MONITORING POST-CONCUSSION SYMPTOMS AND PSYCHOLOGICAL HEALTH-RELATED QUALITY OF LIFE USING ECOLOGICAL MOMENTARY ASSESSMENT THROUGHOUT CONCUSSION RECOVERY

By

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A DISSERTATION

Submitted to
Michigan State University
in partial fulfillment of the requirements
for the degree of

Kinesiology – Doctor of Philosophy

2025

PUBLIC ABSTRACT

Background: Affective post-concussion symptoms negatively impact psychological health-related quality of life (HRQoL), contributing to anxiety and depression symptoms in athletes. Additionally, daily fluctuations in these symptoms remain unclear. Ecological Momentary Assessment (EMA) methodologies allow subjects to repeatedly report their experiences and perceptions in real-time. *Recovering Concussion Update on Progression of Symptoms* (ReCoUPS), a mobile, web-based EMA platform that administers daily symptom surveys via text messages, is a reliable and feasible tool for monitoring concussion symptoms in real time. However, this tool has yet to be used to track psychological HRQoL following a concussion.

Purpose: This dissertation aimed to: 1) investigate the psychometric properties of momentary psychological HRQoL inventories and a post-concussion symptom checklist via ReCoUPS to healthy participants, 2) assess the feasibility for ReCoUPS for montoring traditional post-concussion affective symptoms and psychological HRQoL throughout concussion recovery, and 3) compare changes in affective symptoms and psychological HRQoL throughout concussion recovery using ReCoUPS between concussed college-aged athletes and healthy controls.

Methods: For Aim 1, healthy participants (ages 17-30) completed momentary assessments of post-concussion symptoms and psychological HRQoL via ReCoUPS daily for 7 days, with recalled versions administered at the study closure to assess evidence of test-retest reliability and construct validity. For Aims 2 and 3, college-aged athletes diagnosed with a concussion were enrolled within 3 days post-injury and completed ReCoUPS daily survey text messages daily until the study closure (i.e., within 48 hours after full medical clearance). Healthy matched controls (age, sex, sport) followed the same procedures. All participants completed demographics, injury/ medical history information, and enrolled in the ReCoUPS platform at the acute visit. The SCAT6 Symptom Checklist, PROMIS-SF Anxiety, and PROMIS-SF Depression were completed via ReCoUPS text messages daily throughout recovery. Recovery information and recalled psychological HRQoL were collected at the study closure visit.

Results: For Aim 1, 93 college-aged healthy athletes (mean age: 21.37±2.63 years; 64 female, 29 male) completed the study with 86.02% (n=80) completing over 70% of daily ReCoUPS surveys. Momentary PROMIS-SFs demonstrated moderate-to-excellent agreement with recalled measures and acceptable reliability. Both PROMIS-SFs were strongly correlated with affective symptoms. For Aim 2, we enrolled 36 college-aged athletes with a concussion (mean age: 20.36±1.25 years; 23 female, 13 male), with 66.67% (n=24) completing over 70% of daily surveys. Both momentary PROMIS-SFs were strongly correlated with affective symptoms. Descriptive statistics and heat plots demonstrated variability in outcome measures throughout concussion recovery. For Aim 3, in addition to concussed participants, 34 healthy controls (mean age: 20.35±1.37 years; 21 female, 13 male) were enrolled. Multi-level mixed-effects models revealed that concussed athletes reported significantly higher symptoms than healthy matched controls. **S**ymptom variance was explained by within-athlete and between-athlete differences.

Conclusion: Among healthy college-aged athletes, momentary assessments of psychological HRQoL via ReCoUPS demonstrated evidence of strong reliability and validity. ReCoUPS was a feasible, usable, and effective method of tracking psychological HRQoL and affective symptoms throughout concussion recovery in injured athletes. Concussed athletes reported significantly higher affective symptom and psychological HRQoL scores than healthy controls, with both between-athlete and within-athlete symptom variability. These results support ReCoUPS as a remote symptom monitoring tool, allowing clinicians to make timely and targeted treatment decisions. Further, we support variability in concussion symptoms daily throughout recovery.

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Background: Affective post-concussion symptoms negatively impact psychological health-related quality of life (HRQoL), contributing to anxiety and depression symptoms in athletes. Additionally, daily fluctuations in these symptoms remain unclear. *Recovering Concussion Update on Progression of Symptoms* (ReCoUPS), a mobile, web-based ecological momentary assessment platform that administers daily symptom surveys via text messages, is a reliable and feasible tool for monitoring concussion symptoms in real time. However, this tool has yet to be used to track psychological HRQoL following a concussion.

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Results: For Aim 1, 93 college-aged athletes (mean age: 21.37±2.63 years; 64 female, 29 male) completed the study with 86.02% (n=80) completing over 70% of daily ReCoUPS surveys. Momentary PROMIS-SFs showed moderate-to-excellent agreement with recalled measures (Anxiety: ICC=0.99, 95% CI=0.99-1.00, $p<0.001$; ($\kappa=0.44$; Expected: 51.73%, Actual: 73.12%, p<0.001; Depression: ICC=0.99, 95% CI=0.99-1.00; ($\kappa=0.58$; Expected: 50.99%, Actual: 79.57%, p<0.001) and acceptable reliability (Anxiety $\alpha=0.80$; Depression $\alpha=0.91$). Both PROMIS-SFs were strongly correlated with affective symptoms (Anxiety: $r_s=0.77$, $p<0.001$; Depression: $r_s=0.66$, $p<0.001$). For Aim 2, we enrolled 36 college-aged athletes with a concussion (mean age: 20.36±1.25 years; 23 female, 13 male), with 66.67% (n=24) completing over 70% of daily ReCoUPS surveys. Both the momentary PROMIS-SFs were strongly correlated with affective symptoms (Anxiety: $r_s=0.85$, $p<0.001$; Depression: $r_s=0.74$, $p<0.001$). Descriptive statistics and heat plots demonstrated psychological HRQoL and affective symptom variability throughout concussion recovery. For Aim 3, in addition to concussed participants, 34 healthy controls (mean age: 20.35±1.37 years; 21 female, 13 male) were enrolled. Multi-level mixed-effects models revealed that concussed athletes reported significantly higher symptoms than healthy matched controls ($p<0.001$-0.05). **S**ymptom variance was explained by within-athlete and between-athlete differences.

Conclusion: Results of this dissertation provide evidence of the psychometric properties of momentarily assessing post-concussion symptoms and psychological HRQoL via ReCoUPS in healthy individuals. We also support the acceptability, feasibility, and usability of ReCoUPS to remotely monitor and detect variance in concussion symptoms throughout recovery**.**

This dissertation is dedicated to my mom and dad. I love you more.

ACKNOWLEDGEMENTS

First and foremost, I want to thank my mentor and advisor, Dr. Tracey Covassin, for her unwavering guidance and support over the past four years. Dr. Covassin took a chance on a girl from Philly with a big dream and no master's degree, and now here we are. I would also like to acknowledge my committee members, Dr. Abigail Bretzin, Dr. Kimberly Kelly, and Dr. Matthew Pontifex, for their mentorship, time, and constant support of both this dissertation and my journey as an aspiring concussion researcher. Special thanks to Dr. Doug Wiebe and the entire University of Michigan Injury Prevention Center Team for numerous opportunities for me to grow personally and professionally. Thank you to Dr. Nikki Hoffman and Dr. Matthew Harkey for their additional support and guidance through the wild ride that is a PhD.

To my family, thank you for never giving up on me, even when I wanted to give up on myself. Mom and Dad (Jim and Lynne), your love and support made this possible. To my sisters, Zena and Taylor, my brother-in-laws, Kyle and Brent, and my adopted brother, Willis, thank you for your support, making me the "doctor" of the family (aside from Andre), and giving me my nephews, Brycie, Brody, and Ryan, who got me through the toughest days. And to Dr. Andre Bateman, the best big brother ever, you know I couldn't have done this without you.

To my incredible friends, the "Philly ones" (Emily, Tay, the Fox Chase girls), the "Michigan ones" (Hippo, Megan, Corinne, Logan, Aaron, Caitlin, Abby), and my entire MSU family (including Newton's friends Orla, Chili Luisa, Norman, and Monte), thank you for being you. You have made this grad school thing seem "not that bad."

Finally, to Colin and our doggies (Newton, Louis, and Theo), our little family has been my anchor, and I cannot wait to come home. You have been truly amazing and I'm endlessly grateful for you, for your love, and for your belief in me. I can only hope to make you all proud.

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CHAPTER 1 : INTRODUCTION

1.1 **Overview of the Problem**

Approximately 300,000 sport-related concussions occur annually in the United States.[7] The most recent epidemiological study of concussions in NCAA collegiate sports reported that 3,497 concussions occurred between the 2014-2015 and 2018-2019 school years.[8] Collegiate athletes are at an increased risk of experiencing affective symptoms (e.g., anxiety and depressive symptoms) throughout concussion recovery (i.e., approximately 0 to 90 days post-injury).[9,10] Further, approximately 94.7% of collegiate athletes[9] may endorse at least one affective (i.e., psychological, emotional) symptom post-concussion. Experiencing affective symptoms, which can include sadness,[11] irritability,[11] and anxiety and depressive symptoms,[12] can elicit a cognitive appraisal in the athlete during which they assess the limitations that these symptoms impose on their everyday life (i.e., inability to participate in work, school, and social activities).[13] These limitations can lead to further negative emotional responses, which can ultimately impact the individual's overall psychological health and well-being. Therefore, affective post-concussive symptoms may yield negative impacts on psychological health-related quality of life (HRQoL).[1-6]

HRQoL is an individual's perception of their overall health and well-being specifically relating to health, disease, and injury,[14] and comprises of varying domains, including psychological health.[15] Research suggests psychological HRQoL is worse between 3-10 days post-concussion;[5,6] however, it is not known if psychological HRQoL changes, or fluctuates, on a day-to-day basis throughout recovery making it difficult for sports medicine providers to manage, particularly in the acute phase (i.e., within 7-14 days post-injury).[1,5] Failure to intervene when psychological HRQoL and affective symptoms are heightened throughout recovery can lead to chronic post-concussive symptoms (>3 months)[16,17] and can hinder efforts to effectively manage concussion.

Ecological Momentary Assessment (EMA) is a set of methodologies which allows subjects to repeatedly report their experiences and perceptions in real-time, in their natural environment, over time and across contexts.[18] EMA is an advantageous tool for remotely monitoring concussion symptoms and predicting recovery outcomes,[19,20] including recovery time. Furthermore, symptoms collected via EMA methods were better predictors of recovery time than traditional clinical survey assessment (i.e., in-person with a clinician).[19] *Recovering Concussion Update on Progression of Symptoms* (ReCoUPS) is a mobile EMA platform in which participants are enrolled using a smart phone and are prompted via text message to report concussion symptoms throughout recovery.[20] This protocol is a reliable and feasible method of collecting concussion outcomes (i.e., symptoms) for clinicians to remotely monitor patients in real time.[20,21] For example, Wiebe et al.[20] determined that symptoms reported via ReCoUPS had excellent agreement with symptoms reported in-person at a clinical visit the same day (intraclass correlation coefficient= 0.97) and participants successfully reported their symptoms throughout concussion recovery over 80% of the days enrolled in the study. However, ReCoUPS has yet to be used to collect outcomes such as psychological HRQoL throughout recovery; therefore, it is unclear if ReCoUPS is a feasible method of collecting psychological HRQoL outcomes. Further, monitoring psychological HRQoL in real time throughout concussion recovery using the ReCoUPS platform could offer health care providers (e.g., athletic trainers, sports medicine specialists) with information regarding how these outcomes change on a day-to-day basis.

Despite known impairments in psychological HRQoL following concussion, there is a lack of reliable evidence to support the understanding of psychological HRQoL post-concussion in real-time. Psychological components of HRQoL include anxiety and depression symptoms (e.g., feeling overwhelmed, helplessness, hopelessness),[22] which can impact an individual's overall health and well-being. Psychological domains of HRQoL are among the most impacted post-concussion.[1,3-6,23] Unfortunately, concussion studies often rely on global health scales assessing an individual's recall of HRQoL (i.e., within the past 7 days),[5,6] limiting the ability for researchers and health care providers to understand how psychological HRQoL changes momentarily (i.e., from day to day). While utilizing an EMA platform such as ReCoUPS could be a potential method of monitoring momentary psychological HRQoL, current research has yet to explore this method. Therefore, there is a need to assess the real-time psychometric properties (i.e., reliability) of a psychological HRQoL inventory to ensure the robustness and generalizability of employing these measures via ReCoUPS in both healthy and concussed populations. This will enable healthcare providers to reliably monitor outcomes throughout concussion recovery for timely and precise treatment strategies.

The results of this study will (1) provide evidence of the psychometric properties of utilizing a post-concussion symptom checklist and a psychological HRQoL inventory for EMA in a healthy population, (2) elucidate a novel EMA platform, ReCoUPS as a feasible method of measuring post-concussion affective symptoms and psychological HRQoL in real-time throughout recovery, and (3) measure changes in affective symptoms and psychological HRQoL throughout concussion recovery in high school and collegiate athletes. This study is the first step in guiding subsequent clinical and implementation studies, aiding healthcare providers in making effective and timely treatment recommendations. Implementation of more efficient treatment strategies may reduce the risk of chronic concussion symptoms and prolonged recovery. Subsequent studies based on these results will greatly benefit high school and collegiate athletic trainers and healthcare providers managing concussions (e.g., sports medicine physicians, neuropsychologists), as they will provide a more comprehensive understanding of post-concussion outcomes and recovery trajectories. The outcomes of this study will fill a crucial gap in literature, as little is known about how concussion symptoms and psychological HRQoL change and fluctuate throughout concussion recovery.

1.2 **Purpose of the Study**

The purpose of this study was to examine the utility, acceptability, and feasibility of a novel mobile EMA platform, ReCoUPS, to monitor post-concussion symptoms and psychological HRQoL throughout concussion recovery in college-aged athletes.

1.3 **Specific Aims and Hypotheses**

1.3.1 Specific Aim 1

To investigate evidence of the psychometric properties of a momentary psychological HRQoL inventory and post-concussion symptom checklist administered using the mobile EMA platform, ReCoUPS, to healthy participants.

1.3.1.1 Hypothesis 1a

Momentary assessment of psychological HRQoL via ReCoUPS will demonstrate evidence of high test-retest reliability and a high level of agreement with recalled HRQoL.

1.3.1.2 Hypothesis 1b

Momentary assessment of psychological HRQoL will be strongly correlated with post-concussion affective (i.e., more emotional, sadness, irritability, trouble falling asleep)[11] symptoms.

1.3.2 Specific Aim 2

To assess the acceptability, feasibility, and usability of a mobile EMA platform, ReCoUPS, to monitor fluctuations in traditional post-concussion affective symptoms and psychological HRQoL throughout athlete concussion recovery.

1.3.2.1 Hypothesis 2

Utilizing the ReCoUPS platform will be an acceptable, feasible, and usable method of measuring post-concussion symptoms and psychological HRQoL throughout concussion recovery.

1.3.3 Specific Aim 3

To determine changes in affective symptoms and psychological HRQoL throughout concussion recovery using the EMA platform, ReCoUPS.

1.3.3.1 Hypothesis 3a

Athletes with a concussion will demonstrate significant within-athlete changes in post-concussion symptoms and momentary psychological HRQoL throughout recovery.

1.3.3.2 Hypothesis 3b

Athletes with a concussion will demonstrate significant between-athlete changes in post-concussion symptoms and momentary psychological HRQoL throughout recovery when compared to healthy age, sex, and sport matched controls.

CHAPTER 2 : REVIEW OF THE LITERATURE

2.1 **Introduction**

Concussion is an injury which can lead to several maladaptive outcomes. Existing literature continues to develop the understanding of these outcomes specifically related to mental health post-concussion. Concussion is a complex and heterogenous injury which can be challenging for healthcare providers to diagnose, manage, and treat. Therefore, researchers have attempted to structure symptom patterns and domains. For example, some studies have classified symptoms as physical, cognitive, affective, and sleep domains.[24,25] Chandran et al.[12] used this symptom structure to determine the dependencies between specific concussion symptoms and domains (e.g., headache symptom with physical domain). Further, more recent studies, such as that of Kontos et al.,[26] have continuously worked to develop the evolving conceptual model for concussion sequalae by defining the five clinical profiles of concussion: (1) vestibular, (2) ocular, (3) cognitive/fatigue, (4) migraine, and (5) anxiety/mood. The impairments caused by incurring a concussion have been found to result in functional limitations related to physical activity, academic activity, electronic use, work, and social activity.[26]

Specific clinical profiles and affective symptoms of concussion, such as anxiety/mood are associated with mental health outcomes which may have psychological implications. Further, the psychological implications of concussion have also been found to negatively impact health-related quality of life (HRQoL).[1-3] Moreover, research is continuing to explore how mental health outcomes post-concussion influence HRQoL and how this may further impact concussion recovery in the acute phase. Therefore, the purpose of this literature review is to examine the maladaptive mental health outcomes of concussion specifically related to HRQoL. Furthermore, this literature review will also discuss ecological momentary assessment (EMA) as a method of assessing these outcomes throughout concussion recovery.

2.1.1 Concussion Definition

Recently, the 6th Consensus Statement on Concussion in Sport, held in 2022, defined concussion as a traumatic brain injury induced by biomechanical forces caused by a direct blow to the head, face, neck, or elsewhere on the body with a force transmitted to the head.[27] In addition to this definition, the initial blow initiates a neurotransmitter and metabolic cascade, with possible axonal injury, blood flow change and inflammation affecting the brain.[27] Consequently, the terms concussion and mild traumatic brain injury (mTBI) are often used interchangeably; however, there is validated criteria which specifically defines concussion and differentiates the two. Concussion can result in acute impairments of neurological function that resolves spontaneously or persistent impairments which may evolve over minutes or hours.[25] However, it is important to clarify that concussion impairments largely reflect a functional disturbance rather than a structural injury with symptoms presenting as cognitive, sleep-related, balance, gait, ocular, and/or vestibular that may or may not involve loss of consciousness.[25]

2.1.2 Epidemiology of Sport-Related Concussion

It has been reported that approximately 1.6-3.8 million concussions occur annually in the United States.[28] Of these, approximately 300,000 have reported that the mechanism of injury is due to sport.[7] Therefore, the incidence of concussion has become a public health and sports medicine concern in the United States and internationally.[28] Over the past several years, researchers have worked tirelessly to present an accurate estimation of the incidence of concussion to support the need for attention for this epidemic. Furthermore, it has become increasingly evident that concussions are unreported which would significantly affect incidence statistics. Moreover, considering sex and sport disparities in concussion incidence rates, it is also crucial for a comprehensive understanding of the implications of the public health issue that concussion poses.

Several studies have reported national concussion rates among high school athletics. Gessel and colleagues[7] investigated the epidemiology of concussions in a nationally representative sample of high school athletes. Data was collected using the High School RIO injury surveillance system throughout the 2005-2006 school year. Researchers collected injury and exposure data for athletes participating in 9 US high school sports, including boys' football, soccer, basketball, wrestling and baseball and girls' soccer, volleyball, basketball, and softball. The rate of injury was calculated as the ratio of injuries per 1,000 total athlete exposures (A-E; 1 athlete's participation in practice or competition). Of note, it was observed that in the 2005-2006 school year, 4,431 injuries were reported, of which 8.9% were concussions. Of these concussions, 65.4% occurred during competition while 34.6% occurred during practice. These percentages indicated that the resulting overall concussion injury rate was 0.23 concussions per 1,000 A-Es in competition, 0.11 concussions per 1,000 A-Es in practice, and 0.53 concussions per 1,000 A-Es in competition. Based on these rates, it was estimated that approximately 135,901 concussions were sustained in all sports nationally during the 2005-2006 school year. Furthermore, these estimates indicated that most concussions were sustained in football (40.5%), girls' soccer (21.5%), boys' soccer (15.4%) and girls' basketball (9.5%). Additionally, this study compared high school concussion incidence rates to those reported via the NCAA Injury Surveillance System. It was yielded that during the 2005-2006 school year, there were a total of 8,293 injuries, 482 (5.8%) of which were concussions. Ultimately, it was determined that the overall rate of concussion was higher in collegiate sports than high school sports, despite concussion representing a greater proportion of injuries sustained by high school athletes. While this study was conducted several years ago, it is notable as one of the first studies to evaluate concussion rates for multiple sports in high school populations compared to collegiate populations.

More recent studies have reported on concussion incidence rates in high school athletes using nationally representative data.[29-31] For example, O'Conner et al.[30] described concussion incidence rates for 27 high school sports reported via the NATION surveillance system between the 2011-2012 and 2013-2014 school years. Overall, 2,004 concussions were reported with a rate of 3.89 per 10,000 A-Es. Concussion rates were the highest among football (9.21 per 10,000 A-Es), boys' lacrosse (6.65 per 10,000 A-Es), and girls' soccer (6.11 per 10,000 A-Es). Furthermore, Kerr and colleagues[29] examined concussion incidence in 20 high school sports during the 2013-2014 to 2017-2018 school years using data collected in the High School RIO surveillance system. Results of this study indicated that 9,542 concussions were reported, with 63.7% occurring during competition and 36.3% occurring during practice. This represents an overall concussion rate of 4.17 per 10,000 A-Es, with 10.37 vs 2.04 per 10,000 A-Es occurring in competition and practice, respectively. The highest concussion rates occurred in boys' football (10.40 per 10,000 A-Es), girls' soccer (8.19 per 10,000 A-Es), and boys' ice hockey (7.69 per 10,000 A-Es).

Other studies have focused on reporting concussion incidence rates in collegiate athletes. Zuckerman et al.[32] reported concussion incidence rates for 25 NCAA sports during the 2009-2010 to 2013-2014 school years using information collected through the NCAA Injury Surveillance Program. It was reported that 1,670 concussions occurred within this time period for an overall concussion rate of 4.47 per 10,000 A-Es. The highest concussion rates were reported for men's wrestling (10.92 per 10,000 A-Es), men's ice hockey (7.91 per 10,000 A-Es), women's ice hockey (7.50 per 10,000 A-Es), and men's football (6.71 per 10,000 A-Es). However, men's football and women's soccer had the largest annual estimate of reported concussions (3,417 and 1,113 respectively). A similar, yet more recent, study conducted by Chandran and colleagues[8] determined concussion incidence rates during the 2014-2015 through 2018-2019 school years. Only 23 NCAA sports were included in this study, and it was reported that 3,497 concussions occurred for an overall rate of 4.13 per 10,000 A-Es. The highest concussion rates were observed in men's ice hockey (7.35 per 10,000 A-Es) and women's soccer (7.15 per 10,000 A-Es). While the overall concussion rate decreased between the time frames reported by Zuckerman et al.[32] and Chandran et al.,[8] rates in women's soccer and volleyball notably increased indicating that concussion incidence is gradually rising in specific sports.

While several studies have examined the incidence of reported concussions, some studies have focused on the incidences when athletes do not report when they have sustained a concussion. As a result, undisclosed concussions might not be factored into the general or national concussion statistics, raising concerns that there may be a higher incidence of concussion than previously believed. The University of Pittsburgh Medical Center Sports Medicine Concussion Program reports that 5 in 10 concussions go unreported or undetected.[33] Researchers believe that concussion underreporting may be heavily attributed to knowledge of the injury. Several studies have reported that concussion education improves concussion reporting behaviors.[34,35] Meanwhile, other studies have found that higher concussion knowledge may endorse reasons for an athlete to not disclose a concussion (i.e., knowing that they will be removed from play).[36] Additionally, a recent systematic review concluded that evidence for athletes failing to disclose concussion symptoms can be attributed to interpersonal dynamics among the athlete, teammates, and coaches.[37] Moreover, the impairments typically experienced immediately following concussion (e.g., loss of consciousness, slowed reaction time) present with such rapid onset and resolve spontaneously, it may be difficult for an athlete or athletic trainer to recognize the injury.[38] Lack of education on concussion symptomology may also present as a factor in injury or symptom nondisclosure.[36] Taking these unreported injuries into account, it becomes understandable why the estimation range of 1.6 to 3.8 million annual concussion occurrences is so wide; however, this estimate might still be low.[28]

Unlike the findings of Langlois et al.,[28] which indicate that males are about twice as likely to experience traumatic brain injury in general, several studies report that in sports both sexes played in, high school girls experienced higher rates of concussions than boys. This is also true for collegiate sports, with women demonstrating higher concussion rates than men. Such differences may be attributed to style of play and biomechanical differences (e.g., females have demonstrated weaker neck muscles,[39] less total mass in head and neck when compared to males,[40] and females demonstrate greater angular acceleration and displacement of the head and neck[41]). This also provides insight as to why there is a need to address concussion as a distinct public health issue. For example, Kerr et al.[29] found that when examining sex-comparable sports (i.e., soccer, basketball, cross country, baseball or softball), girls demonstrated higher concussion rates than boys (3.35 vs 1.51 per 10,000 A-Es). Furthermore, a study conducted by Bretzin et al.[42] examined sex differences in injury rates in high school athletes. Results yielded that females were at 1.9 times greater risk for enduring concussions than males in sex comparable sports. Chandran et al.[8] also noted that among sex comparable sports (i.e., basketball, soccer, baseball or softball, and swimming) at the collegiate level, concussion rates were higher among women when compared to men. While researchers continue to learn more about the burden of concussion in the United States, concussion incidence has continued to rise and disparities in occurrences between sport and sex have become more evident. Therefore, it has been suggested that the push for new technologies to better aid documenting these risks will help understand the true burden of concussion[43] as well as assist in the development and prescription of efficient management and rehabilitation of the injury.

2.1.3 Pathophysiology of Sport-Related Concussion

As previously mentioned, the most recent consensus statement on concussion in sport[27] has defined concussion as a biomechanical force to the brain in the absence of macroscopic neural damage. Additionally, the blow to the head, neck, or body which results in concussion may also initiate a neurotransmitter and metabolic cascade which involves bioenergetic challenges, cytoskeletal and axonal alterations, impairments in neurotransmission, and vulnerability to delayed cell death and chronic dysfunction.[44,45] This neurometabolic cascade of concussion has been laid out in the research lead by Giza and Hovda.[46] Consequently, the discussion of translational clinical implications of the injury has stemmed from this understanding of the acute pathophysiology of concussion.[47]

In the research of Giza and Hovda,[46] the acute pathophysiology, physiological perturbations, and clinical corelates of concussion have been generously outlined. As previously mentioned, concussion is caused by a biomechanical force or jolt to the head, neck, or body,[25] which then leads to a metabolic cascade involving an ionic flux, energy crisis, axonal injury, impaired neurotransmission, protease activation, altered cytoskeletal proteins, and ultimately cell death.[46] Each step of this cascade has been deemed to be associated with clinical symptoms of concussion such as migraine, photophobia, impaired cognition, and slowed reaction time. The metabolic cascade begins with an initial ionic flux following this blow. This ionic flux and depolarization triggers voltage-or ligand-gated ion channels that create a 'spreading depression-like' state that may be the biological substrate for very acute post-concussive impairments. Studies have indicated that these impairments may be associated with migraine headache, photophobia, and/or phonophobia.[48,49]

To restore ionic and cellular homeostasis, an energy crisis occurs during which the adenosine tri phosphate (ATP)-requiring membrane begin excessively working and cause hyperglycolysis, or an increase in glucose utilization,[50] leading to a depletion in intracellular energy reserve and increases in adenosine di phosphate (ADP).[51] This event causes an increased demand for energy and results in an uncoupling, or mismatch, between energy supply and demand. Essentially, this is an impairment in cellular metabolism which may cause prolonged diminution of oxidative capacity and metabolic vulnerability. Some animal studies including adult rat models have shown that repeated injury during this phase may lead to worse neurocognitive function and traumatic axonal injury,[52-55] while human studies have shown delayed recovery following a second impact during this phase.[56] Conclusively, this phase is seemingly associated with vulnerability to a second injury and a contact risk for concussed athletes.

The biomechanical forces caused by concussion can also cause cytoskeletal damage and axonal dysfunction. Following a concussion, neurons and glia can be damaged, causing complex degenerations of microstructural components including dendritic arbors, axons, and astrocytic processes.[57] This damage to neurofilaments and microtubules then can lead to axonal dysfunction and potential disconnections.[58] Further, such disconnections impede the neuron from normal functioning. Several studies have found that neuronal dysfunction such as this is related to cognitive impairments in mild TBI models.[54,59] Specifically related to concussed individuals, this damage may also be related to impaired cognition, slowed processing, and slowed reaction time.[46]

Impaired neurotransmission has also been observed following concussion. In vivo experimental TBI studies have shown changes in ligand-gated excitatory inhibitory neurotransmission. More specifically, alterations in glutamate receptor (NMDAR) subunit composition have been reported in immature[60] and mature[61] brain models. This has been heavily associated with abnormal development plasticity, electrophysiology and memory in pup rodent models and functional alterations including differential patterns of calcium in adult models.[61] This has been found to be associated with impaired cognition, slowed processing, and slowed reaction time.[46]

Finally, the neurometabolic cascade of events following concussion also includes protease activation, altered cytoskeletal proteins, and possibly cell death. For example, changes in inflammatory markers have been historically reported in more severe TBI studies,[62] including the activation and infiltration of microglia.[63] Microglia activation has been associated with the increased risk of parkinsonism after TBI.[64] Additionally, while most studies have shown little cell death following mild TBI, ongoing cerebral and hippocampal atrophy have been described in adult rat models,[65] as well as chronic losses in dopaminergic neurons in the substantia nigra.[64] Overall, these upsets have been noted to be affiliated with chronic atrophy and ongoing development of persistent impairments.[46]

As previously mentioned, in a review conducted by Howell and Southard[47] of the molecular pathophysiology of concussion, the cascade of disruptive processes to the brain which occur following concussion were sufficiently summarized. It was essentially concluded that an energy crisis ensures following injury, during which there is a mismatch between the need for energy to restore disruptions in the brain and a reduced ability to produce and deliver energy in the brain. Furthermore, the individual pathophysiological processes which occur during this cascade (i.e., ionic flux, energy crisis, axonal injury, inflammation, cell death), have each been associated with specific symptoms of concussion including migraine headache, impaired cognition, and development of persistent impairments. This has laid the groundwork for subsequent human-based studies which have focused on the symptom sequelae, recovery, and treatment of concussion, which will be discussed in the proceeding sections of this literature review.

2.2 **Signs, Symptoms, Impairments of Sport-Related Concussion**

As previously mentioned, due to the heterogenous nature of concussion symptom presentation, researchers have worked to stratify and organize symptom patterns and presentations.[12,26] For example, in 2019 Kontos and colleagues introduced the clinical profile-based approach to the conceptualization of concussion.[26] Using the model initiated by Collins et al.[66] based upon the empirical evidence supporting that a homogenous, or 'one size fits all', approach to concussion was not feasible, it was proposed that there are five clinical trajectories or profiles which symptoms fall into: (1) cognitive/fatigue, (2) vestibular, (3) ocular, (4) migraine, and (5) anxiety/mood. Further, researchers such as Chandran et al.[12] have also used the known empirical evidence of concussion symptomology to conceptualize symptoms patterns and relationships among symptoms associated with concussion. Ultimately, this study identified predictors of concussion symptom presentations and symptom presentation patterns, elucidating that concussion symptoms follow patterns of physical (e.g., headache, nausea, sensitivity to light and sound), cognitive (e.g., difficulty concentrating, balance, disorientation), affective (e.g., hyperexcitability, irritability) and sleep. Based on these pattern models, the following sections outline the most relevant signs, symptoms, and impairments of concussion.

2.2.1 Vestibular

The vestibular system is a complex sensory network which can be heavily disrupted by concussion. The sensory network itself provides information to the brain regarding motion, equilibrium, and special orientation via neural pathways to direct motor output and vestibular-oculomotor reflexes.[67] The vestibular clinical profile of concussion symptomology is classified by a disruption in this network, leading to outcomes which can include dizziness, motion sensitivity, mental fogginess, and balance problems.[26] As noted by Kontos et al.'s[26] review of clinical characteristics of concussion symptom profiles, nearly half of athletes report symptoms consistent with the vestibular profile (e.g., balance and dizziness) post-concussion.[68,69] Furthermore, a review of literature conducted by Valovich McLeod and Hale[70] indicated that approximately 67-77% of concussed individuals experience dizziness, which may be a risk factor for prolonged recovery. Additionally, balance impairments are common after concussion, primarily lasting between 3-10 days post-injury.

A study conducted by Sinnott et al.[71] investigated the role of persistent vestibular-ocular symptoms and impairments following concussion on recovery time. This study included a total of 50 male and female adolescent athletes and found that individuals with persistent vestibular-ocular symptoms took significantly longer to recover than individuals without these impairments. Additionally, Sufrinko et al.[72] examined sex differences in vestibular and oculomotor symptoms and impairments post-concussion. It was found that females experienced worse vestibular-ocular reflex symptoms when compared to males, but there were no other sex differences on other vestibular-related symptoms. This indicates that perhaps females only experience certain vestibular reflexes worse than males post-concussion.

2.2.2 Ocular

Unlike the vestibular profile, the ocular profile of concussion symptoms is typically characterize by vision impairments and symptoms such as blurred or double vision, frontal headache, pressure behind eyes, difficulty with visually demanding tasks, abnormal eye movement and function.[26] Deficits in convergence and accommodative functions that facilitate the maintenance of near vision may also be observed in athletes with ocular symptoms.[73] Master et al.[74] sought to determine the prevalence of vision diagnoses after concussion in adolescents and found that 69% of concussed individuals included in the study had at least one vision diagnosis including accommodative disorders, convergence insufficiency, and saccadic dysfunction. These visual impairments could also have prolonged effects for the athlete as they may result in visual discomfort and visual functional impairments (e.g., slowed reading and compromised attention).[75]

Ocular and visual impairments post-concussion can have serious adverse effects for athletes. As previously stated, the functional impairments that result from symptoms of this profile may lead to impaired academic, work, and sport performance.[75] Furthermore, athletes with such impairments may also be at higher risk for prolonged recovery. In a study conducted by Master et al.,[76] it was sought to determine which vision or vestibular problems predict prolonged recovery in children. It was determined that symptoms associated with the vestibulo-ocular reflex, abnormal balance and accommodative amplitude predicted prolonged recovery. It is believed that a history of motion sickness[76] or history of an oculomotor abnormality (e.g., strabismus)[66] may be a risk factor for these symptoms; however, there is little research to support this assumption.

2.2.3 Cognitive/Fatigue

Kontos et al.[26] have defined the cognitive/fatigue profile of concussion symptomology as slowed cognitive or thinking abilities as well as the presence of fatigue or tiredness when engaged in mental activities. Symptoms, or deficits, which are classified by this profile include low energy, fatigue, global cognitive deficits, and experiencing symptoms later in the day.[77] Several studies have explored the transient decline and deficits that athletes may face post-concussion. In 2021, Kontos et al.[78] examined the relationship between concussion and cognitive symptoms in male and female high school and collegiate athletes. Cognitive deficits such as verbal and visual memory, as well as reaction time, were observed in the acute phase of concussion. Furthermore, Sandel et al.[79] explored sex-based differences in post-concussive neurocognitive functioning in adolescent male and female athletes. Cognitive performance tasks were presented as verbal memory, visual memory, visual motor speed, and reaction time. It was found that athletes performed more poorly on these computerized cognitive screening tools in the acute phase of concussion, and females performed significantly worse than males across all neurocognitive measures. Additional studies have suggested that these impairments may translate to functional inabilities in academic and occupational settings.[80] Furthermore, Kontos et al.[26] has indicated that while the risk factors of cognitive impairments post-concussion are unknown, it is speculated that continuing to play or engage in daily activities while symptoms are still present or previous presence of neurodevelopment conditions (e.g., learning disorders)[81] may be contributing factors.

This specific symptom pattern classification is also characterized by fatigue and disruption in sleep schedules. A review conducted by Jaffee et al.[82] identified common sleep-related complaints related to concussion to include excessive daytime somnolence, insomnia, and unusual behaviors during sleep or transition stages. It is believed that these sleep impairments can affect athletic and neurocognitive performance. For example, Sufrinko et al.[83] examined the effects of restricted sleep and related symptoms on neurocognitive performance in male and female high school athletes. It was found that sleep-related symptoms and reduced sleep duration were associated with poor neurocognitive performance post-concussion. It has also been found that preinjury sleep difficulties may exacerbate neurocognitive impairments post-concussion.[84] A more recent study conducted by Hoffman et al.[85] explored relationships between days to symptom recovery and varying aspects of sleep and found that sleep-wake disturbances and overall poorer sleep throughout recovery may be associated with longer symptom recovery.

2.2.4 Posttraumatic Migraine

A posttraumatic headache is a headache attributed to trauma or injury to the head and/or neck, such as a concussion. While the headache may occur as an isolated symptom following an injury (i.e., posttraumatic headache), it can also present as a combination of symptoms including dizziness, difficulty concentrating, fatigue, sensitivity to light and noise, nausea, and slowed psychomotor abilities (i.e., posttraumatic migraine).[86] Several studies have reported that headaches are the most common symptom reported after concussion.[87-89] For example, in a study of 544 high school concussions, it was reported that headache was experienced in 93.4% of the injuries. Meanwhile, another study of 17,549 concussed football players reported that posttraumatic headache was present post-concussion in 86% of athletes.[90] Typically, headaches are experienced by concussed individuals within the first week of injury;[89] however, it is possible that these symptoms may persist intermittently past this timeframe.[48] Although existing literature suggests that posttraumatic migraine (PTM) is of the most prevalent symptom post-concussion, it is still apparent that little is understood of the impact that this symptom cluster may have on athletes in the acute or prolonged phase following concussion.

It has been speculated that PTM after concussion may influence clinical outcomes and recovery after injury. Kontos et al.,[89] examined if PTM during the first week after injury predicted cognitive impairment and symptoms in the second week after injury and overall recovery time. In a sample of 138 male high school football players, participants were grouped according to whether they had PTM, headache without PTM symptoms, or no PTM or headache at all. It was found that participants in the PTM group had worse verbal memory, visual memory, reaction time, and symptoms when compared to the headache group in the first- and second-week post-injury. Furthermore, the PTM group was 7.3 times more likely than the no headache group and 2.6 times more likely than the headache group to have a prolonged recovery (i.e., greater than 20 days). Similarly, in a study conducted by Mihalik et al.,[48] symptom status and neurocognitive functioning was compared between PTM, headache and no headache groups. In a sample of 261 high school aged athletes, it was determined that the PTM group exhibited greater neurocognitive deficits (e.g., memory, reaction time) and symptom deviation from baseline (e.g., headache, nausea, sensitivity to light and noise, irritability) than the headache and no headache groups. These results suggest that individuals with PTM post-concussion may have worse clinical outcomes and delayed recovery.

2.2.5 Anxiety/Mood

Anxiety has been defined by the Diagnostic and Statistical Manual (DSM-V) as excessive worry and apprehensive expectations regarding a number of events or activities.[91] Symptoms include restlessness, difficulty concentrating, and irritability. Mood is defined by "a set of feelings, ephemeral in nature, varying in intensity and duration, and usually involving more than one emotion."[92] Consequently, the anxiety/mood clinical profile of concussion is associated with emotional and behavioral changes as well as depression, anxiety, moodiness, and irritability.[26] In 2017, Covassin and colleagues[93] conducted a review of psychological issues which may be associated with concussion in youth and collegiate athletes, which synthesized the literature examining the psychological consequences and effects of concussion. The findings of this review yielded that mood disturbance, anxiety and depression, were among the most prevalent psychological consequences of concussion.

One study which examined mood disturbances post-concussion found that athletes with concussion reported higher levels of depression, confusion, and total mood disturbance when compared to healthy controls at 14 days post-injury with symptoms resolving within the first 3 weeks following the injury.[94] As for anxiety, symptoms are difficult to disentangle from post-concussive symptoms and the symptomologies overlap. However, it has been reported that over one-third of collegiate athletes with concussion report state anxiety (i.e., transient emotional response to a situation that can result in feelings of apprehension and tension)[95] following the injury.[10] More recent research has indicated that 13% of patients with concussion exhibit clinical levels of post-injury anxiety[96] associated with increased stress, lack of team involvement, lack of social support, or uncertainty in recovery time.[97]

Some studies have found that there are specific indicators that may allude to the presence of anxiety/mood symptoms post-concussion. Henry et al.[77] reported that inconsistencies in symptoms reporting and misalignment in self-reported symptoms and performance on objective neurocognitive testing may suggest the individual is experiencing these symptoms. Meanwhile, other studies have indicated that there may be several risk factors predisposing individuals to anxiety/mood symptoms. Iverson and colleagues [98] examined the prevalence of post-concussion-like symptoms in patients with depression. Essentially, the goal of this study was to determine any alignment between clinically diagnosed depression and post-concussion symptoms. It was found that factors which might cause or maintain the reporting of post-concussion symptoms included prior diagnosis of depression or other psychiatric conditions, chronic disturbance, sleep disturbance or fatigue, and/or life or family stress. Another similar study conducted by Sandel et al.[99] sought to present evidence to support factors contributing to the anxiety/mood profile and found that mental health history and biological sex were of the most notable risk factors.

The previously mentioned studies which display anxiety and mood-related consequences post-injury have helped inform the anxiety/mood clinical profile following concussion. Moreover, studies such as that of Iverson[98] and Sandel et al.[99] have further expanded on the risk factors and treatment of this profile. The relevance of understanding the risk factors and treatment of the anxiety/mood profile lie with the fact that if not properly treated, mood changes can lead to chronic post-concussive symptoms, especially in patients with pre-existing mood conditions.[16,17] Therefore, it was concluded that the general mechanisms which may lead to emotional disturbance after concussion are pre-injury risk factors, brain changes from concussion, psychological responses to injury, and concurrent situational risk factors that may engender the anxiety/mood profile subtype after concussion.[99]

2.3 **Management of Concussion**

When considering the management, diagnosis, symptomology, treatment, and recovery of concussion, it is also important to consider the heterogeneity of the injury as a one-size fits all approach is not an effective strategy. While early concussion research recommended strict cognitive and physical rest following concussion,[100] over the past several years, there has been a significant shift in the approach of recognizing, diagnosing, and treating concussion. This shift comes on the basis of several advances in research which have introduced and supported multifaceted approaches to concussion management supported by empirical evidence.[26,66,77] Scheider et al.[101] have presented an adaptation of the recursive model of sport injury[102] to concussion, indicating that when a concussion is suspected the athlete should undergo a multifaceted assessment to diagnose the injury. If a diagnosis is made, the athlete should undergo relative cognitive and physical rest for the first 24-48 hours following the injury then engage in symptom-limited activity. If the athlete is asymptomatic, they may begin return to learn (i.e., RTL, return to preinjury learning status with no additional accommodations or support)[27] and return to sport (i.e., RTS, completion of the RTS strategy with no symptoms at rest or maximal physical activity)[27] strategies, which will then lead to medical clearance to RTS. If the athlete is symptomatic following symptom-limited activity, they should once again undergo multifaceted assessment, which may indicate relevant targeted rehabilitation to initiate RTL and RTS strategies for medical clearance. The following sections explore the advances in such research over the years and explore the current methods of concussion assessment and diagnosis, treatment, and recovery.

2.3.1 Sport-Related Concussion Assessment and Diagnosis

As stated by the 6th consensus statement,[27] the first step in initiating management of concussion is recognition of the injury. concussion is recognized by the presence of one or many signs and symptoms shown on or off the playing field immediately following head impact. Some symptoms that are more severe in nature and warrant immediate removal from play and medical attention include loss of consciousness (LOC), seizure, tonic posturing, ataxia, poor balance, confusion, behavioral changes, or amnesia.[103] More common symptoms that may be less severe in nature but still warrant further assessment include headache, "pressure in head," neck pain, nausea or vomiting, vertigo, blurry vision, balance problems, sensitivity to light and noise, difficulty remembering and concentrating, and affective impairments (e.g., nervous or anxious, irritable, more emotional than usual).[104]

As previously noted, concussion symptoms have been stratified into clinical profiles for more effective identification and management;[26] however, immediately following injury it is important to recognize the overt symptoms of concussion which may require immediate and specific intervention. For example, headache is the most common symptom immediately following concussion, with studies reporting that approximately 94% of concussed individuals will experience this symptom.[30,88] Further, approximately 75% of athletes will experience dizziness, and approximately 60% will experience difficulty concentrating.[30,88] Almost half of athletes will also experience confusion/disorientation (46.0%) and vision changes/sensitivity to light (37.5%).[88] As previously stated, recognizing concussion is the first step in injury management. Therefore, a symptom checklist is often used for the assessment of signs of symptoms of concussion.[105] To date, there are several symptom reports available for clinicians to utilize, including the Post-Concussion Symptom Scale (PCSS),[106] Post-Concussion Symptom

Inventory (PCSI), Graded Symptom Checklist (GSC),[107] Head Injury Scale (HIS),[108] Rivermead Post Concussion Symptoms Questionnaire (RPQ),[109] and the Sport-Concussion Assessment Tool (SCAT).[110]

Recognition of a concussion may be based on an athlete's reported symptoms (i.e., listed above) or signs and symptoms observed by other players or medical staff and professionals.[27] Common assessment tools used in the clinical evaluation and assessment of concussion include the SCAT6,[110] Balance Error Scoring System (BESS),[111] Vestibular Ocular Motor Screening (VOMS),[112] King Devick (KD),[113] and Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT).[114] The SCAT6 is the most updated version of the SCAT and is commonly used in the acute sideline assessment of concussion, implementing assessments including orientation, immediate memory, concentration, the BESS, and delayed recall.[103] The BESS is an instrument focused on evaluating postural stability following concussion[111] and can be utilized independently or in conjunction with the SCAT6. The VOMS is a validated instrument used to evaluate the function of vestibular and oculomotor systems in individuals with a concussion and captures symptoms (e.g., headache, dizziness, nausea, and fogginess) for component tests including smooth pursuits, saccades, near point of convergence, vestibular-ocular reflexes, and visual motion sensitivity.[112,115,116] Another tool utilized in sideline assessment of the visual system following concussion is the KD, which requires patients to read single digit numbers as fast as they can without making errors and increases with difficulty over time.[113] Sideline assessment of concussion has also incorporated technology advances with computer based screening tools. The ImPACT is a computer-based neurocognitive test that measures concentration, attention, memory, visual motor speed, and reaction time.[114] Once a diagnosis of concussion has been made, proceeding steps can be taken in the treatment and recovery protocol.

2.3.2 Sport-Related Concussion Treatment

Following diagnosis of concussion, it is recommended that immediately following injury (i.e., within the first 24-48 hours of injury), rest is implemented including reduced participation in activities of daily living and screen time.[27,117] Following this, it is recommended that individuals systematically advance exercise and involvement in activities of daily living based on the degree of symptom exacerbation.[27,117] However, due to the previously noted heterogeneity of symptomology of concussion and unlikelihood that a "one size fits all" approach to concussion recovery is acceptable, a multifaceted approach to treatment should also be considered. For example, behavioral management strategies which address positive lifestyle changes (e.g., adequate hydration/diet, some degree of daily activity, regulated sleep, stress management) are recommended for athletes following concussion.[26,118] Evidence has also supported the targeted approach to treatment of concussion symptoms as stratified by concussion clinical profiles (e.g., cognitive/fatigue, affective/anxiety/mood, migraine, vestibular, ocular).[26]

Individuals with symptoms which fall into the cognitive/fatigue clinical profile might experience difficulties with cognitive or thinking skills, as well as low energy and difficulty sleeping.[26] Targeted treatments for these symptoms might include academic/work accommodations, behavioral regulation, and/or stimulant medications.[26] Affective symptoms following concussion (e.g., emotional, anxiety, depression) may benefit from psychotherapeutic intervention[119,120] and possibly even psychopharmacological intervention.[99] A systematic review conducted by Al Sayegh et al.[119] found that cognitive behavioral therapy (CBT) may be effective in the treatment of post-concussion symptoms. This was further supported by a more recent and similar review conducted by Tracey et al.[120] which found that cognitive rehabilitation and neurocognitive training may be the most effective interventions for improving mental health impairments post-concussion. Symptoms presenting in the migraine profile are typically treated with manual therapy and treatment of headache disorder[121] (i.e., massage, ice, contrast therapy).[122] Meanwhile, individuals suffering from vestibular dysfunction following concussion might benefit from vestibular therapies which reduce dizziness and improve gait and balance function after concussion.[123] Individuals presenting with ocular complaints (e.g., blurred or double vision) may benefit from neurovestibular therapy and oculomotor training. In a study conducted by Thiagarajan and Ciuffreda,[124] it was found that oculomotor training had a significant, positive effect on most aspects of versional tracking in individuals with mTBI.

2.3.3 Sport-Related Concussion Recovery, Return to Learn, and Return to Sport

Current research has presented substantial variability in the definition of clinical recovery from concussion and how it is measured. Some studies have functionally defined clinical recovery as return to normal activities, including school and sports, following injury,[125] while others have defined it as return to baseline functional domains including symptoms, cognitive performance, and postural stability.[126] To address these variations in definition of clinical recovery, the 6th International Consensus Statement[27] adopted definitions for specific recovery factors including symptom resolution at rest (i.e., resolution of concussion symptoms at rest), complete symptom resolution (i.e., resolution of concussion symptoms with no return during or after maximal physical and cognitive exertion), RTL, and RTS. With the implementation of these definitions, studies may identify clinical recovery of concussion as it related to symptom resolution, RTL and/or RTS.

As previously noted, concussion clinical recovery is contingent upon the resolution of symptoms and ability of the athlete to return to activities. It is important for clinicians to understand the timeline which symptom resolution might follow when measuring recovery.

Within the first 24 hours of injury, it can be expected that athletes will experience the most adverse effects on cognitive function and balance.[127] Other symptoms, such as cognitive deficits,[128] balance,[129] and symptoms[27] typically improve within the first 2 weeks of injury.[125] To further support this, the 6th international consensus statement[27] reported that the typical timeframe for symptom resolution is 2 weeks for most adults and 4 weeks for most children. Historically, several studies have indicated that typical RTS timeframe is 10 days;[129,130] however, more recent studies have indicated that athletes may RTS before their symptoms have entirely resolved and recovery is much longer than 10 days.[77] Furthermore, it is also important to note that despite the typical recovery trajectories, several athletes may experience prolonged recovery, or experience symptoms well past 4 weeks. McCrea et al.[129] found that prolonged recovery typically lasts between 20 to 90 days, but does not exceed 90 days. However, the majority of adults will recover within 3-12 months after injury otherwise the symptoms may be attributed to other non-injury factors.[131]

The duration of concussion clinical recovery can be attributed to several modifying factors. For example, in a study conducted by Meehan et al.,[132] it was sought to determine which variables predict prolonged recovery (>28 days) from concussion. Age, sex, LOC, symptom burden as measured by the PCSS, amnesia, history of concussion, prior treatment for headaches, history of migraines, and family history of concussions were all evaluated as possible predictors. However, it was found that only symptom burden (i.e., higher PCSS scores) was associated with prolonged recovery. Further, in a review conducted by Nelson et al.,[126] a proposed integrated model of clinical (i.e., resolution of both symptoms and functional impairment) and physiological recovery (i.e., resolution of physiological impairment) after concussion indicated full recovery as full resolution of clinical and physiological symptoms. This study indicated that recovery was mediated by factors including sex/gender (e.g., hormones, musculature, cerebral organization, and neuropsychological deficits), age (e.g., physiologic and situational factors), and neurodevelopmental disorders (e.g., cognitive impairments). Other studies have also supported preinjury characteristics (e.g., age, sex, prior concussion diagnosis), injury severity characteristics (e.g., LOC, retrograde amnesia), and clinical characteristics (e.g., acute headache, dizziness) as modifying factors of recovery.[125] The extensive body of literature concerning the defining features of concussion clinical recovery and the factors which mediate it has contributed to an increasingly comprehensive grasp of clinical evaluation, management, and treatment approached for concussion.

Athletes who are also students may require cognitive rest and academic accommodations while recovering from concussion.[121] A four-step RTL strategy has been introduced to provide academic support for students with concussion, which addresses mediating factors of RTL, including social determinants of health and symptom burden.[27] This can be done by adjusting environmental, physical, curricular, and testing factors. The first step of this strategy involves having the student complete daily activities that do not result in more than mild exacerbation (i.e., no more than a 2-point increase on a 10-point scale of cognitive symptoms, with 10 representing the worst symptoms imaginable) of symptoms related to the current concussion. This step should be implemented within the first 24-48 hours following injury. The proceeding steps (i.e., steps 2-4) involve an incremental increase in cognitive overload. The second step is an introduction to school activities such as homework, reading or other activities outside of the classroom. The third step then involves returning to school part time and includes the gradual introduction of schoolwork with potential half days or rest breaks throughout the day. The final and fourth step is full return to school as the student gradually progresses in school activities until a full day can be tolerated without mild symptom exacerbation. However, just like any concussion outcome, RTL may vary across individuals based on symptoms and tolerance. Additionally, while RTL and RTS strategies can occur simultaneously, students should complete RTL before completing RTS.

While concussion symptoms should be resolved prior to RTS, there is also a stepwise RTS strategy which implements gradual return to exercise.[27,121] The RTS strategy, as presented in the 6th consensus statement,[27] consists of steps which typically take 24 hours each. Additionally, if symptoms occur with activity, the progression should be halted to preceding steps and should not be revisited until the athlete is symptom-free.[121] The first step of the strategy, which should occur within the first 24 hours of injury, involves allowing the athlete to engage in daily activities which do not result in more than a mild exacerbation of symptoms and serves the purpose of gradually returning the athlete to typical activities. The second step encourages introduction of aerobic exercise[117,133] to increase heart rate to light (55% of max heart rate) and moderate (70% of max heart rate) levels. The third step builds on the proceeding step as an introduction to individual sport-specific exercise including additional movements and changes in direction. However, if sport-specific training involves risk of inadvertent head impact, then medical clearance should occur prior to the third step. Steps 4-6 should be monitored by a health care provider (e.g., team doctor, athletic trainer) and start with non-contact training drills which resume usual intensity of exercise, coordination, and increased thinking. Following this, the fifth step involves full contact practice where the athlete will participate in normal training activities. If athletes experience symptoms at steps 4 or 5, they should return to step 3 until full symptom resolution is reached. Once step 5 is achieved at full symptom resolution, the athlete may be cleared for full RTS.

2.4 **Mental Health Impairments Post-Sport-Related Concussion**

Approximately 20% of individuals may experience mental health impairments up to 6 months post-injury,[134] and 14.1% of athletes may experience anxiety or depression symptoms post-injury.[10] Mental health has been defined as an individuals' ability to cope with normal stresses of life and activities of daily living.[135] As previously noted, the anxiety/mood profile of concussion symptoms is most associated with mental health outcomes and implications.[26] Furthermore, concussion may result in negative psychological outcomes that impact mental health, including depression, anxiety, mood disturbances, aggression, and impulsivity.[93,136,137] The following section will review existing literature which has explored these mental health impairments post-concussion.

2.4.1 Anxiety and Depressive Symptoms

As previously mentioned, when discussing the anxiety/mood clinical profile of concussion symptomology, concussion can lead to several mental health impairments, including anxiety and depression symptoms. Furthermore, concussion and anxiety symptoms often overlap as shared symptoms include anxiousness, fatigue, nervousness, and sleep difficulties.[93] Additionally, depression is defined by feelings of sadness and worthlessness, loss of interest or pleasure in activities, fatigue, and decreased concentration. Compared to the previously noted one third of athletes who will experience anxiety post-concussion,[95] approximately 20% of athletes will experience depression post-concussion.[10] It is thought that post-concussion anxiety may be attributed to heightened perceived injury severity, lack of prognostic time-lime for RTP, or loss of athletic identity.[93,138] Additionally, depression post-concussion may be attributed to physiological (e.g., similar affected brain regions including prefrontal, hippocampus, and white matter disruptions for concussion and depression)[139] and psychological (e.g., response to removal from sport participation and activities of daily living)[140] factors. Several studies have explored anxiety and depression outcomes post-concussion in varying levels of sport and play.

Collectively, it has been noted that anxiety is a prevalent symptom post-concussion.[10,16,138,141,142] For example, Yang and colleagues[10] compared baseline psychological symptoms to post-concussion symptoms among concussed collegiate athletes. It was found that depression at baseline was the strongest predictor of post-concussion depression and anxiety, and post-concussion depression and anxiety were significantly associated with each other. Corwin et al.[16] and Grubenhoff et al.[141] also examined psychological factors that were associated with anxiety symptoms post injury. In a sample of adolescent participants (i.e., between the ages 5-18 years), Corwin and colleagues[16] found that depression or anxiety, initial complaints of dizziness, abnormal convergence or abnormal oculomotor examination, and history of prior concussion were all associated with prolonged recovery and emotional morbidities post-concussion. Additionally, Grubenhoff and colleagues[141] found that anxiety symptoms were higher in children whose concussion symptoms persisted for greater than one month when compared to children whose symptoms resolved within a week of injury. Therefore, it can be concluded that pre-injury (e.g., previous mental health diagnosis) and post-injury risk (e.g., prolonged symptoms) factors may contribute to heightened anxiety post-concussion.

Post-concussion anxiety has also been examined more acutely throughout concussion recovery. For example, a recent study conducted by Covassin et al.[142] sought to compare state and trait anxiety symptoms in high school and collegiate athletes throughout concussion recovery. It was determined that concussed high school and collegiate athletes exhibited significantly higher state and trait anxiety throughout recovery when compared to healthy matched controls. However, trait anxiety decreased over time throughout recovery in the concussed group, indicating that concussion may primarily impact state anxiety, or a temporary response to the injury rather than overall changes to personality. Furthermore, another study conducted by Covassin et al.[138] compared postinjury anxiety between orthopedic injuries and concussions in collegiate athletes. While it was found that concussed athletes experienced heightened state and trait anxiety postinjury, there were no significant differences between concussed and orthopedic injury groups. These findings support that post-concussion anxiety may be attributable to the state of being injured.

While it has been previously noted that anxiety and depression post-concussion are heavily associated, several studies have turned their attention to primarily examining depression outcomes postinjury.[10,78,143,144] In a study conducted by Kontos et al.,[78] the relationship between concussion and depression and neurocognitive performance was examined in high school and collegiate athletes, with sex differences being noted. Concussed athletes showed significantly higher levels of depression at 2 days, 7 days, and 14 days post-concussion, and collegiate athletes demonstrated significantly higher levels of depression at 14 days postinjury than high school athletes. Additionally, it was found that higher levels of depression were related to neurocognitive deficits such as reaction time and visual memory. The results of this study support that post-concussion depression could be related to limitations in cognitive abilities, and thus day to day activities. Roiger at colleagues[143] produced similar results when they examined the extent to which NCAA Division I athletes demonstrated post-concussion depressive symptoms. Results of this study yielded that concussed athletes experienced heightened depressive symptoms 1-week postinjury. This may have been attributed to lost time from practice and/or competition.

Other studies have focused on pre-injury risk factors for depressive symptoms post-concussion as well as long term effects of post-concussion depressive symptoms. Yang et al.[10] determined that depression at baseline was the strongest predictor of post-concussion depression, indicating that pre-existing mental health conditions may heavily influence mental health outcomes post-concussion. Furthermore, Kerr et al.[145] explored depression outcomes in individuals who reported a history of multiple concussions. This study included former NCAA collegiate athletes, both male and female, from various sports (e.g., football, women's rowing, fencing, track and field). It was found that individuals who reported a history of three or more concussions were 2.4 times more likely to experience moderate to severe depression later in life than individuals who reported that they had never had a concussion. These results were further supported in a study conducted by Chrisman et al.,[146] who determined that history of concussion was associated with higher prevalence of diagnosed depression in adolescents (i.e., 12-17 years old). Decq et al.,[144] also examined the long-term effects of recurrent concussions in adult retired rugby players compared to retired sportsmen from other sports (e.g., fencing, swimming, skiing, horseback riding) and found that regardless of sport played, history of multiple concussions was significantly associated with higher levels of depression.

2.4.2 Mood Disturbances

As previously stated, the concept of mood possesses several definitions. However, one of the most generalized definitions has been offered by Gardner[147] who offers that mood is feeling or emotional states that are subjectively perceived by individuals and are mild, transient, general, and pervasive. Mood can range from pleasurable to unpleasurable feeling states.[148] While concussion has been noted to result in mood disturbances, as discussed specifically related to the anxiety/mood clinical profile, there are limited studies which have explored this impact. One of the first studies to examine mood disturbances post-concussion was conducted by Mainwaring and colleagues.[94] The purpose of this study was to compare emotional functioning of concussed collegiate athletes to that of uninjured teammates and fellow students. This study utilized a shortened version of the Profile of Mood States (POMS), a widely used measure of mood in physical activity research that includes seven subscales: tension, depression, anger, vigor, fatigue, confusion, and self-esteem.[149] Further, total mood disturbance is calculated by subtracting positive mood score (i.e., vigor) from the sum of negative mood scores.[149,150] It was found that athletes with concussion showed a significant postinjury spike in depression, confusion, and total mood disturbances when compared to health controls. However, elevated mood disturbances seemed to subside within 3 weeks postinjury. These results supported the link between sport injury and emotional distress and were notably the first documentation of serial mood disturbance post-concussion.

Another study, conducted by Hutchinson and colleagues,[150] examined mood disturbances in athletes with concussion compared to athletes with minor musculoskeletal injuries. This study also utilized the POMS to measure emotional responses. The results of this study suggest that athletes with concussion demonstrated significantly elevated fatigue and decreased vigor, while athletes with musculoskeletal injuries demonstrated significant increases in anger. Ultimately, these results suggest that emotional responses and mood disturbances are different for concussed athletes compared to athletes with other injuries. A more recent study conducted by Hunt et al.[151] explored changes in mood in youth with persistent post-concussion symptoms following a six-week active rehabilitation program. The results of this study indicated that mood was significantly better following the six-week active rehabilitation program. These results, however, do support that mood disturbances are present as an outcome of concussion.

2.4.3 Aggression and Impulsivity

While anxiety, depression, and mood disturbances are of the most common mental health and psychological outcomes post-concussion, other outcomes, such as aggression and impulsivity, may also be observed post-concussion. It has been consistently noted that athletes engage in higher levels of risk-taking behaviors,[152,153] which often includes acts of aggression and impulsivity.[154] Chronic traumatic encephalopathy (CTE), a progressive neurodegenerative disorder predominantly observed in athletes participating in high-contact sports with history of repetitive concussion, is also heavily associated with aggressive and impulsive behaviors.[155,156] Aggression has been defined as an act that harms another individual with affective intent (i.e., anger).[157] In terms of TBI, impulsivity has been defined as a multidimensional concept which includes emotional and behavioral changes, dyscontrol, and lack of impulse control.[158] Of note, Kerr et al.[145] is one of the first studies to examine the association between recurrent concussion in athletes and aggression and impulsivity. It was found that collegiate athletes with a history of concussion reported higher levels of aggression and impulsivity when compared to collegiate athletes with no history of concussion. Further, Gallant et al.[159] found that collegiate athletes with decreased physiological arousal post-concussion exhibited higher levels of aggression, while Banks et al.[160] determined that mixed martial art fighters with history of repeated concussion exhibited higher levels of impulsivity. Consistent with the overall heterogenous nature of concussion sequalae, mental health impairments which an individual may experience post-concussion are also heterogenous with no two athletes experiencing the same impairments. Furthermore, mental health impairments, as well as other impairments post-concussion (e.g., physiological and functional), may also lead to overall health and well-being deficits, specifically pertaining the HRQoL.

2.5 **Health Related Quality of Life**

2.5.1 Domains of Health-Related Quality of Life

The World Health Organization Quality of Life Assessment (WHOQoL) group have defined quality of life as an "individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns."[15] This is a generalized concept which incorporates varying factors such as an individual's physical health, psychological state, level of independence, social relationships, and features of their environment.[15] Essentially, quality of life (QoL) encompasses multi-dimensional distinctions in varying conceptualizations and domains. For example, HRQoL is the conceptualization of an individual's quality of life, or perception of overall well-being, as it relates to specific disease-related issues.[14] Further, HRQoL has been organized into six broad domains: physical, psychological, level of independence, social relationships, environment, and spirituality/religion/personal beliefs.[15]

In a review of Spilker's hierarchical QoL model, Arnold et al.[22] described the ranges of highly general to more specific domains and subdomains of HRQoL. For example, the generalized perception of well-being is at the top of the model, and as more specific concepts of HRQoL are considered, the specific domains (i.e., physical health, psychological health, social relationships), become more relevant in the second level. It is also important to note with this that physical, psychological, social, and environmental functioning are among the most used domains of HRQoL.[22] Further, each domain of HRQoL is mediated by specific factors, or subdomains, that can be influenced by an individual's beliefs, perceptions, values, and experiences.[161] These specific aspects of the domains of HRQoL comprise the third level of Spilker's model.

Although little research has been done to confirm the notion, Spilker's model assumes that the subdomains at the lower level of the model determine the HRQoL variables at higher levels.[22] For example, specific variables such as depression and anxiety may influence higher level psychological health. Additionally, functional limitations and impairments may mediate physical health, while abilities to fulfill societal roles will be associated with social functioning. Measuring these variables at the lower level of the model, or subdomains of HRQoL, can help researchers better understand the generalized or specific aspects of HRQoL in an individual.

2.5.2 Depression and Anxiety

Based on Spilker's model of HRQoL, depression and anxiety are specific aspects of the domain of psychological functioning.[22] Psychological functioning plays a significant role in the achievement of good HRQoL; however, factors such as "psychological distress," "loneliness," and "adjustment and coping," contribute to decreased HRQoL.[162] Furthermore, symptoms related to depression and anxiety often affect functioning in varying domains including social functioning, productivity, and physical functioning,[163-165] and may exacerbate symptoms related to chronic illness and injury.[166,167] Therefore, researchers believe that depression and anxiety also impact HRQoL. For example, Gaynes et al.[163] examined the effects of depression on HRQoL using data from a study of health and illness in the United States, and found that in the context of chronic medical conditions (e.g., diabetes, hypertension, arthritis), depression is significantly associated with decrements in HRQoL. Similarly, Verma et al. found that depression was a significant determinant of decreased HRQoL in individuals with diabetes,[168] while Omachi et al. found that patients with chronic obstructive pulmonary disease were more likely to experience depressive symptoms and detriments to HRQoL.[169]

Other studies have explored the impact of anxiety on HRQoL. Creed et al.[170] assessed whether depression and anxiety are associated with reduced HRQoL in medical inpatients, yielding that these were significantly associated. Another study, conducted by Strine et al.,[171] examined the association of self-reported anxiety symptoms with HRQoL and health behaviors among a representative sample of United States citizens. It was found that individuals who reported frequent anxiety symptoms were more likely than those without to report poor general health, frequent physical distress, and frequent mental distress. These individuals were also more likely to smoke, be obese, and to be less physically active, indicating that anxiety symptoms and decreased HRQoL may also promote poor health behaviors. There is also evidence to support that while both depression and anxiety negatively impact HRQoL, depression may be more strongly associated with decreased HRQoL. In a study conducted by Aminisani et al.,[172] the relationship between psychological distress and HRQoL was examined in colorectal cancer patients. Responses on anxiety and depression inventories were significantly negatively correlated with HRQoL; however, the correlation between depression inventories and HRQoL domains was significantly higher. Considering the body of literature indicating that anxiety and depression adversely impact psychological HRQoL, there is reasonable cause to assess both of these factors when evaluating psychological HRQoL.

2.5.3 Health-Related Quality of Life in Athletes versus Non-Athletes

Several health-related factors influence overall quality of life, as well as specific domains (e.g., physical, psychological, social)[22] including chronic injuries or illnesses and sport or physical activity participation. Therefore, it is important to understand overall HRQoL in varying populations. For example, Juenger et al.[173] assessed HRQoL in patients with congestive heart failure to compare to the generalized population as well as individuals with other chronic diseases in Germany. Using the SF-36, which included eight domains of HRQoL (e.g., physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, mental health), it was determined that quality of life significantly decreased with indicators of congestive heart failure. Additionally, when compared to the general population, five of the eight domains of HRQoL were significantly lower in individuals with congestive heart failure. However, there were no significant differences between patients with congestive heart failure and patients with chronic hemodialysis and hepatitis C on any domains of the SF-36. Ultimately, these results suggest that chronic illnesses have a negative impact on HRQoL. Further, these findings were supported by a study conducted by Heyworth et al., who examined the impact of combinations of chronic illnesses on HRQoL. HRQoL as measured by the EQ-5D, a HRQoL measure that assesses mobility, self-care, usual activities, pain/discomfort, and anxiety/depression was compared between patients with six common chronic diseases (i.e., asthma, chronic obstructive pulmonary disease, ischemic heart disease, hypertension, diabetes, and cerebrovascular disease). Findings from this study yielded that there were significant correlations between lower HRQoL and the presence of increased number of chronic conditions. However, it is important to note that as the number of chronic diseases in an individual increased, sample size decreased, thus making it difficult to generalize these results.

On the other hand, other factors such as physical activity may be positively associated with HRQoL. Anokye et al.[174] explored the relationship between HRQoL and physical activity as measured objectively (i.e., via an accelerometer) and subjectively (i.e., via participant reporting). The findings of this study suggest that higher levels of physical activity are associated with better HRQoL (r= 0.026), and objective measures of physical activity are better indicators of increased HRQoL (r=0.072). Furthermore, a recent systematic review also supported the positive relationship between physical activity and HRQoL, specifically in the general adult population. Bize et al.[175] concluded that cross-sectional evidence supports that higher physical activity levels are consistently associated with better HRQoL in various domains. However, the association between HRQoL and physical activity varies across domains as higher physical functioning and vitality are more associated with higher physical activity levels. While it is evident that there is an association between physical activity and HRQoL, there is little evidence to support a causal link between the two, and thus the results of such studies must be interpreted with caution.

Some factors associated with physical activity, however, might negatively impact HRQoL such as injury resulting from sport participation and exposure to high contact sports. For example, Houston et al.[23] compared HRQoL in a sample of 467 collegiate athletes based on injury history, participation status, and injury severity. It was reported that while injury did negatively influence HRQoL in athletes who were presently injured, athletes playing through injury reported higher HRQoL than athletes who were sidelined due to injury. However, there were no significant differences between athletes with injuries of varying severities. Additionally, Simon et al.[176] evaluated HRQoL in former collegiate athletes (ages between 40-65 years old) and found that athletes who had suffered chronic injuries, major injuries, and daily limitations had significantly worse HRQoL when compared to non-athletes. Exposure to contact sports may also impact HRQoL as former collegiate athletes who participated in collision sports (e.g., football, diving) reported worse HRQoL when compared to contact (e.g., basketball, soccer, volleyball, wrestling) and limited contact athletes (e.g., baseball, rowing, tennis).[177] Additionally, athletes who competed in collision sports reported worse bodily pain and physical role functioning (i.e., limitations on normal physical activity).[177]

Existing literature also suggests that there is reason to believe that athletes and non-athletes may report different HRQoL. In a systematic review and meta-analysis conducted by Houston et al.,[178] existing literature was synthesized to determine if HRQoL is different among adolescent and collegiate athletes and non-athletes. Ultimately, athletes reported better HRQoL than nonathletes; however, the overall effect size (0.27) was small and thus these results may not be clinically meaningful. Additionally, Kerr et al.[179] found that in a sample of 3,657 former collegiate athletes, HRQoL, specifically psychological health and physical health domains, were not different than normative scores in the United States, before factoring in injury history and participation in collision or contact sports. Therefore, these inconsistent findings suggest that more research should be done examining the difference in HRQoL between athletes and non-athletes.

2.5.4 Health-Related Quality of Life and Mild Traumatic Brain Injury

Recent evidence suggests that mTBI has a negative impact on HRQoL. However, this has not always been the case, specifically related to pediatric populations. A study conducted by Petersen et al. found that mTBI resulted in no decline in children's health after injury.[180] This has been strongly disputed by more recent studies. For example, a systematic review of HRQoL after pediatric mTBI included studies between 2008-2014 and found that patients with mTBI have diminished HRQoL up to a year or longer post-injury. These deficits were overall observed in psychological health and physical health domains.[181] Furthermore, Zonfrillo and colleagues[182] reported that 11.3% of mTBI pediatric patients reported decrease HRQoL based upon PedsQL scores up to 3 months post-injury, and 12.9% reported decreased HRQoL up to 12 months post-injury.[182,183] This study also examined factors which may influence poor HRQoL post-mTBI, which included less parental education and low household income.

Recent evidence has also supported that mTBI has a negative impact on HRQoL in adult populations. Voormolen et al. assessed the implications of post-concussion syndrome following mTBI on HRQoL. In a sample of 731 mTBI patients, it was found that 40% experienced PCS, which negatively impacted HRQoL. Furthermore, psychological health and physical health were the most negatively affected domains of HRQoL following mTBI.[184] A similar study conducted by Yousefzadeh-Chabok and colleagues[185] included 123 mTBI patients and evaluated mental and physical domains of HRQoL post-mTBI. The results of this study found individuals between 18 to 35 years old, as well as women, had lower HRQoL compared to other participants up to six months post-injury. Additionally, cognitive impairments post-mTBI may also be associated with worse HRQoL, specifically impacting depressive symptoms and emotional functioning.[186] Overall, given the evidence which supports that injured athletes and individuals with mTBI experience decrements in HRQoL, it is important to now examine the literature on HRQoL post-concussion.

2.5.5 Sport-Related Concussion

In previous sections of this review, it was noted that symptoms and impairments resulting from concussion may impact the overall livelihood of an individual. This may impact sport participation, activities of daily living, and overall well-being. Consequently, impairments in these areas may ultimately impact HRQoL and specific domains. In studies conducted by Kuehl et al.[1] and McLeod et al.[3] it was found that prior history of concussion is associated with lower perceived HRQoL. Kuehl and colleagues administered the SF-36, a 36-item instrument aimed at assessing HRQoL for a variety of conditions and populations to a variety of collegiate athletes across varying collegiate divisions. Participants were grouped according to their number of reported past concussions (e.g., 0 concussion, 1-2 concussion, or 3 or more concussion). It was found that participants who had reported a greater number of concussions (i.e., 3 or more) scored significantly lower for factors associated with HRQoL such as bodily pain, vitality, and social functioning when compared to those without a history of concussion, indicating that a history of concussion may result in lower HRQoL. Furthermore, McLeod et al.[3] examined the relationship between concussion history and HRQoL in adolescent athletes, resulting in similar findings with individuals with a history of concussion reporting lower HRQoL as measured by the SF-36 subscales including bodily pain, general health, vitality, and mental health.

While the previously mentioned studies have found that a history of concussion negatively impacts general HRQoL, additional studies have narrowed their investigations to specific domains of HRQoL which are believed to be impacted by prior concussion history.[4-6] For example, McLeod and colleagues[4] sought to develop a tool to specifically measure HRQoL in youth athletes following concussion. In doing so, the researchers identified that the following HRQoL domains were important to adolescents following concussion: social (e.g., school), psychological (e.g., mood and emotions), and physical (e.g., activities of daily living and sport participation). Another study, conducted by Williams et al.[5] evaluated perceived HRQoL in adolescent athletes using the Patient-Reported Outcomes Measurement Information System Pediatric-25 subscale throughout concussion recovery. Similar to previous studies, it was also found that physical (e.g., physical function mobility and pain) and psychological (e.g., depression and anxiety) domains were the most impacted by concussion. This was further supported by Weber et al.[6] who found that physical domains were the most likely to be worsened followed by concussion.

Overall, the previously noted studies indicate that physical, psychological, and social domains of HRQoL are most associated with concussion. Additionally, subdomains such as school (social), mood, emotions, depression, and anxiety (psychological), and activities of daily living, functional mobility, and pain (physical) have been identified as factors which mediate these. Consequently, some studies have examined other subdomains of HRQoL that may be associated with prior concussion history. Tracey et al.[187] recently sought to determine the impact of prior concussion history on emotional and behavioral dyscontrol subdomains (associated with psychological health domain) of HRQoL. Unlike previous studies, it was found that individuals with a history of concussion did not have worse perceived emotional and behavioral dyscontrol when compared to individuals without a history of concussion. While this study did not yield significant findings, it does support the notion that further investigation of the specific factors related to concussion which mediate the domains of HRQoL is necessary.

While it is important to note that overall, concussion may impact HRQoL, it is also important to note at which stages of concussion recovery is HRQoL is most affected. Consequently, several studies have produced findings which indicate that symptom severity post-concussion is correlated with lower HRQoL and HRQoL may fluctuate based on the time point during recovery.[2,5,6] Williams and colleagues et al.[5] found that the severity of problems associated with concussion symptoms and HRQoL (e.g., physical and psychological health), were the lowest at 3 days post-concussion and decreased at 10 days post-concussion and return to play. Further, Weber at al.[6] found that HRQoL, as measured by the physical scale associated with the Short Form-12 version 2 (a global-HRQoL measure aimed at assessing perceived health status),[188] was worse within 24-48 hours following injury when compared to return to play and 6-month assessments. However, there were no differences observed by the mental health scale when compared between the acute phase of concussion and return to play. Therefore, perceived HRQoL, and possibly only specific domains, may be lower in the acute phase following concussion, warranting further examination of the effects of concussion symptomology on HRQoL within this timeframe.

2.6 **Ecological Momentary Assessment and ReCoUPS**

2.6.1 Ecological Momentary Assessment Definition

Ecological Momentary Assessment (EMA) is a set of methodologies which allows subjects to report their experiences and perceptions in real-time, in real-world settings, over time and across contexts, repeatedly.[18] The term EMA was coined in 1994 by Stone and Shiffman;[189] however, the methodologies of EMA have been prevalent in various research and clinical settings for years prior. Consequently, the development of modern EMA methodologies are based heavily on the Experience Sampling Method (ESM), developed by Hektner and colleagues.[190] Essentially, these investigators developed electronic diaries which utilized pagers to "beep" participants at random times to prompt them to complete diary entries which described their activities, moods, and/or thoughts. ESM is a valid and reliable set of methodologies which provides descriptions of the patterns of an individual's daily experiences and studies the dynamics of emotions and other subjective states.[191] Csikszentmihalyi and Larson[191] provided practical and methodological issues of ESM and presented evidence for the short-term and long-term reliability of (1) frequency and patterning of daily activity and social interactions, (2) frequency, intensity, and patterning of psychological states, and (3) frequency and patterning of thoughts including intensity and disturbance. Furthermore, validity evidence from this study supported significant correlations between outcomes measures with ESM methodologies and one-time measures and tests.[191] Ultimately, the development of this technique using technological methods paved the way for EMA protocols which expanded the approach to collecting self-report data.

There are key features of EMA which are also encompassed by similar methodologies such as diaries, self-monitoring, and experience sampling. [192] Therefore, EMA is not one single method or technology. Data collected from EMA methods are "ecological" in the sense that they are collected in real-world environments as participants go about their everyday tasks. EMA assessments are focused on how the subject is feeling at any given time over a longer period, and thus are "momentary." These moments are assessed based on the particular research or clinical feature of interest (e.g., symptoms of injury or illness). Furthermore, EMA studies involve several repeated measures and can cover varying extents of time (e.g., every 30 minutes or daily) with varying intensity of assessment. Most importantly, the goal of EMA is to recognize that many behaviors and experiences can be affected by context and therefore the data collected via EMA should be collected in the subject's natural environment to ensure that they are generalizable to real-world and real-life experiences.

2.6.2 Use in Behavioral Medicine and Healthcare

The overarching goal of behavioral medicine is to understand the relationship between social, psychological, and behavioral factors and health. As previously discussed, EMA has been used as a means of assessing behaviors in real time; thus, researchers such as Smyth and Stone[192] have presented a rationale for the use of EMA techniques in behavioral medicine to address researcher questions. First and foremost, behavioral medicine can be a complex phenomenon which requires complex and time-sensitive research designs. EMA addresses this issue by allowing investigators to collect data that can answer questions that cannot be answered via more conventional approaches. Second, as behavioral medicine research typically investigates processes that are sensitive to transient states, external validity is a common issue in this research. The ecological validity (i.e., observing events happening in the real world outside of the laboratory) and generalizability of findings that EMA provides allows researchers to capture relevant experiential changes in a natural environment. Furthermore, EMA has been used in several studies pertaining to behavioral medicine which further explicate the relevance of the data collection technique.

In their review, Smyth and Stone[192] also provide examples of studies which have produced positive results that support the use of EMA in behavioral medicine research. For one, Stone and colleagues sought to study psychological coping with stressful events by assessing self-reported marital or employment in real time (i.e., using EMA through an electronic diary at the time of the event) and 1-2 days later. When comparing the results between real time measurement of stress and recall of stress, it was found that much of what was reported in real time was forgotten at recall.[193] Another study utilized EMA to capture physiological data rather than self-reported psychological data by collecting saliva samples at random times daily to detect cortisol levels for studies focused on the hypothalamic-pituitary-adrenal axis and found that momentary findings throughout the day were significantly different than one-time assessments.[194]

EMA has also been utilized in the assessment of post-concussion symptoms and recovery outcomes. Specifically, Sufrinko and colleagues[19] sought to evaluate mobile EMA as an approach to measure concussion symptoms, explore the relationships between clinical outcomes and EMA, and determine if EMA was advantageous for predicting recovery outcomes compared to traditional recovery reporting. This study included 20 athletes between the ages of 12 to 19 years old with concussion. Throughout recovery, surveys were administered via mobile EMA at 3-time blocks daily, at the initial clinical visit within 72 hours post-injury, and at the second clinical visit 6-18 days post-injury. Data regarding post-concussive symptoms (i.e., the Post-

Concussion Symptom Scale), neurocognitive testing, and vestibular/ocular screening (i.e., VOMS) were collected. It was found that response rate for EMA was 52.4% for prompts and ultimately EMA symptom score was a better predictor of recovery time than symptoms collected at either clinic visit (p= 0.021). The results of this study suggested that EMA is a strategic tool in capturing fluctuations in symptoms in real-time throughout concussion recovery and can provide clinicians with adequate information to refine symptom management strategies.

2.6.3 ReCoUPS

The prevalence of the use of EMA in behavioral medicine and healthcare, as well as successful use in concussion symptom and recovery research, has prompted the development of an application which implements EMA techniques to assess concussion symptoms and outcomes randomly each day throughout concussion recovery. Recovering Concussion Update on Progression of Symptoms (ReCoUPS) is a mobile application which prompts participants to report real-time symptoms and activities throughout their concussion recovery via text message multiple times per day.[20,21] Furthermore, Wiebe and colleagues[20] demonstrated the use of ReCoUPS to measure recovery in a randomized trial of exercise after concussion. In this study, participants were asked to install the ReCoUPS application on their smartphone, which then prompted the report of Post-Concussion Symptom Inventory (PCSI) symptoms three times per day. The PCSI is a widely used and validated tool which aims to capture concussion symptom severity by prompting individuals to respond to a list of 21 symptoms rated on a scale of 0 to 6 (i.e., not at all to severe).[195] The app was designed to randomly prompt participants to respond to the PCSI at random times in the morning (9 am- 1 pm) and afternoon (4 pm- 7 pm) and provided 60 minutes for response to eliminate the ability for participants to choose to respond when they are feeling better.[20] Ultimately, this study found that ReCoUPS is a useful and acceptable method of capturing daily symptom reports from patients with concussion. Acceptability and feasibility data for ReCoUPS has also been collected, which will be discussed in the proceeding section.

2.6.4 Acceptability and Feasibility of ReCoUPS

In a pilot study, Wiebe and colleagues[21] determined the feasibility of the app ReCoUPS to capture symptom progression and physical and cognitive activities of patients following a concussion. In a sample of 34 youths with concussion, it was found that participants responded to more than 80% of the prompts suggesting that the EMA application provides a feasible approach to capture objective measures of physical and cognitive activity, as well as symptoms in real-time post-concussion. However, a limitation to this study was the small sample size which impeded the ability to produce generalizable findings. This was addressed in a follow-up study by Wiebe and colleagues who examined 118 youths, to determine the reliability of concussion symptom reports assessed by ReCoUPS compared to weekly clinical visits. It was found that there was excellent agreement between the two methods (ICC: 0.97), indicating that adherence to using ReCoUPS was high and that ReCoUPS provided a reliable method to assess symptoms relative to reporting at clinical visits.[20] While the acceptability and feasibility of the use of ReCoUPS to monitor real-time concussion symptoms has been established, there are still several outcomes which occur during the acute phase of concussion that have yet to be explored using EMA, such as HRQoL.

As previously stated, research has found that HRQoL impairments are more prevalent in the acute phase of concussion. It has also been noted that impaired HRQoL is associated with post-concussive physical and psychological symptoms. Therefore, given the existing support for ReCoUPS' capacity to recognize fluctuations in symptom manifestation throughout concussion recovery, there is reason to speculate its potential to detect variations in HRQoL as well.

Identifying fluctuations in HRQoL throughout the recovery phase can inform sports medicine providers of the specific impairments which are occurring acutely and thus enable the development and prescription of timely, effective, and targeted treatment strategies to improve overall health outcomes of concussed individuals.

2.7 **Conclusions**

Concussion is an undeniable health risk in sports. Extensive research to date has identified concussion as a complex injury with a unique and heterogeneous symptom presentation. While several researchers have dedicated time and efforts to classifying the symptomology and identifying the most feasible management and treatment strategies, there are still several gaps in the knowledge pertaining to concussion sequalae. Deficits related to concussion can cause serious setbacks for athletes in their given sport, schoolwork, and life. These deficits ultimately lead to impairments in an athlete's perception of their overall health and well-being, or their HRQoL. Again, several studies have identified impairments in HRQoL, specifically psychological domains, in the acute phase of concussion; however, existing research in this area has failed to address the issue that concussion recovery is not uniform across all athletes. The lack of homogeneity in concussion recovery gives reason to believe that it is possible there may be fluctuations (e.g., "highs" and "lows") of recovery, specifically related to HRQoL. The use of EMA in concussion research has already shown that fluctuations in self-reported symptoms exist throughout concussion recovery in the acute phase. As literature has indicated that concussion symptoms may lead to impairments in HRQoL, it is plausible to speculate that EMA may be a valuable tool in the identification of fluctuations in psychological HRQoL throughout concussion recovery.

CHAPTER 3 : METHODOLOGY

3.1 **Experimental Design**

For Specific Aim 1 (to investigate the psychometric properties of a momentary psychological HRQoL inventory and post-concussion symptom checklist administered using the mobile EMA platform, ReCoUPS, to healthy participants), a test-retest reliability design was used. The reliability of momentary psychological HRQoL measures administered by daily ReCoUPS survey text messages was assessed. Additionally, the consistency and agreement between momentary assessments of psychological HRQoL captured via ReCoUPS and recalled psychological HRQoL (i.e., within the past 7 days) captured in-person was assessed. Finally, associations between momentary assessment of psychological HRQoL and post-concussion symptom clusters, specifically the affective cluster, measured via ReCoUPS were determined. For Specific Aim 2 (to assess the acceptability and feasibility of utilizing a mobile EMA platform, ReCoUPS, to monitor fluctuations in traditional post-concussion affective symptoms and psychological HRQoL throughout athlete concussion recovery) and Specific Aim 3 (to determine changes in affective and psychological HRQoL throughout concussion recovery using the EMA platform, ReCoUPS), a longitudinal repeated measures study design was used. Specific Aim 2 focused solely on outcomes measured in concussed college-aged athletes throughout recovery, while Specific Aim 3 also included comparing these outcomes between concussed college-aged athletes and healthy matched controls. This study was approved by the Michigan State University Institutional Review Board (IRB; STUDY00008359).

3.2 **Operational Definitions**

3.2.1 Concussion

A concussion is defined as a direct or indirect blow to the head, face, neck, or body that results in an altered mental status and can present with immediate or delayed heterogenous clinical signs and symptoms.[27] All athletes with a suspected concussion were evaluated by licensed healthcare providers (e.g., physicians, physician assistants, nurse practitioners) and involved the following criteria: 1) the presence of at least one on-field sign (e.g., instability, loss of consciousness, confusion, amnesia), 2) symptoms (e.g., headache, dizziness, blurred vision, fatigue, irritability), and/or 3) any impairment on sideline assessments (e.g., SCAT6 cognitive screening, VOMS).

3.2.2 Affective Concussion Symptoms

As previously mentioned, concussion symptoms typically follow patterns of physical (e.g., headache, nausea, sensitivity to light and sound), cognitive (e.g., difficulty concentrating, balance, disorientation), affective (e.g., hyperexcitability, irritability) and sleep.[12] Affective symptoms are conditions or disorders which affect a person's emotional and psychological well-being.[10] The SCAT6 symptom checklist includes symptoms which an individual might experience post-concussion symptom patterns.[110] For healthy individuals, these patterns included affective, cognitive-fatigue, and migraine symptoms while for individuals with a concussion, these patterns included affective, cognitive-ocular, and migraine symptoms. A recent investigation of the factor structure of the 22-item SCAT-5 symptom checklist,[11] the same checklist used on the SCAT6, revealed that for healthy, uninjured athletes, symptoms which commonly co-occurred or were reported similarly included affective items: more emotional, irritability, sadness, nervous or anxious, and trouble falling asleep. Additionally, for acutely concussed collegiate athletes, symptoms which commonly co-occurred or were reported similarly included affective items: more emotional, irritability, sadness, and nervous or anxious. Therefore, for Specific Aim 1 (i.e., healthy, uninjured participants), affective symptoms will include those indicated for healthy, uninjured athletes (i.e., more emotional, irritability, sadness, nervous or anxious, and trouble falling asleep). Meanwhile, for Specific Aims 2 and 3, (i.e., acutely concussed collegiate athletes), affective symptoms will include those indicated for concussed athletes (i.e., more emotional, irritability, sadness, and nervous or anxious).

3.2.3 Additional SCAT6 Symptom Clusters

While the analysis for this dissertation primarily focused on affective concussion symptoms, it is important to note that concussion symptom profiles and clusters are not mutually exclusive.[11,12,26] For example, the severity of a migraine symptom such as headache may be associated with an affective symptom such as irritability. Therefore, other symptom patterns were included in the analysis. For healthy individuals, cognitive-fatigue symptoms included feeling slowed down, feeling like “in a fog”, “don’t feel right,” fatigue or low energy, confusion, and drowsiness, and migraine symptoms included headaches, pressure in head, neck pain, sensitivity to light, and sensitivity to noise. For individuals with a concussion, cognitive-ocular symptoms included blurred vision, balance problems, difficulty remembering, and confusion, while migraine symptoms included headache, pressure in head, don’t feel right, sensitivity to light, and sensitivity to noise.

3.2.4 Psychological Health-Related Quality of Life

Psychological HRQoL is an individual’s perception of their psychological well-being and mental health within the context of injury, disease, or illness.[15] Negative psychological responses to health including "psychological distress," "loneliness," and "adjustment and coping," contribute to decreased HRQoL.[162] Furthermore, these symptoms intersect with the symptom presentation of depression (e.g., helpless, hopeless) and anxiety (e.g., uneasy, overwhelmed).[22] Depressive and anxiety symptoms often affect functioning in varying domains of HRQoL including psychological health, social functioning, productivity, and physical functioning.[163-165] Therefore, for the purpose of this study, psychological HRQoL will refer to depressive and anxiety symptoms related to health.

3.2.5 Full Medical Clearance

3.2.5.1 Athletes Managed by a Certified Athletic Trainer or Health Care Provider

Full Medical Clearance (FMC) was when concussed athletes were cleared for full unrestricted activity by their licensed healthcare provider (e.g., physician, physician assistant, nurse practitioner). Criteria for achieving FMC were: (1) participants with concussion reported symptom resolution or return to baseline symptom scores, (2) had a normal vestibular assessment, and (3) completed all six stages of the Concussion in Sport return to play step-wise protocol.[27,196] Clinicians can expect athletes to complete the stepwise protocol in a minimum of 1 week as each step takes 24 hours; however, if symptoms were exacerbated at any stage, the participant remained in that stage until reaching symptom resolution. Athletes could return to full unrestricted activity in their sport with no limitations following FMC, which was 72 hours after full symptom resolution.

3.2.5.2 Athletes Without Access to a Certified Athletic Trainer or Healthcare Provider (i.e., Club and Recreational Athletes)

Several athletes included in this study did not have access to a certified athletic trainer or regular care from a health care provider who could oversee a stepwise RTP protocol. Therefore, it is possible that these athletes were not granted official FMC from a health care provider. In these situations, FMC was defined as 72 hours after the athlete reported complete symptom resolution and remained free of symptoms. This was meant to reflect the sixth step of the Return to Sport strategy outlined in the most recent consensus statement on concussion in sport[27] where return to sport occurs following non-contact training drills and full contact practice without symptom exacerbation (i.e., 72 hours).

3.3 **Population and Sampling**

All participants, including healthy college-aged individuals (Specific Aim 1), concussed college-aged athletes (Specific Aim 2, Specific Aim 3), and healthy college-aged athlete matched controls (Specific Aim 3) were recruited from Division I, Division III, and National Association of Intercollegiate Athletics universities in Michigan. Healthy college-aged individuals were recruited through social media, print publications, and referrals from graduate teaching assistants. Healthy college-aged individuals were also asked to refer a friend interested in the study and who fit the inclusion criteria. Concussed college-aged athletes and healthy college-aged athletes were referred to the research team by an athletic trainer or a licensed healthcare provider at the university student health center. Prospective participants contacted the researchers via email or phone call and were informed of the purpose, procedures, risks, and benefits of participating in the study. This initial communication also determined if inclusion criteria were met. If inclusion criteria were met and the prospective participant agreed to participate, they met with researchers in either a designated school-affiliated location (e.g., athletic training room) or in the research laboratory to complete informed consent and for the initial visit. For participants who were 17 years of age, but were college students, study information was presented to a parent or legal guardian and a parental consent form with participant assent was completed.

3.3.1 Inclusion Criteria

3.3.1.1 Specific Aim 1

The inclusion criteria for healthy college-aged individuals were: (1) age 17-30 years old, and (2) current or recent (i.e., within the past year) participation in a club, recreational, junior varsity, or varsity collegiate level sport.

3.3.1.2 Specific Aim 2

The inclusion criteria for concussed college-aged athletes were: (1) age 17-30 years old, (2) physician or health care provider (e.g. physician assistant, nurse practitioner) diagnosed concussion based on criteria from the sixth consensus statement on concussion in sport within 72 hours of enrollment,[27] and (3) currently participating in a club, recreational, junior varsity, or varsity collegiate level sport.

3.3.1.3 Specific Aim 3

The inclusion criteria for healthy college-aged athlete matched controls were: (1) age 17-30 years old, (2) current or recent (i.e., within the past year) participation in a club, recreational, junior varsity, or varsity collegiate level sport, and (3) age, biological sex, and sport participation was matched to those of a concussed participant.

3.3.2 Exclusion Criteria

3.3.2.1 Specific Aim 1 and Specific Aim 3

The exclusion criteria for healthy participants in Specific Aim 1 and Specific Aim 3 were the same. Exclusion criteria were: (1) history of diagnosed or suspected concussion within the past 6 months, (2) no English proficiency, and (3) limited or no access to a cellular device.

3.3.2.2 Specific Aim 2

The exclusion criteria for concussed collegiate athletes were: (1) moderate to severe traumatic brain injury with a Glasgow Coma Scale <13 or abnormal or positive diagnostic imaging (i.e., CT scan or MRI), (2) injury involving loss of consciousness for more than 30 minutes or post-traumatic amnesia for greater than 24 hours, (3) history of diagnosed or suspected concussion within the past 6 months, (4) no English proficiency, and (5) limited or no access to a cellular device.

3.3.3 Sample Size Estimation

3.3.3.1 Specific Aim 1

The sample size estimation for Specific Aim 1 was based upon both an intraclass correlation coefficient (ICC) two-way mixed effects model[20] as well as a Spearman's rho correlation coefficient.[20,197] The estimation to achieve high reliability between recalled psychological HRQoL and momentary HRQoL (as measure by ReCoUPS) was based on the ICC two-way mixed effects model and a medium to large effect size (η^2= 0.14),[198] an acceptable power of (1-β) 0.80 and a-priori alpha level of 0.05, estimated that 63 participants are required to identify excellent agreement between momentary psychological HRQoL, recalled psychological HRQoL. Furthermore, the estimation for construct and convergent validity for a momentary psychological HRQoL assessment was based on the Spearman's rho correlation coefficients with a small, positive coefficient of determination ($\rho H_1 > 0.1$), an acceptable power of (1-β) 0.80 and a-priori alpha level of 0.05, yielding that 60 participants are required to identify positive associations. Previous studies with ReCoUPS reported most participants responded to more than 80% of prompts with remuneration;[20,21] thus, to account for anticipated dropout and missing 20% of daily prompts, and our ability to remunerate participants, it was anticipated that a minimum of

72 participants was required. To ensure that power was met, and to account for any additional missing data, 98 participants were enrolled in this study.

3.3.3.2 Specific Aim 2 and Specific Aim 3

For Specific Aim 2, to estimate the sample size needed to determine significant feasibility of measure post-concussion affective symptoms and psychological HRQoL in real time using ReCoUPS was based on a one-tailed bivariate normal model correlation. A large effect size of r=0.5 was used,[198] α was set at 0.05, and an acceptable power of (1-β)= 0.80 was set to estimate a sample size of 23 participants to yield significant results. However, taking into consideration the within and between group factors for Specific Aim 3, a fixed model, R^2 increase linear regression model was selected, a large effect size f^2 (0.35) was used,[199,200] α was set at 0.05, an acceptable power of (1-β)= 0.80 was set, 2 groups (i.e., concussed collegiate athletes and healthy matched controls) were indicated to estimate a sample size of 31 participants per group. Therefore, to also account anticipated dropout and missing 20% of daily prompts,[19,20] 74 participants (i.e., 37 concussed collegiate athletes and 37 healthy matched controls) were needed to ensure 62 completers. However, we continued to enroll participants past the sample size to ensure that power was met and halted enrollment for data analysis at the end of the Fall 2024 academic semester. Hence, we enrolled 39 participants with a concussion; however, 3 withdrew. Furthermore, data collection was halted at 35 healthy matched controls at the end of the Fall 2024 semester; however, 1 was withdrawn by the study team due to data being impacted by technical issues with the ReCoUPS platform (**Appendix B**).

3.4 **Instrumentation**

3.4.1 Demographics Form

The demographics form was created by the research study team. First, participants were asked personal information including age, biological sex, gender, race, ethnicity, year in school, and their level and current sport participation. Participants were also asked questions about personal and family medical history including any medications which they take, any previous concussions, and personal/family history of headache or migraine disorder, learning disorder/dyslexia, ADD/ADHD, depression/anxiety, and motion sickness. Finally, if the participant had a concussion, they were asked questions related to their injury (e.g., date of concussion, time of injury, mechanism of injury, if loss of consciousness occurred following injury, if they remember the injury, and if they continued to play following the concussion or were removed immediately).

3.4.2 Sport Concussion Assessment Tool-6 (SCAT6) Symptom Checklist

The Sport Concussion Assessment Tool6 (SCAT6) Symptom Checklist is a standard, validated symptom report which determines total number of symptoms and symptom severity post-concussion.[110] This checklist is derived from the Post-Concussion Scale[201] and includes 22 symptoms which often co-occur or cluster together (e.g., physical, affective, sleep, and cognitive).[12] Symptoms are rated on 6-point Likert scale (i.e., None to Severe); therefore, scores greater than 0 indicate the presence of the outcome with severity increasing with score. The SCAT6 symptom checklist was used to determine symptoms present throughout concussion recovery as well as those related to impaired HRQoL, specifically symptoms which cluster as affective (healthy: more emotional, sadness, irritability, nervous or anxious, trouble falling asleep; concussion: more emotional, sadness, irritability, nervous or anxious).[11]

3.4.3 The Patient Reported Outcomes Measurement Inventory System Item Bank v1.0- Emotional Distress- Anxiety Short Form 4a (PROMIS-SF Anxiety)

The PROMIS-SF Anxiety is a standard HRQoL inventory specific to the psychological subdomain of anxiety related to emotional distress,[202] measuring autonomic arousal and experience of threat.[203] This inventory includes 4 questions which report on fear, focus, overwhelming feelings, and uneasiness related to anxiety on a 5-point Likert scale (i.e., Never, Rarely, Sometimes, Often, Always), within the past 7 days with scores greater than 4 indicating the presence of the outcome with severity increasing with score. While this inventory demonstrated support for construct validity as a domain-specific assessment of health in the general population ($r > 0.95$),[204] initial validity evidence for the general population, nor concussion, collegiate, or high school athlete populations has been published. This is also true for the PROMIS-SF Depression ($r > 0.95$),[204] which is mentioned below. For the purposes of this dissertation, responses measured via momentary assessment were changed to a 7-point Likert scale to match the response choices to the SCAT6 symptoms and eliminate participant confusion. The language in the questions was modified to reflect that the participant is currently in the present moment experiencing outcomes rather than in the past 7 days (i.e., "I felt fearful…" will be presented as "I feel fearful…"). Thus, for momentary assessments, scores greater than 0 indicated the presence of the outcome with severity increasing with score. These changes enabled the accurate capture of momentary outcomes. The original version of this inventory was completed at study closure in REDCap for the inter-item comparison for the adjusted Likert scale and momentary/recalled HRQoL.

3.4.4 The Patient Reported Outcomes Measurement Inventory System Item Bank v1.0- Emotional Distress- Depression Short Form 4a (PROMIS-SF Depression)

The PROMIS-SF Depression is another short form included in the PROMIS Emotional Distress inventories meant to measure low levels of positive affect.[203] This inventory includes 4 questions regarding feelings of worthlessness, helplessness, depression, and hopelessness related to overall depression on the same 5-point Likert scale as the Anxiety form. Using the same procedures as mentioned above for the PROMIS-SF Anxiety, response choices were adjusted accordingly to lessen respondent burden and determine the reliability and agreement between momentary and recalled HRQoL.

3.4.5 Recovering Concussion Update on Progression of Symptoms (ReCoUPS)

ReCoUPS is a novel, mobile ecological momentary assessment platform and is a is a reliable and feasible method of collecting concussion symptoms for clinicians to remotely monitor patients in real time (intraclass correlation coefficient= 0.97).[20,21] When enrolling in the online database, participants provided their cell phone number (stored in the database with a unique identifier) and a 6-hour time frame during which they would like to receive the daily survey prompts (i.e., between 9:00 am-3:00 pm, between 12:00 pm-6:00 pm, or between 3:00 pm-9:00 pm). Participants were then be sent an invitation via text message to receive surveys from the MSU Sport Concussion Research Laboratory (**Figure 1**). Once the invitation was accepted, the participant began to receive survey questions (i.e., the SCAT6 Symptom Checklist, momentary PROMIS-SF Anxiety, and momentary PROMIS-SF Depression) at random times within the selected time frame once daily throughout their recovery (**Figure 2**). This allowed participants to repeatedly report on their symptoms and HRQoL in real-time, in their natural environment and across varying contexts (e.g., in class, at home, in social settings).

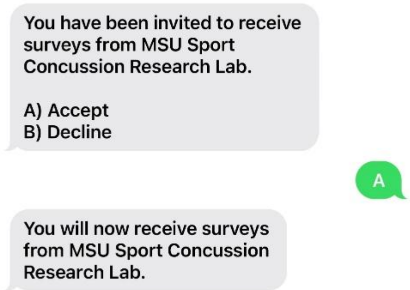

Figure 1. Invitation and acceptance to participate enroll in ReCoUPS surveys.

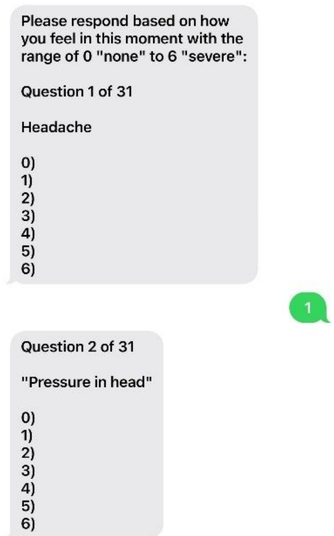

Figure 2. The first survey question sent via ReCoUPS text messages and response, prompting the second survey question to be received.

3.4.6 ReCoUPS User Feedback Survey

All participants, regardless of specific aim, completed a user feedback survey related to the ReCoUPS platform following the termination of daily survey text messages. This survey was a modified version of the System Usability Scale (SUS), the most widely used standardized questionnaire for the assessment of perceived usability.[205,206] The SUS consists of 10 questions focused on the usability and learnability of task-based system tasks, with each statement rated on a scale of 1- “Strongly Disagree” through 5- “Strongly Agree.” The SUS consistently demonstrates an acceptable level of reliability (α= 0.83-0.97), and estimates of concurrent validity have had significant correlations ranging from 0.22 to 0.96.[206] For the purpose of this study, several of the questions from the SUS were modified to more adequately measure user ratings of the ReCoUPS platform specifically. More specifically, the survey consisted of 7 questions on the 1-5 Likert scale which asked participants about their perceived usability of the daily survey text messages. Items consisted of positive questions (i.e., responses towards strongly agree favored the text messages) and inverted questions (i.e., responses towards strongly agree did not favor the text messages). Participants then answered a question regarding their perceived response rate with a follow-up open-ended question asking why they responded when they did. Finally, participants were asked an optional open-ended question on ways to improve the survey text messages and platform.

3.4.7 Recovery Information Form

The Recovery Information Form was created by the study team and all participants diagnosed with a concussion completed this form at their study closure visit. Participants were first asked questions related to academics, including if they missed any school days and how many days were missed, if they received any kind of academic accommodations as a result of their concussion, and if they felt that their coaches and teachers were understanding of their concussion. Then, they were asked questions specifically related to their symptom resolution and FMC to return to sport (if applicable). This included questions regarding the date when their symptoms were completely resolved, the date they first returned to limited or full practice (if applicable), and the date when they were cleared for full, unrestricted sport participation (if applicable). Participants were also asked if they engaged in a RTP protocol managed by a relevant health care provider (e.g., athletic trainer). If so, they were asked to report their self-rated adherence to the protocol. If not, they were asked if they engaged in any informal exercise throughout their recovery, what that exercise was, and if it exacerbated any symptoms. All questions on this form included a “not applicable” option or were able to be skipped if the participant could not provide a response.

3.5 **Data Collection and Management**

3.5.1 Specific Aim 1

Healthy college-aged individuals were recruited from kinesiology and exercise classes. Following recruitment, interested participants met with the researcher in-person to review study procedures and complete informed consent. For participants under 18 years old, legal parents or guardians complete informed parental consent and the participant signed child assent. Following the completion of informed consent, participants were administered the demographics page. All data for all specific aims that was not collected in the ReCoUPS platform (i.e., demographics page, medical history, injury information, recovery information, recalled PROMIS-SF forms) was collected in REDCap (Research Electronic Data Capture), a secure, web-based software platform designed to support data capture for research studies.[207,208] Next, they were enrolled in the ReCoUPS online database to receive survey questions. Participants provided their cellphone number and a 6-hour timeframe when they were most likely to respond to text messages (i.e., 9:00 am-3:00 pm; 12:00 pm- 6:00 pm; 3:00 pm-9:00 pm). They then responded to a text message invitation to receive survey messages. For the next 7 days, participants responded to a total of 30 survey questions via text messages administered by ReCoUPS, including the 22-item symptom checklist from the SCAT6 and 8 total momentary psychological HRQoL questions from PROMIS-SF Anxiety and PROMIS-SF Depression. They were prompted to respond to questions once daily at random times within the 6-hour timeframe selected at study enrollment. We anticipated that it would take participants approximately 3-5 minutes to complete all 30 questions. After completing survey text messages for 7 days, participants met with the research team in-person (i.e., 8 days after study enrollment). Participants were instructed to respond to all survey prompts when they could, including if they received them on the day of their study closure prior to the visit. The research personnel terminated the ReCoUPS survey text messages in the online platform. Then, a recalled (i.e., if they have experienced symptoms within the past 7 days) psychological HRQoL (i.e., PROMIS-SF Anxiety and PROMIS-SF Depression) inventory and the ReCoUPS User Feedback survey were completed at this time in REDCap. At the study closure visit, participants were remunerated $15 for completing the study procedures (if enrolled in Fall 2023) or offered extra credit in a participating Kinesiology course (if enrolled in Fall 2024). Due to limited funding sources, we were unable to remunerate healthy participants in Fall 2024. **Figure 3** demonstrates the timeline for participants responding to ReCoUPS text messages in *Specific Aim 1*.

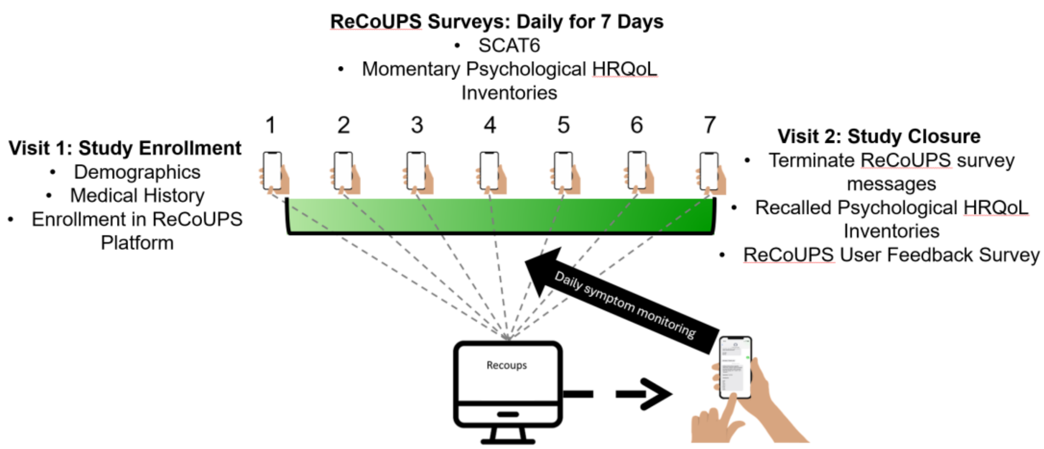

Figure 3. The timeline and method of monitoring post-concussion symptoms and PHRQoL in healthy participants. After completing enrollment procedures, participants responded to ReCoUPS survey text messages, which were displayed on the online platform to the study team members, for 7 days. Surveys were terminated at the study closure visit.

3.5.2 Specific Aim 2 and Specific Aim 3

Concussed college-aged athletes (i.e., recreational, club, intramural, varsity) and healthy matched controls (i.e., age, biological sex, sport) were recruited from NCAA Division I, NCAA Division III, and NAIA universities in the mid-Michigan area. Concussed participants were enrolled no more than 3 days (i.e., 72 hours) post-injury to capture acute symptoms.[27] Following recruitment, interested participants met with the researcher in-person to review study procedures and complete informed consent. After completion of informed consent or parental consent/child assent, participants were administered the demographics page. Next, they were enrolled in the ReCoUPS online database to receive survey questions. Participants provided their cellphone number and a 6-hour timeframe when they were most likely to respond to text messages (i.e., 9:00 am-3:00 pm; 12:00 pm- 6:00 pm; 3:00 pm-9:00 pm). They then responded to a text message invitation to receive survey messages. Participants then responded to the same survey questions administered by ReCoUPS as previously mentioned in *Specific Aim 1*.

Concussed participants continued to respond to survey text messages throughout the duration of their concussion recovery until they were granted FMC by a healthcare provider. Participants then returned to a second in-person visit within 48 hours after FMC or full symptom resolution for 72 hours[27] to accommodate college student schedules. At this visit, daily surveys were inactivated in the ReCoUPS database, and one last round of survey questions in REDCap and study closure was completed. Participants were instructed to respond to all survey prompts when they could, including if they received them on the day of their study closure prior to the visit. Controls followed the same procedures and completed ReCoUPS survey text messages for the same duration as their concussed counterparts. At the study closure visit, all participants (i.e., participants with concussion and healthy matched controls) completed the recalled psychological

HRQoL inventories, and the ReCoUPS User Feedback survey. Participants with a concussion also completed the Recovery Information form at the study closure visit. **Figure 4** demonstrates the method and timeline for how symptoms and PHRQoL were remotely monitored via ReCoUPS text messaging and the online platform throughout concussion recovery in *Specific Aims 2 and 3.*

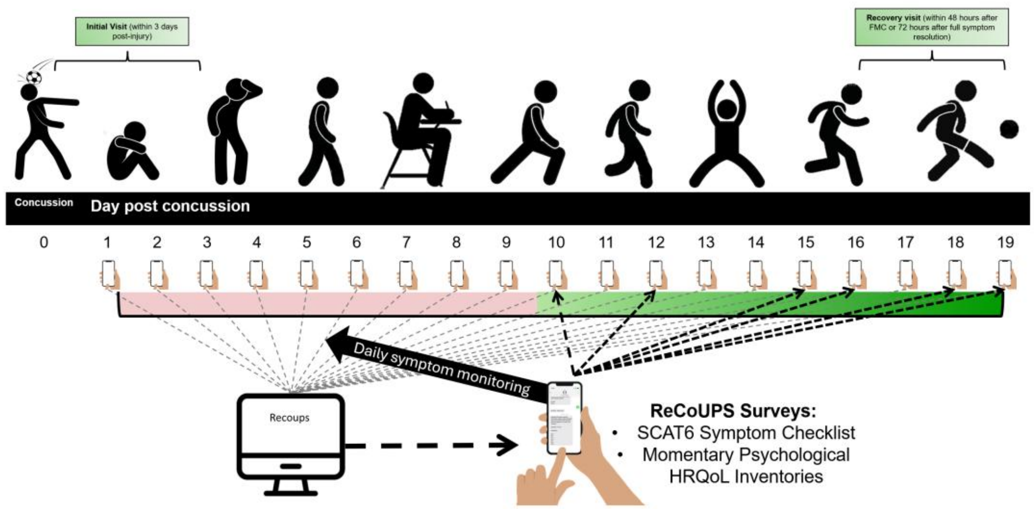

Figure 4. The timeline and method of monitoring post-concussion symptoms and PHRQoL throughout concussion recovery. Participants were enrolled in the study within 3 days after sustaining their injury, completed ReCoUPS survey text messages every day throughout their recovery, which are displayed in the ReCoUPS online platform for the study team. Surveys were terminated at the recovery visit within 48 hours after receiving FMC from a health care provider or 72 hours after full symptom resolution.

In addition to enrolling in the ReCoUPS study, concussed and healthy participants were also enrolled in the Sport Concussion Research Laboratory's on-going prospective cohort study. Therefore, both concussed athletes and healthy controls were remunerated $75 at the initial visit and $75 at the second post-FMC visit, equaling a total of $150 for complying with all study procedures (i.e., demographics and medical history, injury information, enrollment in ReCoUPS, SCAT6, VOMS, and four patient reported outcome measures of psychosocial concussion outcomes selected by other lab members (but unrelated to the present study), recovery information).

3.6 **Data Analysis**

Demographic statistics were reported as frequencies (%) for categorical variables (e.g., sex, personal medical history, sport participation, etc.) and means (standard deviations) for continuous variables (e.g., age). Independent samples t-tests were conducted to determine group differences (i.e., concussed vs. control) for continuous variables and chi-square tests were conducted to determine significant associations between groups and categorical variables (i.e., sex, race, ethnicity, year in school, current sport, sport type, level of play, and medical history). Fisher's exact test determined differences in categorical variables where row values were less than 5. All statistics were conducted using Stata Release 18.5 (Stata Statistical Software, College Station, TX).

3.6.1 Agreement Coding

As previously mentioned, the Likert scale for the recalled PROMIS SF-Anxiety and PROMIS SF-Depression was transformed from a 5-point Likert scale (i.e., 1= Never, 2= Rarely, 3=Sometimes, 4= Often, 5= Always) to a 7-point Likert scale (i.e., 0= none, 6=severe) for momentary assessment. The minimum possible raw score for both the PROMIS-SF Anxiety and PROMIS-SF Depression is 4, with any greater score indicating the presence of the outcome being measured (i.e., anxiety and depression symptoms).[209] Further, on the 7-point Likert scale, any score greater than 0 indicates the presence of the outcome.[110] Therefore, when assessing the agreement between the recalled and momentary assessments of the PROMIS-SF Anxiety and Depression, data for the recalled PROMIS assessments was recoded so any score of 4 was transformed to 0 and any score greater than 4 was transformed to 1. Similarly, data for the momentary PROMIS assessments was recoded so any score of 0 remained 0 and any score greater than 0 was transformed to 1.

3.6.2 Specific Aim 1

Daily response rates for participants were reported for all participants in specific aims 1, 2, and 3 as frequencies to determine the percentage of participant responses to daily surveys. To calculate response rates, the number of surveys the participant completed was divided by the number of days that the surveys that were sent to their phone ([Surveys Completed / Surveys Sent]*100]) throughout their participation in the study. This is consistent with what has been done in previous feasibility studies using ReCoUPS.[20,21] ICC 2-way mixed-effects models determined repeatability, consistency, and agreement of variability between mean momentary assessment of HRQoL (i.e., PROMIS Anx and PROMIS Depress) and mean recalled psychological HRQoL.[210-212] ICCs were reported with 95% confidence intervals (CI) and interpreted as poor (<0.5), moderate (0.5-0.75), good (0.75-0.9), or excellent (>0.9).[213] Additionally, Spearman's rho (r_s) correlation coefficients and a heat plot correlation matrix determined if there was a monotonic relationship between psychological HRQoL and affective post-concussion symptoms. Correlation coefficient r_s were interpreted as weak (0.1-0.3), moderate (0.4-0.6), or strong (0.7-0.9).[214] Spearman correlations also determined evidence of construct validity of items and convergent validity between items,[202] as using a factor analytic approach was not recommended due to our small sample sizes. Cohen's kappa was used to assess the level of agreement between recalled and momentary PROMIS assessments following agreement coding. Kappa value κ was interpreted as poor (<0.00), slight (0.00-0.20), fair (0.21-0.40), moderate (0.41-0.60), substantial (0.61-0.80), and almost perfect (0.81-1.00).[215] Cronbach's alpha (α) determined the internal consistency and reliability of momentary assessments of psychological HRQoL and were interpreted as acceptable (>0.70, with closer to 1 as better) or unacceptable (<0.70).[216] Finally, frequencies of quantitative responses and descriptive statistics for emerging themes of qualitative responses were reported for the ReCoUPS User Feedback Survey. Cronbach's alpha (α) also determined the internal consistency and reliability of the ReCoUPS User Feedback complete survey, positive items, and inverted items for all participants included in specific aims 1, 2, and 3.

3.6.3 Specific Aim 2

Daily response rates were calculated for all participants. Multiple spearman rank correlation coefficients and a heat plot correlation matrix assessed the relationship between momentary symptoms and momentary psychological HRQoL collected daily via ReCoUPS to determine the feasibility of administering these assessments at the same time. Chronbach's alpha (α) determined the internal consistency and reliability of momentary assessments of psychological HRQoL and were interpreted as stated in specific aim 1. ICCs with 95% CIs and Cohen's kappa were again used to assess the level of agreement between momentary and recalled assessments of psychological HRQoL.

Descriptive statistics (i.e., range of scores, mean, standard deviation) demonstrated within-person variability of momentary symptoms and psychological HRQoL collected daily throughout concussion recovery via ReCoUPS. Heat plots depicted the change in severity of all outcome measures (i.e., PROMIS Anxiety, PROMIS Depression, affective symptoms, cognitive-ocular symptoms, migraine symptoms, and total symptoms) every day since sustaining their concussion. Finally, responses to the ReCoUPS User Feedback survey from participants with a concussion were analyzed and reported the same as in specific aim 1.

3.6.4 Specific Aim 3

Daily response rates were calculated for all participants. Because EMA data regularly results in a different number of observations between subjects, multilevel modeling (MLM),[18,198,217] were used to analyze the hierarchy of the data collected from this study. In the literature, multilevel modeling is also referred to as hierarchical linear modeling,[218] hierarchical model,[219] mixed-effects model, or random coefficient model,[220] which all generally refer to any data that has a hierarchical structure and correlations among units within hierarchy levels. At the within-subject level, or within-athlete level (i.e., daily measurements provided by each athlete), the repeated measurements of HRQoL and symptoms within each athlete throughout recovery were observed. Initially, the null model (i.e., Model 1) was fit:

$$Outcome_{ij}=\gamma_{00}+u_{0j}+r_{ij}$$

with the outcome representing psychological HRQoL or symptom cluster scores and the intercept and error term representing the mean score of each outcome. Next, concussion status (i.e., concussion or healthy matched control) was added to the model (i.e., Model 2) to determine the relationship between types of athletes and psychological HRQoL and symptom clusters. Therefore, the following model was fit:

$$Outcome_{ij}=\gamma_{00}+\gamma_{01}ConcussionStatus_{ij}+u_{0j}+r_{ij},$$

where group and individual level differences were observed based on athletes having a concussion or being a healthy matched control. Finally, athlete-level predictor variables which may have influenced outcome measures for each group were added to the model (i.e., Model 3) and the following equation was used:

$$Outcome_{ij}=\gamma_{00}+\gamma_{01}ConcussionStatus_{ij}+\gamma_{02}[\text{Athlete Predictors}]+u_{0j}+r_{ij}$$

where the intercept and slope for each group and *γ* represented the fixed effect coefficients of athlete-level predictor variables. Predictor variables were selected based on the significance of results from univariate robust standard error linear regressions with known variables that effect concussion recovery outcomes and/or EMA responses (e.g., sex, pre-existing mental health conditions, sport participation, exercise or activity throughout recovery).[98,198,221,222]

More specifically, to account for the nested structure of the data and repeated measures nested within individuals, multilevel mixed-effects linear regression analyses with fixed and random effects were used. Random intercept models were specified to evaluate the between and within-person variance components. For the null model (i.e., Model 1), the random-effect variances were estimated separately for each outcome measure. For the addition of concussion status and athlete-level predictors, an independent covariance structure for the random effects was used. To ensure that MLM analyses were warranted, the fixed effects and random effects model fit for Model 1 was assessed using likelihood ratio tests ($\chi 2$). Nested model fit (i.e., Model 2 and Model 3) was assessed using significant likelihood ratio tests ($\chi 2$) and the lowest Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) values. Intraclass correlation coefficients (ICCs) quantified how much of the total variance of an outcome was explained by differences between individuals. The following formula was used: ICC= σ^2constant / (σ^2constant + σ^2residual). ICCs were reported as the percentage of variance due to differences between individuals and within-individuals (i.e., day-to-day variability).

Missing data were present due to a combination of factors: participants forgetting to complete the daily survey, participants choosing not to report symptoms due to the absence of symptoms, and technical issues with the ReCoUPS platform (**Appendix B**). Therefore, the missing data was classified as Missing at Random (MAR). However, to avoid introducing bias through imputation and considering that some data was missing due to external factors such as platform malfunctions, data analysis proceeded using available data without imputing missing values.

CHAPTER 4 : RESULTS

4.1 **Specific Aim 1**

4.1.1 Demographic Information

For specific aim 1, a total of 98 healthy college-aged individuals were enrolled in the study. Of those, one participant withdrew from the study, one participant was instead used as a healthy matched control in specific aim 3 of this dissertation, and three participants had data compromised by a technical issue with the ReCoUPS platform (**Appendix B**). Thus, a total of 93 healthy college-aged individuals who currently or recently (i.e., within the past year) played a sport (mean age: 21.37 ± 2.63 years; 64 female; 29 male) completed the study. Demographic variables are presented in **Table 1** with the sample presenting as predominantly White (n=76, 81.72%), non-Hispanic (n=86, 92.47%), and currently playing a sport (n=71, 76.34%). Additionally, **Table 2** presents information on medical history, including concussion history.

Table 1. Descriptive Statistics for Demographic Variables of Healthy College-Aged Individuals.

Variable	Mean (SD) / N (%)
Age (years)	21.37 (2.63)
Sex	
Female	64 (68.82%)
Male	29 (31.18%)
Race	
Asian or Pacific Islander	10 (10.75%)
Black	6 (6.45%)
White/Caucasian	76 (81.72%)
Biracial	1 (1.08%)
Ethnicity	
Hispanic	6 (6.45%)
Non-Hispanic	86 (92.47%)
Prefer not to say	1 (1.08%)
Year in School	
College Freshman	20 (21.51%)
College Sophomore	6 (6.45%)
College Junior	23 (24.73%)
College Senior (4^{th} year)	29 (31.18%)
College Senior (5^{th} year)	2 (2.15%)

Table 1 (cont'd).

Graduate Student	13 (13.98%)
Currently Play a Sport	71 (76.34%)
Recently Played a Sport[a]	22 (23.66%)
Currently Played Sports	
Soccer	9 (9.68%)
Cross Country	5 (5.38%)
Track & Field	3 (3.23%)
Volleyball	5 (5.38%)
Basketball	14 (15.05%)
Other[b]	57 (61.29%)
Recently Played Sports	
Baseball	7 (7.53%)
Soccer	12 (12.90%)
Track & Field	12 (12.90%)
Basketball	14 (15.05%)
Cross Country	7 (7.53%)
Other[b]	41 (44.09%)
Remuneration Type[c]	
$15	53 (57.0%)
Extra Credit	40 (43%)

[a]Recently played sports were within the past year
[b]Other sports include field hockey, dance, cheer, rugby, swimming & diving, gymnastics, rowing, tennis, wrestling
[c]Remunerated $15 if enrolled in Fall 2023, received extra credit in a KIN class if enrolled in Fall 2024
Continuous data are presented as mean (SD) and categorical data are presented as n (%).

Table 2. Descriptive Statistics for Medical History and Concussion History of Healthy College-Aged Individuals.

Variable	Mean (SD) / N (%)
Previous History of Concussion	
No	65 (69.89%)
Yes	28 (30.11%)
Number of Previous Concussions	2.50 (1.93)
Headache or Migraine Disorder	
No	86 (92.47%)
Yes	7 (7.53%)
Learning Disorder or Dyslexia	
No	90 (96.77%)
Yes	3 (3.26%)
ADD/ADHD	
No	77 (82.80 %)
Yes	16 (17.20%)

Table 2 (cont'd).

Depression/Anxiety	
No	70 (75.27%)
Yes	23 (24.73%)
Motion Sickness	
No	86 (92.47%)
Yes	7 (7.53%)

Continuous data are presented as mean (SD) and categorical data are presented as n (%).

4.1.2 Daily Response Rates to ReCoUPS Survey Text Messages

Daily response rates for participants were calculated as the number of surveys the participant completed divided by the number of days that the surveys that were sent to their phone ([Surveys Completed / Surveys Sent]*100]) throughout their participation in the study and were reported as frequencies (%). Participants were enrolled in the study for an average of 8.07 days (±0.33 days) and median 8 days (minimum days=7; maximum days=10). Some participants remained in the study longer than the planned 8 days (i.e., 7 days completing daily surveys, study closure on the 8^{th} day) due to scheduling conflicts. In these instances, participants were still asked to complete all ReCoUPS daily surveys to accurately measure behaviors with the daily symptom reported and were asked to follow the instructions on the recalled measures as directed. As the participants in this specific aim were all healthy individuals and the maximum enrollment was 10 days, we do not believe that recalled assessment scores were skewed by slightly longer than 7 days of enrollment. Response rates are presented in **Figure 5**. Most participants (n=80, 86.02%) completed over 70% of daily ReCoUPS surveys while 5 participants (5.34%) completed 50% or less of daily ReCoUPS surveys.

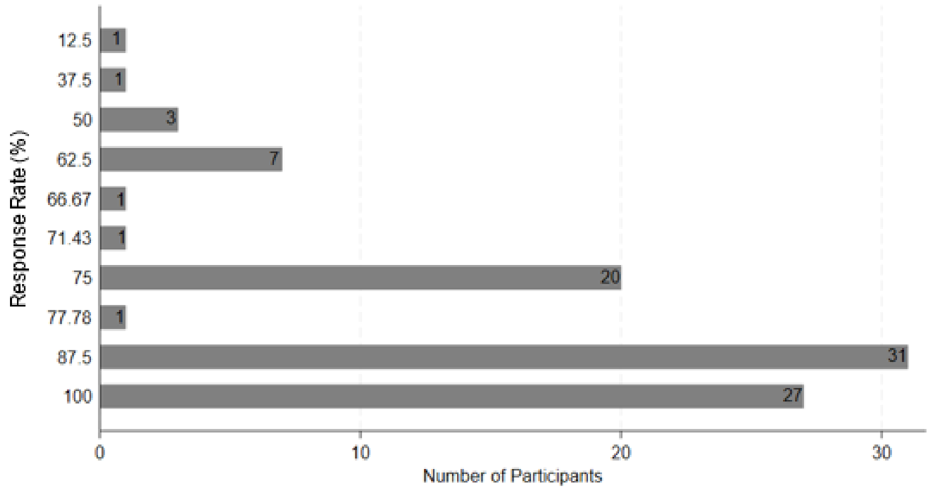

Figure 5. Frequency of healthy reliability participants per response rate of completed daily ReCoUPS survey text messages.

4.1.3 Evidence of Reliability and Validity of Momentary Assessments of PHRQoL and Post-Concussion Symptoms via ReCoUPS Survey Text Messages in Healthy Individuals

Means, standard deviations, ICCs (95% CI), and Cronbach's alpha (α) of recalled and momentary assessments of outcome measures are shown in **Table 3**. Prior to agreement coding, momentary assessments of PROMIS-SF Anxiety (ICC=0.99, 95% CI= 0.99-1.00, p<0.001) and PROMIS-SF Depression (ICC=0.99, 95% CI= 0.99-1.00, p<0.001) demonstrated excellent agreement with their corresponding recalled measures. Following agreement coding, momentary PROMIS Anxiety demonstrated moderate agreement with the recalled measure (κ=0.44; Expected: 51.73%, Actual: 73.12%, p<0.001). Additionally, momentary PROMIS Depression demonstrated moderate agreement with the recalled measure (κ=0.58; Expected: 50.99%, Actual: 79.57%, p<0.001). Both momentary assessments of the PROMIS-SF Anxiety and PROMIS-SF Depression demonstrated acceptable reliability.

Table 3. Descriptive Characteristics of Momentary and Recalled Assessments of Outcome Variables, Agreement, and Reliability.

Assessment	PROMIS-SF Anxiety	PROMIS-SF Depression	Affective Symptoms	Migraine Symptoms	Cognitive Fatigue
Momentary	0.99 (2.25)	0.31 (2.77)	1.90 (3.13)	1.04 (1.95)	2.04 (3.39)
Recalled	6.19 (2.81)[a]	5.48 (2.30)[a]	--	--	--
ICC (95% CI)	0.99 (0.99-1.00)***	0.99 (0.99-1.00)***	--	--	--
Cronbach's Alpha	0.80	0.91	--	--	--

[a]Agreement coding indicates that a score of 0 on momentary assessments is equivalent to a score of 4 on recalled assessments

Statistical significance: *p<0.05; **p<0.01; ***p<0.001

A heat plot correlation matrix depicts spearman correlations for outcome measures via ReCoUPS text messages are shown in **Figure 6.** All momentary assessments of outcome measures were significantly correlated (p<0.001). PROMIS-SF Anxiety and PROMIS-SF Depression scores were strongly correlated (r_s=0.67) with each other, indicating strong effect sizes.[199] Additionally, both the PROMIS-SF Anxiety (r_s=0.77) and PROMIS-SF Depression (r_s=0.66) were strongly correlated with affective symptoms, also indicating strong effect sizes. [199] The PROMIS-SF Anxiety was moderately correlated with migraine symptoms (r_s=0.47) and strongly correlated with cognitive-fatigue (r_s=0.69) and total symptoms (r_s=0.74), with these values corresponding to moderate and strong effect sizes, respectively.[199] The PROMIS-SF Depression was weakly correlated with migraine symptoms (r_s=0.28), representing a small effect size, and moderately correlated with cognitive-fatigue (r_s=0.59) and total symptoms (r_s=0.62), indicating moderate effect sizes.[199]

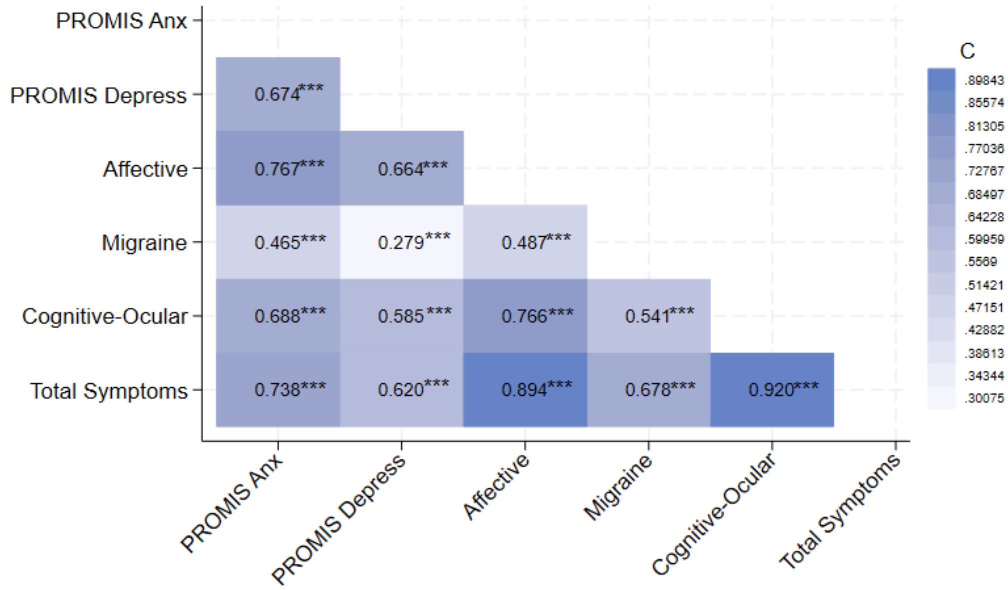

Figure 6. Heat plot of spearman correlation coefficients for momentary outcome measures. Darker blues indicate stronger correlations. Statistical significance: *p<0.05; **p<0.01; ***p<0.001.

4.1.4 ReCoUPS User Feedback

Across all participants in all specific aims of this dissertation, the complete ReCoUPS User Feedback Survey (α=0.87), positive question items (α=0.81), and inverted question items (α=0.78) demonstrated acceptable reliability. Quantitative responses to the ReCoUPS User Feedback Survey are presented in **Figure 7**. Of the participants who completed this survey at their study closure (n=40), the majority indicated ease of use for the ReCoUPS platform. Over half (n=23, 57.5%) of participants indicated that the platform would be beneficial to concussion care and that responding to the survey questions was quick and effective (n=27 ,67.5%). Most participants (n=33 ,82.5%) would recommend others to use the daily surveys to report their concussion symptoms and felt that the platform was easy to use and accurately captured symptoms and feelings (n=34, 85%). For inverted questions, less than a third of participants felt that the survey text messages were difficult (n=4 ,10%) or burdensome (n=7, 17.5%) to use.

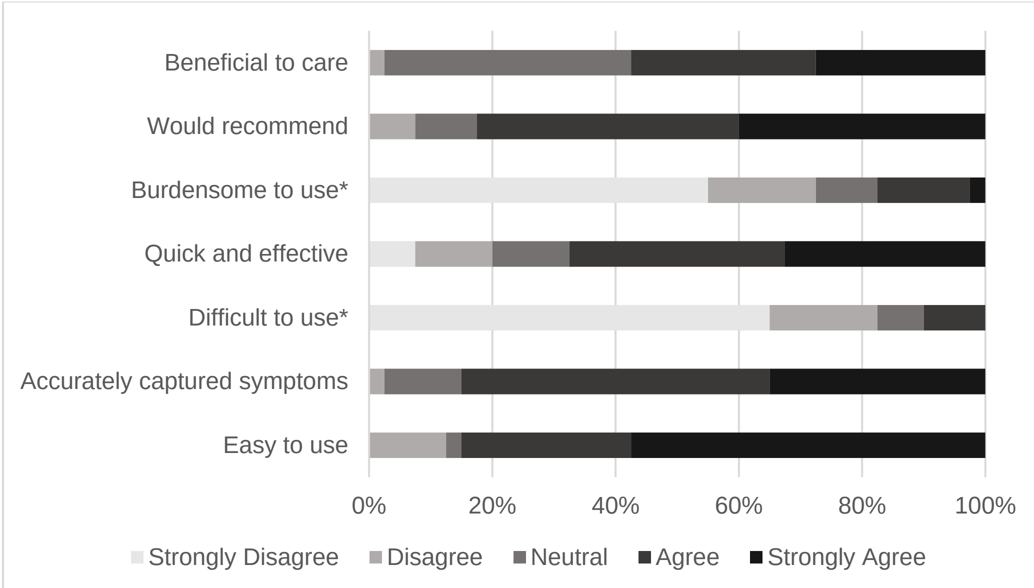

Figure 7. Frequencies of quantitative responses to the ReCoUPS User Feedback Survey. *Denotes "inverted" questions (i.e., "strongly disagree" is a positive response).

Participants were also asked how many of the daily surveys they felt that they completed, with 75% (n=30) indicating that they responded to all questions while 25% (n=10) indicating that they responded to most questions. When asked why they responded the way that they did, themes of "for the benefit of the research study" (n=24, 60%), "responding to text messages was easy to do" (n=8, 20%), "forgot to finish the survey" (n=3, 7.5%), "just because" (n=3, 7.5%), and "technology issues" (n=2, 5.0%) emerged (**Appendix B**). Additionally, participants were asked a final optional question to provide any feedback for improvement of the text messages or platform. Most participants who completed the survey answered this question (n=27, 67.5%). Of these responses, themes of "the text messages came too slow" (n=11, 40.7%), "the texts were great (no additional feedback)" (n=4, 14.8%), "ask questions about more outcomes" (n=2, 7.4%), "the text messages came slow but were overall great" (n=5, 18.5%), "stop double texts" (n=1, 3.7%), and "send multiple text messages at once for bulk response" (n=4, 14.8%) emerged (**Appendix B**).

4.2 **Specific Aim 2**

4.2.1 Demographic Information

For specific aim 2, a total of 39 college-aged athletes with a concussion were enrolled in the study. Of those, three withdrew prior to completing the study procedures. Thus, a total of 36 college-aged athletes (mean age: 20.36 ± 1.25 years; 23 female; 13 male) completed the study. Demographic variables are presented in **Table 4** with the sample presenting as predominantly White (n=34, 94.44%) and non-Hispanic (n=33, 91.67%). Additionally, **Table 5** and **Table 6** present information on medical history and current injury and recovery characteristics.

Table 4. Descriptive Statistics for Demographic Variables of College-Aged Athletes with a Concussion.

Variable	Mean (SD) / N (%)
Age (years)	20.36 (1.25)
Sex	
Female	23 (63.89%)
Male	13 (36.11%)
Race	
Asian or Pacific Islander	1 (2.78%)
White/Caucasian	34 (94.44%)
Biracial	1 (2.78%)
Ethnicity	
Hispanic	3 (8.33%)
Non-Hispanic	33 (91.67%)
Year in School	
College Freshman	10 (27.78%)
College Sophomore	6 (16.67%)
College Junior	8 (22.22%)
College Senior (4th year)	11 (30.56%)
College Senior (5th year)	1 (2.78%)
Currently Played Sports	
Baseball	1 (2.78%)
Basketball	2 (5.56%)
Cheer	2 (5.56%)
Dance	1 (2.78%)
Field Hockey	2 (5.56%)
Football	2 (5.56%)
Ice Hockey	1 (2.78%)
Rowing	3 (8.33%)
Rugby	6 (1.67%)

Table 4 (cont'd).

Soccer	6 (1.67%)
Softball	2 (5.56%)
Track & Field	2 (5.56%)
Volleyball	3 (8.33%)
Wrestling	3 (8.33%)
Level of Play	
NCAA Division I	21 (58.33%)
NCAA Division III	4 (11.11%)
NAIA	3 (8.33%)
Club	2 (5.56%)
Intramural	2 (5.56%)
Recreational	4 (11.11%)

Continuous data are presented as mean (SD) and categorical data are presented as n (%).

Table 5. Descriptive Statistics for Medical History and Concussion History of College-Aged Athletes with a Concussion.

Variable	Mean (SD) / N (%)
Previous History of Concussion	
No	17 (47.22%)
Yes	19 (52.78%)
Number of Previous Concussions	1.74 (1.05)
Headache or Migraine Disorder	
No	33 (91.67%)
Yes	3 (8.33%)
Learning Disorder or Dyslexia	
No	35 (97.22%)
Yes	1 (2.78%)
ADD/ADHD	
No	27 (75.00%)
Yes	9 (25.00%)
Depression/Anxiety	
No	29 (80.56%)
Yes	7 (19.44%)
Motion Sickness	
No	33 (91.67%)
Yes	3 (8.33%)

Continuous data are presented as mean (SD) and categorical data are presented as n (%).

Table 6. Injury and Recovery Information of College-Aged Individuals with a Concussion.

Variable	Mean (SD) / N (%)
Injury Information	
Time to Presentation (days)	2.28 (1.23)
Mechanism of Injury	
Sport-Related	28 (77.78%)
Hit (an object or by an object)	2 (5.56%)
Motor Vehicle Accident	6 (16.67%)
Loss of Consciousness	
No	29 (80.56%)
Yes	7 (19.44%)
Remember the Injury	
No	6 (16.67%)
Yes	30 (83.33%)
Continued to Play[a]	
No	24 (72.73%)
Yes	9 (27.27%)
Recovery Information	
Engaged in a RTP Protocol[b]	
No	2 (5.56%)
Yes	34 (94.44%)
Days to Symptom Resolution	13.72 (8.91)
Days to Full Medical Clearance	19.42 (11.94)

[a]If responded yes, participants either continued to play immediately following injury (n=6, 66.67%) or were removed from play but went back in (n=3, 33.33%)
[b]If responded no, participants may have engaged in structured exercise instead (n=1, 2.78%; one participant was missing data
Continuous data are presented as mean (SD) and categorical data are presented as n (%).

4.2.2 Daily Response Rates to ReCoUPS Survey Text Messages

Daily response rates for participants were calculated using the same formula described in specific aim 1. Participants were enrolled in the study for an average of 19.11 days (±12.31 days) and median 15 days (minimum days=3; maximum days=49). Response rates are presented in **Figure 8.** Response rates were grouped for every 10% for clear representation in the figure. Most participants (n=24, 66.67%) completed over 70% of daily ReCoUPS surveys while 6 participants (16.67%) completed less than 50% of daily ReCoUPS surveys.

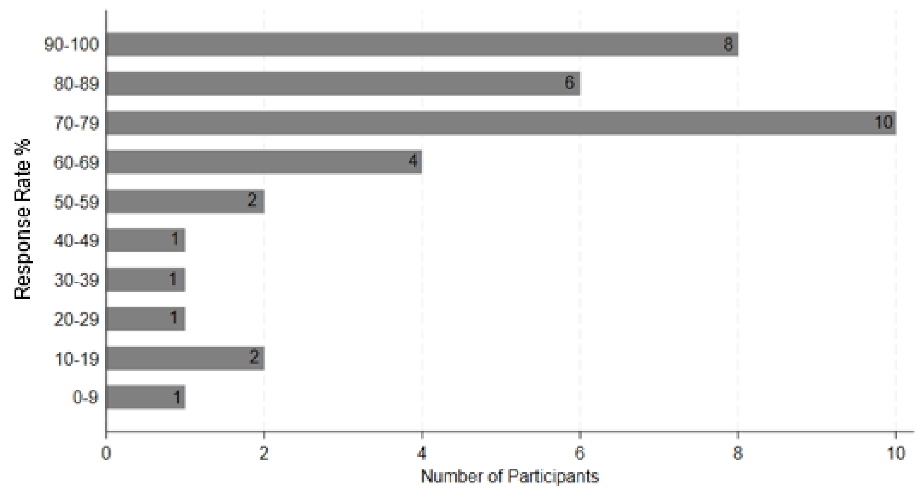

Figure 8. Frequency of participants with a concussion per response rate of completed daily ReCoUPS survey text messages.

4.2.3 Feasibility of Monitoring Post-Concussion Symptoms and Psychological HRQoL daily throughout Concussion Recovery Using ReCoUPS

A heat plot correlation matrix depicts spearman correlations for momentary assessments of outcome measures via ReCoUPS text messages in **Figure 9**. All outcome measures were significantly correlated. PROMIS-SF Anxiety and PROMIS-SF Depression scores were strongly correlated (r_s=0.87), indicating a strong effect size.[199] PROMIS-SF Anxiety scores were strongly correlated with affective (r_s=0.85), cognitive-ocular (r_s=0.77), and total symptoms (r_s=0.77), indicating strong effect sizes, and moderately correlated with migraine symptoms (r_s=0.66), indicating a moderate effect size.[199] PROMIS-SF Depression scores were strongly correlated with affective (r_s=0.74) and cognitive-ocular symptoms (r_s=0.73), indicating strong effect sizes, and moderately correlated with migraine (r_s=0.58) and total symptoms (r_s=0.67), representing moderate effect sizes.[199]

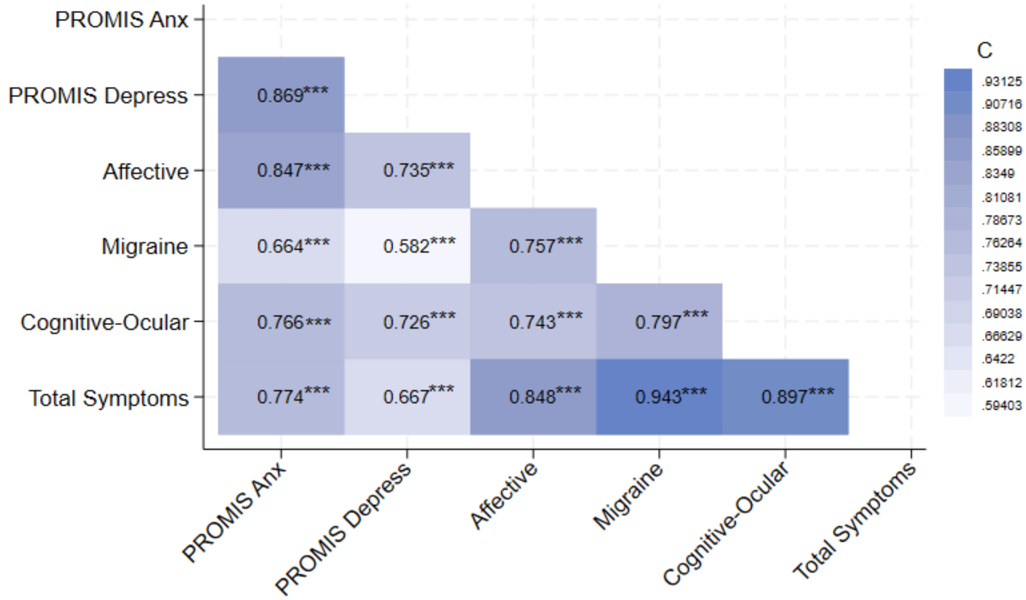

Figure 9. Heat plot of spearman correlation coefficients for momentary outcome measures. Darker blues indicate stronger correlations. Statistical significance: **p*<0.05; ***p*<0.01; ****p*<0.001.

4.2.4 Descriptive Analyses

Means, standard deviations, and ranges of recalled and momentary assessments of outcome measures are shown in **Table 7**. Both momentary assessments of the PROMIS-SF Anxiety (α= 0.91) and PROMIS-SF Depression (0.93) demonstrated acceptable reliability. Prior to agreement coding, momentary assessments of PROMIS-SF Anxiety and PROMIS-SF Depression demonstrated excellent agreement with their corresponding recalled measures. Following agreement coding, momentary PROMIS Anxiety demonstrated slight agreement with the recalled measure (κ=0.20; Expected: 49.88%, Actual: 60.00%, p<0.05) while momentary PROMIS Depression demonstrated fair agreement with the recalled measure (κ=0.39; Expected: 57.96%, Actual: 74.29%, p<0.001).

Table 7. Descriptive Characteristics of Momentary and Recalled Assessments of Outcome Variables and Agreement.

Assessment	Momentary			Recalled			ICC (95% CI)
	Range[a]	Mean	SD	Range[b]	Mean	SD	
PROMIS-SF Anxiety	0-16	1.97	3.25	4-13	5.94	2.88	0.98 (0.91-1.00)***
PROMIS SF-Depression	0-16	1.49	2.87	4-11	4.78	1.69	0.99 (0.94-1.00)***
Affective Symptoms	0-16	2.76	3.96	--	--	--	--
Migraine Symptoms	0-26	5.99	5.97	--	--	--	--
Cognitive-Ocular Symptoms	0-16	2.46	3.64	--	--	--	--
Total Symptoms	0-95	19.85	21.19	--	--	--	--

[a]Minimum possible scores for all momentary assessments was 0. Maximum possible score for PROMIS-SF Anxiety, PROMIS-SF Depression, Affective Symptoms, Cognitive-Ocular Symptoms was 24. Maximum possible score for Migraine Symptoms was 30 and 132 for Total Symptoms.
[b]Minimum possible scores for all recalled PROMIS-SF assessments was 4 and maximum possible score was 20.
Statistical significance: *p<0.05; **p<0.01; ***p<0.001

To further depict changes in symptoms throughout concussion recovery, heat plots were generated. Heat plots assign colors to specific values which represent the severity of symptoms. **Figure 10** demonstrates the severity of total symptoms for each participant every day that they completed their ReCoUPS daily survey from the day of their injury until they have received FMC from a health care provider. Most participants (n=26, 72.2%) had symptoms that changed and decreased in severity throughout their concussion recovery. Moreover, half of participants (n=18, 50%) had total symptom scores greater than an average of 47.5 that progressively decreased throughout their recovery. These figures also emphasize that symptom variability is present within athletes (i.e., symptoms are changing daily throughout recovery) and between athletes (i.e., all concussions are different, and concussions are different than matched controls).

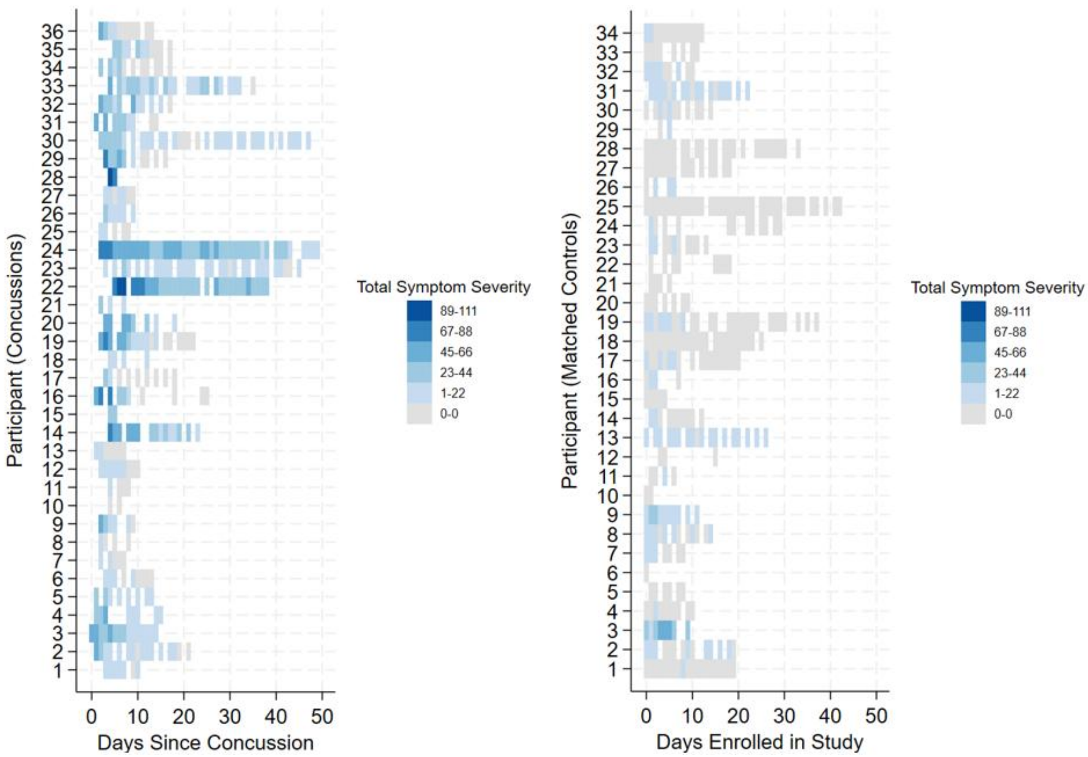

Figure 10. Heat plots demonstrating changes in total symptom severity as collected via ReCoUPS daily survey text messages every day since the date of injury for participants with a concussion and every day enrolled in the study for healthy matched controls. Participants (denoted on the y axis) were assigned a unique identifier. Gray and lighter blue values represent lower total symptom severity while transitioning to darker blues represents increases in symptom severity. Missing values represent days which a participant did not complete their daily survey.

Heat plots (**Figure 11** and **Figure 12**) also demonstrated the change in severity of PROMIS-SF Anxiety, PROMIS-SF Depression, affective symptoms, cognitive-ocular symptoms, and migraine symptoms every day since the athlete sustained their concussion while enrolled in the present study. Again, most participants (n=26, 72.2%) started with more severe symptoms for each outcome that progressively improved throughout recovery.

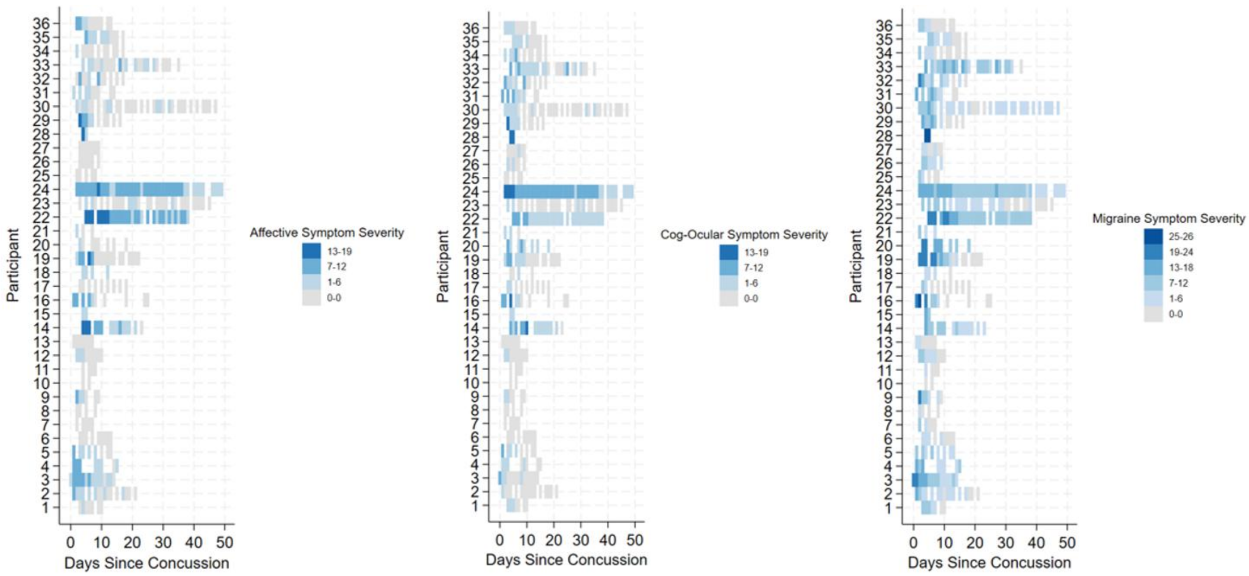

Figure 11. Heat plots demonstrating changes in affective, cognitive-ocular, and migraine symptom severity as collected via ReCoUPS daily survey text messages every day since the date of their concussion. *Note:* Maximum score for affective and cognitive-ocular symptoms is 24 while maximum score for migraine symptoms is 30.

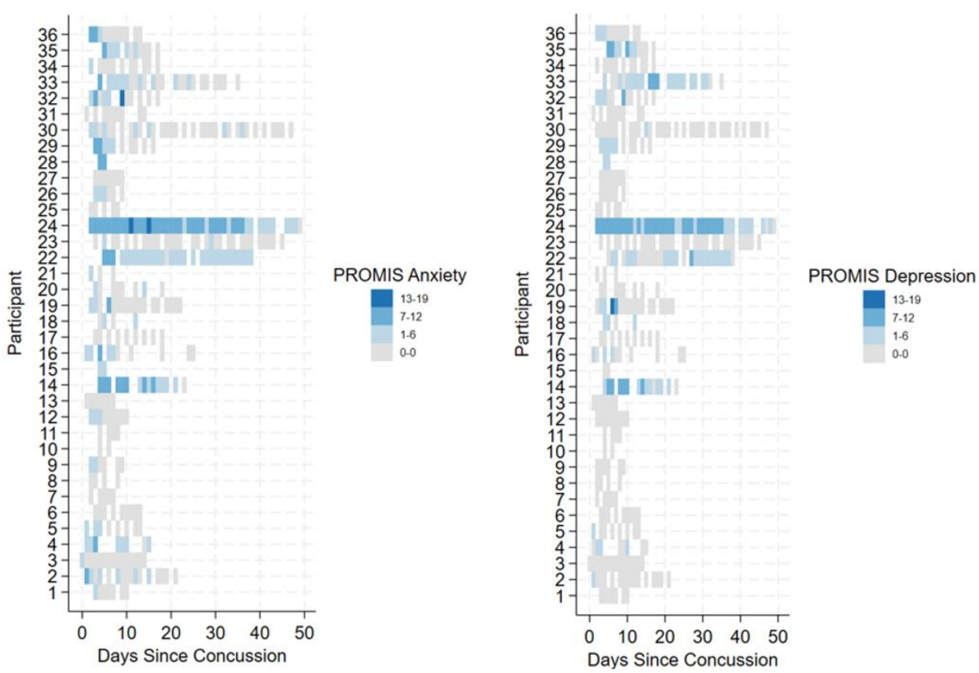

Figure 12. Heat plots demonstrating changes in PROMIS Anxiety and PROMIS Depression severity as collected via ReCoUPS daily survey text messages every day since the date of their concussion.

4.2.5 ReCoUPS User Feedback

Quantitative responses to the ReCoUPS User Feedback Survey are presented in **Figure 13**. Of the participants who completed this survey at their study closure (n=20), the majority indicated ease of use for the ReCoUPS platform. Over half (n=13, 65%) of participants indicated that the platform would be beneficial to concussion care. A little less than half felt that responding to the survey question was quick and effective (n=9, 45%). Most participants (n=13, 65%) would recommend others to use the daily surveys to report their concussion symptoms and felt that the platform was easy to use and accurately captured symptoms and feelings (n=16, 80%). For inverted questions, 20% (n=4) of participants felt that the survey text messages were difficult or burdensome to use.

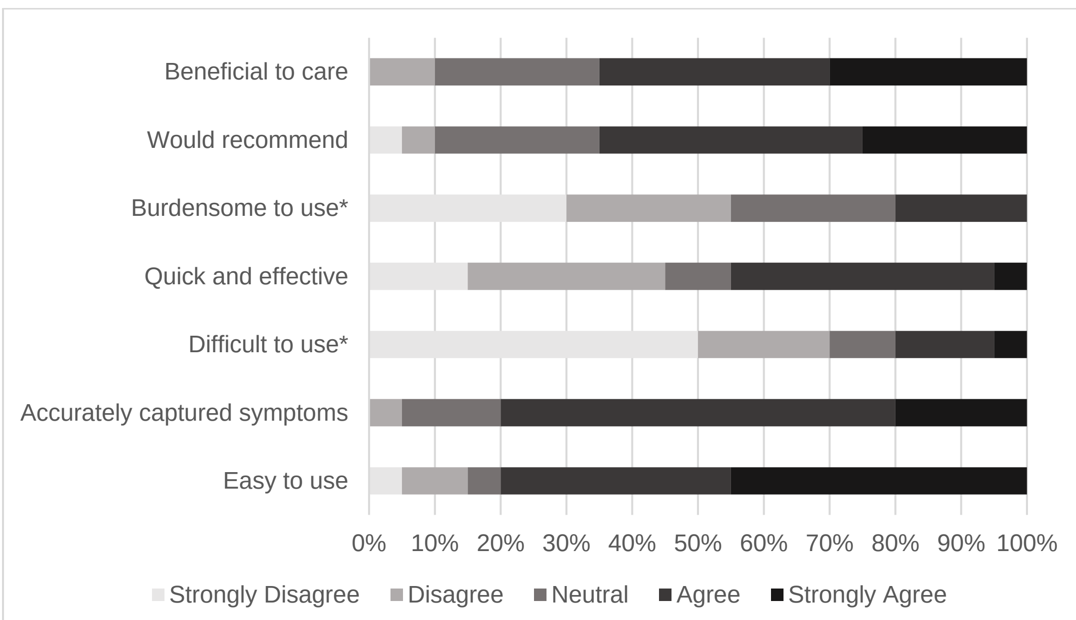

Figure 13. Frequencies of quantitative responses to the ReCoUPS User Feedback Survey. *Denotes “inverted” questions (i.e., “strongly disagree” is a positive response).

Participants indicated that they felt that they completed all (n=9, 45%) or most (n=11, 55%) of daily surveys. When asked why they responded the way that they did, themes of "for the benefit of the research study" (n=7, 35%), "responding to text messages was easy to do and accurately reflected symptoms" (n=3, 15%), "forgot to finish the survey" (n=4, 20%), "exacerbated concussion symptoms" (n=2, 10.5%), "did not respond because all symptoms were 0" (n=1, 5.3%) and "took too long/technology issues" (n=3, 15%) emerged (**Appendix B**). When asked to provide any feedback for improvement of the text messages or platform, most participants who completed the survey answered the question (n=17, 85%). Of these responses, themes of "the text messages came too slow" (n=12, 70.6%), "send multiple text messages at once for bulk response" (n=2, 11.8%), and "use an app that sends notifications instead of text messages" (n=3, 17.6%) emerged.

4.3 **Specific Aim 3**

4.3.1 Demographic Information

For specific aim 3, in addition to our 36 athletes with a concussion, a total of 35 college-aged athletes were enrolled as healthy matched controls in this study. Of those, one was withdrawn by the study team due to data being impacted by technical issues with the ReCoUPS platform (**Appendix B**). Additionally, one of the participants with a concussion was enrolled in the study for 42 days and the study team was unable to find a healthy matched control to complete study procedures prior to the submission of this dissertation. Thus, a total of 34 healthy college-aged athletes (mean age: 20.35 ± 1.37 years; 21 female; 13 male) completed the study. A comparison of demographic variables between participants with a concussion and healthy matched controls are presented in **Table 8** with the sample presenting as predominantly White (n=31, 91.18%) and non-Hispanic (n=30, 88.24%). Further, a comparison of medical and concussion history is presented in **Table 9**. There were no significant differences between groups for any demographic or medical characteristics.

Table 8. Descriptive Statistics for Demographic Variables of College-Aged Athletes with a Concussion and Healthy Matched Controls.

Variable	Concussions Mean (SD) / N (%) n=36	Matched Controls Mean (SD) / N (%) n=34	*p*-value
Age (years)	20.36 (1.25)	20.35 (1.37)	0.96[a]
Days Enrolled in Study	19.11 (12.31)	17.53 (10.34)	0.56[a]
Sex			
Female	23 (63.89%)	21 (61.77%)	0.85[b]
Male	13 (36.11%)	13 (38.23%)	
Race			
Asian or Pacific Islander	1 (2.78%)	2 (5.88%)	0.80[c]
White/Caucasian	34 (94.44%)	31 (91.18%)	
Biracial	1 (2.78%)	1 (2.94%)	
Ethnicity			
Hispanic	3 (8.33%)	3 (8.82%)	0.83[c]
Non-Hispanic	33 (91.67%)	30 (88.24%)	
Prefer not to say	0 (0.00%)	1 (2.94%)	
Year in School			
College Freshman	10 (27.78%)	11 (32.35%)	0.87[c]
College Sophomore	6 (16.67%)	4 (11.76%)	
College Junior	8 (22.22%)	6 (17.65%)	
College Senior (4th year)	11 (30.56%)	13 (38.24%)	
College Senior (5th year)	2.78%)	0 (0.00%)	
Currently Played Sports			
Baseball	1 (2.78%)	1 (2.94%)	0.99[c]
Basketball	2 (5.56%)	2 (5.88%)	
Cheer	2 (5.56%)	2 (5.88%)	
Dance	1 (2.78%)	1 (2.94%)	
Field Hockey	2 (5.56%)	2 (5.88%)	
Football	2 (5.56%)	2 (5.88%)	
Ice Hockey	1 (2.78%)	0 (0.00%)	
Rowing	3 (8.33%)	3 (8.82%)	
Rugby	6 (1.67%)	5 (14.71%)	
Soccer	6 (1.67%)	6 (17.65%)	
Softball	2 (5.56%)	2 (5.88%)	
Track & Field	2 (5.56%)	2 (5.88%)	
Volleyball	3 (8.33%)	3 (8.82%)	
Wrestling	3 (8.33%)	3 (8.82%)	

Table 8 (cont'd).

Sport Type			
Contact	24 (66.67%)	22 (64.71%)	0.71[b]
Non-Contact	12 (33.33%)	12 (35.29%)	
Level of Play			
NCAA Division I	21 (58.33%)	18 (54.55%)	0.25[c]
NCAA Division III	4 (11.11%)	3 (9.09%)	
NAIA	3 (8.33%)	2 (6.06%)	
Club	2 (5.56%)	9 (26.47%)	
Intramural	2 (5.56%)	0 (0.00%)	
Recreational	4 (11.11%)	2 (6.06%)	

[a]T-tests determined differences in continuous variables
[b]Chi-square tests determined differences in categorical variables
[c]Fisher's exact test determined differences in categorical variables where row values were less than 5.
Continuous data are presented as mean (SD) and categorical data are presented as n (%).

Table 9. Descriptive Statistics for Medical History and Concussion History of College-Aged Athletes with a Concussion and Healthy Matched Controls.

Variable	**Concussions Mean (SD) / N (%) n=36**	**Matched Controls Mean (SD) / N (%) n=34**	***p*-value**
Previous History of Concussion			
No	17 (47.22%)	20 (58.82%)	0.33[b]
Yes	19 (52.78%)	14 (41.18%)	
Number of Previous Concussions	1.74 (1.05)	1.67 (0.92)	0.51[a]
Headache or Migraine Disorder			
No	33 (91.67%)	33 (97.06%)	0.62[c]
Yes	3 (8.33%)	1 (2.94%)	
Learning Disorder or Dyslexia			
No	35 (97.22%)	31 (91.18%)	0.35[c]
Yes	1 (2.78%)	3 (8.82%)	
ADD/ADHD			
No	27 (75.00%)	31 (91.18%)	0.12[c]
Yes	9 (25.00%)	3 (8.82%)	
Depression/Anxiety			
No	29 (80.56%)	31 (91.18%)	0.31[c]
Yes	7 (19.44%)	3 (8.82%)	

Table 9 (cont'd).

Motion Sickness			
No	33 (91.67%)	34 (100.00%)	0.24[c]
Yes	3 (8.33%)	0 (0.00%)	

[a]T-tests determined differences in continuous variables
[b]Chi-square tests determined differences in categorical variables
[c]Fisher's exact test determined differences in categorical variables where row values were less than 5.
Continuous data are presented as mean (SD) and categorical data are presented as n (%).

4.3.2 Daily Response Rates to ReCoUPS Survey Text Messages

Daily response rates for healthy matched controls were calculated using the same formula described in specific aims 1 and 2. Healthy participants were enrolled in the study for an average of 17.53 days (±10.34 days) and median 14.5 days (minimum days=3; maximum days=45), which was similar to participants with a concussion (**Table 8**). Response rates are presented in **Figure 14.** Like specific aim 2, response rates were grouped for every 10% for clear representation in the figure. Most participants (n=23, 67.65%) completed over 70% of daily ReCoUPS surveys while 6 participants (17.65%) completed less than 50% of daily ReCoUPS surveys.

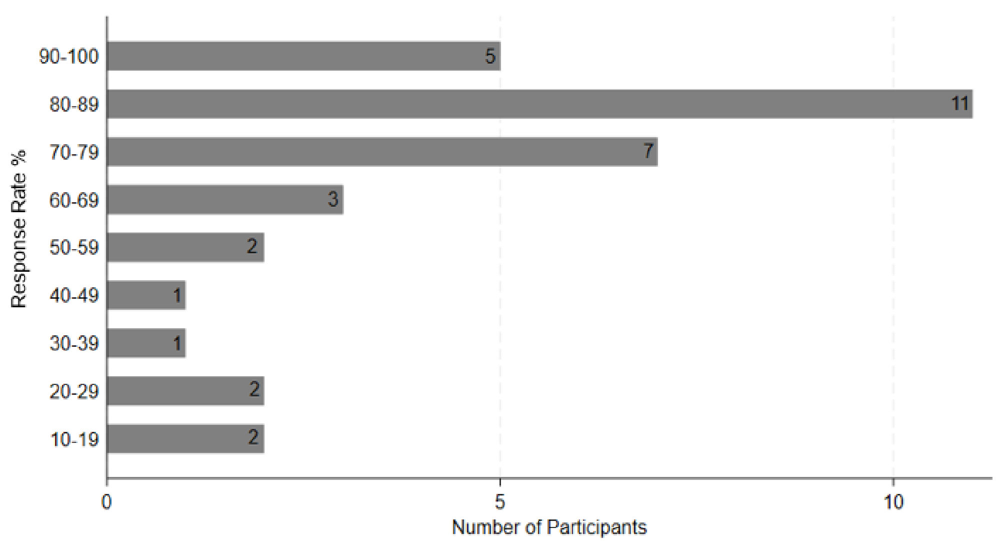

Figure 14. Frequency of healthy matched control participants per response rate of completed daily ReCoUPS survey text messages.

4.3.3 Within and Between Person Variance of Momentary Outcome Measures

4.3.3.1 MLM Fixed and Random Effect Estimates for Momentary Outcome Measures (Model 1)

The models that the data were fit to for this section are presented in **Table 10**. For the null MLM model (Model 1), the fixed and random effects of each outcome measure across all participants (i.e., concussion and healthy matched control) were evaluated (**Table 11**). The fixed effects reflected the weighted average score estimate of the outcome measure across all participants while accounting for the clustered structure of the data (i.e., responses nested within athletes). The mixed effects represented the within and between-athlete variance of the outcome measures. For all outcome measures, the average score was significantly different than 0. Additionally, for all outcome measures, most of the variance was explained by the between-athlete differences (ICCs). Finally, likelihood ratio tests comparing the fixed effects and random effects models for all outcomes were statistically significant, indicating that the inclusion of random effects improved the model, therefore suggesting that multilevel modeling is an appropriate approach to this data.

Table 10. MLM Equations.

Model	Equation
Model 1	$Outcome_{ij}=\gamma_{00}+u_{0j}+r_{ij}$
Model 2	$Outcome_{ij}=\gamma_{00}+\gamma_{01}ConcussionStatus_{ij}+u_{0j}+r_{ij}$
Model 3[a]	$Outcome_{ij}=\gamma_{00}+\gamma_{01}ConcussionStatus_{ij}+\gamma_{02}$[Athlete Predictors] $+u_{0j}+r_{ij}$
Model 3 with Interaction Terms	$Outcome_{ij}=\gamma_{00}+\gamma_{01}ConcussionStatus_{ij}+\gamma_{02}$[Athlete Predictors] + γ_{03}[Concussion Status x Athlete Predictors] $+u_{0j}+r_{ij}$

[a]Athlete predictors were selected based on theoretical relevance and results from univariate robust standard error linear regressions

Table 11. MLM Fixed and Random (Variance Components) Effects Estimates for Momentary Outcome Measures (Model 1).

Variable	Fixed Effects	Random Effects		
	γ_{00} (SE)	Between Person Variance (SE)	Within Person Variance (SE)	ICC
PROMIS Anxiety	1.04 (0.23)***	3.29 (0.62)	3.22 (0.67)	0.51
PROMIS Depression	0.66 (0.19)***	2.23 (0.42)	2.15 (0.11)	0.51
Affective Symptoms	1.48 (0.28)***	4.98 (0.93)	4.47 (0.23)	0.53
Migraine Symptoms	3.16 (0.52)***	17.42 (3.39)	12.29 (0.64)	0.60
Cognitive Ocular Symptoms	1.18 (0.28)***	4.89 (0.95)	3.37 (0.18)	0.59
Total Symptoms	10.47 (1.78)***	201.91 (38.98)	135.58 (7.05)	0.60

Statistical significance: *p<0.05; **p<0.01; ***p<0.001

4.3.3.2 MLM Fixed and Random Effects of Momentary Outcome Measures by Concussion Status (Model 2)

Athletes' concussion status (i.e., concussion or healthy matched control) was added as an athlete-level independent variable and the fixed and random effects were estimated for each outcome measure (**Table 12**). For all outcome measures, participants with a concussion presented with significantly higher mean scores than healthy matched controls. For all outcome measures, the ICCs decreased, indicating that concussion status explained some of the between-athlete differences and that within-athlete differences accounted for a larger proportion of the total variance. More specifically, for PROMIS Anxiety, PROMIS Depression, affective symptom, and total symptom scores, equal variance was explained by between and within-athlete differences (ICCs=0.50). For migraine symptoms, most of the variance was explained by within-athlete differences (ICC=0.47) and more variance was explained by between-athlete differences for cognitive-ocular (ICC=0.52) symptoms when compared to the null model.

Table 12. MLM Fixed and Random (Variance Components) Effects for Momentary Outcome Measures and Concussion Status (Model 2).

Variable	Fixed Effects		Random Effects		
	γ_{00} (SE)	γ_{01} (SE)	Between Person Variance (SE)	Within Person Variance (SE)	ICC
PROMIS Anxiety	0.52 (0.32)	1.00 (0.45)*	1.75 (0.17)	1.80 (0.05)	0.49
PROMIS Depression	0.29 (0.27)	0.73 (0.37)*	1.46 (0.14)	1.47 (0.04)	0.50
Affective Symptoms	0.74 (0.39)	1.44 (0.54)**	2.11 (0.20)	2.11 (0.06)	0.50
Migraine Symptoms	0.42 (0.58)	5.29 (0.80)***	3.09 (0.34)	3.52 (0.09)	0.47
Cognitive Ocular Symptoms	0.20 (0.36)	1.88 (0.50)***	1.98 (0.20)	1.84 (0.05)	0.52
Total Symptoms	2.44 (2.14)	15.54 (2.98)***	11.66 (1.20)	11.66 (0.30)	0.50

Statistical significance: **p*<0.05; ***p*<0.01; ****p*<0.001

4.3.3.3 Comparison of Null Model (Model 1) and Model with Concussion Status (Model 2)

Comparisons of model fit for Model 1 and Model 2 are presented in **Table 13**. For all outcome measures, Model 2 was a better fit as confirmed but likelihood ratio ($\chi2$) tests, AIC, and BIC values. While the BIC values for the PROMIS Anxiety (BIC=3456.20) and PROMIS Depression (BIC=3136.91) model 2 were greater than the BIC values for the nested models (Anxiety BIC=3454.32; Depression BIC=3133.93), the Model 2 AIC values were smaller (Anxiety AIC=3437.38; Depression AIC=3118.09) than the nested model values (Anxiety AIC=3440.21; Depression AIC=3119.82) and the likelihood ratio tests were significant (Anxiety $\chi2$=4.83, p=0.03; Depression $\chi2$=3.73, p=0.05). Therefore, Model 2 was chosen as a better fit.

Table 13. Comparison of Model 1 and Model 2.

Variable	Model 1		Model 2		Likelihood ratio	
	AIC	BIC	AIC	BIC	χ2	*p*-value
PROMIS Anxiety	3440.21	3454.32	3437.38	3456.20	4.83	0.03*
PROMIS Depression	3119.82	3133.93	3118.09	3136.91	3.73	0.05*
Affective Symptoms	3712.77	3726.88	3707.99	3726.80	6.78	0.01**
Migraine Symptoms	4552.77	4566.88	4521.87	4540.69	32.90	<0.001***
Cognitive Ocular Symptoms	3498.08	3512.19	3487.36	3506.18	12.72	<0.001***
Total Symptoms	6514.93	6529.04	6494.26	6513.08	22.67	<0.001***

Statistical significance: $*p<0.05$; $**p<0.01$; $***p<0.001$

4.3.3.4 Pre-selection of Athlete-Level Predictor Variables for MLM Model 3

Univariate regression results indicated that sex, previous concussion history, and sport type (i.e., contact or non-contact) were not significant predictors of any outcome variables (**Table 14**). However, these variables were still selected as predictor variables for the level MLM models based on theoretical relevance and existing literature.[125,222] These regression models were estimated using robust standard errors to account for the nested structure of the data. This procedure accounts for the clustering to an extent but does not account for the correlation among responses within each athlete. Other known factors that influence concussion recovery outcomes such as diagnosis of depression/anxiety disorder and ADD/ADHD were not included in univariate regression analyses or pre-selected as predictors due to the small sample sizes and limited representation of these groups to detect meaningful associations (**Table 8**).

Table 14. Univariate regression results for pre-selected predictor variables.

Variable	β	Robust SE[a]	*p*-value
Sex			
PROMIS Anxiety	0.66	1.23	0.59
PROMIS Depression	0.68	1.09	0.53
Affective Symptoms	-0.05	1.24	0.97
Migraine Symptoms	-0.09	1.55	0.96
Cognitive-Ocular Symptoms	0.96	1.32	0.47
Total Symptoms	1.40	6.71	0.84
Previous Concussion			
PROMIS Anxiety	0.74	0.89	0.41
PROMIS Depression	1.05	0.76	0.17
Affective Symptoms	0.15	1.02	0.88
Migraine Symptoms	0.82	1.32	0.54
Cognitive-Ocular Symptoms	1.04	0.95	0.28
Total Symptoms	3.61	5.28	0.50
Contact Sport			
PROMIS Anxiety	0.51	0.68	0.46
PROMIS Depression	0.43	0.59	0.47
Affective Symptoms	0.56	0.80	0.49
Migraine Symptoms	1.08	1.15	0.35
Cognitive-Ocular Symptoms	1.08	0.67	0.11
Total Symptoms	4.60	4.16	0.27

Statistical significance: **p*<0.05; ***p*<0.01; ****p*<0.001

[a]Because outcomes were assessed each day that the participant was enrolled in the study, data was clustered by participant to account for within-subject correlations

4.3.3.5 MLM Fixed and Random Effects of Momentary Outcome Measures by Concussion Status and Sex, Previous History of Concussion, or Sport Type (Model 3)

The Model 3 results with the addition of concussion status, sex, and the interaction of concussion status x sex are presented in **Table 15**. When accounting for sex, concussion status was a significant predictor of all outcome measures except for PROMIS Anxiety (γ_{01}=0.86, *p*=0.12) and PROMIS Depression (γ_{01}=0.67, *p*=0.15). The constant for PROMIS Anxiety (γ_{00}=0.79, *p*=0.05) and affective symptom (γ_{00}=1.08, *p*=0.02) scores were also significant, indicating that when all predictors are set at 0 at baseline, these values remained significantly greater than 0. Further, males reported slightly lower scores on all outcome measures compared to all other female participants (concussions and healthy controls); however, sex did not significantly influence any outcome measure scores. Additionally, while males with a concussion reported slightly higher PROMIS Anxiety (γ03=0.40, SE=0.93) and PROMIS Depression (γ_{03}=0.18, SE=0.78) scores and lower affective symptom (γ_{03}=-0.16, SE=1.10), migraine symptom (γ_{03}=-1.41, SE=1.65), cognitive-ocular symptom (γ_{03}=-0.06, SE=1.04), and total symptom (β=-2.16, SE=6.15) scores compared to the rest of the sample, the interaction between sex and concussion status did not significantly influence outcome measure scores. For most outcome measures, variance was evenly distributed across within-athlete and between-athlete differences except for migraine symptoms, where most of the variance was attributed to within-athlete differences (ICC=0.46).

Table 15. MLM Fixed and Random (Variance Components) Effects for Momentary Outcome Measures, Concussion Status, Sex, and the Interaction of Concussion Status x Sex (Model 3).

Variable	**Fixed Effects**				**Random Effects**		
	γ_{00} (SE)	**γ_{01} (SE)**	**γ_{02} (SE)**	**γ_{03} (SE)**	**Between Person Variance (SE)**	**Within Person Variance (SE)**	**ICC**
PROMIS Anxiety	0.79 (0.40)*	0.86 (0.55)	-0.75 (0.66)	0.40 (0.93)	1.73 (0.16)	1.79 (0.05)	0.49
PROMIS Depression	0.45 (0.33)	0.67 (0.46)	-0.45 (0.56)	0.18 (0.78)	1.45 (0.14)	1.47 (0.04)	0.50
Affective Symptoms	1.08 (0.48)*	1.49 (0.66)*	-0.95 (0.79)	-0.16 (1.10)	2.07 (0.19)	2.11 (0.05)	0.50
Migraine Symptoms	0.56 (0.71)	5.79 (0.99)***	-0.40 (1.19)	-1.41 (1.65)	3.04 (0.33)	3.51 (0.09)	0.46
Cognitive Ocular Symptoms	0.32 (0.45)	1.90 (0.63)**	-0.31 (0.75)	-0.06 (1.04)	1.98 (0.20)	1.84 (0.05)	0.52
Total Symptoms	3.47 (2.65)	16.28 (3.68)***	-2.85 (4.41)	-2.16 (6.15)	11.53 (1.18)	11.66 (0.30)	0.50

Statistical significance: *p<0.05; **p<0.01; ***p<0.001

Comparisons of model fit for Model 2 and Model 3 when accounting for sex are presented in **Table 16**. For all outcome measures, Model 2, which added concussion status (i.e., concussion or healthy matched control) and did not account for sex were better fits as confirmed but likelihood ratio (χ2) tests, AIC, and BIC. Therefore, the addition of sex as a predictor variable did not improve model fit and thus may not explain meaningful differences between outcome measures.

Table 16. Comparison of Model 2 and Model 3 with Sex Added as Predictor.

Variable	**Model 2**		**Model 3**		**Likelihood ratio**	
	AIC	**BIC**	**AIC**	**BIC**	**χ2**	***p*-value**
PROMIS Anxiety	3437.38	3456.20	3439.84	3468.06	1.54	0.46
PROMIS Depression	3118.09	3136.91	3121.20	3149.42	0.90	0.64
Affective Symptoms	3707.99	3726.80	3708.51	3736.74	3.48	0.18
Migraine Symptoms	4521.87	4540.69	4523.32	4551.55	2.55	0.28
Cognitive Ocular Symptoms	3487.36	3506.18	3490.94	3519.17	0.41	0.81
Total Symptoms	6494.26	6513.08	6496.49	6524.72	1.77	0.41

Statistical significance: *p<0.05; **p<0.01; ***p<0.001

The Model 3 results with the addition of concussion status, previous concussion history, and the interaction of concussion status x previous concussion history are presented in **Table 17**. When accounting for previous concussion history, concussion status was a significant predictor of all outcome measures except for PROMIS Anxiety (γ_{01}=1.09, p=0.08) and PROMIS Depression (γ_{01}=0.66, p=0.19). Further, individuals with a previous history of concussion reported slightly higher scores on all outcome measures except for affective symptoms (γ_{02}=-0.03, SE=0.79) compared to all participants without a previous history of concussion; however, previous history of concussion did not significantly influence any outcome measure scores. Additionally, individuals with a concussion and a history of a previous concussion reported slightly lower PROMIS Anxiety (γ_{03}=-0.25, SE=0.90), affective symptom (γ_{03}=-0.22, SE=1.09), and migraine symptom (γ_{03}=-0.19, SE=1.62) scores and higher PROMIS Depression (γ_{03}=0.05, SE=0.75), cognitive-ocular symptom (γ_{03}=0.29, SE=1.01), and total symptom (γ_{03}=1.23, SE=6.01) scores compared to the rest of the sample. However, the interaction between concussion status and concussion history did not significantly influence outcome measure scores. Finally, as indicated by the ICC values in **Table 17**, there remained a substantial amount of variance attributed to both between and within-person differences.

Table 17. MLM Fixed and Random (Variance Components) Effects for Momentary Outcome Measures, Concussion Status, Previous Concussion History, and the Interaction of Concussion Status x Previous Concussion History (Model 3).

Variable	Fixed Effects				Random Effects		
	γ_{00} (SE)	γ_{01} (SE)	γ_{02} (SE)	γ_{03} (SE)	Between Person Variance (SE)	Within Person Variance (SE)	ICC
PROMIS Anxiety	0.38 (0.42)	1.09 (0.61)	0.35 (0.65)	-0.25 (0.90)	1.74 (0.17)	1.80 (0.05)	0.49
PROMIS Depression	0.11 (0.34)	0.66 (0.51)	0.42 (0.54)	0.05 (0.75)	1.44 (0.14)	1.47 (0.04)	0.50
Affective Symptoms	0.75 (0.50)	1.56 (0.74)*	-0.03 (0.79)	-0.22 (1.09)	2.11 (0.20)	2.12 (0.06)	0.50
Migraine Symptoms	0.30 (0.75)	5.36 (1.10)***	0.31 (1.18)	-0.19 (1.62)	3.09 (0.34)	3.52 (0.09)	0.47
Cognitive Ocular Symptoms	0.03 (0.46)	1.68 (0.68)*	0.42 (0.73)	0.29 (1.01)	1.96 (0.20)	1.84 (0.05)	0.52
Total Symptoms	2.08 (2.77)	14.80 (4.07)***	0.91 (4.35)	1.23 (6.01)	11.64 (1.20)	11.66 (0.30)	0.50

Statistical significance: *p<0.05; **p<0.01; ***p<0.001

Comparisons of model fit for Model 2 and Model 3 when accounting for previous history of concussion are presented in **Table 18**. For all outcome measures the AIC and BIC values were larger for Model 3 when compared to Model 2. Additionally, all likelihood ratio tests were insignificant, indicating that the addition of previous concussion history as a predictor variable did not improve model fit and thus may not explain meaningful differences between outcome measures.

Table 18. Comparison of Model 2 and Model 3 with Previous History of Concussion Added as Predictor.

Variable	**Model 2**		**Model 3**		**Likelihood ratio**	
	AIC	**BIC**	**AIC**	**BIC**	**χ2**	***p*-value**
PROMIS Anxiety	3437.38	3456.20	3441.06	3469.28	0.32	0.85
PROMIS Depression	3118.09	3136.91	3120.68	3148.90	1.41	0.49
Affective Symptoms	3707.99	3726.80	3711.87	3740.10	0.11	0.95
Migraine Symptoms	4521.87	4540.69	4525.79	4554.02	0.08	0.96
Cognitive Ocular Symptoms	3487.36	3506.18	3489.99	3518.21	1.37	0.50
Total Symptoms	6494.26	6513.08	6497.95	6526.18	0.31	0.86

Statistical significance: *$p<0.05$; **$p<0.01$; ***$p<0.001$

The Model 3 results with the addition of concussion status, sport type (i.e., contact or non-contact), and the interaction of concussion status x sport type are presented in **Table 19**. When accounting for sport type, concussion status was only a significant predictor of migraine symptoms (γ_{01}=3.28, p=0.02). Further, individuals who play a contact sport reported slightly lower scores on all outcome measures when compared to all other participants who play a non-contact sport; however, sport type did not significantly influence any outcome measure scores. Additionally, athletes with a concussion and who played a contact sport scored reported higher scores for all outcome measures; however, the interaction between concussion status and sport type was only a significant predictor of PROMIS Depression (γ_{03}=1.62, p=0.04) and cognitive-ocular symptom scores (γ_{03}=2.49, p=0.02). Finally, as indicated by the ICC values in **Table 19**, there remained a substantial amount of variance attributed to both between and within-athlete differences.

Table 19. MLM Fixed and Random (Variance Components) Effects for Momentary Outcome Measures, Concussion Status, Sport Type, and the Interaction of Concussion Status x Sport Type (Model 3).

Variable	Fixed Effects				Random Effects		
	γ_{00} (SE)	γ_{01} (SE)	γ_{02} (SE)	γ_{03} (SE)	Between Person Variance (SE)	Within Person Variance (SE)	ICC
PROMIS Anxiety	1.08 (0.59)	-0.20 (0.81)	-0.78 (0.69)	1.70 (0.96)	1.70 (0.16)	1.80 (0.05)	0.49
PROMIS Depression	0.87 (0.49)	-0.41 (0.67)	-0.83 (0.58)	1.62 (0.80)*	1.41 (1.33)	1.47 (0.04)	0.49
Affective Symptoms	1.07 (0.72)	0.62 (0.99)	-0.47 (0.85)	1.17 (1.18)	2.10 (0.20)	2.11 (0.06)	0.50
Migraine Symptoms	0.82 (1.04)	3.28 (1.44)*	-0.56 (1.23)	2.86 (1.71)	2.98 (0.33)	3.52 (0.09)	0.46
Cognitive Ocular Symptoms	0.62 (0.63)	0.13 (0.87)	-0.59 (0.75)	2.49 (1.04)*	1.86 (0.19)	1.84 (0.05)	0.50
Total Symptoms	4.31 (3.84)	7.38 (5.30)	-2.63 (4.55)	11.59 (6.31)	11.20 (1.67)	11.66 (0.30)	0.49

Statistical significance: **p*<0.05; ***p*<0.01; ****p*<0.001

Comparisons of model fit for Model 2 and Model 3 when accounting for sport type are presented in **Table 20**. For all outcome measures except for cognitive-ocular symptoms, Model 2 was a better fit. While the AIC for Model 3 for cognitive-ocular symptoms (AIC=3484.20) was less than the Model 2 value (AIC=3487.36) and the likelihood ratio test was significant ($\chi2$=7.16, *p*=0.03), the Model 3 BIC value (BIC=3512.43) was greater than the Model 2 value (BIC=3506.18). Hence, these inconclusive results suggest that Model 2 is a better fit for all outcome measures and including sport type as a predictor does not significantly improve the model fit.

Table 20. Comparison of Model 2 and Model 3 with Sport Type Added as Predictor.

Variable	Model 2		Model 3		Likelihood ratio	
	AIC	**BIC**	**AIC**	**BIC**	**$\chi 2$**	***p*-value**
PROMIS Anxiety	3437.38	3456.20	3438.27	3466.50	3.11	0.21
PROMIS Depression	3118.09	3136.91	3118.06	3146.28	4.03	0.13
Affective Symptoms	3707.99	3726.80	3710.94	3739.17	1.04	0.59
Migraine Symptoms	4521.87	4540.69	4522.01	4550.24	3.86	0.15
Cognitive Ocular Symptoms	3487.36	3506.18	3484.20	3512.43	7.16	0.03*
Total Symptoms	6494.26	6513.08	6493.87	6522.10	4.38	0.11

Statistical significance: *$p<0.05$; **$p<0.01$; ***$p<0.001$

CHAPTER 5 : DISCUSSION

5.1 **Overview**

There were three primary specific aims of this study: 1) to evaluate the evidence of the psychometric properties of momentary psychological HRQoL assessments (the PROMIS-SF Anxiety and PROMIS-SF Depression) administered via daily text messages from a novel, EMA platform, ReCoUPS in healthy college-aged individuals, 2) to assess the acceptability, feasibility, and usability of ReCoUPS to remotely monitor fluctuations in affective symptoms and psychological HRQoL throughout concussion recovery, and 3) to examine the within-athlete and between-athlete variance in affective symptoms and psychological HRQoL throughout concussion recovery. Results from specific aim 1 supported the corresponding hypothesis and revealed that momentary versions of the PROMIS-SF Anxiety and PROMIS-SF Depression were valid and reliable methods of assessing psychological HRQoL daily. The hypothesis for specific aim 2 was also supported as results indicated that ReCoUPS is an acceptable and feasible method of remotely monitoring affective symptoms and psychological HRQoL throughout concussion recovery. College-aged athletes with concussions also reported the usability of the platform to do this. Finally, the hypothesis for specific aim 3 was also supported as concussion status was a significant predictor of all outcome measures (i.e., psychological HRQoL, affective symptoms, and all other SCAT6 symptom clusters) with athletes with a concussion reporting worse symptoms and psychological HRQoL than healthy matched controls. Additionally, variance was almost equally explained by both within-athlete and between-athlete differences, indicating that athletes with a concussion have symptoms that change day-to-day throughout recovery and each athlete's symptoms vary from athlete to athlete. Finally, this study also found that potential confounding variables supported by some current literature such as sex,[72,222-228] previous concussion history,[6,125] and sport[8,125,229] type did not significantly predict any daily symptom reports or variance in symptoms.

5.2 **Evidence of Psychometric Properties of Momentary Psychological HRQoL Assessments via ReCoUPS Survey Text Messages in Healthy Individuals**

To our knowledge, this is the first study to evaluate evidence of the psychometric properties of the PROMIS-SF Anxiety and the PROMIS-SF Depression in a population of college-aged athletes and for repeated measures using EMA. PROMIS measures are generally preferred when assessing patient reported outcomes, including psychological HRQoL, due to their precision and having fewer items than conventional measures, alleviating respondent burden while maintaining acceptable reliability and validity.[230] Other studies assessing HRQoL following concussion have utilized comparable measures including the PROMIS Pediatric-25 Profile,[5] the Short Form-36 Version 2.0,[1] and Short Form-12 Version 2,[6] however; these forms are not specific to psychological HRQoL and include 12 items or more, requiring participants to respond to more questions. Additionally, these forms have yet to be validated specifically in populations with a concussion and ask participants to reflect on their HRQoL in general or over the past few days.

For the present study, to assess psychological HRQoL in real time, we needed to modify the language from “recalled” assessments to “momentary” assessments. Hence, we ensured that the modified “momentary” versions of the PROMIS-SF Anxiety and PROMIS-SF Depression were truly measuring their respective outcomes (i.e., autonomic arousal and experience of threat; low levels of positive affect)[203] in our present population. The results of the present study revealed that in a population of healthy college-aged current and recent athletes, momentary assessments of PROMIS-SF Anxiety (α=0.80) and PROMIS-SF Depression (α=0.91) both demonstrated acceptable reliability. This is consistent with a large methodological research study validating the traditional (i.e., "recalled") PROMIS-SFs where both measures demonstrated acceptable reliability (α>0.90),[204] indicating that our momentary versions have preserved consistency and reproducibility. Further, to assess the validity of the momentary assessments of these measures, we compared average momentary responses to those obtained by the traditional recalled version at the study closure visit. This method is comparable to other studies using EMA in TBI research.[20,231] Prior to agreement coding, both PROMIS-SF measures demonstrated excellent agreement with their corresponding recalled measures and following agreement coding, both measures demonstrated moderate agreement with their corresponding recalled measures. While this further confirm the validity of the momentary assessment of these measures, the slight change in agreement between the two statistical methods (i.e., ICCs and Cohen's Kappa) is likely attributed to the dichotomous nature of the recoded data, reduction in variability of the outcome, and not accounting for the severity of the outcome measures (i.e., symptoms).[232-234] However, our findings add supporting evidence for a reliable and valid inventory to measure momentary assessments of psychological HRQoL.

We also correlated the momentary PROMIS measures with all SCAT6 symptom clusters for healthy individuals (affective, migraine, cognitive-fatigue) to ensure that the measures were truly capturing their intended outcomes. We found that both PROMIS measures were significantly correlated with all SCAT6 symptom clusters and total symptom severity, but more specifically, they were both strongly correlated with the affective cluster. As previously noted, affective symptoms are conditions or disorders which affect a person's emotional and psychological well-being, including anxiety and depressive symptoms (e.g., nervous or anxious, irritability, more emotional, trouble falling asleep).[10] Therefore, our findings support that the

PROMIS-SFs meant to measure psychological HRQoL, specifically anxiety and depression outcomes, are strongly associated with symptoms representing similar psychological well-being outcomes.

This evidence of the psychometric properties of the PROMIS-SFs administered via ReCoUPS daily text messages is also supported in the observed acceptability and perceived usability of ReCoUPS by the participants in this specific aim. We found that most participants (n=80, 86.02%) completed over 70% of daily ReCoUPS surveys while only 5 participants (5.34%) completed 50% or less of daily surveys. While participants were receiving some form of minimal remuneration (i.e., $15 or extra credit in a KIN course) for their participation in this study, qualitative responses on the ReCoUPS User Feedback Survey indicated that most participants responded to the surveys for the benefit of the research and because they were easy to do (n=32, 80%). This provides additional support for the ReCoUPS approach as Weibe and colleagues[21] observed that 82% of their participants with a concussion responded to more than 80% of daily prompts. For this study, participants were remunerated; however, the remuneration strategy was not made clear.

Our approach in specific aim 1 was designed to reflect the use of ReCoUPS to remotely monitor symptoms and psychological HRQoL in real time throughout concussion recovery. Overall, the results ensure the reliability, validity, acceptability, and usability of measuring psychological HRQoL using ReCoUPS in a healthy college-aged athlete population. Further, these results contribute to the growing body of literature examining the use of EMA or ambulatory assessments to remotely monitor symptoms and mental health outcomes,[189,192,235-237] specifically in concussion and TBI populations.[19-21,231,238-241] In turn, this lays the foundation for evaluating the usability of ReCoUPS within a comparable population diagnosed with a concussion to help researchers and clinicians alike to understand injury severity and outcomes and streamline effective and targeted treatments.

5.3 Acceptability, Feasibility, and Usability of ReCoUPS to Remotely Monitor Fluctuations in Affective Symptoms and Psychological HRQoL throughout Concussion Recovery

Specific aim 2 of this dissertation evaluated the acceptability, feasibility, and usability of ReCoUPS as a remote symptom monitoring tool in college-aged athletes with a concussion. Results from this longitudinal repeated-measures study indicate that ReCoUPS is an acceptable and feasible method of monitoring symptoms and psychological HRQoL acutely post-injury. More specifically, most college-aged athletes with a concussion (n=24, 66.67%) responded to over 70% of the ReCoUPS daily surveys and momentary assessments of psychological HRQoL demonstrated fair to excellent agreements with traditional recalled measures. Heat plots visualized symptom fluctuations throughout recovery, with most participants (n=26, 72.2%) experiencing symptom severity changes that gradually decreased over time. Our findings support the growing body of evidence regarding the feasibility of EMA and ambulatory assessments to measure real time concussion outcomes and reflect the need to integrating remote symptom monitoring into concussion care. Furthermore, the ease of use of ReCoUPS suggests that daily survey text messages may be a preferred method of monitoring symptoms, highlighting the potential for text messaging-based EMA to enhance concussion management and treatment.

Results from our study support previous evidence that demonstrates ReCoUPS as an acceptable and feasible method of remotely monitoring post-concussion symptoms throughout recovery.[20] Our results are also consistent with additional studies which have found other EMA methodologies, specifically mobile applications, as acceptable and feasible remote symptom monitoring tools for concussion and brain injury populations.[19,231] For example, Sufrinko and colleagues evaluated the usefulness of an EMA application, Ilumivu, to assess post-concussion symptoms and recovery outcomes in 20 adolescent athletes within 72 hours post-injury to 6-18 days post-injury. The application prompted athletes to report their symptoms and activity levels 3 times per day and findings revealed an average response rate of 50.4% per participant and symptom severity significantly decreased throughout recovery ($\beta = -0.37$, 95% CI: −0.4 to −0.3, $p<0.001$). Similarly, to further support findings in existing literature, in our specific aim 2, we reported evidence of variability of daily momentary assessments of post-concussion symptoms and psychological HRQoL with wide ranges and standard deviations of severity scores and favorable response rates.

We also found that momentary assessments of psychological HRQoL were strongly and significantly correlated with all SCAT6 symptom clusters and specifically affective symptoms, indicating that the momentary psychological HRQoL inventories were measuring their intended constructs in college-aged athletes with a concussion. This was further supported by the acceptable reliability of both momentary PROMIS-SFs and agreement with traditional recalled versions of the inventories. When evaluating the feasibility and validity of a mobile health (mHealth) system for EMA of mood-related symptoms once per day in adults with TBI over an 8 week period, Juengst et al.[231] reported a compliance rate of 73.4% and strong correlations between momentary assessments and traditional telephone-based interviews of outcome measures (r_s= 0.81-0.97); however, it was unclear if participants were remunerated for completing study procedures. Thus, the findings from our study contribute to the growing body of literature supporting the reliability and validity of EMA measures. Additionally, descriptive statistics of the momentary assessments of the PROMIS-SFs indicated that there was a wide range and slight variance of total average scores, suggesting that future research or clinical settings may consider assessing other patient reported outcomes in addition to traditional concussion symptom reporting tools when using EMA.

The findings of specific aim 2 also support the EMA methodology which ReCoUPS uses (i.e., SMS text messaging) to remotely monitor concussion symptoms in college-aged athletes. As previously mentioned, the growing body of literature in EMA methodologies for post-concussion or post-TBI care heavily focuses on smartphone applications.[19,231,241] In these studies, participants were required to download a smartphone application to their personal devices or those without access to a smartphone were provided one by the study team. While downloading an application imposes minimal participant burden and in some instances ease of use was reported,[231] ReCoUPS eliminates this step entirely by delivering survey questions directly via text message. Additionally, ReCoUPS requires only a standard text messaging plan, whereas smartphone applications may necessitate access to a cellular data network or Wi-Fi. College-aged athletes with a concussion in the present study indicated the ease of use of the platform as most participants (>65%) felt that it was beneficial to concussion care, they would recommend it to others to report their concussion symptoms, and that it accurately captured symptoms and feelings. However, while ReCoUPS presents a theoretically promising approach, certain feedback did not fully support its effectiveness. Specifically, 12 (70.6%) participants reported concerns such as "the text messages came too slow" which may have been related to technical issues described further in the limitations section. In addition, two of 17 (11.8%) participants suggested a preference to "send multiple text messages at once for bulk response," and three provided a suggestion to "use an app that sends notifications instead of text messages" (17.6%). However, targeted bug fixes such as eliminating delays between survey texts or multiple questions being sent at once might improve user experience and preferences for this methodology to report concussion symptoms daily. Additionally, while the results of this study indicated text messaging as a favorable method of remotely monitoring post-concussion symptoms, we were unable to compare our methodology to application based assessments. Therefore, future implementation research with ReCoUPS may be warranted to determine whether survey texts are truly preferred over a smartphone application for symptom monitoring.

Unlike other studies,[19,231,239,241] we only prompted participants to respond to daily symptom reports and psychological HRQoL inventories once per day throughout their concussion recovery. For example, Sufrinko and colleagues[19] examined if symptoms significantly varied at different times of the day. Three symptom clusters and total symptom severity were assessed, but it was revealed that only cognitive-migraine-fatigue symptoms were significantly higher in the morning compared to other times of the day.[19] Additionally, an overall response rate of 52.4% (n=1,155) was reported with no association found between response rate and time of day.[19] Moreover, in a previous study utilizing ReCoUPS, Wiebe and colleagues[20] administered symptom reports 3 times per day finding that symptom scores were, on average, 1.2 points significantly higher in the morning versus the afternoon, 0.9 points significantly higher in the morning versus the evening, and 0.3 points, but not significantly, higher in the afternoon versus evening. Although symptoms appeared to be slightly worse in the morning, these differences were small and may not be clinically meaningful. Further, while the overall response rate was 86.7%, 42.7% of participants completed the surveys once per day, 34.7% completed the surveys twice per day, and 22.6% completed all three prompts per day. However, in this study an association between response rate and time of day was not analyzed.[20] Therefore, our decision to prompt athletes once per day at their preferred time was justified, as it reduced participant burden while still capturing affective symptoms and psychological HRQoL reports. These findings suggest that for remote post-concussion symptom monitoring, a single daily report may be sufficient.

The results of specific aim 2 further support our initial hypotheses that ReCoUPS is an acceptable, feasible, and usable method for remotely monitoring post-concussion symptoms and psychological HRQoL in real time daily throughout recovery in college-aged athletes with concussion. As the findings of this specific aim build upon those of specific aim 1, which sought to provide evidence of the psychometric properties and usability of ReCoUPS in healthy college-aged individuals to remotely monitor symptoms and psychological HRQoL, we also again lay the groundwork for our specific aim 3. Our findings provide evidence to evaluate the variance, or fluctuations, of daily symptoms and psychological HRQoL in college-aged athletes with a concussion and healthy matched controls to provide clinical recommendations for the use of EMA in concussion care and management to improve recovery outcomes.

5.4 **Within-Athlete and Between-Athlete Variance in Affective Symptoms and Psychological HRQoL throughout Concussion Recovery**

The purpose of specific aim 3 of this dissertation was to determine changes, or fluctuations, in affective symptoms and psychological HRQoL throughout concussion recovery using the EMA platform, ReCoUPS. We hypothesized that athletes with a concussion would demonstrate significant within-athlete changes in these outcomes throughout concussion recovery in addition to between-athlete changes when compared to healthy age, sex, and sport matched controls. To match our 36 college-aged athletes with a concussion, we enrolled 34 controls with approximately two-thirds who responded to over 70% of daily ReCoUPS surveys. When examining the within-athlete and between-athlete variance of all outcome measures, we found that for the null model (i.e., model 1), for all outcome measures, the average score was significantly different than 0 and most of the variance was explained by between-athlete differences. This suggests that, on average, all participants reported measurable symptoms (i.e., SCAT6 symptom clusters, total symptoms, and PROMIS-SF outcomes) and most of the variance is attributed to different types of participants reporting different symptoms. Likelihood ratio tests also confirmed that MLM was an appropriate approach to this data as random effects significantly improved the model, suggesting the MLM would capture both individual trajectories and population-level trends. Hence, for model 2, concussion status was added revealing that for all outcome measures, participants with a concussion reported significantly higher mean scores than healthy matched controls, indicating that symptom severity is different between athletes. Further, within-athlete differences accounted for a large portion of the variance for all outcome measures, indicating that symptoms changed day-to-day for each athlete. Finally, when predictor variables (i.e., sex, sport type, concussion history) were added to the model (model 3), effects did not significantly vary. All comparisons of model fit assessments indicated that model 2 was the best fit for the data. Therefore, our hypotheses were supported and there was a substantial amount of within-athlete variance of affective symptoms and psychological HRQoL throughout concussion recovery and athletes with a concussion demonstrated worse symptoms than their healthy matched controls.

Our findings are supported by a substantial body of growing literature related to concussion symptom burden when compared to healthy controls and contribute meaningfully to this expanding field. Several studies have explored differences between individuals with a concussion and healthy matched controls related to post-injury symptoms of anxiety, depression, mood disturbances, and HRQoL.[142,242-244] The inclusion of a control group in concussion research enhances the generalizability of findings by ensuring that changes in mood, mental health, and psychological outcomes are specifically attributable to the injury rather than individual differences or external factors. For example, Covassin et al.[142] examined state and trait anxiety throughout concussion recovery compared to uninjured matched controls by assessing anxiety within 72 hours of injury, five days post-injury, and within two days after FMC, yielding that state anxiety (i.e., related to a specific event) was higher in the concussion group than controls across all time points. Our present findings support significantly higher anxiety symptoms in athletes with concussion compared to controls on average when measured daily throughout recovery. Moreover, Walton and colleagues[244] compared mood, psychological, and behavioral HRQoL differences between concussed and controls at 72 hours post-injury, 7 days after the first assessment, and following symptom resolution. Results revealed that sleep disturbance was significantly greater in concussed athletes at the first assessment and stigma was significantly higher in concussed athletes at all time points, further endorsing the observed heightened affective symptoms in the present study. Although the aforementioned studies support the finding that individuals with concussion experience a greater symptom burden than healthy controls throughout recovery, they do not provide insight into whether and how these symptoms fluctuate over time. Findings from this specific aim address this gap, as our results suggest that between- and within-athlete variability underscores the need for daily symptom monitoring.

Specific aim 3 sought to examine whether and how psychological HRQoL varies throughout concussion recovery. This hypothesis was based on existing research demonstrating that concussion significantly impacts overall health and well-being, or HRQoL.[13] This likely can be explained in part by the results of specific aim 2, which revealed significantly strong correlations between momentary psychological HRQoL assessments and affective symptoms.

Affective symptoms, such as feelings of sadness and irritability, can contribute to limitations related to school, work, or activity and sport, which in turn may elicit negative emotional responses in the athlete. These negative emotional responses then influence impaired overall health and well-being, reinforcing the complex relationship between concussion and psychological HRQoL. This relationship is heavily dependent on the interaction of internal and external factors that shape emotional responses in an athlete's natural environment, which can dynamically change based on circumstances in their natural environment. Our findings align with previous research showing that HRQoL is worse in the acute phase of concussion recovery.[1,3-6,23] Several of these studies have assessed HRQoL at various timepoints throughout concussion recovery, such as at three days, 10 days, and at RTP[5] or 24-48 hours post-injury, at symptom resolution, RTP, and 6-months post-injury.[6] While infrequent and retrospective assessments have revealed nonlinear recovery trajectories for these outcomes, we are unable to truly understand the day-to-day changes throughout recovery. The results of the present study confirm that in fact, there is significant between- and within-athlete variance of psychological HRQoL daily throughout recovery. Understanding these daily variations are crucial for the proper care of athletes post-concussion.

Following the addition of concussion status to our model 2 to determine between- and within-athlete differences for concussions and matched controls, we adjusted for athlete-level predictors (i.e., sex, previous history of concussion, and sport type) in model 3 to determine their effects on our outcome variables. Additionally, by examining the interaction of concussion status and athlete-level predictors, we examined if the athlete-level predictors' effect on the outcome variables changed over time. Our results indicated that when adjusting for athlete-level predictors, they did not have a significant effect on post-concussion symptom cluster severity, total symptom severity, or worse psychological HRQoL. That is, there were no individual differences between males and females, contact sport and noncontact sport athletes, or individuals with or without a history of concussion in the variability of symptom severity throughout concussion recovery. While previous literature has indicated that athlete-level predictors may influence concussion recovery outcomes due to several factors (e.g., physiological differences and differences in symptom perception between males and females, increased injury exposure and sport culture in contact versus noncontact sport, increased neurobiological vulnerability and psychological influences in individuals with a history of concussion),[125,222] it is possible that the symptom variability observed in the present study is driven more by individual differences in athletes rather than group differences. This is supported by our observed substantial variance attributed to within-person differences in models 2 and 3. This implies that it is likely that individual differences such as coping mechanisms,[243] stress response,[245,246] or athletic identity[247] may contribute more to daily symptom fluctuations throughout concussion recovery than demographic or sport related differences. Clinicians should continue to be mindful of individual characteristics of their athletes when utilizing daily symptom monitoring and providing concussion care.

One possible athlete-level (or between-person level) predictor commonly included in EMA MLM analyses but not examined in the present study is the duration of enrollment in EMA assessments (i.e., time).[198] Often, EMA studies will instruct participants to complete surveys for a specific amount of time to examine temporal dynamics of experiences, behaviors, and symptoms in real-world settings.[192-194] However, in the present study, time was not considered an independent variable. Athletes were asked to complete the daily ReCoUPS surveys every day throughout their concussion recovery, which was dependent upon their symptom severity and progression through their RTP protocol.[27] Additionally, time could not be initially fixed in this study as our results in specific aim 2 revealed that concussion recovery was highly variable across athletes. Thus, in the present study it was not appropriate to examine time as a predictor of fluctuations in concussion symptoms and psychological HRQoL throughout recovery due to the reverse causality relationship between symptom severity and duration of recovery. Therefore, future studies should consider examining the influence of symptom burden as a predictor of recovery time.

5.5 **Clinical Implications**

The evidence provided from this specific aim indicates that athletes with a concussion have symptoms that significantly vary day-to-day throughout recovery and that each athletes' symptoms may be different. The methodology of utilizing EMA to monitor concussion symptoms in real time shows promise, as supported by the extant literature and the results of the present study. Additionally, daily symptom monitoring offers significant clinical benefits, especially due to the stepwise and gradual return-to-activity protocols currently recommended. However, recommendations for concussion management and recovery criteria remain highly diverse.[27,248,249] For example, for RTS, the Concussion in Sport Group recommends a six step strategy starting with a brief rest period followed by gradual introduction of light exercise and sport-specific training as symptoms permit,[27] while a recent systematic review revealed high variation in initial resting period after injury, the implementation of sport-specific training drills, and the time needed to complete a protocol before returning to competition.[248] Moreover, definitions of clinical recovery from concussion differ substantially, which is dependent on various factors, including returning to normal physiological responses during exercise, return to normal and physical cognitive function, self-reported symptom resolution, and bias towards clinical decisions.[27,117,250-252] Despite these discrepancies, one consistent theme in the literature is the underscored importance of personalized assessment and management plans tailored to the individual's specific circumstances and the context of their activities. Remote daily symptom monitoring, specifically with ReCoUPS, provides clinicians with a powerful tool to track symptoms in real-world contexts, allowing for more informed, tailored decision-making in concussion management, an approach strongly supported by our findings.

As previously noted, concussion has a heterogenous symptomology, as supported by our findings, and requires a multifaceted approach to care. Daily symptom monitoring also provides clinicians with the information necessary to make decisions about precisely which treatments may be required for a given athlete based on their reported symptoms. Our results indicated that all SCAT6 symptom clusters (i.e., affective, cognitive-ocular, and migraine), total symptoms, and psychological HRQoL all varied significantly throughout concussion recovery. This further supports the need for a multifaceted approach to treatment and intervention.[27,253] By identifying specifically which symptoms an athlete is reporting, clinicians can streamline the prescription of vestibular and active rehabilitations or psychological interventions.[27,117,120,252,253] Furthermore, early intervention may improve post-concussion outcomes such as eliminating risk for persistent post-concussion symptoms or delayed recovery.[254-256]

Relatedly, the ReCoUPS platform provides clinicians with a quick and effective way to review patients' symptoms in real time. **Figures 15** and **16** illustrate the clinician's perspective of the ReCoUPS platform, where they can view their patients' daily symptoms and how they are changing day-to-day. **Figure 15** is a club sport athlete who received infrequent and unstructured care from an athletic trainer due to the athlete not meeting with the athletic trainer regularly. **Figure 16** is an NCAA Division 1 athlete who was receiving regular care from an athletic trainer. These visualizations also reinforce the variability in concussion recovery, highlighting that symptom patterns differ across individuals (e.g., between athletes of different levels of play with different activities of daily living, motivations, or expectations) and may fluctuate throughout recovery, potentially prolonging symptoms. Additionally, they underscore the need for future research examining differences in concussion recovery and outcomes between athletes with consistent access to athletic trainers or clinical care and those without.

Figure 15. Clinician's view of the ReCoUPS platform demonstrating total daily symptom scores daily throughout recovery. Light gray circles indicate incomplete daily assessment. Participant is a club sport male rugby player.

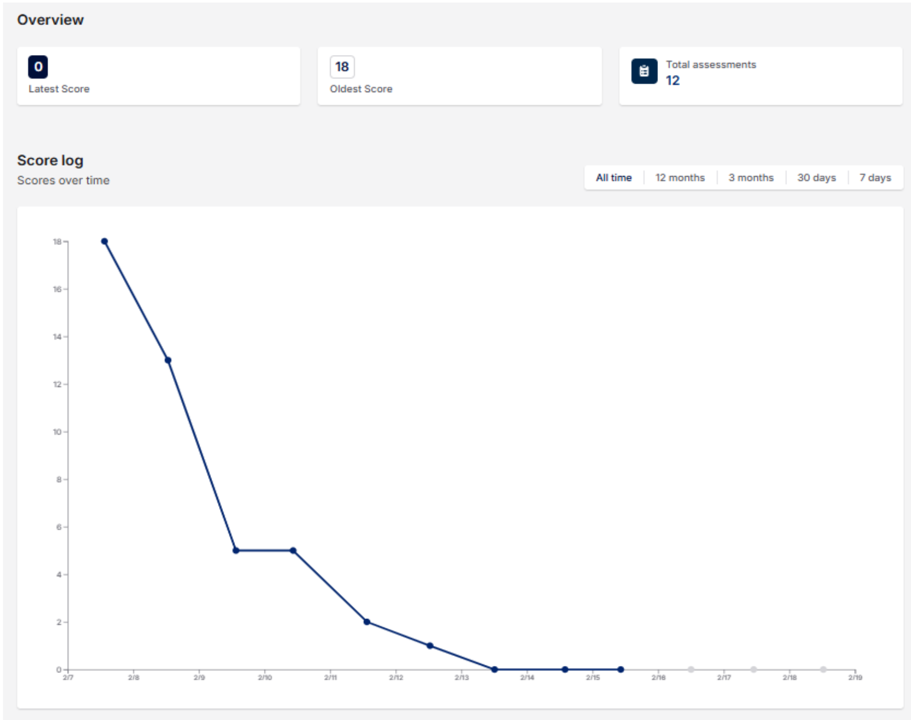

Figure 16. Clinician's view of the ReCoUPS platform demonstrating total daily symptom scores daily throughout recovery. Light gray circles indicate incomplete daily assessment. Participant is a NCAA Division 1 female volleyball player.

Another advantage that remote symptom monitoring presents for clinicians is the ability to capture athletes' symptoms in natural contexts, potentially eliminating dishonest responses. Studies have indicated the issue of under-reporting concussion symptoms due to the pressures from coaches, teammates, parents, and fans.[257-259] If an athlete has the opportunity to report their symptoms through the privacy of their cell phone without environmental pressures, they may be more likely to be honest about their symptoms. This may also explain findings in a previous study utilizing ReCoUPS[20] and other EMA studies,[19] which found that daily symptom reports were better predictors of recovery than traditional in-clinic symptom assessments. Overall, while our results present evidence to support ReCoUPS as a daily symptom monitoring tool, we are also able to provide significant clinical relevance and highlight the need for remote symptom monitoring to improve concussion treatment, management, and outcomes.

5.6 **Limitations**

This study is not without limitations. Firstly, the absences of a baseline measure of psychological HRQoL prevents understanding of how a concussion truly may have impacted an athlete's overall psychological well-being. Future research may consider including baseline assessments of psychological well-being. Additionally, while most athletes have baseline assessments of the SCAT6 symptom checklist, we did not include these in our analyses as it was outside of the goals of our specific aims. However, this might also be considered with future research. Also related to the SCAT6 symptom checklist, the factor structure which informed the symptom clusters used in this dissertation was published in 2020 using a sample of athletes participating in high school, collegiate, and youth sports programs from 2013-2018.[11] Therefore, it is possible that the factor structures may have changed with time or may not be entirely generalized to current samples. While this factor structure was chosen because of the acute timepoint of assessment (i.e., 72 hours post-injury), which is relevant to the study timeline of this dissertation, authors cautioned that it may not be generalized to the subacute or chronic periods after concussion.[11] Future research should consider exploring more current factor structures of the SCAT6 symptom checklist. Furthermore, our study was limited to college-aged athletes participating in varying levels of play; therefore, results may not be generalizable to other age groups such as adolescents. Relatedly, while our sample sizes reached power for the specific aims of this dissertation, we were unable to compare participants' results across different levels of play (e.g., NCAA Divisions I and III, NAIA, club/recreational/intramural sports) and thus access to a health care provider to manage concussion recovery due to a small sample size. Future research might consider examining access to an athletic trainer and prescribed RTP protocols as modifiers of daily symptom variance within athletes.

Another possible limitation in this study is the participant remuneration. For one, we were unable to remunerate all participants across all specific aims equally (i.e., specific aim 1 participants received $15 in Fall of 2023 and extra credit in a KIN class in Fall of 2024, specific aim 2 and 3 all received $150 total for completing study procedures). While remuneration or lack thereof may have influenced participants' willingness to respond to daily surveys, if they attended both of their study visits (i.e., initial visit and study closure visit) to complete study procedures, they received their full promised remuneration, regardless of their response rate to the daily surveys. Therefore, we do not believe that remuneration had a significant impact on our findings. Furthermore, we did examine other factors that may have influenced response rates in our statistical analyses such as sex, level of play of sport, initial symptom severity, and completing the surveys on weekends and/or holidays. While this was not pertinent to the current specific aims, future analyses of this data will consider these factors. Another variable that we did not include in our analyses, which was previously addressed, was time enrolled in the ReCoUPS platform as a predictor of responses. Because of the nature of recovery of concussions and time is a dependent of symptom severity, we could not use it as a predictor variable in our MLMs. However, future research should investigate the association between duration of recovery and symptom burden with symptom burden as a predictor of time to recovery. A common issue with EMA data which we faced was missing data. Missing data in EMA studies can sometimes be imputed; however, as we were unable to determine if data was missing by choice (i.e., the participant did not respond because they did not want to) or due to technical issues (i.e., the participant could not respond), we did not feel that multiple imputations were appropriate. Additionally, we still had sufficient data to observe significant effect sizes and results.

Finally, the most significant limitations of this study were the technical issues which the ReCoUPS platform faced throughout the duration of this study. Case by case issues were tracked in detail, in addition to the solutions provided by the study team, and reported in **Appendix B.** As to be expected with all novel technologies, there were some unforeseen issues. While ReCoUPS was used in studies before this, a different developer supported the current version of ReCoUPS used in this dissertation (Logic Solutions Inc., Plymouth Township, MI). One issue which we faced was daylight savings time (November 5-6, 2023; November 3-4, 2024) which caused some survey text messages to be sent to athletes outside of their selected time frame or more than once per day due to turning clocks back one hour in the eastern time zone. In instances when this happened, participants were instructed to fill out the surveys when they could and if they were prompted twice in one day, to only respond to the first prompt. The second prompt in a day was dropped from the data set. In a few instances, the platform crashed, causing text messages to stop mid survey. We worked with the developer to solve these issues immediately but could not impute responses from impacted participants as they intended to respond. Finally, another bug issue which began around November 1, 2024, caused multiple survey messages to be sent at once, rather than only being sent when a response was recorded for the previous question. Participants were instructed to respond with separate text messages in the order which the questions were received. We were able to confirm that this worked well when matching participants' text message responses to what was recorded in the online platform. If the text messages did not match with what was recorded in the platform, then the participant was dropped from the study. Fortunately, only four of 172 total enrolled participants (2.3%) were forced to be dropped from the study. Therefore, while our response rates should be interpreted with some caution, we still believe that they are an accurate representation of college-age athletes' behavior with the platform. Future research and clinical implementation studies using ReCoUPS, or any technology-based daily symptom monitoring tool, should ensure that potential bugs are resolved prior to the use of the platform, or a feasible troubleshooting protocol is in place.

5.7 **Conclusions**

The purpose of this dissertation was to examine the utility, acceptability, and feasibility of a novel EMA platform, ReCoUPS, to monitor post-concussion symptoms and psychological HRQoL throughout concussion recovery in college-aged athletes. Among healthy college-aged individuals, momentary assessments of PROMIS-SF Anxiety and PROMIS-SF Depression via ReCoUPS demonstrated evidence of strong reliability and validity for monitoring psychological HRQoL. Among athletes with a concussion, ReCoUPS was a feasible, usable, and effective method of tracking psychological HRQoL and affective symptoms throughout recovery. Findings revealed that athletes with a concussion experience significantly higher affective symptoms and psychological HRQoL scores than healthy controls, with both individual (between-athlete) and daily (within-athlete) symptom variability. This dissertation confirms that concussion symptoms not only differ between athletes but can also fluctuate daily throughout recovery. Our results also support ReCoUPS as a remote symptom monitoring tool, providing the necessary groundwork for future implementation studies and clinical use of ReCoUPS.

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APPENDIX A: INSTITUTIONAL REVIEW BOARD (IRB) APPROVAL FORM

MICHIGAN STATE
UNIVERSITY

Initial Study APPROVAL
Revised Common Rule

November 9, 2022

To: Tracey Covassin

Re: **MSU Study ID:** STUDY00008359
IRB: Biomedical and Health Institutional Review Board
Principal Investigator: Tracey Covassin
Category: Expedited 7
Submission: Initial Study STUDY00008359
Submission Approval Date: 11/9/2022
Effective Date: 11/9/2022
Study Expiration Date: **None; however modification and closure submissions are required (see below).**

Title: Monitoring concussion in high school and college athletes using ecological momentary assessment app Recoups

This submission has been approved by the Michigan State University (MSU) Biomedical and Health Institutional Review Board. The submission was reviewed by the Institutional Review Board (IRB) through the Non-Committee Review procedure. The IRB has found that this study protects the rights and welfare of human subjects and meets the requirements of MSU's Federal Wide Assurance (FWA00004556) and the federal regulations for the protection of human subjects in research (e.g., 2018 45 CFR 46, 21 CFR 50, 56, other applicable regulations).

Office of Regulatory Affairs
Human Research Protection Program

4000 Collins Road
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Lansing, MI 48910

517-355-2180
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How to Access Final Documents
To access the study's final materials, including those approved by the IRB such as consent forms, recruitment materials, and the approved protocol, if applicable, please log into the Click™ Research Compliance System, open the study's workspace, and view the "Documents" tab. To obtain consent form(s) stamped with the IRB watermark, select the "Final" PDF version of your consent form(s) as applicable in the "Documents" tab. Please note that the consent form(s) stamped with the IRB watermark must typically be used.

Expiration of IRB Approval: The IRB approval for this study does not have an expiration date. Therefore, continuing review submissions to extend an approval period for this study are not required. **Modification and closure submissions are still required (see below).**

Modifications: Any proposed change or modification with certain limited exceptions discussed below must be reviewed and approved by the IRB prior to implementation of the change. Please submit a Modification request to have the changes reviewed.

APPENDIX B: RECORD OF ReCoUPS EVENTS

Table 21. Record of technology issues and events related to the ReCoUPS platform for each participant impacted.

Participant ID	Participant Type	Enrollment Date	Study Closure Date	Problems?	Platform match texts?	Included in Final Analysis?	Additional Notes
QOL_001	healthy reliability	10/27/2023	11/6/2023	Study team error in enrollment process caused surveys to revert to central time zone during DST and send two surveys on 11/1-11/3 outside of the selected 6 hour time frame	Yes	Yes	Only the first completed assessment was included in the final analysis on days that two surveys were sent to the participant's phone.
QOL_003	healthy reliability	10/30/2023	11/8/2023	Study team error in enrollment process caused surveys to revert to central time zone during DST and send two surveys on 11/1-11/3 outside of the selected 6 hour time frame	Yes	Yes	Only the first completed assessment was included in the final analysis on days that two surveys were sent to the participant's phone.
QOL_005	healthy reliability	10/30/2023	11/7/2023	Study team error in enrollment process caused surveys to revert to central time zone during DST and send two surveys on 11/1-11/3 outside of the selected 6 hour time frame	Yes	Yes	Only the first completed assessment was included in the final analysis on days that two surveys were sent to the participant's phone.
QOL_006	healthy reliability	10/30/2023	11/7/2023	Study team error in enrollment process caused surveys to revert to central time zone during DST and send two surveys on 11/1-11/3 outside of the selected 6 hour time frame	Yes	Yes	Only the first completed assessment was included in the final analysis on days that two surveys were sent to the participant's phone.
QOL_007	healthy reliability	10/30/2023	11/7/2023	Study team error in enrollment process caused surveys to revert to central time zone during DST and send two surveys on 11/1-11/3 outside of the selected 6 hour time frame	Yes	Yes	Only the first completed assessment was included in the final analysis on days that two surveys were sent to the participant's phone.
QOL_008	healthy reliability	10/30/2023	11/7/2023	Study team error in enrollment process caused surveys to revert to central time zone during DST and send two surveys on 11/1-11/3 outside of the selected 6 hour time frame	Yes	Yes	Only the first completed assessment was included in the final analysis on days that two surveys were sent to the participant's phone.
QOL_009	healthy reliability	10/30/2023	11/7/2023	Study team error in enrollment process caused surveys to revert to central time zone during DST and send two surveys on 11/1-11/3 outside of the selected 6 hour time frame	Yes	Yes	Only the first completed assessment was included in the final analysis on days that two surveys were sent to the participant's phone.
QOL_010	healthy reliability	10/30/2023	11/7/2023	Study team error in enrollment process caused surveys to revert to central time zone during DST and send two surveys on 11/1-11/3 outside of the selected 6 hour time frame	Yes	Yes	Only the first completed assessment was included in the final analysis on days that two surveys were sent to the participant's phone.
QOL_011	healthy reliability	10/30/2023	11/7/2023	Study team error in enrollment process caused surveys to revert to central time zone during DST and send two surveys on 11/1-11/3 outside of the selected 6 hour time frame	Yes	Yes	Only the first completed assessment was included in the final analysis on days that two surveys were sent to the participant's phone.
QOL_012	healthy reliability	10/30/2023	11/8/2023	Study team error in enrollment process caused surveys to revert to central time zone during DST and send two surveys on 11/1-11/3 outside of the selected 6 hour time frame	Yes	Yes	Only the first completed assessment was included in the final analysis on days that two surveys were sent to the participant's phone.
QOL_014	healthy reliability	10/30/2023	11/7/2023	Study team error in enrollment process caused surveys to revert to central time zone during DST and send two surveys on 11/1-11/3 outside of the selected 6 hour time frame	Yes	Yes	Only the first completed assessment was included in the final analysis on days that two surveys were sent to the participant's phone.

Table 21 (cont'd).

QOL_015	healthy reliability	10/31/2023	11/8/2023	Study team error in enrollment process caused surveys to revert to central time zone during DST and send two surveys on 11/1-11/3 outside of the selected 6 hour time frame	Yes	Yes	Only the first completed assessment was included in the final analysis on days that two surveys were sent to the participant's phone.
QOL_016	healthy reliability	10/31/2023	11/8/2023	Study team error in enrollment process caused surveys to revert to central time zone during DST and send two surveys on 11/1-11/3 outside of the selected 6 hour time frame	Yes	Yes	Only the first completed assessment was included in the final analysis on days that two surveys were sent to the participant's phone.
QOL_017	healthy reliability	10/31/2023	11/8/2023	Study team error in enrollment process caused surveys to revert to central time zone during DST and send two surveys on 11/1-11/3 outside of the selected 6 hour time frame	Yes	Yes	Only the first completed assessment was included in the final analysis on days that two surveys were sent to the participant's phone.
QOL_018	healthy reliability	10/31/2023	11/8/2023	Study team error in enrollment process caused surveys to revert to central time zone during DST and send two surveys on 11/1-11/3 outside of the selected 6 hour time frame	Yes	Yes	Only the first completed assessment was included in the final analysis on days that two surveys were sent to the participant's phone.
QOL_019	healthy reliability	10/31/2023	11/8/2023	Study team error in enrollment process caused surveys to revert to central time zone during DST and send two surveys on 11/1-11/3 outside of the selected 6 hour time frame	Yes	Yes	Only the first completed assessment was included in the final analysis on days that two surveys were sent to the participant's phone.
QOL_020	healthy reliability	10/31/2023	11/8/2023	Study team error in enrollment process caused surveys to revert to central time zone during DST and send two surveys on 11/1-11/3 outside of the selected 6 hour time frame	Yes	Yes	Only the first completed assessment was included in the final analysis on days that two surveys were sent to the participant's phone.
QOL_023	healthy reliability	11/1/2023	11/9/2023	Study team error in enrollment process caused surveys to revert to central time zone during DST and send two surveys on 11/1-11/3 outside of the selected 6 hour time frame	Yes	Yes	Only the first completed assessment was included in the final analysis on days that two surveys were sent to the participant's phone.
QOL_025	healthy reliability	11/1/2023	11/9/2023	Study team error in enrollment process caused surveys to revert to central time zone during DST and send two surveys on 11/1-11/3 outside of the selected 6 hour time frame	Yes	Yes	Only the first completed assessment was included in the final analysis on days that two surveys were sent to the participant's phone.
QOL_026	healthy reliability			Study team error in enrollment process caused surveys to revert to central time zone during DST and send two surveys on 11/1-11/3 outside of the selected 6 hour time frame	Yes	Yes	Only the first completed assessment was included in the final analysis on days that two surveys were sent to the participant's phone.
ReCoUPS_021	concussion	9/6/2024	N/A	N/A		No	Participant never responded and was withdrawn from the study due to recovery complications
ReCoUPS_025	concussion	9/24/2024	11/5/2024	Participant indicated that they had no issues.	Yes	Yes	
ReCoUPS_030	concussion	10/7/2024	11/18/2024	Multiple messages started on 11/1 and persisted for a few days. Some days were normal, some were multiple messages at a time since then.	Yes	Yes	
ReCoUPS_031	concussion	10/7/2024	11/25/2024	Was getting multiple text messages at a time for about a week starting 11/1 but it went back to normal.	Yes	Yes	
ReCoUPS_037	concussion	10/25/2024	12/9/2024	Multiple messages started on 11/1 but for most days the survey worked normally.	Yes	Yes	
ReCoUPS_035	concussion	10/25/2024	12/5/2024	Participant indicated that some days there were multiple surveys coming at once and some days it was fine starting 11/1.	Yes	Yes	

Table 21 (cont'd.)

ReCoUPS_036	concussion	10/25/2024	11/7/2024	Participant indicated that multiple survey questions started coming on 11/1. On 11/4-11/5 it was normal, but problem persisted 11/6.	Yes	Yes	
ReCoUPS_038	concussion	10/25/2024	11/7/2024	Survey stopped at question 3 on 10/31. Survey started sending multiple questions on Monday 11/4 and that was the only day.	Yes	Yes	
ReCoUPS_039	concussion	10/31/2024	11/19/2024	Multiple texts started on 11/1, but some days it got better.	Yes	Yes	
ReCoUPS_040	concussion	11/4/2024	12/7/2024	Multiple messages came for the first few days, was normal for a few days, then periodically multiple messages would come at once. For the most part though it was fine.	Yes	Yes	Participant was enrolled after the study team became aware of the technical issues that started on 11/1/2024. Participant was instructed to respond to multiple questions at one time.
ReCoUPS_041	concussion	11/12/2024	11/27/2024	Only sent multiple questions at one time on 11/25	Yes	Yes	Participant was enrolled after the study team became aware of the technical issues that started on 11/1/2024. Participant was instructed to respond to multiple questions at one time.
ReCoUPS_042	concussion	11/13/2024	11/27/2024	Multiple messages started on 11/1 and persisted for a few days. Some days were normal, some were multiple messages at a time since then.	Yes	Yes	Participant was enrolled after the study team became aware of the technical issues that started on 11/1/2024. Participant was instructed to respond to multiple questions at one time.
ReCoUPS_043	concussion	11/14/2024	11/26/2024	Multiple messages started on 11/1 and persisted for a few days. Some days were normal, some were multiple messages at a time since then.	Yes	Yes	Participant was enrolled after the study team became aware of the technical issues that started on 11/1/2024. Participant was instructed to respond to multiple questions at one time.
MC_022	healthy matched control	10/14/2024	11/22/2024	Impacted by DST and received 2 texts, one outside of window; only received multiple texts for a few days starting on 11/1 but always received all questions	Yes	Yes	
MC_025	healthy matched control	10/21/2024	11/8/2024	Impacted by DST and received 2 texts, one outside of window; received multiple texts at once every day after 11/1.	Yes	Yes	
MC_026	healthy matched control	10/25/2024	11/7/2024	Impacted by DST and received 2 texts, one outside of window. Participant indicated that the survey started sending multiple questions at a time on 11/1 but the problem persisted through 11/6.	Yes	Yes	
MC_027	healthy matched control	10/25/2024	12/9/2024	Multiple texts started around 11/1, some days were better but for the most part she received multiple messages at once daily.	Yes	Yes	
MC_028	healthy matched control	10/28/2024	12/10/2024	Participant reported during study enrollment that they were receiving multiple survey text messages starting on 11/1. Some days were normal. Participant's surveys also stopped after Question 12 on 11/10.	Yes	Yes	
MC_030	healthy matched control	10/30/2024	11/6/2024	Sometimes it will only send a few of the questions at one time and then will send them later on in the day but other than that it's going great!	Yes	Yes	
MC_031	healthy matched control	10/31/2024	11/19/2024	Multiple survey text messages started 11/1. Participant states that it got better over the past couple of weeks.	Yes	Yes	
MC_032	healthy matched control	11/6/2024	12/10/2024	Multiple messages started on 11/1 and persisted for a few days. Some days were normal, some were multiple messages at a time since then.	Yes	Yes	Participant was enrolled after the study team became aware of the technical issues that started on 11/1/2024. Participant was instructed to respond to multiple questions at one time.

Table 21 (cont'd).

MC_033	healthy matched control	11/11/2024	12/10/2024	Multiple messages were sent at one time just a few days during enrollment	Yes	Yes	Participant was enrolled after the study team became aware of the technical issues that started on 11/1/2024. Participant was instructed to respond to multiple questions at one time.
MC_034	healthy matched control	11/12/2024	11/27/2024	Multiple messages were sent at one time on 11/24 and 11/26	Yes	Yes	Participant was enrolled after the study team became aware of the technical issues that started on 11/1/2024. Participant was instructed to respond to multiple questions at one time.
MC_035	healthy matched control	11/19/2024	12/11/2024	Participant received multiple texts every day throughout her enrollment.	Yes	Yes	Participant was enrolled after the study team became aware of the technical issues that started on 11/1/2024. Participant was instructed to respond to multiple questions at one time.
MC_036	healthy matched control	11/21/2024	12/4/2024	Messages not delivering to platform on 12/2 & 12/3. No notes were taken about multiple messages being sent	Yes	Yes	Participant was enrolled after the study team became aware of the technical issues that started on 11/1/2024. Participant was instructed to respond to multiple questions at one time.
MC_037	healthy matched control	11/21/2024	12/3/2024	Participant was enrolled after 11/1 and indicated that she had the multiple questions coming at one time problem only a few times.	Yes	Yes	Participant was enrolled after the study team became aware of the technical issues that started on 11/1/2024. Participant was instructed to respond to multiple questions at one time.
MC_038	healthy matched control	11/25/2024	12/19/2024	Participant indicated that she did not receive the surveys on 12/5 or 12/6.Surveys resumed for a few days, but due to issues with the developer and service provider Vonage, surveys stopped on 12/12. Participant was unenrolled from the study.	N/A	No	Participant was enrolled after the study team became aware of the technical issues that started on 11/1/2024. Participant was instructed to respond to multiple questions at one time.
MC_039	healthy matched control	11/26/2024	12/10/2024	Multiple messages were sent at one time just a few days during enrollment. Messages stopped on 12/9 after question 6.	Yes	Yes	Participant was enrolled after the study team became aware of the technical issues that started on 11/1/2024. Participant was instructed to respond to multiple questions at one time.
QOL_083	healthy reliability	10/28/2024	11/5/2024	Impacted by DST and received 2 texts, one outside of window. Received multiple texts per day starting on 11/1 and continued every day	Yes	Yes	
QOL_084	healthy reliability	10/30/2024	11/7/2024	Multiple surveys started 11/1 and persisted through 11/6. Survey texts did not match platform, so participant was disincluded from final analysis.	No	No	
QOL_085	healthy reliability	10/30/2024	11/7/2024	Double messages started on 11/1but were normal on 11/6 & 11/7.	Yes	Yes	
QOL_086	healthy reliability	10/30/2024	11/7/2024	Multiple survey messages started on 11/1 and persisted through 11/6.	Yes	Yes	
QOL_087	healthy reliability	10/30/2024	11/7/2024	Multiple surveys started on 11/1 and persisted through 11/7. On 11/7, questions were also out of numerical order. Survey texts did not match platform, so participant was disincluded from final analysis.	No	No	
QOL_088	healthy reliability	10/30/2024	11/7/2024	Multiple surveys started on 11/1 and got worse over the weekend, and participant was trying to answer right away. Problem persisted through 11/6, but 11/6 they were a little better.	Yes	Yes	
QOL_089	healthy reliability	10/30/2024	11/7/2024	Multiple surveys started on 11/1 and persisted through 11/7, sometimes were out of order	Yes	Yes	

Table 21 (cont'd).

QOL_090	healthy reliability	10/30/2024	11/7/2024	problems started 10/31 through 11/6. 11/4 questions stopped after #9	Yes	Yes
QOL_091	healthy reliability	10/30/2024	11/7/2024	Multiple surveys started on 11/2 and persisted through 11/7, sometimes were out of order	Yes	Yes
QOL_092	healthy reliability	10/30/2024	11/8/2024	Multiple surveys started on 11/1 and if participant answered fast enough the survey worked normally.	Yes	Yes
QOL_093	healthy reliability	10/30/2024	11/7/2024	Impacted by DST and received 2 texts, one outside of window.	Yes	Yes
QOL_094	healthy reliability	10/30/2024	11/7/2024	Multiple surveys started on 11/1 and persisted through 11/7, but participant says they better throughout the week.	Yes	Yes
QOL_095	healthy reliability	10/30/2024	11/7/2024	Multiple survey questions started 11/1, but surveys worked normally on 11/4 & 11/5. Problem happened on 11/6.	Yes	Yes
QOL_096	healthy reliability	10/30/2024	11/7/2024	Multiple surveys started on 11/1 and persisted through 11/6, questions were always in order	Yes	Yes
QOL_097	healthy reliability	10/31/2024	11/8/2024	Multiple surveys started on 11/1 but were normal on 11/7. Impacted by DST and received 2 texts, one outside of window.	Yes	Yes
QOL_098	healthy reliability	10/31/2024	11/8/2024	Multiple surveys started on 10/31 but were normal on 11/7.	Yes	Yes
QOL_099	healthy reliability	10/31/2024	11/8/2024	Impacted by DST and received 2 texts, one outside of window. Participant indicated that problem started on 10/31, but it was normal on 11/6 & 11/7	Yes	Yes
QOL_100	healthy reliability	10/31/2024	11/8/2024	Multiple survey questions started 11/1 but were normal on 11/7. Survey texts did not match platform, so participant was disincluded from final analysis.	No	No