1], %	35.2±5.6	4.254	-0.130	0.214	0.879

1. Coefficient of Variation, target <36%

Table 3.4 Diabetes Related Variables and TIR Association by Univariate Linear Regression Analysis (N=26)

Variables	Coef.	CI		P-Value
Age at Diagnosis, years	0.005	-0.014	0.024	0.575
Diabetes Duration, years	-0.003	-0.022	0.016	0.733
Attended Diabetes Camp: Yes, %	-0.091	-0.280	0.098	0.331
Daily Insulin Dose, Units/kg	-0.263	-0.553	0.026	0.073
Regimen, % Pump Injections	-0.003	-0.033	0.026	0.828
Using hybrid closed loop, Yes, %	0.087	-0.072	0.246	0.271
Pump Initiation: By Healthcare Provider, %	-0.037	-0.143	0.069	0.475
Sensor Usage, %	0.110	-0.162	0.383	0.411
A1C, %	-0.041	-0.072	-0.010	**0.011**
Glucose CV[1], %	-0.006	-0.021	0.009	0.415

1. Coefficient of Variation, target <36%

Self-Report Survey Results

SMOD-Diabetes Care Total score (p=0.025), PAID-T (p=0.021), P-PAID-T (p=0.001) were statistically significant in its association with A1C. Alternatively, P-PAID-T was the only statistically significant variable (p<0.001) in its association with TIR, higher distress level associated with decrease in TIR.

Table 3.5 Self-Report Results and A1C Association by Univariate Linear Regression Analysis (N=35)*

Variable	Mean±Std.Dev	Coef.	CI		P-Value
SMOD[1]-Collaboration Total Score	13.4±7.3 range: 3-37	0.022	-0.110	0.154	0.730
SMOD-Diabetes Care Total Score	29.9±6.6 range: 16-43	-0.153	-0.286	-0.021	**0.025**
SMOD-Problem Solving Total Score	14.6±3.7 range: 7-21	-0.113	-0.372	0.146	0.378
SMOD-Communication Total Score	13.9±5.9 range: 6-26	-0.014	-0.192	0.164	0.874
SMOD-Goals Total Score	15.6±3.6 range: 9-21	-0.170	-0.433	0.094	0.198
PAID[2] Teen Total Score	37.2±13.6 range:15-78	0.078	0.013	0.143	**0.021**
PAID Parent Total Score	44.2±14.5 range:21-82	0.097	0.044	0.149	**0.001**
FAD[3]-GF12 Total Score	1.7±0.5 range:1-3.17	0.413	-1.649	2.476	0.685
PIP[4] Frequency Total Score	91.5±25.8 range: 48-145	0.013	-0.024	0.051	0.472
PIP Difficulty Total Score	90.2±28.9 range: 46-179	0.007	-0.027	0.041	0.662

1. Self-Management of Diabetes-Adolescents (SMOD-A) Total scores ranging from 0 to maximum possible scores are 39 (Collaboration with Parents), 45 (Diabetes Care Activities), 21 (Diabetes Problem-Solving), 30 (Diabetes Communication), and 21 (Goals).

2. Problem Areas in Diabetes (P-PAID-T) for parents and (PAID-T) for teens

3. Family Assessment Device (FAD) – General Functioning(GF12)

4. Pediatric Inventory for Parents (PIP)

* To note, the data collection phase coincided with the first year and a half of the shelter-in-place due to the COIVD-19 pandemic.

Table 3.6 Self-Report Variables and TIR Association by Univariate Linear Regression Analysis (N=26)*

Variable	Coef.	CI		*P-Value*
SMOD[1]-Collaboration Total Score	0.001	-0.010	0.013	0.799
SMOD-Diabetes Care Total Score	0.011	-0.001	0.022	0.064
SMOD-Problem Solving Total Score	0.016	-0.005	0.037	0.138
SMOD-Communication Total Score	0.005	-0.010	0.019	0.510
SMOD-Goals Total Score	0.014	-0.009	0.037	0.226
PAID[2] Teen Total Score	-0.008	-0.015	-0.001	**0.023**
PAID Parent Total Score	-0.010	-0.014	-0.005	**<0.001**
FAD[3]-FG12 Total Score	-0.003	-0.197	0.203	0.977
PIP[4] Frequency Total Score	-0.002	-0.005	0.001	0.134
PIP Difficulty Total Score	-0.002	-0.006	0.001	0.138

1. Self-Management of Diabetes-Adolescents (SMOD-A) Total scores ranging from 0 to maximum possible scores are 39 (Collaboration with Parents), 45 (Diabetes Care Activities), 21 (Diabetes Problem-Solving), 30 (Diabetes Communication), and 21 (Goals).
2. Problem Areas in Diabetes (P-PAID-T) for parents and (PAID-T) for teens
3. Family Assessment Device (FAD) – General Functioning(GF12)
4. Pediatric Inventory for Parents (PIP)
* To note, the data collection phase coincided with the first year and a half of the shelter-in-place due to the COIVD-19 pandemic.

The results for multivariable model for A1C and TIR had similar variables included. For A1C, P-PAID-T total score and parent's age explained for 61.7% of the variance (Table 3.7). For multivariable model for TIR, P-PAID-T total and parent's education level explained for 59.0% of the variance (Table 3.8). All the variables which made it into the model was from the family domain, specifically related to the parent.

Table 3.7 Multivariable Regression Model for A1C

Variable	Coef.	CI		P-Value
PAID Parent Total Score	0.076	0.027	0.124	**0.004**
Income, More than U.S. $100,000/year	-2.339	-3.862	-0.816	**0.004**

Table 3.8 Multivariable Regression Model for TIR

Variable	Coef.	CI		P-Value
PAID Parent Total Score	-0.007	-0.012	-0.003	**0.004**
Parent Highest Level of Education: Bachelors Degree and Above	0.165	0.031	0.299	**0.019**

Discussion

The purpose of this study was to perform a theory-based analysis to determine the association of factors in the individual, family, community, and healthcare systems domains and with glycemic outcomes in adolescents with T1D as defined by A1C and TIR. We recruited adolescents 12 to 17 years of age, since this is when the glycemic outcome is typically at its least optimal state.[33] In our study, the mean A1C was 8.48±2.6%, and the mean TIR was 60.5%±19.5%. Though goal A1C should be individualized, the recommended A1C goal by the ADA and ISPAD is less than 7%, and the target TIR is 70%. [34] This study finding is similar to the outcome in state of T1D study according to the T1D Exchange finding where the mean A1C of 4,914 adolescents 13 to 17 years of age was 9.0±1.8%.[33, 35] This state of T1D study also noted only 17% of adolescents with T1D meeting target glycemic outcome.[35] Our sample size showed 30% of the group with A1C less than 7% and 33% of the group with TIR greater than 70% -

indicating this study's cohort demonstrated slightly higher percentage of adolescents meeting goal A1C. Lastly, TIR and A1C were moderately negatively correlated at r=-0.48

As per our hypothesis, the multivariable analysis with A1C and TIR concluded in similar findings. Higher levels of parental diabetes-related stress measured by P-PAID-T were associated with higher A1C levels. A higher P-PAID-T score was associated with lower TIR, both indicating higher levels of parental diabetes-related distress is associated with suboptimal glycemic outcomes. In addition, family income and parent education were also associated with glycemic control.

This finding aligns with the recommendation which encouraged clinicians to utilize the CGM time in ranges (within target, below and above target) to use as clinical target and goals that complement A1C, especially since CGM can guide the day-to-day self-management decision-making process.[36] Another study reported TIR to be strongly associated with microvascular complications, and that it should be also used as an outcome metric in clinical trials in addition to the "gold-standard" A1C.[37] In our data, A1C and TIR are moderately correlated in the negative direction (r=-0.481), which is expected. Future higher-powered studies are needed to validate TIR against A1C, but our study descriptively demonstrates factors associated with A1C are similar to the variables included in TIR.

Parents' report of diabetes distress associated with A1C and TIR suggest higher levels of diabetes-related emotional distress due to one's adolescent with T1D will result in higher A1C and lower TIR for the adolescent. This finding contradicts a correlational study looking at children younger than 9 years of age, which showed that higher parental diabetes-related distress measured by P-PAID-C scores were associated with lower A1C, indicative of better control.[38] Our target age range of 12 to 17 years of age demonstrated the opposite, where the higher levels

of parental distress, the higher the A1C, or the worse the glycemic outcome. This is also reflected on a systematic review finding from 2013, which showed a positive association with parenting stress level for school-aged and adolescents (7 to 17 years of age) with A1C.[39] Alternatively, parenting stress levels for younger children (0 -11 years of age) showed no association or even negatively association with A1C (meaning higher diabetes related distress level was a protective factor).[39] The negative association with parental stress levels and A1C for the younger children less than 11 years of age may be due to the fact that the majority of the self-management care is completed by the parent or the primary caregiver. Higher parental distress might encourage parents to be more careful about managing their children's diabetes. In adolescents, the transition of daily self-management diabetes care starts to become more prominent, as the majority of the time may be spent independent from parental supervision. A higher level of parental distress may be indicative of the challenging or conflicts between parents and adolescent in transitioning from dependence to independence in adolescent's diabetes self-management.

The majority (n=26, 74.3%) of our study participants used CGM. This prevalence is more than twice as high in comparison to the 38% reflected in the literature.[35] The average A1C of US pediatric patients according to the T1D Exchange data from 2013/2014 was 8.7%, which is slightly higher than our average of 8.5%, but only 18% met the ISPAD target A1C of less than 7.5%, where about 45% of our participants reported A1C less than 7.5%. Studies show consistent use of CGM is associated with more optimal A1C.[40, 41] There are studies looking at use of CGM and its association with lower parental distress, and the use of CGM associated with lower A1C.[42, 43] Our results show having higher parental distress is associated with less time spent in the target range of 70 to 180mg/dL. Unfortunately, the causality cannot be determined due to the

cross-sectional nature of this study's design. Regardless of the glycemic control directions, we must acknowledge the significant amount of distress experienced by the parents and the primary care givers with children with T1D.

Family income was negatively associated with A1C, where those reporting having greater than U.S. $100,000/year had lower A1C. Parent's education level was positively associated with TIR, indicating higher the parent's education level, the higher the time spent in target range. There is an abundance of data supporting better glycemic control as evidenced by A1C associated with higher levels of parental education, but not specifically looking at the sensor's TIR data as per the analysis.[44, 45]

The adoption of the sensor became more readily acceptable with its improvement in accuracy, which allows the user to simply use the BG value provided by the sensor in lieu of finger stick BG measures.[36] Many providers recommend using CGM regardless the insulin delivery regimen, because the ability to visualize one's BG has shown efficacy to remain in target range of 70-180mg/dL.[46-49] In this study, more than half of the insulin pump users were using HCL, where 2 teenagers 14 and 16 years of age reported using DIY loop with Fiasp (faster acting insulin aspart) with a tubeless pump, and one 17 year old using looping technology with OpenAPS system. OpenAPS is an open source database which allows for patients to program his or her own closed-loop system.[50] As the diabetes technology develops rapidly, many insulin pump companies will have obtained F.D.A. clearance on HCL devices, which means the HCL pump will soon become the norm. Future studies may need to explore the use of HCL in diabetes management and factors associated with diabetes management.

The goal of diabetes technology development is to decrease the day-to-day burden for the adolescents, and it has been shown to be safe and efficacious for glycemic control. It is

important to identify the reason for lack of diabetes technology use, otherwise a greater "glycemic control gap" between those who are adapting well to the technology use versus those who are not able to adapt will arise. More data to support the efficacy of insulin pumps and CGM, the stronger case to make the resources and technology available to those in need.

Limitations

The goal of this study was to incorporate many more variables from the family, community, and healthcare system domains. In the reality of patient recruitment with limited resources in the midst of the pandemic, recruitment was a challenge – thus resulting in a small sample size (See Supplement-1). Though the sample size was small, the range of A1C ranged from 5.5% to 13%, and included MDI patients highly adaptable to diabetes technology (using DIY loops and Fiasp). The second limitation is the data collection from a single tertiary, multidisciplinary pediatric diabetes center with a very high rate of diabetes technology use, therefore limiting its generalizability to the general population. Lastly, the study was a cross-sectional design and therefore causality cannot be determined.

Conclusion

Parent variables displayed a stronger association to glycemic outcomes. Specifically, the parent's diabetes-related distress level was identified to be a modifiable attribute to be targeted for future interventions. T1D management in all age ranges does not happen in a silo, but rather it requires the entire family's attention and collaboration, and family factors are a key domain associated with the adolescent's glycemic outcome.[51] Lastly, this suggests that family interventions aimed to optimize A1C or TIR are more likely to succeed when they target reduction of diabetes-related parental stress.

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CHAPTER FOUR

Diabetes Technology Use and Its Relationship with Parental Stress in Caring for Adolescents with Type 1

Introduction: Diabetes-related distress by the parent has been identified as an important role in influencing the adolescent with type 1 diabetes (T1D) in their diabetes self-management, which ultimately impacts the glycemic outcome. This study aimed to identify factors associated with diabetes-related distress in parents caring for adolescents with T1D. The second aim is to describe diabetes-related distress in parents related to diabetes technology use.

Methods: In this cross-sectional study, parents of adolescents with T1D were enrolled. Self-report and open-ended questions were collected. The primary outcome of interest was parent diabetes-related distress level measured by P-PAID-T. Independent variables included parenting stress, family functioning scale, adolescent's diabetes related-distress, self-management, and diabetes technology use. Univariate and multivariable regression models were conducted for association with parent diabetes-related distress. Qualitative data from the open-ended text about barriers and facilitators of insulin pump use was categorized into themes.

Results: The mean score of P-PAID-T from the 35 parents was 44.2 ± 14.5 (clinical distress cut-off score =54). The diabetes-related parent distress was only moderately correlated with parent distress ($r=0.49$), indicating the two appear to be separate concepts. The adolescent's satisfaction of diabetes technology use was associated with lower parent diabetes-related distress. The thematic analysis of the qualitative data showed structural, psychological, and physical barriers and facilitators in using insulin pumps.

Conclusion/Implications: The relationship between the individual and family in T1D management

is complex. These association findings may guide future studies on the association between

parent and teen distress and diabetes technology use.

Introduction

Type 1 Diabetes is a Family Ordeal

Type 1 Diabetes (T1D) management is a challenge not only for the individual with the diagnosis but for the entire family. Currently, there is no clear etiology as to what causes T1D, nor is there a cure or way to reverse it, which means if a child is diagnosed, it will be a life-long condition. It's particularly difficult for the parent of younger children when managing the disease requires "hurting" the child with repeated finger sticks or injections.[1],[2] It's also difficult in adolescence because of the inability to be like others – due to loss of spontaneity or freedom.[3],[4] The success of the transition of diabetes management duties as the child grows older is also challenging to measure, because there is no such thing as a "standard" family, and the dynamics and timing of how these transitions occur will vary across households. The parental role in T1D management grow and evolve in parallel with the adolescent, emerging through young adulthood, but the overall support from family and peers have been identified as an important component of successful diabetes management.[5]

Self-Management in T1D

T1D requires never-ending management to monitor blood glucose (BG) levels via BG meter or continuous glucose monitoring (CGM). It also requires dosing of insulin through an insulin pump or injection. In addition to this, carbohydrate counting is required at each meal and snack times in order to determine the prandial insulin dose. Lastly, the impact of the activity – whether it is exercising or sleeping, can have a different impact on the BG. Constant surveillance of BG is necessary to prevent severe hypo or hyperglycemic episodes.[6] The acute consequences can result in seizures, comas, and even death due to low BGs, or diabetic

ketoacidosis (DKA) if insufficient insulin is given. The long-term complications are also well documented to result in damage to multiple organ systems, including the brain.[7]

Diabetes Technology

Insulin pump use is most commonly seen amongst adolescents in the U.S., and its use has been shown to improve A1C. CGM is another technology being used widely amongst adolescents with T1D to decrease hypoglycemic episodes.[8, 9] Its recent improvement in accuracy has effectively almost eliminated the need to take into account the numbers of BG checks performed per day, which was historically used as a proxy for optimal glycemic control. Due to the great advancement in the diabetes technology, the use of diabetes technology greatly increased in youth, particularly for families in the higher socioeconomic status (SES).[10, 11]

Theoretical Framework

Bronfenbrenner's social-ecological theory indicates that the individual behaviors embedded within larger social and environmental influences and understanding the complex relationship between the bio-psycho-social domains are necessary to improve the individual health outcomes.[12, 13] This model also has been applied to understand families with children diagnosed with T1D.[14] In analyzing data for T1D adolescents 12 to 17 years of age, family is one of the most important spheres and this paper will focus on variables associated with diabetes-related distress for the parents.[5]

Study Aims

The first aim of this study is to determine the factors associated with diabetes-related distress in parents caring for adolescents with T1D. The second aim is to describe diabetes-related distress in parents related to diabetes technology use.

Research Question/Hypothesis

The research question is for parents with T1D adolescents 12 to 17 years of age, what modifiable variables are associated with diabetes-related distress? And how does the use of diabetes technology impact the parent's diabetes-related distress? We hypothesize that the higher self-management competence of the adolescent and the use of diabetes technology will be associated with less parent diabetes-related distress.

Methods

Study Design, Population, Setting

In this cross-sectional study, adolescents with T1D and one caregiver were recruited from telehealth visits at a tertiary, multidisciplinary pediatric diabetes center to complete a self-report survey. Patients were screened for eligibility and permission was obtained from the provider prior to joining the telehealth visit. After providing verbal consent, families were contacted via email for e-consent documentation using REDCap. A series of self-report surveys were completed in English by one parent followed by the adolescent. Diabetes self-management, diabetes technology use, diabetes distress, parenting stress, and family functioning factors were measured by standard measures. Age, gender, BMI, insurance type, daily insulin dose, insulin regimen, and A1C were collected by medical chart review. CGM data were collected from device software. Univariate and multivariable regression models were conducted for association with parent diabetes-related distress. The study protocol was approved by University of California (UCSF) Institutional Review Board. The parents filled out series of 4 surveys including Problem-Areas in Diabetes for Parents of teens with T1D (P-PAID-T), Pediatric Inventory for Parents (PIP), Family Assessment Device – General Functioning (FAD-GF12), and

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sociodemographic questionnaire. The adolescent filled out series of 3 surveys including Problem-Areas in Diabetes for Parents of teens (PAID-T), Self-Management of Diabetes in Adolescents (SMOD-A), and Diabetes Technology Questionnaire (DTQ).

Measures

Problem Areas in Diabetes (PAID)

Distress is defined as a negative state in which "coping and adaptation process fail to return to physiological or psychosocial homeostasis", and while stress is a normal response as a reaction to the environment, distress occurs when stress is severe and prolonged.[15] Diabetes-related distress was measured by a self-report survey consisting of 15 items in the Problem Areas in Diabetes (PAID) by parent caring for T1D teen (P-PAID-T). Problem Areas in Diabetes (PAID) is a survey administered to the adolescent and the parent dyad. The parents answer a 15-item self-report survey which primes the respondent with acknowledging that living with T1D can be difficult, and there are minor to major life "problems and hassles" in T1D management. Next, the respondent is asked to reflect upon the past 30 days and indicate how much each of the items has been problematic, where 1 = Not A Problem to 6 = Serious Problem.[16] Internal consistency of the 15-items has Cronbach's alpha of 0.94, and strong reliability for all factors of alphas from 0.81 to 0.92 .[17, 18] For the parents, diabetes-related distress was identified into two factors 1) emotional burden and 2) regimen-specific distress. For example, feeling sad or angry when I think about my child having and living with diabetes is an example of an emotional burden, and feeling like I am often failing with managing my child's diabetes regimen is an example of regimen-specific distress. The higher the total score indicates higher distress.

Pediatric Inventory for Parents (PIP) – Difficulty

Pediatric Inventory for Parents (PIP-Diff) is a 42-item survey, and it prompts the respondent to rate how difficult series of events associated with being a parent of a child with a serious illness over the past 7 days, where 1=" Not at all" to 5 = "Extremely". The range of possible scores for PIP is 45 to 195, where the higher the score indicates greater difficulty.[19, 20]

Family Assessment Device – General Functioning

Family Assessment Device – General Functioning is a 12-item abridged version, and a total score is calculated by adding up the items where 1=Strongly Agree, 4=Strongly Disagree. The total sum is divided by 12 to yield an average score, where a greater than 2.0 score indicates problematic family functioning.[21, 22] This study has adequate reliability and validity reported in other studies.[22, 23]

Diabetes Technology Questionnaire (DTQ)

DTQ is a 30-item survey measuring the impact of the technological device as it relates to the management of T1D[24]. Unpublished psychometric data were obtained from American Diabetes Association abstract for a poster reporting data from 115 youth with T1D. DTQ has internal consistency Cronbach's alpha of 0.94 for the adolescents, where it tested the DTQ against initiation of the hybrid closed loop system, which delivers automatic micro boluses of insulin based on the continuous glucose sensor BG values. It is one of the only measure that is available, specifically asking respondents about the type of diabetes devices currently being used as part of diabetes management. The four options are MDI, insulin pump, MDI with continuous glucose monitor (CGM), and sensor-augmented pump (SAP) or insulin pump with CGM. The survey is designed for longitudinal follow-up (at the initiation of the new diabetes technology and at a follow-up visit), but for the purposes of this study, the baseline version was

administered. It is scored on a five-point Likert scale (1=Very Much, 5=Not At All), where high scores indicate higher satisfaction with use of diabetes technology.

Open-Ended Questions

Parents had an optional opportunity to answer two open-ended questions at the end of the demographic questionnaire addressing barriers and facilitators in insulin pump use. The questions were "what is one thing that makes use of insulin pump most difficult" and "what is one thing that makes use of insulin pump most helpful?".

Analysis

Quantitative data were summarized using descriptive statistics; continuous variables were summarized using mean and standard deviation, and categorical variables using percentage. Univariate analysis was conducted to explore the association between independent variables and the outcome variable (diabetes-related distress reported by parents). Multivariable linear regression models were used to evaluate the measures of diabetes-related distress by the parents while accounting for covariates from the individual and family domains. Multivariable analysis was created by taking into account the modifiable variables in the family domain, as long as the correlation between PAID-Parent total score was less than 0.6. Moreover, variables were selected to be included if it was a modifiable variable about the adolescent with T1D. For instance, SMOD-DCA and DTQ total scores are modifiable variables in the individual (about the adolescent with T1D) domain, and the FAD-GF12 was included although it was filled out by the parent, since it is a reflection of the family including the adolescent. PIP was specifically asking the parent's stress level in taking care of a child with a chronic condition, and was not included. The final model included FAD-GF12, SMOD-DCA total score, and DTQ total score. Beta

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coefficients with 95% confidence intervals are reported for this analysis. Stata/SE 16.1

(StataCorp. 2019.Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC.)

was used to perform statistical analysis. A priori value p-value of less than 0.05 was set.

Results

Of the 59 families approached, 35 parents and adolescents completed the e-consent and

filled out the self-report survey. The mean age of the adolescents with T1D included in this study

was 14.9 ± 1.7 years, with a mean diabetes duration of 7.3 ± 4 years. 63.6% of the adolescents

were female, and 82.9% of the self-report surveys were completed by mothers. The mean age of

the parents of the adolescents with T1D was 46 ± 6 years of age. The majority of the respondents

reported having an education level of having a bachelors degree or greater, and a family income

of greater than U.S. $100,000/year. Lastly, 71.0% reported having private insurance, and the

three participants reporting MDI use all reported having public insurance (CCS). The

convenience sampling population had unusually high usage of insulin pumps and CGM, where

only three families reported using MDI, and 30 (90.1%) reported using insulin pumps.

Moreover, more than half of the insulin pump users reported being on a hybrid closed loop

system. All but one participant has reported CGM use at one point, and 27 participants had

sensor TIR data at the time of enrollment. Amongst the three MDI users, only one participant

had CGM TIR data. The two MDI users also reported having lower than average DTQ scores (92

and 93), where the overall mean DTQ score for this sample was 96.0 ± 15.1.

The primary outcome of interest was the P-PAID-T total score. The possible score

ranges from 14 to 84, where higher scores indicate higher diabetes-related distress. The mean

PAID-Parent total score was 44.23 ± 14.5 ranging from 21 to 82. As expected, the PAID-Parent

and the PAID-Teen scores were positively correlated with r=0.612. The two measures of

glycemic outcomes (A1C and TIR) were statistically significant in their association with P-PAID-T scores (p=0.001 and p<0.001, respectively), showing higher PAID-Parent score was associated with higher A1C and lower TIR (suboptimal glycemic control).

Univariate linear regression analysis was used to analyze variables of interest in the individual and family domain (See Table 1). Significant associations were found between P-PAID-T scores and parental stress level (PIP-Diff), general family functioning (FAD-GF 12), diabetes care self-management by the adolescent (SMOD-A, DCA), and adolescent's satisfaction level with diabetes technology use (DTQ). The parent stress level was positively associated with diabetes-related distress (r=0.49, p=0.004). The family functioning scale was also positively associated with diabetes-related distress, indicating higher the family dysfunction, the higher the diabetes-related distress (p=046, r=0.354). Higher self-management of diabetes care activities reported by the adolescent was negatively associated with the parent's diabetes-distress level (p=0.003, r=-0.519). Moreover, the adolescent's satisfaction with diabetes technology use was negatively associated with parental distress (p=0.031, r=-0.408).

Table 4.1 Individual and Family Variables and PAID-Parent Total Score Association by Univariate Linear Regression Analysis

Variables (n)	M±SD or Percentage (%)	β-coeff	CI		P-Value
Parent related variables					
Parent Age, years (32)	46±6.0	-0.686	-1.540	0.167	0.111
Survey By Mother (35)	82.9%	-8.776	-21.827	4.276	0.181
Parent Education, bachelors and above (27)	55.6%	-6.933	-18.267	4.400	0.219
Family Income > U.S. $100,000/year (29)	68.7%	-10.678	-4.085	0.700	0.159
Pediatric Inventory for Parents (PIP) Diff Total Score (33)	90.2±28.9	0.240	0.084	0.360	**0.004**
Family Assessment Device – GF12 Total Score (32)	1.7±0.5	10.610	0.183	21.034	**0.046**
Teen related variables					
Age of Adolescent, years (35)	14.92±1.7	-0.236	-3.245	2.773	0.874
SMOD-Diabetes Care Activities Total Score (30)	29.9±6.6	-1.172	-1.918	-.0425	**0.003**
PAID Teen Total Score (29)	37.22±13.4	0.667	0.327	1.007	**<0.001**
Diabetes Technology Questionnaire Total Score (28)	95.92±15.1	-0.360	-0.684	-0.035	**0.031**

The multivariable regression model showed the adolescent's dissatisfaction with the diabetes technology was associated with a higher level of diabetes-related distress reported by the parents p=0.045, β coeff = -0.333, with an adjusted R^2 value of 0.229(See Table 2).

Table 4.2 Multivariable Regression Model for Modifiable Individual Variables and Parent Diabetes-Related Distress

Variables (n)	M±SD or Percentage (%)	*β*-coeff	CI		P-Value
Family Assessment Device –GF12 Total Score (32)	1.7±0.5	8.695	-3.710	21.098	0.160
SMOD-Diabetes Care Activities Total Score (30)	29.9±6.6	-0.554	-1.314	0.206	0.145
Diabetes Technology Questionnaire Total Score (28)	95.92±15.1	-0.333	-0.659	-0.008	**0.045**

The qualitative data from the optional free-text by the parents inquiring about barriers and facilitators of using an insulin pump is summarized in Table 3. Total 28 parents out of 35 responded to the free-text questions addressing barriers and facilitators to using an insulin pump. Parents shared the inconvenience of changing supplies, such as insulin insertion sites, and cartridges every three days associated with using an insulin pump. Also, it is challenging when the insulin pump gets disconnected from the body physically due to tubing getting into door handles, or inadvertent movement. Also, the connectivity issue with the sensor was challenging. The constant reminder from the alarm and the cost of the pump was also a challenge. Parents also reported many benefits and how the insulin pump has been helpful. Many parents reported that not having to deal with multiple injections daily in order to administer insulin was beneficial. The pump's ability to administer insulin was more accurate when compared to the manual injections and not having to carry as many supplies. Parents also mentioned the benefits of using a hybrid closed loop: it can make up for "neglect or mistakes", and the HCL's ability to shut off when BG is too low versus increasing basal insulin when BG is rising.

The barriers to diabetes technology use can be categorized into three domains: structural, psychological and physical.[25] In our data, structural barriers were the inability of a guardian or

primary caretaker and the adolescent to attend pump training courses due to lack of time or availability or the cost and coverage of the technology by the insurance. Psychological barriers were the intimidation or anxiety associated with being prescribed a new diabetes technology or the constant need to address the alarms. Physical barriers are also associated with skin trouble from the diabetes infusion set adhesive or running out of skin spaces to insert insulin infusion sites or sensors.

Table 4.3 Barriers and Facilitators of Insulin Pump Use

How Insulin Pump is Difficult?	How Insulin Pump is Helpful?
Structural	**Structural**
Cost	Not having to deal with syringes daily, easy to administer insulin, insulin ready to go at all times
Lack of "loop"	Accurate dosing of insulin, not have to calculate doses manually
Changing supplies (e.g. cannula and insulin cartridge every 3 days)	Ability to adjust basal rates
Psychological	HCL making up for "neglect or mistakes" Basal shutting off when BG too low, and increasing bolus when BG high, auto-correction
Intimidating	Not having to carry supplies
Not being able to see it or control it from parent's perspective, not getting real time data from the pump about boluses so the parent can stay out of the "child's space" and information about insulin on board.	**Psychological**
Alarms, a constant reminder	Freedom!
Physical	**Physical**
Being in the hospital	Not having tubes
Running out of "spaces" for insertion of insulin infusion or sensors	
When it gets disconnected (from the body, CGM)	

Discussion

The purpose of this study was to explore factors associated with diabetes-related distress in parents caring for adolescents with T1D. The second aim was to qualitatively describe insulin pump-related barriers and facilitators by parents. Diabetes-related parent distress is a modifiable variable and is amenable to behavioral intervention. It is also a variable that has been associated with the glycemic outcome of adolescents with T1D. Moreover, family variables are one of the most important domains to be mindful of in adolescent chronic disease management.[26]

In the univariate regression analysis, the two modifiable variables associated with parental diabetes-related distress for adolescents 12 to 17 years of age appear to be related to the *act* of diabetes care. None of the non-modifiable variables, such as age of the parent, who the survey was completed by, parent education level, or annual household income had a statistical significance in its association with diabetes-related distress. Two modifiable variables by the parent (parents stress level, family functioning scale), and three modifiable variables by the adolescent (self-management, diabetes care, diabetes distress of teen, and diabetes technology satisfaction) were found to be statistically significant in its association with parent diabetes-related distress.

A significant part of diabetes self-management involves the use of diabetes technology, from monitoring of the BG levels, administration of insulin to reviewing of the data making dose adjustments or behavioral modifications.[27] As the adolescent reports feeling more confident in self-management of diabetes care activities, and satisfaction with diabetes technology, the less parents report feeling distressed. This also intuitively makes sense, because if the adolescent is showing confidence, positive attitude towards interacting with their diabetes care via using insulin pumps and sensor, the parent will be able to trust and feel less helpless or in distress.

In the current literature, there are varying levels of distress across different levels of diabetes technology adaptors.[25] The DTQ survey included all of the devices which were part of the adolescent's insulin regimen, including glucose meters, insulin pumps, sensor-augmented insulin pumps, hybrid closed-loop and CGM. The MDI users in this study reported had lower than average scores indicative of lower diabetes technology satisfaction, while users of advanced technology (e.g. HCL or looping with APS), reported some of the highest levels of diabetes technology satisfaction.

The multivariable regression analysis associated parent diabetes-related stress with modifiable variables involving the adolescents showed that *only* satisfaction with diabetes technology was statistically significant. Increased adolescent satisfaction with diabetes technology was associated with lower parental distress level related to diabetes reporting was lower. Many of the participants of this study were using diabetes technology, such as an insulin pump with or without a hybrid closed loop and CGM as a way of self-managing diabetes. A recent study conducted in Germany reported a negative correlation between PAID score and diabetes treatment satisfaction score, where high diabetes-related distress can negatively affect treatment satisfaction.[28] This study only assessed the variables within the individual domain and did not indicate the impact of the diabetes-related distress of the parent of the adolescent with T1D. In addition, it looked at the diabetes treatment satisfaction as a whole, unlike our study looking specifically at the adolescent's diabetes technology satisfaction. In our study, if the adolescent reported positive attitude towards interacting with their diabetes technology as their primary tool of diabetes care, the parents were less likely to feel distressed about the adolescent's diabetes. As the adolescents build more independence in diabetes self-management through utilization of diabetes technology, the parents' roles and distress-related to diabetes management

decreases the positivity in satisfaction observed from the adolescent will enable the parent to more easily relinquish the control over diabetes care to the adolescent.

Parental internal conflict to relinquish control and surveillance over the diabetes technology of the adolescent is reflected in the open-text analysis from the parent, indicating barriers to insulin pump use as "not being able to see or control" pump. The desire to stay "out of the child's space", is reported, but at the same, wishing for real-time data from the diabetes technology to be accessible by the parent is also shown. This is reported in the literature, for instance a qualitative study also revealed the theme of "fear" in negotiation of developmental transitions. The concern about whether the child will navigate through normal growth and developmental processes safely, realizing they need to encourage independence to promote normal development, was a significant source of distress for the parents with adolescents with T1D.[29]

Our data also reflects the literature, where more non-Hispanic whites with private health insurance, higher income, and parent with higher education are more likely to be on pump therapy.[30] Transition into adolescence results in a shift of increase in peer influence over parents. This transition period is critical for families with adolescents with T1D, and a whole-person approach inclusive of variables both the individual and the family is important for achieving optimal glycemic outcome.[31]

The major limitation of this study is the cross-sectional design of a small study sample comprised of predominantly higher SES groups. As with many studies, the nature of convenience sampling is over-representative of adolescents and families with familiarity with technology in general since all of the recruitment was done during a telehealth visit, and the family had to be willing to fill out a corresponding self-report survey via email. The patient

recruitment phase coincided with the first year and a half of the COVID-19 pandemic, therefore the population successfully attending Telehealth visits were also likely biased to a higher SES population. Lastly, the DTQ's psychometric validation was published as an abstract, but has not yet been published.[32] The relationship between glycemic control, diabetes technology acceptability, and variables in the individual, family, community and health care systems is an important topic to continue to explore in order to minimize the gap. Furthermore, additional research including additional members of the family, like siblings, and close friends while also being inclusive of ethnic and cultural diversity will be needed.

Conclusion

The use of diabetes technology has been shown to decrease the risk for both short-term and long-term complications by improving glycemic outcomes.[8, 16, 33] Still, the complexity associated with effectively using the diabetes technology involves a steep learning curve for families, and there is a need to future need to investigate the gap or discrepancy between the families who adapt successfully when compared to those who discontinue use, or have never been prescribed. Moreover, the transition of care of T1D into adolescence and young adulthood is a challenging time, and factors in the family, community, and health care systems domains must be considered in understanding or addressing the gap.

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CHAPTER FIVE

Conclusion: Bringing It All Together, Implications and Future Research

Purpose of the Dissertation

This study aimed to describe the relationship between diabetes self-management, factors in the individual and family domains and its association with glycemic outcomes in adolescents with type 1 diabetes (T1D).

Summary of the Findings

The literature review over the past two decades showed decrease in insulin pump discontinuation in pediatric patients with type 1 diabetes (T1D). There was a lack of studies exploring variables in the family, community, and healthcare systems related to discontinuing insulin pumps. Higher hemoglobin A1c (A1C), older age, and female gender were frequently reported to be significantly associated with insulin pump discontinuation.

The cross-sectional study compared factors from the individual and family domains and their association with glycemic control defined by two outcomes, A1C and time spent in range (TIR) from 70-180mg/dL. Parental diabetes-related distress level was statistically significant in its association with both glycemic outcomes, A1C and TIR. Higher income was associated with lower A1C, and higher levels of parental education was associated with greater TIR. The two models indicate parental diabetes-related distress and socioeconomic status (SES) levels are key factors related to the adolescent's glycemic outcomes, which were more significant than any other individual for family factors. Lastly, parent diabetes-related distress was analyzed in a multivariable model. This analysis showed that the higher level of satisfaction of the adolescent with their diabetes technology the lower the parent's diabetes-related distress.

Common findings across the three papers include that 1) the relationships between glycemic outcome, diabetes technology use, and how it relates to the variables in the individual, family,

community, and health care systems domain is a complex one, 2) when trying to understand the factors contributing to glycemic outcomes in adolescents, variables in the family domain must be taken into account, and 3) that there is a gap between those who adapt well and use diabetes technology when compared to those who are either not prescribed or continue the diabetes technology use to self-manage T1D. This disparity appears to be related to SES, but modifiable variables such as parent's level of diabetes-related stress should also be considered.

Significance and Implications

The participants in this study represent a unique subset of the population with higher than usual use of diabetes technology use, including more than half of the participants utilizing hybrid closed-loop (HCL) systems, and almost all of the participants were using CGM. The mean A1C of the participants was at $8.5\pm2.6\%$, which meant the majority did not meet the target glycemic outcome of less than 7% recommended by the American Diabetes Association (ADA) and the International Society for Pediatric and Adolescent Diabetes (ISPAD). Twenty-six of the thirty-five participants also had TIR data. The mean of $60.5\pm20\%$ which was lower than the recommended target value of greater than 70%, but the standard deviation varied greatly. Our sample size was small. It is notable that even within this group of highly adapted to diabetes technology, the glycemic control in the 12 to 17 years of age is a challenge.

Many of the variables between the individual and family domains are interrelated, meaning the direction or the causality is difficult to establish. Moreover, since this study was a cross-sectional study, we can only able to assume the associations among the variables. It is important to note that only parental factors were statistically significant in its association to glycemic outcome for both modifiable and non-modifiable categories in this model. On the other hand, the only statistically significant modifiable variables associated with parental diabetes-related distress was the adolescent's satisfaction level with diabetes technology. This implies that the parent's diabetes distress level must be considered when addressing the adolescent's glycemic outcome. Moreover, since diabetes technology satisfaction was associated with parent distress level, helping the adolescent feel more confident and satisfied with their

diabetes technology device may be key to improve glycemic outcomes and decreasing parent diabetes-related distress. A wide body of literature has shown that use of diabetes technology such as an insulin pump, CGM, and HCL technology, improve glycemic outcomes. Providing education for both the individual and the parent to improve satisfaction of diabetes technology may be critical to help adolescents with T1D to improve glycemic outcomes. Clinicians, researchers and policymakers must work on making this diabetes-technology equally accessible to families across all socioeconomic status.
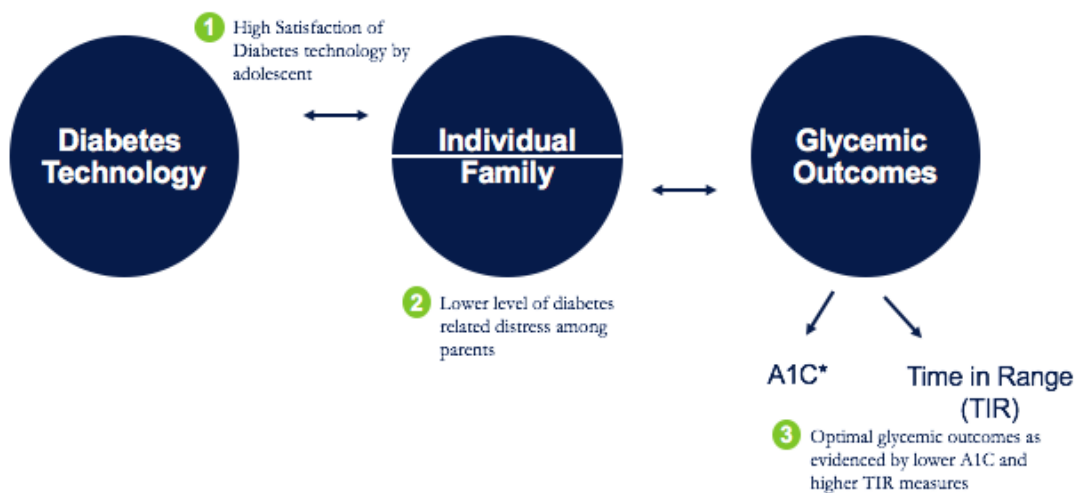
Study Conclusion

Figure 5.1 Study Conclusion

Limitations

The limitations of this study are that it is a cross-sectional study of a small sample size, and therefore the generalizability of the findings is limited. The data collection process also was a convenient sampling of those families who were attending a virtual telehealth visit and had access for the parent and

the adolescent to fill out an online survey. Most importantly, the initial aim of this study was to create a model including factors from all four domains (individual, family, community, and health care systems), but due to the lack of sample size, only the first two domains were explored.

Recommendations for Future Research

There is a need to consider community and health care systems factors in order to further understand the relationship between the individual and what ultimately has the most important impact on the glycemic outcome. Also, a study looking at how the conversation about diabetes technology use is initiated between the providers and the family with T1D, and what are the barriers and the facilitators of the maintenance or continual use of the diabetes technology. Lastly, there are many options available for both insulin pumps and sensor. The decision process by the family and the provider on helping to identify the best diabetes technology, or the best match, will be necessary.

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