Abstract

Affective and Physical Symptom Experiences in Type 2 Diabetes: An Evaluation of Bidirectionality using Ecological Momentary Assessment and Qualitative Analysis

Background: Physical symptoms (SXS) are commonly reported among adults with type 2 diabetes (T2D) and have a significant impact on functioning and diabetes self-management. Although there is evidence that symptom reporting and symptom attribution (SA) are closely linked to the experience of negative affect (NA), the directionality of this relationship remains unclear. This study used ecological momentary assessment (EMA) and qualitative interviewing to evaluate potential bidirectional associations of NA with SXS and SA among adults with sub-optimally controlled T2D.

Methods: The present study is a secondary analysis of EMA and qualitative data from a diverse sample of adults with T2D (N = 61; Age = 55.6 (9.6 years); Women = 64.5%; Black = 61%; Latino = 36%; HbA1c = 8.6(2.3)) that participated in a pilot study assessing affective states, physical symptoms, and diabetes self-management behaviors 3-times daily over a 14-day period via EMA. Path modeling (within same day) and cross-lagged path analyses (survey to survey, day to day, over full study period) were used to evaluate directional relationships of total number (range: 0-13) of SXS reported and subsequent levels of NA (range: 0-5), and vice-versa. SA was evaluated used using 2 questions following reports of SXS which asked the extent to which participants attributed their SXS to diabetes or diabetes medications on a scale of 0-4. Thematic analysis was conducted to evaluate qualitative exit interviews, highlighting the potential impact of NA, SXS, and SA from the patient perspective.

Results: The directional pathway from NA to SXS was shown to be significant on both the same-day and lagged levels, in both fixed effects within-persons and between-persons analyses.

Same-day analyses demonstrated that, on a within-persons level, a 1-point increase in NA from one's personal mean was associated with a 0.42-point increase in subsequent physical symptom experience within the same day (95% CI: 0.25-0.59, p <.01). Cross-lagged path analysis demonstrated a 1-point increase in NA from one's personal mean was associated with a 0.14-point increase in subsequent symptom experience (95% CI: 0.03 - 0.25, p <.01). Similar trends were found on the between-persons level. The directional pathway from SXS to NA was shown to be significant for both same-day within-person fixed effects, and between-person fixed effects levels. Same-day analyses demonstrated that, on a within-persons level, a 1-point increase in SXS from one's personal mean was associated with a 0.12-point increase in subsequent NA within the same day (95% CI: 0.08 - 0.17, p <.01); on a between-persons level, a 1-point increase in SXS from one's personal mean was associated with a 0.52-point increase in subsequent NA within the same day (95% CI: 0.31 - 0.69, p <.01). Day-level results indicate bidirectionality, with pathway significance identified in both the NA to SXS and SXS to NA directions. The NA to symptom attribution to T2D pathway was found to be significant as a 1-point increase in NA from one's personal mean was associated with a 0.16-point increase in attribution score (95%CI: 0.01 - 0.32, p <.01) between-persons. Moderation analyses demonstrated that symptom attribution did not significantly moderate the relationship between symptom experience and NA, such that attributing symptoms to diabetes and/or diabetes medication was not predictive of a significant increase in NA. Qualitative analysis supported similar patterns to those observed in quantitative findings with participants reporting impactful connection between NA and SXS, though direct illustration of the bidirectional relationship between symptom experience and affect could not be concluded.

Discussion: Results showed a bidirectional pathway between NA and SXS, on the day-level, with the NA to SXS pathway further supported in cross-lagged analyses. Pathways illustrated that an increase in NA was related to an increase in SXS as next time point both overtime and within same day. The reverse relationship was seen within same day, but not overtime. The salience of the relationships between NA and SXS was also observed through qualitative analysis of exit interviews with participants. These findings from predominantly ethnic minority adults with T2D largely supported hypotheses. If these associations are causal, these results suggest that interventions that reduce negative affect would also reduce the experience of physical symptoms and vice versa. Given prior evidence linking these NA and SXS to self-management, functioning, and health outcomes in T2D, such interventions could have a substantial impact. The current study's findings contribute to the literature supporting relationships among NA, SXS, and SA and also demonstrate the necessity for future research to understand the complexities of influence among the examined variables to inform future intervention design.

Affective and Physical Symptom Experiences in Type 2 Diabetes: An Evaluation of Bidirectionality using Ecological Momentary Assessment and Qualitative Analysis

by
Sarah R. Fishman

Submitted in partial fulfillment of requirements for the degree of
Doctor of Philosophy
In the Ferkauf Graduate School of Psychology
Yeshiva University
May 2022

The committee for this dissertation consisted of:

Jeffrey S. Gonzalez, PhD, Chairperson
Ferkauf Graduate School of Psychology, Yeshiva University
Albert Einstein College of Medicine
NY-Regional Center for Diabetes Translational Research (CDTR)

Betsy Seng, PhD, Committee Member
Ferkauf Graduate School of Psychology, Yeshiva University
Albert Einstein College of Medicine
Research Associate Professor, Department of Neurology

Andrea Weinberger, PhD, Committee Member
Ferkauf Graduate School of Psychology, Yeshiva University
Albert Einstein College of Medicine
Research Assistant Professor, Department of Epidemiology and Population Health

The readers of the dissertation consisted of:

Jill Crandall, MD, Reader
Albert Einstein College of Medicine
Jacob A. and Jeanne E. Barkey Chair Medicine
Professor, Department of Medicine (Endocrinology)
Chief, Division of Endocrinology

Bari Hillman, PhD, Reader
Ferkauf Graduate School of Psychology, Yeshiva University
Director of Clinical Training, Ferkauf Graduate School of Psychology

Acknowledgements

I am so thankful to my committee members, classmates, lab-mates, family, and friends – their support throughout this process has been remarkable and has had such a positive impact on the process of completing my dissertation. Specifically, I would like to thank Dr. Jeffrey Gonzalez for being my mentor throughout graduate school. I have immense gratitude for his support, guidance, and mentorship throughout my doctoral training. You have supported me in combining my clinical and research interests and have encouraged me to explore analytical methodology beyond what I thought I was previously capable of. I would also like to thank my committee members, Dr. Betsy Seng and Dr. Andrea Weinberger, for your thoughtful feedback, advice and support throughout this project. It has been such a pleasure to be your student, and I have learned so much from both of you within your classrooms and beyond. Thank you to Dr. Jill Crandall and Dr. Bari Hillman for your time and willingness to contribute to this process as readers and for agreeing to contribute your feedback to my dissertation. Lastly, I would like to express my deepest gratitude and appreciation to my family. To my parents, Robin and Matt, I am so appreciative of your consistent support, unconditional love, and willingness to believe in me no matter what path I choose to take, or how long that path may be. To David and Caity, thank you for your ever-present positivity and encouragement, and thank you for always being willing to distract me. To Dan, thank you for your patience, willingness to listen to my presentations multiple times, and for providing unwavering love and humor throughout this journey.

Table of Contents

List of Tables

List of Figures

List of Appendices

Chapter I: Background and Significance

Diabetes Introduction

Diabetes Mellitus is a chronic health condition identified as the eighth leading cause of death in the United States (U.S.) in 2020, previously ranking as the seventh leading cause of death in 2019 (Ahmad & Anderson, 2021). Though this change in ranking may at first appear positive, the CDC rankings for leading causes of death in the U.S. were impacted by COVID-19. As such, diabetes prevalence continues to increase. Over the past 20 years, the number of adults diagnosed with diabetes has doubled, and estimates suggest that if current trends continue, 1 in 3 adults in the U.S. population will be living with diabetes by 2050 (Center for Disease Control and Prevention, 2010). This chronic metabolic disease group, including Type 1 Diabetes, Type 2 Diabetes, Gestational Diabetes, and Prediabetes, accounts for millions of individuals managing diagnoses and navigating various treatment options (Center for Disease Control and Prevention, 2020; American Diabetes Association, 2020b). It is estimated that over 37 million individuals within the United States were living with a diabetes diagnosis in 2019 and more than 8 million of these individuals are living with undiagnosed diabetes (Center for Disease Control and Prevention, National Diabetes Report, accessed April 2022). The cost and burdens of diabetes management represent a significant public health challenge within the U.S. As diabetes is a primary cause of kidney failure, lower-limb amputations, and adult blindness (Center for Disease Control and Prevention, 2020), these trends represent a major threat to the nation's health and economy.

Type 1 & Type 2 Diabetes Overview

Both Type 1 and Type 2 Diabetes involve dysregulation in the production and use of insulin, a vital hormone that regulates blood sugar (also called glucose) levels in the body.

Approximately 5-10% of individuals with a diabetes diagnosis have Type 1 Diabetes (Center for Disease Control and Prevention, 2020). Individuals with Type 1 Diabetes tend to produce none or very little insulin, which in turn impacts the ability of blood sugar to enter cells, leading to a build-up of glucose in the bloodstream over time. Although Type 1 Diabetes usually develops in children and young adults, it can be diagnosed at any age. Symptoms include frequent urination, excess thirst, frequent hunger, weight loss, blurred vision, and general fatigue, and treatment requires daily administration of exogenous insulin (World Health Organization, 2018). Hyperglycemia (when the body has too little insulin to use the sugar in blood; high blood glucose) episodes can happen daily for individuals with T1D and involve a variety of possible symptoms: extreme thirst, increased urination, fatigue, challenges with concentration, stomach pain/nausea, sweet-smelling breath, unexplained weight loss, and cuts or sores that do not heal (Juvenile Diabetes Research Foundation, Accessed April 2022). Treatments required to control hyperglycemia can sometimes cause hypoglycemia (low blood sugar, insulin reaction, insulin shock), including symptoms of feeling shaky, nervousness/anxiousness, sweating/chills, irritability/impatience, confusion, increased heartbeat, lightheadedness, hunger, nausea, pallor, fatigue, blurred/impaired vision, facial tingling/numbness, headaches, challenges in coordination, and nightmares. In its most dangerous cases, hypoglycemia can cause outcomes including seizures, unconsciousness, comas, or death (Briscoe & Davis, 2006).

Type 2 Diabetes Mellitus (T2D) accounts for 90-95% of individuals diagnosed with diabetes and most commonly develops in individuals over 45-years old, though the age of onset is trending younger over time (World Health Organization, 2018). T2D involves two primary challenges – (1) the pancreas does not produce enough insulin, and (2) cells respond poorly to insulin and take in less glucose. T2D is often caused by insulin resistance, and general inability

for cells to normally respond to insulin. The pancreas produces insulin in an attempt to prompt a response from cells and when the pancreas cannot keep up with insulin production requirements, blood glucose rises. Hyperglycemia is also a serious concern for individuals managing T2D and can also cause other health problems (heart disease, vision loss, kidney disease) (Center for Disease Control and Prevention, 2020). Symptoms of T2D include increased urination and thirst, hunger, unintentional weight loss, fatigue, blurred vision, slow-healing sores, and frequent infections (World Health Organization, 2018). As mentioned with T1D, treatments required to manage and treat hyperglycemia can sometimes lead to hypoglycemia and poor health outcomes (myocardial infarction, seizures, brain damage, coma, death) (Yun & Ko, 2016).

The diagnosis, progression, and symptom burden of T2D have a significant impact on the life of the patient and their ability to function. This impact increases throughout disease progression, often accompanied by increasing burden of treatment and self-management regimens (Russell et al., 2005; Redekop et al., 2002; Wexler et al., 2006). Treatment may include oral medications, insulin administration, blood sugar monitoring, and typically requires changes to lifestyle and daily routine (e.g., diet, exercise, weight management). The self-management of diabetes is critical to preventing potentially fatal complications for those that suffer from this disease and has also been noted to be time-intensive (e.g., medication adherence, exercise) and costly (e.g., accessing non-processed and low-sugar food, cost of medication, insulin, and other health insurance) for patients and families (American Diabetes Association, 2021c).

Type 2 Diabetes Symptom Impact

The burden of T2D experience can influence one's ability to manage symptoms, side-effects, and treatment regimens. This burden may prove to become more challenging over time as self-management and self-efficacy abilities have been previously linked to diabetes control

outcomes (Al-Khawaldeh et al., 2012). When well-controlled, T2D typically presents as asymptomatic. However, symptoms are commonly reported by patients (Lustman et al., 1986) and can have a significant impact on functioning (Redekop et al., 2002; Wexler et al., 2006). Individuals may experience a variety of ongoing symptoms associated with glycemic dysregulation including fatigue, blurred vision, pain, interrupted sleep, increased urination, and increased thirst (Chen, Magliano, Zimmet, 2012).

Over time, the health impacts of diabetes can become more challenging. T2D can damage the heart, blood vessels, eyes, kidneys, and nerves (World Health Organization, 2018). Further, adults with T2D are at increased risk for heart attacks and strokes (Emerging Risk Factors Collaboration, 2010). When combined with reduced blood flow, nerve damage (neuropathy) can increase the likelihood of foot ulcer development, infection in limbs, as well as amputation. Neuropathy also significantly impacts an individual's mobility and independence (World Health Organization, 2018), presenting additional challenges for those that need to incorporate physical activity as a part of their T2D treatment plan. Nearly 1 million people experience blindness due to diabetes, as diabetic retinopathy occurs as a result of long-term damage to the retina's small blood vessels (Steinmetz et al., 2021). Diabetes is also among the leading causes of kidney failure (USRDS, 2015). Taken together, the experience of such advanced symptoms and side effect development is associated with higher levels of negative affect and emotional distress (Skaff et al., 2009; McAndrew et al., 2014; Fisher et al., 2009; Hernandez et al., 2019; Perrin et al., 2017).

Disease Experience and Treatment

To achieve and maintain adequate control of diabetes, treatment often requires several medications and consistent medication adherence over time. Although diabetes medications can

substantially decrease disease related morbidity, mortality, and progression, the extent of treatment benefits is often limited by patient adherence (Rubin, 2005). For example, when comparing real world efficacy and Randomized Control Trial (RCT) settings, poor medication adherence was found to be the primary reason that real world effectiveness of treatment is slightly less than that observed in efficacy RCTs of diabetes medications (Carls et al., 2017). This presents a challenge, as much of diabetes management takes place outside of the treatment setting, leaving maintenance and monitoring up to the patient.

Managing treatment outside of the medical and research setting may feel burdensome and challenging. Increased diabetes treatment burden (increase in reported burden by individuals over time) is associated with emotional distress and difficulties in adhering to self-management behaviors (Delahanty et al. 2007). This relationship has been shown to further elevate disease-related distress, disappointment, and self-blame regarding self-management behaviors (Snoeck et al., 2012; Tannenbaum et al., 2016). The T2D treatment experience can be particularly challenging as patients report that increases in treatment intensity and regimen complexity (e.g., insulin, glucose control, oral medication adherence) are associated with anticipated negative changes in quality of life and symptom experience (Rubin & Peyrot, 1999; Huang & Brown, 2007). These anticipated negative effects often contribute to resistance on the part of patients to accept treatment intensification such as the addition of insulin to an oral medication regimen. This has been referred to as “psychological insulin resistance” (Polonsky, et al., 2005).

Diverse populations (e.g., non-Hispanic Black and Hispanic individuals) experience greater incidence of T2D, worse T2D-realted health outcomes, and higher mortality rates compared to non-Hispanic White individuals (Golden et al., 2012). As of 2019, diagnoses of new diabetes cases were substantially higher among non-Hispanic Black individuals (12.1%) and

people of Hispanic origin (11.8%) than non-Hispanic Asian individuals (9.5%%) and non-Hispanic White individuals (7.4%) (Center for Disease Control and Prevention, 2020). Further, meta-analyses show that both Hispanics individuals and non-Hispanic Black individuals have worse glycemic control than non-Hispanic White individuals with T2D (Kirk et al., 2006; Kirk et al., 2008; Cavagnolli et al., 2017). As previously mentioned, the progression of sub-optimally controlled T2D can lead to complications such as retinopathy, nephropathy, heart, and kidney disease as well as foot problems (Center for Disease Control, 2018), highlighting the importance of disease management and maintenance, especially in minority groups given prevalence rates (Center for Disease Control, 2020; Stratton et al., 2000; Fonseca, 2009).

The monitoring of diabetes symptoms and screening for the development of complications is a crucial priority for health care providers (Lustman et al., 1989). While T2D has various causes, genetic/family history, and environmental factors (e.g., access to non-processed food, ability to exercise) may influence predisposition to the condition, as do lifestyle factors (e.g., obesity, insulin resistance due to weight) (Center for Disease Control, 2020). Diabetes treatment-related side effects may also cause barriers to treatment adherence, causing symptoms that last upwards of 1-month, which can be chronic (Grant et al., 2003). Side effects of treatment are common and may include nausea, vomiting, diarrhea, pain, kidney complications, and fatigue (Care, 2019; Maruthur et al., 2016). Side effects of treatment have also been identified as an influence on challenges with treatment adherence, greater emotional distress, and increase in negative beliefs about treatment (Horne et al., 1999; Chao et al., 2007; Catz et al., 2000; Grant et al., 2003). Emotional distress may impact and exacerbate side effects, as supported by the symptom perception hypothesis, which posits that the predisposition to

frequently experienced negative emotions is associated with inflated physical symptom reporting (Love et al., 1989).

Symptom Endorsement

Symptoms are typically understood as a signal to an individual that some internal bodily activity is different. This signal causes assessment of the process by which feelings, sensations, perceptions, and cognitions have changed. These changes are ultimately due to the individual's response to the initial stimuli (Teel et al., 1997). When individuals are given a diagnosis, they generally search for symptoms that fall under the diagnostic umbrella of the given illness, even when the illness experience is asymptomatic (Petrie, 2006). For example, an individual that is given the diagnosis of arthritis may be more aware of stiffness, pain, and shifts in range of motion than they were prior to diagnosis, even if their symptom experience did not change post-diagnosis. This symptom identification effort illustrates the desire that many individuals have to make sense of their illness.

Many individuals with diabetes fear the consequences of having hyper- or hypoglycemic episodes, causing frequent monitoring of symptoms, often accompanied by significant worry (Vallis et al., 2014). Individuals fearing a hypoglycemic episode may be more acutely aware of shortness of breath, nausea, fatigue, dry month, and confusion, among others. Hypoglycemia symptoms of focus may include irregular heartbeat, shaking, fatigue, sweating, and pale skin. Further, symptoms of abnormal blood glucose levels may prompt action to alleviate short term discomfort (e.g., increased urination, thirst, blurred vision). However, to avoid long-term complications and frequent occurrence of hyper- and hypoglycemic episodes, there is an emphasis placed on preventative and proactive symptom monitoring. (Wild et al., 2007; Hampson 1997). Although self-monitoring of blood glucose through finger-stick and use of a

glucose meter is a common component for many patients living with T2D and is recommended to ascertain blood glucose levels that can change without symptom variation, research suggests that patients often rely on symptoms to guide their appraisals of their blood glucose (Allemann et al., 2009; Hampson, 1997).

Tracking and accurately endorsing diabetes-related symptom occurrence and intensity can be quite challenging, especially when using retrospective self-report data collection. Retrospective symptom assessments are often biased (Walentynowicz et al., 2017) when compared to momentary assessments of symptoms (Van den Berghn & Walentynowicz, 2016; Walentynowicz, et al., 2015). In-the-moment symptom experience and symptom labeling provides the opportunity to name each feeling as it is experienced and associated with each symptom stimulus in real time, avoiding potential issues of inaccurate symptom recall (Teel et al., 1997).

Symptom Attribution and Communication

Symptom attribution is another important aspect of the appraisal of physical symptoms that is expected to have an influence on emotional responses and self-management and care-seeking behaviors. Symptom reporting and categorization provides an organizational basis for symptom recognition and attribution. Deciding what to do about a symptom (e.g., seek care, worry, ignore) often depends on what the individual believes is the cause of the symptom (e.g., cause by illness or illness-related medication; Gonder-Frederick & Cox, 1991; Robbins & Greenley, 1983; Robbins & Kirmayer, 1986).

As individuals with T2D experience their illness overtime, they develop frameworks to make sense of their illness experience. These illness perceptions and intuitive ‘common sense

models' guide behaviors and activities in daily life, which in turn impact how the individual will respond to and manage their illness (Leventhal et al., 2003; Petrie & Weinman, 2006).

As previously explained by The Symptom Perception Hypothesis, negative affectivity acts as a predictor of increased physical symptom reporting such that the presence of NA typically magnifies minor physical experiences to be reportable symptoms (Watson & Pennebaker, 1989). Because symptoms may be ambiguous and subjectively dependent on the patient's attribution and experience, it is important to evaluate symptoms in conjunction with emotion and/or psychological variables (Robbins & Kirmayer, 1991).

Prior research suggests that, compared to those without depression and anxiety, individuals experiencing mood and anxiety-related symptoms and disorders are more likely to report an increased number of physical symptoms, sometimes lacking medical explanation (Katon et al. 2007). Medically unexplained symptoms are strongly and consistently associated with increased emotional distress, depression, and anxiety (Kolk et al., 2002). Additionally, increased negative affectivity has been repeatedly associated with heightened awareness of physical sensations and somatic symptoms (Skaff et al., 2009; McAndrew et al., 2014; Fisher et al., 2009). As research suggests that illness perceptions may change over time and due to lived experience with symptoms, particularly within diabetes, (Petrie & Weinman, 2006), it is important to evaluate the opportunity to improve the overall illness experience, taking both physiological and psychological symptoms into account.

Patient-provider communication within chronic illness care is a key element in successful (or detrimental) disease self-management. When communicating with providers, patients may present symptoms in obscure terms which can lead to abnormal illness behavior and general confusion about symptom causation, attribution, and illness perception (Robbins & Kirmayer,

1986). This may occur due to general challenges in communication between patients and providers (e.g., a patient's uncertainty of medical jargon, concerns that their needs may not be met). This effort to prioritize patient-provider communication has been previously addressed by Bodenheimer's Chronic Care Model (CCM). The CCM posits that productive interactions between an informed, empowered patient and a prepared, proactive practice team have the potential to produce productive interactions, which in turn, lead to improved health outcomes (Bodenheimer et al., 2002).

Treatment and self-management decisions are often guided by how providers and patients interpret perceived symptoms and how these interpretations influence beliefs, behavior, and the attribution of symptoms (Gonder-Frederick & Cox, 1991). As such, understanding and evaluating attribution can be particularly challenging when evaluating symptoms versus side effects. Everyday thinking about disease and illness experience is influenced by underlying disease schema, illness, and side-effect experience. Incongruence and confusion of attribution between patients and clinicians can lead to challenges in treatment and disease complications (Gillespie & Bradley, 1988). Patients may use symptom attribution as a method to monitor illness, creating representations based on experience and knowledge that can be learned and reinforced (Petrie, 2006; MacLeod, 1998).

As symptom attribution has been previously described as a monitoring strategy and a means of coping, patients are encouraged to think about what may have "caused" the experienced symptom as a method of tracking over time or attaining a deeper understanding of their illness. Illness perceptions directly influence coping strategies which in turn influence outcomes (Leventhal, 1996). Understanding the preliminary illness perception therefore provides the opportunity to further evaluate illness experience and behavior.

Examining symptom attributions as a moderating variable in the relationship between symptom experiences and emotional responses may be important in understanding the effect of symptoms on the T2D patient's experience. Although the moderating role of symptom attribution on affect has been previously evaluated in other chronic illnesses (specifically on self-efficacy in Rheumatoid Arthritis, and quality of life in hemodialysis) (Schiaffmo & Revenson, 1992; Pucheu, et al., 2004; Chaney et al., 1996), it has not yet been examined using momentary data collection in T2D. These studies depicted a pattern that underscores the relationship of self-management, symptom experience, and affect that is illustrated by Leventhal's Common Sense Model – individuals that experienced lower controllability, lower self-efficacy, or symptom flares tended to experience depressive feelings, increased impairment, and attribution of symptom experience to poor disease control (Schiaffmo & Revenson, 1992; Pucheu, et al., 2004; Chaney et al., 1996).

Positive and Negative Affect

Affect is defined as a relatively stable lens through which individuals perceive experiences, and in modern psychology, often refers to the mental counterpart of internal bodily representations associated with emotions (Barrett & Bliss-Moreau, 2009; Johnson & Tversky, 1983). Affect can involve degree of motivation, intensity, and personality disposition, and can either directly influence health outcomes through bodily systems or indirectly through behaviors (Barrett & Bliss-Moreau, 2009; Cross & Pressman, 2017; Pressman & Cohen, 2005). Positive affect (PA) reflects the extent to which a person feels enthusiastic, active, and alert. Individuals experiencing high levels of PA are often high energy, able to concentrate, and enjoy pleasurable activities. Contrastingly, negative affect (NA) is a general sense of distress and unpleasurable engagements including various mood states (anger, contempt, disgust, guilt, fear, and

nervousness) (Tellegen, 1988). Although depression has been clearly linked to poor health outcomes and studied via measures that overlap with negative affect (Denollet & de Vries, 2006), there is growing literature specifically linking negative affect and neuroticism to negative health outcomes as well (Williams, O'Brien, & Codler, 2004; Lahey, 2009). NA is also defined as a state that occurs when one has failed to achieve a goal, avoid a threat, or is not satisfied with their current state (Cross & Pressman, 2017).

Negative Affect and Symptom Reporting

The predisposition to frequently experience a variety of negative emotions, or negative affectivity, is associated with increased physical symptom reporting (Howren & Suls, 2011). This relationship has been shown in individuals with chronic illness (Chiang et al., 2018; Trick et al., 2014), as well as in patients receiving intensive chronic illness treatments such as hemodialysis (Sousa et al., 2018; He et al., 2017) and chemotherapy (Manne et al., 1994; Buick et. a., 2008). The Symptom Perception Hypothesis supports the theory that negative affectivity may be a predictor of increased physical symptom reporting as the presence of NA may magnify minor physiological experiences to be reportable symptoms (Watson & Pennebaker, 1989). Further, the Symptom Perception Hypothesis suggests that negative affect is associated with the tendency to inflate both the frequency and severity of physical experiences. Even in the absence of illness, misattribution of benign physical experiences may contribute to non-illness related physical experiences being attributed to illness (Howren & Suls, 2011).

Those with elevated NA typically show greater recall of negative stimuli, particularly in relation to the self (Mineka, Watson & Clark, 1998). This internal focus may increase the attention that is paid to otherwise hardly noticed minor or routine physical sensations, making these individuals more frequent and potentially accurate reporters (Dunn et al., 2010). In turn,

this tendency leads to a lower threshold of reporting symptoms in general, especially those that may be ambiguous or un-attributed to a specific illness (Cienchanowski et al., 2003; Suls & Howren, 2012). The perception of physical symptoms is generally preceded by physiological changes and can arise from fluctuations in normal bodily processes from disease, emotions, or environmental conditions (Kolk et al., 2002). Salovey and Birnbaum (1989) argued that negative affect contributes to an increase in self-focus, which consequentially prompts increased symptom detection (Howren, 2009). Therefore, more attention is paid to the stressor (e.g., pain), highlighting instances of potentially minor factors becoming major points of focus (Watson & Pennebaker, 1989; Duncko et al., 2009). Further, in the context of negative affect experience, symptoms that may be considered minor or unrelated to disease experience become a chief complaint.

Evaluating subclinical and sub-diagnostic threshold variables, such as affect, provides the opportunity to go beyond diagnostic categories and to explore the general implications for health outcomes and well-being in individuals with T2D. Within the T2D population, NA has been previously associated with increased symptom reporting, poor glycemic control, and overall poor health outcomes (Hood et al., 2004; Pressman 2005; Skaff et al., 2009). Further, research has confirmed that the observed relationship between mood and blood glucose is connected to negative affect (Skaff et al., 2009; Ryff et al., 2006).

Links Between Psychological and Physical Symptoms

Leventhal's Common Sense Model (CSM) presents a framework for understanding the impact of cognitive and affective processes on health and illness-related behaviors. The CSM initiates the generation of an individual's perception and representation of threats to health, management of the illness, and a system for creating action plans and implementing such plans

(Leventhal, 1996). This process is typically started by the experience of a symptom or physical sensation that may stray form the norm. When a symptom is experienced, individuals are prompted to seek observation or discussion of illness (e.g., from a medical provider), and consume information presented in media or other environmental cues. These stimuli further prompt memories of experience of illness and generation of mental representations of illness threats, treatment, and action plans (Leventhal, Phillip & Burns, 2016). As such, individuals with elevated NA and negative illness representation are expected to respond to typically normal sensations by labeling these symptoms as connected to illness (Leventhal, 1996).

Within T2D, depression and anxiety have been previously associated with symptom reporting and symptom attribution such that higher levels of anxiety are associated with increased symptom reporting and attribution of symptoms to diabetes-related experiences. Further, depression and anxiety have been shown to play a causal role in the increase of physical experiences, which then may lead to attributing these experiences to diabetes medications (Asman et al., 2020). As individuals with elevated NA have been previously shown to have greater recall of negative stimuli (Mor, 2002; Mineka, 1998), it is then plausible for this recall to be associated with physical symptom experiences.

Affect and Symptom Bidirectionality

Previous studies have shown that symptom experience can directly impact physical and psychological feelings, just as feelings can directly impact symptom experience. Specifically, individuals that report high levels of NA are more likely to report increase of symptoms over time across chronic illnesses such as cancer (Koller, et al., 1999), diabetes (McAndrew et al, 2014; Deary, Clyde & Frier, 1997) and rheumatoid arthritis (Griffin et al., 1999) as well as with acute illness (Leventhal et al., 1996). The reverse relationship, that individuals with higher levels

of symptoms at timepoint 'A' are more likely to later endorse higher levels of NA at timepoint 'B', has also been confirmed (Diefenbach et al 1996). This relationship has been conceptualized as the Disability Hypothesis, specifically, that physical disease, disability, and discomfort related to poor health predict and results in future affective distress (e.g., higher levels of NA) (Diefenbach et al., 1996). This relationship has also been shown with pain, as the progression of chronic pain is associated with development of increased NA (Yang & Chang, 2019; Apkarian et al., 2005; Elman, Borsook & Volkow, 2013).

Previous work has highlighted diabetes-related symptoms as contributors to stress, and vice versa (Al-Khawaldeh & Al-Hassan, 2012; Watkins et al., 2000; Rubin & Peyrot, 1999; Coffey et al., 2002; Huang & Brown, 2007). Although the bidirectional relationship between affect and physical health over time has been previously documented in other patient populations and disease groups (Wiese et al., 2019), this relationship has yet to be evaluated in individuals with T2D.

Ecological Momentary Assessment

In the fields of clinical and health psychology, data collection is typically comprised of retrospective self-reports that are collected at clinic-based or research visits. This methodology has been previously and frequently used in evaluations of affect and symptom endorsement (Geisser et al., 2000; Leventhal et al., 1996; Deshields et al., 2014; McKellar, Humphreys & Piette, 2004). This style of retrospective assessment is limited by recall bias and is often not well-suited to capture multiple behavioral or emotional changes over time (Shiffman, Stone & Hufford, 2008).

EMA is sensitive to biological and temporal changes that occur on a moment-to-moment basis through repeated assessments to be completed within the individual's natural environment

throughout the span of one day (or a pre-determined period) (Bresin, Carter & Gordon, 2013) – capturing data in the moment with minimal recall involved. EMA data collection is defined by four qualities: (1) phenomena are assessed temporally – as they occur, (2) assessments are dependent upon specified (often pre-determined) intervals, (3) assessments usually involve a substantial number of repeated observations, (4) assessments are usually made in the environment that the participant inhabits (as opposed to a medical or lab setting) (Stone & Shiffman, 1994).

This method of data collection is rooted in daily diary entries, self-monitoring, and recounts of relevant events (Shiffman, Stone & Hufford, 2008). Initial developments of daily diary entries were first seen using pagers to "beep" participants at random time points to prompt diary entries documenting mood, thoughts, and activity (DeVries 1992, Hektner et al. 2007). This "beep" phenomenon is now easily engrained in modern technology, through the use of smartphones, and has evolved to the point of queuing and collecting responses, all on the same interface and in the individual's personal environment.

Using EMA data collection allows for the analysis of variables as they are naturally experienced – focusing on in-the-moment responses, as opposed to retrospective self-report responses. Previous studies evaluating affectivity have compared EMA data collection to retrospective self-report methods. This work demonstrated that EMA data collection provided significantly stronger predictive abilities than did retrospective self-report when evaluating symptoms associated with mood disorders, major depressive disorder, and dysthymia (Ebner-Priemer, Ulrich, & Günther Sawitzki, 2007; Solhan et al., 2009). Research on daily stressors has evolved using diary methods that obtain repeated measurements from individuals during their

daily lives (Almeida, 2005). Using a time-sensitive method to capture moment-to-moment experiences allows for an advanced evaluation to further support claims of timely self-focus.

EMA may further serve to empower patients to experience self-efficacy in their self-management capabilities (McKeon et al., 2018). EMA symptom and self-management tracking prompts reflection at multiple time-points, which in the context of chronic illness management, can provide an opportunity to quickly evaluate patient-level variables. This has previously been evaluated as, if EMA itself impacted symptoms, it would become an ethically questionable instrument measure, and instead would be applied as an intervention (van Ballegooijen et al., 2016). Further, magnitude of EMA reactivity has been previously evaluated and noted to be small (Hufford et al., 2002) and inconsistent (Rowan et al., 2002).

Momentary and daily diary data collection has been previously used to capture both affect (Shahar & Herr, 2011; Mroczek & Almeida, 2004; Armey et al., 2015) and chronic illness symptom experience (Mulvaney et al., 2018; Okifuji et al., 2011; Kratz, Murphy & Braley, 2017). However, minimal work has been done using momentary data to evaluate bidirectionality of affect and symptom experience among individuals with diabetes.

Ecological Momentary Assessment and Directionality

Ecological momentary assessment methods have previously been applied to understand directional and temporal relationships. Such methodology was used to explore the directionality among stressors, affect, and physical health (Schultchen et al., 2019). To evaluate temporal relationships, previous studies have used EMA to investigate the association between NA and symptom reporting, using same-day and day-after timeframes. Gibson and colleagues found that NA was consistently reported on the same day as and day after reports of vasomotor symptoms, but the reverse of this relationship was not evaluated (Gibson et al., 2011). Similarly, Liao and

colleagues used EMA to examine potential existence of bidirectional relationships between affect, physical feeling, and physical activity (Liao et al., 2016). Although bidirectional relationships were not found in this study, the use of EMA provided a level of data sensitivity to evaluate sequential and time-oriented reactions of affect based on physical activity and vice-versa.

EMA has been used to examine bidirectional pathways in other populations, including sleep patterns and anxiety disorders (Thielsch et al., 2015), impulsivity and alcohol use (Stamates, 2019), as well as binge eating and restrictive eating (DeYoung, et. al 2014). Given the lack of previous research focusing on the potential bidirectional relationship between affect and symptom experience within diabetes, this secondary analysis will investigate this set of pathways. As such, the stress accumulated from symptom experience may contribute to negative affect, just as experienced negative affect may contribute to exacerbation of symptoms (Mohr, 2002, Mineka, 1998). Further, it is possible that negative affect endorsement is predictive of symptom burden endorsement, and that symptom endorsement is predictive of negative affect, supporting a bidirectional relationship.

Given the potential bidirectional influence between NA and symptoms, it is important to evaluate this relationship using a time-sensitive and intensive longitudinal design. The use of EMA serves to avoid the limitations inherent in retrospective self-report surveys that rely on inaccurate autobiographical memory. As experienced pain at the time of recall has been previously shown to lead to overestimation of retrospective pain reports, (Eich, et al. 1985), it is important to evaluate symptom experience on a momentary level to avoid such bias. By collecting affective and symptom experience data at multiple time points within each day over a 2-week study period, longer-term recall concerns will be minimized, and conceptualization of

directionality will be available at multiple time-points (e.g., concurrent, within day, over course of study period).

Path Modeling and Cross-Lagged Analysis Approach

In order to capture and evaluate information collected at two or more timepoints, cross-lagged panel design can be applied. Cross-lagged panel design is a type of structural equation modeling and is primarily used to assess causal relationships (and potential bidirectionality) in a non-experimental setting (e. g., where variables are recorded without manipulation) (Selig & Little, 2012). The term "panel" specifically refers to passive and/or observation studies without experimental design elements. Cross-lagged analysis design is often applied to datasets that contain variables measured on repeated occasions and when hypotheses exist in both causal directions (Newsom, 2015). Cross-lagged models are intended to examine causal factors and one variable's impact on another (e.g., does "a" cause "b" or does "b" cause "a"?) over the course of time. The same structure can be applied to path modeling (also known as multilevel regression modeling; without the cross-lagged syntax) for day-level variables.

Within path modeling and cross-lagged analyses, the addition of a time-related covariate can improve fit and accuracy of model. This is seen specifically when the covariate (e.g., time) is correlated with evaluated variables (Newsom, 2015). Including the covariate within a correlated sample minimizes the bias of the model, thus improving fit. As later detailed, the structure of this secondary analysis followed this outline, using a time-oriented variable as a covariate to minimize bias within highly correlate variables (negative affect, symptom experience, and symptom attribution) across time.

Similar models and analytical designs have been previously applied within diabetes and mood-related studies. Specifically, cross-lagged panel analysis was successfully applied to

evaluate the existence of a relationship between depressive symptoms and diabetes distress, finding significant relationships across all hypothesized paths (Burns, et al., 2015). A similar study design detected bidirectional pathways of association between anxiety, depression, and health-related quality of life (HRQoL) (Liu, et al., 2020). The consistent use and application of this statistical design supports the decision to use cross-lagged analysis with a time-oriented covariate for our methodology.

Qualitative Analysis

To better understand the patient's perspective in an open-ended format, qualitative research has been used to further evaluate patient-reported experiences (Hennink et al., 2017). This has been done through focus groups, semi-structured interviews and open dialogues between patients and clinicians (Shirazian et al., 2016). These open formats of data collection enable the patient to report their own perspective, likely straying from the typical structure provided in a multiple-choice question (Hennink et al., 2017). Although patient-reported outcomes (PROs) are often evaluated in conjunction with medically-based disease related outcomes (e. g., HbA1c, mortality, morbidity), minimal research is available that evaluates the patient perspective of the disease experience at large (Bodenheimer, Wagner & Grumbach, 2002-b; Hennink et al., 2017; Hamilton, & Finley, 2019).

Using qualitative data can provide an in-depth and ethically sound basis for further evaluating the subjectivity of the patient care experience (Hennink et al., 2017, Kaiser, Sekar & Griswold, 2017). A qualitative evaluation provides an opportunity to communicate about variables or experiences in greater detail than may be seen on a multiple-choice question. Additionally, interview-based data collection can provide an opportunity to communicate about issues that may not be covered or addressed by other study designs. Qualitative analysis has been

previously used to evaluate symptom experience in chronic illnesses such as lung cancer (Molassiotis et al., 2011), rheumatoid arthritis (Halls et al., 2015), and both T1D (Watts, O'Hara & Trigg, 2010) and T2D (Newton, Asimakopoulou & Scambler, 2015). Similarly, qualitative methodology has been previously applied to explore affective states and health behaviors (Huffman, et al., 2016; DiPietro, 2017), although minimal research has been done to evaluate the specific interplay of symptom experience and affective states through the qualitative lens.

Study Rationale/Innovation

As previously illustrated, the pathways between NA and SXS are important mechanisms to evaluate and may help to characterize and identify areas of focus for future treatment. To our knowledge, this is the first study to evaluation the temporal and directional relationships between SXS and NA in individuals with T2D. The proposed combination of evaluating qualitative data and EMA moment-to-moment self-report data provides a unique opportunity to combine different methods of assessing PROs and further understand diabetes-related symptom experience in a setting that is sensitive to the environment, and temporal and psychological influences. Further, qualitative research in diabetes can illustrate the importance of clinical and non-clinical relationships, treatment, complications, self-management, and culturally appropriate education (Ritholz, Beverly & Weinger, 2011).

There is a critical need to understand the patient experience of self- and disease-management in chronic illness using PROs. EMA is sensitive to the ongoing experience of the patient and an innovative data collection technique that provides patient-report data as it is experienced moment to moment, in the patient's natural environment (Goldberg et al., 2017). Using a patient's cell phone as a method for data collection can minimize patient-report burden as it is portable and often adaptable into a typical daily usage routine (Yang, Ryu & Choi, 2019).

The portability of EMA data collection allows for the opportunity to collect a greater quantity of data without requiring patients to make daily corresponding lab visits or keep track of paper surveys over time. Though answering questionnaires multiple times per day is time-consuming and may be burdensome, the incorporation of EMA into each participant's cell phone was designed to minimize inconvenience.

For this secondary analysis, EMA data collection was completed using the MyDay study application. EMA provides novel and useful data regarding an individual's experience that can be used to enhance the assessment, treatment, and clinical experience, specifically in patients with Type 2 Diabetes and reported diabetes distress.

To our knowledge, this is the first study to use a combination of data collection methodology that prioritizes the patient voice in different ways. Through MyDay EMA software, patients are reporting moment-to-moment experiences throughout the course of the study (Conner & Barrett, 2012). By participating in the qualitative exit interview, patients are again given a voice and an opportunity to share their experiences through an open-ended, patient-centered methodology, with room for further reflection and feedback. PROs provide an opportunity to focus on aspects of the patient experience that can provide evidence of treatment benefits and burdens that are not captured by blood tests and clinical measures (Boyce, et al., 2014, Bodenheimer, et al., 2002; Hennink et al., 2017, Hamilton et al., 2019). This secondary analysis fills a current gap in literature both through the methodology combination, and through the time-oriented directionality detection.

This study seeks to evaluate the relationship and directionality of negative affect and symptom experience in individuals with T2D. Through a longitudinal EMA design and thematic analysis on patient interviews, symptom experience and affect were captured and reported in-the-

moment directly from the patient, avoiding retrospective and recall bias, and providing an open forum to discuss disease experience. Investigating this dynamic relationship allows for improved understanding of the associations between NA, physical symptoms, and symptom attribution. Evident pathways between variables of focus may be indicative of future areas of focus within the T2D population, with the potential to expand to other chronic illness groups.

Specific Aims

Aim 1: To evaluate associations of NA with subsequent symptom reports and symptom attribution within the same day and over study period using EMA via smartphones among adults with T2D.

Hypothesis 1A: Higher levels of NA will be positively associated with greater symptom endorsement at the subsequent assessment within persons.

Hypothesis 1B: Higher levels of NA will be positively associated with greater tendency to attribute symptoms to diabetes and to diabetes medications within persons.

Aim 2: To evaluate the association of symptom endorsement and attribution on subsequent NA within the same day and over study period using EMA via smartphones among adults with T2D.

Hypothesis 2A: Greater symptom endorsing will be positively associated with higher levels of NA at the subsequent assessment within persons.

Hypothesis 2B: Symptom attribution will moderate the relationship between symptom reporting and NA such that attributing symptoms to diabetes or diabetes medications will be associated with a greater increase in NA.

Exploratory Aim: **To evaluate patient perceptions of the relationship between NA and symptom experience using qualitative exit interviews among adults with T2D.**

Chapter II: Design and Methods

Overview of Research Design

Description of Parent Study

Patients with Type 2 Diabetes were assessed 3-times daily using an app on a Smart Phone over a 14-day period to examine the general associations, as well as temporal relationships, between patient-reported symptoms and self-management variables. Eligible patients were 18 years of age or older with T2DM diagnosis of at least 1 year and prescribed 1 or more oral diabetes medication with an HbA1c documented within the last 6 months prior to consent, available in medical records. Patients were also required to regularly monitor glucose and own a glucose meter and strips. Patients had to own a smart phone and maintain fluency of English language in order to participate and use the EMA mobile application. This is a secondary analysis of Einstein IRB #2017-8241 (parent study under P.I. Dr. Jeffrey Gonzalez), approved on 10/2017, with conclusion of data collection in 4/2020. This study is financially supported by departmental funds at the Ferkauf Graduate School of Psychology with an overall focus on assessing psychological and physical symptoms in individuals with Type 2 Diabetes. The goal of the parent study was to assess T2D patients over a 14-day period to examine general associations, as well as temporal relationships, between patient-reported symptoms and self-management variables

Description of the Current Study

This secondary analysis focused specifically on evaluating the bidirectional relationship between symptom experience and affect using EMA data and qualitative exit interviews. Eligibility for the parent study and secondary analysis remained largely the same. However, due to use of EMA data, this secondary analysis excluded individuals that were unable to complete

EMA data using the mobile application (e.g., individuals that completed participation using paper printouts of surveys).

MyDay Mobile Application

MyDay is an iOS and Android compatible Smartphone application designed to integrate and provide feedback on a variety of individual data relevant for diabetes self-management. MyDay is a mobile application written in Ruby On Rails (v4.1) with a PostgreSQL database background (Mulvaney et al., 2018). MyDay was developed specifically for use in T1D and has since been adapted for use in the parent study. It provided a secure web interface for administering surveys and collecting data with application and database servers managed through the Vanderbilt University Information Technology department protected by the Vanderbilt University firewall. MyDay is intended for use by individuals with diabetes, enabling evaluation of factors that are critical for patient health behavior decision-making.

Design Consideration

The parent study has completed recruitment of participants with type 2 diabetes from the Bronx, New York, with a resulting sample size of 62. Study staff completed processes of screening, obtaining informed consent, collecting demographic information, administering surveys and training participants in use of the smartphone application.

Screening and Recruitment

Participants were recruited at the Albert Einstein College of Medicine/Montefiore Clinical Diabetes Program through opt-out letters, in-clinic screenings, and direct referral by physicians. The Einstein/Montefiore system is estimated to include over 3,500 type 2 diabetes patients in active clinical care. All participants who were interested were asked exclusion/inclusion questions by study staff, either in person or over the phone, depending on

referral source. Proper care was taken to obtain informed consent during both the recruitment and screening processes to ensure HIPAA guidelines were met. Recruitment began in May 2018 and ended in March 2020. Potential participants were contacted either face-to-face in on-campus clinic visits or via telephone to complete a brief screening. Screening involved following up on participation interest and ability as well as evaluating eligibility criteria.

Justification of Inclusion/Exclusion Criteria

Inclusion criteria were carefully chosen based on the importance of maximizing internal validity of the study, while balancing practical concerns for recruitment and enhanced external validity. We excluded children from the current research study because type 2 diabetes is rare among children and adolescents and self-management would be different for youth as compared to adults. Participants also needed to be prescribed 1 or more oral hypoglycemic medications, so that 1) adherence to medication can be tracked using the MEMS cap, and 2) the sample is representative, given that many diabetes patients are prescribed more than one oral medication and the number of prescribed oral medications can influence medication adherence (Grant, Devita, Singer & Meigs, 2003; Bailey & Kodack, 2011).

Within the parent study, budget constraints at the pilot stage restricted ability to collect blood samples to assess HbA1c. Instead, participants were expected to have HbA1c values collected within the last 6 months prior to participation and have values available in their medical records. Regular self-monitoring of blood glucose was also required, so that adherence to this self-management behavior could be tracked. Further, due to budgetary constraints, participants needed to have a smart phone available for use at time of recruitment and throughout the duration of the study. A report from 2021 assessing cellphone ownership in the United States by income level reported that smartphone ownership was around 76% among individuals with an

annual salary less than $30,000 (PEW Research Center, 2021). We postponed the participation of pregnant women until after delivery because of effects of pregnancy on glycemic control. As such, pregnancy was an additional temporary exclusion criterion.

Participant Incentives

All participants were offered an incentive for completing the baseline (credit card gift card of $25) and follow-up (credit card gift card of $25) assessments (a total of $50). Furthermore, participants received an incentive of $75 (credit card gift card) to complete the daily EMA assessments (based on adherence to daily assessments $\geq$ 70%). If adherence to daily assessments fell below 70% (but remained above 20%) the participant was given an incentive of $50. Adherence below 20% was not incentivized. These incentives included offsetting potential costs associated with smart phone wireless data usage. A participant was eligible to receive up to $125 in total for participation.

Baseline Visit

Participants provided informed consent, completed demographic information form, were asked to complete a psychosocial self-report battery (measures included in sub-study described in Measures section below), were given study materials, and were trained on how to use them. Specifically, participants downloaded the mobile application MyDay, and were trained on how to use the Smartphone app for ecological momentary assessments (EMA). Research assistants provided education on EMA data collection and established data collection scheduled with participants (e. g., creating 3-time-point survey queue within the mobile application). Participants were given MEMS Caps to track adherence of daily oral diabetes medication and were trained on MEMS Caps usage and adherence tracking. MEMS pill bottles were returned at follow up visit.

MyDay and EMA Procedures

EMA questionnaires were completed 3-times daily throughout the 2-week study participation via mobile app on participant's mobile phones. Patients indicated time preferences during ranges of morning (around same time that fasting blood glucose was measured), afternoon, and evening at baseline visit. Participants received prompt notifications to complete measures at this time. Measure completion is estimated to take 10-15 minutes per EMA timepoint.

Follow-up Visit

Participants returned approximately 14 days post baseline visit to complete the follow-up psychosocial self-report battery (measures included in sub-study described in Measures section), as well as to return the MEMS cap and review adherence to both MEMS cap usage and MyDay application. During visit 2, dates and glucose values were downloaded from the participants' glucose monitor. Finally, the qualitative exit interview was administered by an RA to gather feedback and user experience data. These interviews also provided patients with an opportunity to discuss behavioral change, patterns, and general diabetes experience. Interviews were audio recorded for and transcribed by research assistants.

Qualitative Exit Interview

At completion of follow-up visit, patients were asked to complete an exit interview which was comprise of a series of 6 questions (Appendix A) to evaluate the patient experience and feasibility of study participation. The interview was constructed to evaluate potential feasibility, burden and overall experience with the mobile application. Patients were given the opportunity to provide feedback in an open-ended interview format and were provided with probes or examples at points of confusion or clarification. Interviews ranged from 10-30 minutes in length,

dependent on amount of information shared by the participant. Interviews were audio-recorded and transcribed by a research assistant. Transcriptions were de-identified and stored in a secure location.

Measures Included in Current Study

Baseline and follow-up questionnaires included a demographic form and psychosocial battery and were administered at baseline and 2-week follow-up visits to the lab by graduate level research assistants. This secondary analysis focuses on the EMA questionnaire portion (daily affect using the Positive and Negative Affect Schedule Short Form and symptom data using the Diabetes Symptom Checklist) and did not include any self-report data collected at baseline and follow-up, with the exception of demographic variables and qualitative exit intervew. EMA questionnaires were conducted 3-times daily throughout 14-day course of study. Timing of questionnaires is illustrated in Figure 1.

Affect

Daily affect was assessed 3-times throughout the day using the shortened 10-item International PANAS-SF to reduce participant burden (Thompson, 2007). This measure was shortened from the 20-item Positive and Negative Affective Schedule (PANAS) (Watson, Clark & Tellegen, 1998) used at baseline and follow up. This secondary analysis specifically focused on the 5 negative-affect-focused questions. The PANAS-SF has been shown to have good psychometric properties when used in the lab and as part of previous daily assessment/EMA studies (Kennedy-Moore et al., 1992) (Appendix C). Affect was evaluated on a 4-point scale ("Right now do you feel…" 0 – 3; not at all; a little bit; quite a bit; extremely). Cronbach's alpha indicated good reliability in this sample for daily measures ($\alpha = .81$). The PANAS has been previously used and validated in diabetes literature, as well as in studies evaluating affect in

lower SES patient demographic groups and using daily diary/momentary design (Wayne et al., 2015; Skaff et al., 2009; Kim et al., 2020).

Symptom Experience and Attribution

Physical symptoms were collected using 13 diabetes-specific physical symptoms (e.g., excessive urination, thirst) selected from the Diabetes Symptom Checklist (Grootenhuis et al., 1994) endorsed on a scale of 0 (not at all) to 3 (extremely) asked 3-times daily (Appendix C). Cronbach's alpha indicated acceptable to good reliability in this sample for daily measures (α = .79). This checklist was adapted from the Identity subscale of the Illness Perception Questionnaire-Revised (IPQ-R) (Moss-Morris, Weinman, Petrie et al., 2002) to track symptom experience and endorsement at day-level timepoints.

We added an additional modification to the scale to ask whether participants attribute symptoms to their diabetes and/or medications to evaluate symptom attribution, created by Dr. Gonzalez for the purpose of this study. Attribution was evaluated for general symptom experience and was not evaluated on an individual symptom-by-symptom level; experienced symptoms caused by my diabetes (0-4; had no symptoms; not at all; a little bit; quite a bit; extremely) or by my diabetes medication (0-4; had no symptoms; not at all; a little bit; quite a bit; extremely). As such, individuals were asked two attribution-related questions after completing the Symptom Checklist portion of EMA. Cronbach's alpha indicated good reliability in this sample for daily measures (α = .88). Both the IPQ-R and Diabetes Symptom Checklist have been previously used to evaluate illness perceptions and symptom experience in chronic illness (McCorry et al., 2013; Weinman et al., 1996; Grootenhuis, et al., 1994).

Missing Data

In the total sample (N=62), 98% of participants participated in daily data collection via MyDay mobile application. Therefore, this secondary analysis has been conducted with participants that engaged in daily data recording through MyDay (N=61). For this project, all (N=61) participants were included regardless of gaps in daily data or missingness of data. Although all participants in the total sample (N=62) completed the exit interview, this analysis of the qualitative data included only the 61 participants who completed the EMA data. This decision was made to prioritize consistency in sample size and interpretation of results.

Additionally, given the pilot nature of this study, participants experienced occasional glitches with mobile application usage or naturally missed occasional survey entries due to daily conflicts or individual-level barriers. The average survey completion rate of daily data collection was 78%. As such, no lag or time-oriented cut off was created as this would prevent use of participant data with any collection gaps.

Data Analysis

Overview of Approach

This secondary analysis evaluated if symptom endorsement was predictive of negative affect, if negative affect predicted symptom endorsement, and if there was a moderating effect of symptom attribution in patients with T2D. Data were analyzed using SPSS software version 27.0 (IBM Corp., 2020) for the sole purpose of preliminary analysis and characterization of the sample. Descriptive statistics were calculated for each of the examined variables as well as demographic variables (e. g., age, race, gender) to characterize the sample.

Statistical Analysis Overview for Quantitative Aims (1 & 2)

To evaluate day-level and lagged analyses, Mplus (Muthén & Muthén, 1998) was used for Aims 1 and 2 using a Bayesian multilevel modeling approach. This maximum likelihood-based approach accommodates for the simultaneous estimation of multiple outcomes (NA and

SXS) within the same model. Mplus software allows for use of time-lagged analyses and incorporates within- and between-participant calculations as well as missing data within syntax. Within- and between-person effects were computed to distinguish between individual variability in negative affect, symptom endorsement, and symptom attribution, across days and between-person variability (Bolger & Laurenceau, 2013). To accomplish this, negative affect, symptom endorsement, and symptom attribution scores were calculated across individuals to develop between-person grand mean centered variables [$MnNA_i$ and $MnSx_i$]. Within-person variables in which deviations from an individual's average NA, symptom endorsement, and symptom attribution across the EMA daily collection period [($NA_{di} – MnNA_i$), ($Sx_{di} – MnSx_i$), and ($SA_{di} – MnSA_i$)] were also calculated using group mean centering.

For the SA variable group specifically, the SUM function in Mplus was used to create a SA total score (combined attribution of SA to diabetes and SA to diabetes medications) that was then group mean centered as previously mentioned for main study variables. As the two SA questions were asked separately, participants may have endorsed both types of SA, simultaneous. As such, the attribution sum variable was created and included in analysis.

Random effects were evaluated using Mplus and were embedded within main analysis models. Random effects tested for between-person differences in the within-person associations between SA and NA. Fixed effects were included within analyses and embedded in results.

To explore the direction of the association between NA and symptom endorsement, path analysis (day level, starting and ending within same day) and cross-lagged path modeling (full study window, continuous over all days with lags including day-to-day) was conducted using Mplus (Muthén & Muthén, 1998). Path analysis and cross-lagged path modeling accommodated for the structure of daily diary data (e.g., time points crossed with participants) (Perndorfer et al.,

2019) and was well suited for intensive longitudinal designs with the goal of elucidating within-person associations and within-person reliability (Bolger & Laurenceau, 2013). Models examined whether EMA measurements of symptom endorsement intensity predicted NA at the following survey time, and vice versa. Day-level (concurrent) and cross lagged models were run separately to accommodate for accuracy in syntax and embedding of appropriate code to indicate time span (e.g., difference between code to lag from one day to the next vs day-level). Repeated measurements of EMA are nested within each participant in both models. General path modeling strcture was the appropriate method to use given the two levels of observation: level of EMA responses (Level 1) and those made at the level of each participant (Level 2), allowing for the evaluation of multiple dependent variables simultaneously.

The Level-1 model included within person effects. In the Level-2 model, the individual intercept is a function of the fixed intercept. The individual effects of the within-person responses are a function of the fixed effects and random effects including time of response and day of response.

For both Aims 1 and 2, a time-oriented variable ("session," representing EMA entry and associated time in survey sequence) was included as a covariate to ensure accuracy of model fit. Time-oriented covariates are strongly encouraged when running lagged and/or time-oriented-analyses for variables that appear to be correlated (as seen within this dataset) (Newsom, 2015). As such, this covariate was used in all models to ensure best possible fit and highest possible level of accuracy.

Within Mplus analyses, multiple outcomes were modeled simultaneously using ITINTERVAL to automatically insert missing observations based on an existing time variable ("session") (Asparouhov & Muthén, 2020). This allowed for maximized use of available data

given the pilot-nature of this study, while also accounting for precise passage of time and integration of different measurement scales.

Statistical Analysis Overview for Qualitative Aim (3)

To evaluate qualitative exit interview data, NVivo 12 qualitative data analysis software (NVivo, qualitative data analysis software; QSR International Pty Ltd. Version 12, 2018) was used for Aim 3 (exploratory aim). An initial codebook served as a flexible and accommodating guide for coding transcripts (Braun & Clark, 2006). Once coders agreed on wording and themes, the edited codebook was applied to ten transcripts. After completion of this phase and reaching saturation in sample of ten transcripts, the codebook was finalized and used to code the remainder of the transcripts. The team of coders independently completed coding of each transcript, meeting weekly to discuss and resolve discrepancies. This qualitative analysis allowed for evaluation of themes as communicated through exit interviews, highlighting the trends of causality as illustrated through quantitative findings.

Aim 1: To evaluate associations of NA with subsequent symptom reports and symptom attribution within the same day using EMA via smartphones

<u>Aim 1A</u>

A path analysis and cross-lagged path model approach was used to evaluate whether negative affect reported in first assessment predicted subsequent symptom endorsement at following assessment within day and over study period. To explore direction of association between NA and symptom endorsement, over time, cross-lagged path models were used to detect changes in symptom endorsement at the following time point, controlling for the effects of the previous NA, and also whether NA predicted changes in the symptom endorsement scores at the following time point (Van Voorhees et al., 2018). This was examined on a within-persons level

as these analyses illustrated directionality within the same participant over time. Cross-lagged path analysis allowed for examination of the association of changes in NA and physical symptoms over the course of the day and study period. Number of endorsements of PANAS for NA and total of endorsed symptoms (Daily Symptom Checklist) were calculated. Through separating within- from between-person variability, within-person findings were strengthened as between-person differences were separated out. Non-informative Bayesian priors were used. Credibility Intervals (Bayesian equivalent of Confidence Intervals) of 95% indicate statistical significance ($p < .05$) when bounds do not include zero. A concurrent (same day) path analysis was also run using the same model structure, removing the over-time lagged effect.

Aim 1B

Cross-lagged models were used to assess the directionality of the relationship from NA to symptom attribution to diabetes/diabetes medications. Non-informative Bayesian priors were used. Credibility Intervals of 95% indicate statistical significance ($p < .05$) when bounds do not include zero.

Aim 2: To evaluate the association of symptom endorsement on subsequent NA within the same day using EMA via smartphones

Aim 2A

Steps in Aim 1, Hypothesis 1A, were conducted using reverse directional structure. A path analysis and cross-lagged path model approach was used to evaluate whether symptom endorsement reported in first assessment predicted subsequent negative affect at following assessment within day and over study period.

Aim 2B

Path analysis was used to examine the day-level moderating effect of symptom attribution (attributing symptoms to diabetes or diabetes medications) on symptom reporting and NA (Figure 2). Markov chain and Monte Carlo with Gibbs sampling (10,000 iterations, thinning =20) were used to obtain posterior distributions. Non-informative Bayesian priors were used. Credibility Intervals of 95% indicate statistical significance (p <.05) when bounds do not include zero. To probe and plot interaction effects, low and high values of each moderator were operationalized (one standard deviation above and below the mean, centered on zero). Figures created using Quantsby Rweb coding (http://quantpsy.org/interact/hlm2.htm).

Exploratory Aim: To evaluate patient perception of relationship between NA and symptom experience using qualitative exit interviews. (Appendix A)

Interviews were transcribed and coded using a thematic analysis process (Braun & Clark, 2006). Interviews were initially given to participants to gather information and feedback about study participation and experience given the pilot-status of this project. However, implementation of a thematic analysis structure was supported by the length and content of these interviews in which participants provided information about their personal experiences with diabetes far beyond mobile application use. In the first phase of this process, two coders (clinical health psychology graduate students with qualitative research training and experience) used open-coding to read five transcripts and highlight relevant theme-oriented text to create a preliminary list of codes (e. g., negative affect, symptom experience, self-management). Open-coding was conducted independently. Coders then met to create an initial codebook to serve as a flexible and accommodating guide for coding the next sequence of transcripts (Braun & Clark, 2006). Once coders agreed on edits to wording and themes, they began the next phase of coding – applying the edited codebook to ten additional transcripts. After completion of this phase, the

codebook was finalized and then used to code the remainder of the transcripts. The team of coders completed coding of each transcript independently, meeting weekly to discuss and resolve discrepancies. Finalized coding of each transcript was entered into NVivo 12 qualitative data analysis software for further evaluation for code saturation and tendencies. Inter-rater reliability was evaluated once the coding team completed individual and independent coding of all interviews.

Power Analysis

Aims 1 & 2

Given the exploratory nature of these secondary analyses to the parent study, it is not appropriate to use power analyses to determine an ideal sample size. This study completed recruitment with a total of 61 participants. Previous efforts to estimate sufficient sample sizes for multilevel modeling call for a sample size of at least 50 at the highest level of model design to account for biased estimates of standard errors (Maas & Hox, 2005). Recruitment efforts for the parent study resulted in a sample size of 62 participants which provided sufficient power for multilevel modeling analyses, surpassing minimum n of 50.

Aim 3

In qualitative interview-based research, there is typically a focus on interviewing stakeholders (e.g., individuals who may be influenced by the implementation of the topic in question) (Hamilton, & Finley, 2019). As the qualitative interview is included in part of overall study participation, each patient will have both quantitative and qualitative data. In a majority of qualitative studies, saturation is reached with smaller samples sizes (n = 10 – 20) than is typically seen in quantitative data (Hamilton, & Finley, 2019). For Aim 3, the saturation will likely be achieved prior to reaching the total sample size (n = 61) of the study. Though saturation was

achieved prior to coding completion, interviews continued to be transcribed and coded to provide for optimal opportunities for mixed methods analysis given the necessity of the quantitative sample size.

Ethics

The current study is included under the larger parent study, which was approved by the Institutional Review Board at the Albert Einstein College of Medicine of Yeshiva University (IRB #2017-8241).

Risks

This study did not involve significant invasive physical procedures, and anticipated risks to participants were assumed to be minimal. Potential and minor risk to participants was seen in burden of answering questions from questionnaires, including responding to 3-times-daily smart phone app-based questions over the 2-week study period. However, participants were told that they have the option of terminating participation at any time or not answering any questions they do not want to answer. Additionally, there was a risk of loss of confidentiality. Steps to reduce this risk are outlined below under "Confidentiality." Two participants endorsed suicidal thoughts on the depression measure (positive scored on item 9 on the PHQ-9), and this was brought to the attention of Dr. Gonzalez, a licensed psychologist, and appropriate psychological referrals were given to the participants.

Benefits

This research may not provide any direct benefits to participants, though participants noted that they were increasingly aware of their diabetes-related self-management, symptoms, and mood. The benefits to others are potentially quite large. The current study had provided the framework to substantially increase our knowledge about the role of patient-reported symptoms

in relation to diabetes self-management and could help build the evidence base for behavioral interventions that could improve diabetes outcomes.

Chapter III: Results

Participants and Descriptive Statistics

In this pilot study, 61 participants completed the EMA and exit interview portions of the study. Table 1 displays the average age of participants (M=55.6), with slightly more females (64.5%) than males (35.5%). All participants were proficient in speaking and reading English (per enrollment criteria) and most were ethnic minorities - 61% identified as Black and 36% identified as Latino.

Descriptive Statistics included mean, median, range, and frequencies, and were examined for each variable included in analyses (Table 2). Scatter plots and histograms were generated to evaluate distribution and visually inspect data. Symptom endorsement was further examined to evaluate frequency of endorsement of physical symptoms as seen on the Diabetes Symptom Checklist (Table 3). All thirteen symptoms were endorsed over the course of the study period, with percentages illustrating reports of symptom frequency (e.g., multiple times over study period) per participant. The most frequently endorsed symptoms were “Very thirsty or dry mouth” (57%), and “Pain” (50%). The least frequently endorsed symptoms were “Dizziness or lightheadedness” (16.7%) and “Nausea or upset stomach” (18.4%), demonstrating a range in symptom endorsement percentage from 16.7% - 57%. As attribution questions were asked once for all symptoms, it was not possible to differentiate attribution frequencies within this dataset.

Main Analyses

Preliminary Results of Bivariate Relationships Among Study Variables

The relationships among continuous patient-related demographic factors (age and HbA1c), negative affect (total score aggregated over course of time and daily mean over study period), symptom experience (symptoms endorsed via Diabetes Symptom Checklist, total score

aggregated over course of time and daily mean over study period), and symptom attribution (attributing symptoms to diabetes and/or to diabetes medications) were examined using Pearson correlations (see Table 4). Age and NA scores aggregated over time (NA Total) were negatively correlated, $r(59)=-0.20$ $p<.01$, as were age and daily mean measurements of NA (NA Total Daily Mean), $r(59)=-0.05$, $p<.01$. Age and total physical symptoms aggregated over time (SXS Total) were positively correlated, $r(59)=0.04$, $p=0.02$. Age and daily mean measurement of total symptoms (SxTotal Daily Mean) were negatively correlated, $r(59)=-0.05$, $p<.01$). Age and symptom attribution to diabetes (T2D Sx Attribution) and symptom attribution to diabetes medications (T2D Med Attribution) were both positively correlated $r(59)=0.12$, $p<.01$; $r(59)=0.13$, $p<.01$. HbA1c and NA scores aggregated over time (NA Total) were negatively correlated, $r(59)=-0.06$, $p<.01$. HbA1c was not significantly correlated with any other main study variable.

Both negative affect variables (NA Total and NA Total Daily Mean) were positively correlated $r(59)=0.92$, $p<.01$, as were both symptom endorsement variables (SXS Total and Sx Total Daily Mean) $r(59)=0.92$, $p<.01$, and both symptom attribution variables (T2D Sx Attribution and T2D Med Attribution) $r(59)=0.80$, $p<.01$. NA scores aggregated over time (NA Total) was positively correlated with both symptom endorsement variables (SXS Total and Sx Total Daily Mean) $r(59)=0.43$, $p<.01$; $r(59)=0.46$, $p<.01$, and both symptom attribution variables (T2D Sx Attribution and T2D Med Attribution) $r(59)=0.21$, $p<.01$; $r(59)=0.17$, $p<.01$. Similar patterns were seen with daily mean measurements of NA and symptom variables (SXS Total and Sx Total Daily Mean) $r(59)=0.46$, $p<.01$; $r(59)=0.48$, $p<.01$, and attribution variables (T2D Sx Attribution and T2D Med Attribution) $r(59)=0.28$, $p<.01$; $r(59)=0.17$, $p<.01$. Finally, both symptom variables (SXS Total and Sx Total Daily Mean) were positively correlated with both

attribution variables (T2D Sx Attribution and T2D Med Attribution) r(59)=0.58, p<.01; r(59)=0.56, p<.01; r(59)=0.57, p<.01; r(59)=0.58, p<.01.

To assess the association of within- and between-effect levels for daily variables, additional correlations were run (Table 5). Significant correlations were found across all levels and variables, further illustrating high levels of correlation in main study variables. Additionally, ICC's were run for main study variables and illustrated more variability between-participants than within-participants (NA Daily Mean = 0.67; Sx Daily Mean = 0.76; T2D SA = 0.59; T2D SA Med = 0.60).

Quantitative Analysis (Aims 1 & 2)

Aim 1a: The directional pathway from NA to SXS was shown to be significant on both the concurrent (same-day) (Table 6) and lagged (over time, multiple time-points) (Table 7) levels, on both within-persons with fixed effects and between-persons analyses, illustrated that the increase in NA was associated with increase in SXS. Same-day analyses (non-lagged path analysis) demonstrated that, on a within-persons level, a 1-point increase in NA from one's personal mean was associated with a 0.42-point increase in subsequent symptom experience within the same day (95% CI: 0.25-0.59, p <.01).

Cross-lagged path analysis was conducted to evaluate the directional relationship of NA and SXS over time (total course of study period). On a within-persons level, a 1-point increase in NA from one's personal mean was associated with a 0.14-point increase in subsequent symptom experience (95%CI: 0.03 - 0.25, p <.01). (Table 6). Between-person levels demonstrated similar trends. On a between-persons level, a 1-point increase in NA from one's personal mean was associated with a 0.53-point increase in subsequent symptom experience within the same day (95% CI: 0.36-0.66, p <.01). Cross-lagged analyses demonstrated a 1-point increase in NA from

one's personal mean was associated with a 0.52-point increase in subsequent symptom experience (95%CI: 0.28 - 0.70, p <.01).

Within this sample, the relationship between NA, SXS, and SA, differed significantly among participants on both same-day and cross-lagged levels (Table 9). By definition, random effects demonstrate a variance around a within-person effect (Field, 2013). Therefore, random effects are estimated at the within-person level, but are reflected as between-person differences, mirroring the nature of differing T2D disease experiences. As such, random effects were included as part of within-person analyses and demonstrated significant NA to SX pathway findings. Same-day analyses with random effects demonstrated that, on a within-persons level, a 1-point increase in NA from one's personal mean was associated with a 0.20-point increase in subsequent symptom experience within the same day (95% CI: 0.10 - 0.36, p <.01). Cross-lagged analyses with random effects illustrated that a 1-point increase in NA from one's personal mean was associated with a 0.05-point increase in subsequent symptom experience (95%CI: 0.01 - 0.18, p <.01). This analysis of random effects suggest that both day-level and cross-lagged relationships differed significantly between individuals.

Aim 1b. Cross-lagged models were used to assess the directional pathway between NA and symptom attribution to diabetes/diabetes medications at subsequent timepoint (Table 7). On the within-persons level with fixed effects, none of these pathways were found to be significant. The pathway evaluating NA and subsequent symptom attribution to diabetes reflected that a 1-point increase in NA from one's personal mean was associated with a 0.01-point increase in attribution score (95%CI: -0.01-0.04, p =0.45). The pathway evaluating NA and subsequent symptom attribution to diabetes medications demonstrated that a 1-point increase in NA from one's personal mean was associated with a 0.02-point increase in attribution score (95%CI: -

0.01-0.04, p =0.13). Lastly, the pathway evaluating NA and subsequent symptom attribution to diabetes and diabetes medication combined (attribution symptoms to T2D and/or T2D medications) illustrated that a 1-point increase in NA from one's personal mean was associated with a 0.03-point increase in attribution score (95%CI: -0.01-0.07, p =0.20).

On the between-persons level, the NA to T2D Attribution pathway was significant as a 1-point increase in NA from one's personal mean was associated with a 0.16-point increase in attribution score (95%CI: 0.01 - 0.32, p <.01). However, the other pathways were not found to be significant on a between-persons levels. A 1-point increase in NA from one's personal mean was associated with a 0.12-point increase in attribution to medication score (95%CI: -0.03 - 0.26, p =0.12) and a 1-point increase in NA from one's personal mean was associated with a 0.27-point increase in sum attribution score (95%CI: -0.03 - 0.57, p =0.72).

Within-person models with random effects demonstrated a similarly significant trend as seen with the NA to SXS pathway. As such, all three pathways were significant, suggesting that this pathway differed significantly between individuals. The NA to T2D Attribution pathway was significant as a 1-point increase in NA from one's personal mean was associated with a 0.57-point increase in attribution score (95%CI: 0.40 - 0.81, p <.01). A 1-point increase in NA from one's personal mean was associated with a 0.48-point increase in attribution to medication score (95%CI: 0.33 - 0.70, p <.01) and a 1-point increase in NA from one's personal mean was associated with a 2.02-point increase in sum attribution score (95%CI: 1.49 – 2.98, p <.01).

Aim 2a. The directional pathway from SXS to NA was shown to be significant on both concurrent (same-day), within-person fixed effects, and between-person levels. Same-day analyses demonstrated that, on a within-persons level, a 1-point increase in SXS from one's personal mean was associated with a 0.12-point increase in subsequent NA within the same day

(95% CI: 0.08 - 0.17, p <.01). Similarly, on a between-persons level, a 1-point increase in SXS from one's personal mean was associated with a 0.52-point increase in subsequent NA within the same day (95% CI: 0.31 - 0.69, p <.01). As such, day-level results indicate bidirectionality, with pathway significance identified in both the NA to SXS and SXS to NA directions.

On cross-lagged level, the within-persons with fixed effects pathway from SXS to NA was not found to be significant, as a 1-point increase in SXS from one's personal mean was associated with a 0.03-point increase in subsequent NA (95% CI: -0.01 - 0.08, p =0.16). On a between-person level, this pathway was found to be significant, as a 1-point increase in SXS from one's personal mean was associated with a .26-point increase in subsequent NA (95% CI: 0.14 - 0.38, p <.01).

As demonstrated in Aim 1, random effects are estimated at the within-person level, but are reflected as between-person differences, mirroring the nature of differing T2D disease experiences. As such, random effects were included as part of within-person analyses and demonstrated significant SX to NA pathway findings, suggesting that this pathway differed significantly between individuals. Same-day analyses with random effects demonstrated that, on a within-persons level, a 1-point increase in SXS from one's personal mean was associated with a 0.03-point increase in subsequent NA within the same day (95% CI: 0.01 - 0.05, p <.01). Cross-lagged analyses with random effects illustrated that a 1-point increase in SXS from one's personal mean was associated with a 0.02-point increase NA (95% CI: 0.01 - 0.04, p <.01).

Though this pathway did not replicate the reverse of the within-persons fixed-effects lagged directional findings as those found between NA and SXS, it underscores the potential consistency of the day-level bidirectionality. Additionally, as seen by between-persons and

random effects findings, patterns of significance may support further bidirectional evaluations for these relationships on these levels of analysis.

Aim 2b. Moderation analyses demonstrated that symptom attribution did not significantly moderate the relationship between symptom experience and NA such that attributing symptoms to diabetes and/or diabetes medication was not indicative of a significant increase in NA at next time point. Moderation analyses were conducted for symptom attribution across both measured domains (attribution to T2D symptoms and attribution to T2D medications), as well as combined attribution (both T2D symptoms and T2D medications as sum attribution score using the SUM feature in Mplus). The first pathway (Figure 3) showed a non-significant positive relationship between symptom endorsement and NA with symptom attribution assigned to T2D. Attributing symptoms to T2D was indicative of a 0.08 decrease in NA (95% CI: -0.50-0.34, p=0.43). The second pathway (Figure 4) showed a non-significant negative relationship between symptom endorsement and NA with symptom attribution assigned to T2D-related medications. Attributing symptoms to T2D related medications was indicative of a 0.05 decrease in NA (95% CI: -0.43-0.34, p=0.40). The third pathway (Figure 5) showed a non-significant positive relationship between symptom endorsement and NA with sum symptom attribution (attribution to T2D-related symptoms and diabetes medication). Attributing symptoms to T2D Attribution sum was indicative of a 0.06 decrease in NA (95% CI: -0.28- 0.15, p=0.22) (Table 8).

Qualitative Analysis (Aim 3)

This exploratory aim focused on evaluating the potential known existence of the relationship between NA and SXS from the patient perspective. Although themes of negative affect and symptom experience were illustrated by results from qualitative analysis of exit

interviews with study participants, it was not possible to deduce consistent bidirectionality or one-way directionality from this qualitative sample.

Bidirectionality detection was not included as a theme within the original codebook (Appendix B) to avoid potential bias in thematic analysis interpretation and initial coding. As such, interpretation of bidirectionality was conducted post-preliminary coding and is considered evident as demonstrated by a patient's description of "x" causing "y" and "y" also causing "x." Bidirectionality was also considered to be evident in quotes describing "x" and "y" in unison (within the same quote from the same patient at the same time) which mirrors levels of same-day and lagged quantitative analyses. However, specific timeframe (e.g., same-day versus over study period) was not included in the codebook or within post-coding analysis.

The previously defined bidirectionality and NA/SXS theme co-occurrence was only seen in 18% of interviews. Within these datapoints, it was not possible to discern specific time periods or predictive and casual relationships (as seen in examples to follow). As such, the content of these responses did not provide adequate saturation to support bidirectional conclusions. Negative affect was coded in 49% of interviews and symptom experience was coded in 57% of interviews. Further, participants shared instances of experiencing increased physical discomfort (including both symptoms and side effects to treatment) and feeling overwhelmed, nervous/anxious, having low mood, among others. Though bidirectionality could not be specifically proven by this thematic analysis, the content and salience of NA and SXS-related challenges is particularly meaningful. As seen in Appendix A, NA and SXS were not specifically evaluated through the exit interview (as the exit interview was initially designed to gather feedback on mobile app and pilot study experience), yet these themes were embedded within participant experience. Natural and spontaneous occurrence of these themes through exit

interviews suggests that participants had knowledge of impact of NA and SXS, though it is not possible to draw broader assumptions about the relationships between NA and SXS with this qualitative dataset.

Negative Affect *(defined as: anger, guilt, fear, nervousness, inability to achieve a goal, sadness, lethargy, distress)*

- "If [I] feel like a failure before, [I am] gonna feel like a failure in the end because you couldn't keep up with your [diabetes] lifestyle."
- "I'm not sad, I'm not depressed, I'm not angry – but at the same time, I'm not happy, I'm just here."
- "Living with diabetes is really scary, it's really scaring me. And I think it's because my mom, she had Type 1, and to be honest, the reason why I was so motivated into this [study], was because I watched my mother and she just gave up because she couldn't handle it, and it is really stressful living with diabetes… There is only so much I can do, because of my health."
- "It is very hard for me. Like the depression and the stress and every day I went through the same thing."
- "I was home alone after going to work, and like I didn't have anything to make me feel happy about."

General Symptoms *(defined as: changes in appetite/eating, thirst/dry mouth, increased urination, nausea/upset stomach, fatigue, pain, dizziness or lightheadedness, blurred vision, concentration challenges, headache, irregular leg/feet sensations)*

- "So it's helped me keep better regulation of how I feel as far as pain, as far as being, uh, better [able] to concentrate, to sleep. All of those things, which to me had been taken for granted but now I find they're very, very important to me"
- "My stomach would feel kind of messed up. And I have to take it [medication] in the morning, and drop my son off, and have to go to work with that nasty feeling."
- "There is only so much I can do, because of my health… I do urinate a lot, and I urinate a lot more when my sugar is high and when its low. I use that bathroom a lot when my sugar is high. And when it is normal, I don't go to the bathroom as much."
- "If [my] mouth was dry, or if you know do have any pain…I always, I always have pain."
- "Last week I woke up with nausea. And I was afraid, and I run to the kitchen to prepare something to eat because I think that the blood [sugar] was very low. And when I ate, everything was okay."

Co-occurring NA and SXS experiences *(defined as: NA and SXS coded in same person/quote; "x" causing "y," and vice versa)*

- "I am upset about taking it [medication] because I am in poor health. If I didn't have to take it, I could do a lot of other things in that time, the little period of time of me having to take my medication, test my glucose. That's like 20 minutes of my day [that is] just stopped."
- "I had some major [health] issues in the last 2 weeks that added to my stress, [like] … I have pain every day, I'm in pain every day, so … you'll see that in the survey. I have pain every day."
- "The nausea… having those feelings overall is like … something that we diabetics have to deal with to last a little bit longer on earth."

- "Like I said, I had a lot of low numbers, which contributed to concentration difficulty, blurred vision difficulties, and feeling shaky that exasperated my already existing anxiety."
- "How overwhelmed do you feel, in regards [to] dealing with diabetes, and having diabetes, and the whole medication part, because it is very overwhelming. It's a two-part thing with diabetes with the fact that, since I was diagnosed at 21, it's like, I feel like, it's a lottery. The numbers could be… you could play a number, but the numbers could be too high, too little. Either way you got to balance it out. And it's difficult to have that balance."
- "My mood has been so down … I didn't really have the motivation and I've been in a lot of pain."
- "Feeling overwhelmed about my diet. Lack of… too much. Those kinds of things. It made me on high alert…. [I am] a little bit more self-conscious, I guess."
- "I'm not a real excited person, but I have gotten nervous and stuff like that when my sugar is acting up."
- "I believe I felt overwhelmed about taking my medications [and] I feel upset about taking it… I am upset about taking it because I am in poor health."
- "I never thought my feelings can impact my diabetes. If I woke up mad, I probably wouldn't test my sugar."
- "Yes, I wake up with depression, I wake up with severe pain"

Chapter IV: Discussion

The purpose of this study was to examine the bidirectional associations of negative affect, with symptom experience and symptom attribution, through day-level and cross-lagged analyses of ecological momentary assessment data (EMA) and exploratory qualitative analysis of participant exit interviews. Significant relationships were found on within-persons levels in quantitative analyses at both day-level and lagged-level pathways between NA and SXS. The reverse pathway, SXS to NA was found to be consistently significant on day-level only. Though bidirectionality was not confirmed through qualitative results, qualitative findings generally supported participant acknowledgement of impact of NA and SXS. To the best of our knowledge, this study was the first to evaluate bidirectionality using EMA and qualitative data among adults with type 2 diabetes.

Summary of Results Testing Study Aims

Bivariate correlations of this secondary analysis demonstrated a significant negative correlation between HbA1c and NA scores aggregated over time. This relationship may underscore associations of NA and diabetes symptoms, though HbA1c and SXS were not correlated. Additionally, age was negatively correlated with NA scores aggregated over time and was positively correlated with total physical symptoms aggregated over time. Both demographically-based correlations highlight importance of patient factors within this sample, and may further impact associations in both the NA to SXS and SXS to NA pathways.

The first aim of this study was to evaluate associations of NA with subsequent symptom reports and symptom attribution. Higher levels of NA at one EMA survey were positively associated with greater symptom endorsement at the subsequent assessment over study period. Higher levels of NA were also associated with greater symptom endorsement within the same

day. This finding supports the NA to SXS directional pathway and was consistent across within- and fixed-effects, between-person, and random effects analyses.

The association between NA and symptoms has been previously evaluated in T1D and T2D patients, with significant associations found between depressive symptoms and greater symptom reporting (Cienchanowski, et al., 2003; Ludman, et al., 2004). Similar relationships specifically citing anxiety as being responsible for elevated reports of momentary symptoms, and depression as being associated with exaggerated recall of past symptoms have also been observed in healthy populations (Howren & Suls, 2012). Similar outcomes have also been found with high NA and increased symptom reporting using retrospective recall assessments (Howren & Suls, 2011) and concurrent day-level assessments (Howren & Suls, 2011; Larsen, 1992). This relationship has also been shown across a longer timeframe (6-months) in both older adults (ages 62-73), and adults experiencing acute illness (Leventhal, et al., 1996).

Additionally, higher levels of NA were associated with greater tendency to attribute symptoms to diabetes on a between-person level and with random effects on within-person analyses. Similar relationships have been previously suggested within the T2D population. Specifically, within a cross-sectional evaluation, self-reported depression has been shown to be significantly associated with greater symptom attribution to diabetes (Asman, et al., 2019). However, within this secondary analysis, higher levels of NA were not significantly associated with symptom attribution to diabetes medication or to combined attribution (attribution to diabetes symptoms and/or diabetes medication). This suggests an area of future evaluation, as NA may predispose individuals to attribute symptoms to their diabetes that may not in fact be associated with their diabetes, as previously seen with depression's association to increased recall, and anxiety's association to hypervigilance of symptoms (Mineka, et al., 1998). In an

evaluation of adults with T2D, those with high trait NA were more likely to attribute somatic and potentially-unrelated symptoms to changes in blood glucose (Wiebe, et al., 1994). Further, NA may cause individuals to become aware of diabetes-related symptoms that they would otherwise not have noticed at low levels of NA. This has been previously shown across chronic illnesses (Katon, 1998) and within diabetes (Lange & Piette, 2005).

The second aim of this study was to evaluate the association of symptom endorsement and attribution on subsequent NA. Greater symptom endorsement was found to be a significant predictor of higher levels of NA at the subsequent assessment within the same day (within- and between-person), at the cross-lagged level between persons, and with random effects (within-persons). This finding supports the SXS to NA directional pathway on the same-day level, confirming day-level bidirectionality, but does not confirm bidirectionality at the cross-lagged level, as a significant pathway was not found from SXS to NA within-persons with fixed effects. This finding illustrates a larger question for future evaluation: understanding the impact of time of day (and carryover into next day/ability to sleep) on T2D management and mood. Further evaluation of this question may help to illustrate the differences in bidirectionality on day and study-period levels.

The association between increased symptom endorsement and NA is supported within the literature, specifically that increased pain is associated with greater risk of depression (Lepine & Briley, 2004; Nicassion & Wallston, 1992). Additionally, chronic physical conditions have been shown to be strongly associated with major depressive disorder (Ohayon & Schatzberg, 2003). Though these studies do not specifically highlight NA, they support the need to track and monitor physical symptoms that may be indicators of depressive symptom development over the course of chronic illness experience. As the results of this analysis supported SXS as a predictor

of subsequent NA on the day level, literature supports that individuals experiencing increased symptom burden often experience negative mood and diabetes distress which may pair with treatment regimen frustration and non-compliance (Kane et. a., 2018). This finding highlights that individuals with T2D experience a range of symptoms and experiences (both physical and mood-related) that individualize their potential challenges and successes with disease management.

As seen in Table 3, the measurement of symptoms in this study accounted for daily evaluation of 13 symptoms used within the symptom endorsement checklist on the MyDay app. As seen by the frequencies indicated, patients endorsed different symptoms over time, varying both at the timepoint-to-timepoint and person-to-person level. The composition of the T2D disease experience varies depending on biological factors and self-management. Oral antidiabetic medications and patient behaviors (such as medication adherence and behavioral changes in real world settings) have been previously cited to influence diabetes outcomes (Cobden, et al., 2010). Further, as the specific treatments for T2D are not consistent across all patients, the disease experience, treatment side-effects, and health outcomes vary on an individual basis.

Although symptom attribution did not demonstrate a consistent moderating effect, it should still be considered as a variable of future evaluation. Given the design of this study, it was not possible to evaluate attribution on a specific-symptom-level. This may have impacted overall attribution-related results, as the presence of attribution endorsement became more generalized to symptoms overall. This limitation of attribution evaluation is also mirrored in moderation analyses, which may have impacted the bounds of SA-related variables as moderators. The causal pathways of attribution within T1D and T2D were recently evaluated by Persky and

colleagues, incorporating the structure of attributional prompts for individual factors that cause or contribute to T2D (Persky et al., 2021). Though this study did not evaluate NA, causal attributions were identified between genetic and behavioral components and the participant's diabetes type (Persky et al., 2021). Similar attribution assessments on the causal factor level have been conducted with T1D and T2D to illustrate genetics as the primary cause that disease development is attributed to (Rose, et al., 2019). Such structure supports future iterations of SA evaluation within NA and SXS (Persky et al., 2021).

Findings of this secondary analysis underscore the necessity to evaluate these directional pathways in greater detail, as random effects illustrated that participants significantly varied from each other. Impact of random effects has been previously evaluated in a bidirectional analysis of pain and physical activity (Rabbitts, et al., 2015), sleep and affect (Shen et al., 2021), and has been used to provide real-world examples of variability from the sample. When evaluating the relationship between seasonal change and affect, significant random effects were used to illustrate differing reactions to darkness and mood (e.g., shortening daylight hours and low mood) (Denissen, et al., 2008). Though fixed-effect models have historically held advantage over random-effects models due to ability to control level 2 variables, fixed-effects models do not allow for effect estimation when variables remain consistent within clusters, supporting the inclusion of both fixed- and random-effects models (Schunk, 2013). Further, random effects have previously been included to evaluate within-subject variance across individuals in momentary data (Dunton, 2017; Hedeker et al., 2008), and have been reported in cross-lagged analyses, even when within-persons fixed-effects are non-significant (Shen et al., 2021).

Taken together, the directional pathway from NA to SXS and SXS to NA in same-day/concurrent analyses support bidirectionality. Bidirectionality has previously been evaluated

within diabetes and depression (Pan, et al., 2010; Chen, et al., 2013), stress, depression, and diabetes (Joseph & Golden, 2017), and depression and diabetes regiment distress (Hessler, et al., 2014). Though these bidirectional relationships are different than those evaluated within this secondary analysis, they support the clear interest in evaluating causal mechanisms within this disease group (e. g., mood, self-management).

The third aim of this study was to evaluate the patient perception and report of the relationship between NA and symptom experience using qualitative exit interviews. As previously mentioned, this exit interview was not originally designed to be an open-ended qualitative experience. As such, the interview structure did not include as many open-ended questions as the typical qualitative interview might entail and followed the structure of a close-ended evaluation. As seen in the interview script (Appendix A), the interview involved prompts and option-list questioning format. Though the qualitative data collected did illustrate an impactful connection between NA and SXS, the time-oriented and sequential content that was aimed for in construct was not found in results. For future iterations of the qualitative portion of this study, it would be beneficial to include more open-ended questions specifically evaluating for mood, symptom experience, and the connection between the two. This design shift would likely lead to a higher quantity of data collected within each interview, therefore providing transcripts with increased depth for analysis. Previous qualitative evaluations within the T2D populations have highlight similar themes to those presented in this secondary analysis. Specifically, symptoms and symptom attribution (Mayer & Rosenfeld, 2006; Funk, et al., 2001), as well as affect, depression, and anxiety (Gask et al., 2011) have been identified through qualitative interviews in the diabetes population.

Summary of Methodology

Regarding methodology within aims 1 and 2, EMA has been previously used to evaluate NA using similar modifications to the PANAS in T1D (Shapira, et. a., 2021), in T2D (Skaff, et al., 2009), and in T2D using the circumplex model of emotion (Wagner, et al., 2017). T1D and T2D symptoms have been previously evaluated using similar diabetes symptom lists (Cienchanowski, et al., 2003). The modified Diabetes Symptom Checklist used within this secondary analysis was also used in recent work with EMA structure (Wagner, et al., 2012).

Ability to report and compare within- and between-person analyses within the EMA data structure has been previously used to describe affect variability, and time-oriented changes in diabetes management (Wagner, et al., 2017). Similar to the findings in this secondary analysis, differences in significance on within- and between-person levels were found, highlighting the importance of distinguishing levels of analysis, and potential problems that may arise from drawing within-person conclusions from between-person associations (and vice versa) (Wagner, et al., 2017). Additionally, similar daily diary methodology has been used to evaluate NA between- and within-persons within the same sample, using lagged models with fixed effects (Skaff, et al., 2009). Within this secondary analysis, within-persons effects evaluate whether increases in NA within a person are associated with increases in SXS within that same person. Similar designs confirm within-person effects as seen in evaluation of NA and increased chronic pain (Frumkin & Rodebaugh, 2021), EMA evaluations of NA and BPD symptoms (Scott, et al., 2017), and longitudinal analysis of NA and cognitive decline symptoms (Zainal & Newman, 2009). Between-persons effects show that people with higher NA also have higher SXS. Similar results with between-persons effects have been previously seen in affect and depressive symptoms (Dejonckheere, et al., 2018), stress and negative emotion (Du, et. al, 2018), and negative and psychotic symptoms (Kramer, et al., 2013).

Though the within-persons effects of this secondary analysis are more compelling, they are not conclusive, as there may be confounding variables that differ from person to person (e.g., comorbidities, sleep, self-management ability). Additionally, there is discrepancy in the magnitude of the within versus between NA and SXS associations. Studies that rely on between-person associations may be over-estimating the magnitude of this effect. As such, reporting both within- and between-person effects allows for full characterization of the results, and has previously been used to illustrate risk pathways between symptoms and substance use (Colder, et al., 2020), the moderation of heart rate on daily stress and NA (da Estrela, MacNeil, Gouin, 2021), the relationship between self-esteem and depressive symptoms (Masselink, et. a., 2018), and the effect of positive affect on daily heart rate (Schwerdtfeger & Gerteis, 2014). As demonstrated by the literature, reporting both between- and within-person effects has been previously done, though has rarely been used to illustrate bidirectionality, as the results of this secondary analysis describe.

The qualitative and quantitative data used in this secondary analysis is a novel combination. Though exit interviews have not received as much attention or use within qualitative literature, they provide an opportunity for eliciting feedback, insights, and personal experience (Young & Hagerty, 2007). The combination of EMA and qualitative/exit interviews has previously been used in evaluating opioid medication and cannabis use in chronic pain (Goodell, et al., 2021), non-suicidal self-injury (NSSI) and suicide risk in Veterans (Gromatsky, et al., 2022), and drug use in vulnerable populations (Markowski, et al., 2021), among others. To our knowledge, this combination of methodology has not yet been applied to individuals with T2D. As such, the methodological combination of this secondary analysis fills a gap in the current diabetes literature and provides a PRO-based evaluation that spans both qualitative and

quantitative methods. As illustrated by the results, this combination yields helpful information in conceptualizing future study iterations and can also be used to create tailored interventions based on directional pathways.

The significance of random effects within this secondary analysis supports the need for patient-centered care as each outcome variable and corresponding lagged relationships was significantly different person-to-person. Patient-centered care has been previously evaluated and positively associated with diabetes self-care (self-management, quality of life) and disease management education (Williams, et al., 2016; Hong et al., 2020). Further, using a patient-centered approach in diabetes care and self-management education creates a foundation for effective and efficient patient-provider interactions (Hong et al., 2020; Schwartz, et al., 2017). As confirmed by the literature, patients feel it is a priority to have their health-related concerns heard by providers (Street, et al., 2009). As previously mentioned, Bodenheimer's Chronic Care Model underscores the importance of patient-provider communication as a factor in producing improved health outcomes (Bodenheimer, et al., 2002). Taken together, the significance of random effects within this secondary analysis supports the need for individualized and patient-centered approaches to disease management.

Limitations

A number of limitations of this secondary analysis should be considered. As the parent study was conducted to evaluate EMA responses at 3 time points per day in addition to baseline and follow-up questionnaires, it is possible that patients experienced study fatigue or frustration based on the quantity and repetitiveness of questions and questionnaires they were asked to complete. This may have also increased awareness of potential stagnant results to treatment (Goldberg et al., 2017). Because this study only evaluated individuals that had access to a smart

phone, it is possible that patients experienced additional distress in needing to spend more time on their phone than they usually would. Given the pilot-nature of this study, participants experienced technological glitches with the mobile application, and/or may have missed surveys due to outstanding reasons (medical hospitalizations, work and family commitments). It would be beneficial for future iterations of this study and analysis to evaluate daily data that had no missing data points. Although this would significantly decrease sample size and the window for lagged analyses, it would provide an opportunity to compare the impact of missing data on overall findings.

Additionally, as patients were given the qualitative exit interview at the end of study participation, their responses may have been impacted by the relief of completing study participation and motivation to receive full study payment. Although payment procedures were completed prior to exit interview to minimize bias responses, it is possible that these efforts were not consistently effective. In order to address this limitation in future studies, it may be beneficial to include a qualitative interview component at the beginning of study participation to provide an opportunity for patients to describe their current symptom burden and self-management experience as well as any anticipatory thoughts they may have about use of the mobile application. Pre- and post-intervention qualitative evaluations have previously been used to describe the impact of study participation (Green-Morris, 2019) which may direct future research in the use of EMA mobile applications. Though this would provide additional burden within patient participation and qualitative analysis, it would allow for consistency in pre- and post- (as well as baseline and follow-up) evaluations.

As previously mentioned, the qualitative exit interview was not specifically designed for this secondary analysis. Therefore, the structure and content of interviews included information

regarding study participation experience and feedback. As such, the quantity and saturation of themes may be different with a qualitative interview that was specifically designed for this secondary analysis. This interview design would contain open-ended questions specifically referencing affect and symptom experience.

Evaluating symptoms, and specifically focusing on physical symptoms, also highlights an area of future improvement and limitation to results interpretation. Given the natural overlap of depressive symptoms (e.g., changes in appetite, difficulty sleeping, psychomotor agitation/retardation) with physical symptoms evaluated in T2D, preforming factorial sensitivity analyses would allow for further exploration and acknowledgement of the potential overlap within these two symptom clusters.

Additional limitations were linked to language fluency and smart phone accessibility of the patient population. Given the recruitment location of this study, future iterations should include translated Spanish study materials. Providing study materials in both English in Spanish would expand the scope of eligible participants and create an opportunity for increased socio-cultural evaluation. Access to smart phones with wifi/internet capability created an additional barrier to participation. By providing participants with the option to use a study-issued smart phone, study participation would reach individuals that do not have reliable or regular access to smart phone devices.

Lastly, sample size and generalizability create limitations in conceptualizing the bidirectional pathways, moderation results, and qualitative analyses on a larger scale. The population of this study consisted primarily of ethnically diverse and socioeconomically disadvantaged patients. Though this population represents a group that has limited representation within clinical research, our findings cannot be easily generalized to the larger population.

Replicating this study within different cultural groups and among individuals of varying socioeconomic status may provide an opportunity to compare and contrast the impact of culture, financial resources, and environmental factors. Additionally, due to the pilot-nature of this study and size of this sample, power analyses were limited. This may have restricted applicability of results to larger populations.

Implications for Future Research

Detected bidirectionality suggests that interventions that reduce negative affect would also reduce the experience of physical symptoms, and that interventions that reduce day-level physical symptom experiences would also reduce negative affect. Due to the cyclical and causal nature of high NA and/or high symptom endorsement, targeting one of these variable groups may have a positive impact on the other. This allows for some flexibility within intervention design, patient and/or clinician goals, and type of treatment. Further, this flexibility underscores the previously mentioned importance of patient-centered care. Results of this study suggest that targeting treatment of NA may improve physical symptom experience at later time points. This may be applicable not only with the T2D population, but across other disease groups, as mood can present a barrier to completing elements of symptom management.

As previously mentioned, this sequence of methodology is relatively underused and provides a unique combination of intensive longitudinal design with qualitative analysis. Although these methods are on opposite sides of a proverbial statistical spectrum, they provide a detailed illustration of the patient experience (within the natural environment and as reported and recorded directly from the patient). The continued use of combining EMA and qualitative data within chronic illness populations would be beneficial in evaluating patient reported outcomes

from multiple data sources. Future iterations of this study would benefit for a genuine open-format qualitative interview.

Clinical Implications and Future Directions

The current study contributes significantly to future research as this secondary analysis combined two different forms of patient-reported outcomes, using vastly different analysis methodology. By employing the combination of EMA and qualitative methodology to explore bidirectionality, the experience of the individual patient was captured on multiple levels, and can be used for future targeted intervention development. As such, many of these participants became active stakeholders in their diabetes management processes if they were not already, as they were empowered to share their study-related experiences and provide feedback that may be incorporated into future iterations of this study. Continuing to provide this reflective post-study opportunity may lead to a more patient-centered approach to disease management and care in chronic illness. The variety in symptom endorsement highlights that individualistic nature of diabetes symptoms – it can be assumed that each participant experienced some combination of symptoms to varying extents, though not the same combination to the same extent. This can be applied to diabetes care at large, as the personalization and individual evaluation may lead to overall improvements in disease knowledge and care. Clinically, these results illustrate the necessity to discuss treatment priorities with patients, and to use the CCM outline to guide productive and proactive interactions and decision making.

Additionally, as previously mentioned, the pathways detected between NA and SXS provide an opportunity to apply interventions to one variable, and evaluate if there are directional effects on the sequential variable. As illustrated by the results of this secondary analysis, higher levels of NA can be quite impactful on subsequent symptom experience. By targeting treatments

towards NA, it is possible that individuals may experience improvements (or even more neutral) symptoms experiences as later timepoints.

Future analyses evaluating the predictive nature of affect would be beneficial. Specifically, using positive affect as a predictor of lower/lesser symptom experience would further support the findings of this secondary analysis. Additionally, focusing on specificity of symptom attribution would provide helpful information on attribution patterns within endorsed symptoms. As previously mentioned, this study design did not allow for evaluation of symptom attribution on an individual symptom level, but rather captured attribution as reflected across all possible endorsed symptoms. Due to this design, it was not possible to tease apart the level of attribution as it connected directly to symptoms.

Lastly, exploring the impact of accountability on disease management and health maintenance is an additional area of future exploration for patient-centered intervention opportunities. Accountability and affect have been previously evaluated and shown to be positively correlated (e.g., increase in supportive structure and/or accountability supports positive affect) in organizational and management structures (Dewi & Riantoputra, 2019), adherence to health interventions (Mohr et al., 2011), as well as in diabetes (Nagelkerk, et al., 2006; Dellasega, et al., 2012). By utilizing the underlying mechanism of accountability, patients may feel supported in their efforts toward positive behavioral change and self-management simply by using a mobile application. This underscores the importance of providing a patient-centered and patient-focused approach, using an individual's self-efficacy as a method to make improvements for the future.

Taken together, this secondary analysis provides the basis for general improvements and personalization in T2D care. Though experiences of chronic illness vary across disease groups

(e.g., differing sets of symptoms, treatments, burden, and outcomes), it is possible that the bidirectional relationship between NA and SXS that has been detected with this T2D population may be seen in other chronic illnesses such as cancer, heart disease, kidney disease, among others. Replicating this study across disease groups may provide additional opportunity to create highly personalized care that spans across illnesses. Further, the results of this secondary analysis provide an exciting opportunity to learn more about bidirectional pathways existing across chronic illness groups.

Tables

Table 1
Baseline Participant Demographic and Diabetes-Related Variables (N=61)

Variable	Mean (SD) or %
Age	55.6 (9.6)
Race	
Black/African American	61%
Asian	5%
White	10%
Other	10%
Did not answer	14%
Ethnicity	
Hispanic/Latino	36%
Not Hispanic/Latino	56%
Did not answer	8%
Female Sex	64.5%
HbA1c	8.6 (2.3)
Insulin Users	43.5%
Years since T2D Diagnosis	
4-10 years	27.4%
11-20 years	40.3%
21+ years	32.3%
Income	
Less than $10,000	25.8%
$10,000-$24,999	27.5%
$25,000-$49,999	22.6%
$50,000-$99,999	17.7%
$100,000-$149,999	1.6%
$200,000 or more	1.6%
Unreported	3.2%
Education	
Some High School	19.4%
High School Diploma	24.2%
Some College	21%
College Degree	17.7%
Some Graduate School	3.2%
Graduate Degree	12.9%
Employment	
Full Time	21.0%
Part Time	6.5%
Student	1.6%
Disabled	21.0%
SSI	27.4%
Retirement	17.7%
Unemployed	3.2%
Unreported	1.6%
Health Insurance	96.8%

Table 2
Main Study Variables

Variable	M(SD)	Min	Max
NA Total	0.86 (1.65)	0.00	9.00
NA Total Daily Mean	0.90(1.53)	0.00	8.00
SXS Total	4.52(3.12)	0.00	13.00
SxTotal Daily Mean	6.02(4.44)	0.00	23.50
T2D Sx Attribution	1.00(.977)	0.00	4.00
T2D Med Attribution	0.89(.879)	0.00	4.00
Sum Attribution	1.87(1.75)	0.00	8.00

Key: Negative Affect (NA); Physical Symptom Experience (SXS); Symptom (Sx); Medication (Med); Type 2 Diabetes (T2D)

Table 3
Distribution and Frequencies of Diabetes symptom endorsement variables

Variable	Mean (SD)	Percentage of Total Surveys Endorsed
Increased appetite or eating	0.43(0.63)	35.3%
Decreased appetite or eating	0.25(0.56)	19.9%
Very thirsty or dry mouth	0.85(0.90)	57.0%
Strong need to urinate	0.67(0.83)	46.3%
Nausea or upset stomach	0.24(0.56)	18.4%
Fatigue or tired	0.66(0.75)	51.3%
Pain	0.75(0.88)	50.3%
Dizziness or lightheadedness	0.20(0.47)	16.7%
Blurred vision	0.35(0.67)	26.0%
Trouble concentrating	0.25(0.50)	21.7%
Headache	0.34(0.62)	27.1%
Leg/feet burning, tingle, ache, tender	0.53(0.65)	44.9%
Other physical symptoms	0.41(0.72)	28.6%

Table 4
Pearson Correlation Coefficients Between Continues Predictor Variables and Outcomes

	HbA1c	NA Total	NA Total Daily Mean	SXS Total	SxTotal Daily Mean	T2D Sx Attribution	T2D Med Attribution
NA Total	*r*=-0.06** *p* <.01	--	--	--	--	--	--
NA Total Daily Mean	*r*=-0.02 *p* =0.37	*r*=0.92** *p* <.01	--	--	--	--	--
SXS Total	*r*=-0.00 *p*=0.82	*r*=0.43** *p* <.01	*r*=0.46** *p* <.01	--	--	--	--
SXTotal Daily Mean	*r*=-0.02 *p*=0.38	*r*=0.46** *p* <.01	*r*=0.48** *p* <.01	*r*=0.92** *p* <.01	--	--	--
T2D Sx Attribution	*r*=-0.013 *p*=0.54	*r*=0.21** *p* <.01	*r*=0.28** *p* <.01	*r*=0.58** *p* <.01	*r*=0.57** *p* <.01	--	--
T2D Med Attribution	*r*=-0.01 *p*=0.82	*r*=0.17** *p* <.01	*r*=0.17** *p* <.01	*r*=0.56** *p* <.01	*r*=0.55** *p* <.01	*r*=0.80** *p* <.01	--
Age	*r*=0-.02 *p* =0.27	*r*=-0.20** *p* <.01	*r*=-0.05** *p* <.01	*r*=0.04* *p* =0.02	*r*=-0.05** *p* <.01	*r*=0.12** *p* <.01	*r*=0.13** *p* <.01

**p<.01, 2-tailed; *p<.05, 2-tailed; Key: Negative Affect (NA); Physical Symptom Experience (SXS); Symptom (Sx); Medication (Med); Type 2 Diabetes (T2D)

Table 5
Day-Level Variable Correlation Matrix

	Sx	SA to Diabetes	SA to Diabetes Meds
NA ^{W}	0.38 **	0.05 **	0.05 **
NA ^{B}	2.62 **	0.42 **	0.62 **
Sx ^{W}	--	0.32 **	0.25 **
Sx ^{B}	--	1.57 **	1.39 **

**p<.01, 2-tailed; ^{W} Within-person effects; ^{B} Between-person effects; all correlations account for session

Table 6
Same Day Analysis: Negative Affect (NA) and Symptom Experience (SXS)

	Estimate	P-value	95% C.I.	
			Lower 2.5%	Upper 2.5%
NA > SXS †	0.42	<.01*	0.25	0.59
SXS > NA †	0.12	<.01*	0.08	0.17
NATD > SXS ‡	0.53	<.01*	0.36	0.66
SXS > NATD ‡	0.52	<.01*	0.31	0.69

*p<.01; † within-person analyses; ‡ between person analyses

Table 7
Cross-lagged Analysis: Negative Affect (NA), Symptom Experience (SXS), Symptom Attribution

	Estimate	P-value	95% C.I.	
			Lower 2.5%	Upper 2.5%
SXS > NA †	0.03	0.16	-0.01	0.08
NA > SXS †	0.14	<.01*	.0.03	0.25
NA > T2D Attribution †	0.01	0.45	-0.01	0.04
NA > T2D Med. Attribution †	0.02	0.13	-0.01	0.04
NA > Attribution (Sum) †	0.03	0.20	-0.01	0.07
SXS > NA ‡	0.26	<.01*	0.14	0.38
NA > SXS ‡	0.52	<.01*	0.28	0.70
NA > T2D Attribution ‡	0.16	0.02*	0.01	0.32
NA > T2D Med. Attribution ‡	0.12	0.12	-0.03	0.26
NA > Attribution (Sum) ‡	0.27	0.72	-0.03	0.57

*p<.05 † within-person analyses; ‡ between person analyses

Table 8
Moderation Analysis: Moderating role of Attribution on Negative Affect

	Estimate	P-value	95% C.I.	
			Lower 2.5%	Upper 2.5%
T2D Symptom Attribution	-.08	.43	-.50	.34
T2D Med Attribution	-.05	.40	-.43	.34
Symptom & Med Attribution	-.06	.22	-.28	.15

*p<.05

Table 9
Random effects of within-analyses of main variables

	Estimate	P-value	95% C.I.	
			Lower 2.5%	Upper 2.5%
SXS > NA [L]	0.02	<.01*	0.01	0.04
NA > SXS [L]	0.05	<.01*	0.01	0.18
NA > T2D Attribution [L]	0.57	<.01*	0.40	0.81
NA > T2D Med. Attribution [L]	0.48	<.01*	0.33	0.70
NA > T2D Sum Attribution [L]	2.02	<.01*	1.49	2.98
SXS > NA [D]	0.03	<.01*	0.01	0.05
NA > SXS [D]	0.20	<.01*	0.10	0.36

*p<.01; [L] Lagged Model; [D] Daily Model

Figures

Figure 1
Timing of EMA questionnaires during study period

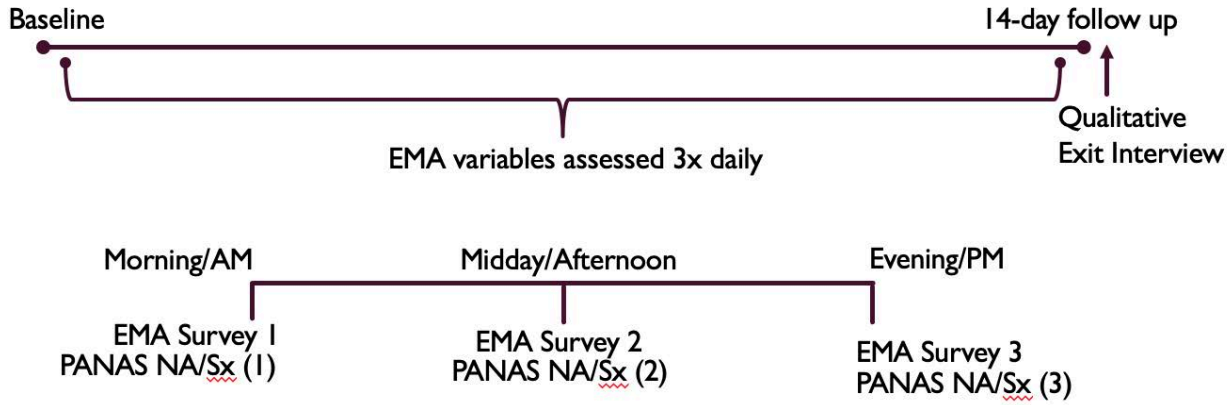


Figure 2
Symptom Attribution as a Moderator on Symptom Experience and Negative Affect

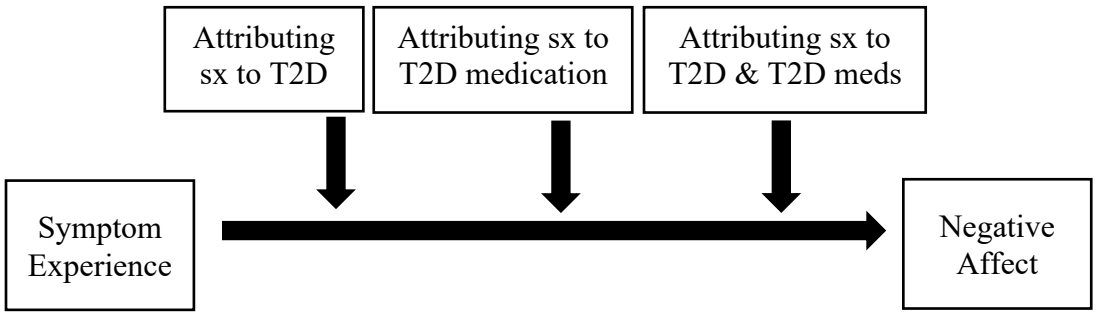
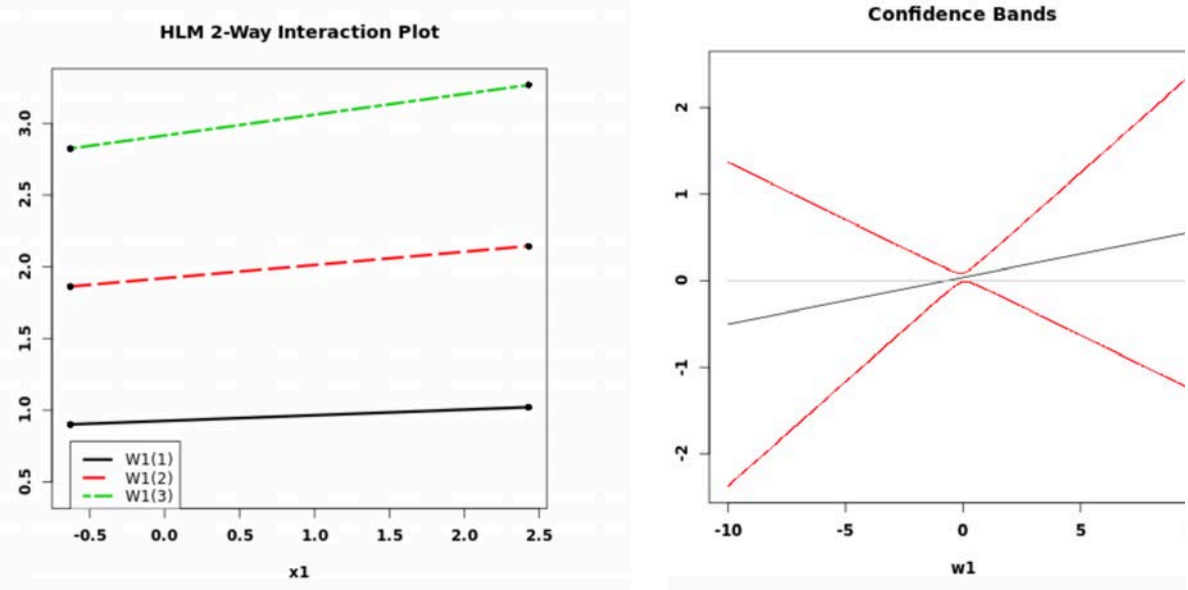
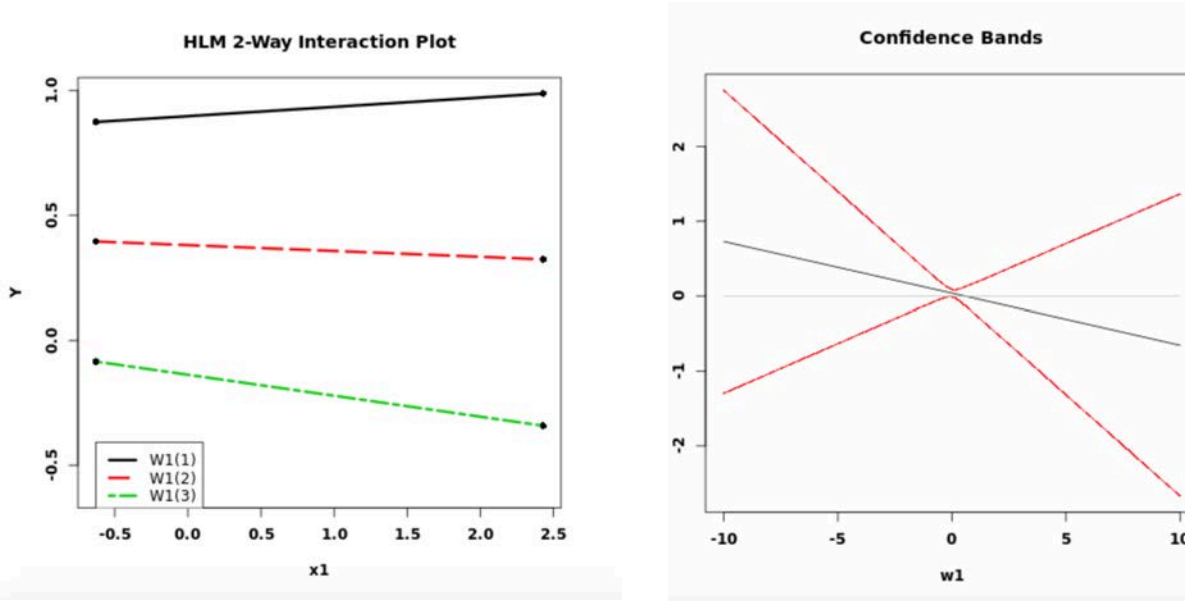


Figure 3
Plots depicting interaction between SXS and SA to Diabetes in the prediction of NA



Left panel: *Interaction between SX and Attribution to T2D (all mean-centered) in the prediction of NA. W1(1) indicates 1 SD below mean (low level NA); W1(2) indicates mean (average NA); W1(3) indicates 1 SD above mean (high NA).*
Right panel: *Confidence bands and regions for interaction between SX and NA (all mean-centered). Confidence bands are shown in red. There is no significance for the simple slope.*

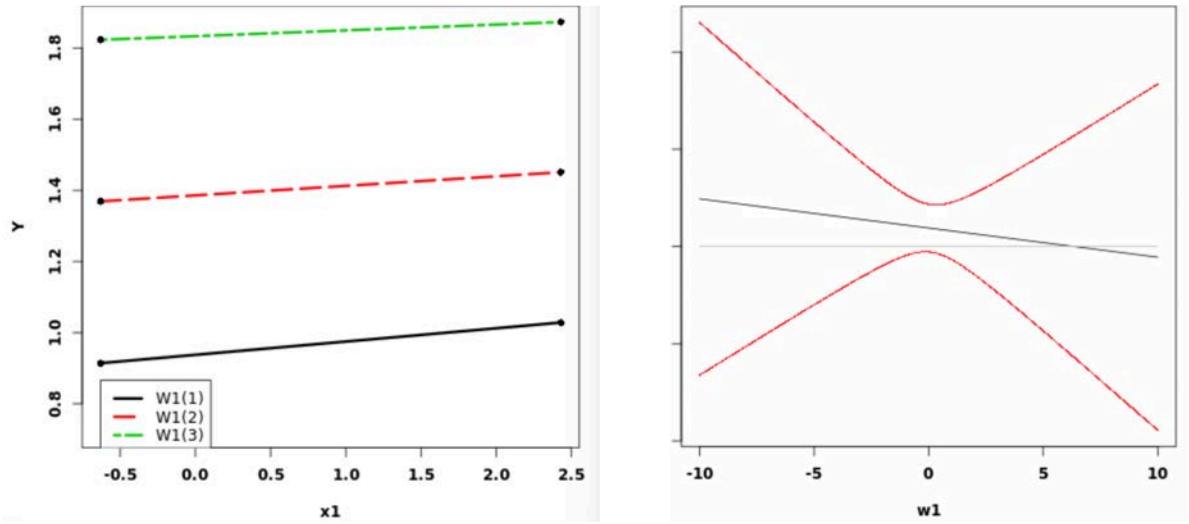
Figure 4
Plots depicting interaction between SXS and SA to Diabetes Medication in the prediction of NA



Left panel: *Interaction between SX and Attribution to T2D Medications (all mean-centered) in the prediction of NA. W1(1) indicates 1 SD below mean (low level NA); W1(2) indicates mean (average NA); W1(3) indicates 1 SD above mean (high NA).*
Right panel: *Confidence bands and regions for interaction between SX and NA (all mean-centered). Confidence bands are shown in red. There is no significance for the simple slope.*

Figure 5

Plots depicting interaction between SXS and SA to Diabetes and Diabetes Medication in the prediction of NA



Left panel: *Interaction between SX and Sum Attribution (all mean-centered) in the prediction of NA. W1(1) indicates 1 SD below mean (low level NA); W1(2) indicates mean (average NA); W1(3) indicates 1 SD above mean (high NA).*

Right panel: *Confidence bands and regions for interaction between SX and NA (all mean-centered). Confidence bands are shown in red. There is no significance for the simple slope.*

Appendices

Appendix A.

EMA Qualitative Exit Interview Questions

Overall Study Participation

1. When you think about the past 2 weeks and your study participation, what comes to mind?
    - What parts of study participation did you like best? Worst?
    - Did you have any issues with measuring your fasting blood glucose every morning?
    - Would you recommend participation in this study to others?

Lab Component of Study

2. How did you feel about the questionnaires and tasks that you completed at baseline and follow-up, while you were here with us in the lab?
    - Would you say that there was too little or too much to do?
    - Did you find any aspects overwhelming or difficult?
    - What aspects did you like best? Worst?
    - Do you have any suggestions for study staff to make participation better or easier?

App Component of Study

3. How user-friendly or challenging did you find the phone app to be?
    - What did you think about font size, interface, and function?
    - How long did it take for you to feel comfortable using the phone app?
    - Did your feelings about the phone app change over the 2-week period?
    - What parts of using the phone app did you like best? Worst?
    - Did using the phone app influence or change how you took care of yourself over the 2 weeks?
    - Would you recommend using the phone app to others?
4. Can you describe a time when the phone app was particularly challenging?
    - How did you deal with that situation?
    - Was there anything study staff could have done to help with this situation?

In Closing

5. Is there anything you would like to add to describe your participation over the past 2 weeks that would help us make the study better for future participants?

Appendix B.

Qualitative analysis codebook.

Negative Affect: anger, guilt, fear, nervousness, inability to achieve a goal, sadness, lethargy, distress, worry, shame

Symptom Experience: changes in appetite/eating, thirst or dry mouth, increased urination, nausea/upset stomach, fatigue, pain, dizziness/lightheadedness, blurred vision, concentration challenges, headache, irregular leg/feet sensation)

- Subcode: Awareness
- Subcode: Side effects

Appendix C.

Daily questions as appearing in MyDay mobile application; Attributions items for this secondary analysis listed in item 5. Negative Affect items for this secondary analysis in item 6 (a, c, f, g, h).

3. **Question Set: Symptoms 1 [6 items]**
    a. Since last survey, have you experienced INCREASED APPETITE OR EATING?
        i. Not At All
        ii. A Little
        iii. Quite A Bit
        iv. Extremely
    b. Since last survey, DECREASED APPETITE OR EATING?
        i. Not At All
        ii. A Little
        iii. Quite A Bit
        iv. Extremely
    c. Since last survey, VERY THIRSTY OR DRY MOUTH?
        i. Not At All
        ii. A Little
        iii. Quite A Bit
        iv. Extremely

    d. Since last survey, STRONG NEED TO URINATE?
        i. Not At All
        ii. A Little
        iii. Quite A Bit
        iv. Extremely
    e. Since last survey, NAUSEA OR STOMACH UPSET?
        i. Not At All
        ii. A Little
        iii. Quite A Bit
        iv. Extremely
    f. Since last survey, FATIGUE OR TIRED?
        i. Not At All
        ii. A Little
        iii. Quite A Bit
        iv. Extremely

4. **Question Set: Symptoms 2 [7 items]**
    a. Since last survey, have you experienced PAIN?
        i. Not At All
        ii. A Little
        iii. Quite A Bit
        iv. Extremely
    b. Since last survey, DIZZINESS OR LIGHTHEADEDNESS?
        i. Not At All
        ii. A Little
        iii. Quite A Bit
        iv. Extremely
    c. Since last survey, BLURRED VISION?
        i. Not At All
        ii. A Little
        iii. Quite A Bit
        iv. Extremely
    d. Since last survey, TROUBLE CONCENTRATING?
        i. Not At All
        ii. A Little
        iii. Quite A Bit
        iv. Extremely
    e. Since last survey, HEADACHE?
        i. Not At All
        ii. A Little
        iii. Quite A Bit
        iv. Extremely
    f. Since last survey, LEGS/FEET BURN, TINGLE, ACHE, TENDER?
        i. Not At All
        ii. A Little
        iii. Quite A Bit
        iv. Extremely

    g. Since last survey, OTHER PHYSICAL SYMPTOM(S)?
        i. Not At All
        ii. A Little
        iii. Quite A Bit
        iv. Extremely

5. **Question Set: Symptoms Follow-up [2 items]**
    a. If you experienced symptoms, were they caused by your diabetes?
        i. (Had No Symptoms)
        ii. Not At All
        iii. A Little
        iv. Quite A Bit
        v. Extremely
    b. If you experienced symptoms, were they caused by diabetes medications?
        i. (Had No Symptoms)
        ii. Not At All
        iii. A Little
        iv. Quite A Bit
        v. Extremely

6. **Question Set: Feelings [8 items]**
    a. Right now, do you feel UPSET?
        i. Not at all
        ii. A Little
        iii. Quite A Bit
        iv. Extremely
    b. Right now, do you feel HAPPY?
        i. Not at all
        ii. A Little
        iii. Quite A Bit
        iv. Extremely
    c. Right now, do you feel IRRITABLE?
        i. Not at all
        ii. A Little
        iii. Quite A Bit
        iv. Extremely
    d. Right now, do you feel ALERT OR ATTENTIVE?
        i. Not at all
        ii. A Little
        iii. Quite A Bit
        iv. Extremely
    e. Right now, do you feel INSPIRED?
        i. Not at all
        ii. A Little
        iii. Quite A Bit
        iv. Extremely

    f. Right now, do you feel DISTRESSED OR STRESSED?
        i. Not at all
        ii. A Little
        iii. Quite A Bit
        iv. Extremely
    g. Right now, do you feel DOWN, DEPRESSED, OR SAD?
        i. Not at all
        ii. A Little
        iii. Quite A Bit
        iv. Extremely
    h. Right now, do you feel LITTLE INTEREST OR PLEASURE in doing things?
        i. Not at all
        ii. A Little
        iii. Quite A Bit
        iv. Extremely

References

Ahmad, F. B., & Anderson, R. N. (2021). The leading causes of death in the US for 2020. *JAMA*, 325(18), 1829-1830.

Al-Khawaldeh, O. A., Al-Hassan, M. A., & Froelicher, E. S. (2012). Self-efficacy, self management, and glycemic control in adults with type 2 diabetes mellitus. *Journal of Diabetes and its Complications*, *26*(1), 10-16.

Allemann, S., Houriet, C., Diem, P., & Stettler, C. (2009). Self-monitoring of blood glucose in non insulin treated patients with type 2 diabetes: a systematic review and meta-analysis. *Current Medical Research and Opinion*, 25(12), 2903-2913.

Almeida, D. M. (2005). Resilience and vulnerability to daily stressors assessed via diary methods. *Current Directions in Psychological Science*, 14(2), 64-68.

American Diabetes Association. (2018). 6. Glycemic targets: standards of medical care in diabetes 2018. *Diabetes care*, *41*(Supplement 1), S55-S64.

American Diabetes Association. (2020b). 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2020. *Diabetes Care*, *43*(Supplement 1), S14–S31. https://doi.org/10.2337/dc20-S002

American Diabetes Association. (2021). 2. Classification and diagnosis of diabetes: Standards of Medical Care in Diabetes—2021. *Diabetes Care*, *44*(Supplement 1), S15-S33.

Apkarian, A. V., Bushnell, M. C., Treede, R. D., & Zubieta, J. K. (2005). Human brain mechanisms of pain perception and regulation in health and disease. *European Journal of Pain*, *9*(4), 463-484.

Armey, M. F., Schatten, H. T., Haradhvala, N., & Miller, I. W. (2015). Ecological momentary assessment (EMA) of depression-related phenomena. *Current Opinion in Psychology*, 4, 21-25.

Asman, A. G., Hoogendoorn, C. J., McKee, M. D., & Gonzalez, J. S. (2020). Assessing the association of depression and anxiety with symptom reporting among individuals with type 2 diabetes. *Journal of Behavioral Medicine*, *43*(1), 57-68.

Asparouhov, T., & Muthén, B. (2020). Comparison of models for the analysis of intensive Longitudinal data. *Structural Equation Modeling: A Multidisciplinary Journal*, *27*(2), 275-297.

Barrett, L. F., & Bliss-Moreau, E. (2009). Affect as a Psychological Primitive. *Advances in Experimental Social Psychology*, 41, 167–218. https://doi.org/10.1016/S0065-2601(08)00404-8

Bodenheimer T, Wagner EH, Grumbach K. (2002) Improving Primary Care for Patients With Chronic Illness. *JAMA.*2002;288(14):1775–1779. doi:10.1001/jama.288.14.1775

Bolger N, Laurenceau JP. Intensive longitudinal methods: *An Introduction to Diary and Experience Sampling Research.* New York, NY: Guilford Press, 2013.

Boyce, M. B., Browne, J. P., & Greenhalgh, J. (2014). The experiences of professionals with using information from patient-reported outcome measures to improve the quality of healthcare: a systematic review of qualitative research. *BMJ Qual Saf*, *23*(6), 508-518.

Braun, V. & Clark, V. (2006). Using thematic analysis in psychology. *Qualitative Research in Psychology*, 3, 77-101.

Bresin, K., Carter, D. L., & Gordon, K. H. (2013). The relationship between trait impulsivity, negative affective states, and urge for nonsuicidal self-injury: A daily diary study. *Psychiatry Research*, 205(3), 227-231.

Briscoe, V. J., & Davis, S. N. (2006). Hypoglycemia in type 1 and type 2 diabetes: physiology, pathophysiology, and management. *Clinical Diabetes*, 24(3), 115-121.

Burns, R. J., Deschenes, S. S., & Schmitz, N. (2015). Cyclical relationship between depressive

symptoms and diabetes distress in people with Type 2 diabetes mellitus: results from the Montreal Evaluation of Diabetes Treatment Cohort Study. *Diabetic Medicine*, *32*(10), 1272-1278.

Care, F. (2019). Standards of Medical Care in Diabetes 2019. *Diabetes Care*, *42*(Suppl 1), S124-S138.

Carls, G. S., Tuttle, E., Tan, R. D., Huynh, J., Yee, J., Edelman, S. V., & Polonsky, W. H. (2017). Understanding the gap between efficacy in randomized controlled trials and effectiveness in real-world use of GLP-1 RA and DPP-4 therapies in patients with type 2 diabetes. *Diabetes Care*, 40(11), 1469-1478.

Catz, S. L., Kelly, J. A., Bogart, L. M., Benotsch, E. G., & McAuliffe, T. L. (2000). Patterns, correlates, and barriers to medication adherence among persons prescribed new treatments for HIV disease. *Health Psychology*, 19, 124.

Cavagnolli, G., Pimentel, A. L., Freitas, P. A. C., Gross, J. L., & Camargo, J. L. (2017). Effect of ethnicity on HbA1c levels in individuals without diabetes: systematic review and meta-analysis. *PloS One*, 12(2), e0171315.

Centers for Disease Control and Prevention. (2020). *National Diabetes Statistics Report 2020. Estimates of Diabetes and its Burden in the United States.* 32.

Centers for Disease Control and Prevention. National Diabetes Statistics Report website. https://www.cdc.gov/diabetes/data/statistics-report/index.html. Accessed April 2022

Centers for Disease Control and Prevention. (2010). Number of Americans with diabetes projected to double or triple by 2050. Atlanta, GA: Center for Disease Control.

Chaney, J. M., Mullins, L. L., Uretsky, D. L., Doppler, M. J., Palmer, W. R., Wees, S. J., ... & Reiss, M. J. (1996). Attributional style and depression in rheumatoid arthritis: The moderating role of perceived illness control. *Rehabilitation Psychology*, 41(3), 205.

Chao, J., Nau, D. P., & Aikens, J. E. (2007). Patient-reported perceptions of side effects of

antihyperglycemic medication and adherence to medication regimens in persons with diabetes mellitus. *Clinical Therapeutics*, 29, 177–180.

Chen, P. C., Chan, Y. T., Chen, H. F., Ko, M. C., & Li, C. Y. (2013). Population-based cohort Analyses of the bidirectional relationship between type 2 diabetes and depression. *Diabetes Care*, 36(2), 376-382.

Chen, L., Magliano, D. J., & Zimmet, P. Z. (2012). The worldwide epidemiology of type 2 diabetes mellitus—present and future perspectives. *Nature Reviews Endocrinology*, 8(4), 228-236.

Chiang, J. J., Turiano, N. A., Mroczek, D. K., & Miller, G. E. (2018). Affective reactivity to daily stress and 20-year mortality risk in adults with chronic illness: Findings from the National Study of Daily Experiences. *Health Psychology*, *37*(2), 170.

Ciechanowski, P. S., Katon, W. J., Russo, J. E., & Hirsch, I. B. (2003). The relationship of depressive symptoms to symptom reporting, self-care and glucose control in diabetes. *General Hospital Psychiatry*, *25*(4), 246-252.

Cobden, D. S., Niessen, L. W., Barr, C. E., Rutten, F. F., & Redekop, W. K. (2010). Relationships among self-management, patient perceptions of care, and health economic outcomes for decision-making and clinical practice in type 2 diabetes. *Value in Health*, 13(1), 138-147.

Coffey, J. T., Brandle, M., Zhou, H., Marriott, D., Burke, R., Tabaei, B. P., ... & Herman, W.H. (2002). Valuing health-related quality of life in diabetes. *Diabetes care*, *25*(12), 2238 2243.

Cohen, J. (1988). The effect size index: d. *Statistical Power Analysis for the Behavioral Sciences*, *2*(1).

Colder, C. R., Lee, Y. H., Frndak, S., Read, J. P., & Wieczorek, W. F. (2019). Internalizing Symptoms and cannabis and alcohol use: Between-and within-person risk pathways with coping motives. *Journal of Consulting and Clinical Psychology*, *87*(7), 629.

Conner, T. S., & Barrett, L. F. (2012). Trends in ambulatory self-report: the role of momentary experience in psychosomatic medicine. *Psychosomatic Medicine*, *74*(4), 327.

Cross, M.P., & Pressman, S.D. (2017). Understanding the connections between positive affect and health. In C.L. Cooper & J.C. Quick (Eds.), The handbook of stress and health: A guide to research and practice (pp. 75–95). Chichester: John Wiley & Sons.

da Estrela, C., MacNeil, S., & Gouin, J. P. (2021). Heart rate variability moderates the between-and within-person associations between daily stress and negative affect. *International Journal of Psychophysiology*, *162*, 79-85.

De Young, K. P., Lavender, J. M., Crosby, R. D., Wonderlich, S. A., Engel, S. G., Mitchell, J. E., ... & Le Grange, D. (2014). Bidirectional associations between binge eating and restriction in anorexia nervosa. An ecological momentary assessment study. *Appetite*, *83*, 69-74.

Dejonckheere, E., Mestdagh, M., Houben, M., Erbas, Y., Pe, M., Koval, P., ... & Kuppens, P. (2018). The bipolarity of affect and depressive symptoms. *Journal of Personality and Social psychology*, *114*(2), 323.

Delahanty, L., Grant, R. W., Wittenberg, E., Bosch, J. L., Wexler, D. J., Cagliero, E., & Meigs, J. B. (2007). Association of diabetes-related emotional distress with diabetes treatment in primary care patients with Type 2 diabetes. *Diabetic Medicine*, *24*(1), 48-54.

Dellasega, C., Añel-Tiangco, R. M., & Gabbay, R. A. (2012). How patients with type 2 diabetes mellitus respond to motivational interviewing. *Diabetes Research and Clinical Practice*, *95*(1), 37-41.

Denissen, J. J., Butalid, L., Penke, L., & Van Aken, M. A. (2008). The effects of weather on daily mood: a multilevel approach. *Emotion*, *8*(5), 662.

Dennick, K., Sturt, J., & Speight, J. (2017). What is diabetes distress and how can we measure it? A narrative review and conceptual model. *Journal of Diabetes and its Complications*, *31*(5), 898-911.

Denollet J, deVries J. Positive and negative affect within the realm of depression, stress, and

fatigue: The two-factor distress model of the global mood scale (gms*) Journal of Affective Disorders*. 2006;91:171–180.

DiPietro, E. K. (2017). Unforgiving Pain: A Qualitative Exploration of Chronic Pain and Self Forgiveness.

Deshields, T. L., Potter, P., Olsen, S., & Liu, J. (2014). The persistence of symptom burden: symptom experience and quality of life of cancer patients across one year. *Supportive Care in Cancer*, 22(4), 1089-1096.

DeVries M, ed. 1992. The Experience of Psychopathology: Investigating Mental Disorders in Their Natural Settings. Cambridge, UK: Cambridge Univ. Press. 429 pp

Dewi, R. C., & Riantoputra, C. D. (2019). Felt accountability: the role of personality and organizational factors. *Journal of Management Development*.

Diefenbach, M. A., Leventhal, E. A., Leventhal, H., & Patrick-Miller, L. (1996). Negative affect relates to cross-sectional but not longitudinal symptom reporting: Data from elderly adults. *Health Psychology*, *15*(4), 282.

Du, J., Huang, J., An, Y., & Xu, W. (2018). The relationship between stress and negative emotion: The Mediating role of rumination. *Clin Res*, *4*(1), 1-5.

Duncko, R., Johnson, L., Merikangas, K., & Grillon, C. (2009). Working memory performance after acute exposure to the cold pressor stress in healthy volunteers. *Neurobiology of Learning and Memory*, *91*(4), 377-381.

Dunn, B. D., Stefanovitch, I., Evans, D., Oliver, C., Hawkins, A., & Dalgleish, T. (2010). Can you feel the beat? Interoceptive awareness is an interactive function of anxiety-and depression-specific symptom dimensions. *Behaviour Research and Therapy*, *48*(11), 1133-1138.

Dunton, G. F. (2017). Ecological momentary assessment in physical activity research. *Exercise and Sport Sciences Reviews*, *45*(1), 48.

Ebner-Priemer, U. W., & Sawitzki, G. (2007). Ambulatory assessment of affective instability in borderline personality disorder. *European Journal of Psychological Assessment*, 23(4), 238-247.

Eich E, Reeves J, Jaeger B, Graff-Radford S. 1985. Memory for pain: relation between past and present pain intensity. *Pain* 223:375–79

Elman, I., Borsook, D., & Volkow, N. D. (2013). Pain and suicidality: insights from reward and addiction neuroscience. *Progress in Neurobiology*, *109*, 1-27.

Emerging Risk Factors Collaboration. (2010). Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. *The Lancet*, *375*(9733), 2215-2222.

Field, A. (2013). *Discovering Statistics Using IBM SPSS Statistics*. sage.

Fisher, L., Mullan, J. T., Skaff, M. M., Glasgow, R. E., Arean, P., & Hessler, D. (2009). Predicting diabetes distress in patients with type 2 diabetes: a longitudinal study. *Diabetic Medicine*, *26*(6), 622-627.

Frumkin, M. R., & Rodebaugh, T. L. (2021). The role of affect in chronic pain: A systematic review of within-person symptom dynamics. *Journal of Psychosomatic Research*, *147*, 110527.

Funk, M., Naum, J. B., Milner, K. A., & Chyun, D. (2001). Presentation and symptom predictors of coronary heart disease in patients with and without diabetes. *The American Journal of Emergency Medicine*, 19(6), 482-487.

Garson, G. D. (2013). Fundamentals of Hierarchical Linear and Multilevel Modeling. In G. Garson, *Hierarchical Linear Modeling: Guide and Applications* (pp. 3–26). SAGE Publications, Inc. https://doi.org/10.4135/9781483384450.n1

Gask, L., Macdonald, W., & Bower, P. (2011). What is the relationship between diabetes and depression? A qualitative meta-synthesis of patient experience of co-morbidity. *Chronic Illness*, 7(3), 239-252.

Geisser, M. E., Roth, R. S., Theisen, M. E., Robinson, M. E., & Riley III, J. L. (2000). Negative affect, self-report of depressive symptoms, and clinical depression: relation to the experience of chronic pain. *The Clinical Journal of Pain*, 16(2), 110-120.

Gibson, C. J., Thurston, R. C., Bromberger, J. T., Kamarck, T., & Matthews, K. A. (2011). Negative affect and vasomotor symptoms in the Study of Women's Health Across the Nation Daily Hormone Study. *Menopause (New York, N.Y.)*, *18*(12), 1270 1277. https://doi.org/10.1097/gme.0b013e3182230e42

Gillespie, C. R., & Bradley, C. (1988). Causal attributions of doctor and patients in a diabetes clinic. *British Journal of Clinical Psychology*, 27(1), 67-76.

Goldberg, R. L., Piccirillo, M. L., Nicklaus, J., Skillington, A., Lenze, E., Rodebaugh, T. L., ... & Piccirillo, J.F. (2017). Evaluation of ecological momentary assessment for tinnitus severity. *JAMA Otolaryngology Head & Neck Surgery*, *143*(7), 700-706.

Golden, S. H., Brown, A., Cauley, J. A., Chin, M. H., Gary-Webb, T. L., Kim, C., ... & Anton, B. (2012). Health disparities in endocrine disorders: biological, clinical, and nonclinical factors—an Endocrine Society scientific statement. *The Journal of Clinical Endocrinology & Metabolism*, *97*(9), E1579-E1639.

Goldman, S. L., Kraemer, D. T., & Salovey, P. (1996). Beliefs about mood moderate the relationship of stress to illness and symptom reporting. *Journal of Psychosomatic Research*, 41(2), 115-128.

Goodell, E. M. A., Nordeck, C., Finan, P. H., Vandrey, R., Dunn, K. E., & Thrul, J. (2021). Feasibility and acceptability of using smartphone-based EMA to assess patterns of prescription opioid and medical cannabis use among individuals with chronic pain. *Internet Interventions*, *26*, 100460.

Gonder-Frederick, L. A., & Cox, D. J. (1991). Symptom perception, symptom beliefs, and

blood glucose discrimination in the self-treatment of insulin-dependent diabetes. In Mental representation in health and illness (pp. 220-246). Springer, New York, NY.

Grant RW, Devita NG, Singer DE, Meigs JB. Polypharmacy and medication adherence in patients with type 2 diabetes. *Diabetes Care*. 2003;26(5):1408-1412.

Green-Morris, G. (2019). An evaluation of the effectiveness of foot care education in rural clinics. *Journal of Diabetes & Metabolic Disorders*, 1-9. Fonseca, V. A. (2009). Defining and characterizing the progression of type 2 diabetes. *Diabetes Care*, *32*(suppl 2), S151-S156.

Griffin, K. W., Friend, R., Kaell, A. T., Bennett, R. S., & Wadhwa, N. K. (1999). Negative affect and physical symptom reporting: A test of explanatory models in two chronically ill populations. *Psychology and Health*, *14*(2), 295-307.

Gromatsky, M., Patel, T. A., Wilson, S. M., Mann, A. J., Aho, N., Carpenter, V. L., ... & Kimbrel, N. A. (2022). Qualitative analysis of participant experiences during an ecological momentary assessment study of nonsuicidal self-injury among veterans. *Psychiatry Research*, 114437.

Grootenhuis P, Snoek F, Heine R, Bouter L. Development of a type 2 diabetes symptom checklist: A measure of symptom severity. *Diabetic Med*. 1994;11(3):253-261.

Halls, S., Dures, E., Kirwan, J., Pollock, J., Baker, G., Edmunds, A., & Hewlett, S. (2015). Stiffness is more than just duration and severity: a qualitative exploration in people with rheumatoid arthritis. *Rheumatology*, *54*(4), 615-622.

Hamilton, A. B., & Finley, E. P. (2019). Qualitative Methods in Implementation Research: An Introduction. *Psychiatry Research*, 112516.

Hampson, S. E. (1997). Illness representations and the self-management of diabetes. *Perceptions of Health and Illness*, 323, 348.

Hedeker, D., Mermelstein, R. J., & Demirtas, H. (2008). An application of a mixed-effects location

scale model for analysis of ecological momentary assessment (EMA) data. *Biometrics*, *64*(2), 627-634.

Hektner JM, Schmidt JA, Csikszentmihalyi M. 2007. Experience Sampling Method: Measuring the Quality of Everyday Life. Thousand Oaks, CA: Sage

Hennink M., Kaiser B. N., Sekar S., Griswold E. P., Ali M. K. (2017). How are Qualitative methods used in diabetes research? A 30-year systematic review. *Global Public Health,* 12(2), 200-219.doi:10.1080/17441692.2015.1120337

Hernandez, L., Leutwyler, H., Cataldo, J., Kanaya, A., Swislocki, A., & Chesla, C. (2019). Symptom experience of older adults with Type 2 Diabetes and Diabetes-Related Distress. *Nursing Research*, *68*(5), 374-382.

Hessler, D., Fisher, L., Strycker, L. A., Arean, P. A., & Bowyer, V. (2015). Causal and bidirectional linkages over time between depression and diabetes regimen distress in adults with type 2 diabetes. *Diabetes Research and Clinical Practice*, 108(2), 360-366.

Hong, Y. R., Jo, A., Cardel, M., Huo, J., & Mainous III, A. G. (2020). Patient-Provider communication with teach-back, patient-centered diabetes care, and diabetes care education. *Patient Education and Counseling*, 103(12), 2443-2450.

Hood, K. K., Butler, D. A., Volkening, L. K., Anderson, B. J., & Laffel, L. M. (2004). The Blood Glucose Monitoring Communication questionnaire: an instrument to measure affect specific to blood glucose monitoring. *Diabetes Care*, *27*(11), 2610-2615.

Horne, R., Weinman, J., & Hankins, M. (1999). The beliefs about medicines questionnaire: The development and evaluation of a new method for assessing the cognitive representation of medication. *Psychology and Health*, 14, 1–24.

Howren, M. B. (2009). Specifying the determinants of bias in reports of physical symptoms and health-related quality of life: The role of depressive affect. The University of Iowa.

Howren, M. B., & Suls, J. (2011). The symptom perception hypothesis revised: depression

and anxiety play different roles in concurrent and retrospective physical symptom reporting. *Journal of Personality and Social Psychology*, *100*(1), 182.

Huang, E. S., Brown, S. E., Ewigman, B. G., Foley, E. C., & Meltzer, D. O. (2007). Patient perceptions of quality of life with diabetes-related complications and treatments. *Diabetes Care*, 30(10), 2478-2483.

Huffman, J. C., DuBois, C. M., Mastromauro, C. A., Moore, S. V., Suarez, L., & Park, E. R. (2016). Positive psychological states and health behaviors in acute coronary syndrome patients: A qualitative study. *Journal of Health Psychology*, *21*(6), 1026-1036.

Hufford, M. R., Shields, A. L., Shiffman, S., Paty, J., & Balabanis, M. (2002). Reactivity to ecological momentary assessment: an example using undergraduate problem drinkers. *Psychology of Addictive Behaviors*, 16(3), 205.

IBM Corp. (2020). *IBM SPSS Statistics for Windows, Version 27.0* (Version 27.0) [Computer software].

Johnson, E. J., Tversky, A. A., & AFFECT, A. (1983). Generalization, and the perception of risk. *J Person Soc Psych*, *45*, 20-31.

Juvenile Diabetes Research Foundation website. https://www.jdrf.org/t1d-resources/about/. Accessed April 2022.

Kane, N. S., Hoogendoorn, C. J., Tanenbaum, M. L., & Gonzalez, J. S. (2018). Physical symptom complaints, cognitive emotion regulation strategies, self-compassion and diabetes distress among adults with Type 2 diabetes. *Diabetic Medicine*, *35*(12), 1671-1677.

Katon, W. (1998, April). The effect of major depression on chronic medical illness. In Seminars in clinical neuropsychiatry (Vol. 3, No. 2, pp. 82-86).

Katon, W., Lin, E. H., & Kroenke, K. (2007). The association of depression and anxiety with medical symptom burden in patients with chronic medical illness. *General Hospital Psychiatry*, 29(2), 147-155.

Kennedy-Moore E, Greenberg MA, Newman MG, Stone AA. The relationship between Daily events and mood: The mood measure may matter. *Motiv Emotion*. 1992;16(2):143 155.

Kim, J., Shah, P., Quilty, L. C., Caravaggio, F., Plitman, E., Iwata, Y., ... & Gerretsen, P. (2020). DAS: The Diabetes Awareness and Insight Scale. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, 14(3), 189-194.

Kirk, J. K., D'Agostino Jr, R. B., Bell, R. A., Passmore, L. V., Bonds, D. E., Karter, A. J., & Narayan, K. V. (2006). Disparities in HbA1c levels between African-American and non-Hispanic white adults with diabetes: a meta-analysis. *Diabetes Care*, 29(9), 2130-2136.

Kirk, J. K., Passmore, L. V., Bell, R. A., Narayan, K. V., D'Agostino Jr, R. B., Arcury, T. A., & Quandt, S. A. (2008). Disparities in A1C levels between Hispanic and non-Hispanic white adults with diabetes: a meta-analysis. *Diabetes Care*, 31(2), 240-246.

Kolk, A. M. M., Hanewald, G. J. F. P., Schagen, S., & van Wijk, C. G. (2002). Predicting medically unexplained physical symptoms and health care utilization: a symptom perception approach. *Journal of Psychosomatic Research*, *52*(1), 35-44.

Koller, M., Heitmann, K., Kussmann, J., & Lorenz, W. (1999). Symptom reporting in cancer patients II: Relations to social desirability, negative affect, and self-reported health behaviors. *Cancer*, *86*(8), 1609-1620.

Kramer, I., Simons, C. J., Wigman, J. T., Collip, D., Jacobs, N., Derom, C., ... & Wichers, M. (2014). Time-lagged moment-to-moment interplay between negative affect and paranoia: new insights in the affective pathway to psychosis. *Schizophrenia Bulletin*, *40*(2), 278-286.

Kratz, A. L., Murphy, S. L., & Braley, T. J. (2017). Ecological momentary assessment of pain, fatigue, depressive, and cognitive symptoms reveals significant daily variability in multiple sclerosis. *Archives of Physical Medicine and Rehabilitation*, 98(11), 2142-2150.

Lahey B. B. (2009). Public health significance of neuroticism. *The American Psychologist*, 64(4), 241256. https://doi.org/10.1037/a0015309

Lange, L. J., & Piette, J. D. (2005). Perceived health status and perceived diabetes control: psychological indicators and accuracy. *Journal of Psychosomatic Research*, 58(2), 129-137.

Larsen, R. (1992). Neuroticism and bias in the encoding and recall of physical symptoms: Evidence from a combined prospective-retrospective study. *Journal of Personality and Social Psychology*, 62, 480-488.

Lépine, J. P., & Briley, M. (2004). The epidemiology of pain in depression. *Human Psychopharmacology: Clinical and Experimental*, 19(S1), S3-S7.

Leventhal, E. A., Hansell, S., Diefenbach, M., Leventhal, H., & Glass, D. C. (1996). Negative affect and self-report of physical symptoms: Two longitudinal studies of older adults. *Health Psychology*, *15*(3), 193.

Leventhal, H. L. B. I., Brissette, I., & Leventhal, E. A. (2003). The common-sense model of self-regulation of health and illness. *The Self-Regulation of Health and Illness Behaviour*, *1*, 42-65.

Leventhal, H., Meyer, D., & Nerenz, D. (1980). The common sense representation of illness danger. *Contributions to Medical Psychology*, *2*, 7-30.

Leventhal, H., Phillips, L. A., & Burns, E. (2016). The Common-Sense Model of Self Regulation (CSM): a dynamic framework for understanding illness self-management. *Journal of Behavioral Medicine*, *39*(6), 935-946.

Liu, X., Haagsma, J., Sijbrands, E., Buijks, H., Boogaard, L., Mackenbach, J. P., ... & Polinder, S. (2020). Anxiety and depression in diabetes care: longitudinal associations with health-related quality of life. *Scientific Reports*, *10*(1), 1-9.

Love, R. R., Leventhal, H., Easterling, D. V., & Nerenz, D. R. (1989). Side effects and emotional distress during cancer chemotherapy. *Cancer*, 63(3), 604-612.

Ludman, E. J., Katon, W., Russo, J., Von Korff, M., Simon, G., Ciechanowski, P., ... & Young, B.

(2004). Depression and diabetes symptom burden. *General Hospital Psychiatry*, 26(6), 430-436.

Lustman, P. J., Clouse, R. E., & Carney, R. M. (1989). Depression and the reporting of diabetes symptoms. *The International Journal of Psychiatry in Medicine*, *18*(4), 295-303.

Maas, C. J. M., & Hox, J. J. (2005). Sufficient Sample Sizes for Multilevel Modeling. *Methodology: European Journal of Research Methods for the Behavioral and Social Sciences*, *1*(3), 86. https://doi.org/10.1027/1614-2241.1.3.86

MacLeod, A. K., Haynes, C., & Sensky, T. (1998). Attributions about common bodily sensations: their associations with hypochondriasis and anxiety. *Psychological Medicine*, *28*(1), 225-228.

Markowski, K. L., Smith, J. A., Gauthier, G. R., & Harcey, S. R. (2021). Practical problems and positive experiences with ecological momentary assessment: reflections from people who use drugs. *The American Journal of Drug and Alcohol Abuse*, *47*(3), 311-318.

Maruthur, N. M., Tseng, E., Hutfless, S., Wilson, L. M., Suarez-Cuervo, C., Berger, Z., ...& Bolen, S. (2016). Diabetes medications as monotherapy or metformin-based combination therapy for type 2 diabetes: a systematic review and meta-analysis. *Annals of Internal Medicine*, *164*(11), 740-751.

Masselink, M., Van Roekel, E., Hankin, B. L., Keijsers, L., Lodder, G. M. A., Vanhalst, J., ... & Oldehinkel, A. J. (2018). The longitudinal association between self–esteem and depressive symptoms in adolescents: Separating between–person effects from within–person effects. *European Journal of Personality*, *32*(6), 653-671.

Mayer, D. D., & Rosenfeld, A. (2006). Symptom interpretation in women with diabetes and myocardial infarction. *The Diabetes Educator*, 32(6), 918-924.

McAndrew, L. M., Mora, P. A., Quigley, K. S., Leventhal, E. A., & Leventhal, H. (2014). Using

the common sense model of self-regulation to understand the relationship between symptom reporting and trait negative affect. *International Journal of Behavioral Medicine*, *21*(6), 989-994.

McCorry, N. K., Scullion, L., McMurray, C. M., Houghton, R., & Dempster, M. (2013). Content validity of the illness perceptions questionnaire–revised among people with type 2 diabetes: A think-aloud study. *Psychology & Health*, 28(6), 675-685.

McKellar, J. D., Humphreys, K., & Piette, J. D. (2004). Depression increases diabetes symptoms by complicating patients' self-care adherence. *The Diabetes Educator*, 30(3), 485-492.

McKeon, A., McCue, M., Skidmore, E., Schein, M., & Kulzer, J. (2018). Ecological momentary assessment for rehabilitation of chronic illness and disability. *Disability and Rehabilitation*, *40*(8), 974-987.

Mineka, S., Watson, D., & Clark, L. A. (1998). Comorbidity of anxiety and unipolar mood disorders. *Annual Review of Psychology*, *49*(1), 377-412.

Molassiotis, A., Lowe, M., Blackhall, F., & Lorigan, P. (2011). A qualitative exploration of a respiratory distress symptom cluster in lung cancer: cough, breathlessness and fatigue. *Lung Cancer*, *71*(1), 94-102.

Mor, N., & Winquist, J. (2002). Self-focused attention and negative affect: a meta analysis. *Psychological Bulletin*, *128*(4), 638.

Mora, P. A., Halm, E., Leventhal, H., & Ceric, F. (2007). Elucidating the relationship between negative affectivity and symptoms: The role of illness-specific affective responses. *Annals of Behavioral Medicine*, *34*(1), 77-86.

Mohr, D., Cuijpers, P., & Lehman, K. (2011). Supportive accountability: a model for providing human support to enhance adherence to eHealth interventions. *Journal of Medical Internet Research*, *13*(1), e30.

Moss-Morris R, Weinman J, Petrie K, Horne R, Cameron L, Buick D. The revised illness perception questionnaire (IPQ-R). *Psychology and Health*. 2002;17(1):1-16.

Mroczek, D. K., & Almeida, D. M. (2004). The effect of daily stress, personality, and age on daily negative affect. *Journal of Personality*, 72(2), 355-378.

Mulvaney, S. A., Vaala, S. E., Carroll, R. B., Williams, L. K., Lybarger, C. K., Schmidt, D. C., Dietrich, M. S., Laffel, L. M., & Hood, K. K. (2019). A mobile app identifies momentary psychosocial and contextual factors related to mealtime self-management in adolescents with type 1 diabetes. *Journal of the American Medical Informatics Association*, *26*(12), 1627–1631. https://doi.org/10.1093/jamia/ocz147

Mulvaney, S. A., Vaala, S., Hood, K. K., Lybarger, C., Carroll, R., Williams, L., ... & Laffel, L. (2018). Mobile momentary assessment and biobehavioral feedback for adolescents with type 1 diabetes: feasibility and engagement patterns. *Diabetes Technology & Therapeutics*, 20(7), 465-474.

Muthén B, Muthén L. Mplus Los Angeles, California: Muthen & Muthen, www.statmodel.com (1998).

Nagelkerk, J., Reick, K., & Meengs, L. (2006). Perceived barriers and effective strategies to diabetes self-management. *Journal of Advanced Nursing*, *54*(2), 151-158.

Newsom, J. T. (2015). Longitudinal structural equation modeling: A comprehensive introduction. Routledge.

Newton, P., Asimakopoulou, K., & Scambler, S. (2015). A qualitative exploration of motivation to self-manage and styles of self-management amongst people living with type 2 diabetes. *Journal of Diabetes Research*, *2015*.

Nicassio, P. M., & Wallston, K. A. (1992). Longitudinal relationships among pain, sleep problems, and depression in rheumatoid arthritis. *Journal of Abnormal Psychology*, 101(3), 514.

Ohayon, M. M., & Schatzberg, A. F. (2003). Using chronic pain to predict depressive morbidity in

the general population. *Archives of General Psychiatry*, 60(1), 39-47.

Okifuji, A., Bradshaw, D. H., Donaldson, G. W., & Turk, D. C. (2011). Sequential analyses of daily symptoms in women with fibromyalgia syndrome. *The Journal of Pain*, 12(1), 84 93

Pan, A., Lucas, M., Sun, Q., van Dam, R. M., Franco, O. H., Manson, J. E., ... & Hu, F. B. (2010). Bidirectional association between depression and type 2 diabetes mellitus in women. *Archives of Internal Medicine*, 170(21), 1884-1891.

Petrie, K., & Weinman, J. (2006). Why illness perceptions matter. *Clinical Medicine*, *6*(6), 536.

Perndorfer, C., Soriano, E. C., Siegel, S. D., & Laurenceau, J. P. (2019). Everyday protective buffering predicts intimacy and fear of cancer recurrence in couples coping with early stage breast cancer. *Psycho-oncology*, *28*(2), 317–323. https://doi.org/10.1002/pon.4942

Perrin, N. E., Davies, M. J., Robertson, N., Snoek, F. J., & Khunti, K. (2017). The prevalence of diabetes specific emotional distress in people with Type 2 diabetes: a systematic review and meta analysis. *Diabetic Medicine*, *34*(11), 1508-1520.

Persky, S., Costabile, K. A., & Telaak, S. H. (2021). Diabetes causal attributions: Pathways to stigma and health. Stigma and Health.

Pew Research Center Mobile Fact Sheet. https://www.pewresearch.org/internet/fact-sheet/mobile/ Accessed April 2022.

Polonsky, W. H., Fisher, L., Guzman, S., Villa-Caballero, L., & Edelman, S. V. (2005). Psychological insulin resistance in patients with type 2 diabetes: the scope of the problem. *Diabetes Care*, 28(10), 2543-2545.

Pressman, S. D., & Cohen, S. (2005). Does positive affect influence health?. *Psychological Bulletin*, *131*(6), 925.

Pucheu, S., Consoli, S. M., D'Auzac, C., Français, P., & Issad, B. (2004). Do health causal

attributions and coping strategies act as moderators of quality of life in peritoneal dialysis patients?. *Journal of Psychosomatic Research*, 56(3), 317-322.

Redekop, W. K., Koopmanschap, M. A., Stolk, R. P., Rutten, G. E., Wolffenbuttel, B. H., & Niessen, L. W. (2002). Health-related quality of life and treatment satisfaction in Dutch patients with type 2 diabetes. *Diabetes Care*, *25*(3), 458-463.

Ritholz, M. D., Beverly, E. A., & Weinger, K. (2011). Digging deeper: the role of qualitative research in behavioral diabetes. *Current Diabetes Reports*, *11*(6), 494.

Robbins J & Krimayer, L. (1991). Attributions of common somatic symptoms. *Psychological Medicine*, *21*, 1029-1045.

Robbins J & Kirmayer, L. (1986). Illness cognition, symptom reporting and somatization in family medicine. *In Illness Behavior* (pp. 283-302). Springer, Boston, MA.

Robbins J & Greenley, J. R. (1983). Thinking about what's wrong: Attributions of severity, cause, and duration in the problem definition stage of psychiatric help seeking. *Research in Community & Mental Health*.

Rose, M. K., Costabile, K. A., Boland, S. E., Cohen, R. W., & Persky, S. (2019). Diabetes causal attributions among affected and unaffected individuals. *BMJ Open Diabetes Research and Care*, 7(1), e000708.

Rowan, P. J., Cofta-Woerpel, L., Mazas, C. A., Vidrine, J. I., Reitzel, L. R., Cinciripini, P. M., & Wetter, D. W. (2007). Evaluating reactivity to ecological momentary assessment during smoking cessation. *Experimental and Clinical Psychopharmacology*, 15(4), 382.

Rubin, R. R. (2005). Adherence to pharmacologic therapy in patients with type 2 diabetes mellitus. *The American Journal of Medicine*, 118(5), 27-34.

Rubin, R. R., & Peyrot, M. (1999). Quality of life and diabetes. *Diabetes/Metabolism Research and Reviews*, 15(3), 205-218.

Russell, L. B., Suh, D. C., & Safford, M. A. (2005). Time requirements for diabetes self

management: too much for many. *J Fam Pract*, *54*(1), 52-56.

Ryff, C. D., Dienberg Love, G., Urry, H. L., Muller, D., Rosenkranz, M. A., Friedman, E. M., Davidson, R. J., & Singer, B. (2006). Psychological well-being and ill-being: do they have distinct or mirrored biological correlates?. *Psychotherapy and Psychosomatics*, *75*(2), 85–95. https://doi.org/10.1159/000090892

Ryu, E. (2011). Effects of skewness and kurtosis on normal-theory based maximum likelihood test statistic in multilevel structural equation modeling. *Behavior Research Methods*, *43*(4), 1066-1074.

Salovey, P., & Birnbaum, D. (1989). Influence of mood on health-relevant cognitions. *Journal of Personality and social Psychology*, 57(3), 539.

Schiaffmo, K. M., & Revenson, T. A. (1992). The Role of Perceived Self-Efficacy, Perceived Control, and Causal Attributions in Adaptation to Rheumnatoid Arthritis: Distinguishing Mediator from Moderator Effects. *Personality and Social Psychology Bulletin*, 18(6), 709 718.

Schultchen, D., Reichenberger, J., Mittl, T., Weh, T. R., Smyth, J. M., Blechert, J., & Pollatos, O. (2019). Bidirectional relationship of stress and affect with physical activity and healthy eating. *British Journal of Health Psychology*, 24(2), 315-333.

Schunck, R. (2013). Within and between estimates in random-effects models: Advantages and drawbacks of correlated random effects and hybrid models. *The Stata Journal*, *13*(1), 65-76.

Schwerdtfeger, A. R., & Gerteis, A. K. S. (2014). The manifold effects of positive affect on heart rate variability in everyday life: Distinguishing within-person and between-person associations. *Health Psychology*, *33*(9), 1065.

Scott, L. N., Wright, A. G., Beeney, J. E., Lazarus, S. A., Pilkonis, P. A., & Stepp, S. D. (2017). Borderline personality disorder symptoms and aggression: A within-person process model. *Journal of Abnormal Psychology*, *126*(4), 429.

Selig, J. P., & Little, T. D. (2012). Autoregressive and cross-lagged panel analysis for longitudinal data.

Shahar, B., & Herr, N. R. (2011). Depressive symptoms predict inflexibly high levels of experiential avoidance in response to daily negative affect: A daily diary study. *Behaviour Research and Therapy*, 49(10), 676-681.

Shapira, A., Volkening, L. K., Borus, J. S., & Laffel, L. M. (2021). Ecological Momentary Assessment (EMA) of Positive and Negative Affect and Associations with Blood Glucose (BG) in Teens with Type 1 Diabetes (T1D). *Journal of Diabetes Science and Technology*, 19322968211035451.

Shen, L., Wiley, J. F., & Bei, B. (2022). Sleep and affect in adolescents: Bidirectional daily associations over 28-day ecological momentary assessment. *Journal of Sleep Research*, *31*(2), e13491.

Shiffman, S., Stone, A. A., & Hufford, M. R. (2008). Ecological momentary assessment. *Annu. Rev. Clin. Psychol.*, *4*, 1-32.

Shirazian, S., Crnosija, N., Weinger, K., Jacobson, A. M., Park, J., Tanenbaum, M. L., ... & Hammock, A. C. (2016). The self-management experience of patients with type 2 diabetes and chronic kidney disease: a qualitative study. *Chronic Illness*, *12*(1), 18-28.

Skaff, M. M., Mullan, J. T., Almeida, D. M., Hoffman, L., Masharani, U., Mohr, D., & Fisher, L. (2009). Daily negative mood affects fasting glucose in type 2 diabetes. *Health Psychology*, *28*(3), 265.

Schwartz, D. D., Stewart, S. D., Aikens, J. E., Bussell, J. K., Osborn, C. Y., & Safford, M. M. (2017). Seeing the person, not the illness: promoting diabetes medication adherence through patient-centered collaboration. *Clinical Diabetes*, 35(1), 35-42.

Solhan, M. B., Trull, T. J., Jahng, S., & Wood, P. K. (2009). Clinical assessment of affective

instability: comparing EMA indices, questionnaire reports, and retrospective recall. *Psychological Assessment*, 21(3), 425.

Stamates, A. L. (2019). The Bidirectionality of Impulsivity and Alcohol Use: An Ecological Momentary Examination Among Emerging Adults.

Steinmetz, J. D., Bourne, R. R., Briant, P. S., Flaxman, S. R., Taylor, H. R., Jonas, J. B., ... & Morse, A. R. F. (2021). Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to VISION 2020: the Right to Sight: an analysis for the Global Burden of Disease Study. *The Lancet Global Health*, *9*(2), e144-e160.

Stone, A. A., & Shiffman, S. (1994). Ecological momentary assessment (EMA) in behavioral medicine. *Annals of Behavioral Medicine*.

Stratton, I. M., Adler, A. I., Neil, H. A. W., Matthews, D. R., Manley, S. E., Cull, C. A., ... & Holman, R. R. (2000). Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ*, *321*(7258), 405-412.

Street Jr, R. L., Makoul, G., Arora, N. K., & Epstein, R. M. (2009). How does communication heal? Pathways linking clinician–patient communication to health outcomes. *Patient Education and Counseling*, 74(3), 295-301.

Suls, J., & Howren, M. B. (2012). Understanding the physical-symptom experience: The distinctive contributions of anxiety and depression. *Current Directions in Psychological Science*, 21(2), 129-134.

Tanenbaum, M. L., Kane, N. S., Kenowitz, J., & Gonzalez, J. S. (2016). Diabetes distress from the patient's perspective: Qualitative themes and treatment regimen differences among adults with type 2 diabetes. *Journal of Diabetes and its Complications*, *30*(6), 1060–1068. doi:10.1016/j.jdiacomp.2016.04.023

Teel CS, Meek P, McNamara AM, Watson L. Perspectives unifying symptom interpretation. *Image J Nurs Sch*. 1997;29(2):175-181. doi:10.1111/j.1547 5069.1997.tb01553.x

Tellegen, A. (1988). Development and Validation of Brief Measures of Positive and Negative Affect: The PANAS Scales. *Journal of Personality and Social Psychology*, *54*(6), 1063-1070.

Thielsch, C., Ehring, T., Nestler, S., Wolters, J., Kopei, I., Rist, F., ... & Andor, T. (2015). Metacognitions, worry and sleep in everyday life: Studying bidirectional pathways using Ecological Momentary Assessment in GAD patients. *Journal of Anxiety Disorders*, *33*, 53-61.

Thompson, E. R. (2007). Development and validation of an internationally reliable short-form of the positive and negative affect schedule (PANAS). *Journal of Cross-Cultural Psychology*, 38(2), 227-242.

United States Renal Data System. (2015). 2015 USRDS annual data report: Epidemiology of kidney disease in the United States.

Vallis, M., Jones, A., & Pouwer, F. (2014). Managing hypoglycemia in diabetes may be more fear management than glucose management: a practical guide for diabetes care providers. *Current Diabetes Reviews*, *10*(6), 364-370.

Van den Bergh, O., & Walentynowicz, M. (2016). Accuracy and bias in retrospective symptom reporting. *Current Opinion in Psychiatry*, 29(5), 302-308.

Van Voorhees, E. E., Dennis, P. A., Elbogen, E. B., Fuemmeler, B., Neal, L. C., Calhoun, P. S., & Beckham, J. C. (2018). Characterizing anger-related affect in individuals with posttraumatic stress disorder using ecological momentary assessment. *Psychiatry Research*, *261*, 274-280.

Wagner, J., Armeli, S., Tennen, H., Bermudez-Millan, A., Wolpert, H., & Pérez-Escamilla, R.

(2021). A daily study of stressors, continuously measured glucose, and diabetes symptoms in latinos with type 2 diabetes. *Journal of Behavioral Medicine*, 44(1), 94-103.

Wagner, J., Armeli, S., Tennen, H., Bermudez-Millan, A., Wolpert, H., & Pérez-Escamilla, R. (2017). Mean levels and variability in affect, diabetes self-care behaviors, and continuously monitored glucose: a daily study of Latinos with type 2 diabetes. *Psychosomatic Medicine,* 79(7), 798.

Walentynowicz, M., Bogaerts, K., Van Diest, I., Raes, F., & Van den Bergh, O. (2015). Was it so bad? The role of retrospective memory in symptom reporting. *Health Psychology*, 34(12), 1166.

Walentynowicz, M., Van Diest, I., Raes, F., & Van den Bergh, O. (2017). Ways of encoding somatic information and their effects on retrospective symptom reporting. *British Journal of Health Psychology*, *22*(2), 362-378.

Watkins, K. W., Connell, C. M., Fitzgerald, J. T., Klem, L. A. U. R. A., Hickey, T., & Ingersoll Dayton, B. E. R. I. T. (2000). Effect of adults' self-regulation of diabetes on quality-of-life outcomes. *Diabetes Care*, *23*(10), 1511-1515.

Watson D, Clark LA, Tellegen A. Development and validation of brief measures of Positive and negative affect: The PANAS scales. *J Pers Soc Psychol*. 1988;54(6):1063.

Watson, D., & Pennebaker, J. W. (1989). Health complaints, stress, and distress: exploring the central role of negative affectivity. *Psychological Review*, *96*(2), 234.

Watts, S., O'Hara, L., & Trigg, R. (2010). Living with type 1 diabetes: a by-person qualitative exploration. *Psychology and Health*, *25*(4), 491-506.

Wayne, N., Perez, D. F., Kaplan, D. M., & Ritvo, P. (2015). Health coaching reduces HbA1c in type 2 diabetic patients from a lower-socioeconomic status community: a randomized controlled trial. Journal of medical Internet research, 17(10), e224.

Wiebe, D. J., Alderfer, M. A., Palmer, S. C., Lindsay, R., & Jarrett, L. (1994). Behavioral self

regulation in adolescents with type I diabetes: negative affectivity and blood glucose symptom perception. *Journal of Consulting and Clinical Psychology*, 62(6), 1204.

Weinman, J., Petrie, K. J., Moss-Morris, R., & Horne, R. (1996). The illness perception questionnaire: a new method for assessing the cognitive representation of illness. Psychology and health, 11(3), 431-445.

Wexler, D. J., Grant, R. W., Wittenberg, E., Bosch, J. L., Cagliero, E., Delahanty, L., ... & Meigs, J. B. (2006). Correlates of health-related quality of life in type 2 diabetes. *Diabetologia*, *49*(7), 1489-1497.

Wiese, C. W., Chen, Z. J., Tay, L., Friedman, E. M., & Rector, J. L. (2019). The role of affect on physical health over time: A cross-lagged panel analysis over 20 years. *Applied Psychology: Health and Well-Being*, *11*(2), 202-222.

Wild, D., von Maltzahn, R., Brohan, E., Christensen, T., Clauson, P., & Gonder Frederick, L. (2007). A critical review of the literature on fear of hypoglycemia in diabetes: implications for diabetes management and patient education. *Patient Education and Counseling*, *68*(1), 10-15.

Williams, P. G., D O'Brien, C., & Colder, C. R. (2004). The effects of neuroticism and extraversion on self-assessed health and health-relevant cognition. *Personality and Individual Differences*, 37(1), 83-94.

Williams, J. S., Walker, R. J., Smalls, B. L., Hill, R., & Egede, L. E. (2016). Patient-centered care, glycemic control, diabetes self-care, and quality of life in adults with type 2 diabetes. *Diabetes Technology & Therapeutics,* 18(10), 644-649.

World Health Organization. (2018). *Diabetes. https://www.who.int/news-room/fact sheets/detail/diabetes*

Yang, S., & Chang, M. C. (2019). Chronic Pain: Structural and Functional Changes in Brain

Structures and Associated Negative Affective States. *International Journal of* M*olecular Sciences*, *20*(13), 3130. https://doi.org/10.3390/ijms20133130

Yang, Y. S., Ryu, G. W., & Choi, M. (2019). Methodological strategies for ecological momentary assessment to evaluate mood and stress in adult patients using mobile phones: systematic review. *JMIR mHealth and uHealth*, *7*(4), e11215.

Young, C., & Hagerty, R. (2007, February). Blending qualitative and quantitative methods for program evaluation: The application and insights of the exit interview. In *4th Annual Meeting of the American Political Science Association Teaching and Learning Conference, Charlotte*.

Young-Hyman, D., De Groot, M., Hill-Briggs, F., Gonzalez, J. S., Hood, K., & Peyrot, M. (2016). Psychosocial care for people with diabetes: a position statement of the American Diabetes Association. *Diabetes Care*, *39*(12), 2126-2140.

Yun, J. S., & Ko, S. H. (2016). Risk Factors and Adverse Outcomes of Severe Hypoglycemia in Type 2 Diabetes Mellitus. *Diabetes & Metabolism Journal,* 40(6), 423–432. https://doi.org/10.4093/dmj.2016.40.6.423

Zainal, N. H., & Newman, M. G. (2021). Larger increase in trait negative affect is associated with greater future cognitive decline and vice versa across 23 years. *Depression and Anxiety*, *38*(2), 146-160.