DISSERTATION

THE EFFECTS OF INTOLERANCE OF UNCERTAINTY AND MEANING IN LIFE ON PSYCHOLOGICAL AND PHYSICAL HEALTH

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ABSTRACT

THE EFFECTS OF INTOLERANCE OF UNCERTAINTY AND MEANING IN LIFE ON PSYCHOLOGICAL AND PHYSICAL HEALTH

Intolerance of Uncertainty (IU) is a dispositional characteristic that informs how people think about, feel, and behave in response to uncertainty. A growing research base suggests IU is a transdiagnostic risk factor for psychopathology (e.g. Koerner & Dugas, 2008; Carleton, 2012), yet few researchers have investigated IU as a risk factor for physical disease. The current investigation adopted a new perspective from the Generalized Unsafety Theory of Stress (GUTS; Brosschot et al., 2016a, 2016b, 2018) to explain how high IU might perpetuate a sense of generalized unsafety (GU), promoting chronic heightened physiological dysregulation that, over time, impairs psychological and physical health. The current studies also examined a potential protective resource, Meaning in Life (MIL), as a buffer against the deleterious effects of IU based on previous research indicating MIL provides a sense of safety and certainty that may counter the effects of IU on GU and health. Structural equation modeling of the hypothesized moderated mediation wherein IU conveys risk for physical and psychological illness via GU (mediator), with MIL (moderator) buffering against this risk, did not yield significant indirect effects in the three distinct samples tested. Moderation effects were significant in one sample, suggesting MIL may provide some protective benefit against GU for people high in IU. Additionally, results of hierarchical models support MIL's role in protecting against negative psychological consequences for high IU individuals. The discussion provides explanations of

these results in the context of GUTS and suggestions for future empirical research to explore risk and protective factors in the development of physical and psychological illness.

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DEDICATION

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CHAPTER I: INTRODUCTION

Uncertainty is embedded in our everyday experiences. Some people find uncertainty highly bothersome, whereas others are less distressed when they feel uncertain. Intolerance of uncertainty (IU) is a dispositional characteristic defined as a, "tendency to react negatively on an emotional, cognitive, and behavioral level to uncertain situations" (Buhr & Dugas, 2009, p. 216). People who are high in IU perceive of stimuli as uncertain more often and experience anxiety and worry more frequently and intensely than those low in IU, enhancing their risk for developing psychopathology. High IU people experience prolonged fear that maintains consistent heightened physiological activation, straining multiple regulatory systems of the body, conveying greater risk for physical ailments. People high in IU are at greater risk for mental and physical illness because they have developed a pervasive, subconscious framework from which they perceive of and experience the world as unsafe. This generalized unsafety (GU, Brosschot, et al., 2016a, 2016b, 2018) helps to explain why, over time, IU is detrimental to both physical and psychological health.

However, the current investigation does not merely focus on factors that convey risk to health, it also considers factors that may promote a sense of safety, counteracting the effects of IU on GU, and contributing to better psychological and physical health. People who report a strong sense of meaning in their lives tend to have better psychological and physical health than those who do not experience their lives as meaningful. Although there are numerous psychological resources associated with well-being and optimal functioning, meaning in life (MIL) may be an especially critical resource because it could provide a sense of safety and certainty that counters the effects of IU on GU and health. People who find uncertainty highly

distressing (high IU) might have access to a sense of MIL that provides them with stability and certainty, protecting them from developing GU, and thus shielding them from the negative effects of IU on health. This paper adopts a new perspective from the Generalized Unsafety Theory of Stress (GUTS; Brosschot et al., 2016a, 2016b, 2018) to explain: 1) why IU is likely to perpetuate a sense of generalized unsafety (GU), which over time damages people's health, and 2) why MIL might convey a sense of safety that buffers against the risk to GU and health that IU conveys. Two studies are outlined as part of the current investigation to examine whether IU conveys risk for physical and psychological illness via GU and if MIL buffers this risk. Results provide critical information about key variables that predict risk for and factors that protect against the development of physical and psychological illness.

Intolerance of Uncertainty (IU)

IU is conceived of as an inclination all humans are born with because being intolerant of uncertainty promotes survival (Brosschot et al., 2016a). IU is thought to diminish with experiences that enhance a person's sense of safety in the world as experiences that promote efficacy in coping with uncertainties reduce the perception of all things as potentially unsafe and promotes learning that experiencing uncertainty does not necessarily result in aversive outcomes (Carleton, 2016; Brosschot, et al., 2016a). However, some individuals do not experience reductions in IU as they age, and thus IU becomes maladaptive. High IU individuals tend to experience chronic anticipatory anxiety about the future, believe uncertainty is aversive, and engage in worrying, reassurance seeking, and hypervigilance in efforts to reduce feelings of uncertainty (Barlow, 2004; Carleton, 2016).

IU and psychological illness

IU is considered to be a transdiagnostic risk factor for a range of psychological disorders, primarily internalizing forms of psychopathology (e.g., McEvoy & Mahoney, 2012; Keefer et al., 2010). IU is present at higher than normative levels in patients diagnosed with social anxiety (Carleton et al., 2010), panic disorder and agoraphobia (Carleton et al., 2014), generalized anxiety (Buhr & Dugas, 2002; Gentes & Ruscio, 2011), posttraumatic stress (Bardeen et al., 2013), obsessive–compulsive symptoms (Jacoby et al., 2013), and depression (McEvoy & Mahoney, 2011; Sexton & Dugas, 2009; van der Heiden et al., 2010), among other disorders.

Several researchers (Carleton, 2016; Grupe & Nitschke, 2013) posit that IU conveys risk for psychopathology due to disruptions in the neural circuitry associated with responding to uncertainty such that high IU people react in a heightened manner to uncertainty that results in maladaptive levels of anxiety. The Uncertainty and Anticipation Model of Anxiety (UAMA; Grupe & Nitschke, 2013) outlines several processes in which high IU people engage when they experience uncertainty. They: 1) inflate estimates of the costs and probabilities of uncertain threat(s); 2) demonstrate hypervigilance in uncertain situations, attending excessively to a potential threat; 3) lack the ability to learn that situations are safe and resolve uncertainty; 4) engage in avoidance of uncertain situations, and 5) exhibit heightened reactivity to uncertainty (Grupe & Nitschke, 2013). All of these processes interact with each other such that high IU people tend to experience anxiety, even in contexts that indicate safety, and this anxiety provokes maladaptive psychological responses as well as prolonged physiological arousal.

Each of these processes is associated with neural and psychophysiological differences in the brains of high versus low IU individuals (see Tanovic and colleagues, 2018). A summary of some of the key differences in neural functioning and structures associated with the five UAMA

processes mentioned above, may help to explain how IU conveys risk for developing psychopathology and physical health ailments.

First, evidence indicates that high IU individuals inflate estimates of the costs and probabilities of uncertain threats and that this overestimation tendency is associated with disruptions in functional aspects of the prefrontal cortex (PFC) and orbitofrontal cortex as well as dopaminergic neurons in the midbrain responsible for error signaling. Deficits in these components impair calculations of expected costs of future events and adjustments of expectancies when events do not occur as expected (Grupe & Nitschke, 2013; Tanovic et al., 2018). High IU individuals exhibit overly pessimistic expectations about the probabilities and costs of uncertain events, and they do not modify their expectations based on previous inaccurate predictions or previous experiences of uncertainty as "not so bad". Overall, the high IU individual's belief that uncertain events will come and that they will be highly distressing contributes to prolonged anxiety and physiological activation that conveys risk for illness.

Second, high IU individuals tend to engage in hypervigilance, which also contributes to heightened physiological arousal. Hypervigilance is associated with disruptions in the amygdala, a vital region of the brain associated with processing of emotions. Neurons in the amygdala are involved in encoding both positive and negative emotional outcomes; however, there are more neurons in the amygdala that encode negative emotional outcomes (Paton et al., 2006) and studies of amygdala activation show a bias toward encoding negative information (e.g., Cunningham et al., 2008). Thus, hyperactivity of the amygdala suggests greater processing of negative and/or threat-related emotions. In high IU people, the amygdala is hyperactive in anticipation of and response to uncertainty of threat which results in biased processing such that they over-identify stimuli as potentially threatening. Not only do high IU people perceive more

stimuli as potentially threatening, but they also tend to pay greater attention to potential threats. These mechanisms likely contribute to the high IU individual's perception of the world as more dangerous and frightening (Grupe & Nitschke, 2013). In fact, heightened amygdala activation has implications for fear learning as well as emotion regulation. High IU individuals experience activation of the amygdala with a wide variety of cues that have previously been associated with uncertainty, which contributes to an internal state of uncertainty about threat in response to many, even objectively predictable, conditions (Grupe & Nitschke, 2013). Thus, the high IU person is wired to look for cues connected to uncertainty and detect cues fairly indiscriminately such that they maintain a heightened vigilance, likely resulting in chronic physiological activation that contributes to risk for mental and physical illness.

Third, deficient safety learning is characteristic of the high IU individual and contributes to chronic feelings of unsafety. Deficient safety learning is thought to result from deficits in the connectivity between components of the PFC and the amygdala. The ventromedial PFC (vmPFC), associated with responding to safety, ideally downregulates activity of the amygdala to signal safety; however, in high IU people, vmPFC-amygdala connectivity is disrupted. Because of this disruption, high IU people tend to have difficulty discriminating between stimuli that are threatening versus those that denote safety (Tanovic et al., 2018; Grupe & Nitschke, 2013). Typically, under conditions of uncertainty, safety signals provide humans with an indication that a threat is not present, relieving their anticipatory anxiety; however, high IU individuals have difficulty identifying these safety signals due to their biased attention toward threat (Grupe & Nitschke, 2013). As a result of deficient safety learning, high IU individuals tend to maintain fear as well as heightened amygdala activity even when a potentially uncertain threat is no longer present, contributing to prolonged stress-like responses under objectively safe conditions. As I

will describe in detail in later sections, deficient safety learning contributes to a sense of generalized unsafety, which conveys risk for physical and psychological health symptoms.

Fourth, high IU individuals tend to engage in cognitive and behavioral avoidance, such as worrying or avoiding thinking about a situation, in response to feeling uncertain. Theory suggests that avoidance is reinforced through operant learning as a mechanism for reducing fear (Grupe & Nitschke, 2013). For high IU individuals, avoidance heightens threat expectancies, yet the events of concern typically fail to occur, resulting in the individual developing a false belief that avoidance prevented the negative outcome from occurring (Grupe & Nitschke, 2013). The amygdala and regions of the PFC underlie this avoidance learning. Avoidance contributes to risk for psychological and physical illness as it prevents fear extinction and thus maintains prolonged, heightened levels of fear that promote physiological dysregulation.

Fifth, heightened reactivity to uncertainty is a characteristic feature of IU. In comparison to healthy controls, individuals with anxiety disorders tend to exhibit elevated startle responses to unpredictable threats. Elevated activation of the bed nucleus of the stria terminalis (BNST) underlies this startle response, as BNST activation is sustained when people perceive potential unpredictable threats. However, individuals with high trait anxiety, and presumably high IU individuals, tend to sustain BNST activation outside of these lab-based threat-inducing paradigms (Grupe & Nitschke, 2013). The anterior insula is also critical in influencing responses to uncertainty as it is involved in neural process related to anticipation, decision making, interoception, and emotional awareness (Grupe & Nitschke, 2013). Grupe and Nitschke (2013) suggest that the anterior insula generates anticipatory emotional responses such that the individual makes presumptions about how potential future events will feel. High IU individuals tend to presume that uncertain situations will feel terrifying, which explains observed heightened

anterior insula activation (Grupe & Nitschke, 2013; Tanovic et al., 2016). Persistent elevations in BNST and anterior insula activity contribute to the behavioral, emotional, and physiological manifestations of anxiety, making "uncertainty particularly 'intolerable' for anxious individuals" (Grupe & Nitschke, 2013, p. 498).

Altogether, these alterations in underlying neural functioning and connectivity align with observable differences in how high versus low IU people respond to uncertainty, and these differences help to explain why high IU individuals are at greater risk than low IU individuals for developing psychological and physical illness. In summary, high IU people tend to experience anticipatory anxiety related to uncertainty, which can be triggered by innocuous cues misperceived as threats, and they maintain a hypervigilant state, experiencing prolonged, heightened anxiety. Because of deficits in safety learning, high IU people do not perceive of indicators of safety, thus they engage in other processes (e.g., avoidance, worry, rumination) to attempt to reduce anxiety. These maladaptive responses are reinforced, further ingraining a fear of the unknown as well as prolonged anxiety that promotes physiological dysregulation. Thus, high IU people have impairments in neural connectivity and functioning and are stuck in a detrimental cycle of thoughts and behaviors that reinforce their IU, conveying heightened risk for psychopathology as well as physical illness.

IU and physical illness

Although much of the extant research on IU focuses on IU as a transdiagnostic risk factor for a range of psychological disorders, there is growing evidence that high levels of IU might also enhance risk for physical disease. First, I will describe existing links between IU and markers of risk for physical illness. Second, I will describe a new theory, GUTS (Brosschot et

al., 2016a, 2016b, 2018), and utilize it to elucidate mechanisms by which high IU may convey risk for disease.

Most studies have looked at the connection between IU and health in the context of ambiguous or unpredictable threats in the laboratory setting. Greco and Roger (2003) found that individuals high in IU had significantly higher blood pressure than those low in IU while awaiting an unpredictable unpleasant stimulus. Presumably, high IU individuals experience more frequent spikes in blood pressure than low IU people due to their processing biases. Frequent spikes in blood pressure can lead to chronic provocation of the cardiovascular system and can contribute to sustained elevations in corticosteroids that impair immune functions and enhance disease risk (Greco & Roger, 2003).

When involved in tasks targeting worry and catastrophizing, high IU participants experience greater worry as well as greater reductions in a component of resting heart rate variability (HRV) termed high frequency (HF-HRV) than low IU participants (Deschenes et al., 2015). HF-HRV is commonly interpreted as an index of parasympathetic nervous system functionality. Results suggest that the high IU participants' pattern of responding may put their cardiovascular health at risk (Deschenes et al., 2015).

Generalized Unsafety Theory of Stress

The Generalized Unsafety Theory of Stress (GUTS; Brosschot et al., 2016a, 2016b, 2018) is a novel theory that further elucidates how IU conveys risk for mental and physical illness, emphasizing HRV as a key mediating factor. Simply, GUTS identifies a lack of perceived safety as the crucial risk factor for developing stress-related physical and psychological illness. Conventional theories of stress tend to argue that stress-related physical illnesses result from disruptions in stress appraisal systems, heightened stress reactivity, poor

coping mechanisms, and a build-up of strain from experiencing frequent and/or intense stressors (e.g., Lazarus & Folkman, 1984; McEwen, 1998). The GUTS theorists suggest that instead of asking "what causes people to experience stress or physiological activation from a perceived stressor?", we should ask, "what allows the stress response to turn off, or be inhibited?" Thus, the perspective shift put forth through GUTS is that the body's inability to maintain or return to homeostasis is not due to the experience(s) of stressors, an accumulation of stressors, or a propensity to react negatively or exaggeratedly to stressors/events, but rather to an organism's inability to perceive safety. When an individual is compromised in his or her ability to perceive safety, his or her body remains in a state of perceived unsafety and prolonged physiological activation occurs, conveying disease risk. This inability to turn off, or inhibit, the stress response is due to deficient safety learning, resulting in perceived generalized unsafety.

A critical predictor of deficient safety learning is high IU. Due to deficient safety learning, high IU people are prone to experiencing generalized unsafety (GU) (Brosschot et al., 2016a). According to theorists (Carleton, 2016; Brosschot et al., 2016a), IU should decrease with experiences of successfully adapting to novelty and change and learning that all unknowns are not aversive (e.g., Timmermans et al., 1994). Humans ideally learn about the predictability and controllability of threats such that things that were once appraised as unknown are learned to be safe, and we gradually generalize experiences across similar contexts, transitioning from perceiving the world as unknown and thus fearful to experiencing only particular new or different experiences as unknown and fearful (i.e., feeling unsafe only in certain contexts) (Brosschot et al., 2016a).

However, this process of learning and generalization does not proceed uniformly for all people, as some people remain highly intolerant of uncertainty due to deficient safety learning.

Because of their tendencies, high IU individuals are more likely to experience deficient safety learning and thus perceive the world as generally unsafe than low IU individuals. As described above in the UAMA model, high IU individuals tend to maintain high levels of fear even in the absence of fear-inducing stimuli. Thus, their brains perceive of threats even when they are not objectively present. As Tanovic and colleagues (2018) state in their description of high IU characteristics, "even when threat is absent and the context indicates safety, the ability to inhibit anxious responding is disrupted…and deficient safety learning contributes to avoidance in uncertain situations (p. 4)." Thus, when high levels of IU are maintained, safety learning is impaired, and impaired safety learning increases susceptibility to GU.

Brosschot and colleagues (2016a, 2016b, 2018) suggest that GU operates at the unconscious level, thus GU is not measurable via self-report, so we need an observable indicator of GU. Brosschot and colleagues suggest that individual differences in resting heart rate variability (HRV) can serve as an indicator of GU. Next, I will describe HRV, then I will outline why low HRV might be an indicator of GU, and finally I will discuss the implications of HRV with regard to physical and psychological health outcomes.

Heart rate variability (HRV)

Heart rate is an integral component of the complex, dynamic systems that regulate the brain and body. Heart rate is mediated by connections between cortical and subcortical systems involved in the regulation of affective and physiological responding (e.g., Deschenes et al., 2015; Thayer & Lane, 2000). HRV is a measure of the variation in intervals between heartbeats, or the beat-to-beat changes over time in heart rate. A healthy heart oscillates spontaneously, responding differentially to environmental and physical demands, which is reflected in high HRV (Thayer et

al., 2012). HRV can also be measured in terms of its high-frequency (HF-HRV) and low-frequency (LF-HRV) components and the LF/HF ratio.

HRV is governed by the autonomic nervous system (ANS). Heart rate is influenced by both components of the ANS: the sympathetic nervous system (SNS) and the parasympathetic nervous system (PNS) (Thayer et al., 2009a). The primary nerve of the PNS is called the vagus nerve. The vagus nerve connects the heart to many other vital organs involved in regulatory processes, including the brain. It also sends signals from other parts of the body to the heart. Heart rhythm and HRV are governed by inputs from the vagus nerve (PNS) and from the sympathetic system (Thayer et al., 2009b).

Although the functioning of the heart is influenced by both PNS and SNS inputs, the PNS inputs are more powerful in dictating the balance of the cardiac system (Thayer et al., 2012). Relative increases in SNS activity cause heart rate to increase whereas relative increases in PNS activity cause heart rate to decrease, thus the interval between heart beats becomes shorter with increases in SNS input and longer with increases in PNS input (Thayer et al., 2012). The sympathetic influences only affect heart rate up to .15Hz (Saul, 1990) whereas parasympathetic influences affect heart rate across the entire frequency range of the power spectrum (Thayer et al., 2012). HRV frequencies below .15Hz are influenced by both the SNS and PNS, whereas HRV frequencies above .15 (HF-HRV) are primarily affected by the PNS (Thayer et al., 2012). Thus, the PNS has more influence on heart rate across the full range. Additionally, due to the differential effects of the neurotransmitters that work for each system, the PNS is capable of rapidly modulating heart rate and HRV whereas SNS effects take much longer (Thayer et al., 2012). Because of these factors, heart rate and HRV are considered to by primarily under PNS control.

When the ANS is balanced, the PNS is largely in control of cardiac functioning whereby the vagal nerve sends a message from the brain to the heart that the organism is safe; this state is referred to as vagal modulation. Under conditions of ANS balance, the SNS and PNS work together to maintain a relatively high HRV wherein the body is prepared to respond flexibly to demands (Bornas et al., 2005). Because the PNS is the dominant system at ANS balance and it works more quickly than the SNS to modify heart rate, respiration rate, and arousal, the system responds well to demands (Porges, 1995). When the ANS is imbalanced, the vagal nerve communicates that the body is not in optimal condition and needs to be ready to respond at all times, thus parasympathetic deactivation occurs and the body is in fight or flight mode. If the body remains in a state of ANS imbalance, parasympathetic deactivation contributes to a prolonged physiological state of activation. HRV is lower when the ANS is imbalanced because in an imbalanced state the SNS is overactive and the PNS is underactive (Weber et al., 2010). A prolonged state of ANS imbalance is evidenced in low HRV and changes in multiple bodily systems involved in physiological regulation, including the cardiac system, the hypothalamic-pituitary-adrenal cortex (HPA), and the vascular system.

Low HRV as an index of GU

Low HRV results from autonomic imbalance wherein the effects of the PNS on cardiac activity are reduced and prolonged physiological arousal is sustained. As mentioned above, when the ANS is balanced, the PNS sends a message that the organism is safe and can rest. The connectivity is reciprocal such that when the organism perceives safety, that perception signals the nervous system to maintain vagal modulation. Thus, it would make sense that people who have impairments in their ability to perceive safety (those who are high in IU) are at risk for prolonged ANS imbalance and low HRV.

In individuals with deficient safety learning, safety is chronically in question, thus the brain and body are always preparing to deal with threats (e.g., Nitschke et al., 2009). Thayer (2009a) suggests that this chronic sense of unsafety means that the organism responds constantly in an undifferentiated pattern to challenges, which is reflected in low HRV. Thus, low HRV is considered "an index of a chronically disinhibited default stress response" (Brosschot et al., 2016a, p.27). People with deficient safety learning chronically feel unsafe and are thus unable to respond to situations differentially because they perceive of all situations as potentially threatening, which is reflected in low HRV, autonomic imbalance, and minimal vagal modulation.

There is significant overlap in the underlying neural connectivity and functioning of people with low HRV and people at high theoretical risk for GU. Low HRV is associated with impairments in the functioning of the PFC and amygdala as well as in PFC-amygdala connectivity. Like people with deficient safety learning, people with low HRV tend to show reduced activity in PFC regions involved in inhibiting over-activation of the amygdala such that individuals with low HRV show impairments in context-appropriate emotional responses (Melzig et al., 2009) and demonstrate heightened perceptions of threat (e.g., Bandler et al., 2000). Similar to individuals with deficient safety learning, individuals with low HRV also show heightened and longer-lasting startle responses to neutral stimuli (Ruiz-Padial et al., 2003), slower extinction in fear-response conditioning paradigms (Pappens et al., 2014), more generalized stress responding, and increased contextual fear conditioning (e.g., Liberzon & Abelson, 2016) than high HRV individuals. These results suggest that low HRV may serve as a marker of theoretically high GU.

Low HRV and physical health outcomes

To reiterate, the model tested in this investigation was that high levels of IU predict GU (indicated by low HRV), and that IU conveys risk for physical and psychological illness via low HRV. Thus, it is important to examine links between HRV and health outcomes.

The vagus nerve, discussed above as a critical modulator of HRV, also plays a key role in regulating a variety of allostatic systems, hypothalamic-pituitary-adrenal (HPA) functions, and inflammatory processes. When the body is under vagal modulation, the vagus sends signals to the brain to release chemicals that inhibit the production of pro-inflammatory cytokines, thus vagal modulation is associated with the circulation of fewer pro-inflammatory cytokines (i.e. tumor necrosis factor alpha and interleukin (IL)-6; Marsland et al., 2007; Janszky et al., 2004; C-reactive protein (CRP) and fibrinogen, Thayer et al., 2009). When vagal modulation is not predominant, individuals tend to have lower HRV, which is associated with HPA dysfunction and increased inflammation. The HPA axis produces a stress hormone, cortisol, which regulates blood pressure and other key functions (Kiecolt-Glaser et al., 2002; Weber et al., 2010). However, under conditions of stress, too much cortisol is produced, and when the body has excessive cortisol for a prolonged period of time, pro-inflammatory cytokines are released into the bloodstream (Kiecolt-Glaser et al., 2002), HRV lowers (e.g., Thayer et al., 2006; Thayer & Brosschot, 2005; Weber et al., 2010), and risk for hypertension increases (e.g., al'Absi et al., 1994; Weber et al., 2008). When HRV is low, systemic inflammation is higher as evidenced by increased presence of inflammatory markers in the blood stream.

Over time, impaired ANS functioning contributes to increased risk for a variety of physical diseases. Low HRV is associated with increased systemic inflammation, which is implicated in Alzheimer's disease (e.g., Thayer & Sternberg, 2010), cardiovascular diseases (e.g., Ridker, 2016), kidney disease (Furuland et al., 2008), fibromyalgia (Staud, 2008), and

others. Low HRV is associated with increased risk for mortality following a myocardial infarction (La Rovere et al., 1998) and heightened risk for future cardiac events (Tsuji et al., 1996) as well as increased levels of various disease precursors such as high cholesterol, glucose, and hemoglobin A1c (Thayer and Fischer, 2009; Jarczok et al., 2014). There is also evidence that low HRV precedes the onset of numerous chronic conditions, including chronic fatigue syndrome (Boneva et al., 2007), fibromyalgia (Staud, 2008), cardiovascular disease (e.g., Thayer, Yamamoto, et al., 2009), chronic pain (Evans et al., 2013), chronic obstructive pulmonary disease (e.g., Carvalho et al., 2011), and others. Low HRV in addition to higher circulating levels of inflammatory proteins (e.g., IL-6, CRP, and fibrinogen) is associated with a higher likelihood of having multiple chronic conditions and greater functional impairment (Friedman et al., 2015).

Not only is low HRV associated with objective indicators of disease, but people with low HRV also tend to rate their physical health as worse than those with high HRV (Jarczok et al., 2014). Similarly, people with low HRV tend to reported greater symptom severity than those with higher HRV (Alvares et al., 2013). Thus, low HRV is linked to both objective and subjective indicators of physical health.

Low HRV and psychological illness

Low HRV is associated with a variety of deleterious physiological processes, and it is becoming evident that low HRV is also a marker of risk for psychological illness. HRV is considered to be an indicator of an individual's self-regulatory capacities and psychological flexibility. People with high HRV use more engagement strategies and less disengagement strategies to cope with distress and negative emotions and are more likely to seek social support when distressed than those low in HRV (e.g. Kemp & Quintana, 2013). Individuals with high

HRV tend to have better emotion regulation abilities (Appelhaus & Luecken, 2006; Thayer & Lane, 2009) and perform better on emotion regulation tasks (Butler et al., 2006) than those with low HRV. High HRV is also associated with facets of wellbeing like positive emotionality (Oveis et al., 2009), cheerfulness (Geisler et al., 2010), and resilience (Kashdan & Rottenberg, 2010). On the other hand, low HRV is associated with affective dysregulation and psychological inflexibility (Kashdan & Rottenberg, 2010). Low HRV is also associated with tendencies that convey risk for psychopathology like negative affect and worry (e.g., Bacon et al., 2004), neuroticism (Cukic and Bates, 2014), and ruminative tendencies (Carnevali et al., 2018). Based on these associations, it seems reasonable that people with low HRV are at higher risk for developing multiple forms of psychopathology. In fact, low HRV is associated with high levels of trait anxiety (Bleil et al., 2008; Miu et al., 2009), ADHD symptoms (Rabbia et al., 2003; Antelmi et al., 2004), depression (e.g., Koenig et al., 2016), and post-traumatic stress disorder (Thome et al., 2016).

Low HF-HRV, another indicator that the PNS is not dominant in regulating cardiac functions, is also considered a risk factor for psychopathology. In fact, Beauchaine and Thayer (2014) denote HF-HRV a "transdiagnostic biomarker for psychopathology" (pp. 338). Low HF-HRV is linked to symptoms associated with internalizing and externalizing psychopathology (see Beauchaine, 2012, 2015; Porges, 2007) such as anxiety (e.g., Kemp et al., 2014), phobias (Ahs et al., 2009), attention problems (see Rash & Aguirre-Camacho, 2012), depression (e.g., Rottenberg, 2007), and others (see Beauchaine & Thayer, 2014). Low HF-HRV is also associated with risk factors for mental illness such as high perceived chronic stress (e.g., Dishman et al., 2000), poor self-regulation and emotion regulation (Beauchaine & Thayer,

2014), neuroticism and trait anxiety (Shepherd et al., 2015), and intolerance of uncertainty (IU) (Deschenes et al., 2015).

Summary

The model laid out thus far identifies people who are high in IU as prone to developing GU (conceptualized as low HRV), which conveys risk for worse psychological and physiological health as indicated by inflammation levels, subjective ratings of physical and psychological health and presence and severity of symptoms of psychopathology.

However, the purpose of the current investigation was not solely to identify risk factors for disease but also to identify potential protective factors. People who find uncertainty highly distressing (high IU) might have access to a sense that their life is meaningful which may give them a sense of stability and certainty, protecting them from developing GU and reducing the negative effects of IU on health. Thus, in the next section, I will explore why a subjective sense of meaning in life might provide a sense of safety that reduces the risk for GU and disease that IU theoretically conveys.

Meaning in life

Meaning in life (MIL) has been the focus of research, philosophical consideration, and existential ponderings for years, spawning various definitions of MIL. In this section, I will first provide a working definition of MIL for use in this investigation, then I will describe extant evidence linking MIL to physical and psychological health and MIL to IU, and finally I will explain why MIL might be a key protective resource for high IU people against GU and poor health.

In recent years, there has been growing definitional consensus amongst psychological researchers studying MIL. MIL is considered to reflect an individual's subjective, global sense

about the nature of his or her existence. This subjective sense that one's life is meaningful is derived from 3 distinct facets: coherence, purpose, and significance (Martela & Steger, 2016; Park & George, 2017; Heintzelman & King, 2014). Coherence refers to the extent to which one's experiences make sense as well as the extent to which one understands oneself and one's fit in the world (e.g., Martela & Steger, 2016; Park & George, 2013). Purpose denotes motivation toward one's overarching goals and aims in life (Martela & Steger, 2016), or having "goals, intentions, and a sense of direction, all of which contribute to the feeling that life is meaningful" (Ryff, 1989, pp. 1071). Significance refers to a sense that one's life is inherently valuable and matters (e.g., Martela & Steger, 2016; Park & George, 2017).

MIL and physical and psychological health

Overall, MIL is considered a key contributor to well-being and health (see Steger, 2009 for a review; see also Heintzelman & King, 2014). Feeling that one's life is meaningful protects individuals from the development of stress-related physical illnesses (see Roepke et al., 2014 for review). High MIL is associated with increased longevity (e.g., Hooker et al., 2018; Hill & Turiano, 2014; Krause, 2009), decreased morbidity (e.g., Kim et al., 2013; Cohen et al., 2016), and reduced risk of mortality (Cohen et al., 2016; Boyle et al., 2010). High MIL predicts reduced risk of myocardial infarction (Kim et al., 2015), stroke (Kim et al., 2013), cardiac events (Cohen et al., 2016), and Alzheimer's disease (Boyle et al., 2010; Boyle et al., 2012).

One facet of MIL, purpose, significantly predicted allostatic load ten years later such that people who report higher levels of purpose experienced less physiological wear and tear from the effects of stress over time (Zilioli et al., 2015). People who report more purpose in their lives tend to have lower levels of inflammatory markers and hemoglobin A1c (e.g. Boylan et al., 2018). Purpose also significantly influences the relationship between people's perceived stress

and their diurnal cortisol patterns such that high levels of perceived stress only impact diurnal cortisol in participants reporting low levels of purpose. Thus, purpose buffers against the negative effects of perceived stress on physiological systems and disease development. Altogether, research indicates that MIL, and the purpose facet of MIL in particular, may protect people from the negative effects of stress on physiological systems that perpetuate disease risk.

MIL is also a vital resource for psychological health. High MIL serves many protective functions, as it is related to higher well-being (e.g. Ryff, 1989) and life satisfaction (Steger et al., 2006; Steger & Kashdan, 2007) and buffers individuals from the negative effects of stressful life events (Park, 2010). People with high levels of MIL are at reduced risk for depression (e.g., Mascaro & Rosen, 2008; Park, 2010; Steger & Kashdan, 2009; Kleftaras & Psarra, 2012), anxiety disorders (e.g., Kashdan & McKnight, 2013), suicidal ideation (e.g., Heisel & Flett, 2004), and more (see Steger, 2013 for review).

Potential relation between MIL and IU

Research results clearly indicate that people who report high levels of MIL report better physical and psychological health whereas research reveals that people who report high levels of IU report poorer physical and psychological health. People with high levels of MIL tend to operate from a framework that their life makes sense (coherence), that they have some ultimate aim (purpose), and that their existence matters (significance). High IU individuals tend to operate from a framework that there are a lot of things about life that are uncertain and that uncertainty is disconcerting and should be avoided or reconciled quickly to minimize distress. Both IU and MIL are described as innate, natural tendencies that are relatively stable over time, guiding how we view our experiences. One might wonder if IU and MIL are diametrically opposed. In other words, is it possible for someone who is high in MIL to also be high in IU? Extant research does

not appear to provide a clear answer to this question. The only study I found investigating both MIL and IU reported a negative correlation between the two, suggesting high IU people tend to report their lives as less meaningful (Garrison & Lee, 2017), which aligns with theoretical predictions.

Although IU and global MIL may tend not to co-exist at high levels in an individual, the relationships between coherence, purpose, significance and IU may differ from the IU and global MIL trend. Thus, each dimension of MIL will be explored next with the purpose of discussing how each might relate to coping with uncertainty and might protect the high IU person from experiencing the negative effects of IU on GU and health outcomes. There is no empirical research on how these dimensions of meaning (separately or altogether) might reduce the effects of IU on people's sense of safety or distress related to uncertainty. Thus, one of the primary purposes of the current studies is to investigate how coherence, purpose, and significance might independently, and altogether, serve as safety resources for high IU people against developing GU and resulting negative health outcomes.

Coherence. Coherence is considered a cognitive process through which people subconsciously assess their environment, detecting patterns and connections, and making judgments such as "this makes sense" of "this does not make sense" (e.g., Baumeister, 1991; Baumeister & Vohs, 2002; King et al., 2006). Detecting patterns and reliable connections in the surrounding environment is a survival-based task as it facilitates finding shelter, food, and safety (Geary, 2004). Humans have an innate capacity for recognizing patterns and detecting reliable associations in the environment that is highly adaptive; they are naturally meaning-makers (Heintzelman & King, 2014). This evolutionary advantage for detecting patterns and connections in the world enables us to perceive events in a stable, consistent manner (e.g., Steger, 2009;

Steger et al., 2011) and keep levels of uncertainty at manageable levels (Hirsh et al., 2012). The Meaning Maintenance Model (MMM; Heine et al., 2006) describes the development of meaning frameworks wherein we develop cohesive, stable lenses from which to view the world that enable us to make sense of our experiences and feel that there is predictability in the world.

When we detect familiar patterns and experience a moment as coherent, we essentially perceive that the environment is safe for us to continue on as we were, pursuing our needs and goals, whereas when we detect something is inconsistent with our expectations, an alert signals us to attend to the immediate environment due to the potential for unsafety. According to the MMM, experiences that dismantle coherence (i.e., ambiguous stimuli) detract from our subjective sense of meaning, and we engage in various compensatory behaviors to reduce the aversive feeling of inconsistency (Heine et al., 2006; Proulx et al., 2012; Heintzelman & King, 2013). The entropy model of uncertainty (EMU; Hirsh et al., 2012) posits that the element of uncertainty is especially powerful in disrupting our sense of coherence. Stimuli that provoke uncertainty are profound in destabilizing our perception of order, reducing our sense of meaning and activating our sense-making processes (e.g. Heine et al., 2006; Park, 2010). When we experience the world as predicted, we tend to feel safe because things make sense. When we experience something unfamiliar, ambiguous, or unpredictable, we feel uncertain, and we engage in behaviors to try to reconcile these discrepancies such that we regain a sense of coherence and safety.

Coherence and IU. Central to MMM and the EMU is the idea that having a coherent framework through which to view the world provides us with a sense of understanding that can minimize uncertainty and uncertainty-related anxiety (Hirsh et al., 2012), which may be especially crucial for people high in IU. People high in IU are prone to perceiving uncertainty

more frequently and experiencing higher levels of uncertainty-related anxiety than those low in IU, so coherence may be a vital compensatory tool for them in reducing uncertainty. If an individual has a well-developed sense of understanding of the self, the world, and the interaction between the two, then they can utilize that framework to make sense of potential uncertain elements, which may reduce the strain IU causes, and reduce the risk of experiencing GU.

A well-developed, stable framework not only provides information moment-to-moment about the predictability of the immediate environment, but a coherent framework also serves as a tool for imposing a sense of understanding and stability onto the world (Stillman & Baumeister, 2009; Baumeister & Vohs, 2002). This may provide an individual with a sense of control, which would be especially beneficial for high IU people in that it could counter the negative effects of IU with regard to perception of and reaction to events. People high in IU who also have a sense of coherence and control may experience fewer stimuli as uncertain and their reactions to uncertainty may be tempered by the certainty that coherence provides. For example, someone who is highly intolerant of uncertainty but who also has an intact, stable framework, perhaps from strong religious beliefs, might be protected from generalizing unsafety across situations because he/she might be able to make sense of situations he/she perceives as uncertain by telling him/herself to "have faith" or "trust in God's plan", which reduces uncertainty-related anxiety and sense of unsafety. Although the individual remains highly intolerant of uncertainty, the effects of IU on GU and health are likely to be less profound as as compared to the high IU individual without an established, coherent belief system.

Essentially, coherence provides people with information about familiarity that puts them at ease and provides a tool to make sense of the unfamiliar and uncertain. High IU people with a strong sense of coherence may be less likely to react as negatively and/or for as prolonged a time

period to events that are perceived as uncontrollable and unpredictable than their high IU-low coherence counterparts. Thus, a strong global sense of coherence may serve as a pervasive safety buffer against the distressing uncertainties that arise in life, reducing the impact of IU on GU and psychological and physical illness.

Theoretical speculations are mixed on whether IU might make it difficult for someone to develop or maintain coherence. People who are high in IU tend to endorse a need for cognitive closure, a preference for order, and close-mindedness (e.g., Berenbaum et al., 2008), which suggest a desire to quickly come to a conclusion rather than entertain many possibilities. On one hand, this may promote coherence because people high in IU might hold strong religious, political, or other beliefs that provide them with quick certainty that reduces the impact of IU on negative outcomes like depression (e.g., Barden & Michel, 2017). Thus, people high in IU who also hold strong religious beliefs might experience this as a coherent framework that gives them a sense of meaning and certainty. On the other hand, this need for quick, absolute certainty may preclude processes that promote the development of robust, flexible meaning frameworks. In attempting to find or maintain meaning when they are uncertain, people high in IU may be drawn to make meaning at concrete levels that provide a quick sense of certainty, whereas people low in IU may be able to explore meaning-related considerations more deeply (Park & Folkman, 1997; Baumeister & Vohs, 2002). High IU people may therefore end up with less "meaningful" meanings such that, in their efforts to assuage the discomfort of not knowing, they quickly grasp to concrete or existing meaning frameworks to re-develop a stable meaning framework for certainty that does not provide them with a lasting or protective sense of coherence.

Overall, it is suggested here that high levels of coherence will likely buffer against the negative impact of IU on GU and health outcomes; however, even high levels of coherence

might not be entirely protective because it might not represent the same robust, flexible tool for high IU people as for low IU people.

Purpose. Purpose is considered a motivational, action-oriented component of MIL that orients people's daily activities to their overarching aims and goals. According to Baumeister (1991), the sense that one's life is meaningful comes from four sources: purpose, self-efficacy, values, and positive self-worth. Purpose denotes an individual's perception that current activities will result in a desired effect on future outcomes, which imbues the current activities with meaning (e.g. reading a psychology text is purposeful because it is expected to benefit one's future career, thus it has meaning).

Having a strong sense of purpose directs attention toward relevant information and valued goals, perhaps directing attention away from daily hassles, challenges, and uncertainties. In their review, Hooker and colleagues (2018) reported that people with high levels of purpose perceive life events, daily hassles, and challenges as less stressful than their lower purpose counterparts. Interestingly, Sumner and colleagues (2015) found participants with higher levels of purpose had lower appraisals of the steepness of a hill and the amount of effort required to summit it than those with low levels of purpose. Having a strong sense of purpose may direct attention toward higher-order goals, focusing people's attention on the "big" things that matter to them rather than getting entangled in day-to-day happenings.

People with high levels of purpose also appear to be better able to cope with stressors as they tend to have more coping resources and are more skilled at coping with challenges (Hooker et al., 2018). Ishida and Okada (2006, 2011) found that individuals with lower purpose demonstrated higher autonomic reactivity to stressors and slower cortisol recovery after stress induction than their higher purpose peers, suggesting purpose may be related to stress reactivity

and its physiological correlates. People with a greater sense of purpose are less reactive to stressful stimuli (van Reekum et al., 2007), view stressful stimuli as less aversive (van Reekum et al., 2007), and are better able to regulate response to negative emotions (Schaefer et al., 2013). Burrow and Hill (2013) also found participants with high levels of purpose as compared to those low in purpose reported less negative affect and higher perceived safety when exposed to unsafe situations. Thus, having a strong sense of purpose may buffer against the perceptions and effects of potential stressors, reducing the impact of challenges on physiological and psychological functioning.

Purpose and IU. High IU people tend to experience daily events as more stressful than those low in IU and are likely to get caught up in the day to day, worrying about what might happen next (e.g., Buhr et al., 2009; Thielsch et al., 2015). Instead of orienting action toward important aims and goals, high IU people likely spend much effort ensuring their basic needs, especially needs for safety, are met. However, a strong sense of purpose may serve as a guiding force that enables them to be less reactive to and less distressed by uncertainty. For example, let's take a high IU person who is strongly motivated by her purpose to provide children with an education. She decides to volunteer as a reading tutor for underprivileged youth. She may be unnerved by the many uncertainties related to the role, but her strong sense of purpose will help her move through the uncertainty-related distress toward valued goals by providing her with a framework from which to interpret uncertainty like, "even though this situation is distressing, this work is worthwhile and I care about making a difference". On the other hand, someone high in IU with low purpose may be easily deterred by the various uncertainties they could encounter in such a position and would not maintain motivation to pursue it.

Essentially, purpose may provide a protective overarching aim that helps people, especially those high in IU, tolerate the distress from uncertainty as they move toward important goals. As high IU people experience distress about the uncertainty of the future, purpose may provide them with a sense of safety because it can give them guidelines as to what they are supposed to do, potentially reducing the effect IU has on worrying about future uncertainty.

Significance. Significance refers to an evaluative component of MIL regarding our assessment of the worth and value of our lives. The sense that one's life has inherent value and is worth living is referred to as significance (Becker, 1997; King et al., 2006; Martela & Steger, 2016). Most people believe that their lives matter (Baumeister, 1991; George & Park, 2016), and this seems to serve an adaptive role. Feeling as though our existence matters may help us cope during difficult times such as bereavement, illness, or trauma (e.g., Janoff-Bulman, 1999). Terror Management Theory (TMT; Greenberg et al, 1986; Greenberg, et al., 2008) views significance as protective, especially against fears related to our own mortality. If we feel that our lives are significant, we acquire a sense of symbolic immortality that assuages death anxiety (Kesebir & Pyszczynski, 2014). A sense of mattering might also help to assuage anxiety related to uncertainty, as uncertainty is a crucial part of what makes thoughts about death so fear-inducing.

Significance and IU. The assurance that comes from having a strong sense that one's life matters may serve as a protective resource for high IU people to grasp onto when they are struggling with unsettling situations (George & Park, 2016). Although there is little empirical research on this topic, there is some theoretical support that a sense of mattering affects information processing in ways that might counter the effects of IU. Self-enhancement theory draws upon the idea that people tend to see themselves in a positive fashion, which extends to the supposition that people tend to perceive their lives as being important (Sedikides & Gregg,

2008). In order to gain and maintain a sense of mattering, people may attend to information that provides them with a sense of significance, seeking out such information or taking in information in a way that fits within this framework (Sedikides & Gregg, 2008). When this framework is utilized, it may counteract the effects of the IU framework, as it may be perplexing to simultaneously perceive stimuli as indicating one's existence is worthwhile and indicating one's existence is full of distressing uncertainty.

Summary

Overall, coherent frameworks that provide the individual with information that helps him/her make sense of experiences, orients the individual toward a purpose, and promotes feelings of mattering likely filter attention and responses to stimuli in ways that minimize the impact of IU. In effect, high IU people who also have high levels of these components of MIL are likely protected to varying extents against the development of GU and negative health outcomes because coherence, purpose, and significance provide the individual with a sense of safety. Due to the dearth of research in this area, it is difficult to speculate as to how these components of meaning will differentially impact people's sense of safety. Thus, exploratory analyses will be conduced in this investigation to examine the impact of each component of MIL and of MIL altogether. It is expected that high MIL will be especially important for the health of people who are highly intolerant of uncertainty as it may reduce their perceived unsafety and uncertainty-related distress.

Daily experiences of meaning and uncertainty

Thus far, IU and MIL have been presented as trait-like characteristics that influence how people tend to operate. However, because these global frameworks are constructed, maintained, and adapted from everyday experiences, it is also vital to consider how IU and MIL as well as

psychological and physical health fluctuate day-to-day. Understanding the daily processes by which uncertainty conveys risk for GU and poor health and ways in which daily experiences of meaning might buffer against risk will provide vital information about how health conditions develop or are prevented over time. Specifically, people's daily experiences of uncertainty and meaning might provide a useful lens through which to understand the processes by which MIL and IU interact to influence GU and various health outcomes.

Although IU may limit people's overall sense of life as meaningful, IU might not preclude experiencing meaning some of the time. Although MIL is relatively stable, research indicates that it can fluctuate daily (e.g., Hofmann et al., 2014). Daily investigations of MIL suggest MIL tends to be higher for people on days when they experience positive social interactions (Machell et al., 2015), when they experience achievement (Machell et al., 2015), positive affect (e.g., King et al., 2006; Tov & Lee, 2016), and more. Thus, various daily experiences can significantly impact people's sense of meaning on a particular day. Fluctuations in MIL may provide insight into important processes related to the development and maintenance of a global sense of MIL as well as ways in which MIL might serve as a protective factor against psychological and physical health symptoms, especially for high IU people.

In the present study, it is expected that on days when people report higher levels of meaning than their average, they will experience fewer negative psychological and health outcomes. This will be particularly important for people who are high in IU as they are at greater risk for GU and negative outcomes that, over time, can contribute to physical and psychological illness. High levels of MIL on a day may provide people with stability and certainty that reduces the impact of IU on GU and emotional and physical well-being. For example, on a day when a high IU individual feels especially motivated by an overarching goal (purpose), he/she may

experience less GU because his/her sense of purpose provides certainty about what to do next (coherence) and enhances his/her belief that his/her existence is worthwhile (significance). It is expected that on days when any component of MIL is higher for an individual than his/her average, he/she will experience less GU and negative physical and psychological symptoms. This will be particularly impactful for people with high levels of IU. Similarly, it is expected that high daily meaning will mitigate risk for daily physical and psychological symptoms in the context of daily uncertainty. On days when people report higher than their average levels of uncertainty, it is expected that they will experience more distress than usual; however, on days when participants experience high levels of uncertainty as well as high levels of meaning, meaning will reduce the impact of uncertainty on outcomes.

In this investigation, it is expected that high trait IU will increase risk for physical and psychological symptoms, especially on days when participants report higher than their average level of uncertainty. However, as discussed above, experiencing a sense of meaning during the same time period may buffer against the risks conveyed by IU and by high daily experiences of uncertainty. Thus, this study will investigate differences in health outcomes on days when high IU people experience uncertainty and they also report their lives as meaningful versus days when they experience those risk factors and report low levels of meaning.

Present studies

The present investigation consisted of two studies. The first study (Studies 1a and 1b) investigated the constructs of interest at the trait level over a multiyear timespan, whereas the second study (Study 2: Part 1) investigated these same constructs every day for one week. Study 1 utilized data from a nationwide sample to examine if IU predicts GU and if GU predicts physical and psychological illness with MIL as a moderator of IU - GU relationship. Study 2

involved the collection of self-report and physiological data via ecological momentary assessment and lab stressor tests over the course of one week using a convenience sample. The focus of Study 2: Part 1 was testing Study 1 hypotheses with a convenience sample. The focus of Study 2: Part 2 was investigating daily changes in IU, MIL, and psychological and physical health to highlight the processes by which these variables interact.

Hypotheses

Study 1

Direct effects:

1. IU will significantly predict GU such that participants with higher levels of IU will have lower resting HRV than those with lower levels of IU.
2. IU will significantly predict various indicators of physical and psychological health such that participants with higher levels of IU will have significantly higher levels of inflammatory markers, worse subjective physical health (Study 1a only), and worse psychological health than those with lower levels of IU.
3. GU will predict various indicators of physical and psychological health such that participants with lower resting HRV will have significantly higher levels of inflammatory markers, worse subjective physical health, and worse psychological health than those with higher resting HRV.
4. Meaning in Life variables (coherence and purpose (Both studies) and significance (Study 1b only)) will significantly predict outcomes such that participants with higher levels of MIL will have significantly lower levels of inflammatory markers, better subjective physical health, and better psychological health than those with low levels of MIL.

Indirect effects:

5. GU will significantly mediate the relationship between IU and outcomes such that the effects of high IU are transmitted via low HRV (GU) resulting in significantly higher levels of inflammatory markers, worse subjective physical health (Study 1a only), and worse psychological health.

Moderation:

6. MIL will moderate the effects of IU on GU such that participants with high levels of coherence, purpose, and/or significance will be protected from the effects of IU on GU. Of particular interest, participants with high levels of IU who also report high levels of coherence, purpose, or significance will have higher HRV than participants with high levels of IU who report low levels of MIL.
7. Participants who are low IU with high MIL will have the highest HRV and best physical and psychological health, whereas participants high in IU with low MIL will have the lowest HRV and worst health.

Moderated mediation:

8. MIL will moderate the effects of IU on GU such that participants with high levels of coherence, purpose, and/or significance will be protected from the effects of IU on GU, which then protect against negative health outcomes. Of particular interest, participants with high levels of IU who also report high levels of coherence, purpose and/or significance will be have higher HRV and will report better psychological and physical health than participants with high levels of IU who report low levels of MIL.

Study 2: Part 1

Between-subject trait-level:

Direct effects:

1. Trait IU will significantly predict GU such that people with higher levels of IU will have lower resting HRV at baseline than participants with low IU.
2. Trait IU will significantly predict various indicators of physical and psychological health such that people with high levels of IU will report significantly worse physical and psychological health than participants with low IU.
3. GU will predict various indicators of physical and psychological health such that people with lower resting HRV at baseline will report significantly worse physical and psychological health than people with higher resting HRV.
4. Trait MIL will significantly predict various indicators of physical and psychological health such that people with higher levels of MIL will report significantly better physical and psychological health than people with low MIL.

Indirect effects:

5. GU will significantly mediate the relationship between trait IU and outcomes such that the effects of high IU will be transmitted via low resting HRV to significantly worse reported physical and psychological health.

Moderation:

6. Trait MIL will moderate the effects of IU on GU such that participants with high levels of coherence, purpose, and/or significance will be protected from the effects of IU on GU. Of particular interest, participants with high levels of IU who also report high levels of coherence, purpose, or significance will have higher HRV than participants with high levels of IU who report low levels of MIL.

7. Participants who are low trait IU with high trait MIL will have the highest levels of HRV (GU) at baseline and best physical and psychological health, whereas participants high in IU with low MIL will have the lowest HRV (GU) at baseline and report the worst health.

Moderated mediation:

8. Trait MIL will moderate the effects of IU on GU such that participants with high levels of coherence, purpose, and/or significance will be protected from the effects of IU on GU, which then protect against negative health outcomes. Of particular interest, participants with high levels of IU who also report high levels of coherence, purpose and/or significance will be have higher HRV and will report better psychological and physical health than participants with high levels of IU who report low levels of MIL.

Study 2: Part 2

Direct effects:

9. Participants with high trait IU will report higher levels of daily anxiety, daily uncertainty, daily negative affect, and daily somatic symptoms than participants low in IU.
10. Participants with high trait MIL will report lower levels of daily anxiety, daily uncertainty, daily negative affect, and daily somatic symptoms than participants low in MIL.

Within-subjects direct effects:

11. On days when participants report feeling more than their average level of uncertainty (about the present day or the future), participants will report higher levels of anxiety, negative affect, and somatic symptoms as compared to days when they report less than their average level of uncertainty.

12. On days when participants report more than their average level of meaning in life, participants will report lower levels of anxiety, negative affect, and somatic symptoms as compared to days when they report lower than their average levels of MIL.

Within and between-subjects moderation:

13. Trait IU will moderate the relationships between daily experiences of uncertainty and daily HRV, anxiety, negative affect, and somatic symptoms such that on days when high IU participants experience high levels of uncertainty, they will experience significantly more anxiety, negative affect, and somatic symptoms than low IU people who report high levels of uncertainty that day.
14. Trait MIL will moderate the relationships between daily experiences of uncertainty, anxiety, negative affect, and somatic symptoms such that on days when high MIL people experience high levels of uncertainty, they will experience significantly less anxiety, negative affect, and somatic symptoms than low MIL people who report high levels of uncertainty that day.
15. There will be significant effects of the interaction between trait MIL and trait IU such that low MIL x High IU participants will experience significantly more daily anxiety, uncertainty, negative affect, and somatic symptoms than high MIL x low IU participants.

CHAPTER 2: METHOD

The purpose of the current investigation was to examine if IU conveys risk for GU and deleterious mental and physical health outcomes over varying timespans and if MIL might serve a protective role, especially for high IU individuals in buffering against GU and adverse health outcomes. Study 1 utilized data collected from the Survey of Midlife Development in the United States (MIDUS) to examine mechanisms within the proposed model over approximately 9 years (Study 1a) and 3 years (Study 1b), whereas Study 2 employed an ecological momentary assessment (EMA) survey design with a convenience sample to examine daily fluctuations in variables of interest over the course of one week.

Study 1 utilized two distinct MIDUS samples selected based on the inclusion of variables of interest and variations in time span. Study 1a utilized a subsample from MIDUS 2 and MIDUS 3 who underwent biomarker collection to examine changes in health over an extended period of time. Study 1b utilized the MIDUS Refresher sample to examine change over a shorter period of time. The advantages of Study 1a as compared to Study 1b include self-reported health as an outcome variable and a gap in time between the collection of HRV and psychological outcomes of interest. An advantage of Study 1b over Study 1a is the inclusion of a new item that assesses the significance component of meaning in life.

Study 1a

Sample and procedure

Data from participants who completed the initial survey for MIDUS 2 (MIDUS 2 Project 1), the MIDUS 2 biomarker project (MIDUS 2 Project 4), and the MIDUS 3 initial survey (MIDUS 3 Project 1) were analyzed. This sample was initially recruited for the MIDUS 1 project

between 1995-1996 by random digit dialing and consists of a national probability sample of non-institutionalized English-speaking adults. MIDUS 2 (Project 1) follow-up was initiated between 2004-2005, approximately 9 years after MIDUS 1. Of the 7,108 MIDUS 1 participants, 4,963 were successfully contacted to complete another phone interview, resulting in a 70% retention rate and a 75% retention rate when adjusted for mortality (Ryff et al., 2017). After the phone interview, self-administered questionnaires (SAQs) were mailed and 4,032 participants (81%) returned them. Of those, 1,054 participants from MIDUS 2 Project 1 were randomly selected to participate in the biomarker project (MIDUS 2 Project 4). Participants in this biomarker sample traveled to a General Clinical Research Center (GCRC) between 2004-2006 where they stayed overnight for data collection. At the GCRC, participants completed another self-administered questionnaire, provided a detailed medical history, underwent a physical exam, provided blood and urine samples, and completed a psychophysiology protocol. Participants from this sample were then contacted in 2013 to participate in MIDUS 3 Project 1, which involved a phone interview and SAQ. 945 participants from MIDUS 2 Project 4 completed MIDUS 3 Project 1.

Measures

Time 1 (from MIDUS 2 Project 1).

Demographic information. An extensive battery of items related to family history and demographic data were collected at Time 1. Demographic items that were considered in this study included age, sex, race, ethnicity, education level, household income, and marital status (see Table 1 for descriptive statistics).

Intolerance of Uncertainty (IU). At the most basic level, someone who is highly intolerant of uncertainty fears the unknown, has negative beliefs about uncertainty, and tends to respond in maladaptive ways to uncertainty (e.g., Carleton, 2016). There was no scale in the

MIDUS survey that explicitly measured IU. Lewis and Bates (2013) conceptualized a related construct, "existential uncertainty", as a scale consisting of two items from the SAQ: "The world is too complex for me" and "I cannot make sense of what is going on in the world". The items were significantly correlated ($r = .44$, $p < .01$; Cronbach's $\alpha = .61$) and were summed into a composite score (Lewis & Bates, 2013). Due to the low Cronbach's alpha value and the poor conceptual alignment between these items and definitions of IU, this study did not utilize these items as indicators of IU. Instead, the following items that align conceptually with IU were used: "In uncertain times, I usually expect the best" (IU1) and "I do not enjoy being in new situations that require me to change my old familiar ways of doing things" (Item 2). Both items were rated on a scale of 1 to 5 where 1 = agree a lot and 5 = disagree a lot. Item 2 was recoded such that high scores equate to high IU. It was expected that people high in IU would disagree with (i.e., score high on) both items. The items were only modestly correlated ($r = .24$) and were thus treated as distinct items in analyses rather than as a scale (see Table 3 for descriptive statistics).

Meaning in Life. Feeling as though one's life makes sense (coherence), has a purpose (purpose), and matters (significance) contributes to a global sense that one's life is meaningful which may serve as a buffer against GU and resulting negative psychological and physical health outcomes.

Coherence. There were no items included in MIDUS 2 that specifically tapped into coherence. However, there is an item that theoretically aligns with coherence as it is conceptualized in MIL research: "I cannot make sense of what's going on in the world". Participants rated this item on a scale of 1 to 7 (1 = agree strongly to 7 = disagree strongly). It is expected that participants with high levels of coherence disagree with this statement (i.e. high scores on this item). See Table 3 for descriptive statistics.

Purpose. Purpose in life was assessed with the 7-item purpose subscale from Ryff's (1989) Psychological Well-Being Scale (see Appendix A). Response options are on a 7-point Likert scale where 1 = strongly agree and 7 = strongly disagree. Items were summed to form a scale score. It was expected participants with high levels of purpose would score high on this scale. This scale has been utilized extensively to measure purpose in life and has excellent psychometric properties (e.g., Springer & Hauser, 2006; Kafka, & Kozma, 2002; Akin, 2008). In this study, the scale demonstrated adequate internal reliability (Cronbach's $\alpha = .71$; see Table 3 for descriptive statistics.

Significance. Significance could not be assessed due to an absence of items related to the construct.

Time 2 (from MIDUS 2 Project 4).

GU. Heart rate variability was measured during the psychophysiology protocol that occurred the morning after an overnight stay at the GCRC. Participants were provided a light breakfast; caffeine was not permitted. ECG electrodes were placed on both shoulders and in the left lower quadrant (Sloan et al., 2017) and ECG was recorded in Lead II. During this baseline time period (prior to stressors), participants were seated and measures of respiration and blood pressure were taken. Analog ECG signals were digitized at 500Hz by a 16-bit National Instruments A/D Board and transmitted to a microcomputer for collection. The ECG waveform was analyzed by customized proprietary event detection software on an R-wave detection machine, resulting in RR interval series (see Ryff et al., 2010 for full description). Errors in R wave marking were corrected using established procedures (see Shcheslavskaya et al., 2010).

The root mean square of successive differences (RMSSD) was utilized as an indicator of HRV (de Geus et al., 2019). RMSSD was computed using an interval method for generating

Fourier transformations based on 300-s epochs (e.g., Sloan et al., 2017; DeBoer et al., 1984). RMSSD is widely used in reports of HRV metrics and is recommended as a well-validated indicator of vagal tone (de Geus et al., 2019). RMSSD is not influenced by respiration rate. Previous researchers using these data have utilized the natural log-transformed RMSSD values as this transformation normalizes the distribution (e.g., Sin et al., 2016). Thus, the natural log transformed RMSSD values was utilized in this study (see Table 3 for descriptive statistics).

Inflammation via biomarker data. At the GCRC, fasting blood draws were taken prior to breakfast. Samples were sent to the MIDUS Biocore Lab for analysis. Three markers of inflammation will be used as indicators of systemic inflammation: proinflammatory cytokine interleukin-6 (IL-6), the clotting factor fibrinogen, and acute-phase protective C-reactive protein (CRP). These biomarkers were selected based on previous research (e.g., Cooper et al., 2015). They are responsive to the psychosocial environment and HRV, and when elevated, contribute to the development and maintenance of many chronic conditions (Boylan et al, 2015). IL-6 was measured at the Biocore lab using Quantikine High-sensitivity ELISA kit #HS600B (R&D Systems, Minneapolis, MN). Fibrinogen and CRP were measured by BNII nephelometer (Dade Behring Inc., Deerfield, IL). See Table 3 for descriptive statistics.

Time 3 (MIDUS 3 Project 1).

Subjective physical health. One observed variable was used to measure subjective physical health: "Using a scale from 0 to 10 where 0 means 'the worst possible health' and 10 means 'the best possible health', how would you rate your health these days?" This item was reverse-coded such that high scores equate to the 'worst possible health' such that the directionality aligned with other outcome variables (see Table 3 for descriptive statistics).

Single-item subjective health measures have good reliability and concurrent and discriminant validity with objective health measures (DeSalvo et al., 2006). This single item has been found to predict future mortality and morbidity, and studies suggest it is not affected by mood (Barger et al., 2007), recent illness (Benyamini et al., 1999) or personality (Chapman et al., 2006).

Psychological health. Several scales measured the presence of psychological distress, including self-rated mental health, negative affect over the past 30 days, generalized anxiety, panic attacks, and depressed affect and anhedonia. Self-rated mental health was measured with a single item, "Would you say your mental or emotional health is excellent, very good, good, fair, or poor?", where higher scores equate to poor mental and emotional health. Refer to Appendix A for a list of items measuring negative affect over the past 30 days, depressed affect, and anhedonia. Assessment for generalized anxiety disorder (GAD) and panic attacks (see Appendix A) were only assessed for participants who endorsed worrying "A lot more" than most people and worried "Every day, Just about every day, or Most days", and worrying about "More than one thing", or having different worries "At the same time" (GAD) and if participants reported having a spell or an attack when they "felt frightened or a spell or an attack for no reason... and the attack happened when a respondent was not in danger or the center of attention" (panic attacks). After exploratory analyses were conducted, an additional item, "History of Depression of Anxiety in the Past 12 months" (yes/no) was included due to higher endorsement rates (18.5% endorsed) and to allow for the estimation of a latent variable (see Tables 1 and 3 for descriptive statistics).

Research suggests that symptoms of psychopathology may represent a common psychopathological factor (e.g., Stochl et al., 2015), and there is strong evidence supporting the

loading of internalizing symptoms such as symptoms of depression and anxiety onto a common factor (Kushner et al., 2013). Furthermore, researchers have modeled psychological health as a latent variable consisting of multiple indicators. Campos and colleagues (2014) found good measurement model fit with a latent factor made up of measures of perceived stress (PSS; Cohen et al., 1983), general mental health (i.e., anxiety, depression, behavioral/emotional control, and positive affect; Berwick et al., 1991), and depressive symptoms (CESD-D; Radloff, 1977). The variables included in this study had not previously been tested as a latent variable. Thus, exploratory analyses were conducted (see Results).

Study 1b

Sample and procedure

The MIDUS Refresher sample (MIDUS Refresher; Ryff et al., 2015) was recruited between 2011-2014 by random digit dialing and consists of a national probability sample of non-institutionalized English-speaking adults (n = 3,577) ages 25-74 (Lein, 2015). At the time of initial recruitment, participants completed telephone interviews. They were then mailed a self-assessment questionnaire (SAQ1) and 2,600 completed and returned the questionnaire. A sub-sample of this MIDUS Refresher sample (n = 863) was assigned to the biomarker sample. Participants in this biomarker sample traveled to a General Clinical Research Center (GCRC) between 2012-2016 where they stayed overnight for data collection. At the GCRC, participants completed another self-administered questionnaire (SAQ2), provided a detailed medical history, underwent a physical exam, provided blood and urine samples (biomarker data), and completed a psychophysiology protocol.

Measures

Demographic information. An extensive battery of items related to family history and demographic data were collected at Time 1. Demographic items considered in this study included age, sex, race, ethnicity, education level, household income, and marital status. (see Table 1 for descriptive statistics).

Intolerance of Uncertainty (IU). The same items described above were collected at time 1 and used in this study to measure IU. As in Study 1a, the items were only modestly correlated (r = .22) and were thus treated as distinct items in analyses rather than as a scale (see Table 4 for descriptive statistics).

Meaning in Life. The same items described above for coherence and purpose were collected at time 1 and used in this study. Additionally, a new item was added to the MIDUS Refresher time 2 questionnaire that assessed people's sense that their lives matter (significance): "To me, my existence here and now, by itself, has meanings". Response options were on a 7-point Likert scale (1 = strongly disagree, 7 = strongly agree). High scores on this item imply high levels of significance. See Table 4 for descriptive statistics.

GU. This was assessed in the same way as Study 1a at the biomarker site (Time 2) (see Table 4 for descriptive statistics).

Inflammation via biomarker data. This was assessed in the same way as Study 1a and collected at Time 2 (see Table 4 for descriptive statistics).

Subjective physical health. There were no items available at Time 2 of the MIDUS Refresher to assess subjective physical health. Thus, this was not included as an outcome in Study 1b.

Psychological health. Various psychological outcomes were measured at Time 2 of the MIDUS Refresher (SAQ2). Several scales measured the presence of psychological distress. A

latent variable including various psychological measures representing psychological health were examined via EFA (see Results) from the following indicators:

Center for Epidemiological Studies Depression Inventory (CES-D). The CES-D assesses for depressive symptoms experienced during the past week, which may be indicative of a depressive disorder. In the MIDUS Refresher (see Appendix A), items were rated as 1 = Rarely or none of the time; 2 = Some or a little of the time; 3 = Occasionally or moderate amount of the time; 4 = Most or all of the time, and were then recoded to match the 0-3 scale typically employed with the CES-D. Items with an (R) were reverse coded and all items were then summed such that higher scores indicate higher levels of depressive symptoms. In this sample, the mean scale score was 9.26 (*SD* = 7.90), and the scale had a Cronbach's α = .88. Previous research indicates that the CES-D has high internal and test–retest reliability, and strong convergent and discriminant validity (Contrada et al., 2006; Radloff, 1977)

Mood and Symptom Questionnaire (MASQ). The MASQ assesses for mood symptoms over the past week, comprised of 5 subscales: depressive symptoms (α = .89), anxious symptoms (α = .89), loss of interest (α = .81), anxious arousal (α = .78), and positive affect (α = .93) (see Appendix A for items). In the MIDUS Refresher, items were rated as 1 = Not at all; 2 = A little bit; 3 = Moderately; 4 = Quite a bit; 5 = Extremely. All items were summed such that lower scores indicate better psychological health (see Table 4 for descriptive statistics).

Study 2

Participants

Community members were recruited from a mid-size college town in the Rocky Mountain region to participate in an experience sampling study investigating the pathways through which chronic stressors affect physical and mental health. Participants were

compensated up to $200. A total of 62 participants took part in Study 2. The sample was 53.2% male, 77.4% White (European Background), 1.6% South Asian, 11.3% Mexican (American), 1.6% Central American, 3.2% South American, 1.6% Other (Spanish American). Sampling was stratified as young adults and older adults were the target sample population. The mean age of the sample was 45.35 (SD= 20.50), with 58% of participants between the ages of 23-35 and 42% between 60-84 years old. 37.1% of participants reported being married, 19.4% cohabitating, 1.6% legally separated, 8.1% divorced, 4.8% widowed, 25.8% never married, 3.2% other. In terms of educational attainment, 1.6% of participants did not complete high school, 3.2% completed high school, 3.2% completed some college without earning a degree, 3.2% earned an associate's degree, 29% completed college and earned a bachelor's degree, 19.4% completed some graduate school, 27.4% completed a master's degree, and 12.9% earned a doctorate degree. 58.1% of participants reported being employed at the time of the study and the mean income of the sample was in the $40,000-$49,000 range.

Participants' height and weight were collected and these were used to calculate BMI. BMI ranged from 18.46-45.72 (M = 25.01, SD = 4.37, Skew = 2.02, Kurtosis = 7.54). Participants were asked if they currently smoke (6.5% endorsed) and if they ever drink alcohol (74.2% endorsed). Participants were asked if they currently take any prescription medications, and 51.6% reported taking at least 1 prescription medication (M = .52, SD = .50). Participants were also asked about chronic health conditions; 21% reported no health conditions and 50% reporting 1 or fewer condition (range = 0-13, M = 2.19, SD = 2.64). Of those who endorsed a chronic condition, 22.6% endorsed arthritis, rheumatism or other bone or joint disease; 4.8% osteoporosis, 22.6% sciatica, lumbago or recurring backache, 11.3% persistent skin trouble, including pressure sores, 8.1% thyroid disease, 6.5% hay fever, 14.5% recurring stomach

trouble, indigestion, or diarrhea, 9.7% urinary or bladder problems, 3.2% constipated all the time, 1.6% gall bladder trouble, 14.5% asthma, bronchitis, or emphysema, 1.6% lung problem, 1.6% deep vein thrombosis, 9.7% persistent foot trouble, 1.6% AIDS or HIV infections, 4.8% persistent trouble with teeth, 14.5% high blood pressure/hypertension, 3.2% low blood pressure, 1.6% alcohol or drug problems, 11.3% migraine headaches, 6.5% chronic sleeping problems, 3.2% diabetes or high blood sugar, 1.6% neurological disorders, 1.6% stroke, 1.6% hernia or rupture, 3.2% cancer, 6.5% pain lasting three months or more not included above, 9.7% other. Participants were asked how much their chronic conditions affects their daily life and 51.6% reported “not at all”, 33.9% reported “a little”, 8.1% reported “somewhat”, and 6.5% reported “a lot”.

Procedure

As part of the study, participants completed 7 days of Ecological Momentary Assessments (EMA) and 5 laboratory visits, including 3 lab sessions, 1 study overview, and 1 follow-up debriefing. Various physiological and psychological measures were collected, including self-report questionnaires in lab, psychophysiological monitors in lab, and EMA surveys in daily life.

Participants visited the lab for an orientation session (“Study Overview”) prior to beginning the 7-day EMA period to learn how to use physiological equipment and take EMA surveys. Following the orientation session, participants completed 7 days of EMA surveys and visited the lab 3 times for approximately 1.0-1.5 hour sessions within the 7 day period. During the lab sessions, self-report questionnaires were administered and physiological measurements were taken before, during, and after a Trier Social Stress Test (TSST). Between lab visits,

participants were notified to complete 6 EMA surveys per day on a Samsung Galaxy J3 mobile phone. After the 7-day period, participants returned materials to the lab and were debriefed.

Measures: Trait level

Intolerance of Uncertainty. IU was measured using the short Intolerance of Uncertainty Scale (IUS-12; Carleton et al., 2007; see Appendix A). The IUS-12 measures reactions to ambiguous stimuli and perceptions of uncertainty. Participants rated 12 items on how characteristic the descriptor is of them on a scale of 1 to 5 (1 = not at all characteristic of me, 5 = entirely characteristic of me). Examples of items include, "Unforeseen events upset me greatly" and "I always want to know what the future has in store for me". The IUS-12 has good construct and concurrent validity, strong internal consistency, and demonstrates measurement invariance across gender and ethnicity (see Hale et al., 2016 for review).

Previous studies suggest scores on the IUS-12 can be captured with one factor (total score) and two factor (prospective and inhibitory anxiety) solutions. Factor analysis conducted by Carleton and colleagues (2007) revealed support for the two factor solution with 5 items loading solely on an Inhibitory Anxiety factor representing an avoidance-orientated responses to uncertainty (Birrell et al., 2011) and 7 items loading solely on a second factor, Prospective Anxiety, reflecting an anxious approach orientation toward uncertainty (e.g., desire for predictability.) Hale and colleagues (2016) sought to clarify mixed results regarding the factor structure of the IUS-12, comparing bifactor and unidimensional models. The bifactor model demonstrated better fit to their sample data, yet they found that a general uncertainty factor accounts for more variance than either subscale (Hale et al., 2016). Based on these results, IU was modeled as 1 latent variable with both subscale scores as indicators in this study (see CFA in

results). In this study, the correlation between IUSi and IUSp was .66 (see Table 5 for additional sample statistics).

Meaning in Life. MIL was measured using the Three-Dimensional Meaning measure (Martela & Steger, 2018; see Appendix A). This new measure includes 12 items total, 4 that measure coherence, 4 purpose items, and 4 significance items. Participants rated each item on a scale from "not at all true of me" to "very true of me". Higher scores indicated higher levels of MIL components. Examples of coherence items include, "Most things happening in my life do make sense" and "By and large, I am able to understand the world around me". Examples of purpose items include, "I have a set of core goals that give my life a sense of direction" and "My daily activities are consistent with a broader life purpose". Examples of significance items include, "My personal existence is significant" and "My life is significant in the grand scheme of things".

Due to the fact that this measure was very recently published, there is no published research regarding its psychometric properties. In this sample, the subscales were correlated modestly (r = .43 to .56) and each subscale demonstrated good internal reliability (α = .83, .85, and .87) (see Table 5 for sample statistics).

CES-D. The Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977; see Appendix A) is a 20-item measure of depression symptomatology comprised of six scales: depressed mood, feelings of guilt and worthlessness, feelings of helplessness and hopelessness, psychomotor retardation, loss of appetite, and sleep disturbance. Participants rated symptoms on a 4-point Likert scale where 0 represents "rarely of none of the time (less than 1 day over the past week)", 1 represents "Some or a little of the time (1-2 days over the past week), 2 represents "Occasionally or a moderate amount of the time (3-4 days over the past week)", and 3 represents

"Most or all of the time (5-7 days over the past week)". Examples of items include, "I was bothered by things that usually don't bother me", "I had trouble keeping my mind on what I was doing", "I thought my life had been a failure", "I lost interest in my usual activities", and "I felt sad". High scores on the CES-D indicate high levels of depressive symptoms.

The CES-D has been used extensively to assess depressive symptoms in the general population (Van Dam & Earleywine, 2010). Examination of psychometric properties in community and student samples indicates the CES-D exhibits high internal consistency, strong factor loadings and good convergent validity with anxiety and negative affect and divergent validity with positive affect (Van Dam & Earleywine 2010). In this study, internal reliability of the scale was high ($\alpha = .90$). (See Table 5 for sample statistics).

Subjective health. The Short-form health survey (SF-36; Ware & Sherbourne, 1992; see Appendix A) was utilized to collect information about participants' subjective physical and psychological health. The SF-36 includes 36 items forming 8 subscales: physical functioning (10 items; ability to attend to personal needs, walk, complete everyday tasks), role limitations due to physical health (4 items; extent to which physical capabilities limit activities), role limitations due to emotional problems (3 items; extent to which emotional problems interfere with activities), energy/fatigue (4 items; overall vitality), mental health (5 items; anxiety and depressive symptoms), social functioning (2 items; extent to which physical or emotional problems have interfered with social interactions), pain (2 items; amount of pain and extent to which pain interferes with activities), and general health (5 items; perception of general health).

Previous research and psychometric analysis indicates scores on the SF-36 subscales can be summarized into two dimensions (e.g., Taylor et al., 2013). The "Physical Health" dimension is compromised of the following scales: role limitations due to physical health, pain,

energy/fatigue, and general health. The "Mental Health" dimension also includes energy/fatigue and general health as well as role limitations due to emotional problems, mental health/well-being, and social functioning. Reliability and validity results provide extensive support for use of the SF-36 as a measure capturing subjective physical and psychological health (Ware & Sherbourne, 1992). High scores on the physical and mental health dimensions are indicative of good physical and mental health. In this study, both physical and mental health demonstrated good internal reliability (α = .83 and 88, respectively). See Table 5 for sample statistics.

HRV. HRV was collected at each lab visit (Time 1, Time 2, and Time 3) and recorded using BioLab software via a Mindware device that records physiological data wirelessly. Electrodes were placed in accordance with recommended practices, and service loops will be placed for all electrodes to minimize noise. The participant was video recorded once physiological recordings begin using Noldus Media Recorder. A five-minute baseline HRV measurement period occurred during which participants were instructed to sit in a chair and complete demographic forms. They were instructed not to use their cell phones and were allowed to read magazines if they finished the forms before the examiner returned. These 5-minute baseline measurements were examined for any potential interference or activities that may impact interpretation of the period as a baseline measurement (e.g., extensive physical activity, cell phone use).

All available data from the three lab visits were utilized to calculate an average baseline HRV (RMSSD). Overall, the mean baseline RMSSD HRV was 28.68 (*SD* = 16.16), ranging from 6.45 to 72.78 with a skew of .88 and kurtosis of .20.

Measures: Repeated Assessment During 1-Week ESM (Study 2: Part 2)

Daily Meaning and Purpose. Daily meaning and purpose were assessed each night using the Daily Meaning Scale (DMS; Steger et al., 2008). The DMS consists of 2 items: "How meaningful did you feel your life was today?" and "How much did you feel your life had purpose today?" These items are rated on a 7-point Likert scale from "not at all" to "very much". Research suggests that average scores on the DMS correlate strongly (r = .55, p <.0001) with validated global meaning in life measures, indicating the DMS is a valid measure of state MIL (Steger et al., 2008) Steger and colleagues also reported very high repeated-measures (within-person) reliability (α = .98).

Across participants, average daily meaning was 3.62 (SD = 1.72) and average daily purpose was 3.69 (SD = 1.72), and daily meaning and purpose were very highly correlated (r = .90). There were also small to moderate correlations between trait MIL and daily meaning and purpose (r ranged from .23 to .47).

Daily uncertainty. Daily uncertainty was assessed each night using a new item developed from theory. The item was "Today, how uncertain did you feel?" Participants responded on a scale of 0 = "not at all" to 6 = "extremely". In the study overview session, participants were told the following, "People experience uncertainty when they lack information about something, and they cannot feel sure. For example, people report uncertainty when they are unsure about a decision, the future (e.g., the outcome of an event), how other people might behave, etc. Some people notice a discomforting or uneasy sensation when they feel uncertain". The intention of this item was to assess how much uncertainty participants felt today, as uncertainty tends to trigger distress in people high in IU. It was expected that participants with high trait IU would report more uncertainty each day of the EMA study than those low in IU and

that those high in trait IU would experience greater distress than those low in IU when they experienced uncertainty. Across participants, average daily uncertainty was 2.56 (*SD* = 1.92). There was also a modest correlation between trait IU and uncertainty (*r* = .31).

Daily negative affect (NA). At each assessment (6 times per day), participants were asked how they were feeling in the moment. They rated the following affect descriptors on a scale of "not at all" (0) to "very strongly" (6): angry, sad, anxious, bored, and tired. Because anxiety was of particular interest in this study due to its strong correlation with IU, anxiety was treated as a separate variable. Scores on angry, sad, bored, and tired were averaged together to form a negative affect (NA) composite each day. Thus, all 6 ratings of anxiety were averaged together to form a participants' daily anxiety score and ratings for each time period of the other negative affect variables were averaged to form a daily NA score.

Across participants, average daily anxiety was 1.61 (*SD* = 1.22) and average daily NA was .99 (*SD* = .78). Correlations between trait mental health and depression and daily anxiety and NA were largely insignificant (*r* ranged from -.035 to .05)

Daily somatic symptoms. Participants were asked, "Have you experienced any of the following symptoms? Please check all that apply: Headache or migraine**,** Bodily pains or aches, Cold/Flu symptoms (e.g., coughing, sore throat, runny nose)**,** Fatigue**,** Irregular heart beats**,** Shortness of breath**,** Other**,** None of the above". Participants were asked about somatic symptoms at 6 times throughout the day. Scores were summed over all time periods each day such that participants received a score of 0-7 physical symptoms for each EMA period, resulting in 0-42 symptoms for the day. The most symptoms reported on any single day by a participant was 30. Across participants, average daily somatic symptoms was 2.74 (*SD* = 3.67). Correlations between trait physical health and daily somatic symptoms was moderate (*r* = - .31). Daily

somatic symptoms also moderately correlated with trait mental health (r = - .36) and depression (r = .34).

Covariates. Gender, age, ethnicity, education level, income, BMI, smoking, alcohol consumption, chronic medical conditions were added as potential covariates in a stepwise manner as described in Study 1 as predictors of trait-level variables.

CHAPTER 3: RESULTS

Study 1 Results

Preliminary Analyses

Descriptive and correlational data are reported in Tables 1, 4 and 5. The maximum likelihood (ML) estimates generated in structural equation modeling (SEM) require that several assumptions about the data be met (McDonald & Ringo Ho, 2002). All predictor, mediator, moderator, and dependent variables were measured on ratio or interval scales. Each observation was independent as auto-correlation testing was non-significant. Intraclass correlations (ICC) based on biomarker data collection site were examined, resulting in ICC <.05, indicating data was not nested within individuals or impacted by biomarker site. Multicollinearity was examined in the predictor and moderator variables using the correlation matrix and no multicollinearity was identified (e.g., no variables correlated $r > .70$).

To test for multivariate normality, each of the variables included in the model were examined for evidence of skew and kurtosis using the SPSS statistical software package (SPSS, 2019). Several variables displayed significant skew and kurtosis. Previous published studies using the MIDUS dataset have employed the natural log transformed RMSSD HRV (e.g., Williams et al., 2015; Laborde et al., 2013) as well as natural log transformations of IL-6 and CRP (e.g., Cooper et al., 2015; Friedman, 2011; Elliot et al., 2018). Natural log transformations of these three variables in this study reduced skew and kurtosis to acceptable levels. For Study 1b, the psychological health variables were also natural log transformed to reduce skew and kurtosis to acceptable levels. These variable transformations ensured the required assumption of normally distributed dependent variables was met.

Linear relationships between predictors and outcome variables is assumed in ML estimation. Very weak relations between predictors and biomarker outcomes contributed to the appearance of non-linearity. However, quadratic or other non-linear relationships were not identified. Homoscedasticity was examined via residual analysis to determine if error terms across the regression are equal, ensuring accurate prediction at low and high levels of predictor values. The homoscedasticity assumption was met for all psychological DV scales based on inspection of residuals in scatterplots. The homoscedasticity assumption was not violated; however, the very weak relations between predictor variables (e.g., IU) and biomarker outcomes contributes to the appearance of heteroscedasticity.

Additionally, upon inspection of data, one case in the Study 1b was identified as likely having an inaccurate BMI at Time 2 (Project 4) as the participants' BMI increased by approximately 52 units from Time 1. Thus, this participant's BMI at Time 2 was coded as missing.

Additionally, BMI values greater than 4SD from the mean were identified and set to the lowest and highest non-outlier values (e.g. Mann et al., 2015). No outliers greater than 3SD from the mean were identified in the predictor or moderator variables. Researchers using the MIDUS biomarker data have transformed the biomarker data to reduce skew (e.g., natural log transformed; Cooper et al., 2015; Graham et al., 2018). However, a review (O'Connor et al., 2009) suggests that removing "outliers" (e.g., CRP values above 10.0 mg/L) may result in a loss of meaningful outcome variance (Elliot & Chapman, 2016). Researchers including Elliot and Chapman (2016) and Eisenlohr-Mohl and Segerstrom (2013) have retained these cases in their analyses.

In addition to multivariate normality, ML estimation requires a sufficient sample size, especially when estimating complex models. A minimum of 10 participants per path is required for most models and a larger sample size is recommended for more complex models (McDonald & Ringo Ho, 2002). This requirement was met given the relatively large number of participants in Study 1a (n = 947) and Study 1b (n = 863).

In Study 1a, approximately 1.5% of biomarker data was missing, 7% of HRV data was missing, and 9% of negative affect scale data was missing. Otherwise, less than 1% of data was missing on variables included in primary analyses. Cases without any biomarker data (n = 5) were excluded from analyses (e.g., Cooper et al., 2015). Little's MCAR test (Missing Completely at Random; Little, 1988) was conducted to test the assumption that data was missing completely at random. Results were not significant, $\chi 2$ (df= 181) = 23.09, p = .21, indicating missing data can be considered missing completely at random.

In Study 1b, 1% of biomarker and psychological outcome variable data was missing and approximately 14% of data (collected at T1) on predictor, mediator, and moderator variables were missing. The item measuring significance, which was collected at T2, had only 1% missing. Cases without any biomarker data (n = 6) were excluded from analyses (e.g., Cooper et al., 2015). Little's MCAR test was conducted and results were not significant, $\chi 2$ (df= 102) = 116.21, p =.16, indicating that missing data can be considered missing completely at random. By default, Mplus software utilizes full-information maximum likelihood (FIML) estimation to handle incompletely observed predictors, and research suggests FIML produces unbiased parameter estimates when data is missing completely at random (e.g., Cham et al., 2017).

Additional preliminary analyses of the descriptive data were completed using t-tests, $\chi 2$ tests, and correlations. Relevant demographic variables (see Table 2) identified as potential

covariates were examined using correlation, t-tests, and $\chi 2$ tests prior to inclusion as predictors in models. Covariates without significant or marginally significant relations in preliminary analysis were not included as paths in models.

Analysis Plan

MPlus statistical software Version 7.4 (Muthen & Muthen, 1998-2012) was used to conduct exploratory and confirmatory factor analyses and to test all hypothesized structural equation models. Structural Equation Modeling (SEM) can incorporate measured and latent variables and can simultaneously estimate hypothesized relationships between multiple variables to provide an estimate of the model's fit to the data (Mann et al., 2015). The hypothesized model included: IU measured as two observed predictors; HRV (indicating GU) as an observed mediator; meaning in life variables (coherence, purpose, and significance (Study 1b only)) as observed moderators of the IU-GU path; psychological health as a latent variable outcome and subjective physical health (Study 1a only) and inflammatory biomarkers Il-6, CRP, and fibrinogen as observed outcomes (see Figures 1 and 2). A model building approach for hypothesis testing was used.

Data were analyzed using maximum likelihood estimation (ML). ML is a method of estimating unknown overall population parameters by using the sample mean and variance as parameters and identifying particular values that make the observed model results the most probable. ML searches for the parameter estimates that will maximize the possibility that the observed sample matrix was drawn from the implied population matrix. To evaluate overall model fit, I utilized model fit criteria suggested by Hu and Bentler (1999) including: comparative fit index (CFI) > .95, Tucker–Lewis Index (TLI) > .95, root mean square error of approximation (RMSEA) < .06, and standardized root mean square residual (SRMR) < .08. The CFI has values

that range from 0 to 1. Values of .90 and higher are considered evidence of a good-fitting model, indicating at least 90% of covariation in the data is represented in the hypothesized model. Values of .95 and higher are considered evidence of excellent model fit. The SRMR is a measure of fit that quantifies the standardized difference between observed and predicted correlations where an SRMR value of zero indicates perfect fit between the observed and predicted correlation. RMSEA is a value that represents the residual difference between the predicted and the observed covariance structure. RMSEA values of less than .06 indicate good fit between the model and observed data (Hu & Bentler, 1999). In addition, the Chi-Square test of model fit was considered despite its sensitivity to large samples. A non-significant Chi-Square test of model fit indicates perfect fit of the model to the data; however, large sample sizes can inflate this statistic, thus the above mentioned model fit criteria were taken into account.

Exploratory Factor Analyses: **Study 1a**. Prior to conducting Exploratory Factor Analysis (EFA), preliminary analyses indicated several items to be included in EFA had highly unbalanced response rates. Only 5.7%, 1.9%, and 10.2% endorsed experiencing symptoms of panic, anxiety, and anhedonia/depression, respectively (see Table 1). These items were recoded into a new dichotomized variable ("Symptoms of Mental Illness") such that 0 = no endorsement of any item, and 1 = any endorsement/symptom endorsed on one of the above items. Negative affect and self-rated mental health were measured on continuous scales and were included in the EFA. Self-rated mental health was recoded such that higher scores equated to worse mental health, in line with the other included scales. An additional item, "History of Depression of Anxiety in the Past 12 months" was included due to higher endorsement rates (18.5% endorsed) and to allow for the estimation of a latent variable. The self-rated physical health outcome item

was normally distributed. It was recoded to align with the direction of other outcomes such that a higher score represented worse health.

The sample was randomly split and one-half of participants' data was utilized for Exploratory Factor Analysis (EFA) conducted in Mplus 7.4. An oblique rotation method (PROMAX) was employed to examine the factor structure and fit of the following continuous psychological symptom scales: Negative Affect PANAS (NA), Self-Rated Mental Health (Self-rated MH), and the categorical items: History of Anxiety/Depression and Symptoms of Mental Illness (MI). Evaluation of the scree plot and eigenvalues support a 1-factor model. The eigenvalues for a 1-factor solution = 2.48, whereas the 2-factor solution has a .58 eigenvalue, and a 3-factor solution has a .52 eigenvalue. The 1-factor model demonstrated excellent fit with $\chi 2$ (df = 2) = .41, p = .82, RMSEA < .001 (.00, .04), SRMR = .011. The factor loadings of each subscale onto the latent factor are all high, NA = .68, Self-rated MH = .63, MI = .74, and History of Anxiety/Depression = .75.

Exploratory Factor Analyses: **Study 1b.** The MIDUS Refresher sample was randomly split and one-half of participants' data was utilized for Exploratory Factor Analysis (EFA) conducted in Mplus 7.4. An oblique rotation method (PROMAX) was employed to examine the factor structure and fit of the following psychological symptom scales: Mood and Anxiety Symptom Questionnaire (MASQ) Depression subscale (MASQ_D), Anxiety subscale (MASQ_A), Anxious Arousal subscale (MASQ_AA), Loss of Interest subscale (MASQ_LI), positive affect subscale (MASQ_PA), and the Center for Depression Scale (CESD).

The MASQ_PA subscale was eliminated because it was the only scale to load on a second factor. The MASQ_AA subscale was eliminated due to its strong correlation with the MASQ_A subscale and its low overall factor loading as compared to the MASQ_A subscale.

Evaluation of the scree plot and eigenvalues support a 1-factor model. The eigenvalues for a 1-factor solution = 3.00, whereas the 2-factor solution had a .42 eigenvalue, and a 3-factor solution had a .30 eigenvalue. The 1-factor model demonstrated excellent fit with χ^2 (df = 2) = .24, p = .89, RMSEA = .00 (.00, .04), SRMR = .003. The factor loadings of each subscale onto the latent factor were all high, MA_D = .88, MA_A = .75, MA_LI = .86, and CESD = .77.

Confirmatory Factor Analyses: **Study 1a.** Data from the other half of the sample was utilized to conduct a Confirmatory Factor Analysis (CFA). Results from the CFA suggest excellent fit for the 1-factor latent variable, Psychological Distress, $\chi 2$ (df = 2) = .49, p = .78, RMSEA < .001, CFI = 1.00, TLI = 1.00, and SRMR = .01 (see Figure 3).

Confirmatory Factor Analyses: **Study 1b.** Data from the other half of the sample was utilized to conduct a Confirmatory Factor Analysis (CFA). Results from the CFA suggest excellent fit for the 1-factor latent variable, Psychological Distress, χ^2 (df = 2) = 3.88, p = .15, RMSEA = .05 (.00, .01), CFI = .99, TLI = .99, and SRMR = .01 (see Figure 4).

Path Analyses: Covariates

Direct and indirect effects identified in hypotheses were tested with potential covariates identified in the analysis plan added in a step-wise manner to each model with non-significant covariates eliminated until models included only covariates significantly associated with hypothesized variables (see Table 2 for all tested covariates).

Demographic factors

Age, sex, race and ethnicity, marital status, and socioeconomic status (SES) were examined as covariates related to HRV and outcome variables. Older age has been significantly related to lower resting HRV (e.g., Umetani et al., 1998), poorer psychological health (e.g., Wolitzky-Taylor et al., 2010), higher systemic inflammation (e.g., Chung et al., 2009), and worse

ratings of subjective physical health (e.g., Chen et al., 2007). Thus, age was considered as a covariate predicting HRV, biomarkers, psychological and physical health and remained in most models as a significant covariate predicting HRV, psychological health, Il-6 and Fibrinogen (see Tables 10 and 11 for results). Age was not a significant predictor of CRP.

Previous research has also found sex to be significantly related to resting HRV, with women exhibiting higher HRV (e.g., Voss et al., 2015). Sex is also related to significant differences in levels of inflammatory biomarkers (e.g., Prather et al., 2013; Toker et al., 2005). Additionally, in the US, there is a higher prevalence of anxiety and depressive disorders among women (e.g., Kornstein et al., 2000). Thus, sex was tested as a covariate predicting HRV, biomarkers, and psychological health. Sex was a significant predictor of Psychological Health, CRP, and Fibrinogen in Study 1a and HRV, CRP, and Fibrinogen in Study 1b (see Tables 10 and 11 for results).

Researchers have observed significant differences in resting HRV across race and ethnicity. For example, African American individuals tend to exhibit higher resting HRV when compared to European Americans (e.g., Hill et al., 2015). Previous research indicates that people who identify as a racial or ethnic minority report significantly more psychological distress (e.g., Taylor et al., 2010), and poorer subjective health (e.g., Schulz et al., 2006) than people of racial and ethnic majority status. Additionally, research suggests that African American women have significantly higher CRP than women of European, Hispanic, or Asian backgrounds (e.g., Albert et al., 2007). Because of the limited studies conducted investigating the relationship between inflammatory biomarkers and race or ethnicity, race and ethnicity were included as potential covariates predicting all three biomarkers in addition to HRV, psychological and physical health. In Study 1a, race was a significant predictor of Fibrinogen and in Study 1b, race was a

significant predictor of IL-6 such that African American and Native American participants had significantly higher levels of these inflammatory markers than White and Asian participants (see Tables 10 and 11 for results).

Research is mixed with regard to the effects of marital status on HRV, biomarkers, and physical and psychological health. Donoho and colleagues (2015) did not find significant differences in HF-HRV between married, divorced, widowed, and never married participants; however, they found that continuously married participants and participants who reported increased satisfaction with their marriage over time had higher HF-HRV than remarried participants and participants who reported increased marital strain. In patients with suspected coronary artery disease, unmarried patients had significantly lower HRV than married patients (Randall et al., 2009). Thus, martial status (continuously married, remarried, never married, divorced, and widowed) was included as a potential predictor of HRV. Marital status has been included as a control variable for IL-6 (e.g., Friedman et al., 2007), fibrinogen (e.g., Engstrom et al., 2006), and CRP (e.g., Donoho et al., 2015) in previous studies. Marital status has also been found to impact subjective health ratings, especially for men, as married men report significantly better physical health than unmarried men (Finkel et al., 2016). Marital status appears to impact psychological health, as happily married individuals tend to have better mental health than unhappy married individuals and single individuals (e.g., Holt-Lunstad et al., 2008). Thus, marital status was included as a potential covariate predicting HRV, biomarkers, psychological and physical health. In the current investigation, marital status did not remain a significant covariate in any model.

Previous studies have found socioeconomic status (SES), especially perceived SES also referred to as subjective social status, significantly related to outcomes. In prior research, low

SES related to higher fibrinogen and CRP (e.g., Jousilahti et al., 2003), higher levels of IL-6 (Gruenewald et al., 2009), and poorer self-rated physical and mental health (e.g., Elliot & Chapman, 2016; Callan et al., 2015). In line with previous studies (Zilioli et al., 2017; Gruenewald et al., 2012), I computed an SES index score based on: educational attainment 1 = no school/some grade school, 5 = high school degree, 9 = 4-year college degree/B.A., 12 = advanced graduate/professional degree), evaluation of current financial situation (11-point Likert scale from "Worst" to "Best"), difficulty in paying monthly bills (where 1 = very difficult, 2 = somewhat difficult, 3 = not very difficult, 4 = not at all difficult), availability of money to meet basic needs (1 = not enough, 2 = just enough, 3 = more than enough), and annual wage from the last calendar year (ranging from 1 = less than $0 to 46 = $500,000–$999,999). Scores from these scales were standardized and summed into a composite with higher scores indicating higher SES. In Study 1a, SES significantly predicted subjective physical health such that higher SES predicted better health ratings, and in Study 1b, higher SES predicted better psychological health and lower Il-6 (see Tables 10 and 11 for results).

There are also numerous health factors that can influence HRV and biomarkers. Based on Laborde and colleagues' (2017) recommendations for measuring HRV in psychophysiological research, a number of health covariates were included based on their relationships with cardiac regulation. Covariates related to medical conditions and treatments were added followed by other health lifestyle factors. Medical conditions and treatments covariates included: the presence of medical conditions including stroke, hypertension, heart disease, hypercholesterolemia, diabetes or hyperglycemia (reviewed in Thayer & Lane, 2007), use of medications affecting parasympathetic activity and inflammation (e.g., antihypertensive medications, blood thinners, statins, steroids, antipsychotics, antidepressants, hormone replacements and hormonal

contraceptives; Lampert et al., 2008; Licht et al., 2008, 2009; Rottenberg, 2007; Cooper et al., 2015; Strohacker et al., 2013). Additionally, body mass index (BMI), smoking (coded as: current smoker, former smoker, never a smoker; Sloan et al., 2017), habitual levels of alcohol consumption (Quintana et al., 2013), and low levels of physical activity (categorized as a dichotomous variable indicating whether or not the participant engaged in at least 20 minutes of exercise at least 3 times per week (Sloan et al., 2017) as well as menstrual status (pre or post-menopausal; Sloan et al., 2017; Cooper et al., 2015) were examined.

In Study 1a, psychotherapeutic agents, cardiovascular agents, hormones or hormone modifiers, smoking status and BMI were significant covariates. Psychotherapeutic agents predicted HRV, IL-6, CRP, and psychological health such that participants taking these drugs reported worse psychological health and had lower HRV and higher inflammatory levels. Cardiovascular agents predicted Il-6 and subjective physical health such that participants taking cardiovascular agents had higher IL-6 and reported worse subjective physical health. Hormones or hormone modifiers predicted CRP such that participants taking hormones or hormone modifiers had higher levels of CRP but reported better subjective physical health. Smoking status predicted Il-6, psychological and subjective physical health such that current smokers reported worse psychological and physical health and higher levels of IL-6 than former smokers or participants who never smoked. BMI predicted HRV, IL-6, CRP, Fibrinogen, and subjective physical health such that higher BMI was associated with lower HRV, worse subjective physical health, and higher levels of inflammatory markers (see Table 10 for results).

In Study 1b, prescription psychotherapeutic agents, hormones, and BMI were significant covariates. Participants taking prescription psychotherapeutic agents had lower HRV and reported worse psychological health than those not taking these drugs. Participants taking

hormones had higher HRV. Higher BMI predicted worse psychological health and higher levels of all three inflammatory markers (see Table 11 for results).

Age was related to IU1; however, when added to the model, age worsened model fit and did not change results so it was not included. Age was the only covariate significantly related to purpose (higher purpose associated with older age) and was included in all models that included purpose.

Study 1a: Direct effects *(see Table 7 for model fit statistics and Table 10 for results)*

Hypothesis 1: IU will significantly predict GU such that participants with higher levels of IU will have lower resting HRV than those with lower levels of IU. The model was saturated, thus traditional model fit statistics are not interpretable (n = 798). The hypothesized direct paths from each IU item to HRV were not significant; however, age, BMI, and psychotherapeutic drugs were significant predictors of HRV (see Table 10).

Hypothesis 2: IU will significantly predict various indicators of physical and psychological health such that participants with higher levels of IU will have significantly higher levels of inflammatory markers and worse psychological health than those with lower levels of IU. Indices indicated adequate overall fit between the hypothesized multivariate model and the observed data (χ^2 [70, n = 832] = 172.55, $p < .001$; CFI = .93, TLI = .89, RMSEA = .04 (.03, .05), SRMR = .10). The hypothesized direct effects from IU to Psychological Distress were significant and in the expected direction such that higher levels of IU predicted more symptoms of psychological distress. Contrary to hypotheses, the direct effect of IU1 on CRP was significant such that higher scores on IU were associated with lower levels of CRP. Direct effects from IU to IL-6 and fibrinogen were not significant (see Table 10).

Hypothesis 3: GU will predict various indicators of physical and psychological health such that participants with lower resting HRV will have significantly higher levels of inflammatory markers, worse subjective physical health, and worse psychological health than those with higher resting HRV. Indices indicated adequate overall fit between the hypothesized multivariate model and the observed data (χ^2 [76, n = 839] = 188.52, p <.001; CFI = .93, TLI = .89, RMSEA = .04 (.03, .05), SRMR = .11). The hypothesized direct effects from HRV to inflammatory markers were significant and in the expected direction such that higher HRV predicted lower levels of IL-6, CRP, and Fibrinogen. The hypothesized direct effect from HRV to Psychological Distress was also significant and in the expected direction such that higher HRV predicted better psychological health. The hypothesized direct effect from HRV to self-rated physical health was non-significant. See Table 10 for estimates and confidence intervals.

Hypothesis 4: Meaning in Life (MIL) variables will significantly predict outcomes such that participants with higher levels of MIL will have significantly lower levels of inflammatory markers, better subjective physical health, and better psychological health than those with low levels of MIL. Indices indicated adequate overall fit between the hypothesized multivariate model and the observed data (χ^2 [91, n =839] = 274.79, p <.001; CFI = .90, TLI = .84, RMSEA = .05 (.04, .06), SRMR =.11). The hypothesized direct effects from both MIL variables (Coherence and Purpose) to Psychological Distress and Subjective Physical Health were significant and in the expected direction, such that higher levels of MIL predicted lower Psychological Distress and better reported health (see Table 10). All direct relations between MIL variables and inflammatory markers were non-significant.

Study 1a: Indirect effects *(see Table 7 for model fit statistics and Table 10 for results)*

To test for mediation, hypothesized indirect effects were incorporated into the model. Mediation occurs when the effect of the independent variable on the dependent variable is transmitted by a mediator (Preacher et al., 2007, p. 186). Temporal mediation can be conducted with longitudinal data, and the assumption is that the independent variable caused the mediator which caused the outcomes and that the relationships cannot be reversed (Winer et al., 2016, p. 948). The path between independent variables and the mediator are labeled $a_{1\text{-}2}$, the paths between the mediator and outcomes are labeled $b_{1\text{-}4}$ and the paths between the independent variable and outcome are $c_{1\text{-}10}$ (see Figure 1). In this study, GU (as indicated by HRV) was hypothesized to mediate the relationship between IU and health outcomes.

The distribution of the product of the coefficients (i.e., a_1b_1) is the most accurate way to test for mediation or indirect effects (Preacher et al., 2007). Further, it is necessary to use asymmetrical confidence intervals to test for statistical significance. The reason for this is that an assumption for mediation analyses is that the product of a_1b_1 is normally distributed; however, this assumption is often violated. With a large sample, the product a_1b_1 is likely to produce a leptokurtotic curve, increasing the risk of making a Type I error (Preacher et al., 2007). Based on results of preliminary analyses, all transformed variables can be treated as normally distributed, thus bias-corrected bootstrapped confidence intervals estimated based on 10,000 bootstrapped samples provides a powerful test of mediation that reduces the likelihood of making a Type I error (Fritz & MacKinnon, 2007). 95% bias-corrected bootstrapped confidence intervals that do not contain zero indicate significant indirect effects.

Hypothesis 5: GU will significantly mediate the relationship between IU and outcomes such that the effects of high IU are transmitted via low HRV (GU) resulting in significantly higher levels of inflammatory markers and worse psychological health.

Traditional fit statistics were not available for this model. All hypothesized indirect effects were non-significant such that HRV did not mediate relations between IU and Psychological Distress or inflammatory markers. All total effects of IU and HRV in predicting the Psychological Distress and Subjective Physical Health outcomes were significant. The total effect of IU1 through HRV predicting CRP was also significant (see Table 10).

Study 1a: Moderation effects (see Table 7 for model fit statistics and Table 10 for results)

Next, hypothesized moderators (Coherence and Purpose) were incorporated into the structural model to test for moderation of the relationship between IU and GU. Moderation occurs when a variable affects the direction and/or strength of the relationship between two other variables. Moderation effects were entered into the model as interaction terms between IU and Coherence and IU and Purpose (Preacher, et al., 2007) and bootstrapped confidence intervals were examined such that 95% confidence intervals that did not contain zero indicate significant moderation. Simple slope tests were conducted at values of -2 (low), 0 (medium), and 2 (high) of the moderators, coherence and purpose.

Hypothesis 6: MIL will moderate the effects of IU on GU such that participants with high levels of coherence or purpose will be protected from the effects of IU on GU. Of particular interest, participants with high levels of IU who also report high levels of coherence or purpose will have higher HRV than participants with high levels of IU who report low levels of MIL. The model was saturated, thus traditional model fit statistics are not interpretable. One of the hypothesized moderation effects was significant. IU2xCoherence predicted HRV such that of participants who report high IU, those with high coherence have higher HRV than those with low coherence. On the other hand, of participants who report low IU, those with low coherence have higher HRV than those high in coherence (see Figure 5).

Simple slopes were calculated in Mplus and the simple slope for IU2xLowCoherence was significant (β = -.11 [-.23, -.02]) and the simple slope for IU2xHighCoherence was significance (β = .08 [.002, .17]). As expected, at high levels of IU, participants high in coherence have significantly higher HRV than those low in coherence. At low levels of IU, participants with low levels of coherence have higher HRV than participants with high coherence.

None of the hypothesized moderation effects were significant for purpose; however, the interaction between IU1xpurpose approached significance in predicting HRV in the direction expected, where high purpose is protective for high IU participants (see Figure 6). The simple effect of IU1(10A) on HRV for people high in purpose is significant such that high IU participants who report high levels of purpose have higher HRV than high IU participants with low or medium purpose scores, whereas low purpose does not appear to affect the relation between IU and HRV in this sample (see Table 10).

Interestingly, when both moderators were incorporated into a single model to test competitive moderation effects, only the simple effect of high purpose remained significant (see Table 10).

Study 1a: Moderated mediation effects (see Table 7 for model fit statistics and Table 10 for results)

To test hypotheses 7 and 8, a moderated mediation model was tested with coherence and purpose as moderators of the IU-GU path and GU as a mediator between IU and physical and psychological health outcomes. The same processes described above were followed such that interaction terms were included to test moderation effects and 95% bias-corrected bootstrapped confidence intervals were examined to determine the significance of conditional indirect effects. Moderated mediation results indicate that if a moderator has a significant effect, then the

mediation process between IU-GU-outcomes differs for individuals based on their levels of the moderators (coherence and/or purpose).

Hypothesis 7 & 8: Participants who are low IU with high MIL will have the highest HRV and best physical and psychological health, whereas participants high in IU with low MIL will have the lowest HRV and worst health. MIL will moderate the effects of IU on GU such that participants with high levels of coherence, purpose, and/or significance will be protected from the effects of IU on GU, which then protect against negative health outcomes. Of particular interest, participants with high levels of IU who also report high levels of coherence, purpose and/or significance will be have higher HRV and will report better psychological and physical health than participants with high levels of IU who report low levels of MIL. Traditional fit statistics were not available for these models. For the coherence moderation model, one of the moderation effects was significant (IU2 (MMr) x Coherence). As described above, IU2xCoherence predicted HRV such that of participants who report high intolerance of uncertainty (IU2), those with high coherence have higher HRV than those with low coherence (see Figure 5). None of the moderated mediation effects were significant; however, all total effects for X1 and X2 were significant for the Psychological and Subjective Physical Health outcomes and total effects of X1 were significant for CRP (see Table 10).

For the model with purpose as a moderator, none of the predicted indirect effects were significant; however, the moderating effect of IU1xPurpose on HRV approached significance. All total effects for X1 and X2 were significant for the Psychological and Subjective Physical Health outcomes and total effects of X1 were significant for CRP (see Table 10). When both

moderators were incorporated into a single model to test competitive moderation effects as only the simple effect of purpose remained significant.

Study 1b: Direct effects (see Table 8 for model fit statistics and Table 11 for results)

Direct and indirect effects identified in hypotheses were tested as outlined in the analysis plan. Potential covariates identified in the analysis plan were added to each model, and non-significant covariates were eliminated and models were re-run until only significant covariates remained. Covariance paths were added between variables correlated at $r = .3$ or greater (e.g., covariance paths between biomarkers, see Figure 2). Results for each hypothesis are presented below.

Hypothesis 1: IU will significantly predict GU such that participants with higher levels of IU will have lower resting HRV than those with lower levels of IU. The model was saturated, thus traditional model fit statistics are not interpretable. The hypothesized direct paths from each IU item to HRV were not significant; however, age, sex, race, psychotherapeutic drugs, and hormones were significant predictors of HRV (see Table 11).

Hypothesis 2: IU will significantly predict various indicators of physical and psychological health such that participants with higher levels of IU will have significantly higher levels of inflammatory markers and worse psychological health than those with lower levels of IU. Indices indicated excellent overall fit between the hypothesized multivariate model and the observed data (χ^2 [46, $N = 645$] = 129.59, $p < .001$; CFI = .97, TLI = .94, RMSEA = .05 (.04, .06), SRMR =.04). The hypothesized direct effects from IU to Psychological Distress were significant and in the expected direction such that higher levels of IU predicted more symptoms of psychological distress. However, direct effects from IU to inflammatory markers (IL-6, CRP, and Fibrinogen) were not significant (see Table 11).

Hypothesis 3: GU will predict various indicators of physical and psychological health such that participants with lower resting HRV will have significantly higher levels of inflammatory markers, worse subjective physical health, and worse psychological health than those with higher resting HRV. Indices indicated excellent overall fit between the hypothesized multivariate model and the observed data (χ^2 [46, n = 651] = 122.81, p <.001; CFI = .97, TLI = .95, RMSEA = .05 (.04, .06), SRMR = .04). The hypothesized direct effects from HRV to inflammatory markers were significant and in the expected direction such that higher HRV predicted lower levels of IL-6, CRP, and Fibrinogen. The hypothesized direct effect from HRV to Psychological Distress was non-significant (see Table 11).

Hypothesis 4: Meaning in Life (MIL) variables will significantly predict outcomes such that participants with higher levels of MIL will have significantly lower levels of inflammatory markers, better subjective physical health, and better psychological health than those with low levels of MIL. Indices indicated excellent overall fit between the hypothesized multivariate model and the observed data (χ^2 [50, n = 651] = 149.34, p <.001; CFI = .96, TLI = .94, RMSEA = .06 (.05, .07), SRMR = .04). The hypothesized direct effects from all 3 MIL variables (Coherence, Purpose, and Significance) to Psychological Distress were significant and in the expected direction, such that higher levels of MIL predicted lower Psychological Distress. Purpose significantly predicted levels of IL-6 and CRP such that higher purpose predicted lower levels of these two inflammatory markers. Significance also predicted levels of CRP as expected such that higher levels of significance was associated with lower CRP. Coherence significantly predicted levels of IL-6; however, in contrast to the hypothesis, higher levels of coherence related to higher levels of IL-6. All other direct relations between MIL variables and inflammatory markers were non-significant (see Table 11).

Hypothesis 5: GU will significantly mediate the relationship between IU and outcomes such that the effects of high IU are transmitted via low HRV (GU) resulting in significantly higher levels of inflammatory markers and worse psychological health. Indices indicated good overall fit between the hypothesized multivariate model and the observed data (χ^2 [55, n = 645] = 215.31, p <.001; CFI = .94, TLI = .90, RMSEA = .07 (.06, .08), SRMR = .06). All hypothesized indirect effects were non-significant such that HRV did not mediate relations between IU and Psychological Distress or inflammatory markers. Total effects of IU and HRV in predicting the Psychological Distress outcome were significant (see Table 11).

Study 1b: Moderation effects (see Table 8 for model fit statistics and Table 11 for results)

Next, hypothesized moderators (Coherence, Purpose, and Significance) were incorporated into the structural model to test for moderation of the relationship between IU and GU. Moderation occurs when a variable affects the direction and/or strength of the relationship between two other variables. Moderation effects were entered into the model as interaction terms between IU and Coherence and IU and Purpose (Preacher, et al., 2007) and bootstrapped confidence intervals were examined such that 95% confidence intervals that do not contain zero were interpreted as significant moderation.

Hypothesis 6: MIL will moderate the effects of IU on GU such that participants with high levels of coherence, purpose, and/or significance will be protected from the effects of IU on GU. Of particular interest, participants with high levels of IU who also report high levels of coherence, purpose, or significance will have higher HRV than participants with high levels of IU who report low levels of MIL. The model was saturated, thus traditional model fit statistics are not interpretable. None of the hypothesized moderation effects were

significant, thus coherence, purpose, and significance do not significantly moderate the relation between IU and HRV (see Table 11).

Study 1b: Moderated mediation effects (see Table 8 for model fit statistics and Table 11 for results)

To test hypotheses 7 and 8, a moderated mediation model was tested with coherence, purpose, and significance as moderators of the IU-GU path and GU as a mediator between IU and physical and psychological health outcomes. The same processes described above were followed such that interaction terms were included to test moderation effects and 95% bias-corrected bootstrapped confidence intervals were examined to determine the significance of conditional indirect effects. Moderated mediation results indicate that if a moderator has a significant effect, then the mediation process between IU-GU-outcomes differs for individuals based on their levels of the moderators.

Hypothesis 7 & 8: Participants who are low IU with high MIL will have the highest HRV and best physical and psychological health, whereas participants high in IU with low MIL will have the lowest HRV and worst health. MIL will moderate the effects of IU on GU such that participants with high levels of coherence, purpose, and/or significance will be protected from the effects of IU on GU, which then protect against negative health outcomes. Of particular interest, participants with high levels of IU who also report high levels of coherence, purpose and/or significance will be have higher HRV and will report better psychological and physical health than participants with high levels of IU who report low levels of MIL. Hypotheses 7 and 8 were tested in the full hypothesized model (see Figure 2). Each MIL variable was examined individually as a moderator.

For the coherence moderation model, indices indicated excellent overall fit

between the hypothesized multivariate model and the observed data (χ^2 [77, n = 652] = 233.99, p <.001; CFI = .94, TLI = .91, RMSEA = .06 (.05, .06), SRMR = .06). None of the predicted indirect effects or moderation effects were significant. For the purpose moderation model, indices indicated adequate overall fit between the hypothesized multivariate model and the observed data (χ^2 [70, n = 649] = 305.47, p <.001; CFI = 0.92, TLI = .87, RMSEA = .07 (.06, .08), SRMR = .07). None of the predicted indirect effects or moderation effects were significant. For the significance moderation model, indices indicated adequate overall fit between the hypothesized multivariate model and the observed data (χ^2 [70, n = 648] = 239.93, p <.001; CFI = .94, TLI = .90, RMSEA = .06 (.05, .07), SRMR = .06). None of the predicted indirect effects or moderation effects were significant (see Table 11).

Because none of the moderation or moderated meditation effects were significant, multiple moderators were not incorporated into a single model to test competitive moderation effects.

Study 2

Preliminary analyses and analysis plan

In addition to SEM, multilevel structural equation models (MSEMs) were run to test several Study 2 hypotheses. Multilevel analysis is necessary when data is nested within persons and/or occasions. MSEM is advantageous in comparison to other multilevel methods because it partitions between- and within-person variance of observed variables into two variables that are not correlated with each other (e.g., Preacher et al., 2010). Also, MSEM centers within-person variables around participants' mean values on the variable(s). MSEM allows paths to have random intercepts and slopes, and Bayesian Credible Intervals can be computed to assess for the

significance of direct, indirect, and moderation effects in nested data (e.g., Muthén & Asparouhov, 2012).

To ensure that MSEM was appropriate for testing daily variables included in Study 2 hypotheses 9-15, intraclass correlations (ICC) were calculated. ICC provides an estimate of the percentage of variance within-persons. ICC values greater than .05 indicate the data is hierarchical, necessitating the use of multilevel analysis (LeBreton & Senter, 2008). In this study, all hypothesized within-person variables had ICC values greater than .05 (ICCs: Daily meaning = .42; Daily purpose = .42; Daily uncertainty = .41; Daily Anxiety = .70, Daily NA = .70; Daily physical symptoms = .39).

Additionally, outliers for each individual and outliers for the sample as a whole were inspected and normality of each variable was examined. No outliers were detected and all variables met normality expectations except daily somatic symptoms which was highly kurtotic. Because daily somatic symptoms was a predictor in all models, kurtosis did not need to be corrected, thus the variable was not transformed. Correlations and descriptive statistics are reported in Tables 5 and 6.

All models were estimated in MPlus version 7.4 (Muthen & Muthen, 1998-2012) using ML estimation. Raw scores were standardized but were not centered as grand-mean centering does not affect results in cross-level models (Preacher et al., 2016).

Path Analysis Results

Part 1: Between-Persons (Trait-Level Only) Model Results

To test hypotheses 1- 8 (see Figure 7), SEM path analysis was utilized to investigate relationships at the between-person level, or level 2. Hu and Bentler's (1999) model fit statistics described above are reported for each model (see Table 9). Direct, indirect, mediation,

moderation, and mediated moderation effects were tested in the same manner as in Study 1 (e.g., using ML estimation with 10,000 bootstrapped samples and bias-corrected bootstrapped intervals). For these level 2 between-persons analyses, the predictor, IU, was measured using the IUS-12 scale. Because there is a known factor structure for the IUS-12 (2 factors), a CFA was conducted to test the fit of the two-factor model as predictive of 1 latent factor (IU). Model fit statistics indicate good fit of a single latent factor (RMSEA < .001, CFI = .99, TLI = .99, SRMR < .001).

The moderator, MIL, was measured with the Three Dimensional Meaning scale that assesses each component of MIL (coherence (α = .83), purpose (α = .87), and significance (α = .85). The mediator, GU, was measured using the RMSSD calculation of baseline HRV. Due to the normality of the data in this study, HRV was not transformed as it was in Study 1. The physical health outcome was assessed via a summed score on the physical dimension of the SF-36 (α = .83). Psychological health was assessed via a summed score on the psychological dimension of the SF-36 (α = .88) and the CES-D (α = .90). Because both the SF-36 and CES-D assess depressive symptoms, these outcomes were modeled with a covariance path (see Figure 7).

Direct and indirect effects identified in hypotheses were tested as outlined in the analysis plan. Potential covariates were added to each model, and non-significant covariates were eliminated and models were re-run until only significant covariates remained. Results for each hypothesis are presented below.

Hypothesis 1: Trait IU will significantly predict GU such that people with higher levels of IU will have lower resting HRV at baseline than participants with low IU. The model was saturated, thus traditional model fit statistics were not available. The hypothesized

direct path from IU to HRV was not significant; however, age was a significant predictor of HRV (see Table 12).

Hypothesis 2: Trait IU will significantly predict various indicators of physical and psychological health such that people with high levels of IU will report significantly worse physical and psychological health than participants with low IU. Indices indicated excellent model fit (χ^2 [5, n = 62] = 5.62, p = .35; CFI = .99, TLI = .99, RMSEA = .05 (.00 , .19), SRMR = .05). The hypothesized direct effects from IU to Psychological health and depressive symptoms were significant and in the expected direction such that higher levels of IU predicted worse mental health. The direct effect from IU to physical health approached significance. Age, total number of chronic conditions, and income were significant covariates (see Table 12).

Hypothesis 3: GU will predict various indicators of physical and psychological health such that participants with lower resting HRV at baseline will report significantly worse physical and psychological health than participants with higher resting HRV. Indices indicated excellent overall fit between the hypothesized multivariate model and the observed data (χ^2 [8, n = 62] = 11.08, p = .20; CFI = .98, TLI = .95, RMSEA = .08 (.00, .18), SRMR = .083). The hypothesized direct effects from HRV to physical and psychological health were not significant; however, the direct effect from HRV to CESD (depression) approached significance in the expected direction such that lower HRV predicted more depressive symptomology. Age and income were significant covariates included in the model (see Table 12).

Hypothesis 4: Trait MIL will significantly predict various indicators of physical and psychological health such that participants with higher levels of MIL will report significantly better physical and psychological health than participants with low MIL. Indices indicated excellent overall fit between the hypothesized multivariate model and the

observed data (χ^2 [25, n = 62] = 26.88, p = .36; CFI = .99, TLI = .98, RMSEA = .04 (.00, .11), SRMR = .08). The hypothesized direct effects from coherence to physical health, psychological health, and depression were significant and in the expected directions, such that higher levels of coherence predicted better mental and physical health. Significance and purpose approached significance in predicting depression and were not significant predictors of physical or mental health. Age, number of chronic medical conditions, income were significant covariates (see Table 12). Alcohol use and gender were significant covariates in predicting coherence and purpose, respectively. Endorsement of alcohol use ("Do you ever drink alcohol?") was positively related to coherence and being female was positively related to purpose.

Each meaning variable was also tested separately. For the coherence only model, indices indicated excellent overall fit between the hypothesized multivariate model and the observed data (χ^2 [6, n = 62] = 8.45, p = .21; CFI = .98, TLI = .95, RMSEA = .08 (.00, .20), SRMR = .07). The hypothesized direct effects from coherence to physical health, psychological health, and depression were significant and in the expected directions, such that higher levels of coherence predicted better mental and physical health and, in this model, alcohol use was no longer a significant predictor of coherence (see Table 12).

For the purpose only model, indices indicated very good overall fit between the hypothesized multivariate model and the observed data (χ^2 [6, n = 62] = 8.79, p = .19; CFI = .98, TLI = .94, RMSEA = .09 (.00, .21), SRMR = .08). The hypothesized direct effects from purpose to physical health, psychological health, and depression remained non-significant, but the direction of all relationships aligned with hypotheses (see Table 12).

For the significance only model, indices indicated good overall fit between the hypothesized multivariate model and the observed data (χ^2 [6, n = 62] = 10.06, p = .12; CFI =

.97, TLI = .92, RMSEA = .10 (.00, .21), SRMR = .08). The hypothesized direct effects from significance to physical health remained non-significant; however, the direct effects from significance to psychological health and depression became significant in expected directions such that higher levels of significance predicted better mental health and lower levels of depression (see Table 12).

Hypothesis 5: GU will significantly mediate the relationship between trait IU and outcomes such that the effects of high IU will be transmitted via low resting HRV to significantly worse reported physical and psychological health. Indices indicated excellent overall fit between the hypothesized multivariate model and the observed data (χ^2 [8, n = 62] = 8.92, p = .35; CFI = .99, TLI = .98, RMSEA = .04 (.00, .16), SRMR = .06). All hypothesized indirect effects were non-significant such that HRV did not mediate relations between IU and psychological or physical health. Total effects of IU and HRV in predicting psychological health and depression outcomes were significant; total effects for physical health were not significant (see Table 12).

Hypothesis 6: Trait MIL will moderate the effects of IU on GU such that participants with high levels of coherence, purpose, and/or significance will be protected from the effects of IU on GU. Of particular interest, participants with high levels of IU who also report high levels of coherence, purpose, or significance will have higher HRV than participants with high levels of IU who report low levels of MIL. The model was saturated, thus traditional model fit statistics are not interpretable. None of the hypothesized moderation effects were significant, thus coherence, purpose, and significance did not significantly moderate the relation between IU and HRV.

Hypothesis 7 & 8: Participants who are low in trait IU and high in trait MIL will have the highest levels of HRV (GU) at baseline and the best physical and psychological health, whereas participants high in IU with low MIL will have the lowest HRV (GU) at baseline and report the worst health. Trait MIL will moderate the effects of IU on GU such that participants with high levels of coherence, purpose, and/or significance will be protected from the effects of IU on GU, which then protect against negative health outcomes. Of particular interest, participants with high levels of IU who also report high levels of coherence, purpose and/or significance will be have higher HRV and will report better psychological and physical health than participants with high levels of IU who report low levels of MIL. Hypotheses 7 and 8 were tested in the full hypothesized model with IU X each MIL variable included as a moderator. The model fit statistics for this full model indicate a poor fitting model (χ^2 [26, n = 62] = 64.04, p <.001; CFI = .79, TLI = .63, RMSEA = .16 (.11, .21), SRMR = .08). None of the moderation or indirect effects in this model were significant. Thus, separate models were run to test each meaning variable independently. For the coherence model, indices indicated poor overall fit between the hypothesized multivariate model and the observed data (χ^2 [14, n = 62] = 44.40, p = .0001; CFI = .83, TLI = .63, RMSEA = .19 (.13, .26), SRMR = .10). None of the predicted indirect effects or moderation effects were significant. For the purpose model, indices indicated good overall fit between the hypothesized multivariate model and the observed data (χ^2 [12, n = 62] = 15.73, p = .20; CFI = .97, TLI = .94, RMSEA = .07 (.00, .16), SRMR = .07). None of the predicted indirect effects or moderation effects were significant. For the significance model, indices indicated good overall fit between the hypothesized multivariate model and the observed data (χ^2 [16, n = 62] = 16.38, p = .29; CFI =

.98, TLI = .97, RMSEA = .05 (.00, .14), SRMR = .07). None of the predicted indirect effects or moderation effects were significant (see Table 12).

Study 2 Part 2: Between-Persons Cross-Level (Trait and Daily) Model Results

Hypotheses 1-8 replicated Study 1 between-person path analyses. Hypotheses 9 and 10 examined direct effects of trait, or between-subjects, level-2 variables (IU and MIL) on participants' daily experiences (level 1). These cross-level direct effects were tested using MSEM (see Figure 8). Trait values on the level 2 variable (IU or MIL) were regressed on the participant's daily experiences (daily anxiety, daily NA, daily somatic symptoms). The regression paths were estimated as fixed (intercept and slope) across individuals and ML estimation was used. Significance of these direct effects were determined based on p-values less than .05.

Hypothesis 9: Participants with high trait IU will report higher levels of daily anxiety, daily uncertainty, daily negative affect, and daily somatic symptoms than participants low in IU. Indices indicated excellent overall fit between the hypothesized multivariate model and the observed data (χ^2 [1, n = 62] = 1.03, p = .31; CFI = 1.00, TLI = .99, RMSEA = .01, $SRMR_{within}$ = .02; $SRMR_{between}$ = .001). Results largely supported the hypothesis as trait IU significantly predicted daily anxiety (β = .45, p <.001), negative affect (β= .34, p = .002), and uncertainty (β = .48, p <.001) such that higher trait IU predicted more daily anxiety, negative affect, and uncertainty. Trait IU approached significance in predicting daily somatic symptoms (β = .20, p = .10) (see Table 13).

Hypothesis 10: Participants with high trait MIL will report lower levels of daily anxiety, daily uncertainty, daily negative affect, and daily somatic symptoms. Indices indicated excellent overall fit between the hypothesized multivariate model and the observed

data (χ^2 [1, n = 62] = 1.02, p = .31; CFI = 1.00, TLI = .99, RMSEA = .01, $SRMR_{within}$ = .02; $SRMR_{between}$ = .001). Total MIL significantly predicted daily anxiety (β = -.26, p = .002) and daily uncertainty (β = -.19, p = .004) such that higher MIL related to lower levels of daily anxiety and uncertainty. Total MIL approached significance in predicting daily negative affect (β = -.19, p = .07).

Trait coherence, purpose, and significance were also tested, resulting in the same model fit statistics. Trait coherence significantly predicted daily anxiety (β = -.51, p <.001), uncertainty (β = -.46, p <.001), and negative affect (β = -.41, p <.001). Trait purpose did not significantly predict any of the daily variables of interest. Trait significance significantly predicted daily anxiety (β = -.19, p = .04) and daily uncertainty (β = -.17, p = .01) (see Table 13).

Within-Persons Model Results

To test hypothesis 11-12 (see Figure 9), within-person analyses (level 1) were conducted to examine fluctuations within participants across days. All variables were group-mean (within-person) centered based on recommendations from Enders and Tofighi (2007). Daily within-person associations were modeled as random slopes such that they can vary across days and across individuals. Thus, the slope between daily uncertainty and daily anxiety, NA, and somatic symptoms (each tested separately) were allowed to vary across occasions within an individual and across individuals (Rush et al., 2019). Similarly, the slope between daily meaning and daily anxiety, NA, and somatic symptoms (each tested separately) were modeled such that the slope can vary across episodes within an individual and across individuals (Rush et al., 2019). The intercepts were also modeled as random such that the latent values could vary across individuals and days. The indirect effects of level 1 paths of interest were tested via ML estimation and significance was determined based on p <.05.

Hypothesis 11: On days when participants report feeling more than their average level of uncertainty, participants will report higher levels of anxiety, negative affect, and somatic symptoms as compared to days when they report less than their average level of uncertainty. Traditional model fit indices were not available due to the estimation of random effects. Results supported this hypothesis. On days participants reported more than their average level of uncertainty, they reported more somatic symptoms (β = .12[.04, .20], p = .002), more anxiety (β = .22[.13, .30], p <.001), and more negative affect (β = .19[.10, .28], p <.001) (see Table 13).

Hypothesis 12: On days when participants report more than their average level of meaning in life, participants will report lower levels of anxiety, negative affect, and somatic symptoms as compared to days when they report lower than their average levels of MIL. Daily meaning and daily purpose were measured and tested separately. Traditional model fit indices were not available due to the estimation of random effects.

For daily meaning, results supported the hypothesis for daily anxiety and negative affect. On days participants reported more than their average level of meaning, they reported significantly less anxiety (β = -.14[-.23, -.04], p = .004), and negative affect (β = -.16[-.27, -.05], p = .003). Results were the same for daily purpose. Results supported the hypothesis for daily anxiety and negative affect. On days participants reported more than their average level of purpose, they reported significantly less anxiety (β = -.16[-.25, -.06], p = .001), and negative affect (β = -.16[-.25, -.06], p = .001) (see Table 13).

Between- and Within-Persons Model Results

Hypotheses 13-15 (see Figure 10) were tested using the Random Coefficient Prediction (RCP) Method with maximum likelihood estimation (e.g., Preacher et al., 2016). With the RCP

method, a latent variable for the random slope is calculated. RCP methodology allows the slope variable to vary as a function of the predictors while minimizing the slope's residual variance (Preacher et al., 2016). Specifying between- and within-level effects splits the between- and within-level variances such that they are not conflated, resulting in a within-level slope that has only within-level variance and a between-level moderator with only between-level variance (Preacher et al., 2016). Moderation is considered present if the moderator significantly predicts the random slope. RCP is especially useful for testing moderation in cross-level interactions (e.g., between-persons IU or MIL and within-persons slopes between daily variables of interest). For these analyses, a moderator variable was calculating by multiplying MIL by the latent variable, IU. This level-2 (between-persons) interaction and the latent trait IU and MIL variables were tested as predictors of random level 1 slopes between daily uncertainty and anxiety, NA, and somatic symptoms. Additionally, models using coherence, purpose, and significance instead of total MIL were tested. Traditional model fit statistics were not available for this type of analysis.

Hypothesis 13: Trait IU will moderate the relationships between daily experiences of uncertainty and daily anxiety, negative affect, and somatic symptoms such that on days when high IU participants experience high levels of uncertainty, they will experience significantly more anxiety, negative affect, and somatic symptoms than low IU people who report high levels of uncertainty that day. IU significantly predicted the daily relation between uncertainty and negative affect ($\beta = .20$, $p = .01$). Thus, on days when participants experienced uncertainty, high trait IU participants tended to experience more negative affect than low IU participants. In other words, the relationship between daily uncertainty and negative affect is

stronger for high IU than low IU participants such that, for high IU participants, experiencing uncertainty on a particular day tends to exacerbate negative affect.

Results of this model indicate the intercepts of all slopes (within-person relations) were significant. Thus, the average within-person slope or relation between daily uncertainty and NA, anxiety, and somatic symptoms were each significant (see Table 14).

Hypothesis 14: Trait MIL will moderate the relationships between daily experiences of uncertainty and daily anxiety, negative affect, and somatic symptoms such that on days when high MIL people experience high levels of uncertainty, they will experience significantly less anxiety, negative affect, and somatic symptoms than low MIL people who report high levels of uncertainty that day. None of the effects of MIL on daily relations between uncertainty, anxiety, negative affect, or somatic symptoms were significant. MIL was tested as an overall global predictor (total score on MIL) and as each dimension (coherence, purpose, and significance), with no significant results (see Table 14).

Hypothesis 15: There will be significant effects of the interaction between trait MIL and trait IU such that low MIL x High IU participants will experience significantly more daily anxiety, uncertainty, negative affect, and somatic symptoms than high MIL x low IU participants. Results of this model indicate MILxIU significantly moderated the daily relationship between uncertainty and negative affect ($\beta = -.20$, $p = .014$). The interaction was probed by calculating simple slopes using the Aiken and West (1991) method. As hypothesized, the daily relationship between uncertainty and negative affect was significantly stronger for participants low in MIL and high in IU than for high MIL x low IU participants (see Figure 11). Thus, on days when high IU x low MIL participants experienced uncertainty, they experienced more negative affect than participants low in IU with high levels of MIL. Additionally, at high

levels of IU, MIL appears to serve a protective, buffering role such that the relation between daily uncertainty and NA is not as strong for high IU x high MIL participants in comparison to high IU x low MIL participants.

Each component of MIL was then examined separately by multiplying the MIL subscale by the latent IU term to create an interaction. Results indicate IU x Coherence significantly moderated the daily negative affect- daily uncertainty slope ($\beta = -.27$, $p < .001$) and the daily anxiety-daily uncertainty slope ($\beta = -.12$, $p = .035$). These interactions were also probed by calculating simple slopes using the Aiken and West (1991) method. Results aligned with hypotheses such that the daily relationship between uncertainty and negative affect and uncertainty and anxiety were significantly stronger for participants low in coherence and high in IU than for high coherence x low IU participants (see Figures 12 and 13). Thus, on days when high IU x low coherence participants experienced uncertainty, they experienced significantly more negative affect and anxiety than participants low in IU with high levels of coherence. Additionally, at high levels of IU, coherence appears to serve a protective, buffering role such that the relation between daily uncertainty and NA and anxiety are not as strong for high IU x high coherence participants in comparison to high IU x low coherence participants. Results indicate IU x Significance significantly moderated the relation between daily negative affect-daily uncertainty ($\beta = -.20$, $p = .02$) in the same manner as coherence and total MIL (see Figure 14).

Thus, it appears that MIL, and specifically the coherence and significance dimensions of MIL, buffer against the negative emotional effects of experiencing uncertainty for high IU participants. The interaction of IU x purpose did not appear to significantly buffer this

relationship. Further, none of the interactions or main effects significantly moderated the relationships between daily uncertainty and daily somatic symptoms (see Table 14).

CHAPTER 4: DISCUSSION

The main purpose of the current investigation was to examine a theoretical pathway based on the GUTS model (e.g., Brosschot et al., 2016a) by which IU might convey risk for psychological distress and poor physical health via autonomic dysregulation caused by chronic feelings of unsafety. Additionally, based on theory and empirical evidence, dimensions of MIL (coherence, purpose, and significance) were examined as potential safety cues that may buffer against the effects of IU on physiological dysregulation and deleterious health consequences. Study 1 examined this hypothesized process over the course of three to nine years in two large, nationally representative samples of US middle-age and older adults (MIDUS 2, 3 and Refresher). Study 2 examined this process with a convenience sample of young and old adults over the course of 1 week. Study 2 (Part 2) also allowed for examination of within-person fluctuations day-to-day in the constructs of interest, providing a narrower perceptual lens through which to explore this process. The primary hypothesis across all studies was that high IU perpetuates chronic feelings of unsafety which conveys risk for physiological dysregulation and inflammation as well as psychological distress, while high MIL provides people a sense of safety which may protect against the deleterious effects of high IU on physiological regulation, inflammation, and physical and psychological health. Thus, participants who report high IU and low MIL are hypothesized to be at greatest risk for poor health.

Study 1 and Study 2 Part 1

In Study 1 and Study 2 Part I, I examined the same hypothesis in a stepwise manner in three distinct samples. Prior to testing hypotheses, split-sample EFA and CFA analyses were conducted to examine the structure and fit of a latent variable for the psychological distress

outcome in Study 1 (see Figures 3 and 4). In both Studies 1a and 1b, single factor solutions demonstrated excellent fit in EFA and were supported via CFA. Prior to testing Study 2 hypotheses, a CFA was conducted with the IUS-12 scale based on its known factor structure and resulted in excellent fit, confirming the extant factor structure of inhibitory and prospective components of IU (e.g., Carleton et al., 2007). Thus, IU was modeled as a latent variable predictor in all Study 2 models.

Hypothesis testing occurred in a step-wise manner, leading up to testing of the full moderated mediation model. Model fit was examined for each model tested (see Tables 7-9). Several models were just-identified models; these saturated models do not produce model fit statistics, but results can be interpreted. All Study 1 models demonstrated adequate model fit that allowed for interpretation of model results; however, several models had model fit statistics slightly lower than desired. In Study 1a, models for hypotheses 2 and 3 had TLI values of .89, which is slightly below the desired .90. Values above .90 are considered evidence of a good-fitting model, indicating at least 90% of covariation in the data is represented in the hypothesized model. These models also had higher than desired SRMR values of .096 (Hypothesis 2) and .11 (Hypothesis 3). Although Hu and Bentler (1999) do not indicate a cut-off score for SRMR, an SRMR value of zero indicates perfect fit between observed and predicted correlations, thus an SRMR value close to zero is desirable. Study 1a Hypothesis 4 also resulted in an SRMR = .11 and a low TLI score (TLI = .84). Modification indices were not available due to the type of analysis run, thus various manipulations were made (i.e., adding additional correlation paths between potential covariates, adding and removing covariates), resulting in no improvement in TLI or SRMR values. It is possible that a critical variable or path was not included in the model that may explain poor model fit statistics; however, all theoretically plausible covariates and

paths were tested. Thus, results of Study 1a Hypothesis 4 (MIL as a predictor of health outcomes) should be interpreted with caution.

In Study 1b, model fit for Hypothesis 5 (mediation model) was adequate; however, the RMSEA values of .07 was slightly above the recommended cut-off of .06. RMSEA represents the residual difference between the predicted and the observed covariance structure. RMSEA values of less than .06 indicate good fit between the model and observed data (Hu & Bentler, 1999). Due to other model fit statistics being in good to excellent ranges, this model is deemed interpretable.

In Study 2, most models with model fit statistics available demonstrated excellent model fit (Table 9); however, there were a few exceptions. For Hypotheses 3 and 4 (coherence and purpose), RMSEA exceeded the recommended value of .06. However, all other indices suggest good model fit. Model fit indices for Hypothesis 7 and 8 (total MIL and coherence) indicate poor model fit. Modification indices were not available due to analysis type, thus each MIL variable was run separately. Based on the results, it appears that the model with coherence as moderator is contributing to poor overall model fit. Additional correlation paths between potential covariates were tested, significant covariates in the model were removed, and other manipulations were made, resulting in no improvement. It is likely a critical variable or path was not included in the model that may improve model fit; however, all theoretically plausible covariates and paths were tested. The model resulted in no significant outcomes, and results from this model will not be interpreted.

As hypothesis testing was conducted, numerous covariates were retained in each model due to their significant relations with study constructs in previous studied (see Table 2). Several hypothesized demographic variables were retained in models. As expected, age predicted HRV

such that older age was associated with lower HRV (e.g., Umetani et al., 1998), and age significantly predicted levels of most inflammatory markers such that older age was associated with higher levels of inflammation (e.g., Chung et al., 2009). Age was significantly related to psychological health in that older adults in Study 1 reported better psychological health than younger adults. Although this may sound surprising, in these studies all participants were middle to older age adults, and researchers have found older adults report greater psychological well-being than middle-age adults (e.g., Steger et al., 2009). Relatedly, age was positively, significantly associated with purpose. Sex was also a significant predictor of several outcomes. In Study 1a, women reported significantly worse psychological health and had higher levels of CRP and fibrinogen. In Study 1b, women again had higher levels of CRP and fibrinogen and had higher HRV. Previous studies have found higher CRP (e.g., Corcoran et al., 2010; Prather et al., 2013) and fibrinogen (Okwuosa et al., 2013) in women than men. Similarly, results of a meta-analysis indicate women tend to show greater vagal activity than men (Koenig & Thayer, 2016). Britton and colleagues (2007) examined longitudinal changes in middle age and older men and women's HRV and found that men experienced reductions in HRV over time whereas women showed increases in HRV, with women's average HRV similar to men's. These results align with results of the current investigation. Similarly, in accordance with previous studies, race significantly predicted levels of fibrinogen (Study 1a) and IL-6 (Study 1b) such that African American and Native American participants had significantly higher levels of these inflammatory markers than White and Asian participants (e.g., Hill et al., 2015). Finally, SES was retained in models in both Study 1a and b. In Study 1a, SES significantly predicted subjective physical health such that higher SES predicted better health ratings, and in Study 1b, higher SES predicted better psychological health and lower Il-6. These results also align with

those of previous studies (e.g., Gruenewald et al., 2009; Elliot & Chapman, 2016; Callan et al., 2015).

In addition to demographic covariates, numerous health covariates were retained (see Table 2). In Study 1a, several types of prescription drugs were related to study variables in the same manner as in previous studies (e.g., Lampert et al., 2008; Licht et al., 2008, 2009; Rottenberg, 2007; Cooper et al., 2015; Strohacker et al., 2013). Participants who reported taking psychotherapeutic agents at the time of biomarker collection reported worse psychological health and had lower HRV and higher inflammatory levels (IL-6 and CRP) as compared to participants not taking psychotherapeutic agents. Participants who reported taking cardiovascular agents at the time of biomarker collection had significantly higher IL-6 and reported worse subjective physical health as compared to participants not taking cardiovascular agents. Participants who reported taking hormones or hormone modifiers at the time of biomarker collection reported better subjective physical health but higher CRP levels than participants not taking hormones. In Study 1b, participants taking prescription psychotherapeutic agents had lower HRV and reported worse psychological health than those not taking these drugs. Participants taking hormones or hormones modifiers had higher HRV than participants not taking hormones. These results align with results of prior research (e.g., Cooper et al., 2015).

In Study 1a, participants' smoking status predicted levels of Il-6, psychological distress, and subjective physical health such that current smokers reported worse psychological and physical health and higher levels of IL-6 than former smokers or participants who had never smoked. This aligns with prior studies that have found significantly higher IL-6 levels in current smokers as compared to former and non-smokers (e.g., Levitzky et al., 2008) as well as a vast body of research linking smoking with psychological disorders and poor overall physical health

(e.g., Choi & DiNitto, 2011). Additionally, BMI was strongly related to several model variables in both Study 1a and b. As expected, in Study 1a, higher BMI was associated with lower HRV (e.g., Koenig et al., 2014), worse subjective physical health, and higher levels of all measured inflammatory markers (e.g., Howren et al., 2009). In Study 1b, higher BMI predicted worse psychological health and higher levels of all three inflammatory markers.

In Study 2, age, income, and total number of chronic conditions were included in models as significant covariates. As in Study 1, older age related to lower HRV and better psychological health. Higher income was related to significantly lower levels of depressive symptoms. As expected, participants who reported more chronic conditions reported significantly worse subjective physical health as compared to participants with fewer chronic conditions.

Because previous studies have been conducted with and without covariates, all models were run both with significant covariates and without, and results of the effects of interest remained the same. Thus, significant covariates were retained in all models.

Direct effects

Results of path models were mixed, as some produced significant results as expected and others did not. Generally, hypothesized relations among psychosocial variables (IU, MIL, and psychological distress) and among physical health variables (HRV, inflammatory markers, subjective physical health) were significant, whereas results of hypotheses examining links between psychosocial predictors (IU and MIL) and physical health variables were mixed (HRV, inflammatory markers, subjective physical health).

Psychosocial variables. As hypothesized, in Studies 1 and 2, direct effects from IU to psychological health outcomes were significant. High IU was associated with increased psychological distress; participants who reported being highly intolerant of uncertainty reported

significantly more symptoms of depression, anxiety, and negative affect than those low in IU. These results align with previous studies that have found moderate to strong associations between IU, anxiety, and depressive symptoms (e.g., Gorka et al., 2017; McEvoy & Mahoney, 2011, 2012). Similarly, in Study 1, direct effects from dimensions of MIL (coherence, purpose, and significance) to psychological health were significant such that high MIL was associated with lower levels of psychological distress. Thus, participants who reported high levels of coherence, purpose, and significance (MIL) tended to report significantly fewer symptoms of psychological distress than participants who reported low levels of MIL. This, too, aligns with results of previous studies linking MIL to psychological health and well-being (e.g., Zika et al., 1982; Kashdan & McKnight, 2013; Mascaro et al., 2008). Surprisingly, in Study 2, purpose did not significantly predict psychological health or depression. Previous studies linking MIL to psychological well-being have primarily focused on purpose as compared to coherence and significance, thus it is especially surprising to find non-significant associations between purpose and psychological well-being. Purpose was measured using a new scale, the Three Dimensional Meaning Scale (Martela & Steger, 2018), thus it is possible that this measure, although conceptually similar to extant measures, does not assess purpose in the same way as prior measures. It is also possible that because Study 2 participants were young and older adults who volunteered to participate in a research study that required multiple in-person visits, they were disproportionally unemployed (41.9% total unemployed; 19% young adults unemployed), and thus may have felt a sense of lacking purpose or lacking engagement in purposeful pursuits at the time of the study.

Physical health variables. Also, as expected, direct effects from HRV to inflammatory markers were significant and in the expected direction such that higher HRV predicted lower

levels of IL-6, CRP, and Fibrinogen in Study 1. When the body is under vagal modulation, as indicated by higher HRV, the vagus nerve sends signals to the brain to release chemicals that inhibit the production of pro-inflammatory cytokines, thus vagal modulation is associated with the circulation of fewer pro-inflammatory cytokines and thus lower levels of IL-6, CRP, and fibrinogen (e.g., Marsland et al., 2007; Janszky et al., 2004; Thayer et al., 2009). When HRV is low, systemic inflammation escalates, as evidenced by increased presence of inflammatory markers in the blood stream (e.g., Kiecolt-Glaser et al., 2002). Although expected associations between HRV and biomarkers were found, hypothesized relations between HRV and subjective physical health were not. This may be due, at least in part, to the primarily older adult samples and the many additional factors that may influence older adults' perceptions of their physical health. Although there are a few studies suggesting people with low HRV tend to rate their physical health worse than those with high HRV (Jarczok et al., 2014), research is not as robust in linking HRV to subjective physical health as in linking HRV to biomarkers.

Psychosocial and physical health variables. Associations between psychosocial (IU and MIL) and physical health variables (HRV, inflammatory markers, subjective physical health) were less consistent and robust. First, IU did not significantly predict HRV in Studies 1 or 2. Although I did not find any prior studies that explicitly measured the association between IU and baseline HRV, previous research suggests low HRV is associated with high levels of trait anxiety (e.g., Bleil et al., 2008; Miu et al., 2009), and depression (e.g., Koenig et al., 2016), which are related to IU. Two studies linked IU with greater decreases in HF-HRV in high worriers (e.g., Deschenes et al., 2016; Ottavani et al., 2016); however, these studies provoked worry, thus examining short-term, state changes in HRV after worry-inducing tasks rather than examining baseline levels of HRV. Perhaps aligning most closely with results of the current study,

Thibodeau and colleagues (2013) found no significant correlation between heart rate and IU. Thus, it could be that IU relates to short-term changes in HRV (i.e. after worry-inducing tasks; Deschenes et al., 2016) but that at the trait level, IU may not be associated with baseline HR or HRV. It is also possible that trait IU is associated with only certain indices of baseline HRV (i.e., HF-HRV). Beauchaine and Thayer (2014) refer to HF-HRV as a "transdiagnostic biomarker for psychopathology" and low HF-HRV is linked to symptoms of anxiety (e.g., Kemp et al., 2014) and high perceived chronic stress (e.g., Dishman et al., 2000). However, I tested all hypothesized models using HF-HRV in place of the RMSSD HRV index and did not find any significant results. Further interpretations of non-significant associations between IU and baseline HRV in the context of the main theory underlying this investigation will be provided in the summary section below.

Secondly, in Study 1, associations between IU and inflammatory markers were inconsistent and largely non-significant. In Study 1a, higher scores on IU predicted lower levels of CRP, which countered the hypothesis that high IU would relate to greater inflammation. All other associations between IU and inflammatory markers were not significant. This was an exploratory hypothesis as I found no previous studies linking IU to inflammatory markers. Results of this investigation provide some preliminary evidence that IU likely does not directly impact systemic inflammation; however, these results should be interpreted with caution for numerous reasons, including issues related to measurement (e.g., single measurement of biomarkers that may be unstable) and the sample, that will be discussed further below. Also, in Study 1a, the relation between IU and subjective physical health was non-significant, whereas in Study 2, IU predicted poorer perceived health amongst high IU participants. This discrepancy in

results in likely due to differences between Studies 1 and 2 in the measurement of IU, which will be further discussed in the limitations section below.

Like IU, MIL was largely unrelated to HRV and inflammatory markers. Direct associations between MIL and HRV were not detected in either study. Direct associations between dimensions of MIL and inflammatory markers were hypothesized and some were significant in Study 1b. In Study 1a, all associations between MIL and inflammatory markers were non-significant. In Study 1b, purpose significantly predicted levels of IL-6 and CRP such that higher purpose predicted lower levels of these two inflammatory markers which aligns with results of prior studies (e.g., Zilioli et al., 2015). Significance also predicted levels of CRP such that higher levels of significance corresponded to reduced CRP. Coherence significantly predicted levels of IL-6 in Study 1b; however, contrary to hypotheses, higher levels of coherence were associated with higher levels of IL-6. No significant relations were found between fibrinogen and dimensions of MIL, and no significant relations were found between any of the inflammatory markers and MIL in Study 1a. It could be these significant associations were not replicated in Study 1a due to the inclusion of subjective physical health as an outcome, which may have reduced the amount of variance for which inflammatory markers could account. In Study 1a and Study 2, subjective physical health, was significantly related to coherence and purpose (Study 1a) and coherence (Study 2) such that higher coherence and purpose were associated with better subjective health ratings. In Study 1, coherence and purpose were more strongly associated with subjective health than IL-6 and CRP (see correlations in Tables 3), potentially reducing the amount of variance for inflammatory levels to explain. Perhaps a more plausible explanation, however, is the difference in time lapse between measurement of MIL and biomarker collection in Study 1a versus 1b. In Study 1b, the time lapse between measurement of

MIL and biomarker collection was much shorter than in Study 1a, suggesting MIL may have a greater impact short term on these inflammatory markers and that perhaps that effect dissipates over time. However, previous researchers have found purpose to predict allostatic load, which incorporates IL-6, CRP, and fibrinogen in its estimation, a decade later (e.g., Zilioli et al., 2015). Thus, results of the current studies suggest the need for further investigation into the temporal nature of the effects of MIL on inflammation.

Finally, the hypothesized effects of HRV on psychological distress were significant in Study 1a and Study 2 but not Study 1b. In Study 1a and Study 2, higher HRV was associated with less psychological distress and fewer depressive symptoms, as expected. It is possible that the Study 1b sample did not report high enough levels of anxiety and depressive symptoms such that an association could be found. In comparing mean scores on the CES-D for Study 1b and Study 2 participants, Study 2 participants reported more depressive symptoms (Study 1b: M = 9.25, SD = 7.9; Study 2: M = 12.4, SD = 8.98). It is also possible the relation between HRV and depressive of anxiety symptoms is not strong enough to be consistently detected in non-clinical samples. Martens and colleagues (2007) found RMSSD HRV was not significantly associated with depressive or anxiety symptoms but rather only with the presence of anxiety disorders. In fact, many of the studies that have found significant associations between HRV and psychiatric symptoms have utilized clinical samples (e.g., Meyer at al., 2016; Agelink et al., 2002). Thus, it is possible significant associations between HRV and psychological outcomes were not found in Study 1b due to the low prevalence of anxiety and depressive disorders among sample participants.

Indirect effects

HRV did not significantly mediate relations between IU and psychological distress or inflammatory markers in Study 1 or 2. Based on the weak and largely non-significant direct effects of IU on HRV and inflammatory markers, insignificant indirect effect results were not surprising. Indirect effects measure the amount of mediation. Baron and Kenny (1986) specify four steps for establishing mediation, most of which were not satisfied in Study 1. First, one must show that the causal variable (IU) is correlated with the outcome (inflammatory markers) and, second, one must show the causal variable (IU) is correlated with the mediator (HRV). In Study 1, associations between IU and inflammatory markers were small (*r* ranged from -.08 to .048) as was the association between IU and HRV (*r* ranged from -.058 to .035). Similarly, in Study 2, the IU-HRV correlation was .031. In Study 1, associations between IU and psychological outcomes (*r* averaged .18) and subjective physical health (*r* = .13) were of small effect size but were relatively larger than associations between IU and inflammatory markers. In Study 2, these relations were stronger (IU-psychological health: *r* = -.42; IU-depression: *r* = .47; IU-physical health: *r* = -.22; See Table 5). However, step 3 (Baron & Kenny, 1986) requires showing that the mediator (HRV) affects the outcome (psychological and physical health). In Study 2, relations between HRV and psychological outcomes (*r* = -.11 and .04) and physical health (*r* = .14) were small. For mediation to occur, the mediator, HRV, must reduce the effect of the predictor (IU) on outcomes (inflammatory markers, subjective physical health, and psychological health). In the current investigation, associations between the predictor (IU) and outcomes were quite small, with the exception of the IU-psychological health outcome, thus perhaps there was not a robust enough direct effect for the mediator to reduce. Additionally, when the direct effect was strong enough (i.e., IU- psychological outcomes), associations between the predictor and mediator (*a*

path) and mediator and outcomes (*b* paths) may not have been strong enough to reduce the direct effect.

Support for this interpretation is provided by the significance of total effects in all models with psychological outcomes. The total effect is the sum of the direct effect from predictor (IU) to outcome (psychological distress) and the indirect effect. Although the indirect effects were not significant, the direct effects of IU on psychological distress and subjective physical health were strong enough to produce significant total effects for these models. Total effects were also significant for CRP in the Study 1a model in which IU1 was significantly predictive of CRP (see Table 10). However, again, mediation likely did not occur due to weak *a* and *b* paths.

Moderation effects

Although tests of indirect effects were not significant, some of the moderation effects in Study 1a were significant such that MIL moderated the relationship between IU and HRV. Interestingly, in Study 1a, when coherence and purpose were tested together, neither significantly moderated the effects of IU on HRV, although a significant simple effect for high levels of purpose was found. However, when coherence was tested alone, coherence moderated the effect of IU2 on HRV. When purpose was tested alone, purpose approached significance in moderating the effect of IU1 on HRV, and the simple effect for high purpose on the IU1-HRV relation was significant. At high levels of IU, coherence served a buffering role, as expected (see Figures 5), such that participants with high levels of IU and high levels of coherence had higher HRV than participants high in IU with low levels of coherence. Surprisingly, coherence did not have the same effect for participants who reported low IU. In fact, simple effects revealed that at low levels of IU, participants who reported low coherence had significantly higher HRV than high coherence participants at low levels of IU. Although coherence was hypothesized to be

protective particularly at high levels of IU, it was expected that high coherence would relate to higher HRV at all levels of IU, as feeling as though life is comprehensible likely conveys a sense of safety for all. It could be that at low levels of IU, participants can better tolerate feeling as though things do not make sense in their lives and do not need as much coherence to maintain vagal regulation. This could also be a spurious result and needs to be replicated.

Purpose approached significance in buffering the effect of IU1 on HRV, and there was a significant simple effect for high purpose. This simple effect indicates participants high in IU who report high purpose have significantly higher HRV than participants high in IU with medium or low levels of purpose (see Figure 6). Thus, as expected, it appears that purpose may have some buffering effect on HRV for high IU participants; however, this moderating effect was not consistent.

Study 1b and Study 2 did not result in any significant moderation results. Moderation occurs when the relationship between two variables (IU and HRV) depends on a third variable (MIL) such that the moderator affects the strength and/or direction of the relation between predictor and outcome (e.g., Frazier et al., 2004). Although the basis of the current investigation theoretically aligns with a moderation model wherein an individual's level of MIL (coherence, purpose, and/or significance) alters the effects of IU on HRV, it is possible that MIL instead serves as a moderator for only high IU individuals and/or that it is better conceptualized as a mediator. I theorized that the effects of IU on HRV depend on level of MIL, particularly for high IU individuals; however, for low IU individuals, effects of IU on HRV may not be influenced by MIL. In the current study, MIL was tested statistically as the moderator which allowed for examining low, medium, and high levels of MIL but not at discrete levels of IU (i.e., only high IU). Perhaps moderation effects would appear if only high IU individuals were

examined. Measurement issues with Study 1 and sample size of Study 2 preclude testing this hypothesis.

It is also possible that MIL serves as a mediator rather than a moderator of the relation between IU and HRV. Because the relation between IU and HRV was not as strong as expected, MIL might better explain how or why IU is related to HRV (mediator) rather than when or for whom (moderator) (Frazier et al., 2004). If it served a significant mediating role, results may indicate IU affects HRV via MIL such that IU influences how much MIL people accumulate or experience, which influences their sense of safety, thus affecting HRV. Further examination of these results in the context of the main theory underlying this investigation will be provided below.

Study 2 Part 2

The purpose of Part 2 of Study 2 was to examine how people's sense of IU and MIL are constructed, maintained, and adapted from everyday experiences of uncertainty and meaning and how fluctuations in these daily states affect psychological and physical health. Understanding the daily processes by which IU conveys risk for and MIL buffers against risk for poor health may provide vital information about how mental and physical health conditions develop and how they can be prevented.

The design of Study 2 allowed for repeated measures (daily) within person. To ensure the structure of these data were hierarchical, or nested within person, intraclass correlations (ICCs) were calculated for each daily variable (uncertainty, anxiety, negative affect (NA), and somatic symptoms). All ICCs were greater than the recommended cut-off of .05, ranging from .39 to .70, indicating a hierarchical structure of daily measures nested within persons. Traditional model fit statistics were not available for most of the models tested due to the estimation of random

effects. However, model fit statistics were excellent for the two models that estimated fixed effects.

Direct effects of Trait IU and MIL on daily experiences

Numerous hypotheses were tested to explore research questions regarding the ways in which trait IU and MIL affect daily experiences of uncertainty, anxiety, NA, and somatic symptoms. Based on UAMA theory (Grupe & Nitschke, 2013) and previous research linking trait IU to anxiety (e.g., Carleton et al., 2012), NA (e.g., Boswell et al., 2013), and somatization (e.g., Fergus & Valentiner, 2016), it was expected that participants who tend to be highly intolerant of uncertainty (high trait IU) would experience more uncertainty day-to-day as well as more negative affect and somatic symptoms as compared to low IU participants. This hypothesis was supported as high trait IU participants reported significantly more daily anxiety, negative affect, and uncertainty as well as marginally more somatic symptoms in comparison to low trait IU participants. Although no extant studies demonstrate relations between trait IU and these daily states, previous research supports strong links between trait IU and trait anxiety and NA and small to moderate associations between IU and somatization (e.g., Carleton et al., 2012; Boswell et al., 2013; Fergus et al., 2016). In line with the current study, one previous study (Thielsch et al., 2015) found trait IU significantly predicted episodic worry such that higher IU participants experienced more worry every day. Thus, in conjunction with previous research, the current study may help to explain why IU is considered a transdiagnostic risk factor for psychopathology (e.g., Beauchaine et al., 2014), as high IU participants experience more anxiety and NA on a daily basis that might additively contribute to the development of anxiety, depression, and other psychological disorders. High IU individuals also appear to experience more uncertainty than low IU individuals, and uncertainty tends to elicit negative emotional,

behavioral, and cognitive responses in people highly intolerant of uncertainty, which could elucidate another pathway (i.e., negative metacognitions; Thielsch et al., 2015) by which IU contributes to heightened risk for psychopathology. Another interpretation of this result is that the daily association between uncertainty and negative affect helps to shape trait IU. From this perspective, it is possible people form self-schemas about IU (i.e., "I am highly intolerant of uncertainty") because they tend to experience stronger daily uncertainty and NA linkages. In other words, when they experience uncertainty, it is often paired with NA, which shapes their perceptions of their ability to tolerate uncertainty. Thus, it is possible that IU both informs and is informed by these daily associations between uncertainty and negative affective experiences.

On the contrary, based on previous research (e.g., Machell et al., 2015; Park & George, 2017; Garrosa et al., 2017) it was expected that participants who tend to experience their lives as highly meaningful would experience fewer daily negative affective and somatic symptoms as compared to participants who report their lives as low in MIL. This hypothesis was partially supported as participants' overall MIL significantly predicted daily anxiety and daily uncertainty such that participants who reported higher MIL reported lower levels of daily anxiety and uncertainty than low MIL participants. The direct effect of MIL on daily negative affect approached significance in the same direction. MIL did not predict daily somatic symptoms. The three dimensions of MIL, trait coherence, purpose, and significance, were also tested independently. Participants high in trait coherence reported significantly less daily anxiety, uncertainty, and negative affect. Participants who reported their lives as high in significance reported significantly lower daily anxiety and daily uncertainty. Trait purpose did not significantly predict any of the daily variables of interest.

Having a well-developed, stable framework from which to view the world (i.e., coherence) tends to make one's life feel predictable, familiar, and compressible (e.g., Stillman & Baumeister, 2009; Baumeister & Vohs, 2002). This familiarity and sense of things going as expected likely puts people at ease and provides them with a tool for making sense of unexpected or unfamiliar experiences as they arise, translating to less anxiety, NA, and uncertainty day-to-day. Similarly, it appears feeling as though one's life matters and is worthwhile (significance), protects against daily anxiety and uncertainty. Although there is little empirical research on the impact of mattering on daily affective experiences, there is some theoretical support that a sense of mattering promotes processing of information in self-enhancing ways that align with one's perception of living a worthwhile existence (Sedikides & Gregg, 2008). More broadly, MIL has been found to promote proactive coping and positive affect (e.g., Miao et al., 2016; King et al., 2006), which may reduce or protect against experiencing anxiety, uncertainty, or NA. Results of the current study indicate experiencing high levels of coherence and/or significance seem to protect people from frequent and/or intense negative daily states.

Surprisingly, purpose, which has received the most empirical attention of the three dimensions in relation to daily experiences, did not significantly relate to any daily state in the current study. Previous studies found high purpose related to better coping (e.g., Hooker et al., 2018), reductions in appraisals of stressors (e.g., Hooker et al., 2018; Sumner et al., 2015) and reactivity to stressors (e.g., Ishida & Okada, 2006; 2011; van Reekum et al., 2007), better emotion regulation (e.g., Schaefer et al., 2013), and less NA (e.g., Burrow et al., 2013). Purpose serves to focus people's attention to their higher order aims and goals, likely directing attention away from daily hassles, challenges, and uncertainties and minimizing deleterious effects of stressors. However, it is also possible that high purpose individuals who experience events that

detract from or obstruct them from moving toward their purpose may experience frustration, uncertainty, and fatigue. Interestingly, in Study 2, purpose was much less strongly correlated with hypothesized related constructs than coherence and significance. For example, whereas coherence and depression were correlated at r = -.55, purpose and depression were only correlated at r = -.17; similarly, coherence and psychological health were correlated at r = .43, whereas purpose and psychological health were only correlated at r = .12. Purpose was also the only dimension of MIL positively correlated with prospective IU (r = .036). Purpose appears to function differently than coherence and significance in this sample despite the fact that its mean and standard deviation are very similar to those of coherence and significance. Thus, it is not the case that Study 2 captured participants with oddly low levels of purpose. It is unclear as to why purpose did not play a predictive role like coherence and significance and may be due to measurement issues discussed further below. It is also somewhat surprising that relations between MIL and daily somatic symptoms were not significant, although there is not much extant research linking MIL and somatic symptoms. This hypothesis was based on strong links between MIL and overall physical health (see Roepke et al., 2014 for review); however, results of the current study suggest the connection between MIL and daily somatic symptoms may not mimic that of MIL and more general indicators of physical health.

Direct effects of daily uncertainty and meaning on daily health

In addition to investigating how trait IU and trait MIL influence daily affective and somatic states, Study 2 Part 2 also examined how daily uncertainty influenced daily affective and somatic states. It was expected that on days when a participant experienced more than his/her average level of uncertainty, he/she would report more negative affective and somatic experiences than on a day when he/she reported lower than his/her average daily uncertainty.

This hypothesis was fully supported. On days participants reported more than their average level of uncertainty, they reported more somatic symptoms, anxiety, and negative affect than they did on days when they experienced less than their average level of uncertainty. The entropy model of uncertainty (EMU; Hirsh et al., 2012) suggests people are motivated to keep uncertainty at manageable levels because uncertainty poses a critical adaptive challenge and tends to be experienced as aversive. In other words, uncertainty requires us to take action to resolve it, which takes our attention away from other desired goals and aims, provoking anxiety. Although everyone has different levels of uncertainty that they can tolerate, more than subjectively tolerable levels of uncertainty triggers discomfort. As no previous studies of daily uncertainty were found, an item was designed to assess daily uncertainty and "greater than tolerable" uncertainty was conceptualized as more than a participant's average daily uncertainty.

Whereas heightened daily uncertainty was expected to trigger negative experiences, heightened daily meaning and purpose was expected to be protective against negative daily states. Results revealed that on days participants reported more than their average levels of meaning or purpose, they reported significantly less anxiety and less negative affect than they did on days they reported less than their average levels of meaning and purpose. Previous studies have found on days when people experience high levels of meaning and/or purpose, they tend to experience more positive social and achievement events, positive affect, and reduced negative affect (Machell et al., 2015; King et al., 2006). Little, if any, research has connected daily meaning and purpose to daily uncertainty or anxiety. Thus, the current study extends knowledge to this area and should be replicated in future studies.

Moderating effects of Trait IU and MIL on relations between daily uncertainty and daily health

It was also expected that trait levels of IU and MIL would influence relations between daily uncertainty and negative daily states. Although heightened uncertainty appears to trigger negative affective and somatic states independent of IU, it was hypothesized that IU would exacerbate these effects. As hypothesized, trait IU significantly moderated the daily relationship between uncertainty and negative affect. Thus, on days when participants experienced more than their average level of uncertainty, high trait IU participants experienced more negative affect than low IU participants. In other words, the relationship between daily uncertainty and negative affect was stronger for high IU than low IU participants such that, for high IU participants, experiencing more uncertainty than usual tends to more drastically exacerbate negative affect.

These results support theoretical assertions that IU serves as a transdiagnostic risk factor for a range of psychological disorders (e.g., Carleton, 2016; Grupe & Nitschke, 2013; Tanovic et al., 2018) as well as empirical studies linking IU with heightened risk for developing anxiety, depression, posttraumatic stress and other disorders (e.g., McEvoy & Mahoney, 2012; Keefer et al., 2010; Bardeen et al., 2013). Results of this study also align with those of the few prior studies investigating related processes. Chen and Hong (2010) found IU moderated relations between daily hassles and anxiety such that high IU participants experienced more anxiety in response to daily hassles than low IU participants, and Klomke and Jeter (2013) found inhibitory IU moderated relations between daily hassles and worry in the same manner.

However, unlike Chen and Hong (2010) and Klomke and Jeter (2013), the current investigation did not find significant moderating effects of IU on the daily relation between uncertainty and anxiety. This is surprising as the relation between uncertainty and anxiety has the strongest empirical and theoretical support (e.g., Dugas & Ladouceur, 2000) of all relations tested in this investigation. It is possible that participants high in trait IU might report

consistently moderate to high levels of anxiety every day, or perhaps participants low in IU report consistently low levels of anxiety, and without much fluctuation, significant differences day-to-day would not be detected. Examination of the heterogeneity of the effects of the predictor (IU) on the outcome (daily anxiety), by group (low, average, and high IU) supported the above assertion: variance in daily anxiety differs by level of IU. Variance in day-to-day in anxiety was significantly smaller for low IU participants ($\beta = .13$) than for average IU participants ($\beta = .30$) and both of those variances were significantly smaller than variance in daily anxiety for high IU participants ($\beta = .45$). Additionally, comparison of standardized means indicate high IU participants reported significantly more daily anxiety ($\beta = .68$) than average ($\beta = -.12$) and low ($\beta = -.33$) IU participants. Thus, it appears from these supplemental analyses that IU significantly relates to daily anxiety; however, it is necessary to group low, average, and high IU participants to see these effects.

Trait IU did not appear to moderate the daily relations between uncertainty and somatic symptoms, even when analyzed by group. In fact, it seems uncertainty triggers somatic symptoms regardless of level of IU. Thus, when people experience more than their average level of uncertainty, they tend to report more somatic symptoms, and this holds true even for low IU participants, suggesting greater than usual uncertainty triggers discomfort for all.

Overall, results of this model add to the literature by elucidating how trait IU affects affective and physiological responses to uncertainty. As UAMA (Grupe & Nitschke, 2013) proposes, people who are highly intolerant of uncertainty tend to experience heightened reactivity to uncertainty, resulting in more NA that likely reinforces their negative beliefs about and maladaptive responses to uncertainty as well as their propensity to develop anxious and depressive symptoms. Further investigation into uncertainty as a trigger for NA, as opposed to

anxiety or worry, may help to explain the transdiagnostic nature of IU in predisposition to psychopathology.

Contrary to hypotheses, MIL did not moderate any of the daily relations between uncertainty and negative affective or somatic states. Even though high trait MIL (coherence and significance) predicts less daily NA, anxiety, and somatic symptoms, it does not appear that trait MIL, or any dimension of MIL independently, buffers against the negative effects of heightened daily uncertainty on NA, anxiety, or somatic symptoms. This suggests heightened uncertainty is quite destabilizing as even people who have a strong sense of mattering, a purposeful existence, and a framework from making sense of the world are not protected from the negative effects of uncertainty.

Future research confirming these results is vital and examination of the moderating effects of MIL at different levels of IU is critical. Additionally, expanding upon the current study by examining the moderating effects of daily meaning and purpose on the relation between daily uncertainty and daily NA, anxiety, and somatic symptoms would provide information about potential buffering mechanisms of meaning and purpose at the daily level. Even though trait MIL does not appear to protect against negative consequences of heightened uncertainty, daily meaning or purpose might.

Moderating effects of IU X MIL on relations between daily uncertainty and daily health.

Although trait MIL did not appear to play a protective role for all participants, it was hypothesized that MIL might be protective for high IU participants. In other words, it was predicted that the interaction between MILxIU at the trait level would significantly moderate daily relations between uncertainty and negative affective and somatic states. As hypothesized, the daily association between uncertainty and negative affect was significantly stronger for

participants low in MIL and high in IU than for high MIL x low IU participants. Thus, on days when high IU x low MIL participants experienced heightened uncertainty, they experienced more negative affect than participants low in IU with high levels of MIL. Further, visual inspection of Figure 11 suggests at high levels of IU, the relation between uncertainty and NA is not as strong for high MIL participants as it is for low MIL participants, indicating MIL has some protective effects for high IU participants.

Each dimension of MIL was investigated separately as a moderator. Results indicated IU x Coherence significantly moderated the association between daily uncertainty and both daily negative affect and daily anxiety (see Figures 12 and 13) such that the daily association between uncertainty and negative affect and uncertainty and anxiety were significantly stronger for participants low in coherence and high in IU than for high coherence x low IU participants. Thus, on days when high IU x low coherence participants experienced more uncertainty, they experienced significantly more negative affect and anxiety than participants low in IU with high levels of coherence. Furthermore, at high levels of IU, relations between uncertainty and NA and uncertainty and anxiety are not as strong for participants high in coherence as they are for participants low in coherence, indicating coherence serves a protective role for those high in IU. Results support significant moderation of the association between negative affect and uncertainty by IU x Significance in the same manner as coherence and total MIL. Therefore, although MIL does not independently moderate daily relations between uncertainty and negative affective experiences, when MIL is examined in conjunction with IU, it appears to serve a protective role for high IU participants. Specifically, the coherence and significance dimensions of MIL buffer against negative emotional effects of experiencing uncertainty for high IU participants,

protecting them from the exacerbations in negative affect and anxiety that high IU x low MIL participants experience.

Results of these models reveal the importance of considering the effects of IU and MIL together, as the protective role of MIL does not appear when MIL is tested independently. This may be due to MIL operating differently at high and low levels of IU as well as the difference in magnitude of the relation between daily uncertainty and daily NA low IU individuals (i.e., very weak), thus not providing a relationship to buffer. As discussed above, at high levels of IU, MIL appears to buffer against the effects of uncertainty on affect. This aligns with theoretical assertions that MIL may serve as a crucial safety resource for individuals who are highly intolerant of uncertainty. Specifically, for high IU individuals, having a coherent framework through which to view the world provides a sense of understanding that can minimize uncertainty and uncertainty-related anxiety (Hirsh et al., 2012). Individuals who have a well-developed sense of themselves, their world, and the interaction between the two can utilize that framework to make sense of potential uncertain elements, which may reduce the strain IU causes, resulting in less NA and anxiety than individuals lacking coherence (e.g., Stillman & Baumeister, 2009; Baumeister & Vohs, 2002). Similarly, the sense that one's life matters appears to serve as a protective resource for high IU people to grasp onto when they are struggling with uncertainty (George & Park 2016).

On the other hand, for low IU participants, uncertainty does not appear to be strongly associated with NA, as slopes approach zero, thus the need for a protective factor is lacking at low levels of IU because uncertainty is not as distressing as it is for high IU participants. Interestingly, uncertainty is more strongly related to anxiety than NA for low IU participants, with slopes around .4 (see Figure 12). For low IU participants, coherence is not protective, as the

relation between daily uncertainty and anxiety is actually stronger for low IU x high coherence participants than low IU x low coherence participants. It could be that low IU x low coherence participants experience less anxiety when faced with uncertainty because they are used to not understanding the world around them and are not particularly bothered by that, whereas low IU x high coherence participants are used to experiencing their world as making sense and uncertainty disrupts that, triggering anxiety and perhaps action to resolve uncertainty (Hirsh et al., 2012). Thus, for high IU people, coherence protects against anxiety provoked by uncertainty, whereas for low IU individuals, coherence might exacerbate anxiety produced by uncertainty, perhaps igniting action to reconcile the disruption in predictability and stability.

As in previous models, purpose did not have significant effects independently or in conjunction with IU. Thus, it appears the overarching aims and goals that purpose tends to provide do not protect against the distress uncertainty provokes. Theory suggests purpose offers a motivating aim that focuses attention and efforts on goal-oriented action, perhaps affording people a clear pathway that distracts from uncertainty or allows them to tolerate distress from uncertainty (e.g., van Reekum et al., 2007; Schaefer et al., 2013). However, purpose did not appear to operate in a protective manner in this study.

Limitations and Future Directions

Overall, results of the current investigation did not provide support for the GUTS model, as IU did not appear to convey risk for inflammation or deleterious physical and psychological health consequences via autonomic dysregulation (low HRV). Non-significant results do not mean GUTS is inaccurate or that processes do not unfold as GUTS proposes. There were numerous limitations to the current studies that may preclude finding significant outcomes.

First, there were a number of measurement-related issues in both studies. One major limitation of Study 1 was a dearth of measured variables that mapped onto the constructs of interest, in particular IU, coherence, and significance. The two items utilized as indicators of IU in Study 1 align conceptually with the main premise of IU; however, neither item was designed with the intention of measuring IU. Thus, it could be that IU was not accurately captured via these items and that poor measurement of the IU construct contributed to non-significant results. Study 2 allowed for choice of measurement instruments, thus IU was measured using a validated scale. In comparing Study 1 and 2, it appears correlations between IU and scores on the CES-D were much weaker in Study 1 (r = .21) than Study 2 (r = .47), lending some support to the assertion IU was not fully or adequately captured by the items selected in Study 1. Additionally, Study 1 did not incorporate any items intended to measure the coherence dimension of MIL. A single item that aligned conceptually with the definition of coherence was selected; however, single item measures are prone to poor validity, reliability, and sensitivity. Similar issues may have affected the single item indicator of significance.

Although Study 2 allowed for selection of measures, measurement issues may have influenced results. First, the Three Dimensional Meaning Scale (Martela & Steger, 2018) is a new measure that has not been extensively utilized or examined. Although the scale demonstrated good internal reliability in the sample, it may be that the measure, particularly of the purpose dimension, does not adequately capture the construct of purpose or may lack sensitivity in discriminating between participants with low versus high purpose. Further investigation of the reliability and validity of this scale is needed. Additionally, previous researchers have noted limitations related to the measurement of IU; however, recent studies suggest the IUS-12 is psychometrically sound (e.g., Hale et al., 2016). Even so, the IUS-12 may

be best suited to detect IU and discriminate between levels of IU in clinical samples as compared to community samples. Relatedly, the Study 1 sample may be under-representative of people high in IU. Although the sample was recruited nationally via probability sampling, it is likely very high IU individuals declined to participate as a portion of the study required in-person lab visits. High IU individuals tend to have high levels of generalized and social anxiety (e.g., Boelen & Reijintjes, 2009) that may preclude in-person attendance. Study 2 also required in-person lab visits and scores on the IUS-12 for this sample align with typical community sample scores, which are much lower than IUS-12 scores in clinical samples (e.g., Carleton et al., 2012). These limitations related to IU measurement and sampling in Study 1 may have precluded significant results. Although Study 2 allowed for measurement of constructs of interest with largely well-validated scales, it had other limitations, including use of a new measure of MIL, a non-clinical sample, small sample size, and lack of biomarker data.

In addition to measurement and sampling limitations, GUTS has not been previously tested empirically. Thus, it is possible the way I conceptualized and tested the GUTS model was not accurate. Based on the lack of significant mediation of HRV across all studies, I question if HRV might function differently in the model than tested and if other critical variables may be missing. For example, it is possible HRV might serve a moderating, rather than mediating role, between IU and psychological and physical health outcomes. If this were the case, HRV might only affect the relation between IU and outcomes at low levels of HRV. It is also possible that some risk or protective factors that may affect the IU-HRV path were missing. In other words, perhaps not all high IU individuals experience the same intensity of perceived unsafety resulting in low HRV. Perhaps only high IU participants who also have a history of abuse or trauma are at high risk whereas people high in IU who have numerous resilience factors are at low risk of GU.

On the other hand, it is also possible that high IU participants experience similar heightened perceived unsafety (GU) but that perceived unsafety does not uniformly translate to physiological dysregulation (i.e. low HRV).

It is also possible that the links between HRV and outcomes were not accurately modeled and tested in the current investigation. Although research suggests HRV predicts levels of inflammatory markers and onset of physical disease (Boneva et al., 2007; Staud, 2008; Evans et al., 2013; Carvalho et al., 2011), much of the research on HRV, inflammation, and disease is correlational rather than longitudinal, indicating low HRV is associated with greater systemic inflammation and disease rather than necessarily predictive of inflammation and disease (e.g., Cooper et al., 2015; Jarczok et al., 2014). Thus, it is possible that bidirectional relationships exist between HRV and outcomes and thus feedback loops between HRV and outcomes need to be included in models. Future studies that can measure HRV and biomarker outcomes at different time points would be helpful in clarifying temporal relationships. There may also need to be a feedback loop between IU and HRV as it is possible that as HRV decreases and the individual operates from a dysregulated autonomic state, uncertainty may become even more intolerable.

It is also possible the HRV index selected (RMSSD), or perhaps HRV itself, is not an accurate indicator of GU. To examine the possibility that RMSSD was not the best HRV index of GU, I re-tested models using HF-HRV due to extant research linking IU and HF-HRV (e.g., Deschenes et al., 2015) as well as theoretical fit of HF-HRV in the model. Results remained non-significant when HF-HRV was substituted. Thus, it is necessary to consider that HRV itself may not be an indicator of GU as Brosschot and colleagues (2016, 2018) theorize. Generalized unsafety remains a relatively new, unexamined and unmeasured construct. Although, theoretically, HRV appears to align with GU, it is possible that GU does not uniformly affect

individuals' physiology in the same way. It is also possible that IU does not predict deficient safety learning and thus does not result in generalized unsafety that perpetuates physiological dysregulation. Further empirical examination of GUTS is necessary prior to making any conclusions about its utility or accuracy.

Implications

Despite insignificant results of the full moderated mediation test of GUTS, the current studies provide some informative takeaways. Although inconsistent across studies, some models revealed support for MIL as a protective factor against the deleterious consequences of IU and uncertainty on health (i.e., HRV, affect). Significant moderation effects of MIL, particularly the coherence dimension, indicate that at high levels of IU, MIL buffers against the negative effects of IU and uncertainty on mental and physical health. It is also evident that effects of IU and MIL translate to the state level, affecting people's daily affective experiences. As expected, people high in trait IU tend to experience more uncertainty and find uncertainty more disconcerting, resulting in more daily NA, anxiety, and somatic symptoms that may contribute to the development of psychopathology, supporting the notion that IU is a transdiagnostic risk factor for psychopathology. A new item was developed to measure people's daily experiences of uncertainty, and, upon initial examination, it appears this item may be useful in future studies based on confirming expected relationships. Further investigation of daily uncertainty and its differential effects may provide beneficial information about how high IU individuals experience daily life.

Also, as expected, results of this study suggest daily meaning and purpose are protective against negative affective states. Additional models were run to examine if trait IU moderates relations between daily meaning and daily uncertainty, NA, and anxiety, and it did not,

indicating daily meaning is protective regardless of level of IU. In the context of the above results, this is crucial, as it indicates cultivating daily meaning or purpose may help high IU individuals better tolerate uncertainty. Interventions that promote cultivation of daily meaning, perhaps particularly coherence, may buffer against the negative affect and anxiety high IU individuals tend to experience when they feel uncertain.

Based on the current investigation, it is unclear if and how IU and MIL affect physiological regulation (i.e., HRV) and physical health. For the most part, relations between both IU and MIL and physical health outcomes were not significant. This could be due to measurement and design issues, or it is possible the constructs are not strongly associated with each other despite numerous studies linking MIL to physical health (e.g., Roepke et al., 2014). Additional research examining if, when, and how MIL and IU affect physiological regulation, inflammation, subjective physical health, and development of disease is needed.

This investigation also adds to the literature by providing information about significant covariates to consider. Although significance of covariates will differ by sample, this study adds to current knowledge of the effects of various demographic and health factors that affect IU, MIL, HRV, inflammatory levels, and physical and psychological health. Other strengths of the current investigation include the replication of the main hypothesis in three distinct samples, two of which were large, nationally representative samples, which suggests generalizability of results. All samples were fairly diverse in terms of SES, ethnic background, religion, and educational background. Study 1 examined only middle aged and older adults and Study 2 examined young and older adults, thus covering the spectrum of adult age. However, both studies required traveling to either a testing center or lab, which may limit the generalizability of results as participants must be healthy enough to travel.

Conclusion

Altogether, results of the current investigation did not support GUTS as it was modeled here. IU did not appear to convey risk for inflammation or deleterious physical and psychological health consequences via autonomic dysregulation (low HRV). However, MIL did appear, albeit inconsistently, to serve a protective role against deleterious physiologic and affective consequences for high IU individuals. Because GUTS has not been previously empirically tested, it is likely that the model examined in the current studies needs refinement. Ideally, future investigation of GUTS with a large, representative sample using validated measures of all constructs, time lapses between measurement of HRV and outcomes, addition of potential bidirectional relations, and examination of the role of HRV (moderator versus mediator) as well as other variables that may exacerbate risk or protect against risk of IU on GU may elucidate the nature of the process outlined in GUTS. If modification resulted in significant outcomes, it would indicate the importance of addressing IU, perhaps through the development of interventions that promote safety learning (i.e. via enhancing MIL), to reduce the negative effects of IU not only on psychological health but also on physical health.

TABLES

Table 1.
Study 1a (MIDUS 2 & 3) and 1b (MIDUS Refresher) Descriptive Statistics

		1a: MIDUS 2 & 3		1b: MIDUS Refresher	
Sex		n	Percent	n	Percent
	Male	420	44.40%	374	43.3%
	Female	525	55.60%	472	54.7%
Race					
	White	875	92.60%	600	69.50%
	Black and/or African American	23	2.40%	56	6.50%
	Native American or Alask Native	13	1.40%	16	1.90%
	Asian	3	0.30%	12	1.40%
	Native Hawaiian or Pacific Islander	0	0.00%	2	0.20%
	Other	29	2.30%	55	6.40%
Ethnicity					
	No	905	95.80%	712	82.50%
	Spanish/Hispanic/Latino Descent	40	4.20%	32	3.70%
Marital Status (T2)					
	Married	672	71%	501	58.10%
	Separated	13	1.40%	20	2.30%
	Divorced	122	12.90%	134	15.50%
	Widowed	49	5.20%	40	4.60%
	Never Married	68	7.20%	156	18.10%
	Living with someone in commited rlts	-	-	12	1.40%
Smoking Status					
	Never Smoker	532	56.30%	501	58.10%
	Former Smoker	303	32.10%	234	27.10%
	Current Smoker	110	11.60%	94	10.90%
Physical Activity (regular exercise 20 min 3x per week or more)					
	No	190	20.10%	233	27%
	Yes	755	79.90%	630	73%
Alcohol Use (past month)					
	None	309	32.70%	241	28%
	Some Use (less than 1 day/week)	260	27.50%	208	24.10%
	Moderate Use (1-4 days/week)	238	25.20%	300	34.70%

	Frequent Use (5+ days/week)	138	14.60%	114	13.20%
Menopause stopped period					
	Pre-menopausal	187	35.60%	173	46.50%
	No	112	21.30%	91	24.40%
	Yes	190	36.20%	106	28.50%
Pacemaker					
	No	916	96.50%	812	94.10%
	Yes	8	0.90%	23	2.70%
RA4XTC_242 (psychotherapeutic agents)					
	No	724	76.60%	627	72.70%
	Yes	144	15.20%	143	16.60%
RA4XTC_97 (hormones)					
	No	657	69.50%	594	68.80%
	Yes	211	22.30%	176	20.40%
RA4XTC_40 (cardiovascular agents)					
	No	533	56.40%	444	51.40%
	Yes	335	35.40%	326	37.80%
Psychological Outcomes					
	Endorsed Panic Attack Symptoms	54	5.70%	-	-
	Endorsed Anxiety Symptoms	18	1.90%	-	-
	Endorsed Anhedonia/Depression Symptoms	96	10.20%	-	-
	Endorsed Hx Anxiety/Depression past 1yr	175	18.50%	-	-

Table 2.
Study 1 and 2 Covariates Examined

Study 1 Covariates	**Variable(s) predicting**
Demographic Covariates	
Age	IU, MIL, HRV, biomarkers, psych hlth, subjective phys hlth
Sex	HRV, biomarkers, psych hlth
Race and ethnicity	MIL, HRV, biomarkers, psych hlth, subjective phys hlth
SES	Psych hlth, subjective phys hlth
Marital status	HRV, Biomarkers, psych hlth, subjective phys hlth
Health Covariates	
Medical conditions	HRV, biomarkers, psych hlth, subjective phys hlth
Medications	HRV, biomarkers, psych hlth, subjective phys hlth
BMI	HRV, biomarkers, psych hlth, subjective phys hlth
Smoking status	HRV, biomarkers, psych hlth, subjective phys hlth
Alcohol consumption	HRV, biomarkers, psych hlth, subjective phys hlth
Physical activity	HRV, biomarkers, psych hlth, subjective phys hlth
Menstrual status	HRV, biomarkers
Site of assessment	HRV, biomarkers
Study 2 Covariates	**Trait-level variable(s) predicting**
Demographic Covariates	
Age	IU, MIL, HRV, psych hlth, subjective phys hlth
Sex	HRV, psych hlth
Race and ethnicity	MIL, HRV, psych hlth, subjective phys hlth
SES	psych hlth, subjective phys hlth
Marital status	HRV, psych hlth, subjective phys hlth
Health Covariates	
Medical conditions	HRV, psych hlth, subjective phys hlth
Medications	HRV, psych hlth, subjective phys hlth
BMI	HRV, psych hlth, subjective phys hlth
Smoking status	HRV, psych hlth, subjective phys hlth
Alcohol consumption	HRV, psych hlth, subjective phys hlth
Physical activity	HRV, psych hlth, subjective phys hlth
Menstrual status	HRV

Table 3.
*Study 1a Correlations, Means, Standard Deviations, Skew, and Kurtosis (*** p<.01, *p<.05)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
1. IU1 (10A)	--															
2. IU2 (MMr)	.24**	--														
3. Coherence	-.19**	-.21**	--													
4. Purpose	-.31**	-.29**	.30**	--												
5. HRV	.04	-002	.03	.02	--											
6. IL-6	-.07*	.04	.002	-.04	-.13**	--										
7. CRP	-.08*	.02	-.02	-.02	-.15**	.51**	--									
8. Fib	-.06	-.01	-.03	-.01	-.13**	.38**	.51**	--								
9. Phys Hlth	.10**	.16**	-.10**	-.20**	-.05	.14**	.17**	-.08*	--							
10. Mental Hlth	.21**	.17**	-.13**	-.29**	-.05	.06	.07*	.02	.59**	--						
11. NA	.20**	.23**	-.19**	-.27**	-.05	.004	.02	.01	.23**	.42**	--					
12. Anh + Dep	.15**	.14**	-.08**	-.19**	-.02	.06	.05	.08*	.25**	.31**	.39**	--				
13. Anxiety	.03	.13**	-.09**	-.16**	.04	.03	.01	-.01	.14**	.21**	.32**	.41**	--			
14. Panic	.08*	.09**	-0.06	-.08*	.02	.05	-0.01	.001	.12**	.24**	.30**	.22**	.21**	--		
15. Age	-.13*	-.04	.02	.09**	-.19**	.17**	.04	.13**	.01	-.05	-.21**	-.14**	-.08**	-.12**	--	
16. SES	-.03	-.10**	.10**	.15**	.04	-.12**	-.09**	-.10**	-.25**	-.22**	-.08*	-.12**	-.12**	-.05	-.32**	--
Mean	2.23	3.64	4.85	39.93	2.86	.68	.31	337.53	2.46	2.31	1.49	.61	.12	.30	54.33	173.00
SD	1.10	1.86	1.76	6.38	.62	.71	1.13	80.63	1.02	.96	.49	1.74	.85	.96	11.06	68.37
Skew	.79	.14	-.39	-.84	.25	.19	.06	.39	.53	.28	1.76	2.71	8.14	3.60	.27	.42
Kurtosis	-.14	-1.30	1.00	.55	.46	.56	-.30	1.18	-.16	-.50	5.18	5.84	70.05	13.04	-.63	-.79

Table 4.
Study 1b Correlations, Means, Standard Deviations, Skew, and Kurtosis

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1. IU1 (10A)	--														
2. IU2 (MMr)	.22**	--													
3. Coherence	-.12**	-.24**	--												
4. Purpose	-.23**	-.30**	.32**	--											
5. Signif	-.21**	-.05	.11**	.27**	--										
6. HRV	.01	-.06	-.05	-.01	-.01	--									
7. IL-6	-004	.05	-.03	-.15**	-.03	-.16**	--								
8. CRP	-.03	-002	-.06	-.15**	-.09**	-.07	.58**	--							
9. Fib	-.07*	.05	-.04	-.06	-.02	-.13**	.46**	.57**	--						
10. MASQ_D	.20**	.17**	-.21**	-.32**	-.22**	.06	.05	.07**	.02	--					
11. MASQ_A	.20**	.17**	-.20**	-.27**	.16**	.07	-.01	.06	-.03	.68**	--				
12. MASQ_LI	.16**	.21**	-.21**	-.39**	-.23**	.04	.16**	.17**	.12**	.79**	.65**	--			
13. CESD	.20**	.23**	-.23**	-.43**	-.26**	.07	.14**	.13**	.07**	.79**	.64**	.77**	--		
14. Age	-.08*	.06	.07	.04	.12**	-.29**	.41**	.08**	.25**	-.21**	-.26**	-.15**	-.19**	--	
15. SES	.01	-.17**	.17**	.22**	.04	-.04	-.28**	-.17**	-.21**	-.11**	-.09*	-.17**	-.16**	.35*	--
Mean	2.37	3.70	4.84	38.83	6.02	3.04	.72	.34	343.36	2.88	2.78	2.46	2.01	51.62	174.67
SD	1.07	1.79	1.77	6.82	1.08	.62	.80	1.21	73.72	.30	.27	.30	.86	13.60	76.32
Skew	.59	.08	-.41	-.73	-1.43	-.03	-.10	.20	.55	.84	.61	.80	-.51	-.13	.32
Kurtosis	-.38	-1.15	-1.03	.24	2.35	-.08	-.19	-.35	.65	.34	-.01	.29	-.16	-1.06	-1.01

** $p < .01$, * $p < .05$

Table 5.
Study 2 Trait-Level Correlations, Means, Standard Deviations, Skew, and Kurtosis

	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1. IUp	(.84)													
2. IUi	.66**	(.81)												
3. IUS	.94**	.87**	(.89)											
4. Coherence	-.07	-.35**	-.20	(.83)										
5. Purpose	.04	-.08	-.01	.42**	(.87)									
6. Significance	-.19	-.22*	-.23*	.51**	.56**	(.85)								
7. HRV	.02	.05	.03	.17	.17	.13	--							
8. CESD	.32*	.58**	.47**	-.55**	-.17	-.41**	-.11	(.90)						
9. Phys Hlth	-.15	-.33**	-.22	.35**	.09	.16	.14	-.51**	(.83)					
10. Mtl Hlth	-.48**	-.35**	-.42**	.43**	.12	.31**	.04	-.77**	.69**	(.88)				
11. Age	-.06	-.11	-.08	.15	.03	.08	-.51**	-.11	-.03	.26*	--			
12. Income	-.15	-.22*	-.19	.26*	.21	.18	-.36**	-.33**	.10	.17	.48**	--		
13. BMI	-.01	-.03	-.02	.01	-.06	-.03	-.17	.05	-.30**	-.06	.28**	.11	--	
14. Hlth Cond	.06	.16	.11	.11	-.01	.06	-.28**	.22	-.49**	-.17	.42**	.16	.47**	--
Mean	19.47	10.08	29.55	21.26	21.98	21.31	28.68	12.40	72.60	72.44	45.35	5.73	25.01	2.19
SD	5.44	3.79	8.43	4.43	4.85	5.53	16.16	8.98	13.61	13.48	20.49	3.18	4.37	2.64
Skew	.03	.66	.37	.62	-.76	-.78	.88	1.31	.83	-.99	.42	.35	1.97	1.97
Kurtosis	-.42	-.37	-.35	.67	-.01	.02	.20	2.24	.39	1.09	-1.62	-1.18	7.37	5.05

** $p < .01$, *$p < .05$

Table 6.
Study 2 State-Level Correlations, Means, Standard Deviations, Skew, and Kurtosis

	1	2	3	4	5	6
1. Uncertain	--					
2. Meaning	.02	--				
3. Purpose	.01	.92**	--			
4. Anxiety	.11*	.16**	.17**	--		
5. NA	.11*	.16**	.17**	.99**	--	
6. Phys Symp	.01	.04	.07	.06	.06	--
Mean	2.56	3.62	3.69	1.61	.99	2.74
SD	1.92	1.72	1.72	1.22	.78	3.67
Skew	.37	-.55	-.49	.38	1.16	2.20
Kurtosis	-.52	-.37	-.49	-.83	1.48	8.10

** $p < .01$, *$p < .05$

Table 7.
Study 1a Model Fit Statistics

	AIC	**Chi Square**	**df**	**p-value**	**RMSEA estimate**	**CFI**	**TLI**	**SRMR**
Hypothesis 1	1454.26	42.48	5	<.001	0	1	1	0
Hypothesis 2	-	172.55	70	<.001	.042 (.034,.05)	0.93	0.89	0.096
Hypothesis 3	-	188.52	76	<.001	.042 (.035,.05)	0.93	0.89	0.11
Hypothesis 4	-	274.79	91	<.001	.049 (.042,.056)	0.9	0.84	0.11
Hypothesis 5	13543.27	-	-	-	-	-	-	-
Hypothesis 6	1448.19	46.91	10	<.001	0	1	1	0
H7 & H8								
IUxCoherence	19471.29	-	-	-	-	-	-	-
IUxPurpose	19580.75	-	-	-	-	-	-	-

Table 8.
Study 1b Model Fit Statistics

	AIC	**Chi Square**	**df**	**p-value**	**RMSEA estimate**	**CFI**	**TLI**	**SRMR**
Hypothesis 1	954.88							
Hypothesis 2	10444.09	129.59	46	<.001	.053 (.042,.064)	0.97	0.94	0.038
Hypothesis 3	11474.16	122.81	46	<.001	.051(.040,.062)	0.97	0.95	0.037
Hypothesis 4	10296.44	149.34	50	<.001	.056 (.045,.066)	0.96	0.94	0.042
Hypothesis 5	11420.76	215.31	55	<.001	.067 (.058,.077)	0.94	0.9	0.056
Hypothesis 6	965.77							
H7 & H8								
IUxCoherence	11721.21	233.99	77	<.001	.056 (.047, .064)	0.94	0.91	0.056
IUxPurpose	11953.06	305.47	70	<.001	.071 (.063, .080)	0.92	0.87	0.074
IUxSignificance	11935.94	239.28	70	<.001	.060 (.052,.069)	0.94	0.9	0.057

Table 9.

Study 2 Model Fit Statistics

	AIC	Chi Square	df	p-value	RMSEA estimate	CFI	TLI	SRMR between	SRMR within
Hypothesis 1	166.06								
Hypothesis 2	394.34	5.62	5	.35	.046(.000, .19)	0.996	0.99	.054	
Hypothesis 3	560.28	11.08	8	.2	.081 (.00, .18)	0.98	0.95	.083	
Hypothesis 4	870.39	26.88	25	.36	.036 (.00, .11)	0.99	0.98	.079	
Hypothesis 5	622.37	8.92	8	.35	.044(.00, .16)	0.99	0.98	.058	
Hypothesis 6	173.17								
H7 & H8 - MIL	631.88	64.04	26	<.001	.16 (.11, .21)	0.79	0.63	.08	
IUxCoherence	554.85	44.4	14	.001	.19 (.13, .26)	0.83	0.63	.095	
IUxPurpose	555.93	15.73	12	.2	.071 (.00,.16)	0.97	0.94	.066	
IUxSignificance	554.43	16.38	16	.29	.054 (.00, .14)	0.98	0.97	.065	
H9	4129.78	1.03	1	.31	0.007	1	0.99	.001	0.023
H10	4193.87	1.02	1	.31	0.007	1	0.99	.001	0.023
H11	4176.8								
H12									
Meaning	4193.87								
Purpose	4189.51								
H13	3272.42								
H14									
Coherence	3382.4								
Purpose	3394.58								
Significance	3397.38								
H15- MIL	3993.89								
IUxCoherence	3982.83								
IUxPurpose	4002.79								

Table 10.
Study 1a (MIDUS 2 & 3) Path Analysis Standardized (STYDX) Results

	Outcomes																	
	HRV			**Psych**			**IL-6**			**CRP**			**Fib**			**Health**		
	B	SE	[95% CI]	*B*	SE	[95% CI]	*B*	SE	[95% CI]	*B*	SE	[95% CI]	*B*	SE	[95% CI]	*B*	SE	[95% CI]
Hypothesis 1																		
IU1 (10A)	.03	.04	[-.05, .10]															
IU2 (MMR)	-.01	.04	[-.08, .062]															
Age	-.18	.03	**[-.24, -.11]**															
RA4XTC_242	-.13	.04	**[-.19, -.06]**															
BMI	-.82	.04	**[-.15, -.01]**															
Hypothesis 2																		
IU1 (10A)				.25	.04	**[.17, .32]**	-.06	.03	[-.13, .00]	-.10	.03	**[-.16, -.03]**	-.04	.04	[-.11, .03]	.09	.03	**[.02, .16]**
IU2				.2	.04	**[.12, .27]**	.02	.03	[-.04, .09]	.01	.03	[-.06, .07]	-.01	.04	[-.07, .06]	.09	.03	**[.02, .15]**
Age				-.18	.04	**[-.26, -.10]**	.16	.03	**[.09, .22]**				.14	.04	**[.06, .20]**			
Sex				.11	.04	**[.03, .19]**				.14	.03	**[.08, .21]**	.16	.03	**[.01, .23]**			
Race													.12	.03	**[.05, .19]**			
BMI							.36	.03	**[.29, .42]**	.42	.03	**[.37, .48]**	.27	.03	**[.20, .33]**	.23	.03	**[.17, .29]**
Smoking				.14	.04	**[.07, .22]**	.08	.03	**[.02, .15]**							.11	.03	**[.05, .18]**
SES																.08	.03	**[.02, .14]**
RA4XTC_40							.09	.03	**[.02, .15]**							.16	.03	**[.09, .23]**
RA4XTC_97										.11	.03	**[.05, .17]**				-.08	.04	**[-.15, -.01]**
RA4XTC_242				.23	.04	**[.16, .31]**	.08	.03	**[.02, .50]**	.07	.03	**[.01, .13]**						
Hypothesis 3																		
HRV				-.08	.04	**[-.17, -.01]**	-.08	.03	**[-.14, -.02]**	-.10	.03	**[-.17, -.05]**	-.08	.03	**[-.14, -.03]**	-.02	.03	[-.09, .04]

Age	-.21	.04	**[-.28, -.14]**	-.25	.04	**[-.35, -.19]**	.15	.03	**[.08, .22]**				.13	.04	**[.06, .19]**			
Sex				.10	.04	**[.01, .18]**				.15	.03	**[.09, .21]**	.17	.03	**[.10, .23]**			
Race													.12	.03	**[.06, .19]**			
BMI	-.10	.03	**[-.17, -.04]**				.36	.03	**[.29, .42]**	.43	.03	**[.37, .48]**	.26	.03	**[.20, .33]**	.23	.03	**[.16, .29]**
Smoking				.16	.04	**[.09, .24]**										.12	.03	**[.06, .18]**
SES																.08	.03	**[.02, .14]**
RA4XTC_40							.09	.03	**[.02, .16]**							.17	.03	**[.10, .24]**
RA4XTC_97	.09	.04	**[.02, .16]**							.12	.03	**[.06, .18]**				-.08	.04	**[-.15, -.01]**
RA4XTC_242	-.15	.03	**[-.22, -.09]**	.25	.04	**[.18, .33]**												
Hypothesis 4																		
Coherence				-.22	.04	**[-.29, -.14]**	.04	.04	[-.03, .11]	.03	.03	[-.04, .093]	-.01	.04	[-.08, .06]	-.07	.03	**[-.14, -.01]**
Purpose				-.34	.04	**[-.41, -.27]**	.001	.03	[-.09, .03]	.02	.03	[-.07, .06]	.01	.04	[-.07, .07]	-.14	.03	**[-.20, -.08]**
Age				-.20	.04	**[-.30, -.14]**	.17	.03	**[.10, .24]**				.14	.04	**[.07, .21]**			
Sex										.15	.03	**[.09, .22]**	.17	.04	**[.1, .24]**			
Race													.12	.04	**[.06, .19]**			
BMI							.37	.03	**[.30, .43]**	.44	.03	**[.38, .49]**	.27	.03	**[.21, .34]**	.23	.03	**[.17, .29]**
Smoking				.16	.04	**[.05, .2]**										.12	.03	**[.06, .18]**
SES																.08	.03	**[.02, .14]**
RA4XTC_40							.09	.03	**[.02, .15]**							.17	.03	**[.10, .24]**
RA4XTC_97										.11	.03	**[.05, .17]**				-.08	.04	**[-.15, -.01]**
RA4XTC_242				.26	.04	**[.18, .32]**												
Hypothesis 5																		
IU1	.02	.04	[-.05, .09]	.23	.04	**[.14 ,.31]**	-.05	.03	[-.11, .02]	-.07	.03	**[-.13, -.01]**	-.03	.03	[-.09, .03]	.10	.04	**[.03, .17]**
IU2	-.01	.04	[-.08, .06]	.22	.04	**[.13, .30]**	.03	.03	[-.04, .09]	.01	.03	[-.05, .07]	-.01	.03	[-.07, .05]	.09	.03	**[.03, .16]**
HRV				-.08	.05	[-.16,	-.08	.04	**[-.14,**	-.01	.03	**[-.16,**	-.08	.03	**[-.14,**	-.03	.03	[-.10,

						.01]			**-.01]**			**-.04]**			**-.03]**			.04]
Age	-.18	.04	**[-.26, -.11]**	-0.20	.04	**[-.29, -.12]**	.13	.03	**[.07, .19]**				.10	.03	**[.04, .16]**			
Sex										.12	.03	**[.07, .18]**	.15	.03	**[.09, .21]**			
Race													.10	.03	**[.04, .15]**			
BMI	-.08	.04	**[-.16, -.01]**				.34	.03	**[.28, .41]**	.42	.03	**[.36, .48]**	.25	.04	**[.18, .32]**	.22	.03	**[.15, .28]**
Smoking				.16	.04	**[.08, .24]**										.13	.03	**[.06, .19]**
SES																.09	.03	**[.04, .15]**
RA4XTC_40							.09	.03	**[.03, .16]**							.12	.03	**[.07, .18]**
RA4XTC_97										.13	.03	**[.07, .18]**						
RA4XTC_242	-.13	.04	**[-.20, -.06]**	.27	.05	**[.18, .35]**												
A1B1				.00	.001	[-.003, .002]	-.001	.002	[-.01, .003]	-.002	.004	[-.01, .01]	-.001	.003	[-.01, .004]	-.001	.002	[-.004, .003]
Total1				.06	.04	**[.04, .10]**	-.04	.02	[-.08, .013]	-.01	.03	**[-.15, -.022]**	-.04	.03	[-.09, .03]	.10	.03	**[.03, .16]**
A2B1				.00	.001	[-.002, .002]	.00	.001	[-.004, .004]	.001	.004	[-.01, .01]	.001	.003	[-.01, .01]	.00	.002	[-.003, .003]
Total2				.05	.02	**[.039, .10]**	.02	.02	[-.02, .07]	.01	.03	[-.06, .08]	-.01	.03	[-.07, .05]	.09	.03	**[.03, .16]**
Hypothesis 6 - Coherence																		
IU1	.03	.04	[-.04,.09]															
IU2	-.03	.04	[-.11,.04]															
Coherence	.03	.04	[-.05,.1]															
Age	-.19	.003	**[-.27,-.13]**															
RA4XTC_242	-.11	.10	**[-.18,-.03]**															
IU1 X Coherence (mod1)	-.01	.04	[-.09, .06]															
IU2 X Coherence (mod2)	.08	.04	**[.01, .15]**															
Simp_LOIU2_Coh	-.11	.04	**[-.23,-.02]**															
Simp_HIIU2_Coh	.08	.04	**[.002,.17]**															
Hypothesis 6 - Purpose																		

IU1	.03	.04	[-.03,.1]															
IU2	-.03	.04	[-.1,.05]															
Purpose	-.02	.04	[-.1,.06]															
Age	-.19	.003	**[-.27,-.13]**															
RA4XTC_242	-.11	.1	**[-.18,-.03]**															
IU1 X Purpose (mod1)	.08	.04	*[-.002,.15]*															
IU1 X Purpose (mod1)	.06	.04	[-.03,.12]															
Simp_HIIU1_Pur	.11	.05	**[.01,.21]**															
Hypothesis 6-Both MIL																		
IU1	.04	.04	[-.02, .11]															
IU2	-.02	.04	[-.10, .05]															
Coherence	.02	.04	[-.05, .10]															
Purpose	-.02	.04	[-.08, .07]															
Age	-.02	.003	**[-.25, -.10]**															
RA4XTC_242	-.24	.10	**[-.20, -.05]**															
IU1 X Coherence (mod1)	-.03	.04	[-.12, .05]															
IU1 X Purpose (mod3)	.06	.04	[-.01, .15]															
IU2 X Coherence (mod2)	.06	.04	[-.02, .14]															
IU2 X Purpose (mod4)	.04	.04	[-.04, .12]															
Sim_Hi1_Purpose	.10	.05	**[.004, .19]**															
Hypothesis 8																		
IUxCoherence																		
IU1	.03	.03	[-.03, .09]	.23	.04	**[.15, .31]**	-.05	.03	[-.12, .02]	-.09	.03	**[-.13, -.015]**	-.04	.03	[-.09, .03]	.10	.04	**[.03, .17]**
IU2	-.02	.04	[-.09, .07]	.22	.04	**[.13, .29]**	.03	.03	[-.03, .10]	.01	.03	[-.06, .06]	-.002	.03	[-.06, .07]	.09	.04	**[.02, .15]**
HRV				-.07	.04	[-.16, .003]	-.07	.04	**[-.15, -.01]**	-.10	.03	**[-.16, -.03]**	-.07	.03	**[-.14, -.01]**	-.03	.03	[-.09, .04]

Coherence	.03	.04	[-.04, .10]															
IU1xCoherence	.003	.04	[-.09, .07]															
IU2xCoherence	.08	.04	**[.003, .15]**															
Age	-.17	.04	**[-.24, -.09]**	-.22	.04	**[-.29, -.14]**	.13	.03	**[.07, .19]**				.10	.03	**[.04, .15]**			
Sex										.12	.03	**[.07, .17}**	.15	.03	**[.09, .21]**			
Race													.10	.03	**[.05, .16]**			
BMI							.35	.03	**[.29, .41]**	.42	.03	**[.38, .48]**	.25	.04	**[.18, .32]**	.22	.03	**[.15, .27]**
Smoking				.02	.04	**[.09, .24]**										.13	.03	**[.06, .2]**
SES																.09	.03	**[.04, .15]**
RA4XTC_40							.09	.03	**[.03, .16]**							.12	.03	**[.05, .18]**
RA4XTC_97										.3	.03	**[.07, .18]**						
RA4XTC_242				.27	.05	**[.17, .36]**												
Total_low_X1				.06	.01	**[.04, .09]**				-.10	.04	**[-.16, -.02]**				.10	.04	**[.02, .16]**
Total_med_X1				.06	.01	**[.04, .09]**				-.10	.04	**[-.16, -.02]**				.10	.04	**[.02, .16]**
Total_high_X1				.06	.01	**[.03, .09]**				-.10	.04	**[-.16, -.03]**				.10	.04	**[.02, .16]**
Total_low_X2				.05	.01	**[.03, .07]**										.10	.04	**[.03, .17]**
Total_med_X2				.05	.01	**[.02, .07]**										.09	.04	**[.03, .16]**
Total_high_X2				.04	.01	**[.02, .07]**										.08	.04	**[.01, .15]**
IUXPurpose																		
IU1	.036	.04	[-.05, .10]	.24	.04	**[.12, .30]**	-.05	.04	[-.12, .03]	-.07	.03	[-.09, .03]	-.03	.03	[-.09, .03]	.10	.03	**[.04, .17]**
IU2	-.03	.04	[-.13, .04]	.19	.04	**[.14, .31]**	.03	.04	[-.02, .11]	.01	.03	[-.06, .06]	-.01	.03	[-.06, .06]	.09	.03	**[.03, .15]**
HRV				-.08	.04	**[-.15, -.01]**	-.08	.04	**[-.16, -.002]**	-.10	.03	**[-.13, -.02]**	-.08	.03	**[-.13, -.02]**	-.03	.03	[-.10, .04]
Purpose	.002	.03	[-.08, .05]															
IU1xPurpose	.07	.04	[-.04, .12]															

IU2xPurpose	.06	.04	*[-.001, .16]*															
Age	-.17	.04	**[-.24, -.10]**	-.21	.03	**[-.25, -.14]**	.13	.03	**[.08, .19]**				.10	.03	**[.02, .15]**			
Sex										.12	.03	**[.07, .19]**	.15	.03	**[.07, .20]**			
Race													.10	.03	**[.04, .14]**			
BMI							.35	.03	**[.27, .41]**	.42	.02	**[.37, .46]**	.25	.03	**[.19, .31]**	.22	.03	**[.15, .28]**
Smoking				.16	.04	**[.07, .24]**										.13	.03	**[.06, .19]**
SES																.09	.03	**[.04, .15]**
RA4XTC_40							.09	.03	**[.05, .16]**							.13	.03	**[.07, .19]**
RA4XTC_97										.13	.03	**[.07, .18]**						
RA4XTC_242				.27	.04	**[.18, .34]**												
Total_low_X1				.06	.01	**[.04, .09]**				-.09	.03	**[-.16, -.01]**				.10	.03	**[.04, .17]**
Total_med_X1				.06	.01	**[.04, .09]**				-.10	.03	**[-.17, -.03]**				.10	.03	**[.03, .16]**
Total_high_X1				.06	.01	**[.04, .08]**				-.11	.03	**[-.17, -.03]**				.09	.03	**[.03, .15]**
Total_low_X2				.05	.01	**[.03, .08]**										.10	.03	**[.04, .16]**
Total_med_X2				.05	.01	**[.03, .07]**										.09	.03	**[.03, .15]**
Total_high_X2				.05	.01	**[.02, .07]**										.09	.03	**[.01, .14]**
Hypothesis 8- Both MIL																		
IU1	.04	.04	[-.02, .11]															
IU2	-.02	.04	[-.09, .05]															
Coherence	.02	.04	[-.05, .10]															
Purpose	-.01	.04	[-.08, .07]															
IU1 X Coherence (mod1)	-.03	.04	[-.12, .05]															
IU1 X Purpose (mod3)	.06	.04	[-.01, .15]															
IU2 X Coherence (mod2)	.06	.04	[-.02, .14]															

IU2 X Purpose (mod4)	.04	.04	[-.04, .12]															
Age	-.16	.04	**[-.24, -.09]**	-.22	.04	**[-.29, -.14]**	.13	.03	**[.07, .19]**				.1	.03	**[.04, .15]**			
Sex										.12	.03	**[.07, .17}**	.15	.03	**[.09, .21]**			
Race													.10	.03	**[.05, .16]**			
BMI							.35	.03	**[.29, .41]**	.42	.03	**[.38, .48]**	.25	.04	**[.18, .32]**	.22	.03	**[.15, .27]**
Smoking				.02	.04	**[.09, .24]**										.13	.03	**[.06, .20]**
SES																.09	.03	**[.04, .15]**
RA4XTC_40							.09	.03	**[.03, .16]**							.12	.03	**[.05, .18]**
RA4XTC_97										.30	.03	**[.07, .18]**						
RA4XTC_242	-.24	.10	**[-.20, -.05]**															
Sim_Hi1_Purpose	.10	.05	**[.004, .19]**															
Total_low_X1				.06	.01	**[.04, .09]**				-.08	.03	**[-.16, -.01]**				.10	.03	**[.04, .17]**
Total_med_X1				.06	.01	**[.04, .09]**				-.10	.03	**[-.17, -.03]**				.10	.03	**[.03, .16]**
Total_high_X1				.06	.01	**[.04, .08]**				-.11	.03	**[-.17, -.03]**				.09	.03	**[.03, .15]**
Total_low_X2				.05	.01	**[.03, .08]**										.10	.03	**[.04, .16]**
Total_med_X2				.05	.01	**[.03, .07]**										.09	.03	**[.03, .15]**
Total_high_X2				.05	.01	**[.02, .07]**										.09	.03	**[.01, .14]**

Table 11.
Study 1b (MIDUS Refresher) Path Analysis Standardized (STYDX) Results

	Outcomes														
	HRV			**Psych**			**IL-6**			**CRP**			**Fib**		
	B	SE	[95% CI]	*B*	SE	[95% CI]	*B*	SE	[95% CI]	*B*	SE	[95% CI]	*B*	SE	[95% CI]
Hypothesis 1															
IU1 (10A)	.03	.04	[-.05,.1]												
IU2 (MMR)	-.06	.04	[-.14,.02]												
Age	-.28	.04	**[-.35,-.22]**												
Sex	.14	.04	**[.06,.21]**												
Race	.09	.04	**[.01,.16]**												
RA4XTC_242	-.15	.04	**[.07,.23]**												
RA4XTC_97	.11	.04	**[.04,.19]**												
Hypothesis 2															
IU1 (10A)				.14	.04	**[.07,.2]**	.02	.03	[-.06,.06]	-.02	.03	[-.09,.4]	-.05	.04	[-.12,.01]
IU2				.13	.04	**[.06,.2]**	-.01	.03	[-.05,.08]	.00	.03	[-.07,.06]	.06	.04	[-.01,.12]
Age				-.29	.04	**[-.36,-.22]**	.36	.03	**[.29,41]**				.22	.04	**[.16,.28]**
SES				-.18	.04	**[-.27,-.1]**	-.12	.03	**[-.19,.07]**						
Sex										.17	.03	**[.11,.22]**	.17	.03	**[.1,.23]**
Race							.08	.03	**[.03,.14]**						
BMI				.13	.04	**[.06,.19]**	.38	.03	**[.33,.44]**	.50	.03	**[.44,.55]**	.32	.03	**[.25,.37]**
RA4XTC_242				.22	.04	**[-.29,-.14]**									
Hypothesis 3															
HRV				-.04	.04	[-.13,.04]	-.15	.04	**[-.22,-.09]**	-.19	.04	**[-.25,-.12]**	-.09	.04	**[-.16,-.02]**
Age				-.32	.04	**[-.4,-.25]**	.33	.03	**[.27,.39]**				.22	.04	**[.15,.28]**
SES				-.18	.04	**[-.27,-.1]**	-.12	.03	**[-.18,-.06]**						
Sex										.17	.03	**[.11,.22]**	.19	.04	**[.12,.25]**
Race							.08	.03	**[.03,.14]**						
BMI				.17	.04	**[.09,.23]**	.37	.03	**[.32,.43]**	.51	.03	**[.48,.56]**	.33	.04	**[.26,.39]**
RA4XTC_242				.22	.04	**[-.3,-.14]**									

Hypothesis 4															
Coherence				-.12	.04	**[-.19,-.05]**	.02	.03	**[-.05,-.08]**	-.02	.04	[-.09,.04]	-.02	.04	[-.09,.05]
Purpose				-.33	.04	**[-.4,-.27]**	-.07	.04	**[-.14,-.002]**	-.08	.04	**[-.15,-.02]**	-.02	.04	[-.10,.05]
Significance				-.10	.04	**[-.17,-.04]**	-.01	.03	[-.07,..05]	-.03	.03	[-.1,.03]	.03	.04	[-.04,.09]
Age				-.25	.04	**[-.32,-.19]**	.35	.03	**[.29,.39]**				.22	.03	**[.16,.27]**
SES				-.11	.04	**[-.18,-.05]**	-.12	.03	**[-.19,-.08]**						
Sex										.17	.03	**[-.19,-.08]**	.16	.04	**[.09,.22]**
Race							.08	.03	**[.02,.13]**						
BMI							.37	.03	**[.30,.42]**	.49	.03	**[.31,.43]**	.32	.04	**[.25,.37]**
RA4XTC_242				.19	.04	**[-.26,-.14]**									
Hypothesis 5															
IU1	.04	.04	[-.04,.13]	.14	.04	**[.07,.22]**	.01	.03	[-.05,.08]	-.01	.03	[-.08,.05]	-.05	.04	[-.12,..02]
IU2	-.08	.05	[-.17,.01]	.13	.04	**[.05,.21]**	-.02	.03	[-.08,.05]	-.01	.04	[-08,.05]	.05	.04	[-.03,.12]
HRV				-.02	.05	[-.11,.07]	-.13	.04	**[-.21,-.07]**	-.19	.04	**[-.17,-.01]**	-.08	.04	**[-.17,-.14]**
Age				-.29	.04	**[-.36,.21]**	.34	.03	**[.29, .41]**				.22	.03	**[.16,.27]**
SES				-.18	.04	**[-.26,.09]**	-.14	.03	**[-.19,-.07]**						
Sex										.18	.03	**[.12,.23]**	.17	.03	**[.11,.23]**
Race							.09	.03	**[.03,.14]**						
RA4XTC_242				.22	.04	**[-.30,-.15]**									
BMI				.13	.04	**[.06,.20]**	.39	.03	**[.32,.43]**	.50	.03	**[.23,.37]**	.32	.04	**[.23,.37]**
A1B1				.00	.00	[-.001,.001]	.00	.01	[-.01,.01]	-.01	.01	[-.03,.01]	-.22	.31	[-.83,.40]
Total1				.04	.01	**[.02,.05]**	.01	.03	[-.05,.06]	-.03	.04	[-.1,.05]	-3.51	2.64	[-8.69,1.66]
A2B1				.00	.00	[-.002,.002]	.01	.01	[-.002,.02]	.02	.01	[-.003,.04]	.48	.39	[-.29,1.26]
Total2				.03	.01	**[.01,.05]**	-.01	.03	[-.06,.04]	.00	.04	[-.08,.08]	4.20	2.70	[-1.13,9.55]
Hypothesis 6															
IU1	.01	.04	[-.07,.08]												
IU2	-.07	.04	[-.15,.01]												
Coherence	.01	.04	[-.08,.08]												

Purpose	-.04	.05	[-.15,.04]												
Significance	.01	.05	[-.08,.08]												
Age	-.29	.04	**[-.36,-.22]**												
Sex	.16	.04	**[.08,.23]**												
RA4XTC_242	.15	.04	**[.06,.22]**												
RA4XTC_97	.12	.04	**[.05,.19]**												
IU1 X Coherence	-.03	.04	[-.12,.04]												
IU1 X Purpose	-.04	.05	[-.13,.03]												
IU1 X Signifcance	.01	.05	[-.08,.09]												
IU2 X Coherence	.02	.05	[-.07,.09]												
IU2 X Purpose	.02	.05	[-.08,.1]												
IU2 X Significance	-.01	.05	[-.09,.07]												
Hypothesis 8															
IUxCoherence															
IU1	.03	.04	[-.03,.06]	.14	.04	**[.06,.21]**	.02	.04	[-.05,.07]	-.01	.04	[-.10,.08]	-.05	.04	[-.03,.06]
IU2	-.04	.04	[-.08,.03]	.14	.04	**[.07,.22]**	.01	.04	[-.05,.06]	-.02	.04	[-.11,.07]	.05	.04	[-.08,.03]
HRV				-.02	.04	[-.11,.06]	-.15	.04	**[-.23,-.07]**	-.20	.04	**[-.28,-.12]**	-.11	.04	**[-.20,-.03]**
Coherence	.01	.04	[-.04,.05]												
IU1xCoherence	-.04	.04	[-.06,.02]												
IU2xCoherence	.02	.04	[-.04,.06]												
Age	-.30	.04	**[-.02,-.01]**	-.30	.04	**[-.37,-.22]**	.34	.03	**[.28,.40]**				.19	.03	**[.13,.25]**
Sex	.16	.04	**[.10,.30]**							.16	.03	**[.10,.21]**	.16	.03	**[.09,.22]**
Race							.10	.03	**[.04,.15]**						
SES				-.15	.04	**[-.24, -.07]**									
Drug 242	.14	.04	**[.07,.34]**	.23	.04	**[-.31,-.16]**									
Drug 97	.13	.04	**[.05,.29]**												
IUXPurpose															
IU1	.01	.04	[-.06,.10]	.14	.04	**[.07,.21]**	.01	.04	[-.06,.09]	-.01	.04	[-.09,.07]	-.05	.04	[-.14,.02]

IU2	-.05	.04	[-.13,.-37]	.14	.04	**[.06,.21]**	.01	.04	[-.06,.08]	-.01	.04	[-.09,.07]	.05	.04	[-.02,.11]
HRV				-.01	.05	[-.11,.07]	-.15	.04	**[-.24,-.07]**	-.20	.04	**[-.28,-.13]**	-.10	.04	**[-.19,-.02]**
Purpose	-.03	.05	[-.12,.07]												
IU1xPurpose	-.06	.04	[-.14,.02]												
IU2xPurpose	.01	.04	[-.07,.10]												
Age	-.30	.04	**[-.37,-.22]**	-.29	.04	**[-.37,-.22]**	.35	.03	**[.29,.41]**				.20	.03	**[.14,.25]**
Sex	.17	.04	**[.08,.24]**							.16	.03	**[.11,.22]**	.16	.03	**[.10,.22]**
Race							.10	.03	**[.04,.15]**						
SES				-.16	.04	**[-.24,-.07]**									
Drug 242	.16	.04	**[.07,.25]**	.23	.04	**[-.30,-.15]**									
Drug 97	.12	.04	**[.04,.20]**												
IUXSignificance															
IU1	.02	.04	[-.06,.13]	.14	.04	**[.06,.20]**	.01	.04	[-.07,.08]	-.01	.04	[-.09,.07]	-.05	.04	[-.13,.02]
IU2	-.04	.04	[-.13,.04]	.14	.04	**[.06,.22]**	.01	.04	[-.06,.08]	-.01	.04	[-.09,.06]	.05	.04	[-.02,.12]
HRV				-.01	.05	[-.11,.07]	-.15	.04	**[-.23,-.06]**	-.20	.04	**[-.28,-.12]**	-.10	.04	**[-.20,-.03]**
Significance	-.01	.04	[-.09,.09]												
IU1xSig	.00	.04	[-09,.08]												
IU2xSig	.00	.04	[-.07,.09]												
Age	-.30	.04	**[-.37,-.22]**	-.29	.04	**[-.37,-.22]**	.35	.03	**[.29,.41]**				.20	.03	**[.14,.26]**
Sex	.16	.04	**[.09,.23]**							.16	.03	**[.1, .22]**	.16	.03	**[.09,.22]**
Race							.10	.03	**[.04,.15]**						
SES				-.16	.04	**[-.25, -.08]**									
Drug 242	-.16	.04	**[.08,.23]**	.23	.04	**[-.31,-.14]**									
Drug 97	.12	.04	**[.05,.21]**												

Table 12.
Study 2 Between Persons Path Analysis Standardized (STYDX) Results

	Outcomes											
	HRV			**Physical Hlth (SF-36)**			**Psychological Hlth (SF-36)**			**CES-D (Depression)**		
	B	SE	[95% CI]	*B*	SE	[95% CI]	*B*	SE	[95% CI]	*B*	SE	[95% CI]
Hypothesis 1												
IU	-.01	.11	[-.23, .20]									
Age	-.51	.10	**[-.70,-.33]**									
Hypothesis 2												
IU				-.20	.12	**[-.42,.03]**	-.41	.11	**[-.62,-.21]**	.42	.10	**[.23,.62]**
Total # chronic conditions				-.37	.09	**[-.56,-.19]**				.10	.09	**[-.06,.27]**
Age							.19	.07	**[.04,.33]**			
Income										-.23	.08	**[-.39,-.06]**
Hypothesis 3												
HRV				.03	.12	[-.21, .27]	.16	.14	[-.11,.43]	-.22	.13	[-.47,.03]
Total # chronic conditions				-.39	.1	**[-.58,-.20]**						
Age	-.55	.09	**[-.28,-.14]**				.24	.09	**[.07,.42]**			
Income										-.29	.09	**[-.47,-.11]**
Hypothesis 4 (all MIL variables)												
Coherence				.38	.13	**[.14,.63]**	.38	.13	**[.13,.63]**	-.47	.12	**[-.70,-.24]**
Purpose				-.13	.13	[-.39,.12]	-.18	.13	[-.44,.08]	.23	.12	[-.01,.47]
Significance				.03	.14	[-.24,.31]	.19	.14	[-.09,.47]	-.26	.13	*[-.51,.00]*
Total # chronic conditions				-.40	.09	**[-.58,-.22]**						
Age							.21	.07	**[.07,.35]**			
Income										-.19	.08	**[-.35,-.03]**
Hypothesis 4 (coherence only)												
Coherence				.34	.10	**[.13,.54]**	.39	.11	**[.18,.60]**	-.49	.10	**[-.68,-.31]**
Total # chronic conditions				-.40	.09	**[-.58,-.22]**						

Age							.21	.07	**[.06,.35]**			
Income										-.18	.08	**[-.34,-.02]**
Hypothesis 4 (purpose only)												
Purpose				.04	.12	[-.19,.28}	.07	.13	[-.17,.32]	-.09	.13	[-.34,.15]
Total # chronic conditions				-.38	.10	**[-.57,-.20]**						
Age							.22	.07	**[.07,.36]**			
Income										-.23	.09	**[-.40,-.06]**
Hypothesis 4 (significance only)												
Significance				.15	.12	[-.08,.38]	.28	.12	**[.05,.51]**	-.36	.11	**[-.57,-.15]**
Total # chronic conditions				-.39	.01	**[-.58,-.20]**						
Age							.21	.07	**[.07,.36]**			
Income										-.21	.08	**[-.38,-.05]**
Hypothesis 5												
IU	-.03	.13	[-.28,.22]	-.18	.12	[-.40,.05]	-.39	.12	**[-.63,-.15]**	.41	.11	**[.19,.64]**
HRV				.05	.1	[-.15,.25]	.19	.11	[-.03,.40]	-.22	.11	**[-.44,-.002]**
Total # chronic conditions				-.37	.13	**[-.63,-.12]**						
Age	-.026	.005	**[-.04,-.02]**				.01	.004	**[.003,.02]**			
Income										-.08	.034	**[-.15,-.01]**
Indirect effect				-.001	.02	[-.03,.03]	-.01	.03	[-.05,.05]	.01	.03	**[-.05,.07]**
Total effect				-.18	.12	[-.40,.05]	-.40	.12	**[-.64,-.15]**	.42	.12	**[.19,.65]**
Hypothesis 6												
IU	.06	.16	[-.22,.39]									
Coherence	.15	.14	[-.11,.44]									
Purpose	.04	.13	[-.25,.27]									
Significance	.07	.16	[-.67,.15]									
Age	-.03	.003	**[-.04,-.02]**									
IU X Coherence (mod1)	-.02	.18	[-.44,.29]									
IU X Purpose (mod2)	.05	.17	[-.26,.27]									

IU X Significance (mod3)	-.13	.22	[-.67,.15]									
Hypothesis 8												
IUxCoherence												
IU	.02	.14	[-.19,.37]	-.18	.11	[-.41,.04]	-.39	.11	**[-.67,-.19]**	.41	.12	**[.21,.64]**
HRV				.05	.10	[-.15,.24]	.19	.12	[-.15,.35]	-.22	.12	**[-.43,-.002]**
Coherence	.18	.09	**[.03,.33]**									
IUxCoherence	-.07	.14	[-.34,.21]									
Total # chronic conditions				-.37	.14	**[-.61,-.04]**						
Age	-.027	.004	**[-.04,-.02]**				.01	.004	**[.004,.02]**			
Income										-.08	.04	**[-.15,-.01]**
Total effect_Low							-.36	.13	**[-.77,-.14]**	.38	.14	**[.08,.66]**
Total effect_Medium							-.39	.13	**[-.70,-.16]**	.41	.13	**[.19,.64]**
Total effect_High							-.41	.13	**[-.68,-.20]**	.44	.14	**[.24,.68]**
IUxPurpose												
IU	-.01	.13	[-.26,.26]	-.19	.11	[-.41,.06]	-.43	.13	**[-.65,-.17]**	.47	.13	**[.21,.66]**
HRV				.04	.10	[-.15,.25]	.05	.10	[-.01,.44]	-.14	.10	**[-.46,-.02]**
Purpose	.17	.11	[-.09,.38]									
IUxPurpose	-.02	.14	[-.29,.27]									
Total # chronic conditions				-.40	.13	**[-.60,-.10)**						
Age	-.02	.01	**[-.04,-.02]**				.01	.004	**[.004,.021]**			
Income										-.08	.03	**[-.15,-.02]**
Total effect_Low							-.42	.13	**[-.66,-.12]**	.46	.14	**[.16,.72]**
Total effect_Medium							-.43	.13	**[-.65,-.16]**	.47	.13	**[.21,.67]**
Total effect_High							-.43	.13	**[-.69,-.15]**	.47	.14	**[.20,.72]**
IUxSignificance												
IU	.04	.13	[-.22,.29]	-.18	.11	[-.41,.06]	-.39	.12	**[-.64,-.17]**	.41	.11	**[.21,.66]**
HRV				.05	.10	[-.15,.25]	.19	.11	[-.01,.44]	-.22	.11	**[-.46,-.02]**
Significance	.14	.11	[-.08,.36]									

IUxSignificance	-.17	.14	[-.51,.02]									
Total # chronic conditions				-.37	.13	**[-.59,-.09]**						
Age	-.03	.01	**[-.04, -.019]**				.01	.004	**[.004,.021]**			
Income										-.08	.03	**[-.15,-.02]**
Total effect_Low							-.32	.15	**[-.64,-.05]**	.33	.13	**[.09,.62]**
Total effect_Medium							-.38	.13	**[-.65,-.15]**	.40	.12	**[.20,.66]**
Total effect_High							-.45	.14	**[-.73,-.20]**	.48	.14	**[.24,.79]**

*Bold values indicates significant paths; italicized values indicate marginally significant paths

Table 13.
Study 2 Cross-Level Path Analysis Standardized (STYDX) Results

	Outcomes							
	Daily Anxiety		**Daily negative affect**		**Daily Somatic Symp**		**Daily Uncertainty**	
	B	SE	*B*	SE	*B*	SE	*B*	SE
Hypothesis 9								
IU	**0.45**	0.12	**0.34**	0.11	0.2	0.12	**0.48**	0.1
Hypothesis 10								
MIL	**-0.26**	0.1	-0.19	0.13	-0.053	0.11	**-0.19**	0.1
Coherence	**-0.51**	0.08	**-0.41**	0.12	-0.21	0.13	**-0.46**	0.1
Purpose	-0.028	0.11	-0.026	0.1	0.044	0.1	-0.022	0.1
Significance	**-0.19**	0.09	-0.12	0.11	0.004	0.08	**-0.17**	0.066
Hypothesis 11								
Daily Uncertainty	**0.22**	0.04	**0.19**	0.04	**0.12**	0.04		
Hypothesis 12								
Daily Meaning	**-0.14**	0.05	**-0.16**	0.05	-0.002	0.03		
Daily Purpose	**-0.16**	0.05	**-0.16**	0.05	0.049	0.027		

*Bold values indicates significant paths; italicized values indicate marginally significant paths

Table 14.
Study 2 Moderation Analysis Standardized (STYDX) Results (Hypotheses 13-15)

	Outcomes								
	Slope: Daily Anxiety-Uncertainty			**Slope: Daily NA-Uncertainty**			**Slope: Daily Somatic-Uncertainty**		
	Intercept	*B*	SE	Intercept	*B*	SE	Intercept	*B*	SE
MIL total									
IUxMLQ	**.47**	-.08	.07	**.29**	**-.20**	.08	**.15**	-.05	.05
IU	**.47**	.02	.06	**.29**	**.16**	.07	**.15**	-.01	.07
MLQ	**.47**	.03	.06	**.29**	-.03	.07	**.15**	-.02	.07
Coherence									
IUxCoherence	**.47**	**-.12**	.06	**.29**	**-.27**	.07	**.15**	-.09	.07
IU	**.47**	.03	.06	**.29**	**.18**	.06	**.15**	-.01	.07
Coherence	**.47**	.02	.06	**.29**	.02	.07	**.15**	-.07	.07
Purpose									
IUxPurpose	**.47**	-.07	.08	**.29**	-.06	.11	**.15**	-.06	.11
IU	**.47**	.01	.08	**.29**	.12	.10	**.15**	-.02	.10
Purpose	**.47**	.05	.05	**.29**	.07	.07	**.15**	-.05	.07
Significance									
IUxSignificance	**.47**	-.04	.04	**.29**	**-.20**	.08	**.15**	-.07	.07
IU	**.47**	.02	.06	**.29**	**.16**	.06	**.15**	-.01	.07
Significance	**.47**	.03	.06	**.29**	-.06	.07	**.15**	-.002	.07

*Bold values indicates significant paths; italicized values indicate marginally significant paths

FIGURES

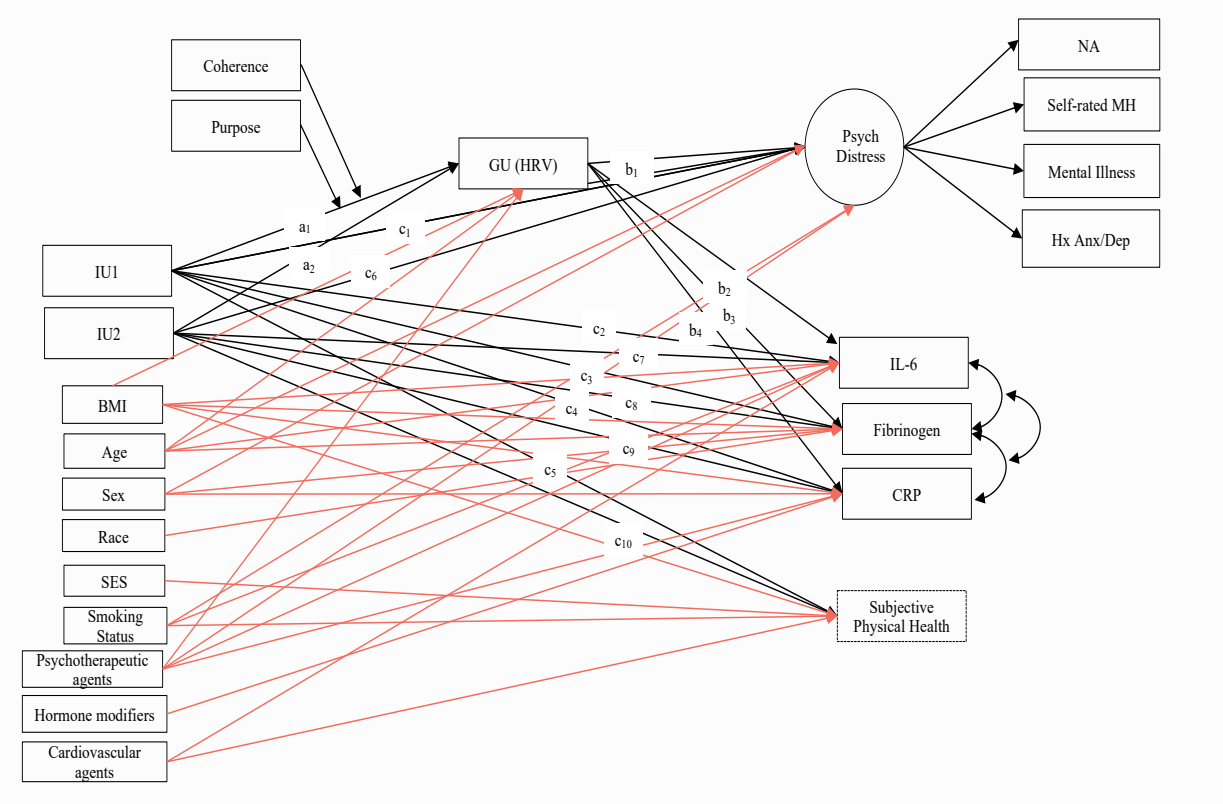

Figure 1. *Study 1a (MIDUS 2 & 3) SEM path model. Colored lines indicate significant paths between covariates and model variables. Black lines indicate paths tested in hypothesized SEM path models.*

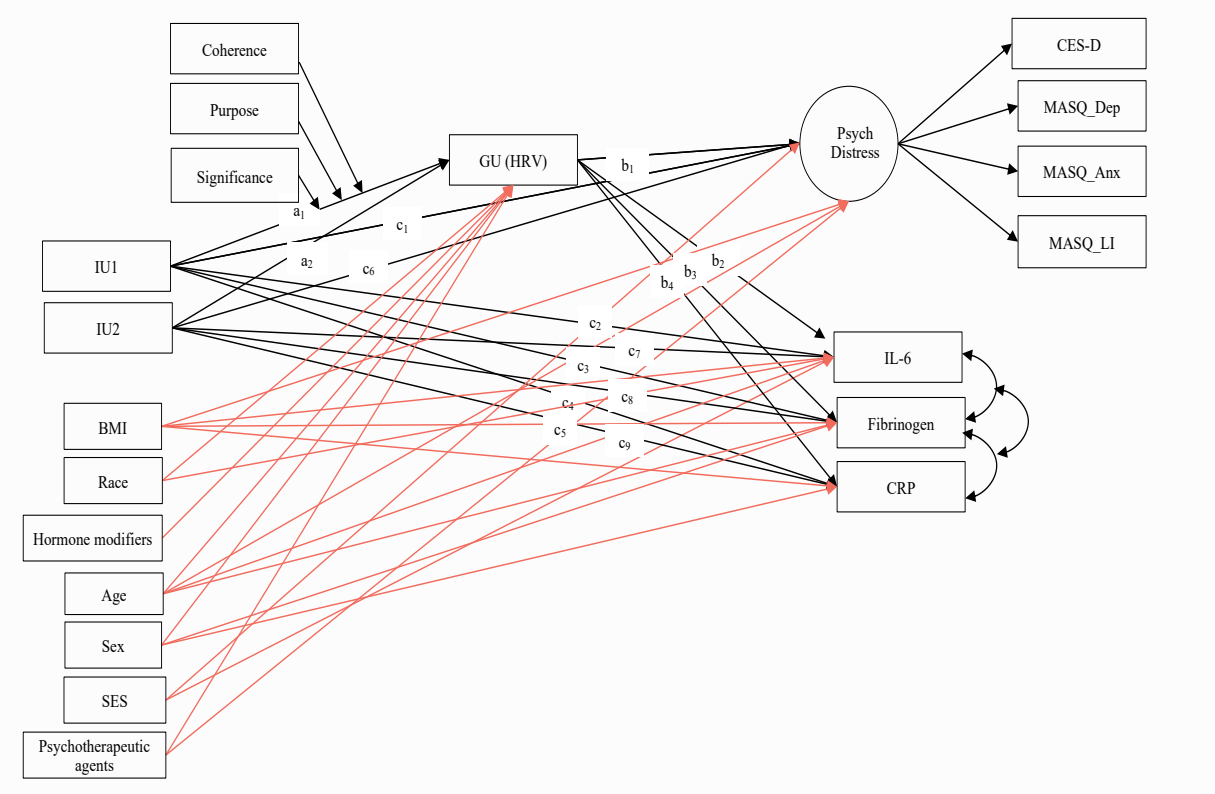

Figure 2. *Study 1b (MIDUS Refresher) SEM path model. Dotted lines indicate significant paths between covariates and model variables. Solid lines indicate paths tested in hypothesized SEM path models.*

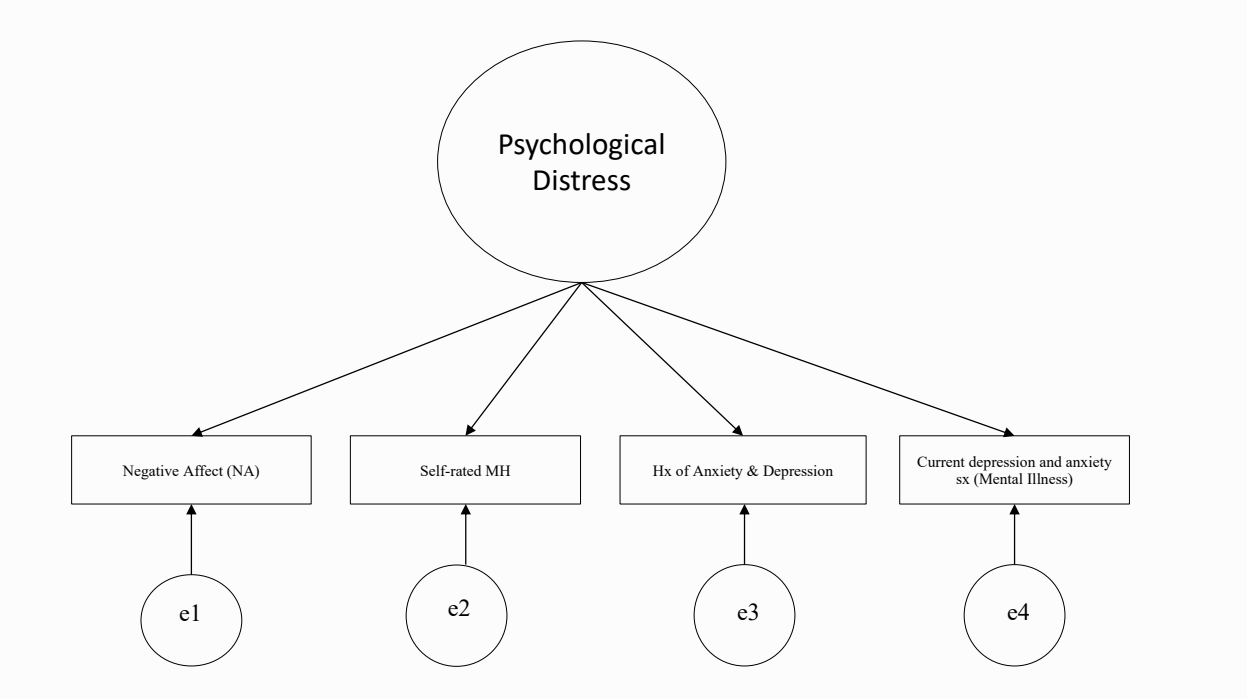

Figure 3. *Measurement model for psychological distress latent variables for Study 1a.*

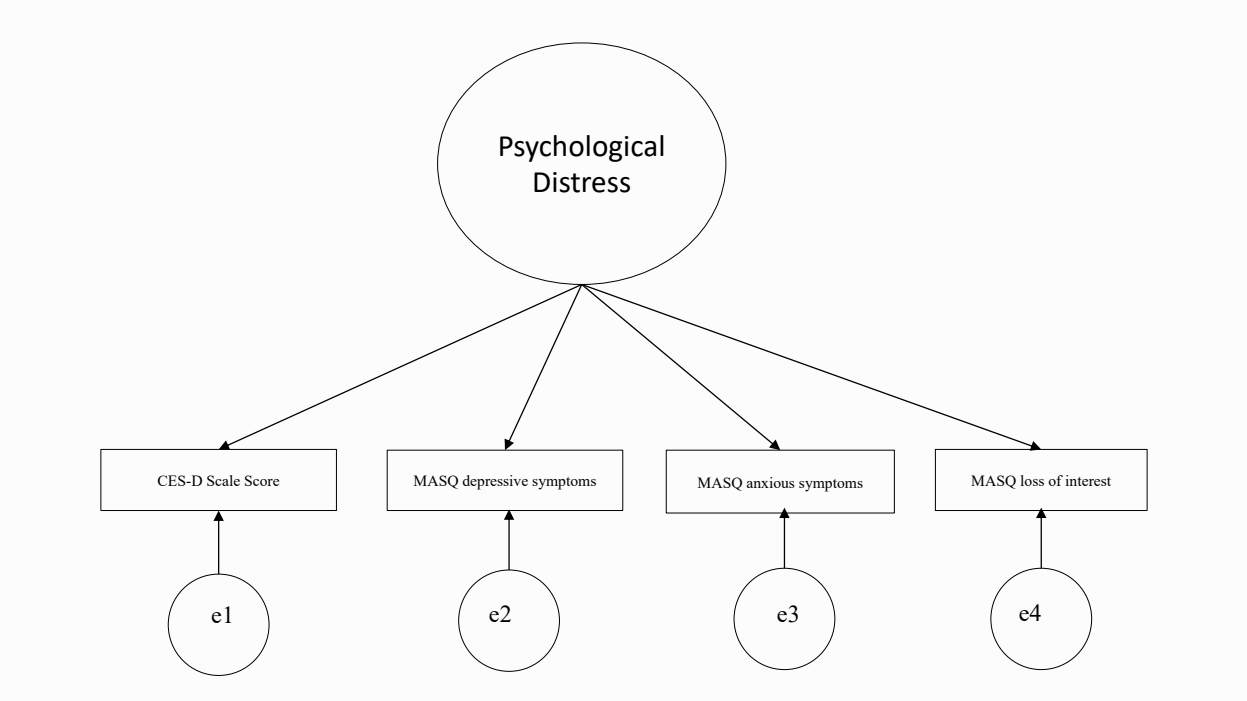

Figure 4. *Measurement model for psychological distress latent variables for Study 1b.*

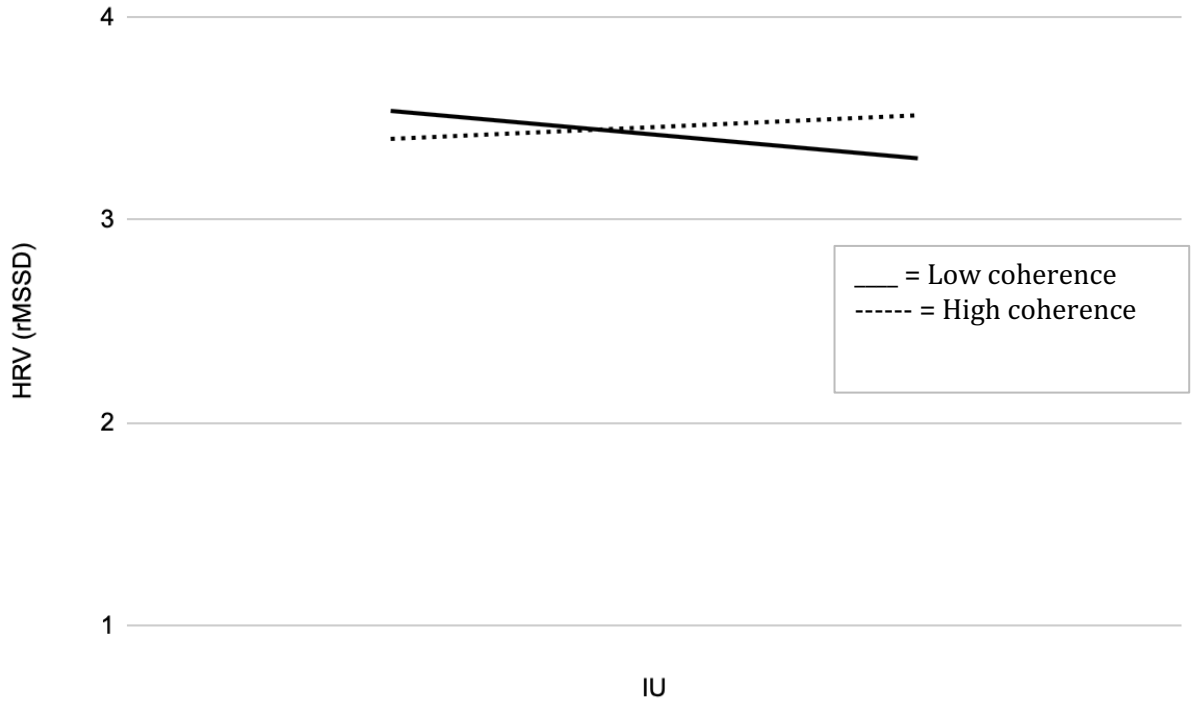

Figure 5. *Study 1a: The interaction of IU (item 2) and coherence predicting resting HRV (lnRMSSD).*

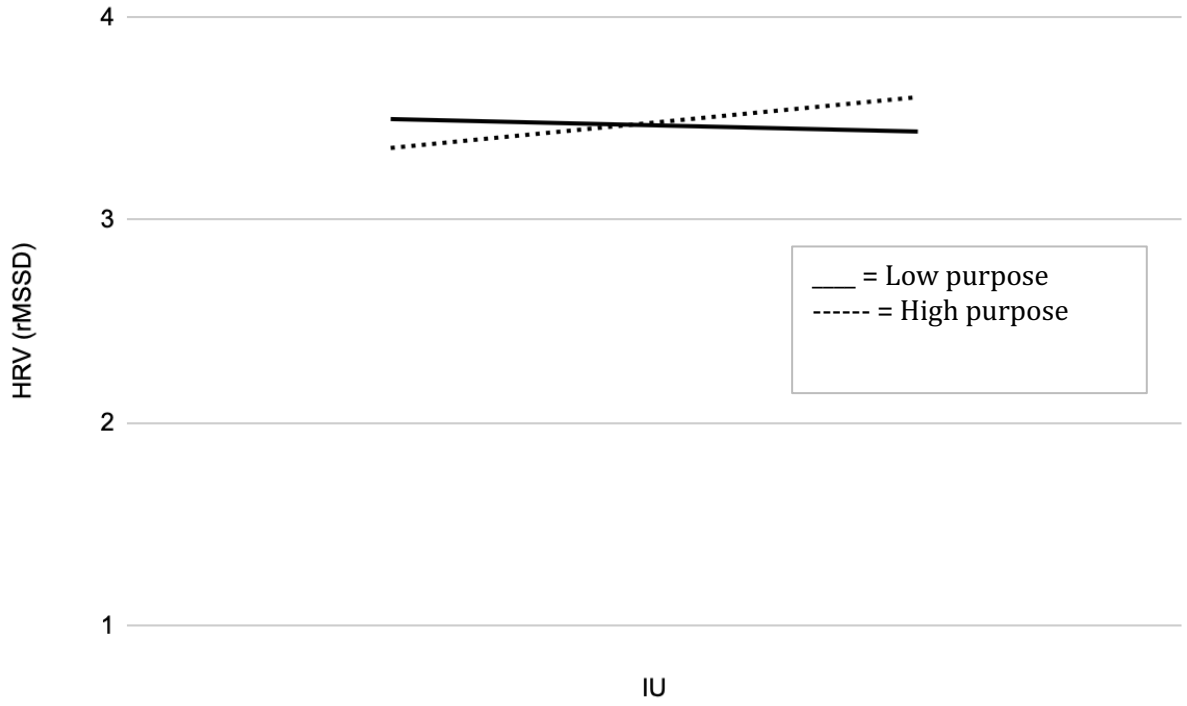

Figure 6. *Study 1a: The interaction of IU (item 1) and purpose predicting resting HRV (lnRMSSD).*

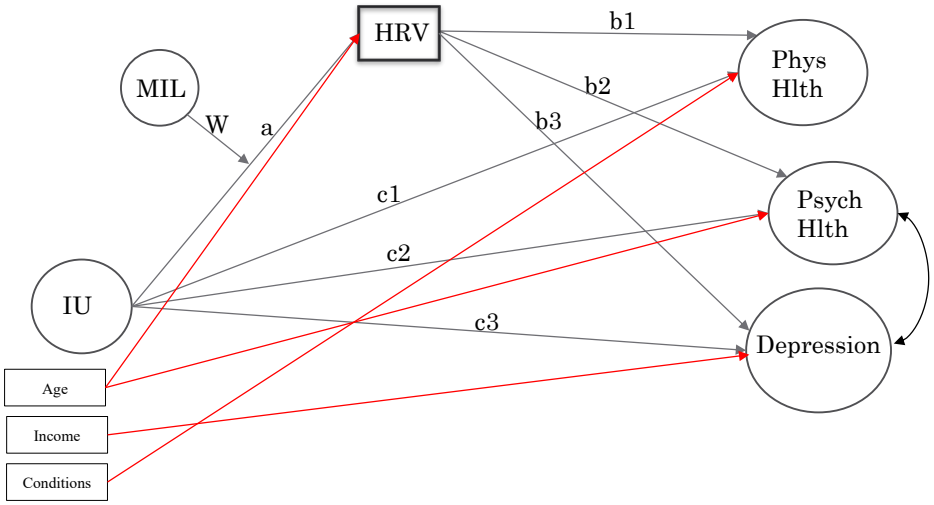

Figure 7. *Path model for Study 2 Hypotheses 1-8*

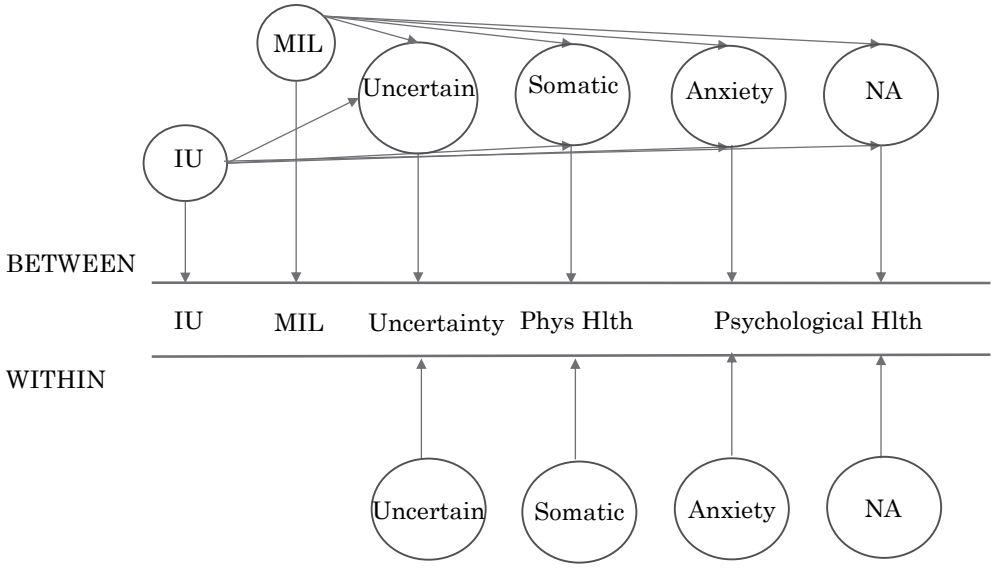

Figure 8. *Path model for Study 2 Hypotheses 9-10 Cross-level direct effects*

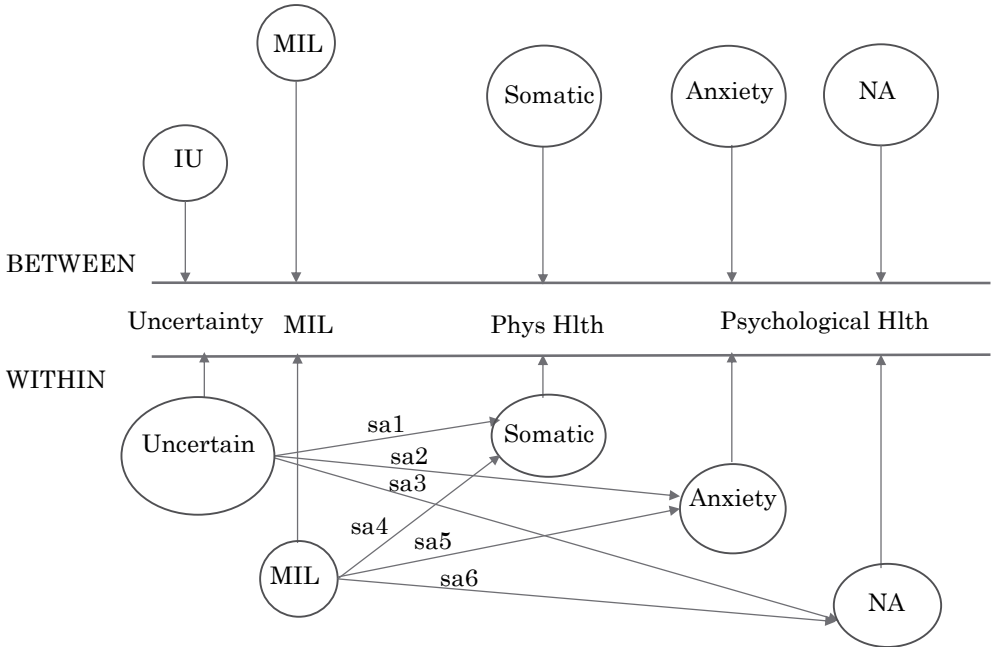

Figure 9. *Path model for Study 2 Hypotheses 11-12 Within-person direct effects where sa1-6 are random slopes.*

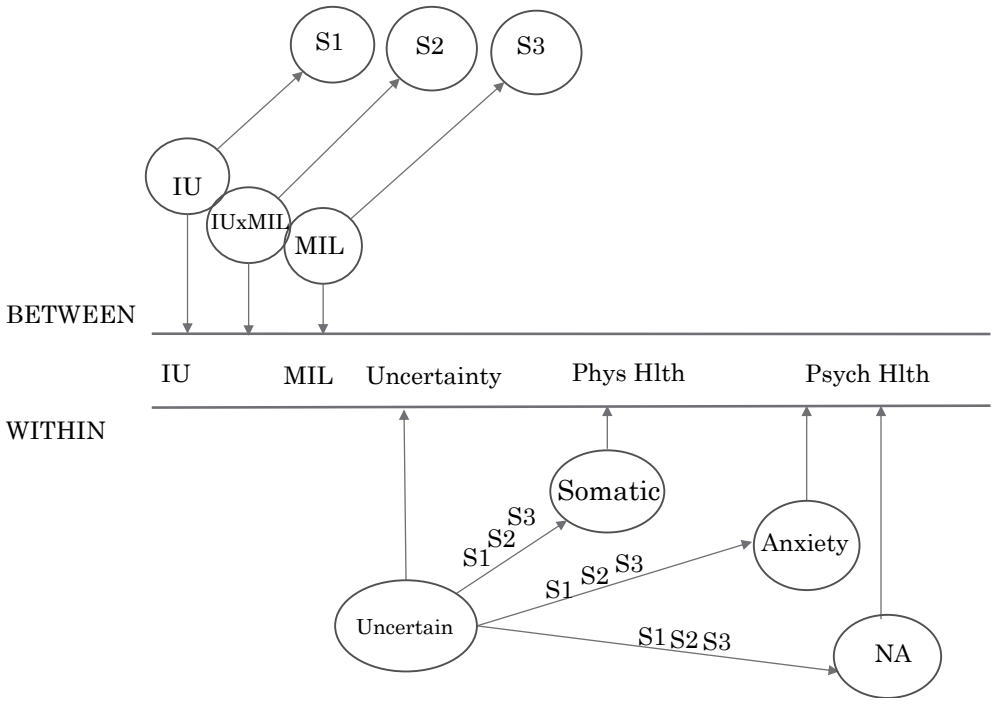

Figure 10. *Path model for Study 2 Hypotheses 13-15 RCP Moderation effects where S1-S3 are random latent slopes*

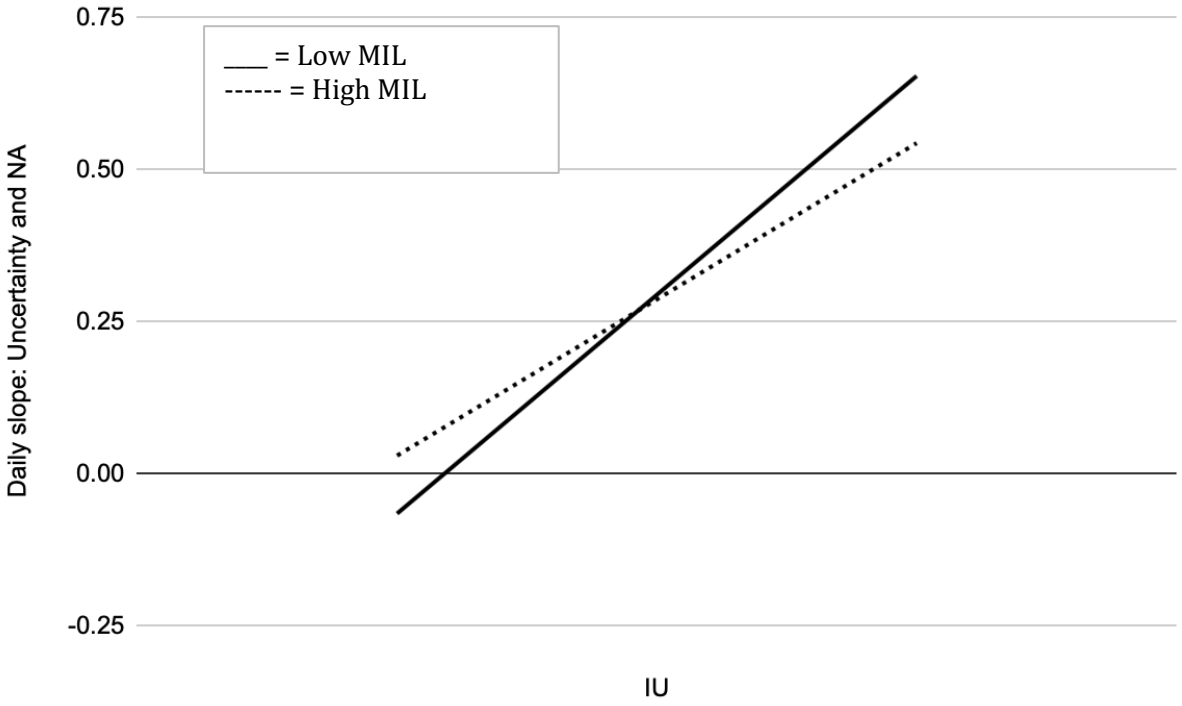

Figure 11. *Study 2: MILxIU moderating the slope of daily uncertainty-daily negative affect*

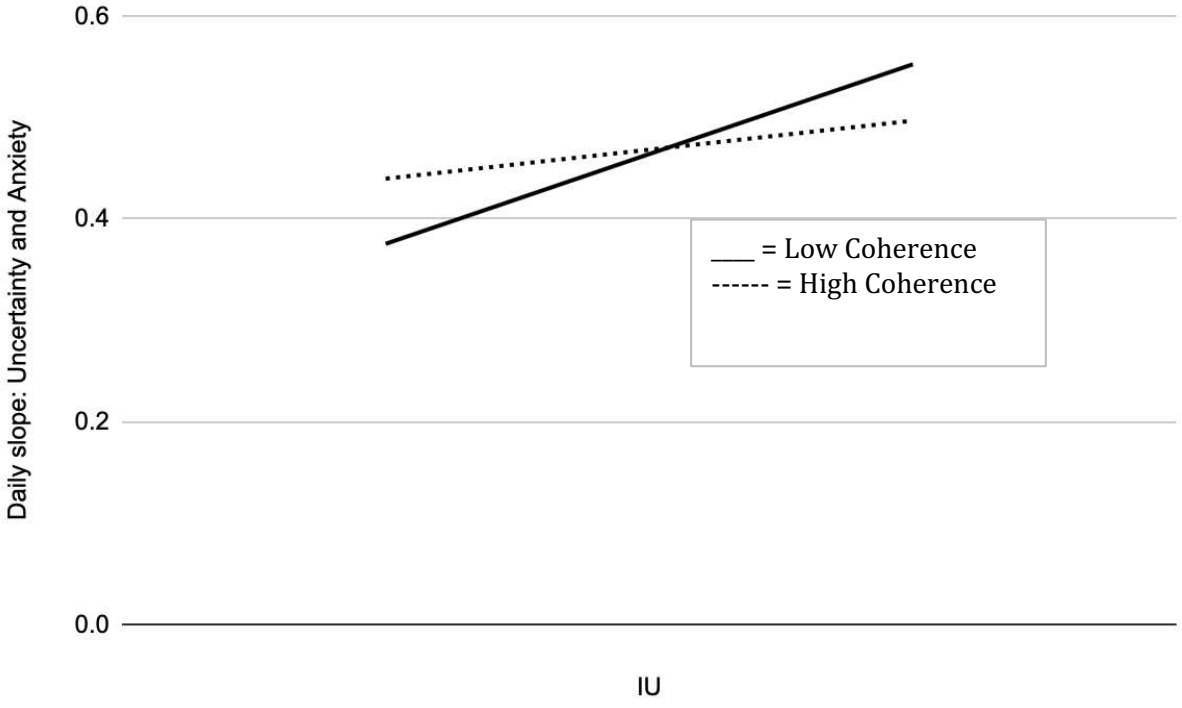

Figure 12. *Study 2: CoherencexIU moderating the slope of daily uncertainty-daily anxiety*

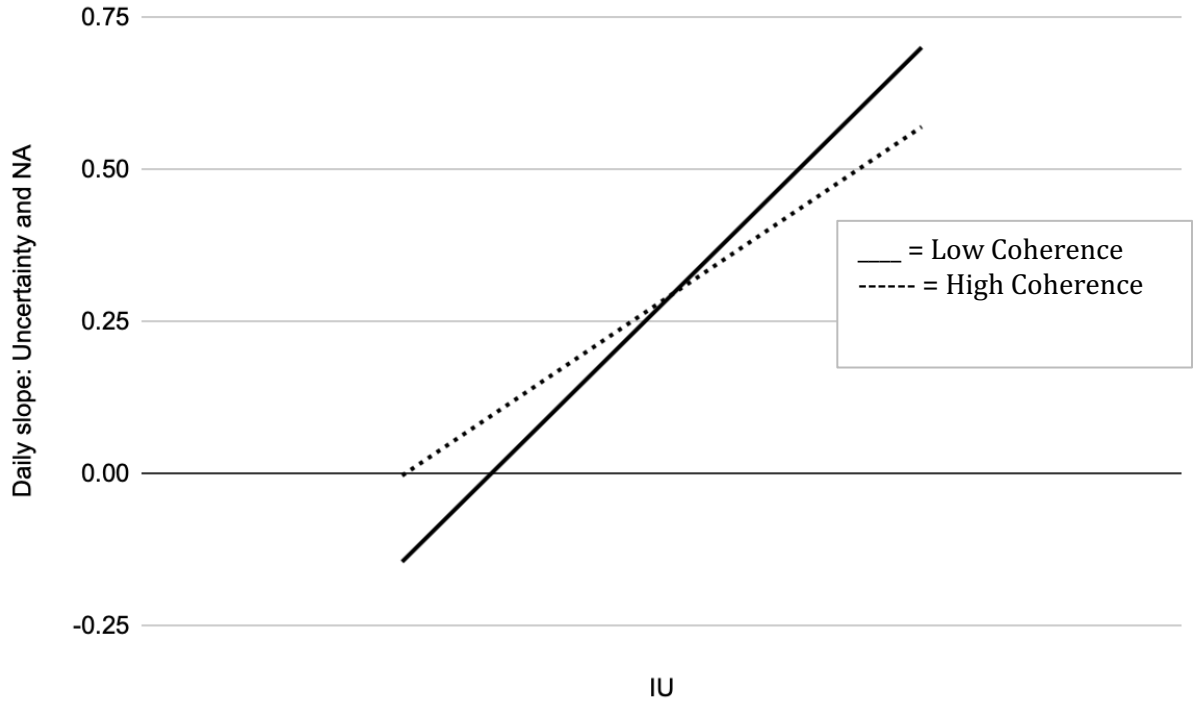

Figure 13. *Study 2: CoherencexIU moderating the slope of daily uncertainty-daily negative affect*

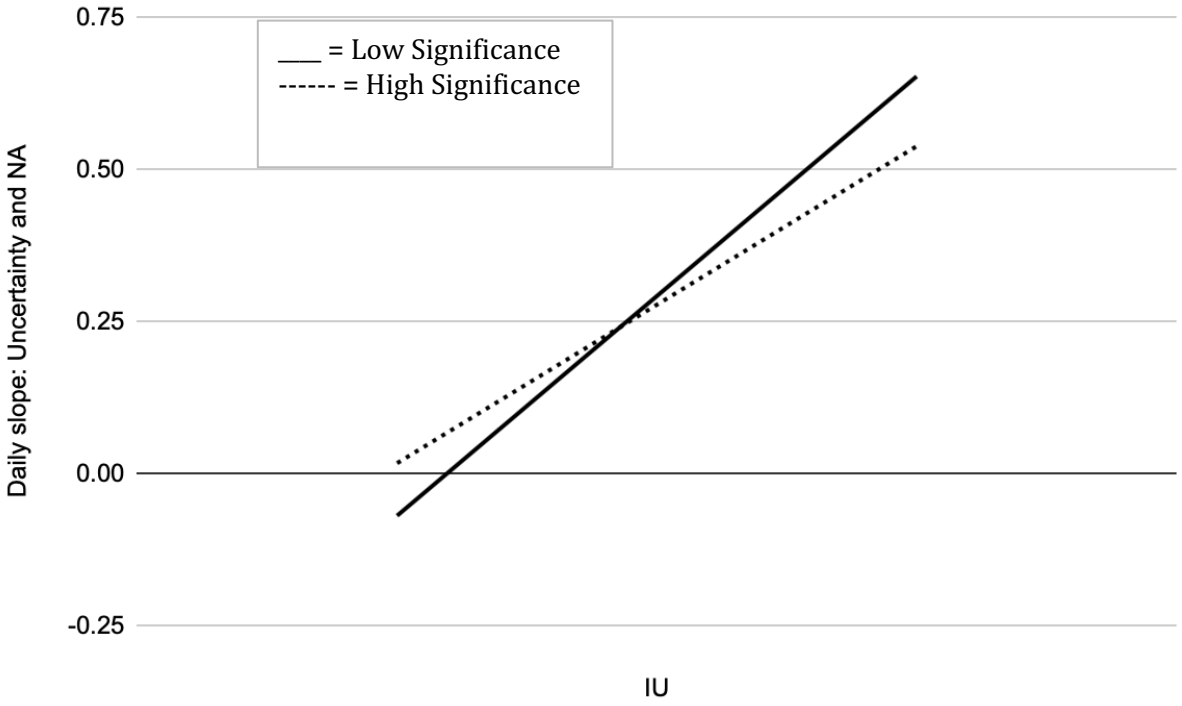

Figure 14. *Study 2: SignificancexIU moderating the slope of daily uncertainty-daily negative affect*

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APPENDICES

Appendix A: Study 1 Measures

Purpose in Life

The next set of items explores your well-being. Please indicate how strongly you agree or disagree with each of the following statements. (Note: only purpose items from the scale are included here)

	Agree Strongly (1)	Agree Somewhat (2)	Agree a little (3)	Neither agree nor disagree (4)	Disagree a little (5)	Disagree Somewhat (6)	Disagree Strongly (7)
I live life one day at a time and don't really think about the future.							
I have a sense of direction and purpose in life. (R)							
I don’t have a good sense of what it is I’m trying to accomplish in life.							
My daily activities often seem trivial and unimportant to me.							
I enjoy making plans for the future and working to make them							

a reality. (R)							
Some people wander aimlessly through life, but I am not one of them. (R)							
I sometimes feel as if I've done all there is to do in life.							

Negative Affect

During the past 30 days, how much of the time did you feel…

	All of the time (1)	Most of the time (2)	Some of the time (3)	A little of the time (4)	None of the time (5)
So sad nothing could cheer you up?					
Nervous?					
Restless or fidgety?					
Hopeless?					
That everything was an effort?					
Worthless?					
Lonely?					
Afraid?					
Jittery?					
Irritable?					
Ashamed?					
Upset?					
Angry?					
Frustrated?					

Depressed Affect

1. The next questions are about your mood. During the past 12 months, was there ever a time when you felt sad, blue, or depressed for two weeks or more in a row?
   - Yes
   - No

- I did not feel depressed because I was on anti-depressant medication
- Don't know/not sure
- Refused

2. Participants who responded yes were then asked, "Please think of the two-week period during the past 12 months when these feelings were worst. During that time, did the feelings of being sad, blue, or depressed usually last all day long, most of the day, about half the day, or less than half the day?
   - All day long
   - Most of the day
   - About half of the day
   - Less than half the day
   - Don't know/not sure
   - Refused

3. During the two weeks when these feelings were worst, how often did you feel this way, every day, almost every day, or less often than that?
   - Every day
   - Almost every day
   - Less often than that
   - Don't know/not sure
   - Refused

4. During those two weeks, did you…

	Yes	No
"lose interest in most things?"		
"feel more tired out or low on energy than is usual for you?"		
"lose your appetite?" or "appetite increased		
"have more trouble falling asleep than usual?"		
"have more trouble concentrating than usual?"		
"feel down on yourself, no good, or worthless?"		
"think a lot about death?"		

Anhedonia

1. During the past 12 months, was there ever a time lasting two weeks or more when you lost interest in most things like hobbies, work, or activities that usually give you pleasure?
   - Yes
   - No
   - I did not feel depressed because I was on anti-depressant medication
   - Don't know/not sure

- Refused

2. Participants who responded yes were then asked, “Please think of the two-week period during the past 12 months when you had the most complete loss of interest in things. During that time, did the feelings of being sad, blue, or depressed usually last all day long, most of the day, about half the day, or less than half the day?
   - All day long
   - Most of the day
   - About half of the day
   - Less than half the day
   - Don’t know/not sure
   - Refused

3. During the two weeks when these feelings were worst, how often did you feel this way, every day, almost every day, or less often than that?
   - Every day
   - Almost every day
   - Less often than that
   - Don’t know/not sure
   - Refused

4. During those two weeks, did you…

	Yes	No
“feel more tired out or low on energy than is usual for you?”		
“lose your appetite?” or “appetite increased		
“have more trouble falling asleep than usual?”		
“have more trouble concentrating than usual?”		
“feel down on yourself, no good, or worthless?” “		
“think a lot about death?”		

Generalized Anxiety

1. People differ a lot in how much they worry. Considering how things have been going in your life over the past 12 months, do you worry more than most people in the same situation, less than most people, or about the same as most people in the same situation?
2. Thinking about the past 12 months, did you worry: every day, just about every day, most days, about half the days, or less than half the days?
3. On days you worry, does the worry usually last all day long, most of the day, about half of the day, or less than half of the day?
4. Do you usually worry about one particular thing or more than one thing?
5. Do you ever have different worries on your mind at the same time?

6. Do you worry about things that are not likely to happen?
7. Do you worry about things that are not really serious?
8. How often is your worry so strong that you can't put it out of your mind no matter how hard you try: often, sometimes, rarely, or never?
9. How often do you find it difficult to control your worry: often, sometimes, rarely, or never?
10. Some people have physical reactions because of their worry. Thinking about the past 12 months, how often did you have each of the following reactions because of your worry? Include only physical reactions that might have been caused by your worry, not those that were caused by something else. "How often over the past 12 months did you experience the following:[SEP](response options: Most days; About half the days; Less than half the days; Never)
    A. "were restless because of your worry"
    B. "were keyed up, on edge, or had a lot of nervous energy"
    C. "were irritable because of your worry"
    D. "had trouble falling asleep"
    E. "had trouble staying asleep because of your worry"
    F. "had trouble keeping your mind on what you were doing"
    G. "had trouble remembering things because of your worry"
    H. "were low on energy"
    I. "tired easily because of your worry"
    J. "had sore or arching muscles because of tension"

11. How much does the worry interfere with your life or activities: a lot, some, a little, or not at all?

Panic attacks

1. During the past 12 months, did you ever have a spell or an attack when all of a sudden you felt frightened, anxious, or very uneasy, in a situation when most people would not be afraid or anxious?
2. During the past 12 months, did you ever have a spell or an attack when for no reason your heart suddenly began to race, you felt faint, or you couldn't catch your breath? When we say, 'for no reason,' we mean that it was NOT due to any physical cause, like a heart problem.
3. About how many attacks did you have in the past 12 months?
4. Did (this attack happen in a situation/ALL of these attacks happen in situations) when you were in danger or were the center of attention?[SEP]
5. "When you have attacks, does (or do)…" (response options: yes or no)
    A. "your heart pound"?
    B. "you have tightness, pain, or discomfort in your chest or stomach"
    C. "you sweat"
    D. "you tremble or shake"
    E. "you have hot flashes or chills"
    F. "you or things around you seem unreal"

Center for Epidemiological Studies Depression Inventory (CES-D)

Center for Epidemiologic Studies Depression Scale (CES-D), NIMH

Below is a list of the ways you might have felt or behaved. Please tell me how often you have felt this way during the past week.

	During the Past Week			
	Rarely or none of the time (less than 1 day)	Some or a little of the time (1-2 days)	Occasionally or a moderate amount of time (3-4 days)	Most or all of the time (5-7 days)
1. I was bothered by things that usually don't bother me.	☐	☐	☐	☐
2. I did not feel like eating; my appetite was poor.	☐	☐	☐	☐
3. I felt that I could not shake off the blues even with help from my family or friends.	☐	☐	☐	☐
4. I felt I was just as good as other people.	☐	☐	☐	☐
5. I had trouble keeping my mind on what I was doing.	☐	☐	☐	☐
6. I felt depressed.	☐	☐	☐	☐
7. I felt that everything I did was an effort.	☐	☐	☐	☐
8. I felt hopeful about the future.	☐	☐	☐	☐
9. I thought my life had been a failure.	☐	☐	☐	☐
10. I felt fearful.	☐	☐	☐	☐
11. My sleep was restless.	☐	☐	☐	☐
12. I was happy.	☐	☐	☐	☐
13. I talked less than usual.	☐	☐	☐	☐
14. I felt lonely.	☐	☐	☐	☐
15. People were unfriendly.	☐	☐	☐	☐
16. I enjoyed life.	☐	☐	☐	☐
17. I had crying spells.	☐	☐	☐	☐
18. I felt sad.	☐	☐	☐	☐
19. I felt that people dislike me.	☐	☐	☐	☐
20. I could not get "going."	☐	☐	☐	☐

Mood and Symptom Questionnaire (MASQ)

Read each item and then circle the number that best describes how much you have felt or experienced things this way during the past week, including today.

	Not at All (1)	A little bit (2)	Moderately (3)	Quite a bit (4)	Extremely (5)
1. Felt sad					
2. Startled easily					
3. Felt cheerful					
4. Felt afraid					
5. Felt discouraged					
6. Hands were shaky					
7. Felt optimistic					
8. Had diarrhea					
9. Felt worthless					
10. Felt really happy					
11. Felt nervous					
12. Felt depressed					
13. Was short of breath					
14. Felt uneasy					
15. Was proud of myself					
16. Had a lump in my throat					
17. Felt faint					
18. Felt unattractive					
19. Had hot or cold spells					
20. Had an upset stomach					
21. Felt like a failure					

22. Felt like I was having a lot of fun					
23. Blamed myself for a lot of things					
24. Hands were cold or sweaty					
25. Felt withdrawn from other people					
26. Felt keyed up, “on edge”					
27. Felt like I had a lot of energy					
28. Was trembling or shaking					
29. Felt inferior to others.					
30. Had trouble swallowing					
31. Felt like crying					
32. Was unable to relax					
33. Felt really slowed down.					
34. Was disappointed in myself.					
35. Felt nauseous					
36. Felt hopeless					
37. Felt dizzy or lightheaded					

38. Felt sluggish or tired					
39. Felt really “up” or lively					
40. Had pain in my chest					
41. Felt really bored					
42. Felt like I as choking					
43. Looked forward to things with enjoyment					
44. Muscles twitched or trembled					
45. Felt pessimistic about the future					
46. Had a very dry mouth					
47. Felt like I had a lot of interesting things to do.					
48. Was afraid I was going to die.					
49. Felt like I had accomplished a lot					
50. Felt like it took extra effort to get started					
51. Felt like nothing was very enjoyable					

52. Heart was racing or pounding					
53. Felt like I had a lot to look forward to					
54. Felt numbness or tingling in my body					
55. Felt tense or “high strung”					
56. Felt hopeful about the future					
57. Felt like there wasn’t anything interesting or fun to do					
58. Seemed to move quickly and easily					
59. Muscles were tense or sore					
60. Felt really good about myself					
61. Thought about death or suicide					
62. Had to urinate frequently					
63. Felt like I am a good person					
64. Felt guilty					

Study 2
Demographic Form

1. Gender
2. Marital status
3. Age
4. Ethnicity
5. Race
6. Who do you live with?
7. Do you have children? If yes, how many?
8. What is your highest level of education?
9. Do you work outside of home?
10. Are you currently employed?
11. What is your primary career?
12. What is your annual income?
13. If applicable, what is the highest level of education of your spouse?
14. If applicable, does your spouse work outside of home?
15. If applicable, what is your spouse's primary career?
16. Medical history
17. Checklist of medical conditions over past 12 months
18. How much do chronic conditions affect your daily life
19. Any prescription medications? List of medications
20. Any non-prescription medications? List of medications
21. Current smoker, alcohol use? (yes/no)

IUS-12

Please circle the number that best corresponds to how much you agree with each item:

	Not at all characteristic of me	**A little characteristic of me**	**Somewhat characteristic of me**	**Very characteristic of me**	**Entirely characteristic of me**
Unforeseen events upset me greatly.	1	2	3	4	5
It frustrates me not having all the information I need.	1	2	3	4	5
Uncertainty keeps me from living a full life.	1	2	3	4	5
One should always look ahead	1	2	3	4	5

so as to avoid surprises.					
A small unforeseen event can spoil everything, even with the best of planning.	1	2	3	4	5
When it's time to act, uncertainty paralyses me.	1	2	3	4	5
When I am uncertain I can't function very well.	1	2	3	4	5
I always want to know what the future has in store for me.	1	2	3	4	5
I can't stand being taken by surprise.	1	2	3	4	5
The smallest doubt can stop me from acting.	1	2	3	4	5
I should be able to organize everything in advance.	1	2	3	4	5
I must get away from all	1	2	3	4	5

uncertain situations.					

Three-dimensional Meaning in Life

Please read each of the following items carefully, thinking about how it relates to your life, and then indicate how true it is for you. Use the following scale to respond:

	1 Not at all true	**2**	**3**	**4 Somewhat true**	**5**	**6**	**7 Very true**
Most things happening in my life do make sense.	1	2	3	4	5	6	7
By and large, I am able to understand the world around me.	1	2	3	4	5	6	7
I can comprehend what my life is all about.	1	2	3	4	5	6	7
I can easily make sense of my life.	1	2	3	4	5	6	7
I pursue one or more big purposes in my life.	1	2	3	4	5	6	7
I am highly committed to certain core goals in my life.	1	2	3	4	5	6	7
I have a set of core goals that give my life a sense of direction.	1	2	3	4	5	6	7
My daily activities are consistent with a broader life purpose.	1	2	3	4	5	6	7
My life is full of value.	1	2	3	4	5	6	7
My personal existence is significant.	1	2	3	4	5	6	7

Every day I experience the sense that life is worth living.	1	2	3	4	5	6	7
My life is significant in the grand scheme of things.	1	2	3	4	5	6	7

Short-form health survey (SF-36)

1. In general, would you say your health is:
    - 1 - Excellent
    - 2 - Very good
    - 3 - Good
    - 4 - Fair
    - 5 - Poor
2. Compared to one year ago, how would you rate your health in general now?
    - 1 - Much better now than one year ago
    - 2 - Somewhat better now than one year ago
    - 3 - About the same
    - 4 - Somewhat worse now than one year ago
    - 5 - Much worse now than one year ago

The following items are about activities you might do during a typical day. Does **your health now limit you** in these activities? If so, how much?

	Yes, limited a lot (1)	Yes, limited a little(2)	No, not at all limited (3)
3. **Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports			
4. **Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf			
5. Lifting or carrying groceries			
6. Climbing **several** flights of stairs			
7. Climbing **one** flight of stairs			

8. Bending, kneeling, or stooping			
9. Walking **more than a mile**			
10. Walking **several blocks**			
11. Walking **one block**			
12. Bathing or dressing yourself			

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of your physical health**?

	Yes (1)	No (2)
13. Cut down the **amount of time** you spent on work or other activities		
14. **Accomplished less** than you would like		
15. Were limited in the **kind** of work or other activities		
16. Had **difficulty** performing the work or other activities (for example, it took extra effort)		

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	Yes (1)	No (2)
17. Cut down the **amount of time** you spent on work or other activities		
18. **Accomplished less** than you would like		
19. Didn't do work or other activities as **carefully** as usual		

20. During the **past 4 weeks**, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

- 1 - Not at all
- 2 - Slightly
- 3 - Moderately
- 4 - Quite a bit
- 5 - Extremely

21. How much bodily pain have you had during the past 4 weeks?
- 1 – None
- 2 - Very mild
- 3 – Mild
- 4 - Moderate
- 5 – Severe
- 6 - Very severe

22. During the **past 4 weeks**, how much did **pain** interfere with your normal work (including both work outside the home and housework)?
- 1 - Not at all
- 2 - A little bit
- 3 - Moderately
- 4 - Quite a bit
- 5 - Extremely

These questions are about how you feel and how things have been with you **during the past 4 weeks**. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the **past 4 weeks**..

	All of the time (1)	Most of the time (2)	A good bit of the time (3)	Some of the time (4)	A little of the time (5)	None of the time (6)
23. Did you feel full of pep?						
24. Have you been a very nervous person?						
25. Have you felt so down in the dumps that nothing could cheer you up?						
26. Have you felt calm and peaceful?						
27. Did you have a lot of energy?						

28. Have you felt downhearted and blue?						
29. Did you feel worn out?						
30. Have you been a happy person?						
31. Did you feel tired?						

32. During the **past 4 weeks**, how much of the time has **your physical health or emotional problems** interfered with your social activities (like visiting with friends, relatives, etc.)?

- 1 - All of the time
- 2 - Most of the time
- 3 - Some of the time
- 4 - A little of the time
- 5 - None of the time

How TRUE or FALSE is **each** of the following statements for you.

	Definitely true (1)	Mostly true (2)	Don't know (3)	Mostly false (4)	Definitely false (5)
33. I seem to get sick a little easier than other people					
34. I am as healthy as anybody I know					
35. I expect my health to get worse					
36. My health is excellent					