Pathways of psychological adjustment to physical health-related stressors: Understanding heterogeneous responses to acute cardiovascular events and the COVID-19 pandemic

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Acute medical events and health-related stressors are complex life events, impacting both body and mind, challenging one’s concept of physical safety, and requiring ongoing psychological adaptation and adjustment. Anxiety sensitivity is an established transdiagnostic risk factor for mental illness; in the context of health-related stressors, physical anxiety sensitivity, or the tendency to interpret somatic sensations as catastrophic and threatening cues, may represent a meaningful mechanism informing longitudinal psychological adjustment and clinical course. This dissertation examines physical anxiety sensitivity and other key mechanisms influencing psychological adjustment following acute health-related events with three empirical studies. Study 1 sheds light on the role of perceived threat and heightened interoceptive threat bias in the development of posttraumatic stress (PTS) symptoms following a suspected acute coronary syndrome (ACS). Studies 2 and 3 share a common computational approach, latent growth mixture modeling (LGMM), allowing for the mapping of trajectory classes of psychological adjustment and highlighting distinct symptom profiles. Using LGGM, Study 2 investigates the role of peritraumatic threat and ongoing cardiac-related anxiety sensitivity on the clinical course of PTS, identifying trajectories of psychological adjustment in the 12-months following a suspected ACS. Study 3 seeks to apply these findings within the context of the
COVID-19 pandemic, exploring the impact of worry and physical anxiety sensitivity on trajectories of depression and anxiety during the first 12-months of the pandemic. Together, these studies provide valuable insights into the naturalistic, heterogeneous course of psychological adjustment to health-related stressors, with particular attention to physical anxiety sensitivity as a potent mechanism driving symptom patterns over time.

**Keywords:** Acute coronary syndrome, COVID-19, posttraumatic stress disorder, depression, anxiety, anxiety sensitivity, enduring somatic threat, trajectories, latent growth mixture modeling
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Chapter 1: General Introduction

We don’t often consider the fragility of our physical form or confront our inherent mortality – that is, until we must. Acute and life-threatening medical events, such as heart attacks, strokes, cancers, and respiratory emergencies, carry all the defining characteristics of a potentially traumatic event, inducing a profound sense of powerlessness in protecting oneself from imminent physical harm and a palpable understanding of one’s own mortality. In light of significant and life-saving medical advances, there is a growing population of individuals who experience acute medical events and survive. Adjustment to a new illness tasks individuals with the process of integrating difficult and nuanced information about the realities of life in their body going forward, including uninvited physical and lifestyle changes, the potential for disease recurrence, and the ever-present risk of premature mortality. Further, many acute medical events result from an existing or indicate a new-onset chronic illness, carrying additional implications.

The process of adjustment to acute health events and chronic illness is complex, requiring biological, behavioral, social, and psychological adaptation (Alonzo, 2000; Scalzo, et al., 2016; Stanton et al., 2007). Particularly for medical events relating to underlying chronic illnesses, which are inherently lifelong, the illness can become inherent to one’s personality and lifestyle, as individuals often must navigate an altered and tenuous relationship with one’s physical body and the reality of corporal impermanence (de Ridder et al., 2008). Medical management of acute medical events and chronic illness is undoubtedly an essential clinical concern; still, these individuals commonly endure a challenging and protracted period of psychological adaptation and adjustment simultaneous to and beyond the acute physical healing process.
The COVID-19 pandemic has expanded our contemporary understanding of the potential scale and severity of physical health-related stressors, serving as an unprecedented and universal symbol of physical risk and mortality, even when compared to prior viral pandemics (Wang et al., 2020). Given the ease of transmissibility, likelihood of severe illness, risk for chronic illness, and immense death toll, the COVID-19 pandemic represents psychological themes quite similar to acute medical events – ongoing and objective physical risk, limited control over ensuring one’s safety, and confrontation with mortality. Of course, the pandemic is distinct in many ways, impacting the nature by which individuals are able to adapt and adjust.

The nature of the virus and subsequent scale of the pandemic allows for community-level observation of individuals’ heterogeneous psychological reactions to an acute health-related stressor. All humans across the lifespan are susceptible to contracting the COVID-19 virus, given the nature of its transmissibility. As opposed to physical health threats impacting a specific population subgroup, the limit of the pandemic’s reach has been ultimately dependent on individual behavior, awareness, and environment (Pecoraro, 2021). In some ways, this sense of extrinsic risk and intrinsic controllability may be empowering, as targeted public health messaging has communicated ways for individuals to mitigate risk through symptom monitoring, mask wearing, social distancing, and vaccination (Brown et al., 2021). However, constant attention to physical health-related risks may confer unintended mental health consequences overtime, due to individual risk perceptions and differing cognitive and affective regulation abilities (Jungmann & Witthöft, 2020; Pepper & Nettle, 2014).

In addition to the overt health-related risks, however, the pandemic’s profound scale of impact has resulted in immense disruptions to society and essential infrastructure. Increasingly conceptualized as a multidimensional stressor, the COVID-19 pandemic has been associated
with myriad psychosocial and systemic impacts, many of which are potential drivers of negative mental health consequences (Bernardini et al., 2021; Breslau et al., 2021; Gruber et al., 2021; Hawes et al., 2021; Kuntz, 2021; Mancini, 2020; Necho et al., 2021; Valiente et al., 2021; Zavlis et al., 2021). Together with the strong public health emphasis on individual control and ownership of risk reduction, the enormous impacts of the pandemic on social systems and community infrastructure creates a complex and highly unique psychosocial stressor.

Despite increasing scientific attention on the heterogeneous process of psychological adjustment to physical health-related stressors, the integral role of mental healthcare and the need for clinical management of psychological sequelae has yet to be fully appreciated in most clinical settings. This clinical translational gap is, in part, the result of a limited understanding of the naturalistic, longitudinal course of psychological adjustment to acute medical events and health-related stressors (Musey et al., 2020). Additionally, despite widespread recognition of the prevalence of mental illness and psychological distress resulting from acute health-related stressors, such as life-threatening medical events and pandemics, less consensus and understanding exists with regard to the underlying psychosocial and regulatory mechanisms at play (de Ridder et al., 2008; Okafor et al., 2021; Petrie & Jones, 2019). Improved understanding of the mechanisms responsible for initiating, sustaining, improving, or worsening the clinical course of adjustment is essential in order to effectively identify, intervene, and educate in clinical settings across levels of care.

1.1 Dissertation Aims

The primary aim of this dissertation is to examine trajectories of psychological adjustment to acute health-related stressors, with particular focus on physical anxiety sensitivity
and other key mechanisms hypothesized to differentially impact mental health. The body of this dissertation consists of three, standalone, empirical studies, included as Chapters 2, 3, & 4. All three included studies examine longitudinal adjustment patterns to health-related stressors, ranging from 1-month outcomes to year-long trajectories of mental health symptoms. Studies 1 & 2 focus on psychological reactions to acute coronary syndrome (ACS), a life-threatening cardiovascular event carrying implications for chronic cardiovascular illness, recurrence, and mortality. Study 3 turns attention to the ongoing COVID-19 pandemic, an aversive and universal public health crisis posing significant risk to physical health and safety.

Unifying the three individual studies, and informed by the Enduring Somatic Threat (EST) model of medically-induced posttraumatic stress disorder (PTSD; Edmondson, 2014), this dissertation also examines a key psychosomatic mechanism—physical anxiety sensitivity. Describing an individual’s propensity to interpret normative physiological signals (i.e., heart rate, respiratory changes, physical discomfort) as threatening cues, physical anxiety sensitivity is a well-established, transdiagnostic risk factor for mental illness shown to differentially impact reactions to health-related stressors (Naragon-Gainey, 2010; Olatunji & Wolitzky-Taylor, 2009; Ong et al., 2006; Schmidt et al., 2006; Wright et al., 2009). Providing the first empirical test of the EST model, Study 1 investigates the role of cardiac-specific anxiety sensitivity on the development and maintenance of ACS-induced PTSD; this study observes the peritraumatic adjustment period, in the 1-month following presentation to the emergency department (ED) for a potential heart attack (Edmondson, 2014; Meli et al., 2017).

Longitudinal trajectory estimates provide a more representative understanding of the natural course of psychological adjustment. Embracing inherent fluctuations in the human response to extreme adversity over time and illustrating heterogeneous symptom patterns,
trajectory analysis provides valuable insight into the clinical course of psychological adjustment (Bonanno, 2012; Galatzer-Levy et al., 2018; Taylor, 2019). Appropriate computational models can account for variability due to important contextual factors, which may attenuate or exacerbate distress, capturing heterogeneity with increased accuracy. Using Latent Grown Mixture Modeling (LGMM), Studies 2 & 3 glean longitudinal trajectory patterns of mental health symptoms in the 12-months following distinct health-related stressors: ED evaluation for a suspected ACS (Meli et al., 2020) and community level exposure to the COVID-19 pandemic. Applying Study 1’s theoretical principles and empirical findings, Studies 2 & 3 further explore the role of physical anxiety sensitivity as a psychosomatic mechanism impacting longitudinal psychological adjustment in the face of physical health-related adverse events.

1.2 Literature Review

The Psychological Impact of Cardiovascular Disease

Cardiovascular disease (CVD), including ACS, remains the leading cause of death in the United States and is among the leading causes of death worldwide (American Heart Association [AHA], 2020; Bertoni et al., 2005). In the US, 26.6 million adults are living with diagnosed, chronic CVDs and there are over 2.2 million emergency hospitalizations each year due to acute cardiovascular events (Blackwell et al., 2014). Approximately half of these hospitalizations result from ACS (Benjamin et al., 2017), a condition where blood flow to the heart is suddenly restricted, often resulting in a heart attack. For many, ACS is a frightening experience associated with significant pain, fear of imminent death, perceived loss of control, and feelings of helplessness (Carmassi et al., 2020; von Känel et al., 2011; Whitehead et al., 2005). Acute
cardiovascular events are also unanticipated, abruptly confronting patients with clear and close reminders of their own mortality (Edmondson, 2014; Ginzburg et al., 2003).

Advances in healthcare have increased survival rates for patients hospitalized for ACS (McManus et al., 2011; Sanchis-Gomar et al., 2016). However, for many, surviving a life-threatening cardiovascular event is not without significant and life-long impacts. For ACS survivors, primary risk of recurrence and mortality remains high, highlighting the critical importance of secondary risk reduction after hospital discharge. Further, among those who survive and receive treatment, heightened distress often continues into the post-discharge recovery period, as patients psychologically and emotionally contend with the realities of chronic illness and increased risk of recurrence and mortality (Alonzo, 2000; Ginzburg et al., 2015; Kutz et al., 1994).

More recently, research has also begun to focus on the ongoing psychological burden impacting survivors of acute CVD events (e.g., Carmassi et al., 2020; Koenen et al., 2017). Due to their sudden onset, unpredictable nature, and acute severity, ACS bears the hallmarks of a traumatic event, capable of inducing a posttraumatic stress reaction (American Psychiatric Association [APA], 2013; Wang et al., 2011). Almost 30 years ago, the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) revised Criterion A for PTSD to include life-threatening illnesses as traumatic events that could induce PTSD (APA, 1994). The DSM-5 defines PTSD as a Trauma- and Stressor-Related Disorder initiated after exposure to a life-threatening, traumatic event; posttraumatic stress (PTS) reactions include psychological distress and impaired functioning due to symptoms related to reexperiencing of the event (i.e. intrusive thoughts and flashbacks), behavioral or cognitive avoidance of event reminders, negative alterations in cognition and mood, and physiological hyperarousal (i.e. increased heart
rate, autonomic activation) in response to reminders of the index event (APA, 2013; Cohen et al., 2009; Shalev et al., 2017).

ACS-Induced PTSD & Health Outcomes

PTSD following life-threatening medical events is a common phenomenon, with estimates indicating approximately 1 in 8 ACS survivors, on average, go on to develop clinically significant PTSD symptoms (Edmondson et al., 2012). However, PTSD following cardiovascular events poses a unique problem for clinicians and survivors, alike, as the consequences of ACS-induced PTSD extend beyond psychological distress. While psychologically debilitating in its own right, PTSD is also prospectively associated with increased risk of CVD event recurrence and mortality (Birk et al., 2019; Edmondson et al., 2012). Thus, whereas all ACS survivors are at high risk for CVD recurrence and mortality, ACS-induced PTS confers yet greater risk.

Regardless of the index event, PTSD has been associated with specific, deleterious health effects that can significantly increase the risk for CVD event recurrence and mortality (Boscarino, 2008; Gradus et al., 2015; Sumner et al., 2015a; Sumner et al., 2015b; Vaccarino et al., 2013). Prolonged exposure to intense psychological stress, characteristic of PTSD, is associated with numerous pathophysiological risk factors for ACS. Through these direct, physiological pathways including chronic inflammation, hypertension, and endothelial dysfunction (Benjamin et al., 2017; Cohen et al., 2009; Hawk et al., 2000; Miller et al., 2001; Sumner et al., 2017; von Kanel et al., 2006; von Kanel et al., 2008; von Kanel et al., 2010), those with PTSD have, on average, double the likelihood for early cardiovascular and all-cause mortality (Boscarino, 2006; Boscarino, 2004; Kubzansky et al., 2007). In light of these established physiological mechanisms, PTSD is recognized as a negative prognostic factor for
those with CVDs, well-known to be associated with coronary heart disease incidence and progression (Akosile et al., 2018; Carmassi et al., 2020; Edmondson et al., 2012; Schoner et al., 2017).

In addition to pathophysiological mechanisms, secondary, behavioral pathways, including maladaptive and avoidant health behaviors resulting from PTS symptoms, indirectly impact known CVD risk factors (Edmondson et al., 2013a; Goldfinger et al., 2014; Koenen et al., 2017). PTSD triggered by acute medical events is associated with decreased medication adherence, an important mechanism of secondary risk reduction and disease maintenance (Kronish et al., 2012; Shemesh et al., 2004; Wasson et al., 2014). In addition, chronic distress can increase tendencies toward behavioral risk factors (i.e., smoking, physical inactivity, poor diet, fragmented sleep, and substance abuse) that are known to increase cardiovascular risk and accelerate disease course (Carmassi et al., 2020, Sumner et al., 2020).

Merging the long-siloed fields of medicine and psychology, psychosomatic research and behavioral medicine have asserted the seriousness of medical event-induced PTSD, particularly for PTSD following ACS. In fact, the current AHA has advised researchers to focus their attention toward psychiatric condition, outside of depression, that may increase risk in patients with ACS (Beer et al., 2020; Lichtman et al., 2014). While research supports that ACS-induced PTSD is an important contributor to risk of recurrence and worse prognosis, comparatively few studies have sought to understand key psychological mechanisms of PTSD following CVD events.
**Psychological Mechanisms Influencing ACS-Induced PTSD**

The increased likelihood of CVD health risk behaviors among individual with PTSD and PTSD’s independent, pathophysiological pathways to CVDs represent a dubious and unfavorable scenario for both physical and mental health outcomes. At present, those with cardiac-induced PTSD are victim to a risk gap, with their psychiatric condition amplifying risk of morbidity and mortality. It is essential for clinicians to implement targeted therapeutic strategies and intervene early. However, it is equally important that interventions and treatment strategies are mechanistically informed in order to effectively reduce public health burden.

PTS may have a unique and independent impact on CVD risk pathways. In the case of behavioral risk factors, studies have shown that maladaptive health behaviors among those with cardiac-related PTSD are largely unrelated to the index event and instead mediated by PTSD symptoms (Alcántara et al., 2014; Breslau et al., 1998; Edmondson et al., 2013a; Kronish et al., 2015). It is important to explore what psychological mechanisms, inherent in symptoms of PTSD, may sustain the behavioral factors and contribute to the physiological CVD risk factors for those with ACS-induced PTSD.

**Interoception & Hyperarousal**

Interoception is a complex neurological process through which individuals gain a sense of their physical bodies. Through a combination of homeostatic and allostatic responses, interoceptive mechanisms support and maintain physiological health. Interoceptive awareness engenders a sense of the physical self and an embodiment through physical sensation. With
interoceptive awareness, we gain the vital ability to recognize irregularities in our physical bodies and engage in behavioral and affective responses that keep us safe.

For approximately one million U.S. adults who develop medically-induced PTSD annually (Sommer et al., 2018), the process of interoceptive awareness is complicated as one’s body is intimately connected to the index trauma. The corporal nature of threat for those with medically-induced PTSD creates clinical nuance, both medically and psychologically. Described in *Criterion E* of PTSD in the DSM 5 as “marked alterations in arousal and reactivity associated with the traumatic event,” hyperarousal is evidenced by hypervigilance and exaggerated startle response (APA, 2013). For those with ACS-induced PTSD, common, normative, and momentary somatic fluctuations can be a source of catastrophic fear and can trigger traumatic stress reactions.

Physiological hyperarousal uniquely complicates interoceptive awareness for those with ACS-induced PTSD. Reexperiencing and hypervigilance, linked to fear-based intrusive memories of the index event or due to ongoing self-monitoring of potentially dangerous somatic sensations, often leads to hyperarousal, or intense, momentary activation of the sympathetic nervous system emblematic of the fight-or-flight fear response. For those with ACS-induced PTSD, the resulting cardiovascular activation (i.e., increased heart rate and blood pressure) along with other somatic experiences of hyperarousal (i.e., dizziness, increased respiration) may be perceived as threatening, reminiscent of their initial medical event reminding patients of their own mortality and fallibility (Edmondson, 2014). Thus, a positive feedback loop emerges with an overall increase in interoceptive attention and an underlying fear of mortality increasing cardiovascular and sympathetic hyperarousal and ongoing, perceived somatic threat. Ongoing interoceptive threat bias toward cardiovascular sensations represents an important psychosomatic
nuance and may play an important role in the development and maintenance of ACS-induced PTSD. The combination of reexperiencing, hypervigilance, and hyperarousal symptoms, along with catastrophic interpretations due to interoceptive threat bias, may uniquely impact ongoing risk and symptom maintenance following ACS.

Creating further complexity, due to autonomic strain caused by continuous hyperarousal activation cycles, enduring somatic threat perceptions may contribute to pathophysiological CVD risk and ACS event recurrence (Seldenrijk et al., 2013). Those with PTSD evidence higher sustained heart rate (HR), which is a well-known, major risk factor for acute cardiac events and increases the risk of mortality in those with pre-existing CVD (Norte et al., 2013; Williamson et al., 2015). PTSD also impacts momentary HR, with frequent peaks following reminders of the index trauma. These frequent HR peaks are perhaps best conceptualized as a physiological sequelae of hyperarousal resulting from PTSD. Hyperarousal’s excessive stress reactivity can also lead to wear and tear on the stress response system. Over time, this can result in hypercortisolism, which reduces the body’s capacity to modulate sympathetic responses (Micieli & Canavero, 2020), further complicating cardiac-related somatic threat perceptions.

Interoceptive threat bias holds increasing promise as a mechanism influencing PTS symptom development after ACS (Otto et al., 2019). In fact, anxiety sensitivity, a transdiagnostic construct describing interoceptive threat bias to anxious arousal sensations, has been widely studied and identified as a mechanism of increased risk for many chronic health conditions (Hornstein et al., 2018). To date, however, scant research has scrutinized the role of interoceptive threat in cardiac-induced posttraumatic stress responses and psychological adjustment. A careful examination of this mechanism and its role in ongoing psychological adjustment is essential for
comprehensive clinical understanding, accurate conceptualization, and targeted intervention for a growing clinical population of ACS survivors and adults living with CVD.

**The Enduring Somatic Threat Model**

Findings have consistently linked acute medical events, and cardiovascular events in particular, to ongoing, intrusive anxiety and PTS symptomology (Gander & von Känel, 2006; Kronish et al., 2012; Whitehead et al., 2005). However, the phenomenological experience of PTSD due to acute cardiovascular events may be different from PTSD due to a discrete, non-medical event. Extant research on survivors of cancer and CVD events instigated discussions on conceptual discrepancies between the traditional PTSD experience and that of medical event-induced PTSD (Gurevich et al., 2002; Kangas et al., 2002). The EST model (Edmondson, 2014) of PTSD due to acute, life-threatening medical events offers a conceptualization of the underappreciated differences between PTSD due to past, discrete/external traumatic events (e.g., combat or natural disaster) and PTSD due to acute medical events that are manifestations of chronic or recurrent disease (e.g., ACS, cancer, or stroke).

The EST model offers that PTSD due to acute, life-threatening medical events hold several unique characteristics distinct from PTSD due to discrete, external traumatic events, such as combat or disaster events, in part due to biased interoceptive awareness. First, whereas external sources of threat can be avoided or ignored, acute health events are unique traumatic experiences because the source of threat is within the body, making it impossible to take space from the trigger to re-establish a sense of safety away from danger. In the context of ACS-induced PTSD, the source of threat – the heart and cardiovascular system – is within and throughout one’s body; taking distance from or escaping the source of threat is not an option.
Second, self-monitoring of cardiovascular and somatic sensations is an essential part of ongoing care following CVD events, as opposed to the innate tendency toward cognitive and behavioral avoidance of sources of threat, fundamental to PTSD diagnostic criteria (Redfern et al., 2009; Smith et al., 2011; Vedin et al., 2012). In ACS-induced PTSD, the index event represents an ongoing, medically valid, and objective source of risk that must be monitored to identify future, potentially life-threatening recurrences. Third, for those who experienced their index event as frightening and painful, continued and medically-necessary hypervigilance toward somatic cues may foster present- and future-oriented traumatic reexperiencing, as opposed to the archetypal past-oriented intrusive memories typically seen in PTSD (Whitaker et al., 2009).

According to the EST model, patients acutely distressed by their index event can become sensitized to normative physical fluctuations and somatic cues, such as perceived increases in heart rate and chest tightening, akin to anxiety sensitization resulting in a fear of cardiac-specific symptoms (Domschke et al., 2010). Individuals without a cardiac history generally ignore these sensations; however, for those who have experienced an ACS event, these cues can initiate a cascade of PTSD-like symptoms including heightened arousal, catastrophic interpretations of interoceptive experience, and intrusive recollections of the index event. Unlike PTSD due to a discrete, non-somatic event, the index event for ACS-induced PTSD often includes the experience of intense chest pain and pressure, along with the objectively verified knowledge that one’s heart functioned improperly, placing one at imminent risk of permanent physical damage or death. Thus, perceptions of normative cardiovascular sensations may be altered, instead perceived as intensely frightening and threatening because of their visceral connection to the index cardiovascular event.
Cardiac-related somatic sensations are also fundamental components of sympathetic nervous system activation. The sympathetic nervous system is responsible for initiating the fight-or-flight stress response, which primarily acts on the cardiovascular system through increased heart rate, blood pressure, and the release of adrenaline through the respiratory system. However, individuals with ACS-induced PTSD are likely to be hypervigilant and highly attuned to cardiac sensations (Edmondson, 2014). Harkening back to their index cardiac event, those with ACS-induced PTSD may be more likely to interpret cardiac sensations as indicators of threat, of develop an interoceptive threat bias, thus lowering the threshold for hyperarousal in the face of normal, somatic cues and cardiovascular variations (Ong et al., 2006). This interoceptive threat bias toward cardiac sensations subsequently increases cardiovascular reactivity, potentially resulting in an inflammatory cycle between sympathetic activation and emotional reactivity (Schiepers et al., 2005; von Kanel et al., 2007).

**Anxiety Sensitivity**

Whereas PTSD is generally considered a disorder of fear memory processing, the EST model suggests the presence of ongoing present and future oriented somatic threat perceptions. The temporality of this interoceptive threat bias may represent an important clinical target and opportunity for intervention. Anxiety sensitivity, or an individual’s propensity to interpret experiences related to anxious arousal as threatening cues, is a transdiagnostic risk factor for mental illness that has been identified as a mechanism of interest in psychological reactions acute stressors (Gallagher, 2017; Manning et al., 2021; Rogers et al., 2021; Schmidt et al., 2021). Similarities between the interoceptive threat bias mechanism described in the EST model and anxiety sensitivity construct provides the opportunity to consider the broader anxiety sensitivity
literature and apply insights to the ongoing exploration of psychological adjustment following acute health-related events (Hornstein et al., 2018; Otto et al., 2018; Reiss et al., 1986).

Anxiety sensitivity is measured using the Anxiety Sensitivity Index – Version 3 (ASI; Taylor et al., 2007), with higher scores indicating higher reactivity to anxious arousal cues. Within the ASI, there are several subscales, categorizing specific types of anxious arousal sensitivity. The ASI physical subscale (ASIp) is uniquely relevant to physical health-related stressors. Physical anxiety sensitivity includes subjective threat perceptions relating to cardiovascular, respiratory, gastrointestinal, and general somatic sensations (e.g., “When I notice my heart skipping a beat, I worry that there is something seriously wrong with me”; “When I feel pain in my chest, I worry that I’m going to have a heart attack”; “When my chest feels tight, I get scared that I won’t be able to breathe properly”).

Providing further promise for the anxiety sensitivity construct as a proxy measure for interoceptive threat bias, numerous studies have examined interventions targeting anxiety sensitivity as a moderator of negative health behaviors (for review, see Hornstein et al., 2018). Given anxiety sensitivity’s transdiagnostic relevance, broad literature base, and proven malleability, physical anxiety sensitivity represents an important clinical and research target. Improving understanding of physical anxiety sensitivity’s role in the longitudinal course of adjustment to acute health-related events may elucidate appropriate points for clinical intervention to support more adaptive psychological reactions over time.

Perceived Threat

Core to the diagnostic criteria of PTSD, the index traumatic experience must invoke an intense stress response due to the individual’s subjective experience of fear and perceived threat
of harm (APA, 2013). Psychological responses to ACS, like anxiety or intense fear during the cardiac event, predict elevated PTSD symptoms (Rocha et al., 2008). The more distressed a patient is in the peritraumatic period, the higher the likelihood of PTS. While a life-threatening cardiovascular event is often frightening, in and of itself, other factors can result in heightened threat perceptions.

Evaluation in an ED setting may result in heightened threat perceptions, compounding the already frightening experience of an ACS event (Birk et al., 2019; White et al., 2017). Exposure and proximity to other critically ill patients and critical care procedures of nearby patients is related to increased PTSD symptoms and worse cardiovascular outcomes (Fishman et al., 2006; Konrad et al., 2017). Particularly in urban environments, crowding in the ED can lead to longer wait times and increased stress among already distressed cardiac patients (Chang et al., 2016; Kellermann, 2006), as well increased risk of long-term cardiac outcomes (Pines et al., 2006; Shen & Hsia, 2011). In ACS patients, ED crowding predicts intense psychological distress and severe PTSD symptoms (Edmondson et al., 2013b).

PTSD occurs as a result of direct or observed threat to life during a traumatic event. Of particular importance to ACS-induced PTSD, this threat is not dependent on objective risk but on subjectively perceived risk (Kronish et al., 2018; Laubmeier & Zakowski, 2004). Millions of adults are evaluated for ACS in emergency departments each year, and nearly half of all patients who present to the ED with symptoms of ACS (chest pain, shortness of breath, left arm pain, documented risk factors for ACS) are not actually having a heart attack (Goodacre et al., 2005). Of those who are not diagnosed with ACS, the majority receive low-risk, minor diagnoses relating to heartburn or benign musculoskeletal pain (Chambers et al., 2015).
However, patients are often unsure of their discharge diagnosis, not knowing whether they were ultimately diagnosed with an ACS or if they received a different discharge diagnosis completely unrelated to their heart. Findings from a recent large study of Medicare claims data that patients evaluated for ACS were only slightly more accurate than chance at reporting whether they were ultimately diagnosed with ACS (Yasaitis et al., 2015). Of note, those who ultimately rule out are at similar risk for PTSD as those who receive a diagnosis of ACS (Kronish et al., 2018). From the point of view of the patient, the experience of going to the ED with ACS symptoms may still be traumatic whether or not they actually had a heart attack. In fact, subjective fear of dying and helplessness are more accurate predictors of who will develop PTSD than common clinical metrics of cardiac event (Guler et al., 2009). Thus, identifying malleable mechanisms responsible for the maintenance or modulation of perceived threat may uncover potent, potential targets for clinical intervention.

Understanding Heterogeneous Psychological Responses to ACS

Of the millions of individuals hospitalized for suspected ACS, many experience these events as traumatic, and some go on to develop PTS symptoms. While PTSD has been declared a “life sentence” based on its relationship with myriad physical health conditions (Koenen et al., 2017), little is known about variations in psychological stress response in the year after evaluation for ACS. Longitudinal studies of adjustment following other index traumas have documented a number of clinically relevant symptom trajectories over time (Bonanno et al., 2012; Bonanno, 2004) These trajectories often include chronic difficulties, acute symptom elevations followed by gradual recovery, delayed-onset symptoms, and stable psychological and physical health or resilience (Galatzer-Levy et al., 2018). In cardiac patients, only depression
(Burton et al., 2020; Burton et al., 2015) and anxiety (Froese et al., 1974; McCarthy et al., 2008) symptom trajectories have been explored.

Perceived threat during the peritraumatic period predicts the development of subsequent PTSD (Holbrook et al., 2001; van Wingen et al., 2011). Unique to life-threatening medical events, the ED environment can be an added source of perceived threat. The EST model suggests that an underlying fear of mortality contributes to PTSD symptoms, leading to ongoing, interoceptive monitoring and catastrophic interpretation of interoceptive signals. With a deeper understanding of the 12-month clinical course of ACS-induced PTSD, with particular respect to the role of interoceptive monitoring and threat perceptions, we will be better able to identify and intervene upon important mechanisms and treatment targets to support ongoing psychological adjustment following evaluation for ACS.

The COVID-19 Pandemic as an Acute Health-Related Stressor

Entering its third year, the COVID-19 pandemic continues to profoundly impact the global community. The virus – due to its remarkable scale of impact and aided by its opportunistic contagion – has repeatedly outpaced efforts to curb its spread, leading to an unprecedented burden on individuals and systems, alike. Appropriately so, the primary public health aim has remained focused on reducing spread and attenuating illness severity. At times, however, these efforts have also contributed to unceremonious disruptions to social, economic, and health systems. Individuals have incurred unpredictable and highly disruptive personal consequences - many losing sources of income, enduring long stretches of isolation or lack of privacy in crowded homes, being plucked from classroom communities, or entering an
unfamiliar virtual workforce. On a social level, lack of human contact and community participation at a time of severe collective adversity run counter to basic social norms.

With the adoption of essential public health measures, advent of safe and effective vaccines, and identification of novel, symptom-reducing treatments, many communities have experienced a tenuous yet hopeful return to the “new normal.” However, the pandemic continues to pose a very real threat to human health, with more than 985,000 deaths and 80.5 million infections nationwide since its onset (World Health Organization [WHO], 2022). Further, its systemic ripple effects continue, causing differential impacts on individuals and communities due to population-specific risk and protective factors. Therefore, clarifying the scale and nature of the pandemic’s impact on mental health remains essential in order to appropriately inform policy changes, direct community-level interventions, and support public dissemination.

Psychological Mechanisms Influencing Psychological Adjustment to COVID-19

Physical Anxiety Sensitivity and COVID-19

Given the significant mortality rate and physical threats of COVID-19, simultaneous to its broader impact as an acute public health disaster, the pandemic has required increased sensitivity to physiological cues that may indicate active, contagious illness. Individuals have been flooded with public health recommendations to remain somatically hypervigilant for physical symptoms like a scratchy throat, cough, fever, malaise, or difficulty breathing. While self-monitoring for potential COVID-19 symptoms has been vital to harm reduction throughout the pandemic, increased self-monitoring and somatic hypervigilance can contribute to emotion dysregulation, evidenced by increased ruminative thoughts and maladaptive behaviors (Barksy & Wyshak, 1990; Jungmann & Witthöft, 2020; Witthöft et al., 2006). Complicating the picture,
many COVID-19 symptoms are similar to uncomfortable somatic experiences of anxious arousal (i.e., body temperature fluctuations, increased respiration and heart rate, dizziness).

Anxiety sensitivity, or an individual’s propensity to interpret experiences related to anxious arousal as threatening cues, is a transdiagnostic risk factor for mental illness that has been identified as a mechanism of interest in psychological reactions to the COVID-19 pandemic (Manning et al., 2021; Rogers et al., 2021; Schmidt et al., 2021). In the face of an acute health-related threat, such as the ongoing COVID-19 pandemic, this interoceptive threat bias appears to have a complex impact on psychological functioning (Alonzi et al., 2020; Avidor et al. 2021; Lenzo et al., 2021; Manzanares et al., 2021; Schmidt et al., 2021; Waqas et al., 2020). The EST model posits that an ongoing mortality threat perpetuates psychological distress in the face of real and proximal physical health-related threats; this mortality threat results in an increased sensitivity to interoceptive monitoring of normal somatic cues and catastrophic interpretations of those interoceptive signals (Edmondson, 2014; Meli et al., 2017). Taken together, individual differences in somatic hyperarousal, degree of hypervigilance, and interoceptive threat bias is likely to differentially impact individuals’ psychological adjustment during the course of the pandemic.

Several studies have examined the role of anxiety sensitivity during the COVID-19 pandemic, both cross-sectionally and longitudinally, and findings support anxiety sensitivity as a risk factor for pandemic-related distress. However, existing longitudinal data on this topic has been limited to 1-month outcomes, warranting additional exploration of this mechanism in longitudinal psychological to the COVID-19 pandemic.
Worry, Uncertainty, & Perceived Threat

Tolerating uncertainty has been a core component of adjusting to life during the COVID-19 pandemic. We have all endured the disquieting experience of having insufficient information in the face of a novel and proximal threat. For many in the U.S., Spring 2020 was punctuated by abrupt, widespread, and fundamental changes to daily life, requiring rapid adaptation. Further, the pandemic’s erratic course has resulted in a barrage of COVID-related media, constant public health alerts, and capricious policies changes, which can lead to greater exacerbation of worry and confusion (Bendau et al., 2021; Neria & Sullivan, 2011).

The inability to tolerate uncertainty and higher perceived threat have been implicated in the development of anxiety and mood disorders (Hollingsworth et al., 2018; Mennin et al., 2004; Morriss et al., 2016), and has emerged as a mechanism of interest in pandemic-related mental health outcomes. Higher intolerance of uncertainty has been shown to moderate psychological distress during the COVID-19 pandemic (Rettie & Daniels, 2020; Satici et al., 2020; Sauer et al., 2020). Given this, we examined feelings of uncertainty and threat as predictors of psychological adjustment trajectories. In line with existing cross-sectional research, we hypothesized that individuals subjectively experiencing higher levels of uncertainty and threat at baseline would exhibit worse psychological adjustment in the first 12-months of the pandemic.

A key source of uncertainty and threat during the pandemic has been its notable impact on the economy. Many studies have highlighted the role of financial concerns in mental health outcomes above and beyond other sources of perceived threat (Bernardini et al., 2021; Haliwa et al., 2021; Zavlis et al., 2021). Controlling for pre-pandemic mental health, finance-related distress has consistently emerged as a predictor of anxious pathology (Benke et al., 2020;
McGinty et al., 2020), and abrupt income loss during the pandemic predicted both anxiety and depression (Hertz-Palmor et al., 2021).

Understanding Heterogeneous Psychological Responses to the Pandemic

While the pandemic is ongoing and many of its impacts are yet to be fully understood, a clearer picture of the pandemic’s initial psychological burden is coming into focus. Though early reports warned of widespread community mental health crises, the data appear to suggest otherwise and instead tell a story of resilience. International studies of psychological adjustment to the pandemic have similarly found heterogeneous trajectories of depression and anxiety symptoms, with the majority remaining resilient and most others reporting consistent, mild symptoms of depression and anxiety with trends toward improvement over time (Chen et al., 2022; Kimhi et al., 2021; Saunders et al., 2021; Shelvin et al., 2021). Notably, high rates of resilience do not suggest that individuals have been emotionally and psychologically impervious to the pandemic. As resilience is defined by a stable course of low symptoms following an aversive event (Bonanno, 2004), those who have shown resilient responses during the pandemic may very well have experienced mild and transient distress reactions without functional interference. Rather, these and other findings speak to the majority’s capacity to flexibly adapt in the face of the COVID-19 pandemic, a novel and acute stressor, in order to achieve and maintain effective emotion regulation.

Disaster events, including pandemics, are inherently dynamic resulting in heterogeneous patterns of psychological adjustment (Bonanno et al., 2010; Galatzer-Levy et al., 2018). The COVID-19 pandemic is undeniably a highly unique adverse event, with few other instances in recent history matching the scale, speed, chronicity of the current pandemic. Despite the
immense psychological and systemic burden, accumulating international research insinuates that the majority of individuals have exhibited natural recovery patterns after initial periods of peritraumatic adjustment. Some reviews show increases in depression and anxiety during the first peak of the pandemic and others highlight high rates of resilience, or a stable pattern of very low, subclinical symptoms (Robinson et al., 2022; Sun et al., 2020). Indeed, emerging reviews and meta-analyses have found higher cross-sectional rates of anxiety and depression within the first several months of the pandemic’s onset, as compared to mental health before the pandemic, with trends toward symptoms returning to baseline over the course of several months (Liu et al., 2021; Necho et al., 2021; Ren et al., 2020; Robinson et al., 2022; Wu et al., 2021).

Taken together, a clearer picture begins to emerge. The majority of individuals appear to experience either an apex of psychological distress at the start of the pandemic and then recovery patterns to a subclinical level or experience no clinically significant changes to their mental health at any point in the pandemic, thus far.

1.3 Rationale for the Studies

This dissertation examines physical anxiety sensitivity and other key mechanisms influencing psychological adjustment following acute health-related events with three empirical studies. Study 1 sheds light on the role of perceived threat and heightened interoceptive threat bias in the development of PTS symptoms following a suspected ACS. Testing a key assumption of the EST model, Study 1 assesses the role of perceived threat and ongoing cardiac-related anxiety sensitivity in the development of PTS symptoms following ED evaluation for a suspected ACS, above and beyond objective medical severity of the event. As a secondary aim of Study 1, we conducted a sensitivity analysis to determine whether the modeled associations
differed by whether participants were ultimately diagnosed with ACS versus another diagnosis. Importantly, the negative consequences of ongoing, distressing somatic threat perceptions do not require that the index event be an objectively verified medical event. Research suggests that the objective severity of cardiac events is unrelated to the development of PTSD (Edmondson & Cohen, 2013; Kronish et al., 2018) and that PTSD is present in as many as one-third of survivors of some index cardiovascular events that cannot be objectively confirmed (Edmondson et al., 2012). Understanding the nature by which interoceptive threat bias relates to psychological adjustment following ACS will begin to clarify the clinical sequelae of cardiac-induced PTSD, providing a mechanistic blueprint for clinical treatment and intervention development. In addition, if ongoing interoceptive distress is indeed a fundamental vulnerability for PTSD after ACS, the current approach to motivating patient self-care – by highlighting the lurking mortality threat in those patients’ bodies – may actually undermine their psychological and physical health.

Applying these findings, Study 2 examined the role of peritraumatic threat and ongoing cardiac-related threat perceptions on the clinical course of ACS-induced PTSD in the 12-months following ED evaluation for ACS. Providing the first longitudinal trajectory estimates of ACS-induced PTSD, Study 2 estimated heterogeneous trajectory classes of PTS symptoms, assessing the role of peritraumatic threat perceptions, cardiac-related anxiety sensitivity, and objective ACS event severity on trajectory group membership. With a deeper understanding of the 12-month clinical course of ACS-induced PTSD, with particular respect to the role of interoceptive monitoring, threat perceptions, and discharge diagnosis, we will be better able to identify and intervene upon important mechanisms and treatment targets to support ongoing psychological adjustment following evaluation for ACS. To further evaluate the role of perceived threat as a predictor of PTS symptom trajectories, Study 2 compared PTS trajectories of those who were
ultimately diagnosed with an ACS versus those who ruled out for an ACS upon discharge, receiving a non-cardiovascular diagnosis.

Study 3 sought to clarify the scale, natural course, and heterogeneous patterns of the COVID-19 pandemic’s impact on community level mental health. This study presented the first 12-month-long trajectory estimates of psychological adjustment to COVID-19 in the U.S., with data collection spanning from April 2020, approximately 1-month after the pandemic’s arrival in the U.S., through April 2021, nearly 5-months after vaccines were adopted publicly. Additionally, Study 3 examined the impact of two psychosocial factors, highly relevant to an individual’s experience of distress during the pandemic: physical anxiety sensitivity and feelings of uncertainty. Anxiety sensitivity, or an individual’s propensity to interpret experiences related to anxious arousal as threatening cues, is a transdiagnostic risk factor for anxiety and depression that has been identified as a mechanism of interest in psychological reactions to the COVID-19 pandemic (Manning et al., 2021; Rogers et al., 2021; Schmidt et al., 2021). Further, higher intolerance of uncertainty is an established risk factor for depressive and anxiety symptoms and has been identified as a moderating factor for psychological distress during the COVID-19 pandemic (Rettie & Daniels, 2020; Satici et al., 2020; Sauer et al., 2020). As the COVID-19 pandemic is ongoing and scientists warn of more pandemic-related disasters in the future, it is of vital public health interest to categorize and understand heterogeneous patterns of psychological adjustment. In doing so, establishing and examining psychosocial mechanisms and social determinants contributing to variations in psychological adjustment at the community level can drive appropriate dissemination, intervention development, and clinical application.

Of note, Study 2 and Study 3 share a common computational approach, latent growth mixture modeling (LGMM), allowing for the mapping of trajectory classes of psychological
adjustment and highlighting distinct symptom profiles. Considering the longitudinal course of psychological adjustment to acutely distressing events is essential to accurately estimate and describe associated mental health outcomes. Reactions to extremely adverse events typically result in a peak of distress as individuals confront novel sources of threats and encounter unwelcome disruptions to familiar ways of being. This peak typically dissipates for the majority, particularly the longer that individuals have to confront, compensate, and ultimately adjust to these events, as individuals find ways to flexibly adapt and effectively cope.

Appropriate computational models can account for variability due to important contextual factors, which may attenuate or exacerbate pandemic-related distress, capturing heterogeneous patterns of psychological adjustment with increased accuracy. Longitudinal trajectory estimates provide a more representative understanding of the natural course of psychological adjustment, embracing inherent fluctuations in the human response to extreme adversity over time and providing valuable insight into patterns of adjustment (Bonanno, 2012; Galatzer-Levy et al., 2018; Taylor, 2019). Using LGGM, Study 2 investigates the role of peritraumatic threat and ongoing cardiac-related anxiety sensitivity on the clinical course of PTS, identifying trajectories of psychological adjustment in the 12-months following a suspected ACS. Study 3 applies the same computational methods within the context of the COVID-19 pandemic, exploring the impact of worry and physical anxiety sensitivity on trajectories of depression and anxiety during the first 12-months of the pandemic.
The Included Studies

**Study 1**

**Study 2**

**Study 3**
Chapter 2: Enduring somatic threat perceptions and posttraumatic stress disorder symptoms in survivors of cardiac events
Enduring somatic threat perceptions and post-traumatic stress disorder symptoms in survivors of cardiac events

Laura Meli¹, Carmela Alcántara², Jennifer A Sumner¹, Brendan Swan¹, Bernard P Chang¹ and Donald Edmondson¹

Abstract
Post-traumatic stress disorder due to acute cardiovascular events may be uniquely defined by enduring perceptions of somatic threat. We tested whether post-traumatic stress disorder at 1 month post–acute coronary syndrome indeed required both high peritraumatic threat during the acute coronary syndrome and ongoing cardiac threat perceptions. We assessed peritraumatic threat during emergency department enrollment of 284 patients with a provisional acute coronary syndrome diagnosis and cardiac threat perceptions and post-traumatic stress disorder symptoms 1 month post-discharge. In a multiple regression model with adjustment for important covariates, emergency department threat perceptions were associated with higher 1 month post-traumatic stress disorder symptoms only among those with high levels of ongoing cardiac threat.

Keywords
cardiovascular disease, enduring somatic threat, peritrauma, stress, trauma

In the United States alone, more than 1 million patients are hospitalized annually for acute coronary syndrome (ACS), which includes myocardial infarction and unstable angina (Bertoni et al., 2005; Saket, 2007). With the adoption of new technologies, interventions, and treatment guidelines over recent decades, survival rates after ACS have steadily improved, even as more patients are treated for ACS each year (Awaida et al., 2006; Theroux et al., 2000). These improvements in care, while of undeniable significance, result in a growing population of ACS survivors in whom the risk of 1-year ACS recurrence or mortality is substantial (Terkelsen et al., 2005). An emerging risk factor for cardiac event recurrence and mortality in these patients is post-traumatic stress disorder triggered by the initial cardiac event (post-traumatic stress disorder (PTSD)) (Edmondson and Cohen, 2013; Edmondson et al., 2012).

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Enduring Somatic Threat Perceptions and Posttraumatic Stress Disorder Symptoms in Survivors of Cardiac Events

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Abstract

Post-traumatic stress disorder due to acute cardiovascular events may be uniquely defined by enduring perceptions of somatic threat. We tested whether post-traumatic stress disorder at 1 month post–acute coronary syndrome indeed required both high peritraumatic threat during the acute coronary syndrome and ongoing cardiac threat perceptions. We assessed peritraumatic threat during emergency department enrollment of 284 patients with a provisional acute coronary syndrome diagnosis and cardiac threat perceptions and post-traumatic stress disorder symptoms 1-month post-discharge. In a multiple regression model with adjustment for important covariates, emergency department threat perceptions were associated with higher 1-month post-traumatic stress disorder symptoms only among those with high levels of ongoing cardiac threat.

Keywords: Cardiovascular disease, enduring somatic threat, anxiety sensitivity, peritraumatic adjustment, stress, trauma
In the United States alone, more than 1 million patients are hospitalized annually for acute coronary syndrome (ACS), which includes myocardial infarction and unstable angina (Bertoni et al., 2005; Saket, 2007). With the adoption of new technologies, interventions, and treatment guidelines over recent decades, survival rates after ACS have steadily improved, even as more patients are treated for ACS each year (Awaida et al., 2006; Theroux et al., 2000). These improvements in care, while of undeniable significance, result in a growing population of ACS survivors in whom the risk of 1-year ACS recurrence or mortality is substantial (Terkelsen et al., 2005). An emerging risk factor for cardiac event recurrence and mortality in these patients is post-traumatic stress disorder triggered by the initial cardiac event (PTSD; Edmondson & Cohen, 2013; Edmondson et al., 2012).

PTSD is currently classified as a trauma- and stressor-related disorder that is diagnosed when an individual experiences four categories of symptoms for at least one month after exposure to a life-threatening traumatic event: persistent re-experiencing of the event, efforts to avoid stimuli related to the event, persistent negative alterations in cognition and mood, and hyperarousal (American Psychological Association, 2013). Since 1994, the *Diagnostic and Statistical Manual of Mental Disorders (DSM)* has identified life-threatening illness as a potentially traumatic event, and research to date suggests that PTSD is relatively common after cardiovascular events. For example, a meta-analytic review of 24 studies of PTSD due to ACS estimated that 12 percent of ACS survivors develop clinically significant PTSD symptoms (Edmondson et al., 2012). However, with the revision of diagnostic criteria in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)*, PTSD symptoms due to medical
events have been called into question, with the suggestion that such events may not qualify as a
Criterion A traumatic stressor and that adjustment disorder may be a more fitting diagnosis

Research in survivors of cancer and acute cardiovascular events has highlighted the
conceptual challenges associated with PTSD due to medical events (Kangas et al., 2002). First,
for many medical events, it is difficult to isolate a single Criterion A traumatic event (e.g., cancer
tests, diagnosis, or treatment) – due to the often-chronic nature of these medical events and their
sequelae (Gurevich et al., 2002). Second, and most important for this study, the underlying
mortality threat implied by an acute medical event lasts long after the index stressor has passed.
This ongoing perception of somatic threat may be important to take into account when
conceptualizing risk for developing PTSD after acute medical events, and it may also affect how
PTSD symptoms manifest. For example, intrusive thoughts may be focused on present and
future-oriented fear of cardiac event recurrence rather than solely keyed to the index cardiac
event (Mehnert et al., 2009).

The Enduring Somatic Threat Model

The enduring somatic threat (EST) model (Edmondson, 2014) of PTSD due to acute life-
threatening medical events was offered to address underappreciated differences between PTSD
due to past, discrete/external traumatic events (such as combat) and PTSD due to acute events
that are manifestations of chronic or recurrent disease (e.g., ACS or stroke). This model
addresses differences such as the external versus somatic source of threat, the predominance of
past versus present/future temporal focus of threatening cognitions, the different types and
consequences of avoidance behavior, and the different character and consequences of hyperarousal.

The EST model proposes that an underlying fear of mortality maintains PTSD symptoms due to both discrete/external and ongoing/somatic events, and that elevated threat perceptions during the traumatic event increase risk for PTSD after both types of traumatic events. However, because many life-threatening medical events (e.g., ACS) are an acute manifestation of a permanently disrupted physiological system (e.g., cardiovascular dysfunction in the case of an acute cardiac event), those medical events represent an ongoing threat originating in the patient’s body – which cannot be avoided (Fox et al., 2006; Goldberg et al., 2004; Tang et al., 2007). Therefore, EST perceptions are both central to an individual’s ACS-induced PTSD symptoms and may be wholly absent in PTSD due to discrete/external traumatic events.

Acute life-threatening medical events such as ACS fundamentally alter a patient’s relationship to their body in a way that may negatively impact mental health. The EST model proposes that patients most distressed by an ACS become sensitized to subsequent somatic cues of threat, which cause significant distress. These cues, such as perceived increases in heart rate, chest tightening, or other normal and frequent somatic experiences that individuals without a cardiac history generally ignore, may initiate a cascade of heightened arousal, catastrophic interpretations of somatic experience, and intrusive recollections of the index cardiac event. This EST and its role in the development of PTSD in ACS patients reflect a key tenet of the EST model, but they have yet to be observed, and their relationship to PTSD has yet to be empirically tested.
Objective Diagnosis: ACS versus non-ACS

Importantly, EST does not require that the index event be an objectively verified medical event. Research suggests that the objective severity of cardiac events is unrelated to the development of PTSD (Edmondson and Cohen, 2013) and that PTSD is present in as many as one-third of survivors of some index cardiovascular events (e.g., transient ischemic attacks (TIA)) that cannot be objectively confirmed (Edmondson et al., 2012).

2.1 The Present Study

We tested the fundamental hypothesis of the EST model in a multi-ethnic sample of cardiac patients recruited in the emergency department (ED) while being evaluated for ACS. Namely, we predicted that for significant PTSD symptoms to emerge in response to the suspected ACS event, patients would have to (1) experience the ACS event as threatening and (2) perceive an EST once the acute event had concluded. We assessed peritraumatic threat perceptions during evaluation for the suspected ACS event, ongoing cardiac threat perceptions 1 month later, and tested their interaction in relation to PTSD symptoms at 1 month after the index cardiac event.

2.2 Method

The REACH Study & Procedures

The REactions to Acute Care and Hospitalization (REACH) study is an ongoing observational cohort study of patients presenting to the ED of Columbia University Medical Center (CUMC) for evaluation of suspected ACS. The study was approved by the Institutional Review Board of Columbia University, and all participants gave informed consent. The primary
aims of the REACH study are to determine the association of ACS-induced PTSD with cardiovascular outcomes and ED contributors to PTSD risk. Most relevant for this study, patients being evaluated for ACS were enrolled and reported on their perceptions of threat and vulnerability during their ED stay. Pre-hospital depression and PTSD symptoms due to prior traumatic events were assessed either in person during inpatient stay or by telephone within 1 week of ED presentation (median time to assessment = 3 days after ED presentation). Ongoing cardiac threat perceptions and ACS-induced PTSD were assessed by telephone at 1 month post-discharge.

Participants

Patients were eligible for the study if they were aged 18 years or older, fluent in English or Spanish, and had a provisional ED diagnosis of ACS. Individuals were not eligible if they were (1) unable to complete the assessment of pre-ACS PTSD and depression within 1 week of hospitalization, (2) deemed unable to comply with the protocol (e.g. patients with a level of cognitive impairment indicative of dementia or with current alcohol or substance abuse), (3) deemed to need immediate psychiatric intervention, or (4) unavailable for follow-up (e.g. patients with a terminal non-cardiovascular illness or those who indicated they were about to leave the United States).

Measures

In the emergency department

Demographic factors. Participants self-reported age, sex, race, and ethnicity.
Peritraumatic threat perceptions during ED evaluation. During evaluation for ACS in the ED, we assessed participants’ peritraumatic perceptions of threat in response to the acute cardiac event with 12 items (e.g., “I am in pain,” “I am afraid,” “I feel helpless,” “I feel vulnerable,” “I worry that I am not in control of my situation”) based on Ozer et al. (2003). Patients rated the extent to which these statements reflected their experience in the ED on a 4-point Likert scale ranging from “Not at all” to “Extremely”; a total score was computed by summing responses to the 12 items. Responses to these items had good internal consistency (Cronbach’s $\alpha = .79$). Previous research (Wiedemar et al., 2008) has utilized similar items to assess perceived threat after acute cardiovascular events. Prior research has found that the measure is sensitive to stressful aspects of ED care, including overcrowding, anxiety-inducing social support, poor clinician-patient communication, and treatment in hallway beds versus private ED rooms (Chang et al., 2016a, 2016b; Edmondson et al., 2013b; Homma et al., 2016; White et al., 2017).

Inpatient interview (or telephone if discharged prior to interview)

Previous PTSD (prior to the suspected ACS event). The PTSD Checklist-Civilian (PCL-C) (Weathers et al., 1993) was administered to assess PTSD due to life events prior to the index ACS event. The PCL-C is a 17-item PTSD screening instrument developed by the National Center for PTSD, and it has been used in numerous patient populations (Walker et al., 2002). Participants rated the extent to which they were bothered by each of the 17 diagnostic criteria for PTSD described by the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) with reference to the most stressful event identified on the Life Events Checklist of potentially traumatic life events (Gray et al., 2004). Responses were rated on a scale from 1 (“Not at all”) to 5 (“Extremely”). The PCL-C has excellent psychometric properties (Blanchard
et al., 1996) and excellent sensitivity and specificity for PTSD clinical diagnosis prediction (Bliese et al., 2008). It yields a continuous PTSD symptom severity score. DSM-IV PTSD symptoms were assessed in this study, as the study was initiated prior to the publication of DSM 5. Internal consistency of the PCL-C in the current sample was excellent (Cronbach’s $\alpha = .93$)

**Depression.** We assessed depressive symptoms in the 2 weeks prior to hospitalization using the Patient Health Questionnaire (PHQ) (Kroenke et al., 2001). The PHQ-8, which consists of eight items scored on a 0-3 scale, is a self-report instrument with excellent psychometric properties (Kroenke et al., 2009) (Cronbach’s $\alpha = .83$).

**Telephone interview at 1-month**

**Cardiac threat perceptions.** We assessed ongoing perceptions of cardiac threat at 1-month follow-up using the four cardiac items from the Anxiety Sensitivity Index – Revised (Peterson & Reiss, 1993). Responses to the four items (“It scares me when my heart beats rapidly”; “When my chest feels tight, I get scared that I won’t be able to breathe properly”; “When I notice my heart skipping a beat, I worry that there is something seriously wrong with me”; and “When I feel pain in my chest, I worry that I’m going to have a heart attack”) were scored on a scale from 0 (“Very little”) to 4 (“Very much”) and summed to create a total ongoing cardiac threat perception score. No time frame is specified for responses (Cronbach’s $\alpha = .80$).

**PTSD symptoms due to suspected ACS (ACS-induced PTSD).** PTSD symptoms were assessed at 1-month follow-up with the PTSD Checklist for a Specific Stressful Experience (PCL-S). The PCL-S is identical to the PCL-C, but participants rated the extent to which they were bothered by the PTSD symptoms in the past month in response to the “heart problem, emergency room visit, and hospitalization” that occurred 1 month ago when they enrolled in the
study. Internal consistency of the PCL-S in the current sample was excellent (Cronbach’s α = .92).

Electronic Health Record

Prior cardiac history. History of prior ACS, percutaneous coronary intervention, or coronary artery bypass graft was extracted from the participants’ health record. Participants with any cardiac history were coded 1.

Discharge ACS status. REACH enrolls participants who are being evaluated for probable ACS in the ED, but many participants receive alternative diagnoses by the time of hospital discharge, such as non-cardiac chest pain, after all diagnostic tests are completed. We included discharge diagnosis of ACS versus non-ACS as a covariate in analyses. We conducted a sensitivity analysis to determine whether the modeled associations differed by whether participants were ultimately diagnosed with ACS versus another diagnosis (Velazquez et al., 2017).

Statistical Analysis Plan

Our primary hypothesis was that the combination of high peritraumatic threat in the ED and high ongoing cardiac threat at 1-month would be associated with the highest ACS-induced PTSD scores. We tested a multiple linear regression model with main effects for peritraumatic threat perceptions during ED evaluation and ongoing cardiac threat perceptions at 1-month post-discharge, as well as their interaction. The model included adjustment for age, sex, confirmed ACS status, pre-ACS PTSD, and pre-ACS depression.
2.3 Results

Participant Characteristics

Participants were 284 patients (age 61±13; 49% women; 46% Hispanic) admitted to the ED with a provisional diagnosis of ACS. A total of 32 percent had a history of coronary artery disease and 35 percent had confirmed ACS diagnosis at hospital discharge. The remaining participants were given diagnoses such as chest pain without a cardiac diagnosis, another symptom/disease process (e.g., pulmonary embolism, costochondritis), or another cardiac disease (e.g., congestive heart failure exacerbation). Means and standard deviations of study variables are given in Table 2.1.

| Table 2.1 Correlations among modeled variables, with mean values and (SD) for continuous variables on the diagonal |
|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|
| 1. ACS-induced PTSD symptoms | 24.53 (10.78) | | | | | | | |
| 2. ED Threat | .46** | 10.29 (3.82) | | | | | | |
| 3. Cardiac threat | .47** | .40** | 6.98 (5.11) | | | | | |
| 4. Pre-ACS depression | .40** | .38** | .34** | 6.46 (6.08) | | | | |
| 5. Pre-ACS PTSD | .46** | .35** | .39** | .43** | 24.87 (11.48) | | | |
| 6. CAD history | -.04 | -.07 | .02 | -.11 | .00 | 33% | | |
| 7. Age | -.12 | -.19* | -.11 | -.01 | -.12 | .13 | 60.1 (12.83) | |
| 8. Female sex | -.11* | -.11 | -.12 | -.16* | -.05 | .20** | -.01 | 49% |

SD: standard deviation; ACS: acute coronary syndrome; PTSD: post-traumatic stress disorder; ED: emergency department; CAD: coronary artery disease.

Initial Bivariate Associations

All variables were significantly associated with each other in expected directions, except for ACS status, which was not associated with any variables except for age and sex (Table 2.1).
Test of the Interaction of ED Threat Perceptions and Ongoing Cardiac Threat

Regression results are given in Table 2.2. The full model \(F (8, 275) = 24.69, p < .001; R^2 \text{ adj} = .40\) explained 40 percent of the variance in ACS-induced PTSD symptoms at 1 month after hospital discharge. Both the main effect of ongoing cardiac threat (\(\beta = .25, p < .001\)) and the main effect of ED threat perceptions (\(\beta = .12, p = .01\)), as well as the interaction of ED threat perceptions and ongoing cardiac threat (\(\beta = .82, p < .001\)) were significant predictors of ACS-induced PTSD symptoms in the final model. The interaction is depicted in Figure 2.1.

The simple slope for the association of ED threat perceptions with ACS-induced PTSD was significantly different from 0 (slope = .99, standard error (SE) slope = .28, \(p < .001\)) only at 1 standard deviation above the mean of ongoing cardiac threat perceptions. In other words, greater peritraumatic ED threat perceptions were associated with higher 1-month PTSD symptoms, but only among those with high levels of ongoing cardiac threat.

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Full sample (N=284)</th>
<th>Confirmed ACS (N=99)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B (SE)   p</td>
<td>B (SE)   p</td>
</tr>
<tr>
<td>ED threat</td>
<td>.40 (.16) .01</td>
<td>-.73 (.49) .14</td>
</tr>
<tr>
<td>Cardiac threat</td>
<td>.54 (.11) &lt;.001</td>
<td>-.82 (.51) .11</td>
</tr>
<tr>
<td>ED threat (\times) cardiac threat</td>
<td>.12 (.03) &lt;.001</td>
<td>.12 (.44) .009</td>
</tr>
<tr>
<td>Age</td>
<td>-.02 (.04) .65</td>
<td>-.19 (.07) .01</td>
</tr>
<tr>
<td>Sex</td>
<td>-.82 (1.04) .43</td>
<td>-8.32 (1.73) &lt;.001</td>
</tr>
<tr>
<td>CAD history</td>
<td>.16 (1.13) .89</td>
<td>3.21 (1.55) .04</td>
</tr>
<tr>
<td>Pre-ACS PTSD</td>
<td>.18 (.05) &lt;.001</td>
<td>-.24 (.09) .01</td>
</tr>
<tr>
<td>Pre-ACS depression</td>
<td>.23 (.10) .02</td>
<td>.78 (.17) &lt;.001</td>
</tr>
</tbody>
</table>

ACS: acute coronary syndrome; PTSD: posttraumatic stress disorder; ED: emergency department; SE: standard error; CAD: coronary artery disease.

Model fit: full sample, \(F (8, 275) = 24.69, p < .001; R^2 \text{ adj} = .40\).

Confirmed ACS, \(F (8, 91) = 14.54, p < .001; R^2 \text{ adj} = .52\).
**Sensitivity Analysis**

We conducted a sensitivity analysis in which we tested the full regression model only in the subset of participants with a confirmed discharge diagnosis of ACS. Results did not differ from those in the full sample. Specifically, the interaction of ED threat perceptions and ongoing cardiac threat ($\beta=.12, p = .009$) remained (Table 2.2).

**Figure 2.1** Interaction of threat perception during emergency department evaluation (centered on the variable mean) and level of ongoing cardiac threat perception in the subsequent month on ACS-induced PTSD symptoms
2.4 Discussion

This is the first study to test a key hypothesis of the EST model of PTSD due to acute life-threatening medical events. We hypothesized that ongoing cardiac threat perceptions would be important contributors to ACS-induced PTSD symptoms and would modify the association of high perceived threat during the ED evaluation for ACS with subsequent ACS-induced PTSD symptom severity. Our hypotheses were supported by the data. Indeed, we found main effects for both ED threat perceptions and ongoing cardiac threat, as well as their interaction. Furthermore, post hoc analyses found that greater ED threat perceptions were associated with 1-month ACS-induced PTSD only in participants who reported high levels of ongoing cardiac threat. Therefore, ongoing cardiac threat seems to be particularly critical for understanding PTSD symptoms after an acute cardiac event.

Although we view these findings as evidence of a unique phenomenon whereby afferent physiological signals trigger traumatic reminders of the index ACS event and future cardiovascular disease (CVD) risk, the associated cognitive processes may be highly similar to those documented in survivors of archetypal PTSD-inducing events such as combat or sexual assault, who are triggered by external reminders of those events. For example, these cardiac threat perceptions may be initiated due to overgeneralization of the fear network. However, they may be distinct in some ways as well. Whereas overgeneralization implies fear network activation to trauma-related but ultimately safe cues (Foa et al., 2006), physiological threat signals may be true prodromes of a new cardiac event. The “true” safety versus threat status of triggering cues is important for both understanding the phenomenon of medical event–induced
PTSD and designing effective treatments for it. This work aims to refine our understanding of the threat appraisal processes that operate in PTSD after acute life-threatening medical events.

The EST perceptions we describe here may represent an important cognitive vulnerability to monitor in the aftermath of acute medical events. They may identify at-risk individuals and serve as targets for intervention. In current medical practice, after a life-threatening cardiovascular event, patients are encouraged to consider the event a “turning point” in their lives and make it a primary driver of many of their day-to-day activities. Because the event itself was an acute manifestation of systemic cardiovascular risk (i.e., atherosclerosis, hypertension, intermittent ischemic episodes will not disappear), patients are asked to actively monitor and combat the cardiovascular threat with interoceptive somatic monitoring, lifestyle changes, medication regimens, and interactions with the medical system – all of which are potent reminders of ongoing vulnerability and of the original event.

However, such reminders can be highly distressing (Whitaker et al., 2009) and have been associated with poor psychological adjustment in CVD patients (Edmondson et al., 2008; Matsuoka et al., 2002). Ironically, it is possible that reducing patients’ perceptions of EST may be a means for reducing both PTSD symptoms and improving cardiovascular prognosis. Innovative therapies such as biofeedback for heart rate variability (HRV) have been shown to improve both PTSD symptoms and HRV in healthy adults (Lande et al., 2010; Tan et al., 2011; Zucker et al., 2009) and may be particularly useful for ACS survivors, as they may serve as a version of exposure therapy.

One reason that reducing EST perceptions may improve subsequent health is through influencing health behaviors (Alcántara et al., 2014; Edmondson et al., 2013a; Kronish et al., 2012, 2013, & 2015). Currently, it appears that patients may develop implicit (i.e., non-
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conscious) or explicit cognitive associations of prescribed treatment – including medications and physical activity – with the initial cardiac event and future mortality. The EST model proposes that patients may avoid medications and physical activity because they serve as reminders of the life-threatening event, and/or direct patients’ attention to the vulnerability of their bodies and ultimately their mortality. Therefore, activities such as medication nonadherence and sedentary behavior confer psychological equanimity in the short term (a form of negative reinforcement), even if patients consciously understand the associated long-term risk. Currently many practitioners attempt to motivate patients by capitalizing on the “teachable moment” that is the life-threatening event, by highlighting the mortality risk associated with adverse health behaviors such as medication nonadherence and sedentary behavior (Demark-Wahnefried et al., 2005). For many patients, however, this may actually work against the ultimate goal of adherence to medication and physical activity recommendations. These hypotheses should be tested in future research.

**Limitations**

This study is important as the first test of the EST model, and it has many unique strengths, including assessment of threat during evaluation for a life-threatening cardiac event in the ED, and a large, ethnically, racially, and socioeconomically diverse sample. However, there are several limitations that must be considered.

First, by measuring cardiac threat perceptions at the same 1-month interview as PTSD symptoms, we may have artificially inflated the association of ongoing cardiac threat perceptions with concurrent PTSD symptoms. However, this limitation should not impact the key result of the article: the synergistic effect of ED threat perceptions and ongoing cardiac threat on PTSD
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symptoms. Similarly, we assessed cardiac threat perceptions only once, at 1 month after hospital discharge, so we were unable to determine whether cardiac threat perceptions increased due to the cardiac event. According to the EST model, if we had measured cardiac threat perceptions prior to the cardiac event, we would have seen substantial change from pre-event to 1 month post-discharge, but we were unable to test that hypothesis in this study. Future studies should measure change in cardiac sensitivity over multiple time points to determine whether change in cardiac threat is associated with the development or maintenance of PTSD symptoms over time.

Second, although all participants were recruited during evaluation for ACS in the ED, over 60 percent of the sample was not diagnosed with ACS at discharge. This finding is in line with results from other studies in which patients were recruited for suspected ACS in the ED (e.g., rates of confirmed ACS have ranged from 16 to 30 percent in recent studies) (Chase et al., 2006; Kwong et al., 2003), and the non-ACS diagnoses were perceived as equally threatening and painful as confirmed ACS diagnoses. Importantly, recent research on the agreement of patient-reported ACS versus claims data found that nearly half of self-reported ACS events (43%) were not supported by claims data, with most corresponding to non-ACS cardiac admissions (Yasaitis et al., 2015). Thus, it is unclear whether patients can distinguish between “true” ACS and other diagnoses for which they are hospitalized after evaluation for ACS. Furthermore, our sensitivity analyses revealed that the key findings held when we limited to only participants with ACS diagnosis at discharge.

Third, because this study was initiated before the DSM-5 was published, our findings reflect PTSD symptoms as defined by DSM-IV. Although some changes were made in revising the PTSD diagnostic criteria from DSM-IV to DSM-5, most of the DSM-5 and DSM-IV PTSD
criteria are highly similar, and *DSM-IV* PTSD symptoms have been found to approximate *DSM-5* estimates of the disorder (Rosellini et al., 2015).

### 2.5 Conclusion

Researchers and *DSM-5* have suggested that the psychological disruption currently termed PTSD symptoms due to medical events do not fit neatly into the current conceptualization of the disorder. However, positive screens for PTSD triggered by life-threatening medical events are a common and important phenomenon to understand. Regardless of conceptualization, they appear to be associated with poor health outcomes. Given the frequency with which life-threatening medical events occur, medically induced PTSD could represent the lion’s share of the PTSD burden in most developed countries. Indeed, it is estimated that as many as 168,000 ACS patients will develop clinically significant symptoms of PTSD this year in the United States alone (Edmondson et al., 2012).

In this article, we identify a potentially novel cognitive vulnerability for ACS-induced PTSD that may reflect a unique aspect of this disorder. Our findings support predictions from the EST model, namely, that PTSD-like symptoms after an acute medical event are particularly likely to result when two conditions are met: the patient experiences significant life threat and vulnerability during the event, and she continues to perceive afferent cardiac signals as highly distressing. We have also shown that these cognitive processes influence PTSD risk in the month after evaluation for an acute cardiac event whether or not the patient ultimately receives an ACS diagnosis. These findings should spur future research into the character and determinants of PTSD due to life-threatening medical events and should be considered in the management of secondary medical risk in patients. If EST is indeed a fundamental vulnerability for PTSD after
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life-threatening medical events such as ACS, our current approach to motivating patient self-care through highlighting the lurking mortality threat in those patients’ bodies may actually undermine their psychological and physical health.

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Chapter 3: Trajectories of posttraumatic stress in patients with confirmed and rule-out acute coronary syndrome
Trajectories of posttraumatic stress in patients with confirmed and rule-out acute coronary syndrome

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ABSTRACT

Many patients evaluated in the emergency department (ED) for acute coronary syndrome (ACS) develop posttraumatic stress symptoms (PTSS), but little is known about symptom trajectories over time. We estimated longitudinal trajectories of PTSS from ED to 1 year after evaluation for suspected ACS (N = 1000), and the effect of threat perceptions and discharge diagnosis. Participants reported on threat perceptions in the ED, ongoing cardiac threat at 1 month, and PTSS at 1, 6, and 12 months. Latent growth mixture modeling identified 3 PTSS trajectories over 1 year: Resilient (81.7%), Chronic-Worsening (13.6%), and Acute-Recovering (4.6%). Chronic-Worsening and Acute-Recovering classes reported significantly higher ED and cardiac threat perceptions than Resilient class. Discharge diagnosis did not differ (χ²(2) = 2.93, p = .231). PTSS are common following evaluation for suspected ACS, and trajectories vary, but targeting threat perceptions may reduce PTSS and improve clinical course, whether or not patients are ultimately diagnosed with ACS.

1. Introduction

Acute coronary syndrome (ACS) is life-threatening, highly distressing, and for many traumatic; 1 in 8 ACS patients screen positive for posttraumatic stress disorder (PTSD) [16,17,22]. However, little is known about variations in ACS patients’ posttraumatic stress symptom (PTS) onset or clinical course. We estimated longitudinal trajectories of PTS following hospitalization for suspected ACS. We also compared patients with confirmed ACS to those who ultimately ruled out, and estimated the influence of threat during hospitalization and subsequent cardiac threat perceptions on longitudinal symptom trajectories.

Cardiovascular disease (CVD) remains the leading cause of death in the United States, accounting for over 900,000 deaths and 2.2 million hospitalizations annually [1,21,42]. After years of steady decline, CVD mortality rates have begun to plateau, and, in some subgroups, increase after nearly 40 years [39]. Patients with ACS (1.1 million hospitalizations per year) are at high risk for recurrent cardiac events and mortality [3,29,37]. Because most ACS patients survive the event, secondary risk reduction and quality of life after hospital discharge are critical. Psychological disorders, such as depression, anxiety, and PTSD, are common after ACS, and negatively impact quality of life [10,16,17,25,40]. Crucially, psychopathology is also an independent risk factor for mortality and cardiac event recurrence [7,8,18,35,36].

For the 12–15% of individuals who screen positive for ACS-induced PTSD [16,17,20], ACS-induced PTSD is associated with cardiac event recurrence and mortality [15,36]. Thus, whereas all ACS survivors are at high risk for CVD recurrence and mortality, ACS-induced PTSD confers yet greater risk.

Millions of adults are evaluated for ACS in emergency departments each year, and those who ultimately rule out are at similar risk for PTSD as those who receive a diagnosis of ACS [24]. This is not surprising, given findings from a recent large study of Medicare claims data that patients evaluated for ACS were only slightly more accurate than chance at reporting whether they were ultimately diagnosed with ACS [43], as the physiological symptoms of ACS can have other etiologies in patients who have enough cardiovascular risk factors to be evaluated for ACS in the first place.

Little is known about variations in psychological stress response in the year after evaluation for ACS. Longitudinal studies of adjustment following other types of trauma have documented a number of clinically relevant symptom trajectories over time (4,51). These trajectories include chronic difficulties, acute symptom elevations followed by gradual recovery, delayed-onset symptoms, and stable psychological and physical health or resilience (Galatzer-Levy, Huang, & Bonanno, 2018). In cardiac patients, only depression [7,8] and anxiety [19,27]...
Trajectories of Posttraumatic Stress in Patients with Confirmed and Rule-Out Acute Coronary Syndrome

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TRAJECTIONS OF POSTTRAUMATIC STRESS AFTER ACS

Abstract

Many patients evaluated in the emergency department (ED) for acute coronary syndrome (ACS) develop post-traumatic stress symptoms (PTSS), but little is known about symptom trajectories over time. We estimated longitudinal trajectories of PTSS from ED to 1 year after evaluation for suspected ACS (N = 1000), and the effect of threat perceptions and discharge diagnosis. Participants reported on threat perceptions in the ED, ongoing cardiac threat at 1 month, and PTSS at 1, 6, and 12 months. Latent growth mixture modeling identified 3 PTSS trajectories over 1 year: Resilient (81.75%), Chronic-Worsening (13.69%), and Acute-Recovering (4.56%). Chronic-Worsening and Acute-Recovering classes reported significantly higher ED and cardiac threat perceptions than Resilient class. Discharge diagnosis did not differ (χ²(2) = 2.93, p = .231). PTSS are common following evaluation for suspected ACS, and trajectories vary, but targeting threat perceptions may reduce PTSS and improve clinical course, whether or not patients are ultimately diagnosed with ACS.

Keywords: Trauma, posttraumatic stress disorder, acute coronary syndrome, threat perceptions cardiovascular disease
Acute coronary syndrome (ACS) is life-threatening, highly distressing, and for many traumatic; 1 in 8 ACS patients screen positive for posttraumatic stress disorder (PTSD; Edmondson, Shimbo, et al., 2013; Edmondson, Kronish, et al, 2013; Holbrook et al., 2001). However, little is known about variations in ACS patients' posttraumatic stress symptom (PTS) onset or clinical course. We estimated longitudinal trajectories of PTS following hospitalization for suspected ACS. We also compared patients with confirmed ACS to those who ultimately ruled out, and estimated the influence of threat during hospitalization and subsequent cardiac threat perceptions on longitudinal symptom trajectories.

3.1 Background

Cardiovascular disease (CVD) remains the leading cause of death in the United States, accounting for over 900,000 deaths and 2.2 million hospitalizations annually (American Heart Association [AHA], 2019; Global Burden of Cardiovascular Diseases Collaboration, 2018; Wright et al., 2018). After years of steady decline, CVD mortality rates have begun to plateau, and, in some subgroups, increase after nearly 40 years (Wall et al., 2018). Patients with ACS (1.1 million hospitalizations per year) are at high risk for recurrent cardiac events and mortality (Beroni et al., 2005; Mozaffarian et al., 2015; Terkelsen et al., 2004).

Because most ACS patients survive the event, secondary risk reduction and quality of life after hospital discharge are critical. Psychological disorders, such as depression, anxiety, and PTSD, are common after ACS, and negatively impact quality of life (Cohen et al., 2009;
TRAJECTORIES OF POSTTRAUMATIC STRESS AFTER ACS

Edmondson, Shimbo et al., 2013; Edmondson, Kronish et al., 2013; Lane et al., 2002; Wasson et al., 2014). Crucially, psychopathology is also an independent risk factor for mortality and cardiac event recurrence (Burton et al., 2020; Burton et al., 2015; Frasure-Smith et al., 1993; Roest et al., 2010; Shemesh et al., 2004). For the 12–15% of individuals who screen positive for ACS-induced PTSD (Edmondson, Shimbo et al., 2013; Edmondson, Kronish et al., 2013; Gander & von Känel, 2006), ACS-induced PTSD is associated with cardiac event recurrence and mortality (Edmondson et al., 2012; Shemesh et al., 2004). Thus, whereas all ACS survivors are at high risk for CVD recurrence and mortality, ACS-induced PTS confer yet greater risk.

Millions of adults are evaluated for ACS in emergency departments each year, and those who ultimately rule out are at similar risk for PTSD as those who receive a diagnosis of ACS (Kronish et al., 2018). This is not surprising, given findings from a recent large study of Medicare claims data that patients evaluated for ACS were only slightly more accurate than chance at reporting whether they were ultimately diagnosed with ACS (Yasaitis et al., 2015), as the physiological symptoms of ACS can have other etiologies in patients who have enough cardiovascular risk factors to be evaluated for ACS in the first place.

Little is known about variations in psychological stress response in the year after evaluation for ACS. Longitudinal studies of adjustment following other types of traumas have documented a number of clinically relevant symptom trajectories over time (Bonanno et al., 2012; Bonanno, 2004). These trajectories include chronic difficulties, acute symptom elevations followed by gradual recovery, delayed-onset symptoms, and stable psychological and physical health or resilience (Galatzer-Levy, Huang, & Bonanno, 2018). In cardiac patients, only depression (Burton et al., 2020; Burton et al., 2015) and anxiety (Froese et al., 1974; McCarthy et al., 2008) symptom trajectories have been explored.
In the present study, we estimated longitudinal trajectories of PTS following emergency department (ED) evaluation for suspected ACS in the REactions to Acute Care and Hospitalizations (REACH) study. Participants in the REACH study are approached in the ED while they are being evaluated for suspected ACS. Thus, upon discharge, some participants are given a discharge diagnosis of confirmed ACS while others ultimately rule-out for ACS and may receive a non-cardiovascular diagnosis. Prior research has shown that there are no differences in rates of PTS at 1-month after evaluation, whether or not the event is diagnosed ACS, as patients who meet our inclusion criteria are high risk for ACS (Lane et al., 2002). Thus, an additional aim of the present study was to compare PTS trajectories of participants diagnosed with “confirmed ACS” vs “rule-out ACS.”

A final aim of the study was to examine threat perceptions as predictors of PTS trajectories. Perceived threat during the peri-traumatic period predicts the development of subsequent PTSD (Holbrook et al., 2001; van Wingen et al., 2011). One source of perceived threat, unique to life-threatening medical events, is the ED environment; ED crowding in the ED and nearby patient acuity have been associated with heightened threat perception in the ED (Edmondson, Shimbo et al., 2013; Konrad et al., 2017). A second source of threat perception stems specifically from the cardiac event. In line with the enduring somatic threat (EST) model (Edmondson, 2014), patients with heightened cardiac threat perceptions in the month after the ACS have the most severe PTS at 1-month post-ACS (Meli et al., 2017). The EST model suggests that an underlying fear of mortality contributes to PTSD symptoms, leading to ongoing, interoceptive monitoring and catastrophic interpretation of interoceptive signals. In the present study, we examined variations in PTS trajectories in relation to ED threat perceptions measured
during the ED visit and ongoing cardiac threat perceptions measured 1-month after hospital discharge.

3.2 Method

Participants

The present study includes the first 1000 English- and Spanish-speaking patients enrolled from November 2013 to February 2016 in the REACH study. REACH is an ongoing prospective observational cohort of a consecutive sample of patients presenting to an urban ED in New York City with symptoms of suspected ACS. All participants had pre-existing risk factors for ACS, reported symptoms consistent with ACS, and were initially considered by ED physicians to (more likely than not) be diagnosed with ACS. We excluded patients with ST elevation myocardial infarction (STEMI) due to hospital emergency department fast track procedures for catheterization. Additional exclusion criteria included inability to follow the protocol (due to dementia or substance abuse), need for immediate psychiatric intervention, and lack of availability for follow-up (e.g., due to terminal non-cardiovascular illness). The study was completed in accordance with the latest version of the Declaration of Helsinki, approved by the Institutional Review Board of Columbia University Irving Medical Center (CUIMC), and all participants gave informed consent before completing study procedures.

Procedure

We first approached participants in the ED during evaluation for suspected ACS and administered informed consent and demographic questionnaires. At this time, participants reported on the ACS symptoms that brought them to the hospital and on current threat
perceptions (in the ED). Upon transfer to an inpatient bed (or by phone, if discharged), we completed the baseline interview, where participants recall prior ED threat perceptions and complete a measure of Acute Stress Disorder symptoms keyed to the ACS event. One month, 6 months, and 12 months after discharge, participants reported on PTSD symptoms specific to the cardiac event (i.e., ACS-induced PTSD) via telephone interview. Participants received a $30 payment for completing assessments.

We extracted discharge diagnosis and baseline medical comorbidities from patient medical records. Patients determined not to have met criteria for “confirmed ACS,” were designated “ruled out” for ACS. The majority of rule-out ACS patients remain at higher-than-normal risk for cardiovascular events, as most had pre-existing coronary artery disease, or other chronic diseases that caused ED physicians to initiate ACS evaluation.

Measures

Demographic Variables

We collected demographic data in the ED. Our participant population is highly diverse, with ~50% of participants identifying as Dominican or Hispanic. A large number of participants identified “Dominican” or “Hispanic” as both their race and ethnicity rather than reporting two distinct racial and ethnic identities. Therefore, for the purposes of this study, we created a combined race/ethnicity variable with categories Black, White, Hispanic, and Other.

Index ACS Status and Medical Covariates

Using medical records, we recorded participants' discharge diagnosis (confirmed ACS or rule-out). Detailed cardiovascular and non-cardiovascular diagnoses (i.e., gastrointestinal
distress, musculoskeletal pain, anxiety/panic attack) in the rule-out ACS participants have been previously reported (Lane et al., 2002). We also recorded whether or not participants had experienced a cardiovascular event in the past. Covariates from the medical record included the Global Registry of Acute Coronary Events (GRACE) risk score (Eagle et al., 2004) and Charlson Comorbidity Index scores (Charlson et al., 1987). GRACE risk scores can range from 1 to 263, with higher scores representing greater risk for mortality. Charlson Comorbidity Index scores can range from 0 to 37, with higher scores indicating more severe medical comorbidity.

*ACS-induced Posttraumatic Stress Symptoms*

We measured ACS-induced Acute Stress Disorder symptoms after ED discharge (median 3 days) using the Acute Stress Disorder Scale (ASDS; Bryant et al., 2000). Participants reported on acute stress symptoms in relation to the “heart problem that brought you to the hospital” (e.g., “did you ever feel numb or distant from your emotions?”). Participants scored responses on a 5-point Likert scale ranging from 1, “Not at all,” to 5, “Very much,” and we summed item responses to compute a total symptom score. As in our prior studies, we did not include 4 dissociation items. We measured ACS-induced symptoms of PTSD (i.e., PTSD with respect to the “heart problem, ED visit, and hospitalization”) at 1-, 6-, and 12-months using the PTSD Checklist (PCL-S) (Weathers et al., 1993). Partway through the study, APA released the DSM-5 and the corresponding PCL-5 was published. We adjusted the assessment used in our study using common items across these two instruments, by creating a 17-item summary score of posttraumatic stress symptoms (PTS) (common to both scales; i.e., DSM-IV criteria) experienced within the past month. Participants rated items on a 5-point Likert scale scored from 1, “Not at all,” to 5, “Extremely,” and we obtained total PTS symptom severity by summing the 17 items.
Psychosocial Covariates

**ED threat perceptions.** We assessed threat perceptions in response to evaluation for suspected ACS in the ED during ED evaluation and after transfer to an inpatient bed using a 7-item measure of ED Threat Perceptions (Cornelius et al., 2018; Ozer et al., 2003). Participants rated the extent to which certain statements (e.g., “I am afraid,” “I feel helpless”) reflected their ED experiences on a 4-point Likert scale ranging from 1, “Not at all,” to 4, “Extremely.” The internal consistency of the ED Threat Perceptions scale was high (Cronbach's α = 0.81).

**Cardiac threat perceptions.** We assessed ongoing perceptions of cardiac threat at 1 month via telephone interview using cardiac threat related items from the Anxiety Sensitivity Index-Revised (ASI; Peterson & Reiss, 1993). This measure was assessed 1-month after the participants' index cardiac events as we were interested in understanding the sequalae specific to cardiac-related interoception that participants experience in an ongoing fashion in the time after hospitalization and discharge. We chose not to include this measure in the ED because, in line with our inclusion criteria, participants were suspected to have had a cardiac event; therefore, participants were likely to experience cardiac-related threat perceptions acutely in the ED. Items included “It scares me when my heart beats rapidly”, “When my chest feels tight, I get scared that I won't be able to breathe properly”, “When I notice my heart skipping a beat, I worry that there is something seriously wrong with me”, and “When I feel pain in my chest, I worry that I'm going to have a heart attack.” Participants responded on a Likert scale ranging from 0, “Very little” to 4, “Very much” and we then summed items to create a total cardiac threat score. Higher scores reflect higher levels of perceived cardiac threat. This variable was introduced after the
study had already begun, and therefore data on this measure were only available for \( N = 526 \).
Internal consistency was high (\( \alpha = 0.87 \)).

**Data Analysis**

We performed latent growth mixture modeling using Mplus 8.0 (Muthén & Muthén, 2010) to identify distinct trajectories of PTS symptoms over the one-year period after evaluation for suspected ACS (baseline and 1-, 6-, and 12-months). Because ASDS (T1) and PTSD symptoms (T2–T4) were scored on different scales, we standardized scores prior to model estimation following (DeRoon-Cassini et al., 2010). For all models, we weighted time intervals between measures to account for nonequivalence. We examined unconditional models with no covariates, comparing only the intercept (no growth), followed by intercept and slope parameters (linear growth), and finally by intercept, slope, and quadratic parameters (nonlinear growth). The linear model provided improved fit over the intercept only model, whereas the nonlinear growth model failed to converge. All subsequent models used linear growth parameters with the variance of the intercept allowed to be freely estimated while the slope variance was fixed. To determine the best fitting trajectory solution, we compared progressive models of 1 to 4 classes using fit statistics, including Akaike (AIC), Bayesian (BIC), sample-size adjusted Bayesian information criterion (SSBIC) indices, entropy values, Lo-Mendell-Rubin (LRT) and bootstrap likelihood ratio tests (BLRT). We selected the final model based on overall model fit and interpretability (Bonanno, 2004; Muthén, 2003).

Little is known about the trajectories of PTS after an ACS event; therefore, after determining the best fitting unconditional model, a number of potentially relevant demographic and medical covariates were tested in addition to our two initial psychosocial covariates of
interest to examine their effect on trajectory class membership. We conducted these analyses initially outside of the model using one-way ANOVA and Chi-Square analyses because of marked reductions in sample size with the ASI cardiac threat perceptions variable. Demographic covariates included age, gender, and race/ethnicity, to assess the extent to which demographic variables predicted class trajectory. Medical covariates were examined to determine whether or not pre-existing cardiovascular risk factors or comorbid illnesses impacted trajectory class. Medical covariates included GRACE risk scores and Charlson Comorbidity Index scores, cardiovascular event history, and discharge ACS status. When examining the effect of discharge ACS status on trajectory class, we used both a Chi-Square analysis outside of the model and an omnibus Wald test as part of a known-class analysis.

In line with Edmondson's EST model (Edmondson, 2014; Meli et al., 2017) and other relevant literature, we examined the association of ED and 1-month cardiac threat perceptions on trajectory class. Based on the results of covariate analyses outside of the model, variables that significantly predicted trajectory class membership were then included in a final conditional model using Least Squares Regression analyses within the LGMM framework.

### 3.3 Results

#### Unconditional Model

We present descriptive characteristics of the sample, stratified by discharge ACS status, in Table 3.1. Information indices (AIC, BIC, SSBIC) for one- to four-class mixture models were progressively smaller as class size increased, suggesting incrementally improved fit (see Supplemental Online Materials 3.1 and 3.2). Entropy remained high and the LRT and BRT indicated significant improvement in fit up to the three-class model solution. However, for a
four-class model solution, entropy decreased and LRT was no longer significant. Based on these considerations, we selected the three-class model as the optimal solution (see Figure 3.1).

Table 3.1 Participant characteristics as a function of ACS status at discharge

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Confirmed ACS Diagnosis (n= 318)</th>
<th>Non-cardiovascular Diagnosis (n= 682)</th>
<th>Total (N=1000)</th>
<th>p-value</th>
<th>Range</th>
</tr>
</thead>
<tbody>
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<td><strong>Demographics</strong></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>62.71 (12.54)</td>
<td>59.91 (13.35)</td>
<td>60.80 (13.15)</td>
<td>.002</td>
<td>22-100</td>
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<tr>
<td>Female</td>
<td>11.50 (115)</td>
<td>34.10 (341)</td>
<td>45.60 (456)</td>
<td>.000</td>
<td>---</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td>.009</td>
<td>---</td>
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<td>White</td>
<td>21.07 (67)</td>
<td>14.37 (98)</td>
<td>16.50 (165)</td>
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<td>Black</td>
<td>16.04 (51)</td>
<td>21.70 (148)</td>
<td>19.90 (199)</td>
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</tr>
<tr>
<td>Other</td>
<td>8.81 (28)</td>
<td>5.57 (38)</td>
<td>6.60 (66)</td>
<td></td>
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</tr>
<tr>
<td>Hispanic</td>
<td>51.57 (164)</td>
<td>56.01 (380)</td>
<td>54.40 (544)</td>
<td></td>
<td>---</td>
</tr>
<tr>
<td><strong>Medical Record Covariates</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>GRACE score</td>
<td>97.30 (30.37)</td>
<td>91.22 (29.98)</td>
<td>93.19 (29.56)</td>
<td>.003</td>
<td>18-200</td>
</tr>
<tr>
<td>Charlson Comorbidity Index</td>
<td>2.16 (1.86)</td>
<td>1.65 (1.99)</td>
<td>1.82 (1.97)</td>
<td>.000</td>
<td>0-11</td>
</tr>
<tr>
<td>Prior cardiovascular event</td>
<td>54.40 (173)</td>
<td>20.97 (143)</td>
<td>31.60 (316)</td>
<td>.000</td>
<td>---</td>
</tr>
<tr>
<td><strong>In-Hospital Assessment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perceived threat in the ED</td>
<td>11.00 (4.13)</td>
<td>10.93 (4.50)</td>
<td>10.95 (4.38)</td>
<td>.814</td>
<td>6-24</td>
</tr>
<tr>
<td>Depressive symptoms at baseline&lt;sup&gt;a&lt;/sup&gt;</td>
<td>6.16 (5.67)</td>
<td>6.68 (6.03)</td>
<td>6.51 (5.91)</td>
<td>.207</td>
<td>0-24</td>
</tr>
<tr>
<td>PTSD total severity score at baseline for prior trauma&lt;sup&gt;b&lt;/sup&gt;</td>
<td>25.26 (12.69)</td>
<td>26.08 (13.59)</td>
<td>25.81 (13.30)</td>
<td>.381</td>
<td>17-85</td>
</tr>
<tr>
<td><strong>1-Month Follow-Up</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perceived cardiac threat</td>
<td>6.85 (5.10)</td>
<td>7.17 (5.20)</td>
<td>7.06 (5.16)</td>
<td>.504</td>
<td>0-16</td>
</tr>
<tr>
<td>ACS-induced PTSD symptoms</td>
<td>25.29 (11.46)</td>
<td>25.06 (11.76)</td>
<td>25.14 (11.64)</td>
<td>.834</td>
<td>17-74</td>
</tr>
<tr>
<td><strong>6-Month Follow-Up</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACS-induced PTSD symptoms</td>
<td>23.39 (11.03)</td>
<td>26.36 (13.41)</td>
<td>25.33 (12.70)</td>
<td>.023</td>
<td>17-83</td>
</tr>
<tr>
<td><strong>12-Month Follow-Up</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACS-induced PTSD symptoms</td>
<td>23.27 (10.45)</td>
<td>24.51 (11.41)</td>
<td>24.10 (11.11)</td>
<td>.291</td>
<td>17-84</td>
</tr>
</tbody>
</table>

*Note. GRACE=Global Registry of Acute Coronary Events. ED=emergency department. PTSD=posttraumatic stress disorder. ACS=acute coronary syndrome.

<sup>a</sup>Past 2-week depressive symptoms assessed with the Patient Health Questionnaire depression scale (PHQ-8).

<sup>b</sup>PTSD total severity score at baseline calculated by summing responses on the PTSD Checklist-Civilian version (PCL-C) with respect to the most stressful event identified on the LEC.
The largest of the three classes, labeled *Resilient* (87.26%), was characterized by low PTS symptoms across all time points with a low intercept \( (b = -0.26, \ SE = 0.02, p < .001) \) and flat, nonsignificant slope \( (b=-0.03, \ SE=0.03, \ p=.28) \). The second largest class, labeled *Chronic-Worsening* (9.56%), described individuals who showed clinically elevated PTS at T1 and T2 and worsening at T3 and T4. This group had a high intercept \( (b = 1.31, \ SE = 0.17, p < .001) \) and a significant positive linear slope \( (b = 1.17, \ SE = 0.17, p < .001) \). The third and smallest class, labeled *Acute-Recovering* (3.19%), was characterized by individuals who had acute initial PTS at T1 and T2, followed by marked reductions across T3 and T4. This group had the highest intercept \( (b = 2.55, \ SE = 0.33, p < .001) \) and significant negative linear slope \( (b = -2.11, \ SE = 0.48, p < .001) \).

**Figure 3.1** Three-class unconditional model of posttraumatic stress symptoms (N = 973)
Preliminary Analyses of Possible Predictors of Class Membership

Analyses of covariates in a conditional model tend to produce better specified solutions relative to an unconditional model (Li & Hser, 2011; Muthén, 2004). We evaluated demographic, medical, and psychosocial variables as predictors of class membership independent of the model using Chi-Square and one-way ANOVAs. No demographic or medical variables showed significant effects, except gender ($\chi^2(1) = 16.74, p < .001$). However, both psychosocial variables of interest, ED threat perceptions ($F[2, 971] = 24.38, p < .001$) and cardiac threat perceptions ($F[2, 525] = 43.70, p < .001$), significantly differentiated trajectory membership.

Conditional Model

To more fully examine how covariates predicted class membership and whether they influence the shape and prevalence of the trajectories, we tested a conditional model that included variables identified in the previous analyses: gender, ED threat perceptions, and cardiac threat perceptions. As previously noted, a considerable amount of data was missing for the cardiac threat perceptions measure because this measure was added after data collection for the study had begun. Of the $N = 1000$, only 526 completed the cardiac threat perceptions measure, lowering the sample size for our conditional model by 45% ($n = 526$).

The conditional model successfully converged. Class membership proportions and shape did not change substantially when compared to the unconditional model (see Supplemental Online Material 3.1). The Resilient class was, again, the largest (81.74%), followed by Chronic-Worsening (13.69%), and the smallest group, Acute-Recovering (4.56%) (Figure 3.2).
To examine the covariates as predictors of class membership, we first used the Resilient class as the reference group. Compared to the Resilient class, ED threat perceptions were significantly higher for individuals in the Chronic-Worsening class \((b = 0.13, SE = 0.03, p < .001)\) and Acute-Recovering class \((b = 0.29, SE = 0.06, p < .001)\). Cardiac threat perceptions were also significantly higher in the Chronic-Worsening class \((b = 0.24, SE = 0.04, p < .001)\) and Acute-Recovering class \((b = 0.35, SE = 0.08, p < .001)\). In a second set of analyses, we used the Chronic-Worsening class as the reference group. Compared to the Chronic-Worsening class, the Acute-Recovering class reported significantly higher ED threat perceptions \((b = 0.15, SE = 0.06, p = .008)\) but no significant difference in cardiac threat perceptions \((b = 0.11, SE = 0.08, p = .213)\). Gender did not significantly differentiate any of the trajectory classes.
Discharge ACS Status

We examined whether PTS symptom trajectories differed by ACS diagnosis. We found no significant difference in proportion of participants in each trajectory in a 2×3 contingency analysis comparing confirmed versus rule-out ACS across PTS symptom trajectories in the unconditional model, \(\chi^2(2) = 1.43, p = .489\), or in the conditional model, \(\chi^2(2) = 2.93, p = .231\). Results are given in Table 3.2. We also tested discharge ACS status as a variable within the LGMM using a known-class analysis and omnibus Wald test in both models. Results of the omnibus Wald test were not significant, indicating that stratification of models based on ACS status (confirmed versus rule-out ACS) did not meaningfully improve model fit (unconditional: \(p = .681\); conditional: \(\chi^2(1) = 0.128, \chi^2(1) = 0.170, p = .720\)).

Table 3.2 Chi-square analyses of trajectory class membership stratified by ACS status in unconditional (N = 973) and conditional (N = 526) growth mixture models

<table>
<thead>
<tr>
<th></th>
<th>Resilient %(%n)</th>
<th>Acute-Recovering %(%n)</th>
<th>Chronic %(%n)</th>
<th>(\chi^2(2))</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unconditional Model</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirmed ACS</td>
<td>88.9% (279)</td>
<td>2.9% (9)</td>
<td>8.3% (26)</td>
<td>1.43</td>
<td>.489</td>
</tr>
<tr>
<td>Rule-out ACS</td>
<td>86.2% (568)</td>
<td>3.9% (26)</td>
<td>9.9% (65)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Conditional Model</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirmed ACS</td>
<td>85.2% (155)</td>
<td>2.7% (5)</td>
<td>12.1% (22)</td>
<td>2.93</td>
<td>.231</td>
</tr>
<tr>
<td>Rule-out ACS</td>
<td>79.9% (275)</td>
<td>5.5% (19)</td>
<td>14.5% (50)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3.4 Discussion

Each year, millions of individuals are hospitalized for suspected ACS. Many experience these events as traumatic, and some go on to develop PTS symptoms. We identified 3 unique trajectories of PTS symptoms over the course of 1-year post-hospitalization in a large, ethnically
TRAJECTORIES OF POSTTRAUMATIC STRESS AFTER ACS

diverse sample. A clear majority of ACS patients in the current study (87%) were classified in a Resilient trajectory denoted by low PTS symptoms at all time points. A smaller group (10%) was classified in a Chronic-Worsening trajectory characterized by high initial PTS symptoms that worsened over the course of the year. Finally, a third, small group (3%) was classified in an Acute-Recovering trajectory characterized by considerably elevated initial PTS symptoms that steadily resolved over the course of the year.

We were particularly interested in whether the PTS trajectories were impacted by threat perceptions during ED evaluation, ongoing interoceptive distress concerning cardiac signals, and by discharge diagnosis (ACS or rule-out). We found that patients who were highly distressed during the ED visit were significantly more likely to show either an acute-recovering or chronic-worsening trajectory (12.7% of the sample combined). In light of current diagnostic criteria for PTSD, this finding is intuitive. According to the DSM-5, peritraumatic factors, including severity of the trauma and perceived threat to life, increase the likelihood of developing PTSD (American Psychiatric Association [APA], 2013). Although our ED threat measure reflected peritraumatic fear of dying and vulnerability, the hectic hospital environment may have exacerbated participants' distress (McCarthy et al., 2008).

Interestingly, however, ED threat perceptions were significantly more strongly associated with acute PTS symptoms that resolved over the ensuing year (i.e., Acute-Recovering pattern) than with the Chronic-Worsening pattern. Thus, although individuals with heightened peritraumatic threat in the ED suffer acute PTS symptoms, they do not necessarily develop chronic PTSD. It will be crucial in future studies to further tease out how threat ED perceptions may inform these different clinical sequelae.
In contrast to threat perceptions during ED evaluation, the perception of ongoing cardiac threat predicted both the Acute-Recovering and the Chronic-Worsening trajectory with equal likelihood. This finding supports the EST model, which theorizes that ongoing somatic threat perceptions are of particular importance for PTS after an acute, life-threatening cardiac event. Heighted cardiac threat is reminiscent of the archetypal hypervigilance and arousal behaviors in response to triggering traumatic reminders characteristic of PTSD. However, unique to our study and this sample, the trigger is a physiological signal both of relevance to the index ACS event and important in identifying a potential future event. Patients are in a unique role of experiencing present cardiac sensations as simultaneously triggering memories of the initial trauma and as potentially signifying a current/future traumatic cardiac event. Whereas PTSD is generally considered a disorder of fear memory processing, the EST model suggests that the present and future temporal focus of cardiac threat perceptions may be an important clinical target.

We also examined other potentially relevant predictor variables. Neither demographic nor medical status variables differed meaningfully across trajectories. Notably, the PTS symptom patterns were also relatively invariant in relation to discharge diagnosis. Despite 68% of patients in our study receiving a rule-out ACS discharge diagnosis, the trajectories for this group and those with a confirmed ACS event were essentially identical, which agrees with prior cross-sectional findings (Lane et al., 2002). While perhaps surprising, our findings suggest that pathophysiology and ultimate diagnosis do not differentially impact PTS reactions following an acute cardiac event. Instead, initial perceived threat, subjective trauma experience, and ongoing concerns about cardiac risk are more powerful and predictive of clinical course and psychological sequelae than clinical diagnosis or severity (Edmondson & Cohen, 2013). Prior findings suggest that patients evaluated for ACS may be uncertain of their discharge diagnosis.
TRAJECTORIES OF POSTTRAUMATIC STRESS AFTER ACS

(Yasaitis et al., 2015). Future studies of PTS in patients evaluated for ACS should determine the influence of patient understanding of discharge diagnosis.

Limitations

Our findings should be interpreted within the context of several limitations. First, the REACH study was conducted at a single site in an urban setting and one of the nation's largest and busiest hospitals. Therefore, these findings may not be generalizable to patients presenting with ACS in other ED settings. A second consideration concerns our measurements of PTS symptoms and cardiac threat. Our study used a self-report questionnaire to assess PTS symptoms rather than a clinical interview. Therefore, we cannot conclude a clinical diagnosis of PTSD and instead report on symptoms of PTS. Further, our study had missing data for our cardiac threat measure. This measure, comprised of cardiac threat related items from the ASI (Peterson & Reiss, 1993), was introduced after data collection for this study had begun, resulting in only half of our total sample completing the cardiac threat measure.

While our study presents novel findings on the predictors of PTS trajectories in the 12-months following a suspected ACS event, our study lacks data on the clinical effects of these trajectories, including event recurrence, future hospitalizations, and mortality. In addition, our study did not formally assess participants' psychological treatment for dysfunction and distress associated with PTS nor medical treatment for CVD. However, prior research has reported self-reported treatment-seeking behaviors in this sample (Wall et al., 2018). Future research should take into consideration clinical outcomes and treatment for PTS and CVD in order to better understand the impact of trajectory status and membership in this population.
3.5 Conclusions

ED treatment for suspected ACS events is a potentially traumatic experience that results in heterogeneous patterns of PTS symptoms. While the majority of individuals are resilient, about 1 in 8 patients report elevated PTS symptoms. Our findings detail the impact of patients' threat perceptions during ED evaluation, as well as the unique relationship of ongoing cardiac threat perceptions with PTS symptom trajectories. It is important for medical and psychological clinicians to consider that PTS symptoms may be present and highly distressing in patients evaluated for CVD events in the ED, regardless of discharge diagnosis. The subjective experience of presenting to the ED with ACS symptoms can be traumatic, and may result in chronic psychological symptoms. Future research should continue to explore symptom trajectories and determinants of PTSD due to other life-threatening medical events. Such research can inform and improve peritraumatic and clinical intervention efforts. Interventions targeting PTS, threat perceptions in the ED, and/or ongoing cardiac/interoceptive threat perceptions may reduce psychological distress, improve quality of life, and perhaps reduce secondary CVD risk after acute cardiac events.

Declaration of Competing Interest: None.

Funding: This work was supported by the National Institutes of Health [HL117832, HL128497, HL128310].
Supplemental Online Material

**Supplemental Online Material 3.1** Fit indices for one- to three-class growth mixture models of posttraumatic stress symptoms (unconditional $N = 973$)

<table>
<thead>
<tr>
<th>Fit index</th>
<th>One-class</th>
<th>Two-classes</th>
<th>Three-classes</th>
<th>Four-classes</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIC</td>
<td>8004.48</td>
<td>7550.45</td>
<td>7401.96</td>
<td>7229.84</td>
</tr>
<tr>
<td>BIC</td>
<td>8038.64</td>
<td>7599.26</td>
<td>7565.40</td>
<td>7307.93</td>
</tr>
<tr>
<td>SSBIC</td>
<td>8016.41</td>
<td>7567.50</td>
<td>7424.12</td>
<td>7257.11</td>
</tr>
<tr>
<td>Entropy</td>
<td>--</td>
<td>0.941</td>
<td>0.936</td>
<td>0.884</td>
</tr>
<tr>
<td>LRT</td>
<td>--</td>
<td>p &lt; .001</td>
<td>p = .035</td>
<td>p = .358</td>
</tr>
<tr>
<td>BLRT</td>
<td>--</td>
<td>p &lt; .001</td>
<td>p &lt; .001</td>
<td>p &lt; .001</td>
</tr>
</tbody>
</table>

*Note.* AIC = Akaike information criterion; BIC = Bayesian information criterion; SSBIC = sample size adjusted Bayesian information criterion; LRT = Lo-Mendell-Rubin test; BLRT = bootstrapped likelihood ratio test

**Supplemental Online Material 3.2** Conditional model description ($N = 526$)

Trajectories in the conditional model were again characterized by low PTS symptoms across all time points, with a low intercept ($b = -0.26$, $SE = 0.03$, $p < .001$) and flat slope ($b = -0.08$, $SE = 0.04$, $p = 0.03$). The second largest class, labeled *Chronic-Worsening* (13.69%), again described individuals who showed clinically elevated PTS symptoms at T1 and T2 and worsening symptoms at T3 and T4, again with a high intercept ($b = .83$, $SE = 0.19$, $p < .001$) and a significant positive linear slope ($b = 1.24$, $SE = 0.16$, $p < .001$). The third and smallest class, *Acute-Recovering* (4.56%), was again characterized by individuals who had acute initial PTS symptoms at T1 and T2, but exhibited marked reductions across T3 and T4. This group had a high intercept ($b = 2.30$, $SE = .21$, $p < .001$) and significant negative linear slope ($b = -2.03$, $SE = 0.21$, $p < .001$).
Chapter 4: Anxiety sensitivity and worry predict trajectories of psychological adjustment in the first 12-months of the COVID-19 pandemic
Anxiety sensitivity and worry predict trajectories of psychological adjustment in the first
12-months of the COVID-19 pandemic

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Abstract

**Background:** The COVID-19 pandemic continues to profoundly impact the global community. The present study seeks to clarify the scale, natural course, and heterogeneous patterns of the pandemic’s impact on mental health. **Methods:** We estimated longitudinal trajectories of depression and anxiety symptoms at three timepoints over the course of 12-months (April 2020, October 2020, April 2021) during the COVID-19 pandemic among a community sample (N=474). At each timepoint, participants completed online, psychosocial questionnaires.

**Results:** Latent growth mixture modeling identified two trajectories of depression (Resilient = 57.32%; High Depression = 42.68%) and four trajectories of anxiety (Resilient = 46.40%; Mild-Improving = 40.45%; Chronic = 9.93%; Worsening = 3.23%). When examining symptoms of depression, younger age, college education, higher interoceptive threat bias, and greater feelings of uncertainty and threat at baseline increased likelihood of membership in the High Depression class, compared to the Resilient class. For anxiety trajectories, the Resilient class was significantly older than all other classes, reporting lower interoceptive threat bias and fewer feelings of uncertainty and threat at baseline than the Mild-Improving and Chronic classes.

**Conclusions:** Given the chronicity, broad impact, and health-related risks of the COVID-19 pandemic, clinically elevated depressive and anxiety symptoms are common responses in the first year of the pandemic; however, the majority of individuals remained resilient. General feelings of uncertainty and threat and interoceptive threat bias are potential foci for community-level mental health interventions targeting depression and anxiety symptoms in younger individuals.

**Keywords:** COVID-19, depression, anxiety, anxiety sensitivity, interoception, trajectory
Anxiety sensitivity and worry predict trajectories of psychological adjustment in the first 12-months of the COVID-19 pandemic

Entering its third year, the COVID-19 pandemic continues to profoundly impact the global community. The virus – due to its remarkable scale of impact and aided by its opportunistic contagion – has repeatedly outpaced efforts to curb its spread, leading to an unprecedented burden on individuals and systems, alike. Appropriately so, the primary public health aim has remained focused on reducing spread and attenuating illness severity. At times, however, these efforts have also contributed to unceremonious disruptions to social, economic, and health systems. Individuals have incurred unpredictable and highly disruptive personal consequences - many losing sources of income, enduring long stretches of isolation or lack of privacy in crowded homes, being plucked from classroom communities, or entering an unfamiliar virtual workforce. On a social level, lack of human contact and community participation at a time of severe collective adversity run counter to basic social norms.

With the adoption of essential public health measures, advent of safe and effective vaccines, and identification of novel, symptom-reducing treatments, many communities have experienced a tenuous yet hopeful return to the “new normal.” However, the pandemic continues to pose a very real threat to human health, with more than 980,000 deaths and 80 million infections nationwide since its onset (World Health Organization [WHO], 2022). Further, its systemic ripple effects continue, causing differential impacts on individuals and communities due to population-specific risk and protective factors. Therefore, clarifying the scale and nature of the pandemic’s impact on mental health remains essential in order to appropriately inform policy changes, direct community-level interventions, and support public dissemination.
Studies of past viral epidemics (e.g., 2002-2003 Sudden Acute Respiratory Syndrome [SARS-CoV] and 2012 Middle East Respiratory Syndrome [MERS-CoV]) have guided important preliminary understandings of COVID-19’s impact on psychological functioning (Chan et al., 2006; Cheng et al., 2004; Chua et al., 2004; Huang et al., 2003; Shi et al., 2003; Wu et al., 2005) and pointed researchers toward the expectation of potential widespread psychological distress (Chau et al., 2021; Jeong et al., 2016; Maunder, 2009; Peng et al., 2010; Sommer, 2020). However, these comparisons have proven limited in their predictive value and clinical application, given COVID-19’s unprecedented scale and unique psychosocial sequelae.

Considering the longitudinal course of the pandemic is essential to accurately estimating pandemic-related mental health outcomes. While cross-sectional studies provide rapid and essential snapshots of population-level symptomology, they are very rarely generalizable in the context of a prolonged and highly dynamic event, such as the COVID-19 pandemic. Reactions to extremely adverse events typically result in a peak of distress as individuals confront novel sources of threats and encounter unwelcome disruptions to familiar ways of being; this peak typically dissipates for the majority, particularly the longer that individuals have to confront, compensate, and ultimately adjust to these events, as individuals find ways to flexibly adapt and effectively cope. In order to capture the natural course of psychological reactions to the pandemic over time, longitudinal studies provide a series of freeze-frames allowing the story of adjustment to unfold and a more complete narrative of the impact of COVID-19 on mental health to emerge. Taking into consideration timelines of data collection, current findings suggest worse psychological adjustment in the weeks and months immediately following the pandemic onset in Spring 2020 in the global community – a highly understandable and in many ways normative response, given the novelty and gravity of the circumstances (Ettman et al., 2020; Holingue et
Disaster events, including pandemics, are inherently dynamic resulting in heterogeneous patterns of psychological adjustment (Bonanno et al., 2004; Galatzer-Levy et al., 2018). The COVID-19 pandemic is undeniably a highly unique adverse event, with few other instances in recent history matching the scale, speed, chronicity of the current pandemic. Despite the immense psychological and systemic burden, accumulating international research insinuates that the majority of individuals have exhibited natural recovery patterns after initial periods of peri-traumatic adjustment. Some reviews show increases in depression and anxiety during the first peak of the pandemic and others highlight high rates of resilience, or a stable pattern of very low, subclinical symptoms (Robinson et al., 2022; Sun et al., 2020). Indeed, emerging reviews and meta-analyses have found higher cross-sectional rates of anxiety and depression within the first several months of the pandemic’s onset, as compared to mental health before the pandemic, with trends toward symptoms returning to baseline over the course of several months (Liu et al., 2021; Necho et al., 2021; Ren et al., 2020; Robinson et al., 2022; Wu et al., 2021). Taken together, a clearer picture begins to emerge. The majority of individuals appear to experience either an apex of psychological distress at the start of the pandemic and then recovery patterns to a subclinical level or experience no clinically significant changes to their mental health at any point in the pandemic, thus far.

Increasingly conceptualized as a multidimensional stressor, the COVID-19 pandemic has been associated with myriad psychosocial and systemic impacts, many of which are potential drivers of negative mental health consequences (Bernardini et al., 2021; Breslau et al., 2021; Gruber et al., 2021; Hawes et al., 2021; Kuntz, 2021; Mancini, 2020; Necho et al., 2021; Rudenstine et al., 2021).
PSYCHOLOGICAL ADJUSTMENT TO COVID-19

Valiente et al., 2021; Zavlis et al., 2021). Appropriate computational models can account for variability due to important contextual factors, which may attenuate or exacerbate pandemic-related distress, capturing heterogeneous patterns of psychological adjustment with increased accuracy. Longitudinal trajectory estimates provide a more representative understanding of the natural course of psychological adjustment, embracing inherent fluctuations in the human response to extreme adversity over time and providing valuable insight into patterns of adjustment (Bonanno, 2012; Galatzer-Levy et al., 2018; Taylor, 2019).

Around the world, longitudinal trajectory studies have replicated findings underscoring heterogeneous psychological adjustment to COVID-19 (Ahrens et al., 2021; Batterham et al., 2021; Chen et al., 2022; Fancourt et al., 2020; Gambin et al., 2022; Kimhi et al., 2021; Pierce et al., 2021; Shevlin et al., 2021), each revealing a common set of prototypical outcome trajectories (Chen & Bonanno, 2020; Galatzer-Levy et al., 2018). To date, however, a limited number of COVID trajectory studies have been conducted in U.S. samples (Shilton et al., 2021). This poses a critical gap in the literature, particularly as the U.S. has maintained the highest global infection and death rates by a substantial margin and currently accounts for approximately 1/6 of the global deaths due to the virus (WHO, 2022).

4.1 The Present Study

The present study seeks to improve understanding of the COVID-19 pandemic’s community level mental health impact. To our knowledge, this study provides the first 12-month-long trajectory estimates of psychological adjustment to COVID-19 in the U.S., with data collection spanning from April 2020, approximately 1-month after the pandemic’s arrival in the U.S., through April 2021, nearly 5-months after vaccines were adopted publicly. We additionally
aimed to examine the impact of two psychosocial factors, highly relevant to an individual’s experience of distress during the pandemic. Previous research has shown that chronic stressors, like the ongoing pandemic, increased emotional reactivity and reliance on maladaptive emotion regulation strategies are known to exacerbate feelings of anxiety and depression (e.g., Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008; Segerstrom, Tsao, Alden, & Craske, 2000). Further, many mental health conditions, including elevated depression and anxiety, are intimately related to an individual’s ability to flexibly adapt and self-regulate in the face of shifting circumstances, ambiguity, and potential threat (Aldao, Sheppes, & Gross, 2015; Bonanno et al., 2004; Hofman, Sawyer, Fang, & Asnaani, 2012; Piguet et al, 2016). Therefore, we sought to identify and examine potential barriers to flexible adaptation and mechanisms disrupting the emotion regulation process.

Tolerating uncertainty has been a core component of adjusting to life during the COVID-19 pandemic. We have all endured the disquieting experience of having insufficient information in the face of a novel and proximal threat; most have been faced with abrupt changes requiring fundamental changes to daily living. Higher intolerance of uncertainty is an established risk factor for depressive and anxiety symptoms and has been identified as a moderating factor for psychological distress during the COVID-19 pandemic (Rettie & Daniels, 2020; Satici et al., 2020; Sauer et al., 2020). Given this, we examined feelings of uncertainty and threat as predictors of psychological adjustment trajectories. In line with existing cross-sectional research, we hypothesized that individuals subjectively experiencing higher levels of uncertainty and threat would exhibit worse psychological adjustment in the first 12-months of the pandemic.

Finally, our study sought to investigate the psychological impact of the COVID-19 pandemic’s threat to physical health and human life. Individuals have been flooded with public
health recommendations to remain somatically hypervigilant for symptoms like a scratchy throat, cough, fever, malaise, or difficulty breathing. While self-monitoring for potential COVID-19 symptoms has been vital to harm reduction throughout the pandemic, increased self-monitoring and somatic hypervigilance can contribute to emotion dysregulation, evidenced by increased ruminative thoughts and maladaptive behaviors (Barksy & Wyshak, 1990; Jungmann & Witthöft, 2020; Witthöft et al., 2006).

Complicating the picture, many COVID-19 symptoms are similar to uncomfortable somatic experiences of anxious arousal (i.e., body temperature fluctuations, increased respiration and heart rate, dizziness). Anxiety sensitivity, or an individual’s propensity to interpret experiences related to anxious arousal as threatening cues, is a transdiagnostic risk factor for anxiety and depression that has been identified as a mechanism of interest in psychological reactions to the COVID-19 pandemic (Manning et al., 2021; Rogers et al., 2021; Schmidt et al., 2021). The enduring somatic threat (EST) model, a leading theoretical model of medically induced PTSD, posits that an ongoing mortality threat perpetuates psychological distress in the face of real and proximal physical or health-related threats; this mortality threat results in an increased sensitivity to interoceptive monitoring of normal somatic cues and catastrophic interpretations of those interoceptive signals (Edmondson, 2014; Meli et al., 2017).

In the face of an ongoing health-related threat, such as the ongoing COVID-19 pandemic, this interoceptive threat bias appears to have a complex impact on psychological functioning (Alonzi et al., 2020; Avidor et al., 2021; Lenzo et al., 2021; Manzanares et al., 2021; Schmidt et al., 2021; Waqas et al., 2020). In line with the EST model and anxiety sensitivity construct and in the context of health-related risks and high mortality rates associated with the COVID-19 virus,
we hypothesized that higher physical anxiety sensitivity would differentially impact trajectories of psychological adjustment in the first year of the COVID-19 pandemic.

4.2 Methods

Participants & Procedure

The present study includes English-speaking, adult participants (N = 404) living in the United States recruited in April 2020. Participants were invited to complete online, psychosocial surveys, using Amazon Mechanical Turk (MTurk), at three equally spaced timepoints over the course of 12 months during the COVID-19 pandemic. MTurk participation requirements and study inclusion parameters included current residence in the United States, English language fluency, and sufficient response validity on each completed survey. The first round of data collection (T1) occurred in April 2020; at T1, participants completed online informed consent and demographic and psychosocial questionnaires. Data collection for timepoint 2 (T2) occurred approximately 6-months later in October 2020 and timepoint 3 (T3) occurred approximately 12-months later in April 2021; at T2 and T3, participants completed an abbreviated battery of psychosocial questionnaires, including follow-up measures from T1.

We excluded participants with more than one incomplete or missing survey. This results in 404 participants at T1, 375 participants at T2, and 278 participants at T3; for demographic information, see Table 4.1. This study was approved by the Institutional Review Board of Teachers College, Columbia University, and all participants gave informed consent before completing study procedures. All procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.
Surveys for all timepoints were created, hosted, and managed on Qualtrics XM, a cloud-based platform facilitating the creation and distribution of online surveys. After accessing the study, participants were directed to study questionnaires housed on Qualtrics XM. We used Qualtrics XM for all data collection. In order to ensure anonymity and confidentiality, we assigned each MTurk participant a unique, six-digit, numerical identification code in Qualtrics XM upon survey completion. This Qualtrics ID code was the sole response identifier connecting MTurk user IDs to their corresponding responses in the Qualtrics database; we did not collect any identifying data from participants. In order to accurately match MTurk participants to their Qualtrics responses across longitudinal timepoints, Qualtrics IDs were saved as metadata in the MTurk platform. When extracting and cleaning data, we downloaded all metadata from MTurk and matched Qualtrics ID codes to MTurk user IDs across the MTurk and Qualtrics datasets.

Table 4.1 Participant characteristics (N=474)

<table>
<thead>
<tr>
<th>Demographics</th>
<th>% (n)</th>
<th>M (SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>--</td>
<td>39.27 (13.25)</td>
<td>18-78</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>215 (45.40)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Male</td>
<td>185 (39.00)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black/African-American</td>
<td>46 (9.70)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Hispanic/Latinx</td>
<td>33 (7.00)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Asian</td>
<td>48 (10.10)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>White</td>
<td>272 (57.40)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic or Latinx</td>
<td>57 (12.00)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Not Hispanic or Latinx</td>
<td>343 (72.40)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No college degree</td>
<td>107 (22.50)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>College degree</td>
<td>297 (62.70)</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Psychosocial Covariates</th>
<th>% (n)</th>
<th>M (SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASIp Total Score</td>
<td></td>
<td>5.94 (2.70)</td>
<td>2-10</td>
</tr>
<tr>
<td>FUTS Total Score</td>
<td></td>
<td>33.37 (10.26)</td>
<td>10-50</td>
</tr>
</tbody>
</table>
Once data was extracted and matched on Qualtrics ID code, we removed data from participants who failed embedded data response validity questions, as well as responders who appeared to be invalid responders. Participants received $3.00 payment via MTurk for valid, high-quality responses at each timepoint; timely completion of questionnaires at T2 and T3 was incentivized with $1.00 bonus payments to those who responded within 2 weeks of follow-up survey launches. We notified participants of bonus incentivization using MTurk’s messaging platform.

We utilized MTurk, a service facilitating efficient, high-quality data collection from a large, diverse pool of online participants (Buhrmester et al., 2018), as a remote data collection solution during the COVID-19 pandemic. While MTurk participants and offline, lab-based participants have been shown to perform similarly, recent studies have drawn attention to data quality concerns due to the increase in “bots” (automated computer programs that automatically complete online surveys) and “farmers” (individuals circumventing MTurk location parameters) engaging with the platform (Kees et al., 2017; Paolacci et al., 2010). To remain vigilant against these potential data quality issues, we followed recommendations to include response validity indicators and metadata to track and remove invalid or low-quality data (Barger et al., 2011). Our study included four embedded response validity questions per timepoint; we also ensured that each online survey included metadata to assess for bots, participants who did not meet demographic inclusion criteria, duplicate responders, and otherwise invalid responders. All invalid and low-quality data was removed before data analysis.

Measures

**Demographic Variables**

We collected demographic data at T1 in April 2020. Demographic variables included self-reported age, gender, race, ethnicity, and highest level of education.
Psychosocial Covariates

**Depression Symptoms.** We measured symptoms of depression at all timepoints using The Center for Epidemiological Studies - Depression (CES-D), a 20-item self-report measure (Radloff, 1977). The CES-D assesses the severity of symptoms associated with depression in the past week, including changes to sleep and appetite, changes to mood and cognition, and social dysfunction. Responses range from 0 (“Rarely or none of the time [less than 1 day]”) to 3 (“Most or all of the time [5-7 days]”). Scores range from 0-60 with higher scores indicating more severe symptomology. Scores equal to or above 16 indicate clinically elevated symptoms of depression. The CES-D has shown good sensitivity and specificity, and high internal consistency (Lewinsohn et al., 1997).

**Generalized Anxiety Symptoms.** We measured symptoms of generalized anxiety at all timepoints using the GAD-7, a brief, 7-item clinical screening tool (Spitzer et al., 2006). The GAD-7 assesses the severity of self-reported anxiety symptoms with responses ranging from 0 (“Not at all”) to 3 (“Nearly every day”). Symptoms include the presence of cognitive, mood, and psychomotor changes over the last 2 weeks (i.e., “Feeling nervous, anxious, or on edge”; “Being so restless that it is hard to sit still”). Scores range from 0-21 with severity cut-off scores of 5 for mild anxiety, 10 for moderate anxiety, and 15 for severe anxiety. The GAD-7 has shown high levels of internal consistency and test-retest reliability (Spitzer et al., 2006).

**Physical Anxiety Sensitivity.** We assessed physical symptoms of anxiety sensitivity at T1 using the physical subscale from the Anxiety Sensitivity Index – Version 3 (ASIp; Taylor et al., 2007). Responses to the six items (“When my stomach is upset, I worry that I might be seriously ill”; “When I notice my heart skipping a beat, I worry that there is something seriously wrong
with me”; “When I feel pain in my chest, I worry that I’m going to have a heart attack”; “When my chest feels tight, I get scared that I won’t be able to breathe properly”; “When my throat feels tight, I worry that I could choke to death;” and “It scares me when my heart beats rapidly”) were scored on a scale from 0 (“Very little”) to 4 (“Very much”) and summed to create a total ASIp score. No time frame is specified for responses. Internal consistency for the ASIp was excellent (Cronbach’s α = .93).

**Feelings of Uncertainty and Threat.** We assessed feelings of uncertainty and threat in various domains at T1 using the Feelings of Uncertainty and Threat Scale (FUTS; adapted from Chen et al., 2015). The FUTS asks participants to rate their thoughts and feelings regarding five potential sources of insecurity in the past week of the COVID-19 pandemic on a scale of 1 (“Not true at all”) to 5 (“Completely true”) for ten items. Sources of insecurity include personal health (“I was concerned about my health”), health of loved ones (“I was concerned about the health of my loved ones”), financial concerns (“I had the feeling that my financial situation is under threat”), situational instability (“I was concerned about how the current situation will evolve”), and food/supply instability (“I was concerned about the scarcity of food and medication”). Scores from the ten items were scored and summed to create a total FUTS score. Internal consistency for FUTS was excellent (Cronbach’s α = .91).

**Data Analysis**

We performed latent growth mixture modeling (LGMM) using MPlus 8.0 to identify distinct trajectories of depression and anxiety. We examined unconditional models (no covariates) of depression and anxiety symptoms over the course of 12-months (3 timepoints), first comparing only the intercept (no growth), followed by intercept and slope parameters (linear
growth). The linear models provided improved fit over the intercept only models. All subsequent models used linear growth parameters with the variance of the intercept allowed to be freely estimated while the slope variance was fixed. To determine the best fitting trajectory solutions, we next compared progressive class models for each measure using fit indices, including Akaike (AIC), Bayesian (BIC), sample-size adjusted Bayesian information criterion (SSBIC), and entropy values, and the Lo-Mendell-Rubin (LRT) and bootstrap likelihood ratio tests (BLRT), which compare the significance of a class solution relative to the previous class solution \((k-1)\). We selected the final models based on overall model fit and interpretability (Bonanno et al., 2004; Lo et al., 2001; Muthén, 2003; Nylund et al., 2007; Ram & Grimm, 2009).

In determining the best fitting unconditional models for each outcome measure, only those models for depression and anxiety converged successfully. In addition to ASIp and FUTS, we also tested a number of potentially relevant demographic and psychosocial covariates to examine their relation to trajectory class membership for depression and anxiety models. Following Muthén (2004), we initially conducted these analyses outside of the model using one-way ANOVA and Chi-Square analyses with depression and anxiety outcomes to determine the most likely predictors for inclusion in conditional models. Psychosocial variables of interest included ASIp and FUTS scores; demographic covariates included age, gender, level of education, race, and ethnicity. The final, conditional models tested these variables using Least Squares Regression analyses within the LGMM framework (see Tables 4.2 & 4.3).

4.3 Results

**Unconditional Model of Depression & Anxiety Symptoms**

We began by estimating three successive models of depression symptoms, one more than the best fitting model, in order to assess fit using multiple parameters (see Table 4.4). Information
indices (AIC, BIC, SSBIC) for one- to three-class mixture models were progressively smaller as class size increased, suggesting incrementally improved fit. Entropy remained high and BRT indicated significant improvement in fit up to the three-class model solution. However, for the three-class model solution, LRT was no longer significant. Based on these fit parameters, we selected the two-class model as the optimal solution.

Next, we estimated successive models of anxiety symptoms, comparing multiple fit parameters throughout, in order to determine the best fitting model for anxiety symptoms (see Table 4.5). Information indices for one- to five-class mixture models were progressively smaller as class size increased, suggesting incrementally improved fit. Entropy remained high and the

<table>
<thead>
<tr>
<th>Table 4.2</th>
<th>Participant characteristics as a function of depression (CES-D) trajectory class membership in unconditional growth mixture model (N=404)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td><strong>Resilient High Depression</strong></td>
</tr>
<tr>
<td>Gender</td>
<td>% (n)</td>
</tr>
<tr>
<td>Female</td>
<td>61.9% (133)</td>
</tr>
<tr>
<td>Male</td>
<td>70.3% (130)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>67.6% (184)</td>
</tr>
<tr>
<td>Non-white</td>
<td>59.8% (76)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
</tr>
<tr>
<td>Hispanic/Latinx</td>
<td>57.9% (33)</td>
</tr>
<tr>
<td>Non-Hispanic/Latinx</td>
<td>66.5% (228)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
</tr>
<tr>
<td>No college degree</td>
<td>60.6% (63)</td>
</tr>
<tr>
<td>College degree</td>
<td>71.4% (264)</td>
</tr>
<tr>
<td><strong>Demographics</strong></td>
<td><strong>Resilient High Depression</strong></td>
</tr>
<tr>
<td><strong>M (SD)</strong></td>
<td><strong>M (SD)</strong></td>
</tr>
<tr>
<td>Age, years</td>
<td>41.37 (13.73)</td>
</tr>
<tr>
<td>Psychosocial Covariates</td>
<td></td>
</tr>
<tr>
<td>ASIp total score</td>
<td>4.61 (5.54)</td>
</tr>
<tr>
<td>FUTS total score</td>
<td>31.08 (10.44)</td>
</tr>
</tbody>
</table>
Table 4.3  Participant characteristics as a function of anxiety (GAD-7) trajectory class membership in unconditional growth mixture model (N=404)

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Resilient % (n)</th>
<th>Mild-Improving % (n)</th>
<th>Worsening % (n)</th>
<th>Chronic % (n)</th>
<th>χ²(3)</th>
<th>p-value</th>
<th>Cramer’s V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>48.4% (104)</td>
<td>29.8% (64)</td>
<td>15.8% (34)</td>
<td>6.0% (13)</td>
<td>6.29</td>
<td>.09</td>
<td>.125</td>
</tr>
<tr>
<td>Male</td>
<td>56.2% (104)</td>
<td>30.8% (57)</td>
<td>8.1% (15)</td>
<td>4.9% (9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>53.3% (145)</td>
<td>29.8% (81)</td>
<td>10.7% (29)</td>
<td>6.3% (17)</td>
<td>3.31</td>
<td>.35</td>
<td>.091</td>
</tr>
<tr>
<td>Non-white</td>
<td>48.0% (61)</td>
<td>32.3% (41)</td>
<td>15.7% (20)</td>
<td>3.9% (5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethnicity*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic/Latinx</td>
<td>38.6% (22)</td>
<td>40.4% (23)</td>
<td>17.5% (10)</td>
<td>3.5% (2)</td>
<td>6.96</td>
<td>.07</td>
<td>.132</td>
</tr>
<tr>
<td>Non-Hispanic/Latinx</td>
<td>54.8% (188)</td>
<td>28.0% (96)</td>
<td>11.4% (39)</td>
<td>5.8% (20)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No college degree</td>
<td>51.0% (53)</td>
<td>27.9% (29)</td>
<td>13.5% (14)</td>
<td>7.7% (8)</td>
<td>3.77</td>
<td>.29</td>
<td>.089</td>
</tr>
<tr>
<td>College degree</td>
<td>58.4% (216)</td>
<td>27.3% (101)</td>
<td>10.3% (38)</td>
<td>4.1% (15)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Resilient M (SD)</th>
<th>Mild-Improving M (SD)</th>
<th>Worsening M (SD)</th>
<th>Chronic M (SD)</th>
<th>F</th>
<th>p-value</th>
<th>Eta-sq</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>42.14 (13.99)</td>
<td>37.16 (12.27)</td>
<td>35.55 (11.42)</td>
<td>31.59 (6.31)</td>
<td>8.54</td>
<td>&lt; .001</td>
<td>.060</td>
<td>18-78</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Psychosocial Covariates</th>
<th>Resilient M (SD)</th>
<th>Mild-Improving M (SD)</th>
<th>Worsening M (SD)</th>
<th>Chronic M (SD)</th>
<th>F</th>
<th>p-value</th>
<th>Eta-sq</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASI Total Score</td>
<td>3.27 (4.40)</td>
<td>8.45 (6.56)</td>
<td>7.94 (6.45)</td>
<td>9.41 (7.54)</td>
<td>28.94</td>
<td>&lt; .001</td>
<td>.178</td>
<td>0-24</td>
</tr>
<tr>
<td>FUTS Total Score</td>
<td>29.64 (13.43)</td>
<td>36.48 (7.85)</td>
<td>37.84 (9.61)</td>
<td>42.00 (6.70)</td>
<td>25.16</td>
<td>&lt; .001</td>
<td>.159</td>
<td>10-50</td>
</tr>
</tbody>
</table>

*Chi-square has at least 1 cell less than expected count.
LRT and BRT indicated significant improvement in fit up to the four-class model solution. However, despite the increase in entropy for the five-class model solution, LRT was no longer significant. Based on these considerations and interpretability, we selected the four-class model as the optimal solution.

Table 4.4  Fit indices for one- to three-class growth mixture models of depression symptoms (CES-D; N=404)

<table>
<thead>
<tr>
<th>Growth Mixture Models</th>
<th>One-class</th>
<th>Two-class</th>
<th>Three-class</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIC</td>
<td>7823.977</td>
<td>7731.401</td>
<td>7694.189</td>
</tr>
<tr>
<td>BIC</td>
<td>7848.944</td>
<td>7768.851</td>
<td>7744.124</td>
</tr>
<tr>
<td>SSBIC</td>
<td>7829.901</td>
<td>7740.287</td>
<td>7706.038</td>
</tr>
<tr>
<td>Entropy</td>
<td>--</td>
<td>0.784</td>
<td>0.800</td>
</tr>
<tr>
<td>LRT</td>
<td>--</td>
<td>p &lt; .001</td>
<td>p = .33</td>
</tr>
<tr>
<td>BLRT</td>
<td>--</td>
<td>p &lt; .000</td>
<td>p &lt; .000</td>
</tr>
</tbody>
</table>

Note. AIC = Akaike information criterion; BIC = Bayesian information criterion; SSBIC = sample size adjusted Bayesian information criterion; LRT = Lo-Mendell-Rubin test; BLRT = bootstrapped likelihood ratio test

Preliminary Covariate Analyses for Conditional Models

Independent of the models, we examined theoretically relevant demographic and psychosocial variables as predictors of class membership using one-way ANOVAs and Chi-Squares. Relative to an unconditional model, appropriate inclusion of covariates in a conditional model produces more accurate and specific trajectory estimates (Infurna & Grimm, 2018; Li & Hser, 2011; Muthén, 2004). For depression symptoms, two demographic variables, age ($F[1, 402] = 20.42, p < .001$) and education level ($\chi^2[1, 403] = 4.41, p = .04$), significantly impacted trajectory membership; both baseline psychosocial covariates of interest, ASIp ($F[1, 403] = 27.79, p < .001$) and FUTS ($F[1, 403] = 42.40, p < .001$), showed significant effects on trajectory class membership. For anxiety symptoms, age ($F[3, 402] = 8.54, p < .001$) was the only
demographic variable to show significant effects; again, both baseline ASIp ($F[3, 403] = 28.94, p < .001$) and FUTS ($F[3, 403] = 25.20, p < .001$) significantly differentiated trajectory class membership. Subsequently, we included each of these covariates in the final, conditional models of depression and anxiety symptoms.

**Table 4.5** Fit indices for one- to five-class growth mixture models of anxiety symptoms (GAD-7; N=404)

<table>
<thead>
<tr>
<th>Growth Mixture Models</th>
<th>Fit index</th>
<th>One-class</th>
<th>Two-class</th>
<th>Three-class</th>
<th>Four-class</th>
<th>Five-class</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIC</td>
<td>6035.039</td>
<td>5915.618</td>
<td>5870.009</td>
<td>5826.177</td>
<td>5811.350</td>
<td></td>
</tr>
<tr>
<td>BIC</td>
<td>6068.329</td>
<td>5961.391</td>
<td>5919.943</td>
<td>5888.596</td>
<td>5886.252</td>
<td></td>
</tr>
<tr>
<td>SSBIC</td>
<td>6042.938</td>
<td>5926.479</td>
<td>5881.857</td>
<td>5840.988</td>
<td>5829.123</td>
<td></td>
</tr>
<tr>
<td>Entropy</td>
<td>--</td>
<td>0.806</td>
<td>0.767</td>
<td>0.796</td>
<td>0.820</td>
<td></td>
</tr>
<tr>
<td>LRT</td>
<td>--</td>
<td>p &lt; .001</td>
<td>p = .04</td>
<td>p = .03</td>
<td>p = .25</td>
<td></td>
</tr>
<tr>
<td>BLRT</td>
<td>--</td>
<td>p &lt; .000</td>
<td>p &lt; .000</td>
<td>p &lt; .000</td>
<td>p &lt; .000</td>
<td></td>
</tr>
</tbody>
</table>

*Note.* AIC = Akaike information criterion; BIC = Bayesian information criterion; SSBIC = sample size adjusted Bayesian information criterion; LRT = Lo-Mendell-Rubin test; BLRT = bootstrapped likelihood ratio test

**Conditional Model of Depression Symptoms**

We next examined covariates within the LGMM framework, as a conditional model of depression symptoms, to estimate the most accurate trajectory membership. In previous analyses, age, educational level, ASIp, and FUTS showed significant effects on class membership and were subsequently included in this model. The conditional model of depression symptoms successfully converged (Figure 4.1). The *Resilient* class was the largest (57.32%) with a low intercept, flat slope, and no clinical elevations in depressive symptoms from Spring 2020 to Spring 2021. The *High Depression* class (42.68%) showed chronic, clinically elevated depressive symptoms with a slightly negative slope, suggesting modest improvement over the first 12-months of the pandemic.
In order to examine covariates as predictors of class membership in the model of depression symptoms, we used the *Resilient* class as the reference group. Compared to the *Resilient* class, individuals in the *High Depression* class were significantly younger ($b = 0.94$, $SE = 0.01$, $p < .001$) and more likely to have a college degree ($b = 0.55$, $SE = 0.21$, $p = .031$). Further, the *High Depression* class exhibited higher baseline ASIp scores ($b = 1.14$, $SE = 0.06$, $p = .021$) and higher baseline FUTS scores ($b = 1.09$, $SE = 0.03$, $p = .002$) than the *Resilient* group.

**Figure 4.1** Two-class conditional model of depression symptoms (CES-D; N=403)
Conditional Model of Anxiety Symptoms

To assess changes to class membership for anxiety symptoms, we examined age, ASIp, and FUTS in the final conditional model. The conditional model successfully converged (Figure 4.2). The Resilient class was the largest (46.40%), endorsing very low, subthreshold symptoms with little-to-no change over the course of the year. The Mild-Improving group (40.45%) described clinically mild anxiety symptoms at all time points, with a negative-trending slope representing slight symptom improvement over the course of the year. The Chronic class was comparatively small (9.93%), representing clinically severe anxiety symptoms beginning in April 2020 and remaining steady throughout the year. The Worsening group (3.23%) represented a pattern of subclinical symptoms of anxiety in Spring 2020, increasing to clinically moderate symptoms of anxiety six months later, and clinically severe symptoms of anxiety one year later in Spring 2021.

Using the Resilient class as the reference group, we explored the abovementioned covariates as predictors of class membership in the conditional model of anxiety symptoms. Compared to the Resilient class, individuals were significantly younger in the Mild-Improving (b = 1.07, SE = 0.02, p < .001), Chronic (b = 1.11, SE = 0.03, p < .001), and Worsening (b = 1.11, SE = 0.04, p = .003) classes. Baseline ASIp and FUTS scores were significantly higher in the Chronic (b = 0.77, SE = 0.05, p < .001; b = 0.83, SE = 0.05, p < .001) and Mild-Improving (b = 0.80, SE = 0.04, p < .001; b = 0.89, SE = 0.02, p < .001) groups, as compared to the Resilient class.
4.4 Discussion

Our findings highlighted heterogeneous patterns of psychological adjustment, namely a resilient majority and variable depressive and anxious reactions, over the first 12-months of the pandemic in a U.S.-based, online, adult community sample. Using LGMM, we identified two unique trajectories of depression symptoms and four unique trajectories of anxiety symptoms. When assessing symptoms of both depression and anxiety, the majority of individuals were classified in Resilient trajectory classes (57.32% in depression analyses; 46.40% in anxiety...
analyses), evidencing no clinical symptom elevations at any time point. For depression, the remaining 42.68% of adults were in the *High Depression* class, endorsing clinically elevated symptoms with negligible change throughout the first year of the pandemic. LGMM of anxiety symptoms, however, revealed a more descriptive model. In addition to the majority *Resilient* group, we saw the following trajectory classes: (a) *Mild-Improving* (40.45%) with clinically mild anxiety symptoms in Spring 2020 resolving steadily over the course of the year toward a subclinical level, (b) *Chronic* (9.93%) with severe anxiety symptoms remaining consistent over the course of the year, and (c) *Worsening* (3.23%) with initial subclinical anxiety symptoms worsening to severe anxiety over the course of the year.

The present study provides the longest trajectory estimates of psychological adjustment during the COVID-19 pandemic in a U.S. sample thus far, with data spanning April 2020 through April 2021. While COVID-19 has, indeed, proven itself a unique and burdensome stressor, our results indicate that psychological reactions at the community level are more or less consistent with prototypical trajectory patterns see following other adverse events (Galatzer-Levy et al., 2018; Shilton et al., 2021). International studies of psychological adjustment to the pandemic have similarly found heterogeneous trajectories of depression and anxiety symptoms, with the majority remaining resilient and most others reporting consistent, mild symptoms of depression and anxiety with trends toward improvement over time (Chen et al., 2022; Kimhi et al., 2021; Saunders et al., 2021; Shelvin et al., 2021).

While the pandemic is ongoing and many of its impacts are yet to be fully understood, a clearer picture of the pandemic’s initial psychological burden is coming into focus. Though early reports warned of widespread community mental health crises, the data appear to suggest otherwise and instead tell a story of resilience. Notably, high rates of resilience do not suggest
that individuals have been emotionally and psychologically impervious to the pandemic. As resilience is defined by a stable course of low or subclinical symptomology following an aversive event (Bonanno, 2012), those who have shown resilient responses during the pandemic may very well have experienced mild and transient distress reactions without functional interference. Rather, these and other findings speak to the majority’s capacity to flexibly adapt in the face of the COVID-19 pandemic, a novel and acute stressor, in order to achieve and maintain effective emotion regulation.

It is of particular importance to recognize that resilience is a multifaceted construct, informed by individual differences in emotion regulation, flexibility, and self-monitoring, exposure severity, family context, and community characteristics (Aldao, 2013; Bonanno et al., 2004; Bonanno & Burton, 2013; Chen et al., 2020; Chen et al., 2022; Chen & Bonanno, 2020; Cheng et al., 2014; Renna et al., 2017; Southwick et al., 2014). While many large-scale disaster events (i.e., natural disasters, war-related exposures) are poised to interrupt one or several of these resilience domains, the pandemic has uniquely blocked or interrupted engagement with many protective factors simultaneously (Gruber, 2020). Therefore, it is essential to consider potential individual and contextual elements specific to the COVID-19 pandemic and its impact in a given community, as individuals who develop symptoms of clinical distress in the context of the COVID-19 pandemic are likely to be those most impacted across one or more of these domains.

Given the pandemic’s protracted and unpredictable course, we were particularly interested in how feelings of uncertainty and threat impacted anxiety and depression trajectories. We were also interested in exploring whether interoceptive threat bias, or physical anxiety sensitivity, differentially predicted psychological adjustment, as the pandemic is highly aversive
event inherently threatening to physical health. We found that individuals with greater feelings of uncertainty and threat and higher physical anxiety sensitivity during the first wave of the pandemic in Spring 2020 were significantly more likely to belong to the **High Depression** (42.68%) trajectory or show clinically elevated anxiety symptoms, belonging to either a **Mild-Improving** or **Chronic** trajectory of anxiety symptoms (50.38% of the sample combined). Neither of these covariates, however, differentially predicted membership in the **Worsening** (3.23%) trajectory of anxiety symptoms.

Greater feelings of uncertainty and threat at the onset of the pandemic predicted worse psychological adjustment 12-months later. For many in the U.S., Spring 2020 was punctuated by abrupt, widespread, and fundamental changes to daily life. Further, the pandemic’s erratic course has resulted in a barrage of COVID-related media, constant public health alerts, and capricious policies changes, which can lead to greater exacerbation of worry and confusion (Bendau et al., 2021; Neria & Sullivan, 2011). The inability to tolerate uncertainty and higher perceived threat have been implicated in the development of anxiety and mood disorders (Hollingsworth et al., 2018; Mennin et al., 2004; Morriss et al., 2016), and has emerged as a mechanism of interest in pandemic-related mental health outcomes (Satici et al., 2020; Sauer et al., 2020). A key source of uncertainty and threat during the pandemic has been its notable impact on the economy. Many studies have highlighted the role of financial concerns in mental health outcomes above and beyond other sources of perceived threat (Bernardini et al., 2021; Haliwa et al., Hertz-Palmor et al., 2021; Zavlis et al., 2021). Controlling for pre-pandemic mental health, finance-related distress has consistently emerged as a predictor of anxious pathology (Benke et al., 2020; McGinty et al., 2020), and abrupt income loss during the pandemic predicted both anxiety and depression (Hertz-Palmor et al., 2021). As financial concerns are such a strong predictor of
mental health outcomes during the COVID-19 pandemic and many experiences relating to financial concerns (i.e., job loss, unemployment, evictions, difficulties with bills/loans) inherently provoke feelings of uncertainty and threat, differential finance-related stressors appear to represent a particularly potent social determinant in understanding longitudinal impacts of the COVID-19 pandemic on mental health.

Our study found that higher interoceptive threat bias in Spring 2020 differentially predicted worse depression and anxiety outcomes over the first year of the pandemic. Given the significant mortality rate and physical threats of the pandemic, simultaneous to its broader impact as a public health disaster, we were particularly interested in the role of interoceptive threat bias, as measured by the ASI-p, on psychological outcomes. Anxiety sensitivity is an established transdiagnostic risk factor associated with increased sensitivity to stressors and is one of the most recognized risk factors of mood and anxiety disorders (Avidor et al., 2021; Naragon-Gainey, 2010; Olatunji & Wolitzky-Taylor, 2009; Reiss & McNally 1985; Schmidt et al., 2006; Stein et al., 2018; Taylor, 2004). The ASI-p measures perceived threat of physiological arousal symptoms, including general malaise, changes in respiratory function or sensation, heart-rate fluctuations and cardiovascular sensations, and sensitivity to temperature change. Several studies have examined the role of anxiety sensitivity during the COVID-19 pandemic, both cross-sectionally and longitudinally (Manning et al., 2021; Rogers et al., 2021; Schmidt et al., 2021), and findings support anxiety sensitivity as a risk factor for pandemic-related distress. However, existing longitudinal data on this topic has been limited to 1-month outcomes. The current findings strengthen the evidence on this risk factor, suggesting that baseline heightened physical anxiety sensitivity, or higher interoceptive threat bias more broadly, predicts worse psychological adjustment up to a year later in the context of the COVID-19 pandemic.
Several demographic factors also emerged as significantly impacting psychological adjustment during the first year of the pandemic. College education level differentially predicted membership in the *High Depression* group. Findings have been mixed with regard to educational attainment level and mental health outcomes during the COVID-19 pandemic (Gloster et al., 2020; Zhou et al., 2020). Given the high concordance between educational attainment and financial outcomes in the broader literature, as well as the bidirectionality of mental health status and education level, future research should further examine the nature of this relationship. Younger individuals were also significantly more likely to be in the *High Depression* class than *Resilient*, when assessing symptoms of depression. When assessing symptoms of anxiety, younger individuals were more likely to be in the *Mild-Improving*, *Chronic*, and *Worsening* classes than *Resilient*. Younger age is a frequently identified risk factor for poor psychological adjustment following adverse events, and the same has consistently been found in the COVID-19 literature (Avidor et al., 2021; Batterham et al., 2021; Gambin et al., 2022; Hawes et al., 2021; Luchetti et al., 2021; Saunders et al., 2021; Shahar et al., 2021; Shilton et al., 2021). While this finding may initially seem counterintuitive given the pandemic’s disproportionate threat to the health of older individuals, theories seeking to explain this age-related finding offer a variety of potential explanations. Many recognize the various strengths that come with the natural aging process (e.g., more life experiences to reflect on, a wider repertoire of coping skills to choose from, better distress tolerance given exposure to challenges inherent in aging), which affords older individuals more emotional stability (Cartensen et al., 2011; Charles, 2010; Klaiber et al., 2021; Palgi et al., 2020; Sardella et al., 2021; Shilton et al., 2021). Specific to our sample, however, “younger” individuals, on average, were in their early-to-mid thirties and “older” individuals were, on average in their early-to-mid forties. Given the relative youth and narrow
age range of our sample, these theories may not fully explain the present findings. Alternatively, generational cohort effects or normative developmental patterns specific to adulthood in the U.S. may account, in part, for our present findings (Nwachukwu, et al., 2020; Zhang et al., 2021).

Typically, earlier stages of adulthood involve an extended process of finding professional, financial, and relational security. As the pandemic’s impact shook each of these domains, younger adults who had less stability prior to the pandemic were likely to have been more acutely impacted by the pandemic’s broader impact on the job market, rental and housing sectors, and school closures (Zhou et al., 2020).

Finally, our anxiety model identified a small Worsening group (3.23%) who, despite having subclinical, very low anxiety symptoms in April 2020, showed emerging anxiety symptoms over the course of the year, resulting in clinically severe anxiety by April 2021. Emerging symptom groups are frequently seen in a minority when examining trajectories of psychological adjustment; these groups are often of particular interest, given their propensity to offer insights into intervention targets and potent mechanisms (Barzilay et al., 2020; Bonanno et al., 2010; Bryant & Harvey, 2002; Sheerin et al., 2018). Of note, our Worsening anxiety group was the only symptomatic trajectory group in which fear of uncertainty and threat and interoceptive threat bias did not predict class membership. Therefore, worsening psychological adjustment in this group appears to be driven by another factor, potentially less related to emotion dysregulation. It may be that a downstream consequence of the pandemic (Batterham et al., 2021) or other mediating factors inadequately measured in the current study inform this pattern of clinical anxiety exacerbation over time. In other trajectory studies, worsening or delayed-onset symptom patterns primarily related to social determinants, including worse financial circumstances (Gambin et al., 2022; Kimhi et al., 2021). Interestingly, the Worsening
trajectory group in our study was, on average, the youngest group (mean age approx. 31 y/o), though not significantly when compared to other trajectory groups. Considering the beforementioned role of younger age and financial instability, the trends seen in our findings may represent additional evidence of age-related social determinants predicting worsening anxiety in the context of the pandemic.

**Limitations**

While our findings provide valuable insights on the long-term patterns of psychological adjustment to the COVID-19 pandemic in the U.S., these results should be considered within the context of several study limitations. As data collection took place during the early stages of the pandemic when lockdowns were in place and in-person contact was restricted, our study utilized online surveying and data collection solutions. Additionally, our sample was fairly homogeneous with regard to sociocultural and racial/ethnic diversity and is not a nationally representative sample. Due to the homogeneity of our sample, we are unable to make conclusions regarding the potential role of many sociodemographic factors on psychological adjustment during the pandemic, including race and ethnicity. Given the obvious and established racial and ethnic health disparities specific to and beyond the COVID-19 pandemic, as well as pervasive and institutionalized sociocultural inequities in the U.S., further studies prioritizing the assessment of psychological adjustment across diverse racial and ethnic groups are critical. Finally, our study used online, self-report surveys as opposed to clinician-administered interviews to assess for clinical symptoms. Therefore, we cannot make assertions about clinical diagnoses, only symptom levels and clinical elevations. However, despite the recognized validity and
generalizability concerns of COVID-19 related research (Pierce et al., 2020), our findings were similar to other mental health trajectory estimates.

4.5 Conclusion

The present study emphasizes resilience as the majority response in the first 12-months of the COVID-19 pandemic in a U.S. community sample. Mild and improving depression and anxiety symptoms were the second most common patterns of psychological adjustment, and approximately 10% of our sample endorsed chronic, severe anxiety over the course of the year. Younger age, greater feelings of uncertainty and threat, and higher interoceptive threat bias consistently predicted year-long symptom elevations in these groups. Further, approximately 1 in every 8 adults reported worsening anxiety over the course of the year; while factors driving this trajectory group remain unclear, worsening anxiety are likely related to sociodemographic determinants, pandemic-related financial consequences, or factors relating to younger age. Our findings highlight the need for further research exploring fluctuations in psychological adjustment overtime in the context of the pandemic. As the COVID-19 pandemic is ongoing and scientists warn of more pandemic-related disasters in the future, researchers should seek to identify and clarify the role of psychosocial mechanisms and social determinants contributing to variations in psychological adjustment at the community level.

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PSYCHOLOGICAL ADJUSTMENT TO COVID-19

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Chapter 5: General Discussion & Conclusions

For many, acute, life-threatening medical events and physical health-related stressors can result in clinically significant affective dysregulation and posttraumatic stress reactions. Challenging one’s sense of physical safety and serving as a tangible reminder of mortality, acute health-related stressors often require ongoing psychological adaptation and adjustment. Theoretical models have proposed specific mechanisms of action thought to be responsible for the complex and nuanced processes underlying affective dysfunction and worse psychological adjustment. One such mechanism, physical anxiety sensitivity, represents an established transdiagnostic risk factor for mental illness, which may hold particular importance in the context of physical health-related stressors. Describing one’s propensity to interpret anxious arousal cues as threatening, heightened physical anxiety sensitivity combines hyperarousal – a symptom inherent to distress reactions – and catastrophic interpretation of the physiological sensations of hyperarousal. Taken together, this bidirectional psychosomatic phenomenon results in an interoceptive threat bias.

With interoceptive awareness, we gain the vital ability to recognize irregularities in our physical bodies and engage in behavioral and affective responses that keep us safe. For those with heightened physical anxiety sensitivity who develop an interoceptive threat bias, the ability to recognize irregularities is lost due to overgeneralization of threat perceptions, resulting in frequent false alarms and persistent affective dysregulation. This dissertation sought to examine physical anxiety sensitivity’s influence on psychological adjustment following acute health-related events.
Together, these studies provide valuable insights into the naturalistic course and heterogeneous patterns of psychological adjustment to acute health-related stressors. Study 1 confirms and emphasizes the deleterious effect of interoceptive threat bias on psychological adjustment following suspected ACS. Recognizing a gap in the literature, Study 2 sought to identify latent, heterogeneous PTS symptom profiles in the 12-months following ED treatment for ACS. Using LGMM, this study found that, while the majority of individuals are resilient, about 1 in 8 patients continue to experience elevated PTS symptoms one year after their hospitalization. While trajectories indicate that symptom patterns vary, Study 2 provides insight into potential mechanisms contributing to variable responses. Applying findings from Study 1, Study 2 identifies heightened physical anxiety sensitivity as a potent mechanism contributing to worse psychological outcomes and highlights the potential benefits of targeting threat perceptions to improve adjustment and clinical course, whether or not patients are ultimately diagnosed with ACS.

Study 3 extended the prior studies’ theoretical assumptions, mapping heterogeneous, longitudinal trajectories of psychological adjustment to the COVID-19 pandemic, an unprecedented, acute health-related stressor representing significant risk to physical safety. Though early reports warned of widespread community mental health crises in response to the pandemic, findings from Study 3 suggest otherwise, instead telling a story of resilience, with low, stable courses of subclinical mood symptoms representing the most common symptom profile. However, in line with findings from Studies 1 and 2, the majority of individuals with clinically elevated anxiety and depression symptoms in the first year of the pandemic endorsed heightened physical anxiety sensitivity at baseline.
The current dissertation sought to address a vital clinical translational gap – the widespread recognition of psychological sequelae in response to health-related stressors and the often-incommensurate clinical response to these needs. With improved understanding of the naturalistic, longitudinal course of psychological adjustment to acute medical events and health-related stressors, patients and practitioners, alike, are afforded increased insight into potential outcomes and clinical patterns. Further, these studies recognize physical anxiety sensitivity and interoceptive threat bias as a highly relevant regulatory mechanisms underlying and informing the likelihood of ongoing clinical distress.

5.1 Empirical Findings

Review of Study 1

Study 1 tested a fundamental hypothesis of the EST model, examining the impact of ongoing cardiac-specific somatic threat perceptions on posttraumatic stress reactions, in a multi-ethnic sample of cardiac patients recruited in the ED while being evaluated for ACS. Informed by the EST model, we theorized that, in order for significant PTS symptoms to emerge in response to a suspected ACS event, patients must experience the ACS event as life-threatening and report ongoing physical anxiety sensitivity, beyond the discrete event. As part of a larger observational cohort study, we assessed peritraumatic threat perceptions during evaluation for the suspected ACS event, ongoing cardiac threat perceptions 1 month later, and then tested their interaction in relation to PTSD symptoms at 1-month after the presenting ACS event.

In line with hypotheses, main effects emerged for both ED threat perceptions and ongoing cardiac threat, as well as their interaction. Speaking directly to mechanistic inquiries, post hoc analyses found that, only among participants who reported high levels of ongoing
cardiac-related anxiety sensitivity, higher ED threat perceptions were associated with 1-month ACS-induced PTS. Therefore, physical anxiety sensitivity appears to represent a critical mechanism in the emergence PTS symptoms after an acute cardiac event.

These findings serve as evidence of a unique psychosomatic phenomenon whereby normative, afferent physiological signals serve as traumatic reminders of the index ACS event and future CVD risk. However, the associated cognitive processes may be highly similar to those documented in survivors of archetypal PTSD-inducing events, such as combat exposure or natural disaster event, wherein individuals are triggered by generalized, external reminders of those events and engage with catastrophic interpretations. That is, interoceptive threat bias toward cardiac sensations is essentially similar to the pathology behind any other traumatic exposure and is likely to be initiated due to overgeneralization of the fear network. However, the psychosomatic mechanisms of ACS-induced PTSD are distinct in other ways. Whereas overgeneralization implies fear network activation to trauma-related, but ultimately safe, cues (Foa et al., 2006), physiological threat signals may indicate dangerous, real symptoms of a new cardiac event. The “true” safety versus threat status of triggering cues is important for both understanding the phenomenon of medical event–induced PTSD and designing effective treatments for it.

The presence of heightened physical anxiety sensitivity following ACS-induced PTSD represents an important cognitive vulnerability to monitor in the aftermath of acute cardiovascular events, and acute health events, more broadly. Ironically, it is possible that reducing patients’ perceptions of EST may be a means for reducing both PTSD symptoms and improving cardiovascular prognosis. Reducing interoceptive threat bias may improve subsequent health behaviors responsible for secondary risk (Alcántara et al., 2014; Edmondson et al., 2013;
Kronish et al., 2012, 2013, 2015). Following an acute, life-threatening medical event, patients may develop implicit or explicit cognitive associations toward prescribed treatments, connecting preventative or maintenance medications, physical activity, and other beneficial lifestyle changes, with the initial cardiac event and future mortality. Therefore, activities such as medication nonadherence and sedentary behavior confer psychological equanimity in the short term (a form of negative reinforcement), even if patients consciously understand the associated long-term risk.

In current clinical settings, patients are encouraged to consider the experience of an acute health events as a “turning point” – an opportunity for broad lifestyle changes. Simultaneously, because index events are typically an acute manifestation of systemic cardiovascular risk (i.e., atherosclerosis, hypertension, intermittent ischemic episodes will not disappear), patients are asked to actively monitor and combat the cardiovascular threat with interoceptive somatic monitoring, lifestyle changes, medication regimens, and interactions with the medical system – all of which are potent reminders of ongoing vulnerability and of the original event. However, innate to the criteria of PTSD, such reminders can be highly distressing (Whitaker et al., 2009) and have been associated with poor psychological adjustment in CVD patients (Edmondson et al., 2008; Matsuoka et al., 2002). Currently many practitioners attempt to motivate patients by capitalizing on the “teachable moment” that is the life-threatening event, by highlighting the mortality risk associated with adverse health behaviors such as medication nonadherence and sedentary behavior (Demark-Wahnefried et al., 2005). For many patients, however, this may actually work against the ultimate goal of adherence to medication and physical activity recommendations. These hypotheses should be tested in future research.
Review of Study 2

Each year, millions of individuals are hospitalized for suspected ACS. Acute coronary syndrome (ACS) is life-threatening, highly distressing, and for many traumatic; 1 in 8 ACS patients screen positive for posttraumatic stress disorder (PTSD) (Edmondson, Shimbo et al., 2013; Edmondson, Kronish et al., 2013; Holbrook et al., 2001). However, little is known about variations in ACS patients' posttraumatic stress symptom (PTS) onset or clinical course. Study 2 estimated longitudinal trajectories of PTS following evaluation for suspected ACS. Further, this study compared patients with confirmed ACS to those who ultimately ruled out upon discharge, and estimated the influence of perceived threat during hospitalization and subsequent cardiac threat perceptions on longitudinal symptom trajectories.

Results indicated 3 unique trajectories of PTS symptoms over the course of 1-year post-hospitalization in a large, ethnically diverse sample. A clear majority of ACS patients in this current study (87%) were classified in a Resilient trajectory, representing low, subthreshold symptoms throughout the year. A smaller group (10%) was classified in a Chronic-Worsening trajectory, characterized by high initial PTS symptoms that worsened over the course of the year. Finally, a third, small group (3%) was classified in an Acute-Recovering trajectory with considerably elevated initial PTS symptoms that steadily resolved over the course of the year.

Interoceptive threat bias, specifically heightened cardiac-related threat perceptions, predicted membership in both the Acute-Recovering and the Chronic-Worsening trajectories. This finding supports the EST model, which theorizes that ongoing somatic threat perceptions are of particular importance for PTS after an acute, life-threatening cardiac event. Heighted cardiac threat is reminiscent of the archetypal hypervigilance and arousal behaviors in response to triggering traumatic reminders characteristic of PTSD. However, unique to our study and this
sample, the trigger is a physiological signal both of relevance to the index ACS event and important in identifying a potential future event. Whereas PTSD is generally considered a disorder of fear memory processing, the EST model suggests that the present and future temporal focus of cardiac threat perceptions may be an important clinical target.

Patients who were highly distressed during the ED visit were significantly more likely to show either an \textit{Acute-Recovering} or \textit{Chronic-Worsening} trajectory (12.7\% combined). Interestingly, however, ED threat perceptions were more strongly associated with acute PTS symptoms that resolved over the ensuing year (i.e., \textit{Acute-Recovering} pattern) than with the \textit{Chronic-Worsening} pattern. Thus, although individuals with heightened peri-traumatic threat in the ED suffer acute PTS symptoms, they do not necessarily develop chronic PTSD. It will be crucial in future studies to further tease out how threat ED perceptions may inform these different clinical sequelae.

Threat perceptions proved impactful, above and beyond objective risk. Participants in this study were approached for recruitment in the ED while being evaluated for suspected ACS. Thus, upon discharge, some participants are given a discharge diagnosis of confirmed ACS while others ultimately rule-out for ACS and may receive a non-cardiovascular diagnosis. Prior research has shown that there are no differences in rates of PTS at 1-month after evaluation, whether or not the event is diagnosed ACS. Despite 68\% of patients in our study receiving a rule-out ACS discharge diagnosis, the trajectories for this group and those with a confirmed ACS event were essentially identical, in agreement with prior cross-sectional findings (Lane et al., 2002). While perhaps surprising, our findings suggest that pathophysiology and ultimate diagnosis do not differentially impact PTS reactions following an acute cardiac event. Instead, initial perceived threat, subjective trauma experience, and ongoing concerns about cardiac risk
are more powerful and predictive of clinical course and psychological sequelae than clinical
diagnosis or severity (Edmondson & Cohen, 2013). Prior findings suggest that patients evaluated
for ACS may be uncertain of their discharge diagnosis (Yasaitis et al., 2015). Future studies of
PTS in patients evaluated for ACS should determine the influence of patient understanding of
discharge diagnosis.

Review of Study 3

Responding to the sudden and unprecedented onset of the COVID-19 pandemic, Study 3
provided the longest trajectory estimates of psychological adjustment during the COVID-19
pandemic in a U.S. sample thus far, with data spanning April 2020 through April 2021. While
COVID-19 has, indeed, proven itself a unique and burdensome stressor, the present findings
suggest that community level psychological responses are more or less consistent with
prototypical trajectory patterns see following other adverse events (Galatzer-Levy et al., 2018;
Shilton et al., 2021). The present study emphasizes resilience as the majority response in the first
12-months of the COVID-19 pandemic in a U.S. community sample. Mild and improving
depression and anxiety symptoms were the second most common patterns of psychological
adjustment, and approximately 10% of our sample endorsed chronic, severe anxiety over the
course of the year.

Our study found that higher baseline interoceptive threat bias in Spring 2020
differentially predicted worse depression and anxiety outcomes over the first year of the
pandemic. Given the significant mortality rate and physical threats of the pandemic,
simultaneous to its broader impact as a public health disaster, we were particularly interested in
the role of interoceptive threat bias on psychological outcomes. The current findings
strengthened evidence on this risk factor. In the context of the COVID-19 pandemic, heightened baseline physical anxiety sensitivity, or higher interoceptive threat bias, more broadly, predicted worse psychological adjustment one year later.

Several demographic factors, namely younger age and college education, also emerged as significantly impacting psychological adjustment during the first year of the pandemic. Younger individuals were also significantly more likely to be in the High Depression class than Resilient, when assessing symptoms of depression. When assessing symptoms of anxiety, younger individuals were more likely to be in the Mild-Improving, Chronic, and Worsening classes than Resilient. Younger age is a frequently identified risk factor for poor psychological adjustment following adverse events, and the same has consistently been found in the COVID-19 literature (Avidor et al., 2021; Batterham et al., 2021; Gambin et al., 2022; Hawes et al., 2021; Luchetti et al., 2021; Saunders et al., 2021; Shahar et al., 2021; Shilton et al., 2021). While this finding may initially seem counterintuitive given the pandemic’s disproportionate threat to the health of older individuals, theories seeking to explain this age-related finding offer a variety of potential explanations.

Finally, our anxiety model identified a small Worsening group (3.23%) who, despite having subclinical, very low anxiety symptoms in April 2020, showed emerging anxiety symptoms over the course of the year, resulting in clinically severe anxiety by April 2021. Emerging symptom groups are frequently seen in a minority when examining trajectories of psychological adjustment; these groups are often of particular interest, given their propensity to offer insights into intervention targets and potent mechanisms (Barzilay et al., 2020; Bonanno et al., 2010; Bryant & Harvey, 2002; Sheerin et al., 2018).
Of note, our *Worsening* anxiety group was the only symptomatic trajectory group in which fear of uncertainty and threat and interoceptive threat bias did not predict class membership. Therefore, worsening psychological adjustment in this group appears to be driven by another factor, potentially less related to emotion dysregulation. It may be that a downstream consequence of the pandemic (Batterham et al., 2021) or other mediating factors inadequately measured in the current study inform this pattern of clinical anxiety exacerbation over time. In other trajectory studies, worsening or delayed-onset symptom patterns primarily related to social determinants, including worse financial circumstances (Gambin et al., 2022; Kimhi et al., 2021).

With the adoption of essential public health measures, advent of safe and effective vaccines, and identification of novel, symptom-reducing treatments, many communities have experienced a tenuous yet hopeful return to the “new normal.” However, the pandemic continues to pose a very real threat to human health, with more than 985,000 deaths and 80.5 million infections nationwide since its onset. Further, its systemic ripple effects continue, causing differential impacts on individuals and communities due to population-specific risk and protective factors. Therefore, clarifying the scale and nature of the pandemic’s impact on mental health remains essential in order to appropriately inform policy changes, direct community-level interventions, and support public dissemination. As the COVID-19 pandemic is ongoing and scientists warn of more pandemic-related disasters in the future, researchers should seek to identify and clarify the role of psychosocial mechanisms and social determinants contributing to variations in psychological adjustment at the community level.
5.2 General Discussion

Through the included studies, results indicated a novel cognitive vulnerability for ACS-induced PTSD that may reflect a unique aspect of this disorder. Further, findings suggest that these psychosomatic cognitive processes influence PTSD risk in the month after evaluation for an acute cardiac event whether or not the patient ultimately receives an ACS diagnosis. If enduring somatic threat perceptions are indeed a fundamental vulnerability for PTSD after life-threatening medical events such as ACS, our current approach to motivating patient self-care through highlighting the lurking mortality threat in those patients’ bodies may actually undermine their psychological and physical health. These findings should spur future research into the character and determinants of PTSD due to life-threatening medical events and should be considered in the management of secondary medical risk in patients.

Interventions targeting medically-induced PTS symptoms and ongoing interoceptive threat perceptions may reduce psychological distress, improve quality of life, and even reduce secondary CVD risk after acute cardiac events. Innovative therapies such as biofeedback for heart rate variability (HRV) have been shown to improve both PTSD symptoms and HRV in healthy adults (Lande et al., 2010; Tan et al., 2011; Zucker et al., 2009) and may be particularly useful for ACS survivors, as they may serve as a version of exposure therapy. Additionally, the broader anxiety sensitivity literature has identified several evidence-based treatments, including interoceptive exposure, in order to target heightened anxiety sensitivity. Of note, while evidence for these interventions in promising, fewer studies have examined these interventions among individuals with heightened physical anxiety sensitivity resulting from or in conjunction with an acute, life-threatening medical event or chronic illness.
Often overlooked, basic psychoeducation may be an important tool in supporting patients experiencing psychological distress amidst a health crisis or in the face of a chronic medical stressor. A study conducted using the same patient sample as Studies 1 and 2 recently found that patients who had received invasive coronary revascularization after their first ACS reported lower PTSD symptoms 1-month later and were more likely to report being “cured” than those who had not received the procedure, irrespective of objective medical severity or complexity (Edmondson et al., 2018). Notably, this study implies that clinician-delivered diagnostic, psychoeducational, and prognostic information has the potential to drastically impact a patient’s somatic perceived threat following an acute health event, resulting in longitudinal mental health outcomes. The patients’ sense of being “cured” after medical doctors visualized their vasculature and made sure that no metaphorical “pipes were clogged” suggests that a recovered physical security and homeostasis is not only possible following ACS, but likely supported through psychoeducation to increase patient understanding. Future clinical research should explore more directly whether a patient’s level of cardiac-related perceived threat, and perhaps physical anxiety sensitivity more broadly, may be amenable to cognitive restructuring delivered by clinical providers in ED and hospital settings.

Importantly, recent research on the agreement of patient-reported ACS versus claims data found that nearly half of self-reported ACS events (43%) were not supported by claims data, with most corresponding to non-ACS cardiac admissions (Yasaitis et al., 2015). Thus, it is unclear whether patients can distinguish between “true” ACS and other diagnoses for which they are hospitalized after evaluation for ACS. Furthermore, our sensitivity analyses revealed that the key findings held when we limited to only participants with ACS diagnosis at discharge. Per these findings, medical and psychological clinicians must recognize and consider that PTS
symptoms may be present and highly distressing in patients evaluated for CVD and other life-threatening medical events, regardless of discharge diagnosis or objective event severity. The subjective experience of presenting to the ED with frightening, painful, or dangerous symptoms can be traumatic and may result in chronic psychological symptoms. Future research should continue to explore symptom trajectories and determinants of PTSD due to other acute or life-threatening medical events. Such research can inform and improve peritraumatic and clinical intervention efforts.

Optimizing psychoeducation for patients is, of course, a key concern in providing adequate patient care in any clinical care setting. However, psychoeducation for providers, particularly when working on interdisciplinary teams or communicating across interdisciplinary lines, holds weight as well. Behavioral medicine aims to bridge academic and clinical gaps among the various professional fields involved in successful health promotion and behavior change; however, silos remain. In line with the spirit of the Consultation-Liaison model, many ED and hospital settings have embedded psychology and psychiatry staff able to consult for acute mental health concerns impacting medical care. Given the typically brief hospital course for patients with ACS presentations and many other acute health events, adequate diagnoses, effective interventions, and appropriate referrals are unlikely to take place bedside in the peritraumatic period. Recognizing these inherent limitations to adequate mental health care in acute healthcare settings, research should explore easily-scalable, low cost psychoeducational, public health, or resource-sharing interventions targeting medical patients with increased physical anxiety sensitivity. Interventions should be studied and identified across the spectrum of healthcare settings – from emergency department and inpatient medical teams to consultation-liaison providers to outpatient medical and mental health providers.
The present findings also indicate that interoceptive threat bias plays an important role in psychological adjustment, not only to acute medical events, but also more broadly in the context of acute health-related stressors, like the COVID-19 pandemic. Baseline heightened physical anxiety sensitivity almost unanimously predicted clinically elevated depression and anxiety symptoms over the first 12-months of the pandemic. As many public health campaigns tend to use fear- or risk-based messaging to encourage health-improving or harm-reducing behaviors, dissemination efforts may be inducing unintended psychological consequences. For those with heightened physical anxiety sensitivity – whether due to a trait-like predisposition, impaired affective regulation processes, comorbid mental health conditions, naturalistic peritraumatic adjustment, or self-monitoring due to a chronic health issue – this messaging may not be sufficient or even beneficial. Dissemination efforts should consider including information regarding how to recognize false positives or ways to balance and understand emotion-driven versus objectively-supported physical health concerns. Future research should continue to examine the role of public health dissemination in the experience of physical anxiety sensitivity, as this mechanism appears to represent a particularly potent mechanism of risk.

Of note, we observed a small group of individuals whose anxiety worsened significantly over the course of the year in Study 3. Emerging symptom groups are frequently seen in a minority when examining trajectories of psychological adjustment and frequently offer insights into intervention targets and potent mechanisms (Barzilay et al., 2020; Bryant & Harvey, 2002; Sheerin et al., 2018). While these patterns are common, the present study’s Worsening group was the only symptomatic trajectory group in which relevant demographic and psychosocial covariates did not differentially predict class membership. Because the size of this trajectory was relatively small, lack of prediction may reflect, at least in part, reduced statistical power to detect
differences. It is also possible, however, that worsening psychological adjustment in this group may be driven by another, unmeasured factor, potentially less related to emotion dysregulation and more to do with social determinants.

Considering the vast systemic consequences of the pandemic and pervasive health disparities observed plainly throughout the pandemic, future research should further examine the relationship between social determinants, particularly as related to worsening or delayed symptom exacerbation. It may be that a downstream consequence of the pandemic (Batterham et al., 2021) or other mediating factors inadequately measured in the current study, such as financial circumstances (Gambin et al., 2022; Kimhi et al., 2021), inform this pattern of clinical anxiety exacerbation over time. These findings suggest the likelihood of a broadening mental health gap that, without concerted scientific and clinical attention, is poised to continue widening.

**Limitations**

The three studies comprising this dissertation have several notable limitations. First, Study 1 and 2 sampled from a large, observational cohort study which was conducted at a single site – an urban medical center recognized as one of the nation's largest and busiest hospitals. Therefore, findings from Studies 1 and 2 may not be generalizable to patients presenting with ACS symptoms in other geographic locations or non-ED settings.

An additional limitation of Studies 1 and 2 relates to measurement procedures. By measuring cardiac threat perceptions at the same 1-month interview as PTS symptoms, the association of ongoing cardiac threat perceptions with concurrent PTSD symptoms may have been artificially inflated. Similarly, we assessed cardiac threat perceptions only once, at 1-month
after hospital discharge, in Studies 1 and 2, so we were unable to determine whether cardiac threat perceptions increased due to the cardiac event. The probable bidirectionality of physical anxiety sensitivity and mechanisms of objective physical illnesses requires future research, providing prospective assessment of anxiety sensitivity in order to more completely understand this nuanced psychosomatic relationship. Given the extensive application of wearable devices in behavioral medicine, future studies may consider the use of ecological momentary assessments in untangling this topic further and measuring effectiveness of interventions.

These limitations, however, should not impact the key result of the pair of studies: the synergistic, longitudinal effect of ED threat perceptions and ongoing cardiac threat on PTSD symptoms. Future studies should measure change in cardiac sensitivity over multiple time points to determine whether change in cardiac threat is associated with the development or maintenance of PTSD symptoms over time. Further, while Study 2 presents novel findings on the predictors of PTS trajectories in the 12-months following a suspected ACS event, this study lacks data on the clinical effects of these trajectories, including event recurrence, future hospitalizations, and mortality. In addition, our study did not formally assess participants' psychological treatment for dysfunction and distress associated with PTS nor medical treatment for CVD.

Findings from Study 3 provide valuable insights on the long-term patterns of psychological adjustment to the COVID-19 pandemic in the U.S. However, these results, too, should be considered within the context of several study limitations. As data collection took place during the early stages of the pandemic when lockdowns were in place and in-person contact was restricted, our study utilized online surveying and data collection solutions. To obtain our sample, we utilized Amazon MTurk, a service facilitating efficient, high-quality data collection from a large, diverse pool of online participants (Buhrmester et al., 2018). While
MTurk participants and offline, lab-based participants have been shown to perform similarly, recent studies have drawn attention to data quality concerns due to the increase in “bots” (automated computer programs that automatically complete online surveys) and “farmers” (individuals circumventing MTurk location parameters) engaging with the Amazon MTurk platform (Kees al., 2017; Paolacci et al., 2010). To remain vigilant against these potential data quality issues, we followed recommendations to include response validity indicators and metadata to track and remove invalid or low-quality data (Barger et al., 2011). However, there may be distinct characteristics between our online sample and traditionally recruited samples for which we were unable to control or measure.

Additionally, our sample was fairly homogeneous with regard to sociocultural and racial/ethnic diversity and is not a nationally representative sample. Due to the homogeneity of our sample, we are unable to make conclusions regarding the potential role of many sociodemographic factors on psychological adjustment during the pandemic, including race and ethnicity. Given the obvious and established racial and ethnic health disparities specific to and beyond the COVID-19 pandemic, as well as pervasive and institutionalized sociocultural inequities in the U.S., further studies prioritizing the assessment of psychological adjustment across diverse racial and ethnic groups are critical.

Finally, all included studies used self-report questionnaires to assess PTS, anxiety, and depression symptoms rather than clinical interviews. Therefore, we cannot make assertions about clinical diagnoses, only symptom levels and clinical elevations.
5.3 Conclusions

Researchers and DSM-5 have suggested that the psychological disruption currently termed PTSD symptoms due to physical health-related events do not fit neatly into the current conceptualization of the disorder. However, positive screens for PTSD triggered by life-threatening medical events or acute physical health stressors are a common and important phenomenon to understand. The EST model and the nuanced, psychosomatic construct of physical anxiety sensitivity provide entry points through which we can understand affective, cognitive, and behavioral elements of psychological adjustment to a broad and inclusive range of acute physical-health stressors. Emerging evidence suggests that interoceptive threat bias plays a crucial role in affective dysregulation and worse psychological adjustment to the pandemic, a universal stressor, emphasizing the broad applicability and great potency of this mechanism.

Regardless of diagnostic conceptualization or index event, physical anxiety sensitivity is associated with worse, longitudinal psychological adjustment and poor health outcomes. Given the frequency with which life-threatening medical events occur, medically-induced PTSD could represent the lion’s share of the PTSD burden in most developed countries. Further, representing an acute and global health-related stressor, the COVID-19 pandemic appears to induce anxious and depressive reactions in a high proportion of individuals who report heightened interoceptive threat bias. Both of these contexts demonstrate the role of interoceptive threat bias as, in part, maintaining these maladaptive reactions and clinically elevated symptom profiles.
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