# Detecting Behavioral Patterns

# for Understanding Long-Term

# Health Behavior Maintenance

by

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A Dissertation Presented in Partial Fulfillment
of the Requirements for the Degree
Doctor of Philosophy

Approved October 2023 by the
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ARIZONA STATE UNIVERSITY

December 2023

ABSTRACT

Sticking to healthy behaviors is difficult. The lack of long-term behavior maintenance negatively impacts health outcomes and increases healthcare costs. Current methods for improving behavior maintenance yield varying and often limited results. This dissertation designs and tests quantitative methods for identifying behavioral strategies associated with long-term maintenance the long-term maintenance of three different health behaviors.

Data were collected from three settings: mindfulness through a commercial app, walking from a randomized controlled trial, and pill-taking from a commercial app-based intervention. Novel pattern-detection methodologies were employed to measure temporal consistency and identify key behavioral strategies.

For mindfulness and walking behaviors, the impact of individual phenotypes on long-term behavior maintenance was analyzed. For medication adherence, the optimal window of time in which pills should be taken was empirically determined, and the impact of consistent timing on long-term medication adherence was analyzed. To perform these analyses, robust and regularized models, panel data models, statistical tests, and clustering algorithms were used. For mindfulness meditation, both consistent and inconsistent phenotypes were associated with long-term engagement. In the walking intervention, those with a consistent phenotype experienced greater increases in walking after the study than inconsistent individuals. However, the effect of consistency was strongest for individuals who either exercised less than 10 or more than 30 minutes per day. Lastly, in the medication adherence incentive program, consistently taking medication within 55 minutes of the goal time had the strongest association with future adherence.

This dissertation demonstrates that certain phenotypes are more advantageous than others for long-term maintenance and interventions. Temporal consistency is likely helpful for maintaining behaviors that offer delayed physical benefits, such as regular walking or medicating for chronic illnesses, but less helpful for cognitive behaviors like mindfulness, which can provide more immediate satisfaction. When designing interventions, the nature of the behavior and observable phenotypes should be taken into consideration. Generally, focusing on consistency is likely to contribute to long-term success; however, this is individual and context dependent. Future research should investigate this further by examining the relationship between behavioral phenotypes and psychological measurement tools to gain a deeper understanding of the successful maintenance of healthy behaviors.

## DEDICATION

To my wife, Deianeira, for always being there and making this possible.

# ACKNOWLEDGMENTS

I acknowledge the faculty, staff, and fellow students at Arizona State University that made this journey enjoyable and rewarding.

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# CHAPTER 1

# INTRODUCTION

## Background

This dissertation aimed to leverage mobile health (mHealth) behavioral data to support individuals in sustaining healthy behaviors over extended periods while also offering insights to guide researchers and policymakers in the development of innovative interventions for promoting well-being. The primary objective was to identify discernible patterns within mHealth data, shedding light on the factors contributing to the sustained success of various health behaviors. Within this dissertation, we examine these behaviors within three distinct contexts: mindfulness meditation in an observational study, physical activity in a randomized controlled trial, and medication adherence in an incentivized program.

Research has consistently demonstrated the manifold benefits associated with maintaining healthy behaviors. It widely acknowledged that sustained engagement with healthy practices yields various advantages, including enhanced mental well-being, increased life expectancy, and a reduced risk of adverse health effects, such as hypertension (Bostock et al., 2019; García et al., 2016; Pokorski & Suchorzynska, 2018; Ponte Márquez et al., 2019; Saeed et al., 2019). Nonetheless, individuals often struggle to maintain these behaviors over time, resulting in the impermanence of these behaviors (Gardner et al., 2012). Therefore, the imperative lies in enhancing long-term adherence in order to optimize disease prevention and curtail healthcare expenditures (Spring Bonnie et al., 2013). In aggregate, the failure of individuals to persist in healthy behaviors incurs significant annual costs for the U.S. government (Iuga & McGuire, 2014; Jardim et al., 2019). Regrettably, the financial cost burdens often trickle down to individuals in the form of additional financial pressure through higher copayments or increased costs to employers for coverage (Iuga & McGuire, 2014).

One potential solution lies in harnessing the psychological phenomenon of habits. Habits are actions that are triggered automatically by a stimulus and demand minimal cognitive effort to perform. As such, if individuals could establish their healthy behaviors as habits, the maintenance of these practices over the long term would theoretically become more manageable. In practice, the study of habit formation in healthy behavior is extremely limited because of the difficulty in distinguishing between individuals who have formed habits and those that have not. In the context of health outcomes, the precise psychological nuances of habit presence are less critical than the actual execution of the behavior. While there is likely a connection between the two, this dissertation prioritizes identifying associations with long-term behavior maintenance, independent of reported habit strength.

Another potential avenue to explore is personalized medicine, which, in the context of behaviors, takes the form of tailored treatments or incentives designed to promote specific behaviors. Current behavioral research grapples with challenges related to the validity of interventions when deployed in real-world settings, particularly with limited understanding of heterogeneous treatment effects in behavioral studies. The research presented in this dissertation contributes to addressing these limitations. For instance, within the context of the randomized controlled trial focused on physical activity, a heterogeneous treatment effect analysis is conducted.

The primary objectives of this dissertation research were twofold: 1) to use machine learning and data modeling techniques in the construction and analysis of behavioral phenotypes and their association with long-term behavior persistence, and 2) to conduct these analyses across diverse behaviors and settings. This data-driven, biomedical informatics approach to studying healthy behaviors aimed to address the current limitations of actionable medicine by generating novel insights into the phenotypes associated with long-term behavior maintenance. To perform the dissertation research, I was given access to multiple longitudinal healthy behavior datasets. The datasets included mindfulness meditation (i.e., the timing of all use of a meditation mHealth application), physical activity (i.e., minutes of moderate-to-vigorous activity), and medication adherence (i.e., timing of pill-taking for individuals managing chronic diseases).

The central hypothesis of the dissertation posits that certain behavior phenotypes offer advantages in terms of long-term behavior maintenance. Furthermore, it was hypothesized that the complexity of the behavior would play a significant role in this context. For example, in the case of medication adherence, where the action requires minimal time and cognitive effort, it is presumed to be a simpler behavior compared to activities like walking, which demand both time and physical exertion. In the case of acute behaviors, such as medication adherence, maintaining consistency (and consequently habit formation) is expected to be most advantageous. However, for more intricate behaviors, this may not necessarily hold true. In any case, the overarching hypothesis of this dissertation revolves around the existence of behavior phenotypes, with some being more closely associated with long-term maintenance, and that association likely depending on the complexity of the behavior and setting.

This research successfully unveiled distinct behavioral phenotypes for each behavior and their associations with long-term maintenance and the effectiveness of treatments where applicable. Furthermore, this dissertation offers in-depth insights into the exploration of treatment heterogeneity, a subject that holds the potential to advance our understanding of habit formation theories (C. J. Bryan et al., 2021). This dissertation research has brought us closer to discovering the true causal relationship between behavior, treatments, and psychological phenomena such as habits. The findings of this dissertation research have brought us closer to unraveling the true causal relationship between behavior, treatments, and psychological phenomena such as habits. In summary, my biomedical informatics approach to studying behavioral data aimed to promote knowledge acquisition that can be leveraged to enhance persistence in healthy behaviors and subsequently reduce healthcare costs for both individuals and society.

## Relevant Literature

Many studies have demonstrated the benefits of practicing mindfulness meditation. One randomized controlled trial found that short, guided mindfulness meditations delivered via a smartphone app improved workplace stress and workers' overall well-being (Bostock et al., 2019). Mindfulness-based interventions have also shown promise as effective treatments for anxiety and depression, however when recommended they should be done with the understanding that additional medications or psychotherapy may be needed (Pokorski & Suchorzynska, 2018; Saeed et al., 2019). In addition to the mental health benefits, other studies have provided evidence for the use of meditation for other health-related outcomes (Herman et al., 2017; Ponte Márquez et al., 2019). For example, for patients with hypertension, a randomized controlled trial provided evidence that mindfulness meditation lowered blood pressure (Ponte Márquez et al., 2019). In another randomized trial, mindfulness-based stress reduction techniques compared with normal at-home treatments done by individuals with chronic back pain had a high probability of being a cost-effective alternative treatment (Herman et al., 2017, p.). Other research, while validating that meditation practices can provide positive outcomes, emphasizes the importance of consistent action. One section of the dissertation demonstrated this by providing empirical evidence for the benefits of mindfulness-based interventions while highlighting the importance of meditation being a daily practice (Lacaille et al., 2018).

Physical activity has long been established as a behavior with healthy benefits (CDC, 2022b). Walking is an easy way to be physically active and it does not require any special skills to perform (CDC, 2022a). One meta-analysis, that included walking samples from over 45,000 adult reports, demonstrated that walking a sufficient amount of steps per day reduces premature death (Paluch et al., 2022). A more recent section of the dissertation done in 2022 used genetic data from over 400,000 individuals and found causal evidence to support the relationship between live-long brisk walking and biological age indicators (Dempsey et al., 2022). A detailed systematic review and meta-analysis showed that walking groups reduced blood pressure, and improved the resting heart rate, body index, cholesterol, and more (Hanson & Jones, 2015). Just like other physical activities, the benefits of walking are not limited to physical health. Brisk walking has also been studied as a potential treatment for mental health disorders. One review study found that there is growing evidence to suggest walking benefits mental health (Kelly et al., 2018). In addition, a detailed meta-analysis concluded that physical activity is safe as a recommendation for treatment of depression and anxiety with the understanding that additional medication or psychotherapy may also be needed (Saeed et al., 2019).

Drugs in the United States must be thoroughly tested and studied before regular use (Research, 2022). It is therefore not surprising that strict medication adherence is strongly associated with better health outcomes. This association has been demonstrated in several studies (Ho et al., 2009). Some research has taken additional steps to account for the health adherer effect (the effect where medication adherers are also likely to perform other healthy behaviors) and still has found that medication adherence has a strongly positive impact on well-being (Ho et al., 2009). Equally important are the associations between non-adherence and adverse health effects (Cutler et al., n.d.). One meta-analysis reports a link between depression and lack of medication adherence in chronic diseases (Grenard et al., 2011).

Unfortunately, the benefits that come from these healthy behaviors do not last, since most individuals fail to continue to perform the healthy behavior over time (Gardner et al., 2012). For a behavior to reach a state of automaticity it is estimated that it may take up to 254 days of consistent action (Lally et al., 2010). This may be one reason why healthy behavior interventions have limited success, since failure often occurs after the incentive period ends (Rohde & Verbeke, 2017; Wood & Neal, 2016a). For example, the benefits of meditation are primarily attained through persistent long-term practice

(Shen et al., 2020; Tang et al., 2012), and many people who initiate meditation struggle to maintain their meditation practice (Huberty et al., 2019; Stecher, Berardi, et al., 2021a; Stecher, Sullivan, et al., 2021a). Healthcare costs will likely be reduced significantly if individuals could stick to their healthy behaviors (Spring Bonnie et al., 2013). Lack of healthy behavior maintenance wastes billions of dollars every year (Iuga & McGuire, 2014; Jardim et al., 2019). Improving widescale persistence in healthy behavior may help alleviate financial pressure on patients who absorb these losses through higher copayments, or increased costs to employers for coverage (Iuga & McGuire, 2014).

Establishing behaviors as habits may help with persistence because of theory that suggests habits can continue even without motivation and require minimal cognitive effort to perform (Gardner et al., 2011a; Lally et al., 2011). This is particularly important for long-term behavior maintenance because although behavior change initially requires cognitive effort, enactment becomes easier as automaticity increases due to repetition in action in context over time (Lally et al., 2011). Habits are characterized as an automatic, or reflexive, response to a contextual queue (Wood & Neal, 2007a). Repeatedly performing a new behavior in response to the same stimuli (or contextual cue) over time is theorized to be the best mechanism in the formation of new reflexive habits (Gollwitzer, 1999; Gollwitzer & Brandstätter, 1997; Hull, 1943; Lally et al., 2010; Marteau et al., 2012; Wood & Neal, 2007a). Currently it is estimated that on average it takes around 66 days for a habit to be formed (Lally et al., 2010), however little is known about why or how this number depends on the behavior or the individual. This dissertation research provides new insights into long-term maintenance which may be connected to the habit formation.

Habit-based strategies are increasingly being incorporated into health behavior interventions to promote long-term behavior maintenance (Badawy et al., 2020). For example, when it comes to medication adherence, a comprehensive systematic review and meta-analysis concluded that medication adherence improvement should focus on habit-based interventions (Badawy et al., 2020). Other studies have attempted to demonstrate the impact habits have on healthy behavior persistence. Evidence supports the idea that habits encourage persistence in health behaviors, such as improved medication adherence (Brooks et al., 2014a; Kronish & Ye, 2013; Liddelow et al., 2020; Phillips, Alison et al., 2013). However, the application of these findings is limited. To date, habit research has relied heavily on self-reported measures, such as the self-reported habit index (Verplanken & Orbell, 2003). Despite the widespread use of self-reported methods, these metrics are known to lack ideal validity due to various biases that individuals have when performing self-assessments, such as respondents guessing the hypothesis of the section of the dissertation and skewing answers to confirm research questions (Heppner et al., 2015). One section of the dissertation found that some self-reported habit index survey respondents lacked confidence in reporting automaticity, struggled to remember behaviors or cues, and misinterpreted words in the questions (Gardner & Tang, 2014). Moreover, little research has been done to establish the concrete convergent validity of these measures (Hagger, 2019). In addition to these psychometric limitations, there are also theoretical concerns with these metrics (Ersche et al., 2017; Hagger et al., 2015; Sniehotta & Presseau, 2012). Specifically, because habitual behaviors are theorized to be automatically or unconsciously initiated, individuals should not be able to recall their experience performing the behavior (Gardner & Tang, 2014).

Therefore, self-reported habit metrics are more likely to capture perceived self-efficacy for the behavior rather than the actual strength of the habit (Hagger et al., 2015; Sniehotta & Presseau, 2012). The constructed measures in this dissertation research may provide new opportunities to address the current limitations of relying on self-reported surveys in determining habit strength.

Another challenge with measuring habits is the specificity of the context of questionnaires, which in practice can vary enormously by individual (Ersche et al., 2017). Variations at the individual level decrease reliability in employing new methods in practice. For instance, not all healthy behaviors impact people in the same way. One weight loss section of a study found that the beneficial health outcomes were dependent on certain individual characteristics (Baum et al., 2017). In addition, the application of habit-based interventions is unreliable at the individual level because randomized control trials estimate the average effect of interventions and are therefore unlikely to be informative about individual patients (Zhu & Gallego, 2020). In addition, behavior interventions themselves have different effects that depend on context and population (C. J. Bryan et al., 2021). One review paper on behavioral nudges (interventions) found evidence for heterogeneity that depended on the "target population, intervention type, target behavior, experimental design, the way of reporting, and the type and number of outcome measures" (Szaszi et al., 2018). Treatment effect heterogeneity likely explains most inconsistency in findings (C. J. Bryan et al., 2021). When it comes to behavioral interventions, "investigating systematic effect heterogeneity is vital for understanding what works, for whom, and under what conditions" (Miller, 2019). This dissertation research will investigate treatment heterogeneity in the context of the physical activity randomized controlled trial by analyzing the relationship between treatment and behavioral phenotypes.

To address the knowledge gap in the current literature, this research focuses on discovering objective phenotypes and individual characteristics associated with persistence in long-term studies. Several papers have attempted to model future behavior, but have relied on survey-based predictors (Son et al., 2010; Strobach et al., 2020). In more recent years researchers have attempted to model future behavior using observational data, however, this research often only looks at short-term behavior maintenance (Zhou et al., 2019). Additionally, the focus of most research has been on predicting future behavior and little has been done to quantitatively analyze the effect size of features (phenotypes) on persistence. For example, two studies (one of which I am an author on) have evaluated objective measures of consistency in behavior timing as indicators of meditation persistence and medication adherence, but both are unclear how these metrics would apply in other settings and to what extent they impact the success of long-term maintenance (Phillips et al., 2021; Stecher, Berardi, et al., 2021a). The field of biomedical informatics can help address these limitations. There is a growing role of biomedical informatics for information extraction in behavioral sciences (Shortliffe & J. Cimino, 2014). Observable behavioral data may be an important source of evidence to characterize cognitive processes (Shortliffe & J. Cimino, 2014). A biomedical informatics approach applied to various behavioral settings in long-term studies will provide new knowledge about the mechanisms of long-term maintenance.

# CHAPTER 2

# MINDFULNESS MEDITATION OBSERVATIONAL STUDY

## Introduction

Mindfulness meditation has been linked to numerous mental and physical health benefits, such as reduced stress, lower blood pressure, and greater overall well-being (Bostock et al., 2019; Herman et al., 2017; Pokorski & Suchorzynska, 2018; Ponte Márquez et al., 2019; Saeed et al., 2019). Additionally, mindfulness meditation-based interventions are effective treatments for anxiety and depression (Pokorski & Suchorzynska, 2018; Saeed et al., 2019), and offer a cost-effective alternative treatment for chronic back pain compared to other at-home remedies (Herman et al., 2017, p.). However, maintaining a mindfulness meditation practice over time is needed to attain the maximal health benefits (Shen et al., 2020; Tang et al., 2012), and behavioral maintenance is a challenge for most health behaviors (Forbes et al., 2018; Howells et al., 2016; Torous et al., 2020).

Mobile health platforms may help to support the maintenance of mindfulness meditation, as they increase accessibility and lower the cost compared to traditional face-to-face mindfulness meditation instruction (Gál et al., 2021; Longyear & Kushlev, 2021; Muñoz et al., 2016). Unfortunately, research has shown that less than 10% of health app users maintain their engagement with the app long-term (Baumel et al., 2019). Even in mobile health interventions, high dropout rates are common, with the average intervention attrition rate estimated to be between 26% and 43% (Meyerowitz-Katz et al., 2020; Torous et al., 2020). Therefore, it is important to identify the behavioral strategies that are associated with the long-term maintenance of app-based mindfulness meditation to help individuals attain the associated health benefits.

One potential mechanism for maintaining mindfulness meditation is to establish a habit. Habits are formed by repeatedly performing a target behavior in response to the same contextual cue, and over time the behavior becomes automatically, or reflexively, initiated upon encountering the contextual cue (Gardner, 2015; Lally et al., 2010; Verplanken & Melkevik, 2008). Habits have been shown to maintain many behaviors (Wood & Neal, 2016b) by reducing the cognitive effort required to perform the behavior (Lally et al., 2011). This allows habits to persist despite waning motivation or distractions (Galla & Duckworth, 2015; Gardner et al., 2011b; Rebar et al., 2014), and habit formation strategies have been used to promote the maintenance of several health behaviors, including physical activity (Kaushal et al., 2017; Phillips et al., 2016; Phillips & Gardner, 2016), dietary behaviors (Keller et al., 2021; McGowan et al., 2013), tooth brushing and flossing (Judah et al., 2013; Wind et al., 2005), and medication adherence (Brooks et al., 2014b; O'Carroll et al., 2013; Phillips et al., 2016). Additionally, many studies have established a link between consistently performing a behavior around the same time of day and the formation of habits (Berardi et al., 2023; Schumacher et al., 2019; Stecher, Berardi, et al., 2021b; van der Weiden et al., 2020), since people often encounter the same contextual cues around similar times in the day (Gardner et al., 2012). Therefore, a pattern of consistently timed mindfulness meditation may be indicative of a habit and an important strategy for long-term mindfulness meditation maintenance.

In addition to habits, several other psychological mechanisms have been shown to promote behavioral maintenance and may support the maintenance of mindfulness meditation. For example, some researchers posit that maintenance requires self-regulation, which broadly refers to an individual's ability to modulate cognitive, affective, or self-related processing to achieve a behavioral goal (Hall & Fong, 2007; Hennessy et al., 2020; Mann et al., 2013). Additionally, both intrinsic motivation (i.e., behavior engagement due to personal enjoyment and interest) and self-efficacy have been found to play important roles in initiating and maintaining behavior change (Gollwitzer & Sheeran, 2006; Ntoumanis et al., 2021; Paganini et al., 2022). Specifically, intrinsic motivation has been associated with initiating and maintaining several different health behaviors (Ntoumanis et al., 2021), including meditation (Cardeña et al., 2015; Ryan et al., 2021). Self-efficacy, which refers to an individual's perceived competence or confidence in performing goal-directed behaviors (Bandura, 1977), has also been cited as a key determinant of health behavior initiation and maintenance (Amireault et al., 2013; Schwarzer, 2008). Lastly, affective processes have also been shown to play an important role in the maintenance of various health behaviors, including meditation (Cohn & Fredrickson, 2010; Dunton & Vaughan, 2008; Van Cappellen et al., 2018). For example, one study found that novice meditators who experienced higher levels of positive affect during meditation were over four times more likely to maintain their medication practice 15 months later (Cohn & Fredrickson, 2010). Overall, these findings suggest that mindfulness meditation may be maintained long-term through the mechanisms of self-regulation, intrinsic motivation, self-efficacy, or affective processes, even in the absence of fully formed habits. Thus, more research is needed to better understand the relative role of habits versus these other potential behavioral mechanisms for maintaining mindfulness meditation (C. J. Bryan et al., 2021; Miller, 2019), as well as how they differ across individuals, which will ultimately enable researchers to design more successful interventions that can enable individuals to successfully attain the health benefits of mindfulness meditation.

## Objective

The purpose of this research was to investigate the importance of habits versus other behavioral mechanisms for maintaining app-based mindfulness meditation among individuals who subscribed to Calm, a commercially available mindfulness meditation app. To do so, we implemented a novel technique for identifying longitudinal behavioral patterns that were associated with long-term mindfulness meditation maintenance. By uncovering the common behavioral patterns behind long-term maintenance, and how these may differ among individuals, this work will enable future researchers to develop more targeted and effective approaches for supporting the maintenance of mindfulness meditation, which may offer solutions for maintaining other important healthy behaviors.

## Methods

### Generalized Pattern Detection Process

We developed the following process for detecting common patterns in longitudinal behavioral data that are associated with long-term behavioral maintenance, which is outlined in Figure 2-1. To illustrate how this process works, imagine that each person in a high-frequency longitudinal dataset of N people has a M x $T_Y$ matrix of behavioral data, where M represents the number of different behaviors that are measured at $T_Y$ sequential time points, where time could be measured in seconds, minutes, or hours. The first step is to split each person's full-time series into shorter sequential time windows of equal length (referred to as chunks of data), e.g., M x ($T_1$ -$T_a$); M x ($T_{a+1}$-$T_{2*a}$); M x ($T_{2*a+1}$-$T_{3*a}$), where a>0 and 3*a=Y. Then, to determine if there was a common time window (or chunk) when behavior significantly changed, e.g., when a large fraction of app users dropped out or shifted to another time-of-day pattern, we calculated the Euclidian distance between every pair of data chunks, i.e., the square root of the squared differences between corresponding elements of two chunks of data. For each chunk of data, we then found the average distance to all other chunks across all people in the sample and constructed a line plot of the average distance by sequential chunks of data to visually identify changes in behavior over time. If a noticeable change in the distance between chunks occurs, this inflection point represents an important moment when many individuals begin to deviate from their initial behavioral pattern.

However, the presence of systematic inflections will vary based on the data and behavior. If an inflection point is present (lines 4-6 in Figure 2-1A), then descriptive behavioral measures should be calculated at the chunks of data that occur immediately before and after the inflection point, and regression models can be used to identify the measures that changed the most at this point. For example, descriptive measures could include the number of mindfulness meditation sessions, total duration of mindfulness meditation, and the consistency in mindfulness meditation time of day, and if an increase in consistency is found to be the largest relative change at the inflection point, this finding would suggest that people are forming a mindfulness mediation habit. When no inflection points are present (lines 8-9 in Figure 2-1A, descriptive behavioral measures should be calculated for all chunks of data, and regression models that use the descriptive behavioral measures to predict behavior during future chunks of data can identify the measures that are most important for understanding behavioral maintenance. In either case, whether observable inflections are present or not, this process will successfully identify the behavioral measures that are important for understanding how behaviors are maintained in a given setting, e.g., is it the overall volume of behavior, frequency of performance, or consistency in the timing of behavior in the day that is most indicative of long-term maintenance?

Figure 2-1: Generalized Schematic for Pattern Detection Procedure

**Algorithm 1:** Processing Behavioral Patterns

**Result:** Categorized Behavioral Patterns
**Input :** Longitudinal Observations
**Output:** Pattern Label

**Step 1:** Split data into chunks of time
**Step 2:** Calculate average distance from each chunk to all others
**Step 3:** Visualize distances through time
**if** *Systematic Inflection Points* **then**
    **Step 4:** Compute descriptive metrics of behavior at the inflection
    **Step 5:** Determine metric changes at inflection point
**else**
    **Step 4:** Compute descriptive metrics of behavior at each chunk
    **Step 5:** Fit regression models for each individual
**end**

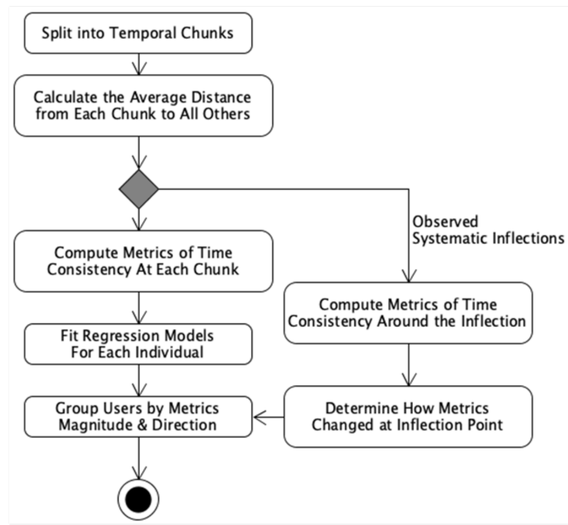



Figure 2-1: Generalized schematic for characterizing behavioral patterns in longitudinal data. (A) (left) The behavioral pattern detection is outlined as a step-by-step algorithm. (B) (right) The process flow diagram outlines how to detect inflection points in behavioral data and determine the important behavioral patterns.

The remaining parts of the methods section detail how we used this generalized process for detecting the behavioral patterns associated with the long-term maintenance of mindfulness meditation.

## Participants and Procedure

Longitudinal behavioral data were collected from the mindfulness meditation app Calm, which had over 4 million paying subscribers at the time of data collection. The data used in this analysis came from a sample of 15,000 randomly selected new users who paid for their first annual membership in 2017. The sample was also selected so that roughly one-quarter of users never renewed their annual subscription, one-quarter of users renewed once, one-quarter renewed twice, and one-quarter renewed three times, which means the data potentially spans from 2017 to 2021 for some users. The data contain the start time and duration of all app sessions performed by each user, but no demographic information was collected by the app. This study was approved by the Arizona State University Institutional Review Board (Study #: 00012530).

## Descriptive Behavioral Measures

Based on the start time and duration of each session, a minute-level time series was constructed for each user that indicated whether they were completing a session using the app. These minute-level data were then split into 4-week chunks, and for each 4-week chunk, we calculated three behavioral measures of temporal consistency to answer our question about the relative role of habits for maintaining mindfulness meditation: 1.)

dynamic time-warping (DTW) distance, 2.) the variance of mindfulness meditation session start times, and 3.) entropy. For the first measure, the temporal consistency between the first 14 days and the last 14 days of each 4-week chunk was computed using the DTW algorithm. This algorithm calculates an adjusted distance measure that allows for flexibility in the timing of similar data patterns. For example, if a user meditated at 10:00 AM on a Monday (day 1) and 11:00 AM on another Monday (day 15), the traditional Euclidean distance between these time series would be 1 hour. However, the DTW distance would be 0 hours since the general pattern of one session at a similar time of day is consistent across these two days. DTW was calculated using the Python software package 'dtw' (Giorgino, 2009), where we used the 'Sakoechiba' window type with a window size set to 2 (to allow for 2 hours of flexibility) and the step pattern of 'symmetric1.' When comparing activity patterns over consecutive days using DTW distance though, it is important to distinguish between temporally consistent app use versus consistency in no app use. In other words, the DTW distance between consecutive time intervals with no meditation is 0 (the minimum distance), which is the same as the DTW distance between perfectly consistent sessions of mindfulness meditation. This complicates the interpretation of the DTW distance measure, potentially making it an inaccurate signal of temporally consistent meditation. Thus, we adjusted the DTW distance measure by penalizing consecutive time intervals with 0 meditations. To do this, the adjusted DTW was defined as 1 when there were no sessions on consecutive 14-day periods, and all other DTW distances were scaled by dividing by the total number of 2-hour windows spent meditating with the app on the previous day (plus 1 to avoid division by 0). This scaling was used so that the penalized distance of 1 would be high relative to the DTW distance calculated on days with actual meditation app use. The adjustment on DTW was done as follows:

$$\text{Adjusted DTW} = \begin{cases} 1, & \text{If no activity in consecutive 14 day periods} \\ \frac{\text{DTW}}{2\text{hrs}+1}, & \text{Otherwise} \end{cases};$$

where 2hrs is the number of 2-hour windows spent meditating with the app on the previous day.

Our second behavioral measure of temporal consistency was the variance of meditation session start times. To calculate this measure within each 4-week chunk, the start times were first transformed into circular distances to avoid overestimating distances between days, e.g., 11 PM on one day and 2 AM the next day is correctly calculated as a 3-hour difference. The resulting variance in session start times was calculated as follows:

$$\sigma^2_{\text{Time}} = \frac{\sum\left(d(t_{i,}\bar{t})\right)^2}{n-1}$$

where $t_i$ represents the start time of a meditation session i, $\bar{t}$ is the average start time, and $d(t_{i,}\bar{t})$ is the cartesian distance on the 24-hour clock.

Finally, the information entropy of meditation sessions was calculated for each 4-week chunk, which captures the uncertainty in mindfulness meditation timing. The entropy was calculated as follows:

$$H = -\sum_{i=1}^{4} P(x_i)\log P(x_i),$$

where H is the entropy and $P(x_i)$ is the empirically calculated probability of meditating during time window i, where i = $\{\text{morning}, \text{midday}, \text{evening}, \text{late night}\}$. H can take values between 0 and 1.39, with 0 representing meditating exclusively in a single time window (i.e., temporal consistent session timing) and 1.39 representing an equal probability of meditating during each of the four windows. Each block of time was defined as follows: morning; between 4:00 AM to 10:00 AM, midday; between 10:00 AM to 4:00 PM, evening; between 4:00 PM to 10:00 PM and late night; 10:00 PM to 4:00 AM.

### Pattern Detection

We calculated the Euclidean distance between all 4-week chunks of data in order to identify any inflection points that would signal points of systematic change in mindfulness meditation behavior. In the absence of an inflection point, we were prepared to use Least Absolute Shrinkage and Selection Operator (LASSO) regression models to predict future app use based on our temporal consistency measures calculated over prior 4-week chunks. To measure future app use, we used the number of mindfulness meditation sessions performed in each 4-week chunk. We determined the optimal number of prior chunks of data to include in the LASSO models, i.e., how many past chunks of data to include as independent variables, by fitting LASSO models with varying amounts of past data and calculating the adjusted-$R^2$ as a measure of goodness-of-fit for predicting future app use. As we add more past chunks of data to the model, the number of complete observations decreases, so we selected the model with the highest adjusted-$R^2$ to optimally balance the tradeoff between more independent variables and a smaller set of complete observations.

We then determined behavioral phenotypes based on the estimated associations between our temporal consistency measures (DTW, variance, and entropy) and future app use. First, a 10-fold cross-validation was used to determine a global regularization penalty for the LASSO models of future app use, i.e., mindfulness meditation sessions. Then, we fit separate LASSO models of future app use for each user. The purpose of the LASSO models was to classify users based on the relative predictive ability of each temporal consistency metric, which was determined based on the size of the sum of all statistically significant coefficients for a given measure. The temporal consistency measure with the largest estimated association to future app use was used to categorize each user into one of three behavioral phenotypes: consistent, inconsistent, or indeterminate. Users whose largest association with future app use was negative (i.e., more temporal consistency was correlated with greater future meditation) were labeled as consistent, while those with a positive largest association were labeled as inconsistent. Users whose model fit was poor (in the bottom $10^{th}$ quantile of adjusted-$R^2$ values) were labeled as indeterminate.

The last step was to assess the quality of our behavioral pattern detection process. Toward this aim, we fit separate panel regression models of future app use among the three behavioral phenotypes using our temporal consistency measures as independent variables. All independent variables were first standardized, and these panel regression models also included fixed effects for each user and controls for the number of days with any app use and the portion of app use that occurred during COVID-19 lockdowns in order to improve model fit. The sign and significance of the estimated associations between the temporal consistency measures and future app use among each phenotype were assessed to verify our categorization process, e.g., the consistent group was expected to show a positive association between improved consistency and future app use.

## Results

### Sample Characteristics

The dataset began with 15,000 randomly selected users who had initiated their first annual membership with Calm in 2017. The app users displayed high dropout rates between 2017 and 2021. Figure 2-2 shows the steep decline in the percentage of users who used the app in any future chunk of data over time. From this figure, we can see that only 60.9% of users would use the app in at least one future chunk of data at chunk 15 (i.e., week 60). By chunk 30 (i.e., week 120), this percentage dropped to 44.99%, and by chunk 45 (i.e., week 180) this number dropped to less than 20%.

Figure 2-2: App Engagement over Time

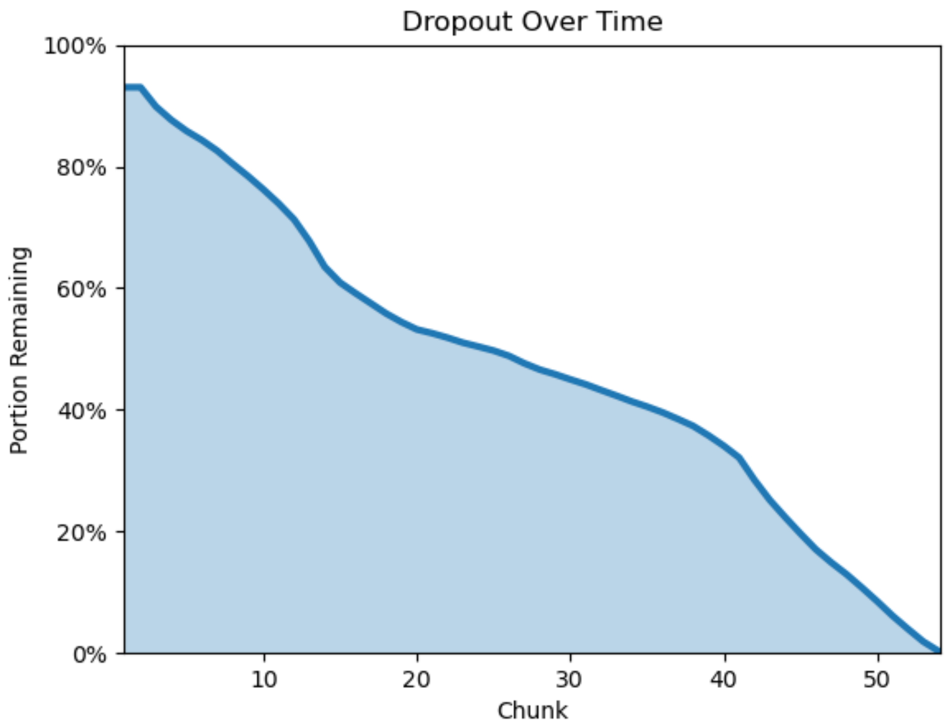



Figure 2-2: The percent of users with any app use in a future chunk of data. Chunk refers to the 4-week interval from the start of users' app subscription.

### Pattern Detection Process

The first step in our behavioral pattern detection process was to calculate the average distance from each chunk of data to all other chunks. Figure 2-3 shows the average distance to all other chunks for each chunk of data averaged among all users. Due to the lack of clear inflection points, we determined that the next step in the pattern detection process would be to compute our chosen behavioral measures for all chunks of data. That is, we calculated our three temporal consistency measures for all users and all chunks of data and proceeded to lines 8-9 in the algorithm shown in Figure 1-1A.

Figure 2-3: Behavior distances over Time

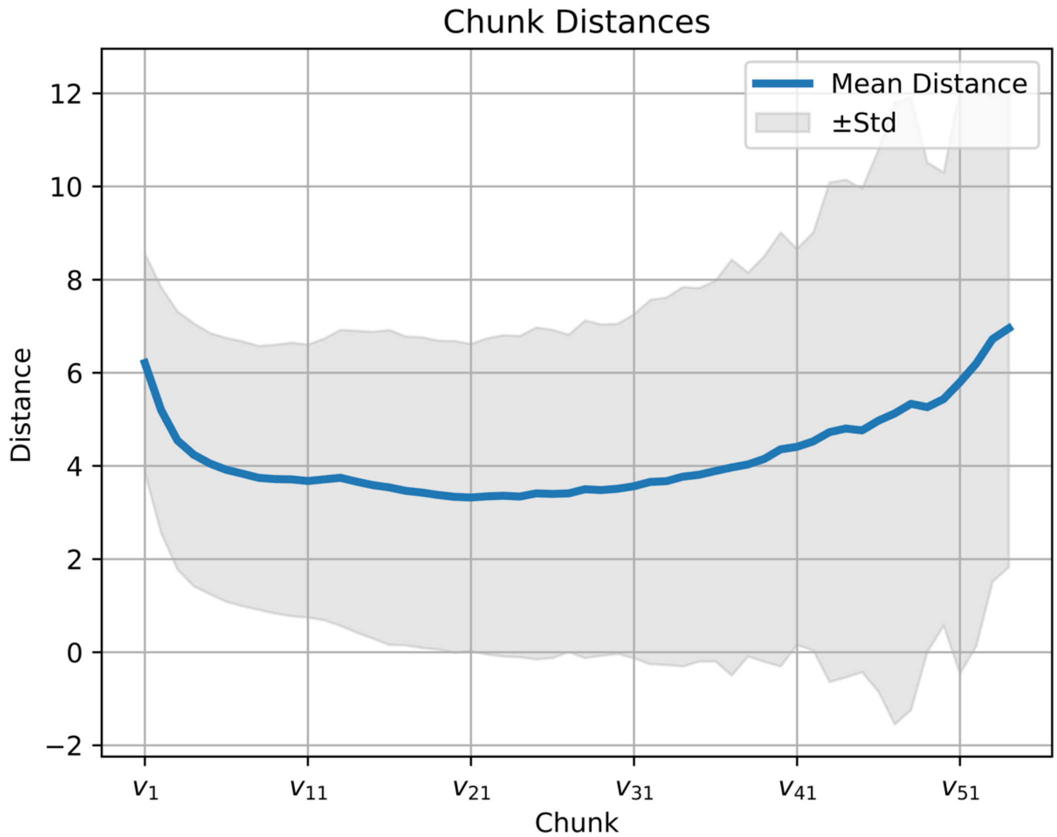



Figure 2-3: The distance between the indicated chunk of data and all other chunks averaged over all users. Chunk refers to the 4-week interval from the start of users' app subscription.

After calculating our temporal consistency measures, the next step was to determine the most appropriate regression model for predicting future app use. Specifically, we needed to determine the optimal number of past observations to include in the model of future app use without sacrificing too many observations. Based on the adjusted-$R^2$, it was determined that the model with information from the previous 2 chunks of data yielded the best goodness-of-fit.

In line with the process outlined in Figure 1-1, we estimated regression models of future app use for each user, which resulted in a smaller final sample of users categorized into our three behavioral phenotypes than in the original dataset. Figure 2-4 describes how the sample size was reduced throughout this pattern detection process. First, 1,874 users were dropped because they had less than three full chunks worth of data before they dropped out of the sample. Then, 8,921 users were dropped because our model of future app use based on their behavioral measures calculated in two prior chunks of data were estimated over few observations and thus did not converge to a meaningful solution. Based on the relative size of the significant coefficients in each user's model of future app use, 1,659 users were categorized in the consistent phenotype, which indicated that the more consistent their mindfulness meditation the more sessions they were likely to perform in the future. Additionally, this categorization process led to 2,326 users being categorized as inconsistent, and the final 222 users as indeterminant.

Figure 2-4: Flow Chart of Sample Size

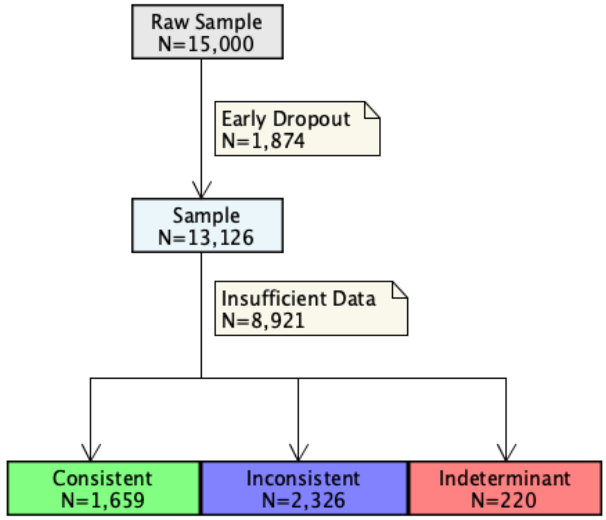



Figure 2-4: Flow chart of sample size. After determining the minimum data requirements, 1,874 individuals were dropped due to insufficient data. Then, when fitting models for each individual, an additional 8,921 were dropped due to model nonconvergence.

The regression results that informed our categorization are displayed in Table 2.1, which shows the descriptive statistics for individual model coefficients for the consistent, inconsistent, and indeterminant behavioral phenotypes. As expected, the average coefficients for the consistent timing group were all negative, i.e., more consistency was associated with more future app use. Likewise, the average coefficients for the inconsistent group were all positive. For the consistent timing individuals, roughly 45% (n=748/1,659) had their biggest estimated association with future app use from the adjusted DTW metric (-6.85, STD=19.53). For those in the inconsistent timing group, roughly 46% (n=1,076/2,326 had their biggest estimated association with future app use from entropy (7.57, STD=10.33).

Table 2.1: Model Coefficients by Behavioral Phenotype

| Variable | Consistent Timing Mean / (STD) | Consistent Timing Count / (Portion) | Inconsistent Timing Mean / (STD) | Inconsistent Timing Count / (Portion) | Indeterminant Mean / (STD) | Indeterminant Count / (Portion) |
|---|---|---|---|---|---|---|
| Adjusted DTW | -6.845 | 748 | 7.160 | 314 | -0.820 | 87 |
| | (19.531) | (45.09%) | (12.289) | (13.50%) | (3.439) | (39.55%) |
| Entropy | -13.389 | 415 | 7.572 | 1,076 | 1.177 | 73 |
| | (63.804) | (25.02%) | (10.337) | (46.28%) | (6.686) | (33.18%) |
| Variance of Time | -38.233 | 496 | 13.810 | 936 | -0.008 | 60 |
| | (253.497) | (29.89%) | (38.327) | (40.24%) | (0.704) | (27.27%) |
| Total | 1,659 | | 2,326 | | 220 | |

Table 2.1: Descriptive statistics of the effect of each temporal consistency measure by behavioral phenotype. Individuals were labeled as consistent if the strongest effects were negative, inconsistent if the strongest effects were positive, and indeterminate if the model fit was poor (below the 10$^{th}$ quantile). Each cell displays the mean (and standard deviation in parentheses) of the estimated coefficients on the independent variable indicated in the row labels.

To evaluate the success of this behavioral pattern detection process, we fit panel regression models for each phenotype to predict their future app use. Table 2.2 presents the results from these panel regression models that used our three temporal consistency measures to predict the number of future meditation sessions among the three phenotypes. For the consistent session timing group, the regression results show that entropy had the strongest negative association with future sessions, with a coefficient of -0.49 (SE=0.08, P<0.001). All other significant associations with future app use in this group were also negative. For the inconsistent session timing group, the regression results show that the variance of time had the largest estimated association with future sessions, with a coefficient of 0.49 (SE=0.06, P<0.001). All other significant associations in this group were also positive. Lastly, in the indeterminate group, the estimated associations with future sessions were insignificant and smaller in magnitude compared to the other two phenotypes. In addition, the signs of the estimated associations were mixed, with a positive association for entropy and a negative association for the adjusted DTW. Among these indeterminate users, the greatest estimated association with future sessions was entropy, with a coefficient of 0.18 (SE=0.16, P=0.27).

Table 2.2: Association Between Temporal Consistency Measures and Future Number of Sessions by Phenotype

| | Consistent Session Timing | Inconsistent Session Timing | Indeterminate |
|---|---|---|---|
| Variable | b / (SE) | b / (SE) | b / (SE) |

| | | | |
|---|---|---|---|
| Adjusted DTW | -0.254*** | 0.372*** | -0.016 |
| | (0.058) | (0.049) | (0.093) |
| Lagged Adjusted DTW | -0.126* | 0.206*** | -0.029 |
| | (0.055) | (0.044) | (0.087) |
| Entropy | -0.491*** | 0.352*** | 0.179 |
| | (0.083) | (0.081) | (0.161) |
| Lagged Entropy | -0.288*** | -0.017 | 0.329 |
| | (0.074) | (0.07) | (0.179) |
| Variance of Time | 0.106 | 0.485*** | 0.012 |
| | (0.056) | (0.056) | (0.103) |
| Lagged Variance of Time | 0.039 | 0.280*** | -0.059 |
| | (0.052) | (0.049) | (0.101) |
| Controls Included | Yes | Yes | Yes |
| Fixed effects | Yes | Yes | Yes |
| Number of Users | 1,659 | 2,326 | 220 |

Standard errors in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table 2.2: This table displays the regression coefficients (with standard errors in parentheses) for panel regression models of future app use, measured by the number of mindfulness meditation sessions, estimated within each of the three behavioral phenotypes indicated in the column headings.

Finally, to assess the relative role of habits versus other behavioral mechanisms for maintaining mindfulness meditation, Table 2.3 describes the mindfulness meditation behavior of each phenotype. Overall, 39.5% (N=1,659) were labeled as consistent, and these users meditated with the app for an average of 34.6 (SD 11.8) consecutive chunks (about 138 weeks). The consistent phenotype completed an average of 8.0 (SD 13.6) sessions in each chunk, and they meditated with the app on an average of 5.6 (SD 8.3) days per chunk. For the 55.3% (N=2,326) of users categorized as inconsistent, the average number of consecutive chunks with any use was 33.4 (SD 12.9). Additionally, the average number of meditation sessions per chunk was 8.2 (SD 13.6) and the number of days with any meditation per chunk was 5.7 (SD 8.4) among the inconsistent phenotype.

The P-values for T-tests comparing these descriptive statistics between the consistent and inconsistent phenotypes are presented in column 4 of Table 2.3. Based on these comparisons, the consistent phenotype maintained their mindfulness meditation for roughly 1.2 chunks longer (approximately 5 weeks) than the inconsistent group (P=0.003). Otherwise, both the consistent and inconsistent phenotypes had a similar average number of meditation sessions per chunk (P=0.184), and a similar variance in the number of meditation sessions per chunk (P=0.496). While the difference in the average number of days with any meditation per chunk was significant (P=0.034), the magnitude of the difference was less than 0.1.

The remaining 5.2% of users (N=220) who were categorized as indeterminate had poor model fits when predicting their future app use, i.e., the $R^2$ values were in the bottom 10% quantile (<.56). Due to the poor model fit, it was unclear if these users had a consistent or inconsistent pattern in their time of day of mindfulness meditation. While the indeterminate phenotype maintained their mindfulness meditation the longest, roughly 42.6 chunks (SD 5.7), users in this phenotype performed fewer meditation sessions per chunk (5.7, SD 11.0; P<0.001) and fewer days with any meditation sessions per chunk (4.0, SD 7.0; P<0.001).

Table 2.3: Mindfulness Meditation Behavior by Phenotype

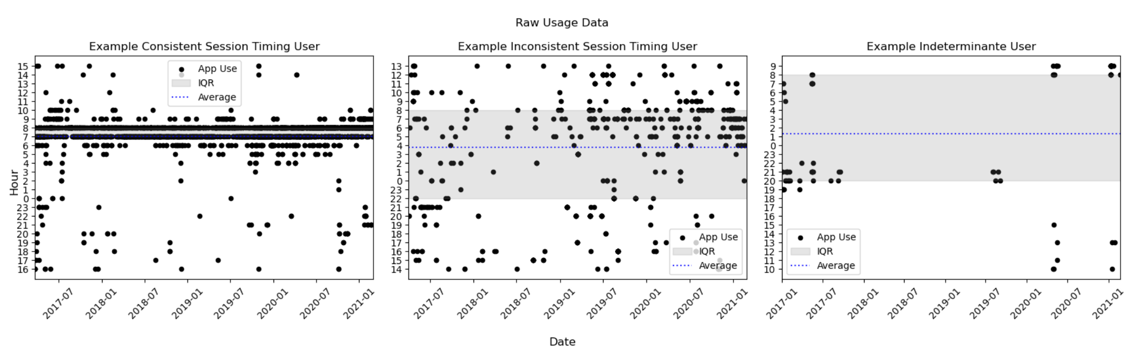
| Variable | Consistent Session Timing Mean / (STD) | Inconsistent Session Timing Mean / (STD) | Indeterminate Mean / (STD) | Consistent vs Inconsistent P-Value | Difference Between all P-Value |
|---|---|---|---|---|---|
| Consecutive Chunks with Any Use | 34.616 (11.786) | 33.405 (12.943) | 42.568 (5.721) | 0.003 | <0.001 |
| Days with Any Use per Chunk | 5.567 (8.346) | 5.665 (8.447) | 4.016 (6.994) | 0.034 | <0.001 |
| Portion of Use During | 0.189 (0.386) | 0.187 (0.384) | 0.235 (0.418) | 0.362 | <0.001 |

| | | | | | |
|---|---|---|---|---|---|
| COVID (2020) | | | | | |
| Number of Meditation Sessions per Chunk | 8.048 (13.553) | 8.147 (13.619) | 5.685 (10.947) | 0.184 | <0.001 |
| Variance in Number of Meditation Sessions per Chunk | 0.015 (0.038) | 0.015 (0.036) | 0.012 (0.037) | 0.496 | <0.001 |
| Individual Model $R^2$ | 0.835 (0.136) | 0.845 (0.134) | 0.465 (0.058) | 0.021 | <0.001 |
| Number of Users | 1,659 | 2,326 | 220 | | |
| Observations | 58,579 | 79,389 | 9,555 | | |

Table 2.3: Descriptive statistics of mindfulness meditation behavior by phenotype. Statistical comparisons of the indicated variables between phenotypes were performed using T-tests.

To visualize our results, Figure 2-5 plots representative users from the consistent, inconsistent, and indeterminate phenotypes. In the top half of Figure 2-5, the time of day of each meditation session is plotted by day, and the bottom of Figure 2-5 shows the number of meditation sessions by chunk of data along with the user's panel regression model predictions for the number of meditation sessions smoothed over the full time period. This figure shows that the panel regression models did a good job of fitting the number of meditation sessions for each phenotype. Importantly, the figure also demonstrates that important differences existed in users' patterns in the time of day of mindfulness meditation sessions. The consistent user (left) is characterized by performing mindfulness meditation at a similar time of day for their entire period of app use. Specifically, this user favored performing mindfulness meditation at and around 7 AM every day. Meanwhile, the inconsistent user (middle) is characterized by constant but variable meditation session start times. In other words, while this user did frequently perform mindfulness meditation, there was no clear pattern in the time of day. Lastly, the indeterminate user is characterized by sparse use. Although this user maintained a low level of mindfulness meditation for at least as long as the other two users, there were several long gaps with no meditation.

Figure 2-5: App Usage over Time for Representative Users from Each Group



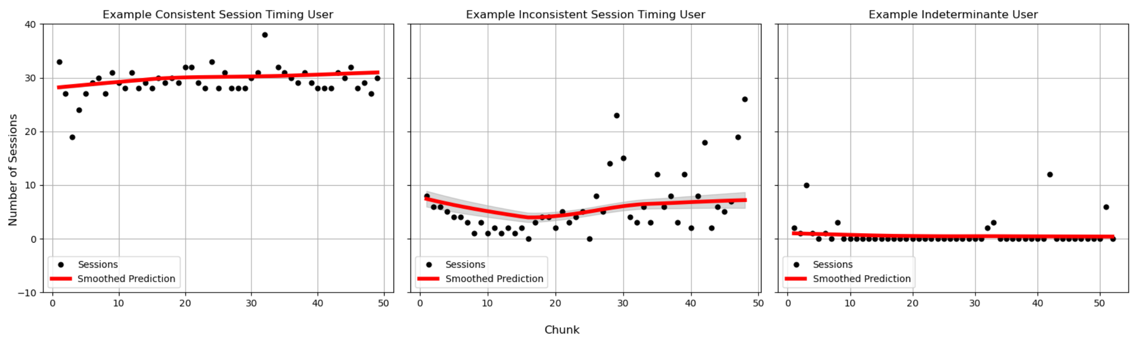



Figure 2-5: Top: (Left) Representative user plot for the consistent session timing group. (Middle) Representative user plot for the inconsistent session timing group. (Right) Representative plot for the indeterminate group. Bottom: (Left) Representative user plot for the consistent session timing group. (Middle) Representative user plot for the inconsistent session timing group. (Right) Representative plot for the indeterminant group. Chunk refers to the 4-week interval from the start of users' app subscription.

Finally, Table 2.4 compares the portion of mindfulness meditation by time of day between the consistent and inconsistent phenotypes. For both phenotypes, the most popular time window for mindfulness meditation was late at night (10 PM – 4 AM), with each phenotype performing more than 40% of their meditation sessions during that time window. The consistent phenotype had a slightly higher portion of their meditation sessions performed in the morning compared to the inconsistent phenotype, but overall, the distribution of mindfulness meditation timing was very similar between these two behavioral phenotypes.

Table 2.4: Time of Day of Mindfulness Meditation by Phenotype

| Time of Day | Consistent Session Timing | Inconsistent Session Timing |
|---|---|---|

| | | |
|---|---|---|
| Morning | 29.84% | 26.64% |
| Midday | 11.94% | 13.70% |
| Evening | 16.34% | 18.35% |
| Late Night | 41.88% | 41.32% |

Table 2.4: The percent of mindfulness meditation sessions by time-of-day windows (morning, midday, evening, & late night) for the consistent and inconsistent phenotypes. Morning is defined as 4:00 AM to 10:00 AM; midday as 10:00 AM to 4:00 PM; evening as 4:00 PM to 10:00 PM; and late-night as 10:00 PM to 4:00 AM.

## Discussion

The purpose of this study was to investigate the importance of habits versus other behavioral mechanisms for maintaining app-based mindfulness meditation by identifying the common patterns in the time of day of mindfulness meditation that were associated with long-term maintenance. We applied our novel pattern detection process to a high-frequency, longitudinal dataset of mindfulness meditation sessions with the Calm app, and ultimately categorized 39.5% (n=1,659/4,207) of users in our final analytic sample as consistent, which indicated that their maintenance of mindfulness meditation was associated with a consistent time of day pattern in their meditation practice. This finding suggests that roughly 40% of long-term mindfulness meditators had formed a habit since habits are frequently performed in the same location around a similar time of day (Gardner et al., 2012). We also found that a larger fraction of users, 55.3% (n=2,326/4,207), maintained their mindfulness meditation practice while displaying an inconsistent pattern in the time of day of their meditation. These results suggest that both habits and other behavioral mechanisms can successfully maintain mindfulness meditation and that the mechanism used for the long-term maintenance of mindfulness meditation differs between individuals.

The finding that roughly 40% of long-term mindfulness meditators displayed a consistent pattern of mindfulness meditation supports the literature on habits, which theorizes that habits are an important behavioral mechanism for maintenance (Gardner, 2015; Lally et al., 2008; Wood & Neal, 2007b). Since forming a habit has been shown to reduce the cognitive effort required to perform a behavior (Lally et al., 2011), it was expected that a large fraction of users with high mindfulness meditation maintenance would display a consistent phenotype indicative of a habit. The ability of consistently timed mindfulness meditation to maintain meditation long-term is also supported by existing interventions that have shown how consistency can promote mindfulness meditation maintenance (Stecher, Sullivan, et al., 2021b). Additionally, the users with a consistent phenotype maintained mindfulness meditation longer than the inconsistent phenotype, although the difference in duration was only 1.2 chunks (approximately 5 weeks). Taken together, these findings suggest that habits play an important role in maintaining mindfulness meditation for many app users, and future research should better characterize these users and collect more information on the location and contextual cue for these habits to inform the targeting and design of habits-based mindfulness meditation interventions.

The majority of long-term mindfulness meditators (55%) displayed an inconsistent time-of-day pattern, which suggests that habits are not the only mechanism for maintaining mindfulness meditation. An inconsistent pattern has been theorized to be a characteristic of dynamic complexity and has been observed in many complex biological and physical systems (Gilden, 2001), which suggests that the complexity of mindfulness meditation may make it difficult for many to perform as a habit. Instead, several other behavioral mechanisms, such as intrinsic motivation, self-efficacy, self-regulation, or affective processes, may be supporting the long-term maintenance of mindfulness meditation among users in the inconsistent phenotype (Amireault et al., 2013; Bandura, 1977; Cardeña et al., 2015; Cohn & Fredrickson, 2010; Dunton & Vaughan, 2008; Gollwitzer & Sheeran, 2006; Hall & Fong, 2007; Hennessy et al., 2020; Mann et al., 2013; Ntoumanis et al., 2021; Paganini et al., 2022; Ryan et al., 2021; Schwarzer, 2008; Van Cappellen et al., 2018), and future research should investigate the relative role of these mechanisms in this health behavior setting. By disentangling the mechanisms that can maintain mindfulness meditation and identifying those that are successfully used by people in the real world, future research can help to better target and personalize interventions that enable more people to attain the health benefits of long-term mindfulness meditation. Additionally, the behavioral pattern detection process introduced in this study should be applied in other health behavior settings to similarly investigate the relative role of habits versus other behavioral mechanisms for maintaining healthy behaviors long-term.

### Limitations

This study utilized high-frequency longitudinal behavioral data from a popular commercial mobile health app, which increased the real-world applicability and generalizability of the results but also introduced several limitations. First, since the data come from a single mindfulness meditation app that contained a range of meditation content and other app-based behavioral supports, such as reminders and an activity tracking feature, the time of day patterns observed in this study may not apply to other mindfulness meditation apps. Second, the data did not contain information about the location, context, or proceeding behaviors for each mindfulness meditation session, which is necessary to accurately identify habits. Third, user characteristics and affective states were not available, which would provide important information for better targeting future interventions and for understanding the behavioral mechanisms underlying mindfulness meditation maintenance. Finally, several data transformation decisions were made that could have influenced the results, such as constructing an hourly time series (versus shorter or longer time intervals) and dividing the time series into 4-week chunks of data. While the impact of these decisions was minimal when tested among a small sample of users, additional research is needed to fully understand how these data transformation choices influence the results of our pattern detection process.

## Conclusion

This study used longitudinal behavioral data to identify common patterns in the time of day of mindfulness meditation that were associated with long-term maintenance and found that roughly 40% of mindfulness meditation app users displayed a consistent pattern of mindfulness meditation indicative of a habit. Another 55% of users displayed inconsistent patterns in the time of day of mindfulness meditation, which suggests that habits are not the only behavioral mechanisms that can maintain app-based mindfulness meditation. Additionally, this study outlines a novel process for identifying the common behavioral patterns associated with long-term maintenance, which can be readily applied to other sources of high-frequency longitudinal behavioral data to understand what mechanisms may underlie maintenance across a range of other important preventative health behaviors.

# CHAPTER 3

# PHYSICAL ACTIVITY RANDOMIZED CONTROLLED TRIAL

## Introduction

Physical activity is deeply understood to provide positive benefits and improve health outcomes. The Center for Disease control promotes physical activity as a way to help individuals feel better, function better, and sleep better (CDC, 2022b). Walking is an easy way to be physically active and does not require any special skills to perform (CDC, 2022a). One meta-analysis, that included walking samples from over 45,000 adult reports, demonstrated that walking a sufficient amount of steps per day significantly reduces the odds of premature death (Paluch et al., 2022). Additionally, genetic data from over 400,000 individuals was analyzed to find causal evidence in support of the relationship between live-long brisk walking and biological age indicators (Dempsey et al., 2022). Another detailed systematic review and meta-analysis showed that walking groups reduced blood pressure, improved resting heart rate, body index, cholesterol, and more (Hanson & Jones, 2015). As with other physical activities, the benefits of walking are not limited to physical health. Brisk walking has been studied as a potential treatment for mental health disorders. One review study found that there is growing evidence to suggest walking benefits mental health (Kelly et al., 2018). Additionally, a detailed meta-analysis concluded that physical activity is safe as a recommendation for treatment of depression and anxiety, with the understanding that additional medication or psychotherapy may also be needed (Saeed et al., 2019).

To receive the health benefits of physical activity, individuals must continually perform the behavior long-term since any stopping or discontinuation can reverse the positive effects. A randomized trial found that stopping exercise (detraining) can result in increases in cardiovascular disease risk factors, such as arterial pressure and body fat percentage (Nolan et al., 2018). Multiple other studies have found a link between persistent physical inactivity with increased prevalence of metabolic syndrome (Kim et al., 2019; Yang et al., 2008). A systematic review that involved over 600,000 individuals linked sedentary behavior and lack of physical activity to obesity, which itself is causally related to many negative risk factors (Censin et al., 2019; Silveira et al., 2022). Even acute prolonged sitting has been linked to significant vascular disfunction in lower limbs (Paterson et al., 2020). Additionally, for healthy behaviors like physical activity, there are significant financial consequences for failing to perform the behavior long-term. In aggregate, it is estimated that lack of maintenance in healthy behavior costs the United States billions of dollars each year (Iuga & McGuire, 2014; Jardim et al., 2019). Unfortunately, these higher costs often result in added financial pressure on patients through higher copayments or increased rates to employers for coverage (Iuga & McGuire, 2014).

In order to mitigate adverse health consequences and rising expenses, healthcare experts often employ a range of behavioral interventions aimed at promoting long-term adoption of healthy behaviors. To date, the impact of behavioral interventions on physical activity have been minimal. Despite the growing efforts to promote physical activity, as of 2022 the World Health Organization reports that global levels of physical activity have not increased since 2001 (*Physical Activity*, n.d.). Surprisingly, some research has demonstrated that physical activity interventions may inadvertently result in increased sedentary time from baseline (Hartman et al., 2020). Additionally, many studies fail to track or assess the effectiveness of treatment post-intervention. Several studies have demonstrated that while physical activity interventions may show strong evidence for improving follow-up outcomes for certain individuals, most provide little or weak evidence for improving post-intervention outcomes (Abdin et al., 2019; Howlett et al., 2018; Sheshadri et al., 2020). To date, researchers have not come to a consensus on the best interventions to increase physical activity (Gormley et al., 2022).

Due to the drawbacks in the efficacy of interventions in the long-term, contemporary research has aimed at helping individuals establish healthy behaviors as habits; automatic actions that are triggered by specific contexts (Skinner, 1938). Consistent action in a behavior has been linked to habit formation and is likely beneficial in long-term maintenance (Peng et al., 2021). For example, several studies have demonstrated that temporal consistency patterns are strong predictors of behavior maintenance and possibly the establishment of habits (Berardi et al., 2023; Fowers et al., 2022; Stecher, Berardi, et al., 2021b). However, it is unclear if treatments impact the long-term level of consistency in performing a behavior or if they simply benefit those with an preexisting consistent phenotype (Howlett et al., 2018). Additionally, while it is known that various behavioral phenotypes in physical activity exist, the extent to which these phenotypes interact with interventions or treatments is unclear (A. D. Bryan et al., 2017; Lee & Park, 2021). For this reason, there is a need to understand how treatments may have varying effects that depend on the individual (i.e., heterogeneous treatment effects) (C. J. Bryan et al., 2021; Ma et al., 2021). In studying heterogeneous treatment effect, researchers primarily have focused on the role that individual demographic characteristics interact with treatments (Gormley et al., 2022). As far as we are aware this is the first study to analyze heterogenous treatment effects based on objectively recorded behavioral phenotypes.

## Objective

The goal of this study was to investigate the role of temporal consistency patterns and walking context in the maintenance of physical activity in the 12 months after a behavioral intervention. In the current study, we call the observable characteristics of an individual's walking pattern a behavioral phenotype. We aim to establish the presence of behavioral phenotypes and analyze their relationship to long-term maintenance and treatment effects. By understanding the mechanisms behind maintenance and how these may differ among individuals, researchers can develop more targeted and effective methods to support individuals during the intervention so that their healthy practices can be better maintained long-term.

## Methods

### Sample Characteristics

Data for this research came from the Walking Intervention Through Texting study that was originally designed to promote walking habits in Maricopa County, Arizona. The study was a federally funded trial registered prospectively at ClinicalTrials.gov and was approved by the Arizona State University Institutional Review Board (NCT02717663). The original study design recruited 512 individuals from a variety of neighborhood types based on measures of walkability and socioeconomic status. A two-week baseline was recorded to assess the initial walking behavior of individuals prior to intervention. Then, each participant in the study was assigned to one of four treatments: 1) adaptive goals with immediate rewards, 2) static goals with immediate rewards, 3) adaptive goals with delayed rewards, and 4) static goals with delayed rewards. The treatment period lasted 12 months. Finally, 6 months after the end of the treatment period (month 18) and 12 months after the end of the treatment period (month 24), follow-up levels of physical activity were recorded. More details of the study design and rationale can be found in the published paper (Adams et al., 2019). For the purposes of the current study, only the individuals that participated in the study for the full intervention period (12 months) were included in the analyses, which left 435 participants. Additionally, for the follow-ups that occurred at month 18 and month 24 we were limited to only those individuals who participated, which left 374 and 364 individuals respectively.

### Variable Construction

Physical movement data was recorded at one-minute intervals, and this was used to define variables that measure consistency. First, the data was split into one-week windows. For each user and each one-week chunk, we constructed three measures of consistent walking behavior: dynamic time warping (DTW) distance, the variance of time, and entropy. Each of the three metrics aims to capture the consistent walking session timing within/between each window.

First, the similarity between the weeks was computed using the dynamic time warping (DTW) algorithm, which calculates an adjusted distance measure that allows for flexibility in the timing and magnitude of similar data patterns. The DTW algorithm is noteworthy because it enables a simultaneous comparison of similarity in the timing and magnitude of movement. This means that when comparing two time-series that include both the timing of each physical activity and the vigor or magnitude of the activity, DTW can determine the similarity in both the timing of the sessions and the amount of movement that occurred within each session. For example, if a participant walked at a fixed magnitude from 10:05 to 10:35 AM on Monday (day 1) and from 11:05 to 11:35 AM at the same magnitude on the next Monday (day 8), the traditional Euclidean distance between these time series would be 60 minutes, while the DTW distance is 0 since the general pattern of a walking session at similar times and days is consistent. The DTW was calculated using the Python software package 'dtw' (Giorgino, 2009). We used the Sakoechiba window type with a window size set to 120 (to allow for 2 hours of flexibility) and the step pattern of symmetric1. When comparing activity patterns over consecutive weeks, it is important to distinguish between temporal consistent physical activity versus temporally consistent inactivity. Specifically, the DTW distance between consecutive time intervals with no walking is 0 (minimum), which is the same as the DTW distance between perfectly consistent intervals of walking. In other words, the algorithm cannot distinguish between two-time intervals of perfectly consistent physical activity and two-time intervals of perfectly consistent inactivity. This complicates the interpretation of the DTW distance, potentially making it an inaccurate signal of consistent walking. Thus, the DTW distance measure was adjusted by penalizing time intervals with consecutive 0 bout minutes. Where this was the case, the adjusted DTW was defined as 1, and all other DTW distances were scaled by dividing by the total number of minutes spent walking with the app (plus 1 to avoid division by 0). This scaling allowed the penalized distances to be high in comparison to days with actual walking activity. The adjustment on DTW was done as follows:

$$Adjusted\ DTW = \begin{cases} 1, & \text{If no activity in consecutive weeks} \\ \dfrac{DTW}{mins + 1}, & \text{Otherwise} \end{cases}$$

Next, to quantify regularity in the timing of walking sessions, the information entropy of walking sessions was calculated for each chunk, which captures the ‘surprise’ or ’uncertainty’ in timing. The entropy was calculated as follows:

$$H = -\sum_{i=1}^{4} \mathrm{P}(x_i) \log \mathrm{P}(x_i),$$

where $H$ is the entropy and $\mathrm{P}(x_i)$ is the empirically calculated probability of activity during time window $i$, where $i = \{\text{morning, midday, evening, late night}\}$. $H$ can take values between 0 and 1.39, with 0 representing activity exclusively in one time window (i.e., temporal consistent walking session timing) and 1.39 representing equal probability of walking during each of the four windows. If an individual did not engage in any physical activity in a given week, they were also considered to have an equal probability of walking during each of the four-time windows, so their value of $H$ was 1.39.

Lastly, the variance of time in walking sessions was calculated for each week. To account for the relative similarity of late walking sessions (e.g., a walking session that occurred at 11:59 PM and a walking session that occurred at 12:00 AM), the start times were mapped onto the 24-hour clock face and converted to cartesian coordinates prior to taking the mean and distance. The resulting variance was calculated as follows:

$$\sigma_{Time}^2 = \frac{\sum\left(d(t_{i,}\bar{t})\right)^2}{n-1}$$

Where $t_i$ represents the start time of a walking session $i$ and $d(t_{i,}\bar{t})$ is the cartesian distance on the 24-hour clock.

## Behavior Grouping

We used our constructed time consistency metrics to categorize individuals into one of two groups: consistent walking behavior or inconsistent walking behavior. First, we applied a k-means clustering algorithm with 3 clusters on the DTW metric. Individuals in the cluster group with the smallest values of DTW were categorized as consistent, while those in the cluster group with the highest values of DTW were categorized as inconsistent. The DTW was used as the main consistency metric for grouping since it was able to capture consistency in both timing and magnitude of movement. For individuals whose DTW series were in the middle cluster, we used the entropy and variance of time to categorize them. We performed k-means clustering separately for both entropy and variance of time using 2 clusters. For those who were in the middle DTW cluster and belonged to the cluster of entropy or variance of time with the smaller values, were categorized as consistent. The grouping schema is presented in Figure 3-1.

Figure 3-1: Behavioral Signal Processing Schema

**Algorithm 1:** Processing Behavioral Patterns

```
Input  : DTW, Entropy, and Variance of Time
Output: Consistent or Inconsistent Label
K-Means Cluster 3 Clusters on DTW series
if in least DTW cluster then
    Label = Consistent
else if in greatest DTW cluster then
    Label = Inconsistent
else if in middle DTW cluster then
    K-Means Cluster 2 Clusters on Entropy Series
    K-Means Cluster 2 Clusters on Variance Series
    if in least Entropy cluster OR in least Variance cluster then
        Label = Consistent
    else
        Label = Inconsistent
else
    Label = Inconsistent
```

Figure 3-1: Generalized schematic for characterizing behavioral patterns in longitudinal data. The behavioral pattern detection is outlined as a step-by-step algorithm.

### Outcome variable

After the 12-month study, follow-up data were collected at two separate times: at month 18 (6 months after the end of the study) and month 24 (12 months after the end of the study). To determine which individuals were able to maintain their behavior long-term, we compared the average daily walking bout minutes during the baseline of the study with those in month 18 and month 24. Specifically, we fit our models using two outcomes: the change in daily bout minutes from baseline at month 18, and the change in daily bout minutes from baseline at month 24.

### Regression Models

We fit multiple linear regression models with heterogeneous robust standard errors to assess the association between consistency during the study and long-term maintenance. Additionally, we fit multiple linear regression models to determine the presence of treatment heterogeneity by including treatment interactions with our consistency category indicator. The treatment heterogeneity models aimed to assess differences in treatment effect between those that had a consistent behavioral phenotype. In all models we controlled for demographics (BMI, age, sex, and race), and the study treatment groups (when they were not already being used to assess heterogeneity). We also took into consideration the overall level of physical activity. Each regression model in the current study was fit using robust standard errors. Finally, we took a deeper dive by describing and visualizing how adaptive goals changed over time and examining reported walking styles.

## Results

In our study, we analyzed the walking patterns of 474 individuals over a 12-month study period with a two-week baseline and follow-ups recorded after the study at month 18 and month 24. We used the study period data to categorize everyone into one of two groups: consistent walking behavior and inconsistent walking behavior. The consistent group had an average age of 47.11 (SD=8.80) and a BMI of 32.49 (SD=5.87). The inconsistent group were slightly younger with an average age of 44.13 (SD=9.16) and slightly more overweight with a BMI average of 34.67 (SD=7.79). Both groups were more female with 58.6% and 68.5% of individuals in the consistent and inconsistent group respectively. The majority of the sample consisted of white individuals with 84.02% reporting white race in the consistent group and 81.64% reporting white race in the inconsistent group. All other demographics and sample characteristics are displayed in Table 3.1.

Table 3.1: Sample Characteristics by Phenotype

| Demographic | Consistent | Inconsistent |
|---|---|---|
| Age | 47.112 | 44.131 |
| | (8.802) | (9.155) |
| BMI | 32.486 | 34.659 |
| | (5.873) | (7.798) |
| Female | 58.58% | 68.52% |
| Black | 2.96% | 6.56% |
| Hawaiian | 1.78% | 0.98% |
| Indian | 2.37% | 2.62% |
| Prefer Not to Say | 5.92% | 6.89% |
| White | 84.02% | 81.64% |
| Hispanic | 14.79% | 20.98% |

*Table 3.1:* Sample characteristics for the individuals in the study. Much of the study sample included white females with the inconsistent group containing a higher proportion of females and both groups consisting of over 80% white race individuals.

In total, 169 individuals were classified as consistent, and 305 individuals were classified as inconsistent. The average number of minutes walking per day were different at baseline between the two groups. The consistent individuals walked on average 16.95 minutes per day (SD=10.19), while the inconsistent group walked on average 11.97

minutes per day (SD=8.39). Both groups saw an increase in walking minutes after the treatment was randomly assigned and given over the 12-month study period. During the study period the consistent group walked on average 31.28 (SD=17.24) minutes per day while the inconsistent group only walked on average 12.51 (SD=10.16) minutes per day. At month 18, 6 months after the end of the treatment period, both groups were still walking considerably more than they were at baseline with the consistent group walking on average 9.17 (SD=19.41) minutes longer per day and the inconsistent group walking 2.91 (SD=12.32) more minutes per day. By month 24, both groups continued to walk more than their initial baseline levels, although their walking activity was not as high as it was at month 18. At month 24 the consistent group was walking 7.23 (SD=20.08) more minutes per day than baseline while the inconsistent group was walking an average of 1.67 (SD=13.37) more minutes per day than baseline. All other descriptive statistics about walking between the two groups (consistent & inconsistent) can be found in Table 3.2.

Table 3.2: Summary Statistics by Phenotype

| | Variable | Consistent mean / (std) | Inconsistent mean / (std) |
|---|---|---|---|
| Baseline | Minutes of PA per Day | 16.946 (10.198) | 11.965 (8.399) |
| | Number of Sessions per Day | 2.366 (1.513) | 1.814 (1.292) |

| | | | |
|---|---|---|---|
| | Session Length (Mins.) | 7.479 (3.308) | 6.537 (2.694) |
| | Number of Individuals | 169 | 305 |
| Study Period (Months 1-12) | Minutes of PA per Day | 31.277 (17.243) | 12.508 (10.16) |
| | Number of Sessions per Day | 3.378 (1.923) | 1.671 (1.264) |
| | Session Length (Mins.) | 10.549 (5.676) | 6.084 (3.176) |
| | Number of Individuals | 169 | 305 |
| Month 18 | Minutes of PA per Day | 25.984 (20.076) | 14.922 (12.865) |
| | Number of Sessions per Day | 3.278 (2.321) | 2.146 (1.689) |
| | Session Length (Mins.) | 6.678 (4.68) | 4.266 (2.813) |
| | Change in Minutes per Day (vs Baseline) | 9.173 (19.413) | 2.91 (12.32) |
| | Number of Individuals | 160 | 232 |
| Month 24 | Minutes of PA per Day | 24.086 (17.637) | 13.727 (13.881) |
| | | 2.936 | 1.998 |

| | | |
|---|---|---|
| Number of Sessions per Day | (2.002) | (1.809) |
| Session Length (Mins.) | 6.709<br>(5.383) | 3.994<br>(2.911) |
| Change in Minutes per Day (vs Baseline) | 7.227<br>(16.768) | 1.668<br>(13.366) |
| Number of Individuals | 158 | 221 |

*Table 3.2:* Descriptive statistics of walking behavior between the consistent and inconsistent groups. The consistent group (left) walked more at baseline and maintained higher walking rates during and after the study. The inconsistent group (right) increased their walking from baseline but on average walked less minutes per day than the consistent group.

Figure 3-2 plots representative users from the consistent walking behavior group (top) and the inconsistent walking behavior group (bottom). In Figure 3-2 the raw data of walking during the study are plotted on the left with the time of the session on the vertical axis and the day in the study on the horizontal axis. Then, the middle and left graphs plot the same raw data but for the follow ups at month 18 and month 24. These representative user plots in Figure 3-2 illustrate the differences in walking behavior patterns over time. The plots allow for a visual representation of the data and provide insight into the behavior patterns of the different groups.

Figure 3-2: Representative User Plots for Consistent and Inconsistent Walkers

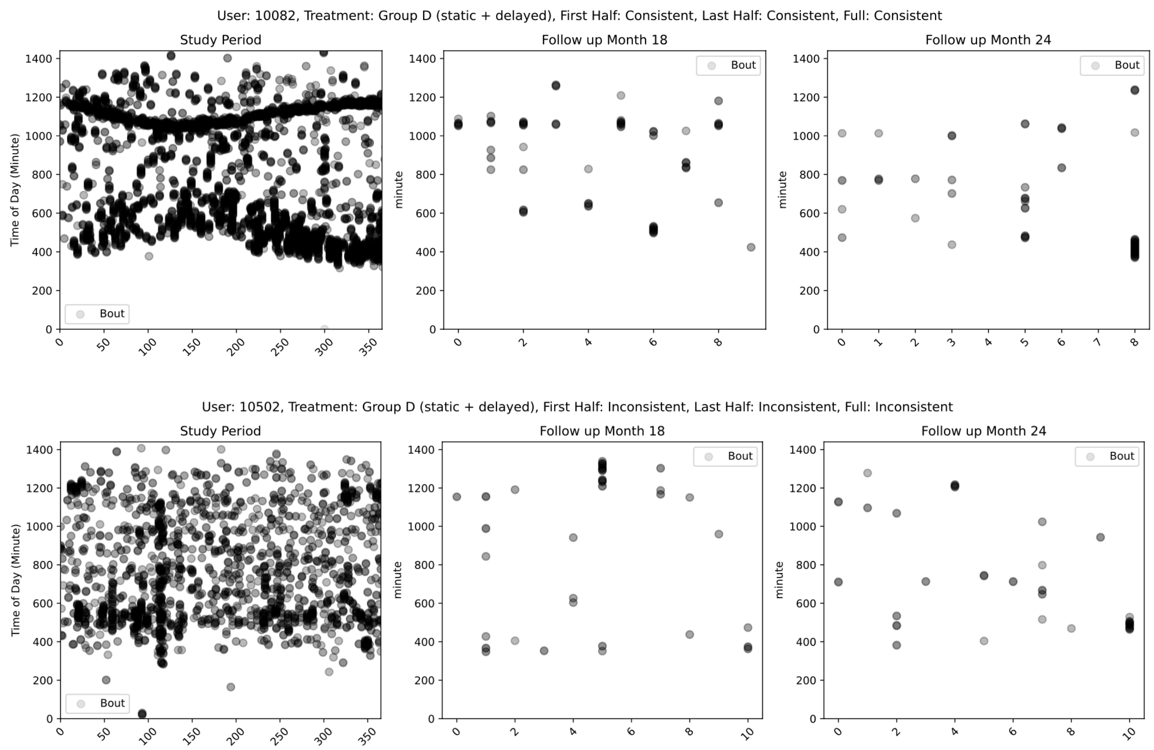



*Figure 3-2:* Representative user plots for the consistent (top) and inconsistent (bottom) groups. The time of day by the minute (ranging from 0 to 1440) is on the vertical axis and the day is on the horizontal axis. The left plot shows the raw walking data during the 12-month study period, the middle plot shows the raw walking data during the follow-up at month 18 (6 months after the end of the study) and the right most plot shows the raw walking data during month 24 (12 months after the study period).

We fit four regression models to assess the association between consistency and long-term maintenance. All models aimed to estimate the effect of consistency on the change in walking minutes per day as compared to baseline (the two-week period prior to the start of the study). We first fit the models without considering exercise level, then we included exercise level interactions. At month 18 those that were consistent were walking on average 6.01 (SE=1.65) more minutes per day than baseline compared to the inconsistent group (P=0.001). Similarly at month 24 the consistent individuals were walking on average 5.08 (SE=1.65) more minutes per day than baseline compared to the inconsistent group (P=0.002). When exercise level interactions were included in the models, at month 18 individuals that exercised over 35 minutes per day on average and were consistent during the study period were walking 15.82 (SE=5.76) minutes more than baseline compared to those that exercised between 21 and 35 minutes (P=0.006). In other words, those that spent less than 35 minutes walking per day saw the smallest change from baseline within the consistent group. At month 24 the interaction between consistency and exercise level is not significant.

Table 3.3: Association Between Consistency and Maintenance

| | Change in Minutes per Day (Month 18 vs Baseline) b/(se) | Change in Minutes per Day (Month 18 vs Baseline) b/(se) | Change in Minutes per Day (Month 24 vs Baseline) b/(se) | Change in Minutes per Day (Month 24 vs Baseline) b/(se) |
|---|---|---|---|---|
| Consistent | 6.011*** | -1.929 | 5.081** | 0.494 |
| | (1.762) | (3.025) | (1.652) | (2.952) |
| Treatment A | 1.521 | 0.379 | 4.940* | 3.880 |
| | (2.299) | (2.183) | (2.257) | (2.245) |
| Treatment B | -2.115 | -2.469 | 1.115 | 0.748 |

| | | | | |
|---|---|---|---|---|
| | (2.088) | (1.973) | (2.062) | (1.944) |
| Treatment C | 0.432 | 0.360 | 1.742 | 1.376 |
| | (2.256) | (2.141) | (2.000) | (1.988) |
| Over 35 Mins per day | | -0.936 | | 9.179 |
| | | (4.481) | | (9.021) |
| Under 21 Mins per day | | -4.019 | | -2.892 |
| | | (2.2313) | | (2.169) |
| Consistent # Over 35 Mins per day | | 15.82** | | 0.625 |
| | | (5.776) | | (9.513) |
| Consistent # Under 21 Mins per day | | 2.623 | | 1.247 |
| | | (3.638) | | (3.632) |
| Observations | 392 | 392 | 379 | 379 |
| Controls | Yes | Yes | Yes | Yes |

*Table 3.3:* Association between consistency and maintenance. This shows that being consistent estimated higher changes from baseline at month 18 and at month 24 compared to the inconsistent group. Additionally, when interacted with walking level at month 18, consistent individuals that walked above 35 minutes per day were walking 16

additional minutes on average than those that walked below. This suggests the estimated effect of consistency worked the best for the highest levels of exercise.

The results of Table 3.3 are visualized in Figure 3-3. In Figure 3-3 we display the change in walking minutes per day by walking group (consistent or inconsistent). The consistent group (left) saw bigger changes from baseline when compared to the inconsistent group (right). The consistent group saw their most dramatic changes for those walking over 35 minutes per day (green) and during the study period.

Figure 3-3: Change in Walking by Phenotype Exercise Level

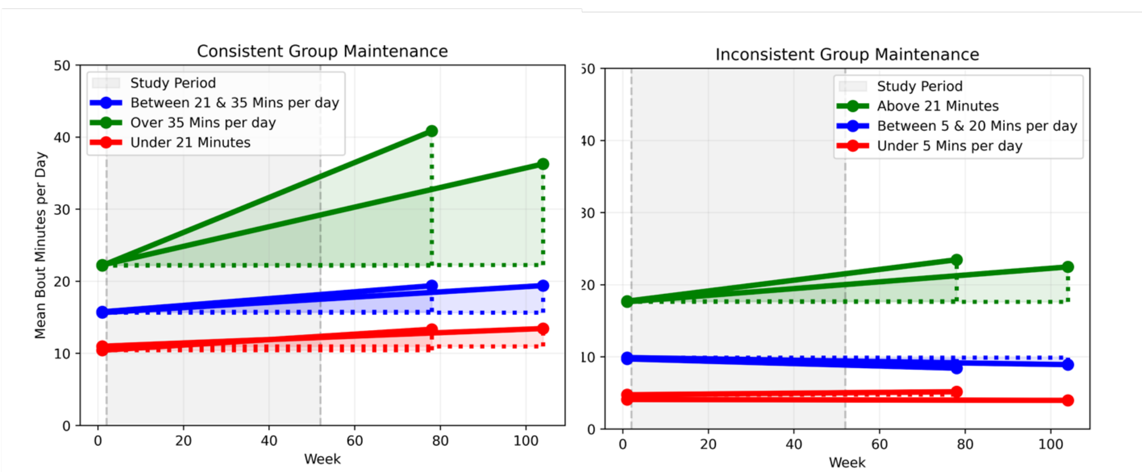



*Figure 3-3:* Change in walking minutes from baseline. Green represents those in the highest level of walking per day during the study. Blue represents those in the middle and red represents those that were walking on average in the lowest group during in the study. The consistent group (left) saw bigger changes from baseline when compared to the inconsistent group (right). The consistent group saw most dramatic changes at when at the highest level of exercise (green).

A survey was given to participants in the study to assess the breakdown of types of walking. Individuals were asked to report the amount of time they spent walking for the purpose of transportation and the purpose of exercise. Table 3.4 displays the portion of walking done for transportation out of the total reported exercise for the consistent and inconsistent phenotypes. Overall, users generally walked slightly more for exercise than for transportation. Individuals with the consistent phenotype reported a smaller proportion of walking done for transportation, ranging from 37.22%-42.31% by exercise level. Comparatively, the inconsistent phenotype reported a larger portion of walking done for transportation, ranging from 46.54% to 48.14% by exercise level. For both phenotypes, the type of reported exercise was similar among all levels of exercise.

Table 3.4: Reported Walking Types by Phenotype and Activity Level

| Physical Activity Level | Consistent | Physical Activity Level | Inconsistent |
|---|---|---|---|
| Under 21 Minutes | 42.31% | Under 5 Minutes | 46.54% |
| Between 21 and 35 Minutes | 37.22% | Between 5 and 20 Minutes | 46.77% |
| Over 35 Minutes | 41.81% | Over 21 Minutes | 48.17% |
| Responses | 169 | Responses | 266 |

*Table 3.4:* Reported (via survey) walking types by phenotype and activity level. Individuals in the study reported how much their walking was either transportation or done for the purpose of exercise. The consistent group spent a smaller portion of their time walking for transportation compared to the inconsistent group.

We assessed the relationship between the consistent and inconsistent categorization and the original randomly assigned study treatment groups. Table 3.5

shows the results of various two-sample test of proportions to check for statistical evidence that the relationship between the categorization into the groups consistent or inconsistent is related to the study randomized treatment. For each of the four treatment groups, being consistent was not related to treatment group. The details of the two-sample test of proportions results are displayed in Table 3.4.

Table 3.5: Test for Differences in Phenotype and Treatment Assignment

| Treatment | Consistent mean/(std) | Inconsistent mean/(std) | p-value |
|---|---|---|---|
| A | 0.231 (0.423) | 0.262 (0.441) | 0.448 |
| B | 0.266 (0.443) | 0.243 (0.429) | 0.570 |
| C | 0.290 (0.455) | 0.236 (0.425) | 0.198 |
| D | 0.213 (0.411) | 0.259 (0.439) | 0.263 |
| Observations | 169 | 305 | |

*Table 3.5:* The relationship between our consistent/inconsistent categorization was unrelated to the original study treatments. Treatment A was adaptive goals with immediate rewards, treatment B was static goals with immediate rewards, treatment C

was adaptive goals with delayed rewards and treatment D was static goals with delayed rewards.

To assess treatment heterogeneity (i.e., differences in treatment effect) based on behavior patterns, we fit a regression model to predict changes in from baseline at month 18 and month 24 using treatment interactions with behavioral signal categorization. Table 3.6 shows that those that were consistent and were assigned treatment A performed significantly better than baseline at month 18 and month 24 compared to all other groups. Specifically, at month 18 being consistent and being assigned the treatment of adaptive goals with immediate rewards was associated with 11.59 (SE = 5.19), P=0.026 and 13.43 (SE=4.77, P=0.005) minute increases than the reference group.

Table 3.6: Heterogenous Treatment Effect Model

| | Change in Minutes per Day (Month 18 vs Baseline) b/(se) | Change in Minutes per Day (Month 24 vs Baseline) b/(se) |
|---|---|---|
| Consistent | 2.621 | 0.642 |
| | (3.243) | (3.037) |
| Treatment A | -3.057 | -0.643 |
| | (2.509) | (2.607) |
| Consistent # treatment A | $11.59^{*}$ | $13.43^{**}$ |
| | (5.186) | (4.767) |

| | | |
|---|---|---|
| Treatment B | -3.155 | 0.289 |
| | (2.251) | (2.631) |
| Consistent # treatment B | 2.992 | 2.609 |
| | (4.560) | (4.293) |
| Treatment C | 0.737 | 1.048 |
| | (2.568) | (2.332) |
| Consistent # treatment C | -0.112 | 2.325 |
| | (4.793) | (4.281) |
| Controls | Yes | Yes |
| Observations | 392 | 379 |

*Table 3.6:* Assessing the heterogeneous treatment effect. Treatment A (adaptive goals with immediate rewards) when combined with a consistent behavioral phenotype saw the largest gains in walking when compared to baseline.

In Figure 3-4 we plotted the change in adaptive goals for those assigned to treatment A during the study period. In the consistent group, those that were walking under 21 minutes per day (red) and between 21 and 35 minutes (blue) saw an increase in the walking goals as the study progressed. For consistent individuals the average goal for those that were walking over 35 minutes per day (green) saw a gradual decline to around

50 minutes. In the inconsistent group, those that walked under 20 minutes per day (blue and red) saw a decrease in their adaptive goals through the study. Those that were walking on average over 21 minutes per day (green), saw a great fluctuation in the average goal time as it jumped up around day 65 and came back down after day 200 in the study.

Figure 3-4*:* Adaptive Walking Goals by Phenotype and Exercise Level

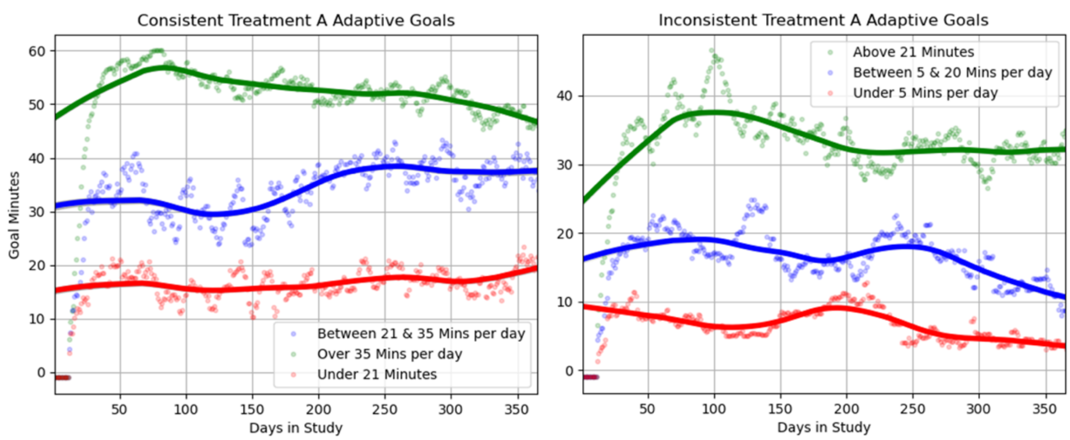



*Figure 3-5:* The change in adaptive goals for treatment group A (adaptive and immediate rewards). (Left) the consistent group saw an increase in goals overtime in the middle (blue) and least walking group (red) and slight decline in goals in the strongest walking group (green). (Right) the inconsistent group saw a slight decline in the goals for the middle (blue) least walking group (red), and a decrease that flattened out in the highest walking group (green.

## Discussion

The goal of this study was to investigate the role of behavioral pattern phenotypes in the maintenance of physical activity in the 12 months after a behavioral intervention. We first used a variety of metrics to quantitatively categorize individuals into two study period behavioral phenotypes: consistent or inconsistent. After the categorization, we found that both groups saw long-term improvements from baseline, at 6 months and 12 months after the conclusion of the study. This result supports the conclusion that behavioral interventions are effective at increasing the mean output. In this randomized control trial design, overall increases in walking behavior were maintained. More details of the efficacy of the original study can be read in the original published paper (Adams et al., 2022). However one common criticism of randomized controlled trials is that they capture the mean benefit and in practice the actual application at the individual level may or may not be effective (C. J. Bryan et al., 2021; Zhu & Gallego, 2020). By focusing on heterogeneous treatment effects randomized controlled trials may be improved by applying the most effective treatments based on specific individual characteristics.

In the current study, we found that those who were characterized as consistent in their walking behavior likely benefited the most from the study treatment. Specifically, being consistent was associated with larger increases in the amount of minutes walking at month 18 (6 months after the study) and 24 (12 months after the study) when compared to baseline. Interestingly our analysis demonstrated that a relationship exists between the level of physical activity and the estimated effect of having a consistent behavioral phenotype. The consistent individuals who at the highest level of physical activity level (i.e., over 35 minutes per day) saw stronger associated increases in walking than lower exercise levels. This suggest that rigid walking routines may be the most beneficial for high ends of physical activity level. To our knowledge this relationship between consistency and physical activity level has not been found or discussed in any other literature.

To further understand the differences between consistent and inconsistent groups we looked at the reported walking types. Individuals in the study were asked to respond to survey questions to report the amount of walking done for transportation and the amount of walking done for the purpose of exercise. We found that overall, the consistent group performed a higher portion of their total walking as exercise. The differences in walking preference provides additional evidence that consistency is associated with more rigid routines done for the purpose of exercise. Since the consistent group was more successful at long-term maintenance, this also suggests that convenient physical activity is likely less sustainable than ridged exercise-driven physical activity.

As we dove deeper into understanding the consistent behavioral phenotype we wanted to examine if any relationship existed between the randomly assigned treatment and our categorization. We wanted to know if it was possible that the treatments themselves was impacting the behavioral phenotype and therefore related to our consistent/inconsistent categorization. We found that our consistent/inconsistent label did not favor any treatment groups. The lack of relationship between the behavioral phenotype and treatment group suggests that our consistent/inconsistent label is likely predetermined (existing prior to the study) rather than impacted by the treatment. In other words, an individual likely already had the consistent behavioral phenotype prior to the start of the study. Given this result we then analyzed the heterogeneous treatment effect based on the differences in behavioral phenotype (consistent/inconsistent).

Our results indicated that being consistent and receiving the adaptive goals with immediate rewards treatment (treatment A) resulted in the best long-term benefits. The original study found that adaptive goals and immediate reinforcement treatment group saw significantly higher increases in MVPA than all other treatment groups (Adams et al., 2022). Additionally, in our study we demonstrated that the consistent behavioral phenotype saw significantly higher increases in walking minutes per day when compared to the inconsistent group (controlled for treatment). After establishing there was no association between consistency and treatment group, it was unclear how the two would interact together. Therefore, it was somewhat surprising to see that the majority of the increase within treatment A (adaptive goals with immediate rewards) came from those with the consistent phenotype. Therefore, individuals who exhibit a consistent phenotype likely benefit greatly from treatments with adaptive goals and immediate rewards. More research should be done to determine the best or most effective treatment types for individuals that fall under that inconsistent behavioral phenotype umbrella. For maximal effectiveness of treatments, it may be necessary to be catered according to individual behavioral phenotype.

When examining the change in adaptive goals during the study, we found that among the consistent walkers the goals increased or had marginal decreases through time (in the highest exercise group). This may indicate that the study treatments had a positive effect on behavior change for the consistent individuals. Specifically, all physical activity levels in the consistency group saw an increase in adaptive goals over first 50 days, then for those who were exercising less than 35 minutes, their goals continued to increase. This may suggest that consistent users were changing their behavior from the start to the end of the study. However, this was not true for adaptive goals in the inconsistent group. For individuals with the inconsistent behavioral phenotype, adaptive goals were less stable and even decreased during the study period. The highest level of physical activity saw a big jump in goal levels near the beginning of the study that quickly fell back down. It is possible the highest exercise level of inconsistent users may have overshot their MVPA and could not maintain it. In contrast the consistent group did not see as much of an over-performance early in the study. Overall, this may suggest that behavior changes were less common in the inconsistent group and provides further evidence that the consistent phenotype benefitted the most from the study treatment.

## Limitations

Despite our results there are a few important limitations to consider. First, the data from this analysis depended on study participants wearing their tracking devices. If an individual failed to wear the device during the study or follow-up, then we would be unable to detect their activity level. Next, this sample consisted mostly of white overweight/obese females from a specific region and may not generalize well to other populations. Lastly, for the reported walking, we recognize that this is not as reliable as objective data. Not every individual participated in the survey, which weakens our ability to extract meaningful information from Table 3.3. For this purpose, we only included survey reports as a single descriptor in understanding walking type preferences between the two behavior groups. Self-reported data were not used anywhere else in the current study.

## Conclusion

This study demonstrates that variety in behavior phenotype exists, and that these phenotypes are likely present and independent to study interventions or treatments. Our study indicated that consistent behavior phenotypes had stronger increases from baseline at 6 months and 12 months after the conclusion of the study when compared to the inconsistent individuals. Additionally, we found that the intervention treatment effects were more likely to be maintained long-term for those who favor more rigid (consistent) scheduled exercise when performed over 35 minutes per day. Finally, this study demonstrates the need to understand heterogeneity in treatment effects. The study treatment worked best for those characterized as having the consistent behavioral phenotype. More study needs to be done to target physical activity treatments more effectively for the inconsistent phenotypic individuals.

# CHAPTER 4

# MEDICATION ADHERENCE INCENTIVE PROGRAM

## Introduction

Medication adherence is essential for both immediate well-being and long-term health, especially among individuals managing chronic health conditions. Multiple studies have demonstrated that following medication instructions improves health outcomes (Ho et al., 2009). When patients adhere to the instructions of their doctors and pharmacists, both health outcomes and overall well-being improve (Aremu et al., 2022). Unfortunately, when individuals do not comply with their medication regimen, it leads to negative health effects. Studies have shown that medication nonadherence leads to adverse health effects (Cutler et al., n.d.). The outcomes of not adhering to medication include worsening conditions, increased comorbid diseases, and premature death (Chisholm-Burns & Spivey, 2012). The negative effects often go beyond the symptoms targeted by the medication. For instance, a comprehensive meta-analysis established a connection between depression and non-adherence to medication in chronic illnesses (Grenard et al., 2011).

Despite the advantages of adhering to medication and the drawbacks of not doing so, many individuals struggle with maintaining it over the long term. The actual rate of adherence per individual is believed to be as low as 50%. In other words, individuals do not take half of their prescribed medication (Brown et al., 2016). In a 2023 study of nearly 5,000 individuals, more than 25% of participants reported not adhering to their medication regimens (Garcia et al., 2022). Numerous factors can detrimentally affect a person's capacity to adhere to their medication regime including the patient's mental state and the type and packaging of the medication (Yap et al., 2016). An additional potential challenge that patients encounter is the cost of medication. A report issued in 2022 underscores a significant connection between the out-of-pocket expense of prescription medication and the rate of complete discontinuation in its use. As the medication cost escalates, the probability of patients entirely ceasing its usage also rises markedly (*IQVIA Insitute Report: Medicine Spending and Affordability in the U.S.*, n.d.). Ironically, the lack of medication adherence adds to the increase in healthcare expenses. Collectively, it is approximated that the inability of individuals to sustain healthy behaviors incurs billions of dollars in costs each year (Iuga & McGuire, 2014). For example, in 2016 the estimated cost of nonoptimized medications was over $500 billion, which accounts for 16% of total healthcare spending in the United States (Watanabe et al., 2018).

In an effort to address both the negative health effects and the escalating costs, researchers have experimented with numerous interventions aimed at enhancing medication adherence, yielding differing levels of success. An analysis of over 770 studies concluded that researchers have tested many intervention methods to increase medication adherence, but with varying and sometimes conflicting results (Conn & Ruppar, 2017). For example, efforts to improve medication adherence for heart failure via intervention resulted in a lower risk of readmission and mortality (Ruppar et al., 2016). However, among the highly adherent, interventions in one study failed to find any significant difference in medication adherence over a 90-day trial (Garza et al., 2016). Conversely, other studies have found success. For example, among mental health conditions, one systematic review found that above all financial incentives were likely the best intervention type to improve medication adherence (García-Pérez et al., 2020).

One of the more promising and effective intervention approaches has been financial incentives, but the effects are often short-term. For instance, a digital intervention that offered financial incentives demonstrated improvements in medication adherence; however, its follow-up period was limited to just two weeks (Guinart et al., 2022). Additionally, a meta-analysis that examined 21 different studies concluded that financial incentives likely are an effective method to increase medication adherence, but that further research is necessary to investigate how financial incentives can consistently lead to lasting effects for chronic diseases (Petry et al., 2012). An example of such an intervention is the app named Wellth, which offers financial incentives to encourage medication adherence. Wellth is a mobile app that provides incentives for daily medication adherence that is both feasible and acceptable, but the long-term success of the Wellth program is unknown. To date, it is not well understood why the most successful interventions still suffer from short-term effects. One possibility is that it may result from people becoming desensitized to incentives or that the initial excitement of receiving incentives fades over time(Royer et al., 2015).

Habit formation may be key in helping individuals take medications long-term. Habit-based strategies are increasingly being incorporated into health behavior interventions to promote long-term behavior maintenance (Badawy et al., 2020). Habits reduce the cognitive demands and conscious effort required to perform a behavior (Lally et al., 2011), which allows individuals to persist in a behavior long-term, despite waning motivation or distractions (Galla & Duckworth, 2015; Gardner et al., 2011b; Rebar et al., 2014). A comprehensive systematic review and meta-analysis concluded that medication adherence improvement should center around habit-based interventions (Badawy et al., 2020). Furthermore, another systematic review and meta-analysis found that the interventions directed at habit formation exhibited the highest degree of success (Conn & Ruppar, 2017). This led the authors to conclude that healthcare providers and researchers should emphasize habit-based interventions to enhance adherence (Conn & Ruppar, 2017).

Recent studies have established a link between consistency in behavior timing and the formation of habits (Berardi et al., 2023; Fowers et al., 2022; Schumacher et al., 2019; Stecher, Berardi, et al., 2021b; van der Weiden et al., 2020). Regarding medication adherence, maintaining consistent timing for pill-taking has been linked to the formation of habits. Moreover, the strength of these habits stands out as the most important predictor for long-term medication adherence (Phillips, Alison et al., 2013). Additionally, individuals with good long-term adherence have reported using temporally consistent pill-taking routines (Phillips, Alison et al., 2013). Thus, consistent pill-taking among Wellth participants may be a successful strategy for maintaining long-term medication adherence.

### Objective

The goal of this study was to examine the association between temporally consistent pill-taking and long-term medication adherence among Wellth participants. Specifically, this study aimed to analyze medication adherence in the context of the Wellth incentive program to determine what mechanisms lead to the best long-term adherence in the specific setting. By varying the flexibility of the pill-timing measure, we also aimed to determine the optimal time range of pill-taking for maintaining long-term adherence in this setting.

## Methods

### Sample Characteristics

Data were collected from a mobile application called Wellth, which is designed to financially incentivize medication adherence through programs. The Wellth app requires participants to submit through the app a daily photo of their pills in their hand, which is used as proof of pill taking. After submitting their pill-taking photographic evidence, participants are immediately notified that they have avoided losing $2 from their potential monthly incentive of $30. For the current study, the data came from participants of 8 different Wellth app programs. Each of the 8 programs was of varying duration, ranging from 3 months to 1 year. The data contained the date and time of day for every photo submitted to the Wellth app, as well as the total monthly incentives awarded to each participant. In addition to submitting a photo, participants must take their pill within a 3-hour window to successfully track medication adherence. That is, if a person's pill-timing goal is 9 AM, then they must take the pill between 6 AM and 12PM in order to record a valid check-in. Importantly, individuals would receive a push notification if they had not already recorded a successful pill-taking. These notifications came at goal time, one and a half hours after goal time, and ten minutes prior to the final window closing. The data contained the total goal for each individual and an indicator if the user was able to provide a valid check-in.

## Pill-Timing and Future Adherence

We hypothesized that the closer in temporal proximity pills were taken to goal time, the better long-term maintenance. To test this hypothesis, we employed a number of methods using STATA/BE 17.0 and Python 3.9. First, we fit multiple regression models using heterogenous robust standard errors that used the average difference in minutes from goal time in the first month of a program to predict last month adherence. The data contained information on individual characteristics such as the number of assigned tasks, age, and the presence of comorbid diseases. To account for the presence of comorbid diseases in our models we defined a comorbid value as a count of various comorbid diseases. For example, a comorbid value of 5 indicated that an individual had 5 comorbid diseases. A comorbid value of 0 indicated an individual had no comorbid diseases. The comorbid diseases included in this study were type 2 diabetes, type 1 diabetes, SUD, schizo, OUD, IHD, hypertension, hyperlipid, hyperchol, hepatitis, HIV, depression, CHF, COPD, CKD, cancer, bipolar, AFIB, and asthma. We also included controls for age, number of tasks, and the current adherence rate. Next, we fit the same model again using the same controls but added in an indicator that tracked whether, on average, the time difference was occurring before or after the goal time (1 for after goal time, 0 otherwise). We included this additional variable to test whether or not the time difference was dependent on being before or after goal time. To investigate this further we fit the same models again but separately using the average pill timing before and after. That is, we fit a model using the average pill timing when pills were taken before goal time to predict future adherence and we fit a separate model using the average pill timing when pills were taken after goal time to predict future adherence.

### Finding the Optimal Time Window

After establishing the estimated effects of pill-timing and the relative difference of whether it occurred before or after, we were ready to estimate an optimal time window. We aimed to find the level of consistency (a window of time) in pill timing that was most associated with future medication adherence. By plotting the average time differences from goal time in the first month against last month adherence we were able to find a window of time that was associated with last month adherence that was above average. To evaluate the timing window, we used both linear and logistical regression model techniques. In the linear models our outcome of interest was future adherence (i.e., portion of pills taken). For the logistic models our outcome of interest was perfect future adherence (i.e., 1 for taking 100% of assigned medications and 0 otherwise). Both models/outcomes were used together to ensure robustness of results. In a panel data setup using cluster robust standard errors, we used the portion of valid check-ins that took place within the time window on a given month to predict next the month's adherence rate.

Our next step was to analyze the relationship between consistent pill timing and long-term maintenance. We again turned to using the first month data to predict last month adherence. In each model we controlled for the program, comorbid value, age, number of tasks and the first month check-in rate (adherence). The logit models were fit using the same binary outcome as before (i.e., 1 for 100% adherence, 0 otherwise). The logistic model equation was given as follows:

$$\Gamma_{last} = W'_{first} \times \beta_{first} + C_{\text{first}} + \epsilon$$

Where $\Gamma_{last}$ is 1 for 100% adherence in the last payment period and 0 otherwise, and $W'_{first}$ is the portion of adherence that occurred within the optimal time window in the first payment period, and $C_{first}$ represent any control variables included in the models (program, age, comorbid number, and number of assigned tasks), and $\epsilon$ is the error term.

Lastly, to further demonstrate the overall estimated impact of pill-timing consistency on long-term medication adherence, we fit a linear regression model to predict the portion of valid check-ins out of the total number of tasks in the last pay period. The final regression equation is defined as follows:

$$Y_{last} = W'_{first} \times \beta_{\text{first}} + C_{\text{first}} + \epsilon$$

Where $Y_{last}$ is the portion of pills taken during the last month of a program, $W'_{first}$ is the portion of adherence that occurred within the optimal time window in the first payment period, and $C_{first}$ represent any control variables included in the models (program, age, comorbid number, program length, and number of assigned tasks), and $\epsilon$ is the error term.

## Results

The sample contained 3,416 participants from 8 different Wellth programs. Each program had a distinct sample size ranging from 229 to 1,997 individuals. Table 4.1 contains sample characteristics for the data used in this study, grouped by program length. The 8 programs had durations ranging from 3 to 12 months. The programs spanning 12 months had the smallest totaling 229 participants. Conversely, the programs running for 5 months had the largest sample, amounting to 1,997 individuals. Medication adherence was highest in the first month across all program durations. Specifically, for 12-month programs the first month adherence was .952 (STD=0.72) and for 5-month programs the first month adherence was .957 (STD=0.075). The last month of each program had lower medication adherence rates compared to the first month of the program. Programs that lasted 12 months saw an average medication adherence drop to .906 (STD=0.182) by the last month. Meanwhile the programs that were 5-months in duration had an average last month adherence of .773 (STD=0.308). All other adherence averages are displayed in Table 4.1.

The participants in this study were majority female, ranging from 54.5% to 100%. The average age for participants by program length ranged from 45 to 57. The comorbid value varied by program length. The programs that lasted 3 months had the greatest average comorbid number (Mean=2.46, STD=1.31) and the programs of 12 months had the lowest average comorbid numbers, at 0.009 (SD= 0.093). Lastly, the number of daily tasks each individual was required to complete was nearly equal across all program lengths with the average ranging from 1.15 (STD=0.361) to 1.3421(STD=0.475).

Table 4.1: Sample Characteristics by Program Length

| | Length 3 Months | Length 5 Months | Length 6 Months | Length 12 Months |
|---|---|---|---|---|
| Age | 52.3 | 47.053 | 56.738 | 45.1 |
| | (9.961) | (12.031) | (10.862) | (13.415) |
| Comorbid Value | 2.458 | 1.977 | 0.83 | 0.009 |
| | (1.311) | (1.45) | (.376) | (.093) |
| English | 0.878 | 0.962 | 0.796 | 0.865 |
| | (512.) | (1921.) | (483.) | (198.) |
| Female | 1 | 0.651 | 0.545 | 0.797 |
| | (583.) | (1300.) | (6.) | (181.) |
| Tasks | 1.328 | 1.187 | 1.341 | 1.153 |
| | (.523) | (.417) | (.475) | (.361) |
| First Month Adherence | 0.962 | 0.957 | 0.965 | 0.952 |
| | (.069) | (.075) | (.057) | (.072) |
| Last Month Adherence | 0.932 | 0.773 | 0.938 | 0.906 |
| | (.141) | (.308) | (.131) | (.182) |
| Individuals | 583 | 1997 | 607 | 229 |

*Table 4.1:* Descriptive statistics for the various program lengths. The average age of individuals in the study ranged between 45 and 64 years old. Most participants were female and spoke English. The 5-month program contained the most individuals at 4,260 while the 7-month program contained the fewest individuals at 360.

In Table 4.2 we plot the adherence rates by month of program completion. This was done to demonstrate the possible effects of seasonality. September was the most popular month to finish a program with 881 individuals in the study finishing in that month with a mean adherence of 0.911. The lowest month for adherence was July with an average adherence of only 0.624. All other adherence levels can be seen in Table 4.2.

Table 4.2: Last Month Adherence by Month

| | Last Month Adherence Rate | | | |
|---|---|---|---|---|
| Last Month | mean | count | 25% | 75% |
| January | 0.933 | 106 | 0.938 | 1 |
| February | 0.933 | 108 | 0.933 | 1 |
| March | 0.908 | 292 | 0.9 | 1 |
| April | 0.933 | 97 | 0.9 | 1 |
| May | 0.906 | 21 | 0.933 | 1 |
| June | 0.917 | 50 | 0.938 | 1 |
| July | 0.624 | 774 | 0.3 | 0.983 |
| August | 0.916 | 237 | 0.911 | 1 |
| September | 0.911 | 881 | 0.911 | 1 |

| | | | | |
|---|---|---|---|---|
| October | 0.868 | 399 | 0.844 | 1 |
| November | 0.863 | 372 | 0.867 | 1 |
| December | 0.923 | 79 | 0.933 | 1 |
| Total | | 3416 | | |

*Table 4.2:* The adherence rate by month end. This table supports the idea that there is some level of seasonality to pill taking, with the end of the year having slightly lower adherence than the beginning of the year. Notably July had the lowest adherence by far.

Among all users, 1,265 were perfectly adherent in their last month of their program. Figure 4-1 plots the distribution of time differences among these perfect adherers. The plot shows a bell-like curve to the distribution around the 0 minute (goal time). On average perfect adherers were taking their pills close to goal time in the first month of the program.

Figure 4-1: Perfect Adherers First Month Pill-timing Distribution

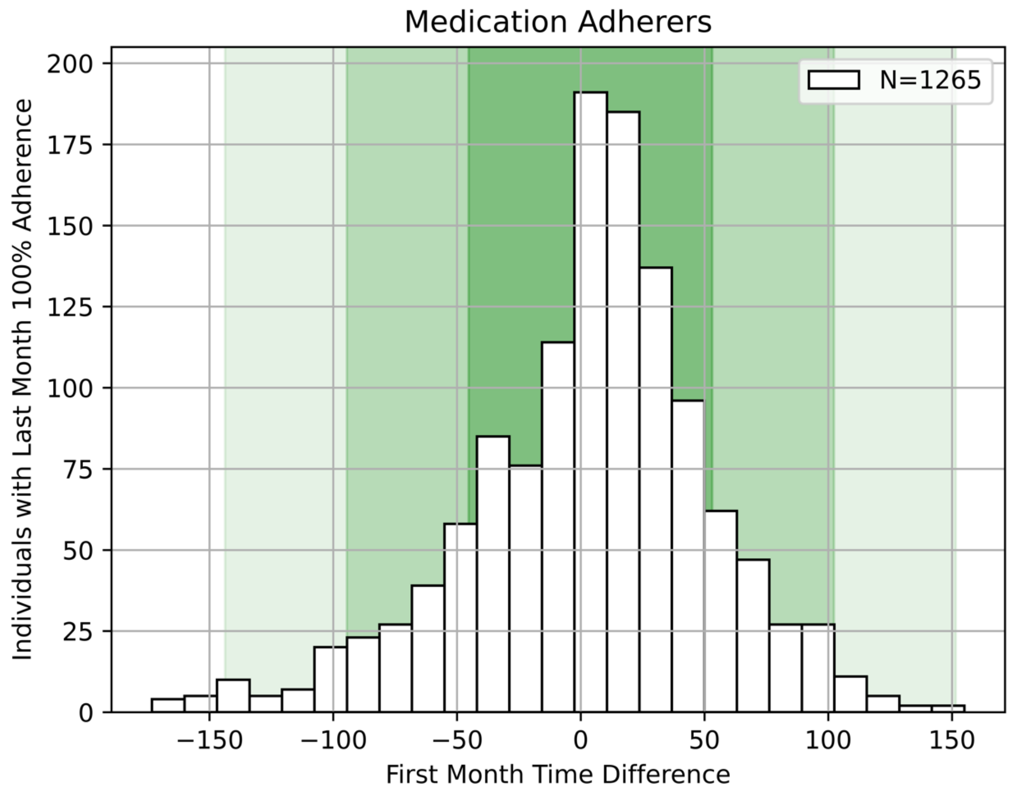



*Figure 4-1:* The distribution of first month time difference among last month perfect adherers. Each shade of green is a standard deviation. The perfect adherers tended to be taking pills close to goal time in their first month of the program.

Table 4.3 shows the regression model results for the models that used average absolute difference from goal time minutes in the first month to predict last month adherence. Firstly, in model (1), the results indicate that the further from goal time pills are taken in the first month the worse for last month adherence (p=0.008). The magnitude of this change is roughly 2 percentage point drop in last month adherence for every 1 hour off from goal time in the first month. When adding an additional variable (model (2)) that indicates if the time difference was occurring before or after the goal, the results show that pill taking after goal time was associated with 1.62% (SE=0.006, P=0.01) worse long-term adherence. For example, the negative effect of being off by 10-minutes was not the same if it was before goal time verses after.

Table 4.3: First Month Pill-timing and Last Month Adherence

| | (1) | (2) |
|---|---|---|
| | Last Month Adherence | Last Month Adherence |
| | b/se | b/se |
| Minutes from Goal | -0.000317** | -0.000314** |
| | (0.000) | (0.000) |
| Comorbid Value | -0.00182 | -0.00215 |
| | (0.003) | (0.003) |
| Age | 0.00136*** | 0.00130*** |
| | (0.000) | (0.000) |
| Number of Tasks | -0.0195** | -0.0185* |
| | (0.007) | (0.007) |
| Any Check-in Rate | 0.874*** | 0.858*** |
| | (0.067) | (0.068) |
| After Goal | | -0.0162* |
| | | (0.006) |

| | | |
|---|---|---|
| Program Control | Yes | Yes |
| Observations | 3416 | 3416 |

*Table 4.3: Model outputs predicting last month adherence given first month average pill timing. Each minute pills were taken away from goal time had an estimated negative effect on last month adherence. When including an indicator for before vs after, taking pills after goal time was worse than taking them before.*

In Table 4.4 this is investigated further by fitting the same models again but separately including the average pill timing for pills taken before goal time and for pills taken after goal time. The first column of Table 4.4 estimated the effect of pill-taking before goal time and the second column of Table 4.4 estimated the effect of pill-taking after goal time. Both variables of interest were significant. Specifically, every hour that pills were taken before goal time was associated with a 1.3% (p=0.027) drop in last month adherence. Meanwhile, every hour that pills were taken after goal time was associated with a 3.9% (P<0.001). That is, the negative effect per minute was 3 times worse for pills taken after goal time when compared to pills taken before goal time.

Table 4.4: Before Vs after Goal Time Pill-timing

| | (1) | (2) |
|---|---|---|
| | Last Month Adherence | Last Month Adherence |
| | b/se | b/se |

| | | |
|---|---|---|
| Minutes Before Goal | -0.000218* | |
| | (0.000) | |
| Comorbid Value | -0.00195 | -0.00229 |
| | (0.003) | (0.003) |
| Age | 0.00134*** | 0.00118*** |
| | (0.000) | (0.000) |
| Number of Tasks | -0.0168* | -0.0183* |
| | (0.007) | (0.007) |
| Any Check-in Rate | 0.889*** | 0.791*** |
| | (0.069) | (0.069) |
| Minutes After Goal | | -0.000646*** |
| | | (0.000) |
| Program Control | Yes | Yes |
| Observations | 3201 | 3362 |

*Table 4.4: Model outputs predicting last month adherence given first month average pill timing for both before and after goal time. Each minute pills were taken after goal time had a larger estimated negative effect on last month adherence compared to pills taken before.*

Figure 4-2 was used to determine the optimal window of time in which pills should be taken for long-term maintenance. Figure 4-2 displays the first month average pill timing on the horizontal axis and the last month adherence on the vertical axis. The raw data are plotted as black data points, and a trend line model fit is displayed as a red line. Additionally, a black horizontal line is included on the plot to show the last month average adherence among all users. To be above the horizontal line (i.e., to be above average in the last month) pills should be taken within 45 minutes before goal time or within 30 minutes after goal time. This can be seen in Figure 4-2 where the red trend line moves above the horizontal average line.

Figure 4-2: Last Month Medication Adherence by First Month Timing

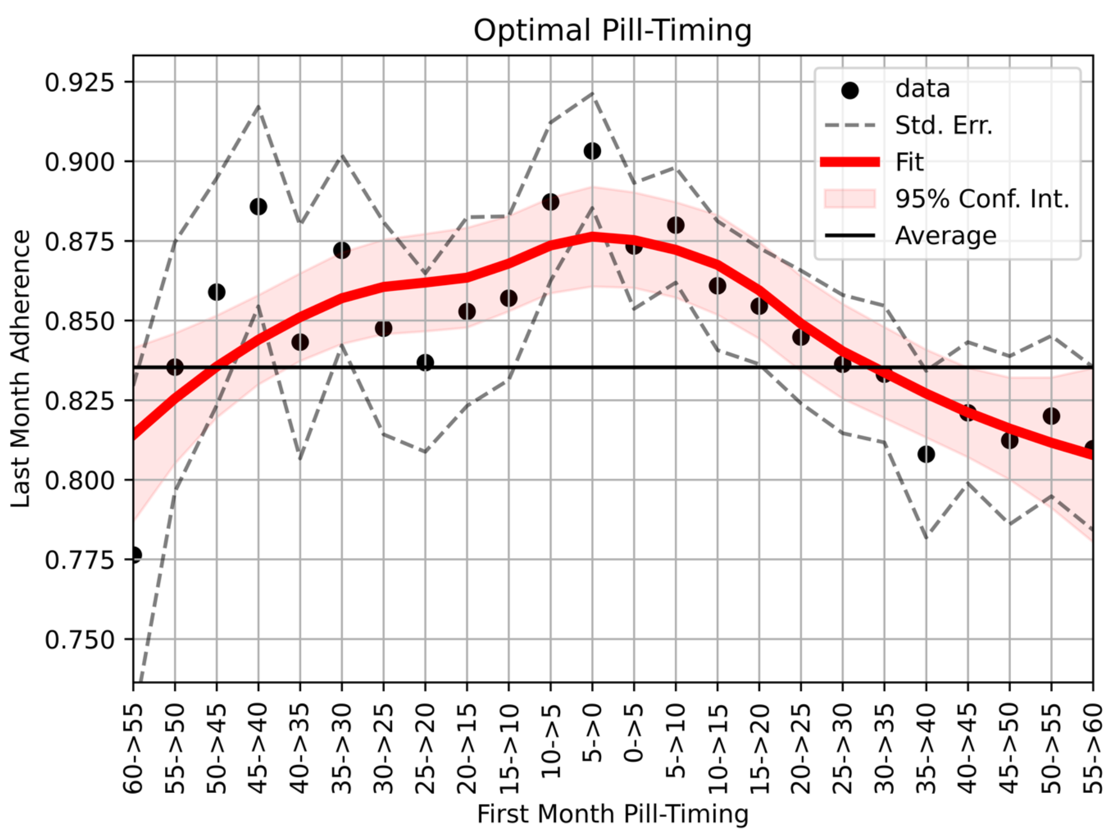



*Figure 4-2:* A plot of the optimal consistency time window. The first month average pill timing is plotted on the horizontal axis and the last month adherence on the vertical axis.

The raw data are plotted as black data points, and a trend line model fit is displayed as a red line. Additionally, a black horizontal line is included on the plot to show the last month average adherence among all users. To be above the horizontal line (i.e., to be above average in the last month) pills should be taken within 45 minutes before goal time or within 30 minutes after goal time.

To estimate the effect of taking pills within the time window, we fit various regression models. First, in Table 4.5 we show the regression model output for using the optimal time window to predict next month adherence in a panel data setup. Results indicated that taking pills within this window (within 45 minutes before goal time or within 30 minutes after goal time) was associated with 2.96-fold increase in the odds ($p<0.001$) of perfect adherence in the next month. Specifically, for every 10% increase in the portion of valid pills taken within the optimal time window in the first month the odds of last month adherence are multiplied by 1.115 ($p<0.001$) The estimated effect on maintenance was the greatest among each time window we modeled.

Table 4.5: First Period Consistency Association with next Period Adherence

| | (1) |
|---|---|
| | Next Month Full Adherence b/se |
| Optimal Window | $2.962^{***}$ |

| | |
|---|---|
| | (0.552) |
| Any Check-in Rate | 34.215*** |
| | (6.931) |
| Observations | 9744 |

*Table 4.5:* The panel data model results for the level of consistency (time window) with the strongest association to future adherence (taking 100% of medication). An increase of 10% in the number of pills taken within 55 minutes (as opposed to within 3 hours) is associated with a 15% increase in log odds of 90% or more pill-taking in the next payment period (month).

After establishing and validating optimal window for pill-taking on next month adherence, the next step was to estimate the impact on long-term adherence by estimating the effect on last month adherence rates (as opposed to next month). Therefore, we fit two additional regression models, as shown in Table 4.6. The first, found in the first column, is another logistic regression model used to predict last month full adherence (1 for 100% adherence, 0 otherwise). The second model is found in the second column and is a linear regression model to predict the raw last month adherence. The results indicated that taking pills within the optimal time window was associated with 2.412 ($P<0.001$) the odds of last month perfect adherence. Specifically, for every 10% increase in the portion of valid pills taken within the optimal time window in the first month the odds of last month adherence are multiplied by 1.092 ($p<0.001$). For the linear regression model, the portion of pills taken within the optimal window was associated with a 5.61% ($P<0.001$) increase in last month adherence. That is, for every 10% increase in the portion of valid pills taken with the optimal time window the expected last month adherence goes up by .5% ($P<0.001$).

Table 4.6. First Period Consistency Association with Last Period Adherence

| | (1) | (2) |
|---|---|---|
| | Maintenance | Last Month Adherence |
| | b/se | b/se |
| Optimal Window | 2.412*** | 0.0561*** |
| | (0.4000) | (0.011) |
| Comorbid Value | 0.925 | -0.00173 |
| | (0.0389) | (0.003) |
| Age | 1.016*** | 0.00134*** |
| | (0.004) | (0.000) |
| Number of Tasks | 0.598*** | -0.0190** |
| | (0.544) | (0.007) |
| Any Check-in Rate | 1502747*** | 0.845*** |
| | (2086732) | (0.068) |
| Program Control | Yes | Yes |
| Observations | 2999 | 3416 |

*Table 4.6:* Regression analysis output using the first-month consistency rate (within 45 minutes before goal time or within 30 minutes after goal time) to predict medication adherence (100% pill-taking) in the last month. Taking pills at a more precise time is strongly associated with long-term maintenance.

To further understand the differences between those that on average favored taking pills at or prior to goal time and those that favored taking pills after goal time, we created a contingency table to plot the time of day in which goals were established and the associated last month adherence for both groups. The results showed that the mean adherence was not significantly different between the before and after groups for the evening (P=0.244, N=736). For all other times of day, the before group had significantly higher last month adherence rates. All these results are displayed in Table 4.7.

Table 4.7: Last Period Adherence by Time of Day

| | Before | | After | | | Total |
|---|---|---|---|---|---|---|
| | Mean / std | Count | Mean / std | Count | P-value | |
| Morning | 0.914 (.204) | 160 | 0.852 (.258) | 506 | 0.005 | 666 |
| Midday | 0.861 (.261) | 627 | 0.81 (.279) | 1044 | <0.001 | 1671 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Evening | 0.851 (.275) | 166 | 0.824 (.257) | 570 | 0.244 | 736 |
| Late Night | 0.922 (.159) | 71 | 0.827 (.276) | 272 | 0.006 | 343 |
| Total | | 1024 | | 2392 | | 3416 |

*Table 4.7:* Contingency table outlying the last month adherence rates between the before and after group by time of day. Those who on average were taking their pills before the goal time had significantly higher last month adherence for the morning, midday, and late night. For the evening there was no significant difference.

## Discussion

The goal of this paper was to estimate the optimal time range of pill-taking to assess the relationship between consistent pill timing and long-term medication adherence. Our results indicated that taking pills closer to goal time was associated with improved future medication adherence in both the next month and last month of a program. Additionally, we found that taking pills within 45 minutes prior to goal time or within 30 minutes after goal time was the window of time associated with higher-than-average long-term adherence. Specifically, a higher portion of valid medication check-ins taken within the optimal time window of the preset goal time was positively predictive of future medication adherence. Observing a window with a generous level of flexibility was not surprising since rigid routines are often less favorable to habit formation than those that allow some level of flexibility (Stecher, Berardi, et al., 2021b). In fact, habit formation theory suggests that occasionally failing to perform a behavior given the associated cue does not seem to weaken the habit formation process (Lally et al., 2010). Therefore, if individuals take their pills at roughly the same time every day, they can still expect the habit-formation process to run its course. Our results seem to suggest that 30 to 45 minutes of flexibility (depending on if it occurs before or after the goal time) was the optimal level of flexibility for the habit formation process in this setting. Notably the window of time was not the same depending on if pills were being taken before or after goal time. One possible explanation for this could be the nature of the program itself. Individuals would receive push notifications to their mobile device if they had not recorded taking their pill. This notification came at goal time, again 1.5 hours after goal time, and one last time at 10 minutes before the close of the 3-hour valid check-in window. It is possible that those who favored taking pills after goal time were relying on the push notifications to their phone to remind them to take the pills. One potential item to consider here is the implications this could have on the habit formation process. If an individual developed a pill-taking habit that was built on the mobile phone notification queue, then after the program was over the performance of the behavior would likely drop off. Since habits are automatic actions in response to a contextual queue, when that queue is no longer present habit formation theory would suggest that the associated behavior would no longer occur.

Taking medication closer to goal time is consistent with other pill timing research that has demonstrated the importance of consistent timing for maintaining medication adherence (Phillips et al., 2021), but has not investigated the optimal flexibility of time consistency. To underscore the long-term significance of maintaining consistent pill timing within an optimal window, our research revealed a positive correlation between taking medication within this timeframe and increased odds of achieving perfect medication adherence rates (100%) in the last month controlled for 8 different programs. The estimated effect size was slightly greater when predicting next month adherence as opposed to last month adherence. This was not surprising since research has demonstrated in the context of healthy behaviors that the closer in temporal proximity an event is to an outcome the better the predictability (Fowers et al., 2022). Our findings support the need for researchers to consider both the temporal proximity and the number of observations when assessing and predicting future behaviors (Fowers et al., 2022).

Lastly, our research provides important implications to be considered when assessing or developing incentive programs to promote long-term medication adherence. The results of this study suggest that when using incentives to increase medication adherence, the timing of pill-taking should be emphasized early, and participants should be encouraged to establish pill-taking routines that occur within a more concise time window. Many pill-taking incentives are not dependent on the timing at which the behavior occurs (Conn & Ruppar, 2017). However, when it comes to medication adherence, pill-timing may be of vital importance to help individuals form habits. Additionally, the presence and timing of notifications should also be carefully considered in the context of the habit formation theory. If researchers focus on pill-timing as a mechanism for habit formation it is possible that medication adherence rates increase, and individuals and society benefit from the associated improved health outcomes and reduced healthcare spending.

## Limitations

The research presented in this paper had some limitations to consider. First, the data used in the analyses were not representative of the general population. Additionally, some key demographic information was missing from the data that may have been informative about the patterns of pill-taking. Such demographic information includes socioeconomic status.

When it comes to our long-term analysis, one limitation was the requirement for individuals to stick with the program for the entire duration. If an individual dropped out early, we were unable to detect their level of adherence in the last month of the study. Although the findings are still of interest, this potentially may have biased the results to this specific population (i.e., those that participated from start to end in the Wellth program). To better gauge the generalized effect of consistent pill-taking on future medication adherence, additional research should be performed in other contexts.

## Conclusion

Our findings support existing research that the time in which pills are taken is likely related to habit formation. When receiving financial incentives for medication adherence, consistency in pill timing is important for sustaining and maintaining both short-term and long-term medication adherence. Specifically, for Wellth participants, individuals who took their medications within 30 minutes prior to goal time or within 45 minutes post goal time likely became optimally engaged with the habit formation process. We found that taking pills outside of this time window at the start of a program was associated with below average adherence in the last month of a given program. Our results highlight the need for behavioral professionals to consider the time of day in which pills are taken as an important factor when designing and implementing medication adherence incentive programs.

# CHAPTER 5

# CONCLUSION

Biomedical informatics is all about leveraging data and technology to extract meaningful knowledge or information to advance biomedicine. In this dissertation, I leveraged novel approaches to detect key behavior phenotypes from longitudinal data that are associated with behavior maintenance. This work has provided new knowledge about the ways in which individuals are successful at maintaining various healthy behaviors. From this dissertation we know more about the role of temporal consistency in maintaining behaviors of varying complexity and across different behavioral settings.

New knowledge was discovered from this dissertation research. More specifically, through the dissertation research I was able to successfully discover behavioral phenotypes in three health settings. Certain phenotypes were more advantageous for long-term maintenance and treatments. For example, temporal consistency may have been beneficial for long-term success in some contexts. However, there were circumstances discovered in the research that may have been less beneficial, such as in mindfulness meditation or walking at lower durations.

Finally, several outcomes result from the dissertation findings. When designing health interventions, both the complexity of the behavior and individual phenotypes should be considered. This will lead to improved health outcomes, lowered healthcare costs and more. For example, in a physical activity intervention the goals and treatment can be catered to the individual capacity and phenotype. Future research should continue to investigate the mechanisms of long-term maintenance. Our current understanding of behaviors stems from psychological measurements. Such measurements should be compared together with quantitative analyses to better study the relationship between different mechanisms of maintenance. Lastly, additional studies of health behavior maintenance should be conducted in new settings and for new behaviors. Together, new research will further expand our knowledge of long-term maintenance so that, ultimately, individuals can be successful in their goals to live healthier lives.

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