IS CONSISTENCY KEY? EXPLORING DAILY VARIABILITY IN STRESS, SELF-DISCLOSURE, MOOD, AND SLEEP AS PREDICTORS OF VACCINE RESPONSE

by

SARAH M. LYLE

(Under the Direction of Katherine B. Ehrlich)

ABSTRACT

Decades of research suggest that positive and negative psychosocial factors are associated with markers of physical health, including response to vaccination (Burns et al., 2003b; Uchino et al., 2020). Additionally, the variability or fluctuations within psychosocial experiences can serve as unique predictors for health (Eizenman et al., 1997; Ross et al., 2013). Findings from past research exploring the role of psychosocial experiences on adaptive immune function are mixed, and little work has explored how the variability within these experiences is associated with adaptive immune function (Jenkins et al., 2018). A sample of 100 adolescents and adults (66% Female, 93% White, M_{age} = 48.3, *SD* = 20.8, *Age Range* = 11 – 86 yrs.) received the influenza vaccine, provided pre- and post-vaccination blood samples (approximately one month apart), and reported on their daily experiences of stressful events, perceived stress, self-disclosure, perceived responsiveness, positive and negative mood, and sleep across seven days. Hierarchical linear regression was used to explore how (a) the average levels of each construct (i.e., a participant's mean value across all seven days) and (b) the

variability within each construct (i.e., a participant's standard deviation across all seven days) were associated with antibody production following vaccination. Contrary to our hypotheses, there were no associations between any of the average-level or variability predictors and antibody response at one month following vaccination for any of the constructs. Future research should focus on recruiting larger samples to further elucidate the influence of psychosocial experiences on antibody production and maintenance following vaccination.

INDEX WORDS: Vaccine response, adaptive immunity, antibody production, daily diary study, daily variability, psychosocial experiences, stress, perceived stress, self-disclosure, mood, positive affect, negative affect, sleep quality, sleep duration, physical health

IS CONSISTENCY KEY? EXPLORING DAILY VARIABILITY IN STRESS, SELF-DISCLOSURE, MOOD, AND SLEEP AS PREDICTORS OF VACCINE RESPONSE

by

SARAH M. LYLE

B.A., Ohio Northern University, 2013

M.S., Nova Southeastern University, 2017

A Dissertation Submitted to the Graduate Faculty of The University of Georgia in Partial Fulfillment of the Requirements for the Degree

DOCTOR OF PHILOSOPHY

ATHENS, GEORGIA

2022

© 2022

Sarah M. Lyle

All Rights Reserved

IS CONSISTENCY KEY? EXPLORING DAILY VARIABILITY IN STRESS, SELF-DISCLOSURE,

MOOD, AND SLEEP AS PREDICTORS OF VACCINE RESPONSE

by

SARAH M. LYLE

Major Professor:	Katherine B. Ehrlich
Committee:	Kalsea J. Koss
	Richard B. Slatcher
	Janet E. Frick

Electronic Version Approved:

Ron Walcott
Vice Provost for Graduate Education and Dean of the Graduate School
The University of Georgia
August 2022

DEDICATION

This dissertation is dedicated to my Grandma Lyle and my late grandparents, Grandpa Lyle and Grandma Stratton. I hope that all this “psycho-babble” is making you proud.

ACKNOWLEDGEMENTS

First, I would like to thank my major professor and mentor, Katie Ehrlich. This dissertation and my success as a scholar would not have been possible without your support. You nurtured my strengths and challenged me to grow in my weak areas. Thank you for never giving up on me and pushing me to become a stronger researcher, writer, mentor, and teacher. I am extremely grateful to have had such an encouraging mentor throughout the last five years, and I am looking forward to working with you throughout my career.

I would also like to extend my thanks to my committee members, Drs. Janet Frick, Richard Slatcher, and Kalsea Koss. I offer my sincere appreciation for your insight, feedback, and contributions to this dissertation project. Additionally, many thanks to my other professors who have helped guide my progress across the years. Thank you, Drs. Michelle vanDellen, Anne Shaffer, Kacy Morris, Stephen Miller, David Wright, Kandauda Wickrama, Jaime Tartar, Jonathan Banks, James Munoz, Phillip Zoladz, Megan Kraynock, and Kristie Payment.

I am also sincerely grateful to the children and adults who participated in this study, the many undergraduate students and Health and Development Lab members who helped screen and schedule these participants, the staff at the Clinical and Translational Research Unit, and Dr. Ted Ross and Michael Carlock at the Center for Vaccines and Immunology. A special thank you to Phuongtin Ta, Gabriella Ross, and

Loren Wray who helped me collect and organize this data. Additionally, I am grateful to Andrew Farkas, William Schiavone, and Benjamin Listyg for answering all my statistics questions throughout my time at UGA (you three are true blessings).

Most importantly, I wish to thank my emotional support system. To my “OG BB-YES” crew (Kelsey, Jack, Rose, Rebekah, Andrew, and Will)—thank you for the Trapeze dinners, craft nights, Sandy Creek dog park dates, and bonfire vent sessions. To my Athens “Framily” (Meghan, Dustin, Courtney, Richie, Kayla, and Michael)—thank you for adopting me into your chosen family. You’ve been a refuge from the stress of graduate school and taught me about loving myself and others unconditionally. To Kelsey Corallo, my lab twin and work-wife—thank you for your friendship. I wouldn’t have survived graduate school without our trashy tv/pizza roll dates and the countless hours we spent playing/snuggling with Phoebe and Eevee. To Alicia Gutlon—thank you for constantly supporting me during this dissertation period. You made sure that I had food to eat and the perfect song to listen (and dance) to during all of my much-needed writing breaks. You are the love of my life. Thank you for making my heart so happy. To my dad, mom, and sister—thank you for loving me through all the ups and downs of these past five years. I am grateful to God for giving me you as my family.

Finally, I want to acknowledge my students at Livingston Elementary School and Mifflin Middle School. I would not have pursued a PhD if it wasn’t for you. Thank you for inspiring me each and every day!

TABLE OF CONTENTS

Page

ACKNOWLEDGEMENTS v

LIST OF TABLES ix

LIST OF FIGURES x

CHAPTER

1 INTRODUCTION 1

Overview of the Immune System 2

Evidence Linking Psychosocial Experiences to Vaccine Response 8

Variability in Psychosocial Experiences 20

Current Study 24

2 METHODS 29

Participants 29

Procedures 30

Measures 31

Vaccination and HAI Titer Production 36

Data Analytic Plan 37

Power Analysis 39

3 RESULTS 42

Participant Demographics 42

Daily Survey Compliance 42
Psychosocial Variables 43
Other Daily Variables 43
Response to Vaccination 43
Intercorrelations Among Study Variables 44
Associations Between Psychosocial Variables and Vaccine Response 46
4 EXPLORATORY ANALYSES 63
Rationale 63
Predictions 65
Results 65
Conclusions 67
5 DISCUSSION 71
Limitations of the Current Study 73
Strengths of the Current Study 75
Future Directions 76
Conclusions 77
REFERENCES 78
APPENDICES
A Institutional Review Board Study Approval 107
B Daily Stress Inventory Item Selection 109
C List of Models 110
D Protocol of Power Analysis 111

LIST OF TABLES

Page

Table 1: Participant Demographics Split by Subgroup 48

Table 2: Psychosocial Variables 50

Table 3: Means and Standard Deviations of Daily Variables Split by Subgroup 51

Table 4: Antibody Values 52

Table 5: Correlation Matrix 53

Table 6: Associations Between Stress Constructs and Vaccine Response 59

Table 7: Associations Between Self-Disclosure Constructs and Vaccine Response 60

Table 8: Associations Between Mood Constructs and Vaccine Response 61

Table 9: Associations Between Sleep Constructs and Vaccine Response 62

Table 10: Age × Average Level Interaction Predicting Vaccine Response 69

Table 11: Age × Variability Interaction Predicting Vaccine Response 70

LIST OF FIGURES

Page

Figure 1: Variability Example 28

Figure 2: Recruitment and Enrollment Flowchart 40

Figure 3: Study Timeline 41

CHAPTER 1

INTRODUCTION

Negative psychosocial experiences across the lifespan are associated with an increased risk for adverse physical health outcomes, including cardiovascular diseases, diabetes, cancer, and early mortality (Cohen & Wills, 1985; Miller et al., 2011; Repetti et al., 2002; Shonkoff et al., 2012; Taylor et al., 1997). For instance, House, Landis, and Umberson (1988) showed that low-quantity and low-quality relationships are major risk factors for early mortality in their seminal paper. Similarly, a meta-analysis of over 70 studies provided additional evidence linking social isolation and loneliness to premature mortality (Holt-Lunstad et al., 2015). More recently, it was shown that the negative affect following daily stressors were associated with poor health outcomes 10 years later (Leger et al., 2018). Indeed, decades of research exploring a variety of stressors, such as low socioeconomic status (Chen & Miller, 2013; Claussen et al., 2003; Cohen et al., 2010; Galobardes et al., 2008), adverse childhood experiences (Danese et al., 2009; Felitti et al., 1998), experiences of discrimination (Assari et al., 2017; Lewis et al., 2014), and work-place stressors (Benthem de Grave et al., 2022) consistently shows that negative experiences are associated with long-term health and well-being.

The immune system has been identified as one possible biological mechanism linking psychosocial experiences to long-term health (Cohen & Herbert, 1996; Hayward et al., 2020; Jemmott & Locke, 1984; Miller et al., 2011; Muscatell, 2022; Segerstrom &

Miller, 2004; Shattuck, 2021). Specifically, psychosocial experiences have been shown to influence immune system function (Kiecolt-Glaser et al., 2002; Segerstrom & Miller, 2004), and these alterations in immune system function often precede the onset of many chronic diseases of aging (Chung et al., 2009; Duncan et al., 2003; Miller et al., 2011; Pearson et al., 2003).

1.1.1 Overview of the Immune System:

The purpose of the immune system is to protect our body against foreign invaders, such as bacteria and viruses (Cohen & Herbert, 1996; Parkin & Cohen, 2001). Two interacting divisions make up the immune system, including the innate immune system and the adaptive immune system (Hoebe et al., 2004; Parkin & Cohen, 2001), and the functioning of these divisions is susceptible to psychosocial influences (Cohen & Herbert, 1999; Dhabhar, 2014; Segerstrom & Miller, 2004).

1.1.1.1 Innate Immunity:

The innate immune system is our first line of defense and is non-specific, meaning that the cells of this system attack, neutralize, and destroy pathogens, including viruses and bacteria, that enter the body. This system is fast-acting and activates within seconds to minutes following the exposure to any foreign invader. In this system, cells called granulocytes are recruited to destroy the pathogens that have entered the body. Macrophages are one class of granulocytes, and these specialized cells are responsible for “eating” up any infected cell and recruiting chemical messengers called cytokines to the area of potential infection. The proliferation, or

influx, of macrophages and cytokines results in inflammation. Minor infections or injuries (e.g., paper cuts) could become deadly without this inflammatory system.

1.1.1.2 Adaptive Immunity:

The adaptive immune system is slower and more specific than the innate system. This system can take weeks to mount a full response. The adaptive system includes both cellular and humoral responses to pathogens. The cellular response directly combats infected cells by releasing T helper (Th) 1 cells. These T-cells recognize the cells in our body that have been compromised by a specific virus or bacteria and destroys them.

The humoral response, alternatively, develops new proteins to combat the pathogen that has entered the body. Specifically, Th2 cells stimulate B-cells to create antibodies. Following exposure to a pathogen, naïve B-cells recognize the invader (also known as the antigen). These cells record the shape of the antigen's surface proteins and respond by building an army of antibodies. Antibodies hold cellular memories for pathogens and circulate throughout the bloodstream, and if the body is exposed to that particular pathogen again, the immune system is equipped to eliminate it.

In addition to building antibodies for antigens that our body is naturally exposed to throughout life, we also build antibodies for antigens that we intentionally expose our bodies to (i.e., the antigens included in vaccines). Vaccines activate the adaptive immune system, and our body responds by producing antibodies in response to the vaccine. An increase in the number of circulating antibodies for a particular pathogen suggests increased immunity to that pathogen (Beyer et al., 2004).

1.1.1.3 Vaccine Paradigm:

Vaccine challenge studies are a convenient tool for researchers to use when studying the links between psychosocial experiences and immunity (Burns et al., 2003b; Burns & Gallagher 2010; Cohen et al., 2001; Madison et al., 2021; Pedersen et al., 2009; Phillips, 2011; Uchino et al., 2020; Vedhara, 2019). In this method, participants receive a vaccination and provide pre- and post-vaccination blood samples[1] (Burns & Gallagher, 2010), and researchers collect assessments of various psychosocial experiences through questionnaires, interviews, and observational paradigms (Burns & Gallagher, 2010; Corallo et al., 2022; O'Connor et al., 2015; Segerstrom et al., 2008). Several different vaccines have been used in vaccine paradigm studies, including the meningococcal vaccine, hepatitis A and B vaccines, rubella vaccine, human papillomavirus vaccine, pneumonia vaccine, typhoid vaccine, varicella zoster vaccine, tetanus vaccine, influenza vaccine, and most recently, the COVID vaccine (Brydon et al., 2009a, 2009b; Burns et al., 2002a, 2002b; Edwards et al., 2006; Gallagher et al., 2008a, 2008b, & 2022; Glaser et al., 2000; Irwin et al., 2011 & 2013; Li et al., 2007; Morag et al., 1998; Wu et al., 2017).

Some research groups who use vaccine paradigms are focused on innate immunity and measure markers of inflammation in the blood following vaccination (Brydon et al., 2009a & 2009b; Glaser et al., 2003; Tronkowski et al., 2004; Vedhara et al., 2002; Wong et al., 2013). For example, Segerstrom and colleagues (2008)

---

[1] In rare cases, pre-vaccine blood samples are not collected (for examples, see Burns et al., 2002b and Gallagher et al., 2022).

demonstrated that caregivers produced greater interleukin-6 (IL-6) following influenza vaccination than non-caregivers.

Vaccine challenge studies, however, are often used to explore how psychosocial experiences influence adaptive immunity. Antibody production following vaccination is an *in vivo* assessment of adaptive immune function (Burns & Gallagher 2010). This method is used to explore how psychosocial factors, such as stress, social support, and sleep, are associated with the antibody titers in the post-vaccine blood samples. The post-vaccination blood draw can occur days (Gallagher et al., 2008b; Vedhara et al., 1999), weeks (Burns et al., 2003a; Corallo et al., 2022; Gallagher et al., 2008a; Li et al., 2007; Miller et al., 2004; Vedhara et al., 1999), months (Burns et al., 2003a; Gallagher et al., 2008a; Kiecolt-Glaser et al., 1996; Miller et al., 2004; O'Connor et al., 2014b; Wong et al., 2013), or a year or more (Burns et al., 2002a; Irwin et al., 2013; Phillips et al., 2006) after the administration of the vaccine.

A variety of methods have been used to assess response to vaccination (Beyer et al., 2004). One approach is to classify individuals as responders or non-responders (for examples, see Afsar et al., 2009; Burns et al., 2003b; Glaser et al., 1998) by dividing participants into those people who demonstrated a two-fold increase in antibody titers to the pneumonia vaccine or a four-fold increase in antibody titers to the influenza vaccine (Gallagher et al., 2009b and Kiecolt-Glaser et al., 1996, respectively) and those who did not. An alternative approach is to classify individuals as seroprotected (Burns et al., 2002b; Talbot et al., 2015) by using clinically-relevant cut-off points to divide participants into those people who produced enough antibodies to be protected against

that virus (e.g., post-vaccination titers ≥ 1:40 for the influenza vaccine or ≥ 1:100 for the hepatitis B vaccine; Talbot et al., 2015 and Burns et al., 2002b, respectively) and those who did not. A third approach, albeit a less clinically-relevant one, is to divide participants into high- vs low-responders (Burns et al., 2002a; Marsland et al., 2001) by splitting participants at the median titer level within the sample. These three approaches yield dichotomous outcomes, and researchers either compare the different groups on their reports of psychosocial function (Burns et al., 2003b) or they use logistic regression to predict group membership from the reports of psychosocial functioning (Burns et al., 2002a).

An alternative to using dichotomous measures of vaccine response is to use a continuous measure to quantify antibody production following vaccination. Here, linear regression is used to examine the association between psychosocial reports and response to vaccination. Antibody titers are not normally distributed, and consequently, most researchers conduct $\log_{10}$, $\log_2$, or natural log transformations on the titer values collected from each blood sample (for examples, see Li et al., 2007; O'Connor et al., 2014b; Taylor et al., 2017). Researchers are usually interested in antibody growth or the change in antibodies from pre-vaccination to post-vaccination. One method of calculating this growth is to subtract pre-vaccination levels from post-vaccination levels (O'Connor et al., 2014b & 2015) and use this new value as the dependent variable in subsequent regression analyses. However, in most cases, regression analyses are conducted on the post-vaccine values while controlling for the pre-vaccine levels (Gallagher et al., 2008a, 2008b, & 2009a).

The body's ability to produce antibodies following vaccination depends greatly on a person's pre-vaccination antibody titer values. Therefore, rather than calculating change scores or controlling for participants' baseline antibody titers, Beyer and colleagues recommend that researchers correct for pre-vaccination levels and use this corrected value as the outcome variable in regressions (Beyer et al., 2004).

To date, studies linking psychosocial experiences and response to vaccination have produced mixed results. Some findings suggest that risk factors, such as stress and negative affect, are associated with diminished antibody response, and promotive factors, such as social support and positive affect, are associated with amplified antibody response (Afsar et al., 2009; Ayling et al., 2018; Brydon et al., 2009b; Gallagher et al., 2022; Glaser et al., 2000; Irwin et al., 2011, 2013; Li et al., 2007; Miller et al., 2004; O'Connor et al., 2014b; Petrie et al., 1995; Philips et al., 2005a; Pressman et al., 2005; Vedhara et al, 1999). However, growing evidence suggests that the link between these psychosocial experience and vaccine response is less straightforward than the field once thought. For example, results from some studies suggest that risk factors are associated with amplified responses, whereas promotive factors are associated with diminished responses, and several studies report no association at all (Burns et al., 2002a; Gallagher et al., 2008a & 2008b; Hallam et al., 2022; Li et al., 2007; Marsland et al., 2001; O'Conner et al., 2014b; Prather et al., 2012; Wong et el., 2013; Wu et al., 2017).

Evidence Linking Psychosocial Experiences to Vaccine Response

1.2.1 Psychosocial Risk Factors and Response to Vaccination

A large majority of the work linking psychosocial experiences and vaccine response has explored how stress-inducing experiences are associated with antibody production following vaccination. Researchers have focused on the effects of caregiving (Gallagher et al., 2009b; Glaser et al., 1998; Glaser et al., 2000; Kiecolt-Glaser et al., 1996; Vedhara et al., 1999), stressful life events (Gallagher et al., 2008a; Phillips et al., 2005a), perceived stress (Li et al., 2007; Miller et al., 2004), and negative mood (Marsland et al., 2001).

1.2.1.1. Chronic Caregiving Stress:

Some of the first work that linked stress to vaccine response compared caregivers to age-matched controls. This work has been conducted in populations of people serving as the primary caregiver for adults with dementia (Glaser et al., 2000; Kiecolt-Glaser et al., 1996; Segerstrom et al., 2008; Vedhara et al., 1999), adults with Alzheimer's disease (Glaser et al., 1998), adults with multiple sclerosis (Vedhara et al., 2002), and children with developmental disabilities (Gallagher et al., 2009a & 2009b).

Two studies using the influenza vaccine explored whether the stress associated with caregiving could influence who mounted a sufficient, or protective, response to at least one of the strains included in the vaccine one-month following vaccination (Glaser et al., 1998; Kiecolt-Glaser et al., 1996). The results from these studies suggest that elderly caregivers of spouses with dementia or Alzheimer's are less likely than age-matched controls to respond to the vaccine. Additionally, parents of children with

developmental disabilities produced fewer antibodies of a composite of all pneumonia serotypes one- and six-months following vaccination (Gallagher et al., 2009b) relative to controls. Collectively, results from these studies suggest that taking care of a sick loved one is negatively associated with response to vaccination.

There is mixed evidence regarding the robustness of these findings. In one example, elderly caregivers whose spouses had dementia had a poorer response to one of the A strains, but not the other A strain nor the B strain, one-month following influenza vaccination (Vedhara et al., 1999) than controls. Alternatively, Gallagher and colleagues (2009a) found that parents of children with developmental disabilities had a poorer response to the B strain, but neither A strain, one- and six-months following influenza vaccination.

Four studies reported that caregivers and controls did not differ in antibody production to the influenza vaccine or the pneumonia vaccine approximately one-month following vaccination (Glaser et al., 2000; Segerstrom et al., 2008; Vedhara et al., 2002; Wong et al., 2013). Two of these four studies collected follow-up measures three-months post vaccination. At this later time point, caregiving was not associated with influenza antibody response in elderly caregivers of spouses who have been diagnosed with Alzheimer’s, Parkinson’s, or stroke (Wong et al., 2013), but was associated with pneumonia antibody response in elderly caregivers of spouses with dementia (Glaser et al., 2000). This difference between caregivers and controls that emerged later for the pneumonia vaccine persisted at the six-month follow up mark (Glaser et al., 2000). Additionally, among elderly caregivers of spouses with dementia (but not age-matched

controls) negative repetitive thought was negatively associated with antibody production for one of the A strains and the B strain (Segerstrom et al., 2008) across a five-year study.

1.2.1.2. Stressful Life Events:

Past research has explored how other stressful life events might predict vaccine response. Several of these studies used Linden's Life Events Scale for Students (Linden, 1984) to capture the total number of negative life events a person experienced over the previous year and that person's accumulated stress across all stress events (i.e., a weighted life event score, which factors in both the number and severity of the stressors). These two concepts, although related, provide unique information. For instance, two people could experience the same stressor, such as a car accident, but experience vastly different amounts of stress following the stressor. One person may leave the accident relatively unharmed, whereas another person may face months of physical therapy and financial stress. Alternatively, one person may experience several negative life events, but these events result in very little stress, collectively. In contrast, another person may only experience a few major life events, but these events lead to huge disruptions in their life.

The number of stressful life events and the weighted life event score have been explored as two unique predictors of vaccine response, and evidence is mixed regarding which characterization of stress is the best predictor of vaccine response. For example, the number of life events a person reported experiencing was negatively associated with post-vaccine titer values for the meningococcal C serotype and the influenza B

strain (but not the meningococcal A serotype or either of the influenza A strains) five-weeks following vaccination in young adults (Phillips et al., 2005a). Five months following vaccination, weighted life event scores were negatively associated with antibody production of the B influenza strain, but neither of the two A strains or the meningococcal serotypes (Phillips et al., 2005a).

Three additional studies suggest that the link between negative life events and vaccine response may look different at earlier time points than at later time points following vaccination. For example, Burns et al. (2002b) assessed whether the weighted life event score predicted seroprotection status in two groups of participants: (a) young adults who had been vaccinated within the previous year, and (b) young adults who had been vaccinated over a year ago. They found no association between weighted life event scores and the likelihood of being seroprotected following hepatitis B vaccine for participants who had been vaccinated within the last year, but weighted life event scores were negatively associated with seroprotection status among participants who were vaccinated over a year ago. Gallagher et al. (2008a) reported that neither the number of negative life events nor the weighted life event score were associated with hepatitis A titer values four weeks following vaccination in young adults, but the expected link emerged at the 18-week follow up. Finally, Burns et al. (2003b) found that young adults classified as responders to the influenza vaccine five weeks following vaccination surprisingly reported more negative life events than those who were classified as non-responders, but this association reversed at the five-month follow-up, such that responders reported fewer negative life events than non-responders.

Two studies explored the links between other kinds of negative life events and antibody production (Jabaaij et al., 1993; Phillips et al., 2006). Daily hassles were negatively associated with hepatitis B vaccine response seven months following vaccination in a sample of medical students (Jabaaij et al., 1993). Similarly, bereavement, a particularly salient stressful event, was negatively associated with one A strain and the B strain of the influenza vaccine in a sample of older adults (Phillips et al., 2006), but weighted life event scores were not associated with antibody response in this same study (Phillips et al., 2006).

Four studies in young adults and youth did not find associations between exposure to negative life events and response to the pneumococcal vaccine, the meningitis vaccine, and the hepatitis B vaccine (Burns et al., 2002a; Gallagher et al., 2008a & 2008b; Marsland et al., 2001; O'Conner et al., 2014), and one study found that exposure to negative life stressors was positively associated with antibody response to the hepatitis B vaccine in a sample of young adults (Petry et al., 1991).

1.2.1.3. Perceived Stress:

Perceived stress has also been explored as a potential factor that predicts vaccine response. Perceived stress is a person's general thoughts and feelings about the level of stress they are experiencing at any given moment (whether tied to specific life events or not; Cohen et al., 1983). Glaser et al. (1992) found that medical students who responded to the hepatitis B vaccine following the first injection reported less perceived stress than students who did not respond to the vaccine until after the second or third injection. Burns et al. (2002a) showed that higher levels of perceived stress were

associated with a greater likelihood of being classified as a low responder to the meningitis vaccine after one month in a sample of young adults. Hayney et al. (2014)[2] found that lower perceived stress was linked to a greater likelihood of being seroprotected three weeks following influenza vaccination in older adults. Moreover, perceived stress was negatively associated with antibody production following tetanus vaccination in adulthood (Li et al., 2007) and influenza vaccination in young adulthood (Miller et al., 2004; Pressman et al., 2005).

Two studies suggested that perceived stress was not associated with vaccine response one month following vaccination but reported statistically significant links at later time points (Sacadura-Leite et al., 2014; Talbot et al., 2015). Despite the null effect at one-month post-vaccination, Talbot et al. (2015) reported that lower perceived stress was associated with a greater likelihood of being seroprotected eight months following vaccination for one of the B strains in the influenza vaccine (but not the two A strains or the other B strain) in older adults. Likewise, Sacadura-Leite et al. (2014) reported that higher perceived stress at baseline was associated with a greater likelihood that a person's titer values for the two A strains (but not the B strain) would decline at the six-month follow up in a sample of hospital nurses.

Two additional studies exploring the link between perceived stress and vaccine response produced perplexing findings. Burns et al. (2003b) found that young adults who were seroprotected five weeks following influenza vaccination reported higher

[2] This research group collected antibodies through nasal secretions (not blood), and they used a more stringent cut-off point to divide their participants into responders and nonresponses. Normally, the responder cut-off is defined as $\geq$ 1:40, but Hayney et al., (2014) used $\geq$ 1:160.

perceived stress at baseline, but young adults who were seroprotected five-months following vaccination reported lower baseline perceived stress. These results were only significant for one of the A strains, and stress was not associated with seroprotection for any of the other strains at either time point (Burns et al., 2003b). In a second example, Corallo et al. (2022) reported a positive link between emotional distress (a composite of perceived stress, loneliness, and depressive symptoms) and influenza antibody production for one of the A strains, but not the other strains in a sample of adolescents.

Finally, six additional studies found no evidence for a link between perceived stress and response to vaccination for the influenza vaccine in younger and older adults, pneumonia vaccine in young adults, hepatitis B vaccine in younger and midlife adults, and human papillomavirus vaccine in young adults (Gallagher et al., 2009b; Hallam et al., 2022; Marsland et al., 2001; Moynihan et al., 2004; Prather et al., 2012; Taylor et al., 2017; Wu et al., 2017).

***1.2.1.4. Negative Affect**:*

Negative affect, or a measure how a person experiences negative emotions, has been shown to influence short- and long-term health outcomes (Leger et al., 2018; Watson, 1988) and has been explored as a psychosocial factor that might influence response to vaccination. For instance, trait negative affect was negatively associated with hepatitis B antibody levels in young adults, such that higher levels of negative affect were linked with a lower antibody response (Marsland et al., 2001), but five studies failed to find this association between negative affect and response to the pneumonia vaccine in young adults, influenza vaccine in younger and older adults, and

COVID-19 vaccine across adulthood (Ayling et al., 2018; Gleeson et al., 1996; Hallam et al., 2022; Moynihan et al., 2004; Pressman et al., 2005).

1.2.2. Psychosocial Promotive Factors and Response to Vaccination

Relative to the number of studies that have explored stress and other risk factors, there are far fewer studies that explore how promotive factors, such as positive relationship quality and satisfaction, social support, or positive affect, are linked to response to vaccination.

1.2.2.1. Relationship Quality and Satisfaction

Relationship satisfaction and high-quality interactions have been shown to influence antibody production (O'Connor et al., 2015; Phillips et al., 2006). Among married or cohabiting people, self-reported relationship satisfaction, or the amount of contentment a person reported, was positively associated with antibody production one month following influenza vaccination for one of the A strains, but not the other strains in older adults (Phillips et al., 2006). Among children, observed mother-child relationship quality was positively associated with antibody production at one month following the meningitis vaccination for one of the four serogroups (O'Connor et al., 2015).

1.2.2.2. Social Support

Structural and functional aspects of social support appear to be associated with response to vaccination (Uchino et al., 2020), although the findings are mixed. Pressman et al. (2005) found a positive link between network size (structural support) and antibody production one and four months following influenza vaccine for one of the A strains, but not the other A strain nor the B strain in a sample of young adults.

Additionally, Gallagher et al. (2008b) reported a positive link between functional social support (e.g., extent to which you have people in your life who listen to you, who help you, and who you spend time with) and one of the five serotypes included in the pneumonia vaccine (but not the other four serotypes) five days following vaccination in young adults.

Functional social support was positively associated with antibody production five weeks and five months following influenza vaccination for one of the A strains (but not the other A strain or B strain), but it was not associated with antibody production to the meningococcal vaccine at the five-week or five-month follow-up in young adults (Phillips et al., 2005a). Similarly, Gallagher et al. (2008a) found a positive link between number of friends (structural support) and pneumonia vaccine response four weeks following vaccination (but not at the 18-week follow-up) in young adults, but it was not associated with antibody production to the hepatitis A vaccine (Gallagher et al., 2008a).

However, results from several studies do not support the notion that social support is beneficial to antibody production. In one study, social support was curiously associated with a poorer response to influenza vaccine three weeks post-vaccination in older adults (Moynihan et al., 2004), and social support was not associated with response to vaccination in various other studies in younger and older adults (Gallagher et al., 2009b; Li et al., 2007; Phillips et al., 2006; Wong et el., 2013). For example, Glaser et al. (1992) found that functional support was not associated with whether a young adult responded to the hepatitis B vaccine following the first injection (i.e., early responder) rather than the second or third injection (late responders).

1.2.2.3. Self-Disclosure and Perceived Responsiveness

Self-disclosure and perceived responsiveness are two distinct factors that help set the stage for social support to occur within ongoing relationships (Clark & Reis, 1988; Laurenceau et al., 1998; Reis & Patrick, 1996). Self-disclosure is the act of sharing facts, thoughts, or feelings with another person, whereas perceived responsiveness is the extent to which that other person listened to you and accepted you (Clark & Reis, 1988; Laurenceau et al., 1998; Reis & Patrick, 1996).

There has been little work exploring the roles of self-disclosure and perceived responsiveness in predicting response to vaccination, but there is a growing body of literature that links these constructs to health more broadly (Frattaroli, 2006; Stanton et el., 2019b). Self-reported self-disclosure has been linked to fewer doctor visits (Greenberg et al., 1996), lower asthma-related gene expression (Imami et al., 2019), and better sleep (Kane et al., 2013). Similarly, perceived responsiveness has been linked with better health behaviors (Britton et al., 2019; Dooley et al., 2018), lower salivary cortisol (Slatcher et al., 2015), and a lower risk for mortality (Alonso-Gerres et al, 2020).

Other studies have experimentally manipulated self-disclosure. In these studies, participants are randomly assigned into a self-disclosure group (e.g., they engage in self-disclosure through speeches, writing, or group discussions) or a control group. Experimental self-disclosure has been linked with lower inflammation (Booth et al., 1997; Bower et al., 2003), fewer physical health symptoms (Gallant & Lafreniere, 2003; Gidron et al., 2002), and lower blood-pressure (Beckwith McGuire et al., 2005).

Two experiments have explored how self-disclosure is associated with antibody production following vaccination, and they produced conflicting results. Petrie et al. (1995) reported that primarily White medical students who disclosed their trauma in a writing intervention mounted a higher antibody response four and six months following hepatitis B vaccination, relative to controls. However, Stetler et al. (2006) found that Black adults who disclosed their trauma related to discrimination in a similar writing intervention mounted a lower antibody response one and three months following influenza vaccination for the two A strains in the vaccine (but not the B strain) relative to controls.

In a large meta-analysis of over one hundred studies, Frattaroli (2006) concluded that experimental self-disclosure was beneficial for mental and physical health; and therefore, the results by Stetler et al (2006) were surprising. However, as Stetler and colleagues (2006) point out, their experiment differed in a major way from most studies that manipulate self-disclosure. In many prior studies, participants were requested to write about a traumatic event from their past, whereas in Stetler et al's (2006) study, the participants were requested to write about the trauma associated with discrimination, which is often an ongoing stressor. These researchers also noted that within the disclosure group, participants who attributed their experiences of discrimination to a specific cause (e.g., systemic racism) mounted a better response to the vaccine than participants who failed to attribute their experiences to something specific. Perhaps the effects of experimental self-disclosure on health are different depending on these contextual factors.

One contextual factor that could potentially influence how self-disclosure influences health, including response to vaccination, is the extent to which a person engages in self-disclosure during their everyday life. However, there have not been any studies that have explored the role of self-reported self-disclosure and perceived responsiveness on antibody production following vaccination.

1.2.2.4. Positive Affect

Positive affect, or a measure of how a person experiences positive emotions, has been linked to better health outcomes (Pressman & Cohen, 2005), and a small number of studies have explored whether positive affect can similarly influence response to vaccination. Indeed, higher positive affect was associated with being classified as a “high” rather than a “low” responder to the hepatitis B vaccine in young adults (Marsland et al., 2006) and was positively associated with influenza antibody production at four- and 16-weeks following vaccination for one of the A strains, but none of the other strains in the vaccine older adults (Ayling et al., 2018). One study suggested that positive affect was not associated with influenza antibody response in older adults (Moynihan et al., 2004).

1.2.3. Sleep and Response to Vaccination

An emerging line of work has explored how sleep and other health behaviors might influence vaccine response. Experimental studies (i.e., studies that manipulate sleep duration) suggest that partial or total sleep deprivation on the day prior to, or day of, vaccination can negatively influence antibody production (Benedict et al., 2012; Lange et al., 2003, & 2011; Speigel et al., 2002). Similarly, college students with

insomnia, a sleep disorder that is characterized by sleep disruptions, produced fewer antibodies relative to healthy controls, and night shift workers mounted a diminished meningococcal antibody response relative to day workers (Ruiz et al., 2020; Taylor et al., 2017).

Results from studies that measure naturally occurring sleep in normative samples (i.e., participants wear actigraphy watches to measure how much sleep they get or they report on their sleep using sleep diaries or questionnaires) also support the notion that sleep is associated with response to vaccination. For instance, actigraphy-derived sleep duration measured for the week surrounding hepatitis B vaccination was positively associated with antibody production (Prather et al., 2012), and self-reported sleep duration was positively associated with influenza antibody production following vaccination (Prather et al., 2021). However, in both of these studies, self-reported sleep quality was unrelated to antibody production (Prather et al., 2012 & 2021). Findings from one additional study suggested that self-reported sleep quality was not associated with response to the pneumonia vaccine (Gallagher et al., 2009b).

Variability in Psychosocial Experiences

As noted, there is mixed evidence in the literature regarding the extent to which both positive and negative psychosocial experiences predict vaccine response. In the majority of these past studies, researchers would rely on a single measure of their construct of interest (e.g., a one-time assessment of perceived stress that represents the average amount of stress that a person experienced over the prior month). However, psychosocial experiences are not static and can change or fluctuate over time,

and a one-time assessment may not capture the complexity that is associated with those experiences. A more nuanced approach would explore how variations in these experiences might be associated with vaccine response.

1.3.1. Yearly Experiences and Response to Vaccination

There is a growing interest in investigating how year-to-year changes in psychosocial experiences are related to vaccine response (Kohut et al., 2012; Lyle et al., in prep; Segerstrom et al., 2008; 2012). In one impressive study, Segerstrom and colleagues (2012) tracked a large cohort of older adults across seven years and found an association between changes in distress and antibody production. Specifically, participants mounted higher antibody responses following vaccination in the years in which they experienced lower than average distress. However, this finding was only significant among participants who also reported higher than average levels of physical activity, suggesting that the links between stress and response to vaccination may vary depending on different lifestyle factors.

1.3.2. Daily Experiences and Response to Vaccination

Diary and ecological momentary assessment studies are the gold standard methods for exploring research questions related to a person's daily experiences (Bolger & Laurenceau 2013), and few research groups have used these methods to explore the link between psychosocial experiences and vaccine response (Ayling et al., 2018; Jenkins et al., 2018; Miller et al., 2004; Prather et al., 2012; Pressman et al., 2005). In almost all of these studies, the daily measures were aggregated to create an average score, which

does not utilize these daily designs to their full potential. Only two studies capitalized on the repeated nature of the daily diary design (Jenkins et al., 2018; Miller et al., 2004)

In one example, Miller and colleagues (2004) collected 14-days of diary assessment and explored whether the average level of stress across all 14 days was associated with antibody production, and they attempted to identify whether there were particular days in which the link between stress and vaccine response was stronger or weaker. Results from this study suggested that averaged perceived stress across the study period was negatively associated with influenza antibody values for one of the A strains (but no other strains) one and four months following vaccination, and the strongest links between daily stress and vaccine response occurred on day-8 through day-10 following vaccination (Miller et al., 2004).

In another example, Jenkins and colleagues (2018) collected 13 days of diary assessments to explore the role of daily fluctuations in positive and negative affect in predicting antibody production (Jenkins et al., 2018). For each participant, these researchers calculated the mean, representing the participant's average value, and the standard deviation, representing the participant's within-person variability, in positive and negative affect across all 13 days. Although there were no main effects of the average positive or negative affect scores or the variability in positive affect on vaccine response, variability in negative affect was negatively associated with influenza antibody production. In other words, participants who experienced greater fluctuations in their negative affect across the study period showed a diminished response to vaccination. Additionally, there was an interaction between average positive affect and variability in

positive affect, such that among individuals with high average levels of positive affect, there was a negative association between variability in positive affect and antibody response, suggesting that variability in positive affect was only detrimental for antibody production when the person had high average levels of positive affect. These results suggest that exploring the variability within daily experiences might provide unique insights into the complexities surrounding the role of daily experiences and vaccine response. See Figure 1 for a visual of three different people who have the same mean values but differ in their variability.

1.3.3. Evidence Linking Variability to Health and Well-Being

Unpredictability in experiences may serve as a unique stressor that can influence health and well-being across the lifespan (Kulman et al., 2017; Liu & Fisher, 2022). For example, children who grew up in unpredictable environments (e.g., frequent moves, disruptions to parental employment) were more likely to engage in substance use as teens than children who had more predictable or stable lives (Doom et al., 2016). In addition to unpredictability in these major life events, the unpredictability in a child's every day experiences has been linked to health. For example, infants whose mothers engaged in more unpredictable behaviors during a 10-minute observed parent-child play task exhibited a blunted cortisol response following vaccination (Noroña-Zhou et al., 2019).

Similarly, the variability in psychosocial experiences from day-to-day or week-to-week has been associated well-being (Eizenman et al., 1997; Kernis et al., 1993). Variability in mood has been negatively associated with life satisfaction, depressive

symptoms, and self-reported health (Chan et al., 2015, 2016; Gruber et al., 2013; Hardy & Segerstrom, 2017). Fluctuations in relationship satisfaction and perceived partner commitment can predict later break-up status (Arriaga, 2001; Arriaga et al., 2006). Greater variability in worry and experiences of negative life events, such as discrimination, have been associated with poorer health behaviors, including substance use and sleep, respectively (Bustamante et al., 2020; Fuller-Rowell et al., 2021; Shadur et al., 2015).

Variability in psychosocial experiences and variability in sleep have also been associated with physical health outcomes. Fluctuations in self-esteem were associated with arterial stiffness, an early warning sign for atherosclerosis (Ross et al., 2013), and fluctuations in perceived control and life satisfaction were associated with mortality status (Boehm et al., 2015; Eizenman et al., 1997). Additionally, variability in bedtime was associated with higher TNF-α (Okun et al., 2011). The current study seeks to build upon this prior work by investigating how variability in daily stress, self-disclosure, perceived responsiveness, mood, and sleep might uniquely predict antibody response following vaccination.

Current Study

1.4.1. Current Study Overview

The present study uses a vaccine challenge to explore how psychosocial factors and sleep influence immune system function. Past research suggests that negative psychosocial factors, including stress and negative affect, are linked with diminished response to vaccination (Pedersen et al., 2009), and positive psychosocial factors,

including social support and positive affect, are linked with enhanced response to vaccination (Uchino et al., 2020). Furthermore, sleep has been examined as a particularly important health behavior that can influence vaccine response (Prather et al., 2012 & 2021). The majority of this past work has assessed these research questions in cross-sectional designs, and therefore, they are limited in their ability to answer more complex questions regarding how the variability or fluctuations in these risk and promotive factors might relate to vaccine response. By examining the daily variation of these experiences, this study can advance our understanding of how these factors relate to immune function. Specifically, by utilizing daily diaries, we can replicate prior work by exploring how average levels of risk and promotive factors influence antibody production. Additionally, a daily diary design allows us to build upon that work by assessing whether variability in those factors predict antibody production.

In this study, a sample of youth and adults completed two surveys every day for seven consecutive days following influenza vaccination. In the morning survey, participants reported on their mood and their sleep quantity and quality. In the evening survey, participants reported on their mood, experiences with a variety of stressors, and any instances of self-disclosure. Additionally, we collected important covariates (i.e., substance use and physical activity) to further clarify the unique influences of stress, self-disclosure, mood, and sleep on vaccine response.

1.4.2. Current Hypotheses

Research regarding how psychosocial factors influence adaptive immune function has yielded mixed results. Some studies report strong associations between

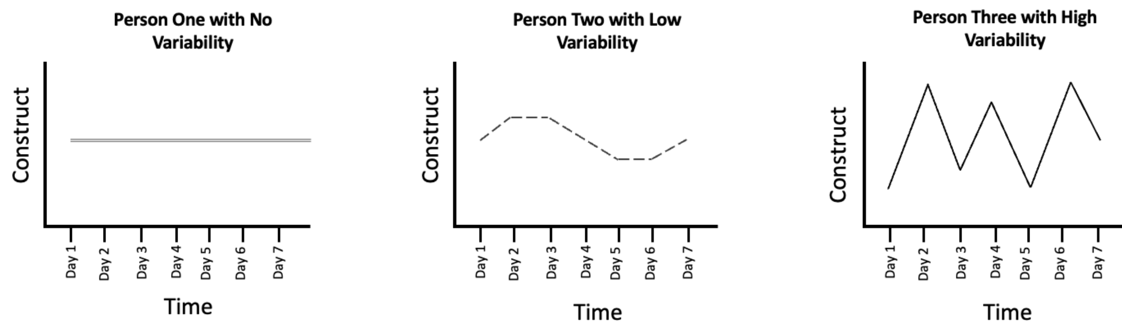
psychosocial experiences and antibody production, while other studies report no associations between these experiences and response to vaccination. Therefore, the first goal of the current study was to evaluate the associations between average levels of risk and promotive factors on vaccine response. To calculate a person's average level for each construct, I calculated the mean of all seven days of data collection. I predicted that antibody production following vaccination would be negatively associated with number of stressors, accumulated stress, and negative mood, and it would be positively associated with self-disclosure, perceived responsiveness, positive mood, sleep duration, and sleep quality.

The second goal of the current study was to investigate the role of daily variations in risk and promotive factors as predictors of vaccine response. To calculate a person's variability within each construct, I calculated the standard deviation across all seven days of data collection, which has been a commonly used method across different kinds of psychosocial constructs (Boehm et al., 2015; Gruber et al 2013; Hardy & Segerstrom et al., 2017, Jenkins et al., 2018; Mezick et al., 2009, Okun et al., 2011; Ross et al., 2013). In light of evidence linking variability in psychosocial factors to health-relevant outcomes, I hypothesized that the variability in daily experiences of stress, self-disclosure, perceived responsiveness, mood, and sleep would be negatively associated with antibody production following vaccination, such that people who have more variability in their daily experiences will have a diminished vaccine response.

I also ran a series of exploratory analyses investigating whether any of these associations varied as a function of age. More information regarding the rationale for these analyses and my hypotheses can be found in chapter 4.

Figure 1

Variability Example



Note. This figure depicts three hypothetical people who all have the same average value for a given construct across the seven days, but they differ on the amount of variability that they exhibited across the study period. Person One has no variability, Person Two has low variability, and Person Three has high variability.

CHAPTER 2

METHODS

Participants:

Participants were recruited via email from a larger longitudinal study exploring the links between psychosocial experiences and vaccine response. (Participants were drawn from the 2021 – 2022 cohort.) Adults and children's legal guardian completed an initial screening phone call to review inclusion and exclusion criteria. Participants were eligible if they were at least 10 years old, were an English-speaking resident of the Athens area, were willing to receive the flu vaccine as an injection, were willing to undergo at least two blood draws across four weeks, and were in good general health. Participants were ineligible if they were immunocompromised, allergic to any component of the vaccine, diagnosed with any severe cognitive impairments, or if they weighed under 110 lbs. (for adult participants). Additionally, participants were ineligible if they had presented any flu-like symptoms in the past four weeks or had recently received or were planning to receive a health intervention that could alter their immune system (e.g., recent or planned vaccinations) during the study period.

Following the initial screening call, all eligible and enrolled participants of the larger study were contacted via email and informed about the current daily survey study. Adults and the legal guardian of youth under 18 yrs. provided informed consent to participate in the daily survey study. When a legal guardian provided informed

consent, I contacted the adolescent via email and text message to obtain assent. Although 152 participants (68.4% Female, 89.5% White, M_{age} = 46.0, *SD* = 20.7, *Age Range* = 11 – 86 yrs.) agreed to participate in the daily survey study, only 100 participants (66% Female, 93% White, M_{age} = 48.3, *SD* = 20.8, *Age Range* = 11 – 86 yrs.) were included in the current study because they completed at least five of the seven morning surveys and five of the seven evening surveys (i.e., 70% of the total diary entries). I selected this threshold following the recommendation of Griffiths et al., (2021). Twenty-eight participants who agreed to participate did not complete any diary entries, and 24 participants completed fewer than 70% of the diary entries. For a flowchart regarding the recruitment and enrollment procedures, see Figure 2.

Procedures:

All participants completed at least two study visits at UGA's Clinical and Translational Research Unit (CTRU) and were asked to complete seven days of at-home surveys on their computer or phone. At the first visit, a trained phlebotomist drew a sample of participants' blood (adults provided a 97.5-mL sample, and adolescents provided a 30-mL sample), and then a registered nurse administered the quadrivalent influenza vaccine (FluZone™, Sanofi Pasteur, Inc., Swiftwater, PA, USA). Approximately one month later (M_{days} = 28.6, *SD* = 1.68, *Range* = 25 – 35 days), participants returned to the CTRU and provided a second blood sample (adults provided a 75-mL sample, and adolescents provided a 27.5-mL sample).

Beginning the day after their first visit, all participants were asked to complete online morning and evening surveys for seven consecutive days. The morning survey

assessed sleep from the previous night and current mood, and the evening survey assessed current mood and experiences of stress and self-disclosure throughout the day. The surveys also captured potential control variables, including physical activity and substance use. Participants were instructed to complete the morning survey within an hour of waking up and the evening survey within an hour of going to bed. All morning surveys were completed between 4:00am and 1:00pm, and all evening surveys were completed between 6:00pm and 3:00am. For a visual depiction of the procedures and timeline for this study, see Figure 3.

All methods and materials were approved by the University of Georgia's (UGA) Institutional Review Board (see Appendix A for the study approval form). Participants were compensated with a $25 Amazon e-Voucher for completing any portion of the daily surveys and an additional $15 for completing at least 80% of the daily surveys. Participants were also compensated up to $100 at the CTRU for receiving their vaccination and participating in additional procedures for the larger study.

Measures:

***Demographics**:*

Participant demographics were collected during the first visit at the CTRU, including age in years, biological sex assigned at birth (0 = female and 1 = male), race (0 = White and 1 = Non-White), and body mass index (BMI). These variables were used as covariates because they have been shown to influence response to vaccination (Haralambieva et al., 2014; Kurupati et al., 2016; Zimmerman & Curtis, 2019). Older individuals tend to produce fewer antibodies following vaccination relative to younger

individuals, males produce fewer antibodies than females, and people with higher BMI produce fewer antibodies than people with lower BMI (Zimmerman & Curtis, 2019). Additionally, there is some evidence that race is associated with antibody production (Haralambieva et al., 2014; Kurupati et al., 2016).

Daily Variables of Interest:

Stress. Participants reported their exposure to daily stress using an adapted version of the Daily Stress Inventory (Brantley et al., 1987). Our study team selected 17 stressors common to both adults and youth (see Appendix B for the complete list of items and the items we selected). Every evening, participants were instructed to rate events on a scale from 0 = *this event did not occur*, 1 = *this event occurred but it was not stressful,* to 7 = *this event occurred, and it caused me to panic*. Example items include: "Had a confrontation with a friend," "Was embarrassed," and "Feared illness/physical discomfort." I derived two variables from our stressor inventory (a) Number of unique stressors experienced, and (b) Amount of accumulated stress.

To calculate the number of unique stressors experienced each day, I counted the number of items in which a participant responded with 1-7 on the scale (the values that indicate an event occurred). Higher scores indicate that the participant experienced a greater number of unique stressors that day. To calculate the amount of accumulated stress experienced each day, I summed the person's responses across all 17 items, with higher scores indicating more accumulated stress on that day.

For both stress constructs, I calculated the mean across all seven days and recorded the variability (i.e., standard deviation). Therefore, each participant received

scores for their average number of unique stressors, variability in the number of unique stressors, average level of accumulated stress, and variability in accumulated stress, across the seven days of diary collection.

Self-Disclosure and Perceived Responsiveness. Every evening, participants were instructed to reflect on the most meaningful conversation they had during the day and respond to six items that assessed self-disclosure and perceived responsiveness. These items included, “Extent to which you talked about facts/information,” “Extent to which you talked about your thoughts,” “Extent to which you talked about your feelings,” “Extent to which the person you were talking to really listened to what you were saying,” “Extent to which the person was responsive to what you were saying,” and “Degree to which you feel accepted by that person.” The participants were asked to respond on a scale from 1 = *not at all* to 5 = *extremely* for each prompt. This measure yielded two constructs: (a) amount disclosed, and (b) perceived responsiveness. These items were adapted from other self-disclosure and intimacy measures used in the past (Laurenceau et al., 1998). Researchers have used similar measures with adults (Kane et al., 2014), and this exact measure was used in a sample of youth (Imami et al., 2019).

To assess the amount of information disclosed, I calculated the mean of the first three items. Higher scores indicate that the participant disclosed more information each day. To assess perceived responsiveness, I calculated the mean of the last three items. Higher scores indicate more responsiveness each day.

First, I calculated the average score across the seven days for amount disclosed and perceived responsiveness. Then, I recorded the variability in the amount disclosed

and perceived responsiveness across all seven days. Therefore, each participant received scores for their mean level of self-disclosure, variability in self-disclosure, mean level of perceived responsiveness, and variability in perceived responsiveness experienced across the seven days of diary collection.

Mood. Every morning and evening, participants completed a condensed version of the Positive and Negative Affect Schedule (PANAS; Watson et al., 1988). Participants responded on a scale from 1 = *not at all* to 5 = *extremely* regarding the extent to which they feel different emotions. For each day, I computed a Positive Affect Index by taking the mean of the five positively valenced items (i.e., happy, excited, relaxed, hopeful, and inspired) collected in the evening questionnaire. Higher scores indicate more positive affect. I also computed a Negative Affect Index by taking the mean of the five negatively valenced items (i.e., mad, sad, nervous, distressed, and irritable) collected from the evening questionnaire. Higher scores indicate more negative affect.

First, I computed the mean of the Positive Affect Index and the Negative Affect Index across all seven days. Additionally, I recorded the variability in positive and negative mood across the seven days. Therefore, each participant received scores for their mean level of positive mood, variability in positive mood, mean level of negative mood, and variability in negative mood experienced across the diary period.

Sleep. Each morning, participants reported their sleep duration and quality from the previous night. To assess sleep duration, participants reported the time they went to bed the prior night, how many minutes it took them to fall asleep, and the time they woke up in the morning. I calculated sleep duration by taking the difference between

when a participant went to bed and when they woke up and then subtracted the number of minutes it took them to fall asleep. Higher scores indicate a longer sleep duration each day. Participants also reported their overall sleep quality on a scale from 1 = *very bad* to 4 = *very good.* These items were derived from the Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989) and have been used in prior daily diary work related to sleep and vaccine response (e.g., Miller et al., 2004; Prather et al., 2021).

For both sleep constructs, I calculated the mean across all seven days and recorded the variability. Therefore, each participant received scores for their mean level of sleep duration, variability in sleep duration, mean level of sleep quality, and variability in sleep quality across the seven days of diary collection.

Other Daily Variables:

Physical Activity. Every evening, participants reported how many minutes they participated in physical activity during the day (e.g., brisk walking, jogging, bicycling, playing sports, or exercising). I calculated the mean of all seven days to yield an average physical activity score to use as a covariate. Physical activity and exercise have been used as covariates in previous studies (For examples, see Burns et al., 2002a, Gallagher et al., 2022; Miller et al, 2004), and evidence suggests that, among older adults, physical activity is positively associated with antibody production (Kohut et al., 2002).

Substance Use. Every evening, participants reported how many substances they consumed during the day (e.g., alcoholic drinks and cigarettes or cigars). I derived two dichotomous variables, including whether the participant (a) drank alcohol or (b) smoked at any point in the seven days (*0 = no, 1 = yes*). These control variables were

selected because they have been shown to be associated with dampened response to vaccination (Zimmerman & Curtis, 2019), although evidence is mixed.

Vaccination and HAI Titer Production:

The 2021-2022 FluZone vaccine included the following four strains: (a) A/Victoria/2570/2019 (H1N1); (b) A/ Tasmania/503/2020 (H3N2); (c) B/Phuket/3073/2013 (B/Yamagata lineage); and (d) B/Washington/02/2019 (B/Victoria lineage). All vaccines were administered via intramuscular injection into the participant's upper arm at the CTRU by a registered nurse[3]. To quantify pre- and post-vaccination hemagglutination-inhibition (HAI) titers to all four strains in the vaccine, researchers at the Center for Vaccines and Immunology at the University of Georgia followed a standard assay protocol used in previous studies (Carlock et al., 2019; Corallo et al., 2022; Nuñez et al., 2017). To account for baseline antibody values (i.e., HAI titers measured from the first blood sample), I applied the correction method developed by Beyer et al. (2004) to the antibody values measured from the second blood sample[4]. Following Segerstrom et al. (2012), I created a standardized composite of the corrected antibody values for all four strains. Higher composite scores reflect greater antibody production following vaccination.

[3] All participants who were 65 years or older were given the option to receive a higher dose of the vaccine (a dose that contains four times the number of antigens than the standard dose). Thirty of the thirty-one older adults (29.7% of the sample) chose to receive the high dose.

[4] I conducted this correction method twice. First, I applied this method to all participants enrolled in the 2021-2022 Flu Study. Then, I applied the method to only those participants included in the current study. These two values were correlated at $r = .997$, $p < .001$. I made the *a priori* decision to retain the value derived from the entire 2021-2022 Flu Cohort.

Data Analytic Plan:

All data cleaning and analyses were conducted in IBM SPSS Statistics version 28 and R version 4.2.0. I calculated the average score across all seven days for my variables of interest (i.e., number of unique stressors, amount of accumulated stress, amount of disclosure, amount of perceived responsiveness, positive mood, negative mood, sleep duration, and sleep quality). I also recorded the standard deviation of each participant's score across all seven days[5] to capture their daily variability. These two steps yielded 16 independent variables (i.e., the average score and the standard deviation for each variable associated with stress, self-disclosure, mood, and sleep). My dependent variable was vaccine response (i.e., the composite Beyer-corrected score).

I included common demographic variables (i.e., age, sex, race, and BMI) and behavioral factors (i.e., alcohol use, tobacco use, and average physical activity) that have been shown to influence response to vaccination in all analyses (Haralambieva et al., 2014; Kohut et al., 2002; Kurupati et al., 2016; Zimmerman & Curtis, 2019). To account

[5] In addition to calculating the simple standard deviation, I followed the steps outlined by Arriaga et al. (2001 & 2006) who suggested taking a multilevel modeling approach to calculating variability. First, I calculated a new variable for each day that reflected an individual's daily deviation from their average score. I regressed the daily values onto time [$VAR_{ij} = \gamma_{00} + \gamma_{01}(time) + r_{ij}$]. I saved the residual (r_{ij}) as a new value which represents that person's daily deviation. Then, I calculated the standard deviation of these residuals, which resulted in one final value representing this participant's "variability" across the seven days of that construct. Gunaydin et al., (2021) used this approach to predict attachment security from average levels of partner responsiveness and the variability within partner responsiveness across a three-week period. In their supplemental materials they indicate that the value produced by Arriaga's method and the simple standard deviation (not using the multilevel approach) were correlated at $r = .999$ and produced nearly identical results when used in subsequent analyses. Across my constructs, the simple standard deviations and the multilevel model standard deviation calculations were correlated at $r = .958$ to $r = 1.00$ where all p's < .001. Therefore, I proceeded to run all analyses with the simple standard deviation calculation.

for any possible influence of receiving the high versus the regular dose, I also included dosage (0 = regular dose and 1 = high dose) as a covariate.

I used multiple regression to determine whether the independent variables predicted response to vaccination while controlling for sex, race, age, BMI, alcohol use, smoking, physical activity, and dose (see Appendix C for a list of all proposed models). First, I explored whether the average scores for each variable predicted vaccine response. I ran separate models for each construct (i.e., number of unique stressors, amount of accumulated stress, amount of disclosure, amount of perceived responsiveness, positive mood, negative mood, sleep duration, and sleep quality) for a total of eight models. For each model, I entered all control variables in the first block, and then I entered the average score for the construct in the second block.

I then explored whether the variability (i.e., the standard deviation) for each variable predicted vaccine response. I ran separate models for each construct (i.e., number of unique stressors, amount of accumulated stress, amount of disclosure, amount of perceived responsiveness, positive mood, negative mood, sleep duration, and sleep quality) for eight additional models. For each model, I entered all control variables in the first block, the average score for the construct in the second block, and the variability score in the third block.

Finally, I planned to conduct one large model with all the independent variables that showed significant associations with antibody response from the prior 16 models. Therefore, if all my independent variables were associated with response to vaccination,

I could potentially have a model with 24 predictors (16 independent variables and all eight covariates).

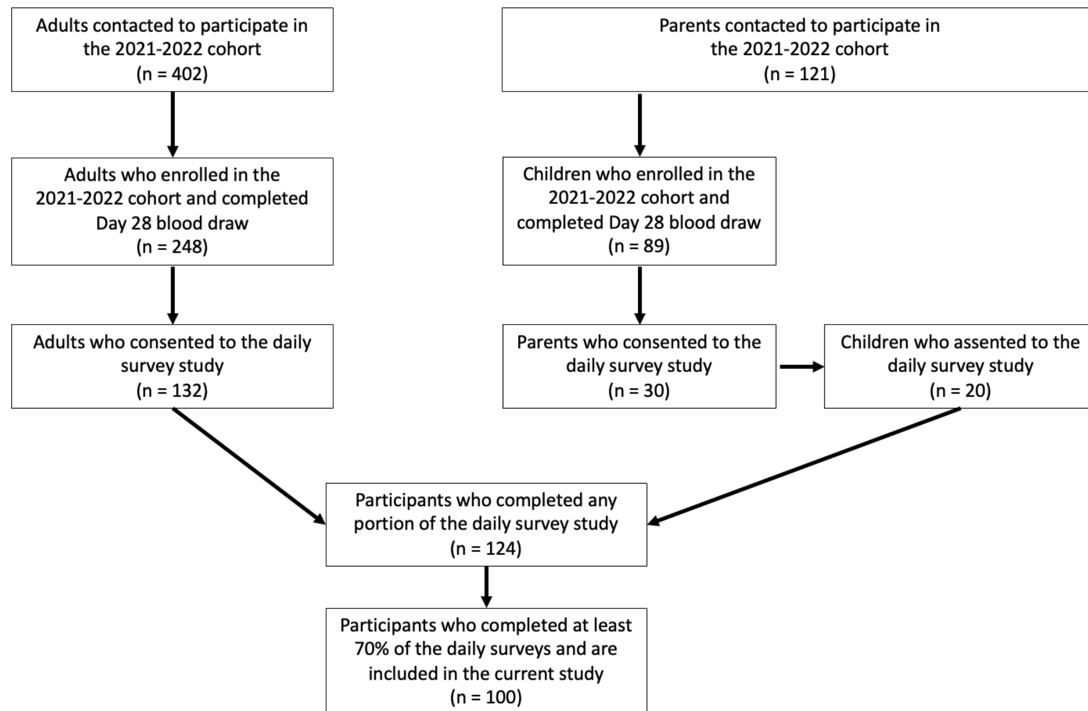
All reported p-values are two-tailed with an *a priori* significance level of $p < .05$, which was reduced to $p < .003$ after Bonferroni correction due to multiple comparisons (n = 16 analyses).

Power Analysis:

A total of 100 participants were included in the analyses for this study. Given this total number of participants and the number of effects I included in each model, I used G*Power Version 3.1 to determine whether my analyses were powered to detect small, medium, or large effects (Faul et al., 2007; Faul et al., 2009). In my individual models, I estimated 10 effects and in my combined model, I could have estimated up to 24 effects. According to G*Power, my sample was adequately powered to detect effects less than or equal to $f^2 = .179$ in my individual models and effects less than or equal to $f^2 = .280$ in my combined model. G*Power's conventional standards suggest that f^2 values = .15 indicate medium effects and f^2 values = .35 indicate large effects (Faul et al., 2007; Faul et al., 2009). Therefore, my sample was adequately powered to detect medium and large effects but may not be sensitive enough to detect small effects. See Appendix D for the protocol of power analysis generated by G*Power.

Figure 2

Recruitment and Enrollment Flowchart



Note. This figure demonstrates the recruitment and enrollment procedures for the current study. A total of 523 adults and parents were contacted to participate in the 2021-2022 Flu Study, and 343 of those participants enrolled. Of the 152 consenting participants who were sent surveys, only 124 people filled out at least one survey. Twenty-four of those participants did not complete at least five morning and five evening surveys and were therefore excluded from the study. The final sample includes 100 adults and youth.

Figure 3

Study Timeline

Recruitment and Enrollment	Day 0	Day 1 ••• Day 7	Day 28
Obtain informed consent and assent	Visit 1 at CTRU: vaccination and blood sample	Survey administration: one survey every morning and one survey every evening	Visit 2 at CTRU: blood sample

Note: This figure depicts the procedures that the participants completed. All participants attended two visits at the Clinical and Translational Research Unit on the University of Georgia's Health Sciences campus. The visits were scheduled approximately one-month apart, and participants completed seven days of surveys starting the morning following their first visit.

CHAPTER 3

RESULTS

Participant Demographics:

A total of 100 participants (66% Female, 93% White, M_{age} = 48.3, *SD* = 20.8, *Age Range* = 11 – 86 yrs.) were included in the current study. Table 1 presents the demographic information for (a) all the participants enrolled in the larger study, (b) those participants who consented or assented to the current study, (c) those participants who completed at least one survey, and (d) those participants who completed five morning and five evening surveys.

I compared the final sample included in the current analyses to the entire 2021-2022 Flu Study. On average, the participants in the current study were older [t (335) = -3.53, p = .023] and more likely to be White [X^2(1, N = 337) = 6.12, p = .013] than the participants in the larger study. There were no differences in sex [X^2(1, N = 337) = 3.33, p = .068] or BMI [t (329) = -1.00, p = .667] between participants in this study and those in the larger study.

Daily Survey Compliance:

A total of 1,400 surveys were expected (i.e., 14 surveys × 100 people). However, because not everyone completed every survey, only 1,295 surveys were completed (92.5% of total possible surveys). Forty-seven people completed every survey. There were no differences in age [t (98) = 1.76, p = .39], BMI [t (98) = -0.32, p = .21], sex [X^2(1,

N = 100) = 0.17, p = .68], or race [X^2(1, N = 100) = 0.05, p = .82] between the participants who had missing data and the participants who had complete data.

Psychosocial Variables:

I presented the means, standard deviations, and intraclass correlations for all psychosocial and sleep variables in Table 2. The intraclass correlations for all variables were high (ICCs ranging from 0.75 to 0.93), indicating that these variables were highly stable across the seven days of data collection. To help visualize the differences between the group of participants who had missing data from the group of participants who had complete data, I presented the means and standard deviations within each group in Table 3, and I reported whether these groups differed on any of the psychosocial constructs.

Other Daily Variables:

Average physical activity (PA) across the seven-day survey period ranged from 0 to 72.86 minutes per day (M_{PA} = 21.84 mins., *SD* = 16.92). Additionally, 50 participants endorsed drinking alcohol and two participants endorsed smoking throughout the study period. Although I planned to use all three of these variables as covariates in my analyses, I eliminated smoking status due to the low endorsement rate.

Response to Vaccination:

Across all four stains included in the vaccine, titer values from the second blood sample were higher than the titer values from the first blood sample [Victoria: t (99) = -6.74, $p < .001$; Tasmania: t (99) = -3.77, $p < .001$; Phuket: t (99) = -4.85, $p < .001$; Washington: t (99) = -4.77, $p < .001$]. Typically, an antibody titer ≥ 1:40 implies

seroprotection against that particular influenza virus strain (Beyer et al., 2004). Across the four strains, approximately 72% to 79% of the sample was seroprotected at Day 28. The raw titer values, % seroprotected, and Beyer-corrected values for each individual strain as well as the composite are presented in Table 4. There was no difference in the Beyer-corrected values for participants who had missing data relative to those who had complete data [t (98) = -0.35, p = .46].

Intercorrelations Among Study Variables:

All bivariate intercorrelations among study variables are presented in Table 5. Average level of positive affect was negatively correlated with average level and variability in negative affect, average number of stressors, average level of accumulated stress, and variability in perceived responsiveness, and it was positively correlated with average level of amount disclosed, average level of perceived responsiveness, and average level of sleep quality ($rs > |.27|$, $ps < .001$). Variability in positive affect was positively correlated with average level and variability in negative affect, variability in number of stressors, average level and variability in accumulated stress, average level and variability in amount disclosed, and variability in perceived responsiveness ($rs > |.22|$, $ps < .02$).

Average level of negative affect was positively correlated with variability in negative affect, average level and variability in number of stressors, average level and variability in accumulated stress, variability in amount disclosed, variability in sleep duration, and variability in sleep quality, and it was negatively correlated with average level of perceived responsiveness and average level of sleep quality ($rs > |.20|$, $ps < .05$).

Variability in negative affect was positively correlated with average level and variability in number of stressors, average level and variability in accumulated stress, average level and variability in amount disclosed, variability in perceived responsiveness, and variability in sleep duration, and it was negatively correlated with average level of sleep quality (*rs* > |.21|, *ps* < .04).

Average number of unique stressors was positively correlated with variability in number of unique stressors, average level and variability in accumulated stress, and average level of amount disclosed, and it was negatively correlated with average level of sleep quality (*rs* > |.32|, *ps* ≤ .001). Variability in number of unique stressors was positively correlated with average level and variability in accumulated stress and variability in perceived responsiveness, and it was negatively correlated with the average level of sleep quality (*rs* > |.25|, *ps* < .01).

Average accumulated stress was positively associated with variability in accumulated stress, average level of amount disclosed, and variability in perceived responsiveness, and it was negatively associated with average levels of sleep quality (*rs* > |.21|, *ps* < .04). Variability in accumulated stress was positively correlated with average level and variability in amount disclosed, and variability in perceived responsiveness, and it was negatively correlated with average level of sleep quality (*rs* > |.23|, *ps* < .01).

Average level of amount disclosed was positively correlated with average level of perceived responsiveness ($r = .63$, $p < .001$). Variability in amount disclosed was positively correlated with variability in perceived responsiveness ($r = .36$, $p < .001$).

Average level of perceived responsiveness was negatively correlated with variability in perceived responsiveness (r = -0.42, $p < .001$). Variability in perceived responsiveness was positively correlated with variability in sleep duration (r = .21, $p < .04$). Average level of sleep duration was positively correlated with variability in sleep quality, and it was negatively correlated with average level of sleep quality ($rs > |.23|$, $ps < .02$). Average level of sleep quality was negatively correlated with variability in sleep quality (r = -0.27, $p < .006$).

Associations Between Psychosocial Variables and Vaccine Response:

Average Levels. I hypothesized that while controlling for sex, race, age, BMI, vaccine dosage, alcohol use, and physical activity, average levels of accumulated stress, number of unique stress events, and negative mood would be negatively associated with antibody production following vaccination (i.e., Beyer-corrected composite). Additionally, I hypothesized that average self-disclosure, perceived responsiveness, positive mood, sleep duration, and sleep quality would be positively associated with antibody response. Contrary to my hypotheses, all models yielded null results, and no associations emerged between any of the psychosocial variables and antibody production following vaccination. I presented the results for the stress-related constructs in models 1A and 2A in Table 6, the self-disclosure-related constructs in 3A and 4A in Table 7, the mood-related constructs in models 5A and 6A in Table 8, and the sleep-related constructs in models 7A and 8A in Table 9.

Variability. Second, I hypothesized that while controlling for sex, race, age, BMI, vaccine dosage, alcohol use, and physical activity, variability within accumulated stress,

number of unique stress events, self-disclosure, perceived responsiveness, positive mood, negative mood, sleep duration, and sleep quality would be negatively associated with antibody production following vaccination. Again, contrary to my hypotheses, all models yielded null results, and no associations emerged between variability within the psychosocial variables and antibody production following vaccination (See models 1B, 2B, 3B, 4B, 5B, 6B, 7B, and 8B in Tables 6 – 9).

Table 1

Participant Demographics Split by Subgroup

Variable	All participants in 21-22 flu cohort[a]		Participants who consented or assented to the current study[a,b]		Participants who completed any portion of the daily surveys[b,c]		Participants included in current analyses[c]	
	n	%	n	%	n	%	n	%
Sex								
Male	140	41.5	48	31.6	40	32.3	34	34
Female	197	58.5	104	68.4	84	67.7	66	66
Race								
White	289	85.8	136	89.5	110	88.7	93	93
Non-White	48	14.2	16	10.5	14	11.3	7	7
Age range	10 - 86		11 - 86		10 - 86		11 - 86	
Age mean (SD)	41.7 (22.5)		46.0 (20.7)		45.0 (20.9)		48.3 (20.8)	
BMI mean (SD)	27.82 (7.5)		29.34 (8.3)		28.81 (8.2)		28.50 (8.0)	
	N = 337		N = 152		N = 124		N = 100	

Note. Sex was coded as female = 0, male = 1; Race was coded as 0 = White, 1 = Non-White; Age is in years; and BMI is kg/cm^2. SD = standard deviation

[a] On average, participants who consented or assented to the diary study were older [t (335) = -3.21, p = .002] and had a higher BMI [t (329) = -3.42, p = .025] than the participants who participated in the larger study but did not agree to participate in the diary study. There was a higher percentage of females in the group of participants who consented or assented to the diary study than in the larger study [X^2(1, N = 337) = 11.32, p < .001]. There was a marginally significant difference in the percentage of

White and Non-White people [X^2(1, N = 337) = 23.13, *p* = .077], such that there was a higher percentage of White people in the group of participants who agreed to participate in to the diary study than in the group of participants who were part of the larger study but did not agree to participate in the diary study.

[b] On average, participants who completed at least one survey did not differ from participants who consented or assented to the study but did not complete any of the surveys in in terms of age [*t* (150) = 0.63, *p* = .782], BMI [*t* (148) = 1.35, *p* = .730], sex [X^2(1, N = 152) = 0.14, *p* = .705], or race [X^2(1, N = 152) = 0.42, *p* = .518].

[c] On average, participants who completed at least 10 surveys did not differ from participants who completed fewer than 10 surveys in terms of age [*t* (122) = -3.15, *p* = .134], BMI [*t* (121) = 1.32, *p* = .237], or sex [X^2(1, N = 124) = 0.72, *p* = .397]. However, those who completed 10 surveys were more likely to be White [X^2(1, N = 124) = 9.50, *p* = .002] than those who completed fewer than 10 surveys.

Table 2

Psychosocial Variables

Variable	Mean	SD	ICC
Number of stressors	5.28	2.34	0.90
Accumulated stress	12.91	8.89	0.89
Amount disclosed	2.92	0.62	0.81
Perceived responsiveness	3.69	0.68	0.85
Positive mood	2.70	0.64	0.93
Negative mood	1.36	0.42	0.90
Sleep duration	7.64	0.87	0.75
Sleep quality	3.06	0.45	0.80
Total N		100	

Note: SD = Standard deviation; ICC = Intraclass correlation.

Table 3

Means and Standard Deviations of Daily Variables Split by Subgroup

Variable	Full sample N = 100		Complete data N = 47		Missing data N = 53		Significant differences
	Mean	SD	Mean	SD	Mean	SD	
Number of stressors							
Mean	5.28	2.34	5.33	2.21	5.23	2.46	
Variability	1.85	0.86	**1.76**	**0.70**	**1.94**	**0.98**	t (98) = -1.02, p = .034
Accumulated stress							
Mean	12.91	8.89	12.75	8.08	13.05	9.62	
Variability	6.64	5.10	6.18	4.12	7.05	5.82	t (98) = -0.85, p = .057
Self-disclosure							
Mean	2.92	0.62	2.98	0.62	2.88	0.61	
Variability	0.66	0.28	0.64	0.26	0.67	0.30	
Perceived responsiveness							
Mean	3.69	0.68	**3.78**	**0.76**	**3.60**	**0.59**	t (98) = 1.36, p = .009
Variability	0.67	0.33	0.65	0.32	0.69	0.34	
Positive mood							
Mean	2.70	0.87	2.67	0.79	2.73	0.59	
Variability	0.40	0.17	0.46	0.22	0.50	0.27	t (98) = -0.83, p = .078
Negative mood							
Mean	1.36	0.42	1.32	0.39	1.40	0.44	
Variability	0.24	0.20	0.26	0.26	0.32	0.28	
Sleep duration							
Mean	7.64	0.87	7.57	0.80	7.70	0.93	
Variability	0.96	0.48	0.96	0.51	0.97	0.45	
Sleep quality							
Mean	3.06	0.45	3.10	0.46	3.03	0.45	
Variability	0.49	0.24	0.48	0.25	0.50	0.24	

Note. Bolded values indicate that there was a statistically significant difference between the participants with complete data and those with missing data. SD = Standard deviation.

Table 4

Antibody Values

	Beyer-corrected titer values				
Vaccine Strain	Mean	SD	Range		
Composite	-0.10	0.66	-1.30 - 2.37		
A/H1N1 - Victoria	2.54	1.21	0.41 - 5.82		
A/H3N2 - Tasmania	2.20	1.20	0.00 - 6.00		
B/Yam- Phuket	1.41	0.75	0.00 - 5.00		
B/Vic - Washington	1.54	0.84	0.26 - 6.00		
	Raw titer values				
Vaccine Strain	Day 0 Mean	Day 0 SD	Day 28 Mean	Day 28 SD	% Seroprotected
A/H1N1 - Victoria	26.63	30.91	95.92	110.18	74
A/H3N2 - Tasmania	78.01	116.85	160.46	281.14	79
B/Yam- Phuket	66.54	114.84	92.07	121.15	72
B/Vic - Washington	53.28	81.40	83.94	104.57	75

Note. Beyer corrected values are presented in the top half of this table, and raw titer vales are presented at the bottom. Seroprotected = a titer value ≥ 1:40. SD = Standard deviation.

Table 5

Correlation Matrix

Variable	1	2	3	4
1. Sex	1			
2. Race	0.05	1		
3. Age	0.07	-0.01	1	
4. BMI	-0.03	0.22*	0.20*	1
5. Dose	0.08	-0.01	0.75***	-0.03
6. Alcohol	0.08	-0.04	0.16	-0.12
7. Physical activity	0.02	-0.15	0.17	-0.13
8. Positive affect (mean)	0.03	-0.04	0.17	0.03
9. Positive affect (sd)	-0.21*	0.15	-0.17	0.03
10. Negative affect (mean)	-0.18	0.23*	-0.27**	-0.11
11. Negative affect (sd)	-0.24*	0.17	-0.20**	0.09
12. Number of stressors (mean)	0.04	0.00	-0.18	-0.12
13. Number of stressors (sd)	0.01	-0.03	-0.23*	-0.09
14. Accumulated stress (mean)	-0.08	0.10	-0.23*	-0.06
15. Accumulated stress (sd)	-0.11	0.06	-0.18	0.03
16. Amount disclosed (mean)	-0.05	0.05	0.09	0.00
17. Amount disclosed (sd)	-0.06	0.20*	-0.08	0.08
18. Perceived responsiveness (mean)	-0.07	-0.01	0.16	0.01
19. Perceived responsiveness (sd)	0.10	-0.03	-0.10	0.05
20. Sleep duration (mean)	-0.17	-0.21*	0.12	-0.17
21. Sleep duration (sd)	-0.04	0.09	-0.31**	-0.05
22. Sleep quality (mean)	0.14	-0.02	0.23*	0.16
23. Sleep quality (sd)	-0.03	0.15	-0.05	0.05
24. Ab composite	-0.22*	0.03	-0.19	0.14

Table 5 Continued

Variable	5	6	7	8
5. Dose	1			
6. Alcohol	-0.04	1		
7. Physical activity	0.27**	-0.09	1	
8. Positive affect (mean)	0.20	0.08	0.43***	1
9. Positive affect (sd)	-0.20	-0.01	-0.05	0.06
10. Negative affect (mean)	-0.24*	-0.13	-0.35***	-0.45***
11. Negative affect (sd)	-0.17	-0.09	-0.22*	-0.22*
12. Number of stressors (mean)	-0.14	0.06	-0.20*	-0.36***
13. Number of stressors (sd)	-0.21*	-0.04	-0.15	-0.18
14. Accumulated stress (mean)	-0.23*	0.01	-0.32**	-0.39***
15. Accumulated stress (sd)	-0.23*	0.03	-0.22*	-0.19
16. Amount disclosed (mean)	-0.05	0.13	0.18	0.28**
17. Amount disclosed (sd)	-0.15	-0.02	-0.11	0.09
18. Perceived responsiveness (mean)	0.13	0.07	0.22*	0.38***
19. Perceived responsiveness (sd)	-0.16	-0.04	-0.27**	-0.18*
20. Sleep duration (mean)	0.15	0.15	0.04	0.08
21. Sleep duration (sd)	-0.21*	-0.09	-0.10	-0.13
22. Sleep quality (mean)	0.23*	-0.02	0.29**	0.42***
23. Sleep quality (sd)	-0.02	0.17	0.01	-0.14
24. Ab composite	-0.16	-0.11	-0.18	-0.18

Table 5 Continued

Variable	9	10	11	12
9. Positive affect (sd)	1			
10. Negative affect (mean)	0.27**	1		
11. Negative affect (sd)	0.56***	0.69***	1	
12. Number of stressors (mean)	0.18	0.60***	0.42***	1
13. Number of stressors (sd)	0.36***	0.38***	0.45***	0.40***
14. Accumulated stress (mean)	0.27**	0.78***	0.57***	0.88***
15. Accumulated stress (sd)	0.45***	0.60***	0.70***	0.52***
16. Amount disclosed (mean)	0.24*	0.08	0.22*	0.32**
17. Amount disclosed (sd)	0.22*	0.20*	0.20*	0.03
18. Perceived responsiveness (mean)	-0.02	-0.23*	-0.08	-0.05
19. Perceived responsiveness (sd)	0.27**	0.18	0.33***	0.12
20. Sleep duration (mean)	-0.01	-0.10	-0.1	-0.14
21. Sleep duration (sd)	0.19	0.24*	0.28**	0.05
22. Sleep quality (mean)	-0.14	-0.43***	-0.21*	-0.36***
23. Sleep quality (sd)	0.06	0.24*	0.2	0.15
24. Ab composite	0.19	0.1	0.23*	-0.03

Table 5 Continued

Variable	13	14	15	16
13. Number of stressors (sd)	1			
14. Accumulated stress (mean)	0.46***	1		
15. Accumulated stress (sd)	0.75***	0.73***	1	
16. Amount disclosed (mean)	0.14	0.28**	0.29**	1
17. Amount disclosed (sd)	0.04	0.18	0.23*	0.07
18. Perceived responsiveness (mean)	-0.07	-0.09	-0.04	0.63***
19. Perceived responsiveness (sd)	0.25*	0.21*	0.35***	-0.20
20. Sleep duration (mean)	-0.11	-0.12	-0.08	0.07
21. Sleep duration (sd)	0.19	0.14	0.19	-0.11
22. Sleep quality (mean)	-0.26**	-0.42***	-0.30**	0.03
23. Sleep quality (sd)	0.11	0.13	0.12	-0.09
24. Ab composite	-0.06	0.03	0.10	-0.08

Table 5 Continued

Variable	17	18	19	20
17. Amount disclosed (sd)	1			
18. Perceived responsiveness (mean)	-0.09	1		
19. Perceived responsiveness (sd)	0.36***	-0.42***	1	
20. Sleep duration (mean)	0.03	0.19	-0.1	1
21. Sleep duration (sd)	0.19	-0.18	0.21*	-0.14
22. Sleep quality (mean)	-0.17	0.18	-0.2	-0.12
23. Sleep quality (sd)	0.14	-0.08	0.0	-0.09
24. Ab composite	0.08	-0.06	0.0	0.06

Table 5 Continued

Variable	21	22	23	24
21. Sleep duration (sd)	1			
22. Sleep quality (mean)	-0.23*	1		
23. Sleep quality (sd)	0.32**	-0.27**	1	
24. Ab composite	0.18	-0.03	0.12	1

Note. Sex was coded as female = 0, male = 1; Race was coded as 0 = White, 1 = Non-White; Dose was coded as 0 = standard, 1 = high, Alcohol use was coded as 0 = no, 1 = yes; Age is in years; BMI is kg/cm^2; and Physical Activity is in minutes per day.

* $p \leq .05$; ** $p \leq .01$; *** $p \leq .001$

Table 6

Associations Between Stress Constructs and Vaccine Response

Variable		Number of unique stressors		Accumulated stress	
		Model 1A	Model 1B	Model 2A	Model 2B
Constant					
	β	—	—	—	—
	95% CI	[-0.49, 1.00]	[-0.41, 1.14]	[-0.48, 0.90]	[-0.47, 0.91]
Sex					
	β	-0.20 ~	-0.19 ~	-0.20 *	-0.20 ~
	95% CI	[-0.55, 0.00]	[-0.54, 0.01]	[-0.56, -0.01]	[-0.55, 0.00]
Race					
	β	-0.02	-0.03	-0.02	-0.01
	95% CI	[-0.58, 0.47]	[-0.60, 0.46]	[-0.57, 0.49]	[-0.56, 0.49]
Age					
	β	-0.25	-0.26	-0.24	-0.25
	95% CI	[-0.02, 0.00]	[-0.02, 0.00]	[-0.02, 0.00]	[-0.02, 0.00]
BMI					
	β	0.16	0.15	0.16	0.15
	95% CI	[-0.01, 0.03]	[-0.01, 0.03]	[-0.01, 0.03]	[-0.01, 0.03]
Dose					
	β	0.08	0.07	0.7	0.08
	95% CI	[-0.35, 0.59]	[-0.40, 0.57]	[-0.36, 0.58]	[-0.35, 0.59]
Alcohol use					
	β	-0.05	-0.05	-0.05	-0.06
	95% CI	[-0.34, 0.22]	[-0.35, 0.21]	[-0.35, 0.21]	[-0.35, 0.21]
Physical activity					
	β	-0.15	-0.16	-0.16	-0.17
	95% CI	[-0.01, 0.00]	[-0.02, 0.00]	[-0.02, 0.00]	[-0.02, 0.00]
Construct mean					
	β	-0.07	-0.03	-0.07	-0.17
	95% CI	[-0.08, 0.04]	[-0.07, 0.05]	[-0.02, 0.01]	[-0.04, 0.01]
Construct variability					
	β	—	-0.1	—	0.14
	95% CI		[-0.25, 0.09]		[-0.02, 0.06]
		R^2 = .13	R^2 = .14	R^2 = .13	R^2 = .14
		F(8,91) = 1.75, p = .10	F(9,90) = 1.66, p = .11	F(8,91) = 1.75, p = .10	F(9,90) = 1.65, p = .11

Note. Sex was coded as female = 0, male = 1; Race was coded as 0 = White, 1 = Non-White; Dose was coded as 0 = standard, 1 = high, Alcohol use was coded as 0 = no, 1 = yes; Age is in years; BMI is kg/cm^2; and Physical Activity is in minutes per day. ß = standardized beta. ΔR^2 from model 1A to model 1B = .009. ΔR^2 from model 2A to model 2B = .008.

~ $p \leq .1$; * $p \leq .05$; ** $p \leq .01$; *** $p \leq .001$

Table 7

Associations Between Self-Disclosure Constructs and Vaccine Response

Variable		Amount disclosed		Perceived responsivness	
		Model 3A	Model 3B	Model 4A	Model 4B
Constant					
	β	—	—	—	—
	95% CI	[-0.62, 1.02]	[-0.73, 1.01]	[-0.75, 1.01]	[-0.75, 1.39]
Sex					
	β	-0.2 *	-0.2 *	-0.2 *	-0.19 ~
	95% CI	[-0.55, -0.01]	[-0.55, 0.00]	[-0.55, -0.00]	[-0.55, 0.01]
Race					
	β	-0.02	-0.03	-0.02	-0.03
	95% CI	[-0.57, 0.48]	[-0.60, 0.47]	[-0.58, 0.47]	[-0.60, 0.46]
Age					
	β	-0.23	-0.23	-0.24	-0.23
	95% CI	[-0.02, 0.00]	[-0.02, 0.00]	[-0.02, 0.00]	[-0.02, 0.00]
BMI					
	β	0.16	0.16	0.16	0.17
	95% CI	[-0.01, 0.03]	[-0.01, 0.03]	[-0.01, 0.03]	[-0.01, 0.03]
Dose					
	β	0.07	0.08	0.08	0.07
	95% CI	[-0.38, 0.58]	[-0.40, 0.59]	[-0.36, 0.59]	[-0.37, 0.57]
Alcohol use					
	β	-0.05	-0.04	-0.05	-0.05
	95% CI	[-0.34, 0.22]	[-0.34, 0.22]	[-0.35, 0.22]	[-0.35, 0.21]
Physical activity					
	β	-0.13	-0.13	-0.14	-0.15
	95% CI	[-0.01, 0.00]	[-0.01, 0.00]	[-0.01, 0.00]	[-0.01, 0.00]
Construct mean					
	β	-0.04	-0.04	-0.01	-0.04
	95% CI	[-0.26, 0.18]	[-0.27, 0.18]	[-0.21, 0.19]	[-0.25, 0.18]
Construct variability					
	β	—	0.04	—	-0.07
	95% CI		[-0.38, 0.60]		[-0.60, 0.31]
		R^2 = .13	R^2 = .13	R^2 = .13	R^2 = .13
		F (8,91) = 1.71, p = .11	F (9,90) = 1.52, p = .15	F (8,91) = 1.70, p = .11	F (9,90) = 1.54, p = .15

Note. Sex was coded as female = 0, male = 1; Race was coded as 0 = White, 1 = Non-White; Dose was coded as 0 = standard, 1 = high, Alcohol use was coded as 0 = no, 1 = yes; Age is in years; BMI is kg/cm^2; and Physical Activity is in minutes per day. ß = standardized beta. ΔR^2 from model 3A to model 3B = .001. ΔR^2 from model 4A to model 4B = .004.

~ $p \leq .1$; * $p \leq .05$; ** $p \leq .01$; *** $p \leq .001$

Table 8

Associations Between Mood Constructs and Vaccine Response

Variable		Positive mood		Negative mood	
		Model 5A	Model 5B	Model 6A	Model 6B
Constant					
	β	—	—	—	—
	95% CI	[-0.40, 1.10]	[-0.62, 0.95]	[-0.80, 1.11]	[-0.57, 1.44]
Sex					
	β	-0.2 *	-0.17 ~	-0.2 *	-0.18 ~
	95% CI	[-0.55, -0.00]	[-0.51, 0.04]	[-0.56, -0.00]	[-0.53, 0.03]
Race					
	β	-0.2	-0.04	-0.02	-0.01
	95% CI	[-0.57, 0.47]	[-0.64, 0.41]	[-0.59, 0.50]	[-0.60, 0.51]
Age					
	β	-0.24	-0.23	-0.24	-0.2
	95% CI	[-0.02, 0.00]	[-0.02, 0.00]	[-0.02, 0.00]	[-0.02, 0.00]
BMI					
	β	0.18	0.18	0.16	0.11
	95% CI	[-0.00, 0.03]	[-0.00, 0.03]	[-0.01, 0.03]	[-0.01, 0.03]
Dose					
	β	0.09	0.12	0.08	0.05
	95% CI	[-0.33, 0.60]	[-0.30, 0.63]	[-0.36, 0.58]	[-0.40, 0.54]
Alcohol use					
	β	-0.03	-0.03	-0.05	-0.07
	95% CI	[-0.32, 0.24]	[-0.32, 0.24]	[-0.35, 0.22]	[-0.37, 0.19]
Physical activity					
	β	-0.09	-0.08	-0.15	-0.16
	95% CI	[-0.01, 0.00]	[-0.01, 0.01]	[-0.01, 0.00]	[-0.02, 0.00]
Construct mean					
	β	-0.12	-0.14	-0.02	-0.18
	95% CI	[-0.35, 0.10]	[-0.37, 0.83]	[-0.40, 0.34]	[-0.77, 0.19]
Construct variability					
	β	—	0.15	—	0.23
	95% CI		[-0.15, 0.93]		[-0.11, 1.24]
		R^2 = .14	R^2 = .16	R^2 = .13	R^2 = .16
		F (8,91) = 1.86, p = .08	F (9,90) = 1.90, p = .06	F (8,91) = 1.70, p = .11	F (9,90) = 1.84, p = .07

Note. Sex was coded as female = 0, male = 1; Race was coded as 0 = White, 1 = Non-White; Dose was coded as 0 = standard, 1 = high, Alcohol use was coded as 0 = no, 1 = yes; Age is in years; BMI is kg/cm^2; and Physical Activity is in minutes per day. ß = standardized beta. ΔR^2 from model 5A to model 5B = .019. ΔR^2 from model 6A to model 6B = .025.

~ $p \leq .1$; * $p \leq .05$; ** $p \leq .01$; *** $p \leq .001$

Table 9

Associations Between Sleep Constructs and Vaccine Response

Variable		Sleep duration		Sleep quality	
		Model 7A	Model 7B	Model 8A	Model 8B
Constant					
	β	—	—	—	—
	95% CI	[-1.90, 0.91]	[-2.30, 0.68]	[-1.07, 0.87]	[-1.554, 0.64]
Sex					
	β	-0.18 ~	-0.17 ~	-0.21 *	-0.2 *
	95% CI	[-0.53, 0.03]	[-0.52, 0.04]	[-0.56, -0.01]	[-0.56, -0.01]
Race					
	β	-0.01	-0.01	-0.02	-0.04
	95% CI	[-0.54, 0.52]	[-0.57, 0.49]	[-0.57, 0.47]	[-0.63, 0.42]
Age					
	β	-0.24	-0.2	-0.24	-0.21
	95% CI	[-0.02, 0.00]	[-0.02, 0.00]	[-0.02, -0.00]	[-0.02, 0.00]
BMI					
	β	0.18	0.18	0.15	0.13
	95% CI	[-0.00, 0.03]	[-0.00, 0.03]	[-0.01, 0.03]	[-0.01, 0.03]
Dose					
	β	0.06	0.06	0.07	0.04
	95% CI	[-0.40, 0.56]	[-0.39, 0.60]	[-0.37, 0.58]	[-0.41, 0.54]
Alcohol use					
	β	-0.06	-0.06	-0.05	-0.09
	95% CI	[-0.37, 0.20]	[-0.36, 0.20]	[-0.35, 0.22]	[-0.40, 0.17]
Physical activity					
	β	-0.14	-0.13	-0.16	-0.18
	95% CI	[-0.01, 0.00]	[-0.01, 0.00]	[-0.02, 0.00]	[-0.02, 0.00]
Construct mean					
	β	0.1	0.11	0.05	0.1
	95% CI	[-0.09, 0.23]	[-0.08, 0.24]	[-0.23, 0.39]	[-0.18, 0.48]
Construct variability					
	β	—	0.13	—	0.15
	95% CI		[-0.11, 0.46]		[-0.17, 0.98]
		R^2 = .14	R^2 = .15	R^2 = .13	R^2 = .15
		F (8,91) = 1.81, p = .09	F (9,90) = 1.78, p = .08	F (8,91) = 1.73, p = .10	F (9,90) = 1.76, p = .09

Note. Sex was coded as female = 0, male = 1; Race was coded as 0 = White, 1 = Non-White; Dose was coded as 0 = standard, 1 = high, Alcohol use was coded as 0 = no, 1 = yes; Age is in years; BMI is kg/cm^2; and Physical Activity is in minutes per day. ß = standardized beta. ΔR^2 from model 7A to model 7B = .014. ΔR^2 from model 8A to model 8B = .018.

~ $p \leq .1$; * $p \leq .05$; ** $p \leq .01$; *** $p \leq .001$

CHAPTER 4

EXPLORATORY ANALYSES

Rationale:

The current study offers a unique opportunity to ask research questions regarding age-related differences in antibody response to vaccination. Most studies in this area have restricted their samples to specific age ranges (e.g., children, young adults, middle-aged adults, or older adults). Work in older adults tends to suggest that psychosocial factors are strong predictors of vaccine response, but research with younger samples has been less conclusive. For example, stress and other risk factors have been negatively associated with vaccine response in several samples of older adults (Glaser et al., 1998 & 2000; Hayney et al., 2014; Kiecolt-Glaser et al., 1996; Phillips et al., 2006; Segerstrom et al., 2008), but these same factors have been positively associated or not associated with vaccine response in younger samples (Burns et al., 2002a & 2003b; Corallo et al., 2022; Gallagher et al., 2008a & 2008b; O'Connor et al., 2014; Vedhara et al., 2002). For example, Burns et al. (2003b) found that undergraduate students protected against the influenza vaccine at five weeks post-vaccination reported more perceived stress and more negative life events than students who were not protected. Similarly, Petry et al. (1991), O'Conner et al. (2014), and Corallo et al. (2021) found positive associations between distress and hepatitis B, meningitis, and influenza antibody production, respectively.

Immune function, including one's ability to produce and maintain antibodies following vaccination, declines across the lifespan (Effros, 2007; Haynes & Swain, 2007; Ogawa et al., 2000). As Kiecolt-Glaser et al. (1996) have proposed, this decline in function could mean that the immune systems in older adults are more vulnerable to negative consequences associated with psychosocial factors, which may explain why there is more consistent evidence linking these factors to antibody production in older samples compared to younger samples. This idea does not, however, explain the seemingly contradictory findings from younger samples suggesting that stress leads to a more robust immune response.

Much less is known about the developing immune system relative to the immune systems in older adults (Hawkley & Cacioppo, 2004; O'Connor et al., 2014a). Increasingly, research suggests that stress may influence the immune systems in younger people differently than it does in older people (O'Connor et al., 2014a). Although stress has been associated with poorer innate immune function in older adults, there appears to be an enhancement in innate immune function following stress in younger samples (Cole et al., 2011; Schleifer et al., 2002). Therefore, many questions remain regarding how age interacts with these psychosocial experiences to influence adaptive immune function.

The following exploratory analyses explore whether the links between response to vaccination and the average levels and the variability in the number of unique stressors, accumulated stress, amount of self-disclosure, amount of perceived

responsiveness, amount of positive mood, amount of negative mood, sleep duration, and sleep quality vary as a function of age.

Predictions:

In line with evidence that immune system function declines with age, I hypothesize that there would be a negative association between the risk factors and antibody production in older adults, but not in younger adults or youth. I also hypothesized that there would be a positive association between the promotive factors and antibody production in older adults, but not in younger adults or youth. Similarly, among older individuals, but not younger individuals, there will be a negative association between variability in the psychosocial experiences and antibody production following vaccination.

Results:

Average Levels: I used PROCESS version 4.0 (Model 1) to test whether age moderated the link between average levels the psychosocial constructs and antibody response. I ran a separate model with the average level of each variable of interest for a total of eight models. Sex, race, BMI, vaccine dosage, alcohol use, and average minutes spent exercising per day were entered as covariates in all analyses. Age, the average level of the construct, and the Age × Average Level of the construct interaction were entered as independent variables. Across the eight different models, two significant interactions emerged, including the Age × Positive Mood interaction (*coeff* = 0.011, p = .026) and the Age × Amount Disclosed interaction (*coeff* = 0.012, p = .040).

I used the Johnson-Neyman technique to probe these interactions. These analyses indicated that for participants who were younger than 37 (31% of the sample), there was a negative association between positive mood and antibody production, but for adults older than 37, positive mood was not associated with antibody production. Also, although the Age × Amount Disclosed interaction yielded a significant main effect, the conditional effect of amount disclosed on antibody production was not statistically significant anywhere across the ages included in this sample. I present the results for these eight models in Table 10.

Variability: I used PROCESS version 4.0 (Model 1) to test whether age moderated the links between daily variability in the psychosocial constructs and antibody response. I ran a separate model with the variability of each variable of interest for a total of eight additional models. Sex, race, BMI, vaccine dosage, alcohol use, average minutes spent exercising per day, and average levels of the construct were entered as covariates in all analyses. Age, the variability in the construct, and the Age × Variability in the construct interaction were entered as independent variables. Across the eight different models, three significant interactions emerged, including the Age × Perceived Responsiveness interaction (*coeff* = -0.020, $p = .033$), the Age × Negative Mood interaction (*coeff* = -0.028, $p = .047$), and the Age × Sleep Quality interaction (*coeff* = -0.047, $p = .002$).

I used the Johnson-Neyman technique to probe these interactions. Among participants who were older than 71 (14% of the sample), there was a negative association between variability in perceived responsiveness and antibody production, but there were no associations between variability in perceived responsiveness and

antibody response in younger participants. Among participants who were younger than 44 (40% of the sample), there was a positive association between variability in negative mood and antibody production, but there were no associations between variability in negative mood and antibody response in older participants. Among participants who were younger than 46 (44% of the sample), there was a positive association between variability in sleep quality and antibody response. Additionally, the Johnson-Neyman technique indicated that among people older than 83 there would be a negative association between variability in sleep quality and antibody response, but only one participant in this sample was in this age range. There was no association between variability in sleep quality and antibody response among people between the ages of 46 and 83. I present the results for these eight analyses in Table 11.

Conclusions:

Results from these analyses support the notion that the influence of psychosocial factors on response to vaccination may look different in younger people than it does in older people. Historically, findings in older adults suggest that negative psychosocial experiences serve as risk factors for antibody production following vaccination. In this study, variability in perceived responsiveness and variability in sleep quality were negatively associated with vaccine response, suggesting that these older individuals are more vulnerable to the daily variability in these two protective factors than younger individuals.

Curiously, average amount of positive mood was negatively associated with antibody production, and similarly, variability in negative mood and sleep quality were

positively associated with antibody production in younger participants. These three findings directly contradict the hypotheses that risk factors lead to a diminished antibody response whereas promotive factors lead to an amplified antibody response. Much larger samples with participants spanning wide age ranges will be needed to better understand how psychosocial factors influence antibody production following vaccination.

Table 10

Average Levels of Psychosocial Factors and Age Predicting Vaccine Response

Variable	Number of unique stressors	Accumulated stress	Amount disclosed	Perceived responsiveness	Positive mood	Negative mood	Sleep duration	Sleep quality
Constant	-0.032	0.010	1.596	1.282	1.909	-0.485	-2.224	0.700
Sex	-0.260 ~	-0.263 ~	-0.260 ~	-0.235 ~	-0.237 ~	-0.262 ~	-0.260 ~	-0.277 ~
Race	-0.042	-0.015	-0.122	-0.154	-0.059	-0.062	-0.027	-0.036
BMI	0.014	0.013	0.015	0.014	0.014	0.014	0.014	0.013
Dose	0.119	-0.091	0.109	0.069	0.129	0.074	0.119	0.090
Alcohol use	-0.052	-0.052	-0.079	-0.067	-0.037	-0.048	-0.069	-0.061
Physical activity	-0.006	-0.006	-0.007	-0.005	-0.004	-0.005	-0.006	-0.006
Age	-0.003	0.004	-0.040 *	-0.035 *	0.015 **	0.005	0.030	-0.022
Construct mean	0.026	0.008	-0.054 *	-0.335	0.272 *	0.393	0.304	-0.189
Age X construct mean	-0.001	-0.000	0.012 *	0.008 ~	0.005 *	-0.009	-0.005	0.005

Note. Sex was coded as female = 0, male = 1; Race was coded as 0 = White, 1 = Non-White; Dose was coded as 0 = standard, 1 = high, Alcohol use was coded as 0 = no, 1 = yes; Age is in years; BMI is kg/cm^2; and Physical Activity is in minutes per day.

~ $p \leq .1$; * $p \leq .05$; ** $p \leq .01$; *** $p \leq .001$

Table 11

Variability in Psychosocial Factors and Age Predicting Vaccine Response

Variable	Number of unique stressors	Accumulated stress	Amount disclosed	Perceived responsiveness	Positive mood	Negative mood	Sleep duration	Sleep quality
Constant	0.197	-0.148	-0.226	-0.277	-0.445	-0.056	-1.097	-1.371
Sex	-0.258 ~	-0.230	-0.280 *	-0.257 ~	-0.219 ~	-0.220	-0.231	-0.320 *
Race	-0.062	-0.017	-0.072	-0.133	-0.243	-0.101	-0.031	-0.186
BMI	0.013	0.012	0.014	0.015	0.017	0.011	0.016 ~	0.014
Dose	0.091	0.089	0.081	0.071	0.128	0.038	0.056	0.101
Alcohol use	-0.069	-0.042	-0.037	-0.081	-0.035	-0.030	-0.077	-0.103
Physical activity	-0.006	-0.006	-0.005	-0.006	-0.003	-0.006	-0.006	-0.007 ~
Construct mean	-0.007	-0.017	-0.050	-0.042	-0.150	-0.312	0.087	0.027
Age	-0.005	-0.001	0.001	0.006	0.004	0.002	-0.001	0.016 ~
Construct variability	-0.006	0.079	0.655	0.770	1.514 *	1.961 *	0.394	2.837 ***
Age X construct variability	-0.002	-0.001	-0.012	-0.020 *	-0.022	-0.028 *	-0.005	-0.047 **

Note. Sex was coded as female = 0, male = 1; Race was coded as 0 = White, 1 = Non-White; Dose was coded as 0 = standard, 1 = high, Alcohol use was coded as 0 = no, 1 = yes; Age is in years; BMI is kg/cm^2; and Physical Activity is in minutes per day.

~ $p \leq .1$; * $p \leq .05$; ** $p \leq .01$; *** $p \leq .001$

CHAPTER 5

DISCUSSION

Promotive factors, including self-disclosure, perceived responsiveness, positive mood, and sleep, are thought to be associated with an amplified immune response (Uchino et al., 2021). In contrast, risk factors, including stress and negative mood, are associated with a diminished immune response (Pederson et al., 2009). Additionally, variability within psychosocial experiences is linked to poorer health (Boehm et al., 2015; Bustamante et al., 2020; Eizenman et al., 1997; Fuller-Rowell et al., 2021; Okun et al., 2011; Ross et al., 2013; Shadur et al., 2015).

The first goal of the present study was to replicate prior work exploring the links between risk and promotive factors (i.e., accumulated stress, number of unique stressors, self-disclosure, perceived responsiveness, mood, and sleep) and vaccine response. The second goal of this study was to explore how variability in these experiences might be associated with vaccine response. Contrary to my hypotheses, I did not find evidence that average levels of these constructs or the daily variability within these constructs were associated with antibody production following influenza vaccination. Despite the notion that psychosocial factors influence antibody production, a growing number of studies have failed to find these associations (Gallagher et al., 2008a; Gleeson et al., 1996; Hallam et al., 2022; Marsland et al., 2001; Taylor et al., 2017; Wong et al., 2013; Wu et al., 2017).

Results from the present study are consistent with prior work that similarly did not find associations between stress and antibody response one month following vaccination. Caregiving stress, exposure to stressful life events, and self-reported perceived stress were not associated with hepatitis A or B, pneumonia, or influenza vaccine response one month following vaccination, but in each of these studies, the expected link emerged at later time points (Burns et al., 2002b; Glaser et al., 2000; Gallagher et al., 2008a; Sacadura-Leite et al., 2014; Talbot et al., 2014; Vedhara et al., 2002). For example, although perceived stress was not associated with whether someone was protected against the influenza vaccine at one month, stress was linked to protection status seven months later, such that higher stress was associated with a greater likelihood of not being protected (Talbot et al., 2015). These studies suggest that antibody maintenance, or a person's ability to maintain antibodies several months after vaccination, might be more susceptible to psychosocial experiences than antibody production itself (Burns et al., 2002b; Talbot et al., 2015). Unfortunately, we did not assess antibody levels at later time points, so we cannot test this hypothesis with our current sample. However, many participants will return for the ongoing study in Fall 2022, so future analyses can explore questions about antibody maintenance using blood samples that will be collected in several months.

Because there is less work exploring how mood, social support, and sleep are associated with antibody production, it is unclear whether a similar pattern regarding antibody maintenance would emerge in these other psychosocial factors. In one study, the effects of social support were present one month following pneumonia vaccination

but were not present three months later (Gallagher et al., 2008a), which appears to contradict the pattern seen with stress. Ayling et al. (2018) found that positive mood was associated with influenza vaccine response one- and four-months following vaccination, but negative mood was not associated with vaccine response at either time point. Similarly, sleep duration was linked with influenza vaccine response one- and four-months following vaccination, but sleep quality was not (Prather et al., 2021). Many questions remain regarding how risk and promotive factors influence the production and maintenance of antibodies following vaccination.

Limitations of the Current Study

This study has several limitations that future research should address. Perhaps the most significant limitation of the present study is the sample size. My initial goal was to recruit 150-200 of the existing flu study participants; however, only 152 people consented to participate in the daily diary portion, only 124 participants completed at least one survey, and only 100 participants were included in the final analyses because they completed at least five morning and five evening surveys. Power analyses suggest that I am only powered to detect medium and large effects, and it is likely that any effects between psychosocial experiences and antibody production are small. Therefore, these findings may be a result of Type II errors. Additionally, the sample size restricts the kinds of research questions that I can address (e.g., questions regarding mediation). Despite this study being underpowered, it is a comparable size to the majority of studies exploring the links between psychosocial factors and antibody response.

Second, because I excluded any participant who did not complete at least five morning and five evening surveys, my sample may not generalize to the broader population. It is possible that the participants who experienced the most variability in their experiences may not have completed enough surveys to be included in the final sample. Historically, researchers used a simple rule of thumb to determine whether participants with missing data should be included or excluded in daily diary studies (e.g., they would include all participants who completed the majority of the surveys; Griffiths et al., 2021). Griffiths et al. (2021) conducted a simulation study to explore how different amounts of missing data might influence conclusions made from daily diary studies, and they concluded that when a researcher is trying to detect changes from day to day, any participant with fewer than five out of seven days of data should be excluded. Therefore, even though my sample size would have increased if I had used the rule of thumb value (four out of seven), I followed Griffiths's recommendation.

Third, this study only collected seven days of diary data, so we cannot make conclusions about how stress after those seven days is associated with antibody production. One study found that the stress experienced on days eight through ten following vaccination were most strongly linked to influenza antibody production following vaccination (Miller et al., 2004). Future studies should explore how stress and other psychosocial experiences collected across the month following vaccination are associated with antibody production.

Fourth, sleep duration and quality were both collected by self-report (a subjective assessment of sleep). Although this method has been used in prior vaccine

studies (Prather et al., 2021), actigraphy or polysomnography could provide more objective measures of sleep (Prather et al., 2012). Prior studies linking sleep to vaccine response have suggested that sleep duration (either experimentally manipulated or collected through the use of actigraphy) was associated with vaccine response (Benedict et al., 2012; Lange et al., 2003; Lange et al., 2011; Prather et al., 2012; Speigel et al., 2002) but self-reported sleep duration was not a predictor of vaccine response in the present study. Objective and subjective assessments of sleep are moderately correlated, and psychosocial factors, like personality and mental health, have been shown to influence the strength of this correlation (Matthews et al., 2017). Future studies could investigate whether the discrepancy between objective and subjective measures is meaningful for health and antibody production following vaccination.

Strengths of the Current Study

Despite the limitations of this study, this project has two major strengths that should be noted. First, I explored how risk *and* promotive factors are associated with antibody production following vaccination. An overwhelming amount of research in this area has focused on how caregiving stress, exposure to negative life events, and perceived stress are linked to vaccine response. There is much less work exploring the link between promotive factors and vaccine response. To address this gap, I included two novel promotive factors that have yet to be explored in the extant literature linking psychosocial factors to adaptive immune function, (a) self-reported self-disclosure and (b) perceived responsiveness. Similarly, there is little work exploring the role of sleep in

predicting vaccine response, and I included both sleep duration and sleep quality in this study.

Second, this study utilizes a daily diary design. Much of the past work has relied on one-time assessments and has required participants to rely on retrospective reports. Some evidence suggests that specific personality characteristics can bias accurate reporting. For instance, Reuben et al. (2016) showed that people high in neuroticism and low in conscientiousness were more likely to over-report negative childhood experiences compared to their actual experiences that were measured prospectively throughout their childhood. These researchers also found that people high in agreeableness under-reported negative childhood experiences compared to their actual experiences growing up (Reuben et al., 2016). Further, prospective measures were better at predicting objective health outcomes, whereas retrospective reporting was more predictive of subjective health reports (Reuben et al., 2016). The current study utilizes a prospective daily diary design, and therefore, may not be as susceptible to the influences of these different personality characteristics as retrospective designs.

Future Directions

Daily diary studies provide a unique opportunity to ask interesting research questions regarding variability in day-to-day experiences. An intriguing line of work inspired by Almeida and colleagues has explored how emotional reactivity to stressors is linked with health and well-being (Almeida et al., 2002; Charles et al., 2013; Leger et al., 2018; Mroczek et al., 2013; Stanton et al., 2019a; Stawski et al., 2008). Specifically, this group of researchers capitalized on daily diary studies that collected assessments of

mood and stress and used multilevel modeling to calculate an emotional reactivity to stress score. This emotional reactivity score has been linked to self-reported mental health, physical health symptoms, and mortality (Charles et al., 2013; Leger et al., 2018; Mroczek et al., 2013; Stanton et al., 2019a; Stawski et al., 2008). Other research groups used this method to calculate emotional reactivity to sleep. For example, emotional reactivity to sleep predicted chronic health conditions eight years later (Sin et al., 2021). I could use Almeida's method to calculate emotional reactivity to stress and emotional reactivity to sleep and test whether these factors are associated with antibody production following vaccination. Similarly, I could extend the use of this method and calculate emotional reactivity to self-disclosure and emotional reactivity to perceived responsiveness.

Conclusions

The results of this study question the notion that psychosocial experiences are linked to antibody production following vaccination. Contrary to our predictions, no links emerged between average levels of psychosocial factors, nor the variability within psychosocial factors, and antibody production following influenza vaccination. Future research should use larger sample sizes to explore whether antibody maintenance over time is more susceptible to psychosocial factors than antibody production and whether these links vary as a function of age.

REFERENCES

Afsar, B., Elsurer, R., Eyileten, T., Yilmaz, M. I., & Caglar, K. (2009). Antibody response following hepatitis B vaccination in dialysis patients: Does depression and life quality matter? *Vaccine, 27*, 5865-5869. https://doi.org/10.1016/j.vaccine.2009.07.055

Almeida, D. M., McGonagle, K. A., Cate, R. C., Kessler, R. C., & Wethington, E. (2002). Psychosocial moderators of emotional reactivity to marital arguments. *Marriage & Family Review, 34*, 89-113. https://doi.org/10.1300/J002v34n01_05

Alonso-Ferres, M., Imami, L., & Slatcher, R. B. (2019). Untangling the effects of partner responsiveness on health and well-being: The role of perceived control. *Journal of Social and Personal Relationships, 37,* 1150-1171. https://doi.org/10.1177/0265407519884726

Arriaga, X. B. (2001). The ups and downs of dating: Fluctuations in satisfaction in newly formed romantic relationships. *Journal of Personality and Social Psychology, 80,* 754-765. https://doi.org/10.1037//0022-3514.80.5.754

Arriaga, X. B., Reed, J. T., Goodfriend, W., & Agnew, C. R. (2006). Relationship perceptions and persistence: Do fluctuations in perceived partner commitment undermine dating relationships? *Journal of Personality and Social Psychology, 91,* 1045-1065. https://doi.org/10.1037/0022-3514.91.6.1045

Assari, S., Lee, D. B., Nicklett, E. J., Moghani Lankarani, M., Piette, J. D., & Aikens, J. E. (2017). Racial discrimination in health care is associated with worse glycemic control among Black men but not Black women with type 2 diabetes. *Frontiers in Public Health, 5*, 235. https://doi.org/10.3389/fpubh.2017.00235

Ayling, K., Fairclough, L., Tighe, P., Todd, I., Halliday, V., Garibaldi, J., Royal, S., Hamed, A., Buchanan, H., & Vedhara, K. (2018). Positive mood on the day of influenza vaccination predicts vaccine effectiveness: A prospective observational cohort study. *Brain, Behavior, and Immunity, 67*, 314-323. https://doi.org/10.1016/j.bbi.2017.09.008

Beckwith McGuire, K. M., Greenberg, M. A., & Gevirtz, R. (2005). Autonomic effects of expressive writing in individuals with elevated blood pressure. *Journal of Health Psychology, 10,* 197-209. https://doi.org/10.1177/1359105305049767

Benedict, C., Brytting, M., Markstrom, A., Broman, J., & Schioth, H. B. (2012). Acute sleep deprivation has no lasting effects on the human antibody titer response following a novel influenza A H1N1 virus vaccination. *BMC Immunology, 13,* 1-5. https://doi.org/doi.org/10.1186/1471-2172-13-1

Benthem de Grave, R., Hasselman, F., & Bijleveld, E. (2022). From work stress to disease: A computational model*. PLoS One, 17,* e0263966. https://doi.org/10.1371/journal.pone.0263966

Beyer, W. E., Palache, A. M., Luchters, G., Nauta, J., & Osterhaus, A. D. (2004). Seroprotection rate, mean fold increase, seroconversion rate: Which parameter

adequately expresses seroresponse to influenza vaccination*? Virus Research, 103,* 125-132. https://doi.org/10.1016/j.virusres.2004.02.024

Boehm, J. K., Winning, A., Segerstrom, S., & Kubzansky, L. D. (2015). Variability modifies life satisfaction's association with mortality risk in older adults. *Psychological Science, 26,* 1063-1070. https://doi.org/10.1177/0956797615581491

Bolger, N. & Laurenceau, J. (2013). Intensive longitudinal methods: An introduction to diary and experience sampling research. The Gilford Press.

Booth, R. J., Petrie, K. J., & Pennebaker, J. W. (1997). Changes in circulating lymphocyte numbers following emotional disclosure: Evidence of buffering. *Stress Medicine, 13*, 23-29.

Bower, J. E., Kemeny, M. E., Taylor, S. E., & Fahey, J. L. (2003). Finding positive meaning and its association with natural killer cell cytotoxicity among participants in a bereavement-related disclosure intervention. *Annals in Behavioral Medicine, 25,* 146-155.

Brantley, P. J., Waggoner, C. D., Jones, G. N., & Rappaport, N. B. (1987). A daily stress inventory: Development, reliability, and validity. *Journal of Behavioral Medicine, 10,* 61-74.

Britton, M., Haddad, S., & Derrick, J. L. (2019). Perceived partner responsiveness predicts smoking cessation in single-smoker couples. *Addictive Behaviors, 88*, 122-128. https://doi.org/10.1016/j.addbeh.2018.08.026

Brydon, L., Walker, C., Wawrzyniak, A., Whitehead, D., Okamura, H., Yajima, J., Tsuda, A., & Steptoe, A. (2009). Synergistic effects of psychological and immune

stressors on inflammatory cytokine and sickness responses in humans. *Brain, Behavior, and Immunity, 23,* 217-224. https://doi.org/10.1016/j.bbi.2008.09.007

Brydon, L., Walker, C., Wawrzyniak, A. J., Chart, H., & Steptoe, A. (2009). Dispositional optimism and stress-induced changes in immunity and negative mood. *Brain, Behavior, and Immunity, 23,* 810-816. https://doi.org/10.1016/j.bbi.2009.02.018

Burns, V. E., Carroll, D., Drayson, M., Whitham, M., & Ring, C. (2003). Life events, perceived stress and antibody response to influenza vaccination in young, healthy adults. *Journal of Psychosomatic Research, 55,* 569-572. https://doi.org/10.1016/s0022-3999(03)00073-4

Burns, V. E., Carroll, D., Ring, C., & Drayson, M. (2003). Antibody response to vaccination and psychosocial stress in humans: Relationships and mechanisms. *Vaccine, 21,* 2523-2534. https://doi.org/10.1016/s0264-410x(03)00041-0

Burns, V. E., Carroll, D., Ring, C., Harrison, L. K., & Drayson, M. (2002). Stress, coping, and Hepatitis B antibody status. *Psychosomatic Medicine, 64,* 287-293.

Burns, V. E., Drayson, M., Ring, C., & Carroll, D. (2002). Perceived stress and psychological well-being are associated with antibody status after meningitis C conjugate vaccination. *Psychosomatic Medicine, 64,* 963-970. https://doi.org/10.1097/01.psy.0000038936.67401.28

Burns, V. E., & Gallagher, S. (2010). Antibody response to vaccination as a marker of in vivo immune function in psychophysiological research. *Neuroscience & Biobehavioral Reviews, 35,* 122-126. https://doi.org/10.1016/j.neubiorev.2010.01.005

Bustamante, C. M. V., Rodman, A. M., Dennison, M. J., Flournoy, J. C., Mair, P., & McLaughlin, K. A. (2020). Within-person fluctuations in stressful life events, sleep, and anxiety and depression symptoms during adolescence: A multi-wave prospective study. *Journal of Child Psychology and Psychiatry, 61,* 1116-1125. https://doi.org/10.1111/jcpp.13234

Buysse, D. J., Reynolds III, C. F., Monk, T. H., Berman, S. R., & Kupfer, D. J. (1988). The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. *Psychiatry Research, 28*, 193-213.

Carlock, M. A., Ingram, J. G., Clutter, E. F., Cecil, N. C., Ramgopal, M., Zimmerman, R. K., Warren, W., Kleanthous, H., & Ross, T. M. (2019). Impact of age and pre-existing immunity on the induction of human antibody responses against influenza B viruses. *Human Vaccines and Immunotherapeutics, 15,* 2030-2043. https://doi.org/10.1080/21645515.2019.1642056

Chan, D. K., Zhang, X., Fung, H. H., & Hagger, M. S. (2015). Does emotion and its daily fluctuation correlate with depression? A cross-cultural analysis among six developing countries. *Journal of Epidemiology and Global Health, 5,* 65-74. https://doi.org/10.1016/j.jegh.2014.09.001

Chan, D. K., Zhang, X., Fung, H. H., & Hagger, M. S. (2016). Affect, affective variability, and physical health: Results from a population-based investigation in China. International Journal of Behavioral Medicine, 23, 438-446. https://doi.org/10.1007/s12529-015-9510-2

Charles, S. T., Piazza, J. R., Mogle, J., Sliwinski, M. J., & Almeida, D. M. (2013). The wear and tear of daily stressors on mental health. *Psychological Science, 24,* 733-741. https://doi.org/10.1177/0956797612462222

Chen, E., & Miller, G. E. (2013). Socioeconomic status and health: Mediating and moderating factors. *Annual Review of Clinical Psychology, 9*, 723-749. https://doi.org/10.1146/annurev-clinpsy-050212-185634

Chung, H. Y., Cesari, M., Anton, S., Marzetti, E., Giovannini, S., Seo, A. Y., Carter, C., Yu, B. P., & Leeuwenburgh, C. (2009). Molecular inflammation: Underpinnings of aging and age-related diseases. *Ageing Research Reviews, 8,* 18-30. https://doi.org/10.1016/j.arr.2008.07.002

Clark, M. S., & Reis, H. T. (1988). Interpersonal processes in close relationships. *Annual Review of Psychology, 39*, 609-672.

Claussen, B., Davey Smith, G., & Thelle, D. (2003). Impact of childhood and adulthood socioeconomic position on cause specific mortality: The Oslo Mortality Study. *Journal of Epidemiology and Community Health, 57*, 40-45.

Cohen, S., & Herbert, T. B. (1996). Health psychology: Psychological factors and physical disease from the perspective of human psychoneuroimmunology. *Annual Reviews of Psychology, 47*, 113-142.

Cohen, S., Janicki-Deverts, D., Chen, E., & Matthews, K. A. (2010). Childhood socioeconomic status and adult health. *Annals of the New York Academy of Sciences, 1186*, 37-55. https://doi.org/10.1111/j.1749-6632.2009.05334.x

Cohen, S., Kamarck, T., Mermelstein, R. (1983). A global measure of perceived stress. *Journal of Health and Social Behavior, 24*, 385-396.

Cohen, S., Miller, G. E., & Rabin, B. S. (2001). Psychological stress and antibody response to immunization: A critical review of the human literature. *Psychosomatic Medicine, 63,* 7–18.

Cohen, S., & Wills, T. A. (1985). Stress, social support, and the buffering hypothesis. *Psychological Bulletin, 98,* 310-357.

Cole, S. W., Arevalo, J. M., Manu, K., Telzer, E. H., Kiang, L., Bower, J. E., Irwin, M. R., & Fuligni, A. J. (2011). Antagonistic pleiotropy at the human IL6 promoter confers genetic resilience to the pro-inflammatory effects of adverse social conditions in adolescence. *Developmental Psychology, 47,* 1173-1180. https://doi.org/10.1037/a0023871

Corallo, K. L., Lyle, S. M., Carlock, M. A., Ross, T. M., & Ehrlich, K. B. (2022). Emotional distress, targeted rejection, and antibody production after influenza vaccination in adolescence. *Psychosomatic Medicine, 84,* 429-436. https://doi.org/10.1097/PSY.0000000000001054

Danese, A., Moffitt, T. E., Harrington, H., Milne, B. J., Polanczyk, G., Pariante, C. M., Poulton, R., & Caspi, A. (2009). Adverse childhood experiences and adult risk factors for age-related disease. *Archives of Pediatric and Adolescent Medicine, 163,* 1135-1143.

Dhabhar, F. S. (2014). Effects of stress on immune function: The good, the bad, and the beautiful*. Journal of Immunology Research, 58,* 193-210. https://doi.org/10.1007/s12026-014-8517-0

Dooley, M. K., Sweeny, K., Howell, J. L., & Reynolds, C. A. (2018). Perceptions of romantic partners' responsiveness during a period of stressful uncertainty. *Journal of Personality and Social Psychology, 115,* 677-687. https://doi.org/10.1037/pspi0000134

Doom, J. R., Vanzomeren-Dohm, A. A., & Simpson, J. A. (2016). Early unpredictability predicts increased adolescent externalizing behaviors and substance use: A life history perspective. *Development and Psychopathology, 28,* 1505-1516. https://doi.org/10.1017/S0954579415001169

Duncan, B. B., Ines Schmidt, M., Pankow, J. S., Ballantyne, C. M., Couper, D., Vigo, A., Hoogeveen, R., Folsom, A. R., & Heiss, G. (2003). Low-grade systemic inflammation and the development of type 2 diabetes: The Atherosclerosis Risk in Communities Study. *Diabetes, 52*, 1799-1805.

Edwards, K. M., Burns, V. E., Reynolds, T., Carroll, D., Drayson, M., & Ring, C. (2006). Acute stress exposure prior to influenza vaccination enhances antibody response in women. *Brain, Behavior, and Immunity, 20,* 159-168. https://doi.org/10.1016/j.bbi.2005.07.001

Effros, R. B. (2007). Role of T lymphocyte replicative senescence in vaccine efficacy. *Vaccine, 25*, 599-604. https://doi.org/10.1016/j.vaccine.2006.08.032

Eizenman, D. R., Nesselroade, J. R., Featherman, D. L., & Rowe, J. W. (1997). Intraindividual variability in perceived control in an older sample: The MacArthur successful aging studies. *Psychology and Aging, 12,* 489-502. https://doi.org/10.1037/0882-7974.12.3.489

Faul, F., Erdfelder, E., Buchner, A., & Lang, A. G. (2009). Statistical power analyses using G*Power 3.1: Tests for correlation and regression analyses*. Behavior Research Methods, 41,* 1149-1160. https://doi.org/10.3758/BRM.41.4.1149

Faul, F., Erdfelder, E., Lang, A.-G., & Buchner, A. (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods, 39*, 175-191.

Felitti, V. J., Anda, R. F., Nordenberg, D., Williamson, D., Spitz, A., Edwards, V., Koss, M. P., & Marks, J. S. (1998). Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults: The Adverse Childhood Experiences (ACE) Study. *American Journal of Preventive Medicine, 14,* 245-258.

Frattaroli, J. (2006). Experimental disclosure and its moderators: A meta-analysis. *Psychological Bulletin, 132,* 823-865. https://doi.org/10.1037/0033-2909.132.6.823

Fuller-Rowell, T. E., Nichols, O. I., Burrow, A. L., Ong, A. D., Chae, D. H., & El-Sheikh, M. (2021). Day-to-day fluctuations in experiences of discrimination: Associations with sleep and the moderating role of internalized racism among African

American college students. *Cultural Diversity & Ethnic Minority Psychology, 27,* 107-117. https://doi.org/10.1037/cdp0000342

Gallagher, S., Phillips, A. C., Drayson, M. T., & Carroll, D. (2009). Caregiving for children with developmental disabilities is associated with a poor antibody response to influenza vaccination. *Psychosomatic Medicine, 71,* 341-344. https://doi.org/10.1097/PSY.0b013e31819d1910

Gallagher, S., Phillips, A. C., Drayson, M. T., & Carroll, D. (2009). Parental caregivers of children with developmental disabilities mount a poor antibody response to pneumococcal vaccination. *Brain, Behavior, and Immunity, 23,* 338-346. https://doi.org/10.1016/j.bbi.2008.05.006

Gallagher, S., Phillips, A. C., Ferraro, A. J., Drayson, M. T., & Carroll, D. (2008). Psychosocial factors are associated with the antibody response to both thymus-dependent and thymus-independent vaccines. *Brain, Behavior, and Immunity, 22,* 456-460. https://doi.org/10.1016/j.bbi.2007.10.018

Gallagher, S., Phillips, A. C., Ferraro, A. J., Drayson, M. T., & Carroll, D. (2008). Social support is positively associated with the immunoglobulin M response to vaccination with pneumococcal polysaccharides. *Biological Psychology, 78,* 211-215. https://doi.org/10.1016/j.biopsycho.2008.01.001

Gallagher, S., Siobhan, H., Muldoon, O. T., & Whittaker, A. C. (2022). Social cohesion and loneliness are associated with the antibody response to COVID-19 vaccination. *Brain, Behavior, and Immunity, 103*, 179-185. https://doi.org/10.1016/j.bbi.2022.04.017

Gallant, M. D., & Lafreniere, K. D. (2003). Effects of an emotional disclosure writing task on the physical and psychological functioning of children of alcoholics. *Alcoholism Treatment Quarterly, 21*, 55-66. https://doi.org/10.1300/J020v21n04_05

Galobardes, B., Lynch, J. W., & Davey Smith, G. (2008). Is the association between childhood socioeconomic circumstances and cause-specific mortality established? Update of a systematic review. *Journal of Epidemiology and Community Health 62,* 387-390.

Gidron, Y., Duncan, E., Lazar, A., Biderman, A., Tandeter, H., & Shvartzman, P. (2002). Effects of guided written disclosure of stressful experiences on clinic visits and symptoms in frequent clinic attenders*. Family Practice, 19,* 161-166.

Glaser, R., Kiecolt-Glaser, J. K., Bonneau, R. H., Malarkey, W. B., Kennedy, S., & Hughes, J. (1992). Stress-induced modulation of the immune response to recombinant hepatitis B vaccine. *Psychosomatic Medicine, 54*, 22-29.

Glaser, R., Kiecolt-Glaser, J. K., Malarkey, W. B., & Sheridan, J. F. (1998). The influence of psychological stress on the immune response to vaccines. *Annals of the New York Academy of Sciences, 840,* 649-655. https://doi.org/doi.org/10.1111/j.1749-6632.1998.tb09603.x

Glaser, R., Robles, T. F., Sheridan, J., Malarkey, W. B., & Kiecolt-Glaser, J. K. (2003). Mild depressive symptoms are associated with amplified and prolonged inflammatory responses after influenza virus vaccination in older adults. *Archives in General Psychiatry, 2003*, 1009-1014.

Glaser, R., Sheridan, J., Malarkey, W. B., MacCallum, R. C., & Kiecolt-Glaser, J. K. (2000). Chronic stress modulates the immune response to a pneumococcal pneumonia vaccine. *Psychosomatic Medicine, 62,* 804–807.

Gleeson, M., Pyne, D. B., McDonald, W. A., Clancy, R. L., Cripps, A. W., & Horn, P. L. (1996). Pneumococcal antibody responses in elite swimmers. *Clinical, Experimental Immunology, 105*, 238-244.

Greenberg, M. A., Wortman, C. B., & Stone, A. A. (1996). Emotional expression and physical health: Revising traumatic memories or fostering self-regulation? *Journal of Personality and Social Psychology, 71*, 588-602.

Griffiths, P., Williams, A., & Brohan, E. (2021). How do the number of missing daily diary days impact the psychometric properties and study results arising from a weekly average summary score? https://doi.org/10.21203/rs.3.rs-799794/v1

Gruber, J., Kogan, A., Quoidbach, J., & Mauss, I. B. (2013). Happiness is best kept stable: Positive emotion variability is associated with poorer psychological health. *Emotion, 13,* 1-6. https://doi.org/10.1037/a0030262

Gunaydin, G., Selcuk, E., Urganci, B., & Yalcintas, S. (2020). Today you care, tomorrow you don't: Differential roles of responsiveness variability and average responsiveness in romantic attachment. *Social Psychological and Personality Science, 12,* 839-849. https://doi.org/10.1177/1948550620944111

Hallam, J., Jones, T., Alley, J., & Kohut, M. L. (2022). Exercise after influenza or COVID-19 vaccination increases serum antibody without an increase in side effects. *Brain, Behavior, and Immunity, 102*, 1-10. https://doi.org/10.1016/j.bbi.2022.02.005

Haralambieva, I. H., Salk, H. M., Lambert, N. D., Ovsyannikova, I. G., Kennedy, R. B., Warner, N. D., Pankratz, V. S., Poland, G. A. (2014). Associations between race, sex and immune response variations to rubella vaccination in two independent cohorts. *Vaccine, 32,* 1946-1953.

Hardy, J., & Segerstrom, S. C. (2017). Intra-individual variability and psychological flexibility: Affect and health in a National US sample. *Journal of Research in Personality, 69*, 13-21. https://doi.org/10.1016/j.jrp.2016.04.002

Haynes, L., & Swain, S. L. (2006). Why aging T cells fail: Implications for vaccination. *Immunity, 24,* 663-666. https://doi.org/10.1016/j.immuni.2006.06.003

Hayney, M. S., Coe, C. L., Muller, D., Obasi, C. N., Backonja, U., Ewers, T., & Barrett, B. (2014). Age and psychological influences on immune responses to trivalent inactivated influenza vaccine in the meditation or exercise for preventing acute respiratory infection (MEPARI) trial. *Human Vaccines & Immunotherapeutics, 10,* 83-91. https://doi.org/10.4161/hv.26661

Hayward, S. E., Dowd, J. B., Fletcher, H., Nellums, L. B., Wurie, F., & Boccia, D. (2020). A systematic review of the impact of psychosocial factors on immunity: Implications for enhancing BCG response against tuberculosis. *SSM Population Health, 10*, 100522. https://doi.org/10.1016/j.ssmph.2019.100522

Hawkley, L. C., & Cacioppo, J. T. (2004). Stress and the aging immune system. Brain, Behavior, and Immunity, 18, 114 – 119. https://doi.org/10.1016/j.bbi.2003.09.005

Hoebe, K., Janssen, E., & Beutler, B. (2004). The interface between innate and adaptive immunity. *Nature Immunology, 5*, 971-974. https://doi.org/10.1038/ni1004-971

Holt-Lunstad, J., Smith, T. B., Baker, M., Harris, T., & Stephenson, D. (2015). Loneliness and social isolation as risk factors for mortality: A meta-analytic review. *Perspectives on Psychological Science, 10*, 227-237. https://doi.org/10.1177/1745691614568352

House, J. S., Landis, K. R., & Umberson, D. (1988). Social relationships and health. Science, 241, 540-545.

Imami, L., Stanton, S. C. E., Zilioli, S., Tobin, E. T., Farrell, A. K., Luca, F., & Slatcher, R. B. (2019). Self-disclosure and perceived responsiveness among youth with asthma: Links to affect and anti-inflammatory gene expression. *Personality and Social Psychology Bulletin, 45,* 1155-1169. https://doi.org/10.1177/0146167218808497

Irwin, M. R., Levin, M. J., Carrillo, C., Olmstead, R., Lucko, A., Lang, N., Caulfield, M. J., Weinberg, A., Chan, I. S., Clair, J., Smith, J. G., Marchese, R. D., Williams, H. M., Beck, D. J., McCook, P. T., Johnson, G., & Oxman, M. N. (2011). Major depressive disorder and immunity to varicella-zoster virus in the elderly. *Brain, Behavior, and Immunity, 25,* 759-766. https://doi.org/10.1016/j.bbi.2011.02.001

Irwin, M. R., Levin, M. J., Laudenslager, M. L., Olmstead, R., Lucko, A., Lang, N., Carrillo, C., Stanley, H. A., Caulfield, M. J., Weinberg, A., Chan, I. S., Clair, J., Smith, J. G., Marchese, R. D., Williams, H. M., Beck, D. J., McCook, P. T., Zhang, J. H., Johnson, G., & Oxman, M. N. (2013). Varicella zoster virus-specific immune responses to a herpes zoster vaccine in elderly recipients with major depression and the impact

of antidepressant medications. *Clinical Infectious Diseases, 56,* 1085-1093. https://doi.org/10.1093/cid/cis1208

Jabaaij, L., Grosheide, P. M., Heijtink, R. A., Duivenvoorden, H. J., Ballieux, R. E., & Vingerhoets, A. J. J. M. (1993). Influence of perceived psychological stress and distress on antibody response to low dose rDNA hepatitis B vaccine. *Journal of Psychosomatic Research, 37*, 361-369.

Jemmott, J. B., & Locke, S. E. (1984). Psychosocial factors, immunologic mediation, and human susceptibility to infectious diseases: How much do we know? *Psychological Bulletin, 95*, 78-108.

Jenkins, B. N., Hunter, J. F., Cross, M. P., Acevedo, A. M., & Pressman, S. D. (2018). When is affect variability bad for health? The association between affect variability and immune response to the influenza vaccination. *Journal of Psychosomatic Research, 104*, 41-47. https://doi.org/10.1016/j.jpsychores.2017.11.002

Kane, H. S., Slatcher, R. B., Reynolds, B. M., Repetti, R. L., & Robles, T. F. (2014). Daily self-disclosure and sleep in couples. *Health Psychology, 33,* 813-822. https://doi.org/10.1037/hea0000077

Kernis, M. H., Cornell, D. P., Sun, C., Berry, A., & Harlow, T. (1993). There's more to self-esteem than whether it is high or low: The importance of stability of self-esteem. *Journal of Personality and Social Psychology, 65*, 1190-1204.

Kiecolt-Glaser, J. K., Glaser, R., Gravenstein, S., Malarkey, W. B., & Sheridan, J. (1996). Chronic stress alters the immune response to influenza virus vaccine in older

adults. *Proceedings of the National Academy of Sciences, 93,* 3043-3047. https://doi.org/doi.org/10.1073/pnas.93.7.3043

Kiecolt-Glaser, J. K., McGuire, L., Robles, T. F., & Glaser, R. (2002). Psychoneuroimmunology: Psychological influences on immune function and health. *Journal of Consulting and Clinical Psychology, 70,* 537-547. https://doi.org/10.1037//0022-006x.70.3.537

Kohut, M. L., Lee, W., Martin, A., Arnston, B., Russell, D. W., Ekkekakis, P., Yoon, K. J., Bishop, A., & Cunnick, J. E. (2005). The exercise-induced enhancement of influenza immunity is mediated in part by improvements in psychosocial factors in older adults. *Brain, Behavior, and Immunity, 19*, 357-366. https://doi.org/10.1016/j.bbi.2004.12.002

Krnic, E., Gagro, A., Kozaric-Kovacic, D., Vilibic, M., Grubisic-Ilic, M., Folnegovic-Smalc, V., Drazenovic, V., Cecuk-Jelicic, E., Gjenero-Margan, I., Kuzman, I., Jeren, T., Sabioncello, A., Kerhin-Brkljacic, V., Kaic, B., Markotic, A., Gotovac, K., Rabatic, S., Mlinaric-Galinovic, G., & Dekaris, D. (2007). Outcome of influenza vaccination in combat-related post-traumatic stress disorder (PTSD) patients. *Clinical and Experimental Immunology, 149,* 303-310. https://doi.org/10.1111/j.1365-2249.2007.03410.x

Kuhlman, K. R., Chiang, J. J., Horn, S., & Bower, J. E. (2017). Developmental psychoneuroendocrine and psychoneuroimmune pathways from childhood adversity to disease. *Neuroscience & Biobehavioral Reviews, 80*, 166-184. https://doi.org/10.1016/j.neubiorev.2017.05.020

Kurupati, R., Kossenkov, A., Haut, L., Kannan, S., Xiang, Z., Li, Y., Doyle, S., Liu, Q., Schmader, K., Showe, L., & Ertl, H. (2016). *Oncotarget, 7*, 62898 – 62911.

Lange, T., Dimitrov, S., Bollinger, T., Diekelmann, S., & Born, J. (2011). Sleep after vaccination boosts immunological memory. *The Journal of Immunology, 187,* 283-290. https://doi.org/10.4049/jimmunol.1100015

Lange, T., Perras, B., Fehm, H. L., & Born, J. (2003). Sleep enhances the human antibody response to hepatitis A vaccination. *Psychosomatic Medicine, 65,* 831-835. https://doi.org/10.1097/01.psy.0000091382.61178.f1

Laurenceau, J. P., Barrett, L. F., & Rietromonaco, P. R. (1998). Intimacy as an interpersonal process: The importance of self-disclosure, partner disclosure, and perceived partner responsiveness in interpersonal exchanges*. Journal of Personality and Social Psychology, 74*, 1238-1251.

Leger, K. A., Charles, S. T., & Almeida, D. M. (2018). Let it go: Lingering negative affect in response to daily stressors is associated with physical health years later. *Psychological Science, 29*, 1283-1290. https://doi.org/10.1177/0956797618763097

Lewis, T. T., Williams, D. R., Tamene, M., & Clark, C. R. (2014). Self-reported experiences of discrimination and cardiovascular disease. *Current Cardiovascular Risk Reports, 8,* 365. https://doi.org/10.1007/s12170-013-0365-2

Li, J., Cowden, L. G., King, J. D., Briles, D. A., Schroeder, H. W., Jr., Stevens, A. B., Perry, R. T., Chen, Z., Simmons, M. S., Wiener, H. W., Tiwari, H. K., Harrell, L. E., & Go, R. C. (2007). Effects of chronic stress and interleukin-10 gene polymorphisms on

antibody response to tetanus vaccine in family caregivers of patients with Alzheimer's disease. *Psychosomatic Medicine, 69,* 551-559. https://doi.org/10.1097/PSY.0b013e3180cc2c61

Linden, W. (1984). Development and initial validation of a life event scale for students. *Canadian Counsellor, 18,* 106-110.

Liu, S., & Fisher, P. A. (2022). Early experience unpredictability in child development as a model for understanding the impact of the COVID-19 pandemic: A translational neuroscience perspective. *Developmental Cognitive Neuroscience, 54*, 101091. https://doi.org/10.1016/j.dcn.2022.101091

Madison, A. A., Shrout, M. R., Renna, M. E., & Kiecolt-Glaser, J. K. (2021). Psychological and behavioral predictors of vaccine efficacy: Considerations for COVID-19. *Perspectives on Psychological Science, 16*, 191-203. https://doi.org/10.1177/1745691621989243

Marsland, A. L., Cohen, S., Rabin, B. S., & Manuck, S. B. (2001). Associations between stress, trait negative affect, acute immune reactivity, and antibody response to hepatitis B injection in healthy young adults. *Health Psychology, 20,* 4-11.

Marsland, A. L., Cohen, S., Rabin, B. S., & Manuck, S. B. (2006). Trait positive affect and antibody response to hepatitis B vaccination*. Brain, Behavior, and Immunity, 20,* 261-269. https://doi.org/10.1016/j.bbi.2005.08.009

Matthews, K. A., Patel, S. R., Pantesco, E. J., Buysse, D. J., Kamarck, T. W., Lee, L., & Hall, M. H. (2018). Similarities and differences in estimates of sleep duration by polysomnography, actigraphy, diary, and self-reported habitual sleep in a

community sample. Sleep Health, 4, 96-103. https://doi.org/10.1016/j.sleh.2017.10.011

Mezick, E. J., Matthews, K. A., Hall, M., Kamarck, T. W., Buysse, D. J., Owens, J. F., & Reis, S. E. (2009). Intra-individual variability in sleep duration and fragmentation: Associations with stress. *Psychoneuroendocrinology, 34,* 1346-1354. https://doi.org/10.1016/j.psyneuen.2009.04.005

Miller, G. E., Chen, E., & Parker, K. J. (2011). Psychological stress in childhood and susceptibility to the chronic diseases of aging: Moving toward a model of behavioral and biological mechanisms. *Psychological Bulletin, 137,* 959-997. https://doi.org/10.1037/a0024768

Miller, G. E., Cohen, S., Pressman, S., Barkin, A., Rabin, B. S., & Treanor, J. J. (2004). Psychological stress and antibody response to influenza vaccination: When is the critical period for stress, and how does it get inside the body? *Psychosomatic Medicine, 66,* 215-223. https://doi.org/10.1097/01.psy.0000116718.54414.9e

Morag, M., Yirmiya, R., Lerer, B., & Morag, A. (1998). Influence of socioeconomic status on behavioral, emotional, and cognitive effects of rubella vaccination: A prospective, double-blind study. *Psychoneuroendocrinology, 23,* 337-351.

Moynihan, J. A., Larson, M. R., Treanor, J., Duberstein, P. R., Power, A., Shore, B., & Ader, R. (2004). Psychosocial factors and the response to influenza vaccination in older adults. *Psychosomatic Medicine, 66,* 950-953. https://doi.org/10.1097/01.psy.0000140001.49208.2d

Mroczek, D. K., Stawski, R. S., Turiano, N. A., Chan, W., Almeida, D. M., Neupert, S. D., & Spiro, A., 3rd. (2015). Emotional reactivity and mortality: Longitudinal findings from the VA Normative Aging Study. *Journals of Gerontology: Series B, 70,* 398-406. https://doi.org/10.1093/geronb/gbt107

Muscatell, K. A. (2021). Social psychoneuroimmunology: Understanding bidirectional links between social experiences and the immune system. *Brain, Behavior, and Immunity, 93,* 1-3. https://doi.org/10.1016/j.bbi.2020.12.023

Norona-Zhou, A. N., Morgan, A., Glynn, L. M., Sandman, C. A., Baram, T. Z., Stern, H. S., & Davis, E. P. (2020). Unpredictable maternal behavior is associated with a blunted infant cortisol response. *Developmental Psychobiology, 62,* 882-888. https://doi.org/10.1002/dev.21964

Nunez, I. A., Carlock, M. A., Allen, J. D., Owino, S. O., Moehling, K. K., Nowalk, P., Susick, M., Diagle, K., Sweeney, K., Mundle, S., Vogel, T. U., Delagrave, S., Ramgopal, M., Zimmerman, R. K., Kleanthous, H., & Ross, T. M. (2017). Impact of age and pre-existing influenza immune responses in humans receiving split inactivated influenza vaccine on the induction of the breadth of antibodies to influenza A strains. *PLoS One, 12,* e0185666. https://doi.org/10.1371/journal.pone.0185666

O'Connor, T. G., Moynihan, J. A., & Caserta, M. T. (2014). Annual research review: The neuroinflammation hypothesis for stress and psychopathology in children--developmental psychoneuroimmunology. *Journal of Child Psychology and Psychiatry, 55*, 615-631. https://doi.org/10.1111/jcpp.12187

O'Connor, T. G., Moynihan, J. A., Wyman, P. A., Carnahan, J., Lofthus, G., Quataert, S. A., Bowman, M., & Caserta, M. T. (2014). Depressive symptoms and immune response to meningococcal conjugate vaccine in early adolescence. *Development and Psychopathology, 26*, 1567-1576. https://doi.org/10.1017/S0954579414001242

O'Connor, T. G., Wang, H., Moynihan, J. A., Wyman, P. A., Carnahan, J., Lofthus, G., Quataert, S. A., Bowman, M., Burke, A. S., & Caserta, M. T. (2015). Observed parent-child relationship quality predicts antibody response to vaccination in children. *Brain, Behavior, and Immunity, 48*, 265-273. https://doi.org/10.1016/j.bbi.2015.04.002

Ogawa, T., Kitagawa, M., & Hirokawa, K. (2000). Age-related changes of human bone marrow: A histometric estimation of proliferative cells, apoptotic cells, T cells, B cells, and macrophages. *Mechanisms of Ageing and Development, 117*, 57-68.

Okun, M. L., Reynolds, C. F., 3rd, Buysse, D. J., Monk, T. H., Mazumdar, S., Begley, A., & Hall, M. (2011). Sleep variability, health-related practices, and inflammatory markers in a community dwelling sample of older adults. *Psychosomatic Medicine, 73*, 142-150. https://doi.org/10.1097/PSY.0b013e3182020d08

Parkin, J., & Cohen, B. (2001). An overview of the immune system. *The Lancet, 357*, 1777-1789. https://doi: 10.1016/S0140-6736(00)04904-7.

Pearson, T. A., Mensah, G. A., Alexander, R. W., Anderson, J. L., Cannon, R. O., 3rd, Criqui, M., Fadl, Y. Y., Fortmann, S. P., Hong, Y., Myers, G. L., Rifai, N., Smith, S. C., Jr., Taubert, K., Tracy, R. P., Vinicor, F., Centers for Disease, C., Prevention, &

American Heart, A. (2003). Markers of inflammation and cardiovascular disease: Application to clinical and public health practice: A statement for healthcare professionals from the Centers for Disease Control and Prevention and the American Heart Association. *Circulation, 107,* 499-511. https://doi.org/10.1161/01.cir.0000052939.59093.45

Pedersen, A. F., Zachariae, R., & Bovbjerg, D. H. (2009). Psychological stress and antibody response to influenza vaccination: A meta-analysis. *Brain, Behavior, and Immunity, 23,* 427-433. https://doi.org/10.1016/j.bbi.2009.01.004

Petrie, K. J., Booth, R. J., Pennebaker, J. W., Davison, K. P., & Thomas, M. G. (1995). Disclosure of trauma and immune response to a hepatitis B vaccination program. *Journal of Consulting and Clinical Psychology, 63,* 787-792.

Petrie, K. J., Fontanilla, I., Thomas, M. G., Booth, R. J., & Pennebaker, J. W. (2004). Effect of written emotional expression on immune function in patients with human immunodeficiency virus infection: A randomized trial. Psychosomatic Medicine, 66, 272-275. https://doi.org/10.1097/01.psy.0000116782.49850.d3

Petry, L. J., Weems, L. B., & Livingstone, J. N. (1991). Relationship of stress, distress, and the immunologic response to a recombinant hepatitis B vaccine. *The Journal of Family Practice, 32*, 481-486.

Phillips, A. C. (2011). Psychosocial influences on vaccine responses. *Social and Personality Psychology Compass, 5,* 621-633. https://doi.org/10.1111/j.1751-9004.2011.00378.x

Phillips, A. C., Burns, V. E., Carroll, D., Ring, C., & Drayson, M. (2005). The association between life events, social support, and antibody status following thymus-dependent and thymus-independent vaccinations in healthy young adults. *Brain, Behavior, and Immunity, 19*, 325-333. https://doi.org/10.1016/j.bbi.2004.10.004

Phillips, A. C., Carroll, D., Burns, V. E., Ring, C., Macleod, J., & Drayson, M. (2006). Bereavement and marriage are associated with antibody response to influenza vaccination in the elderly. *Brain, Behavior, and Immunity, 20,* 279-289. https://doi.org/10.1016/j.bbi.2005.08.003

Prather, A. A., Hall, M., Fury, J. M., Ross, D. C., Muldoon, M. F., Cohen, S., & Marsland, A. L. (2012). Sleep and antibody response to hepatitis B vaccination. *Sleep, 35,* 1063-1069. https://doi.org/10.5665/sleep.1990

Prather, A. A., Pressman, S. D., Miller, G. E., & Cohen, S. (2021). Temporal links between self-reported sleep and antibody responses to the influenza vaccine. *International Journal of Behavioral Medicine, 28*, 151-158. https://doi.org/10.1007/s12529-020-09879-4

Pressman, S. D., & Cohen, S. (2005). Does positive affect influence health? *Psychological Bulletin, 131*, 925-971. https://doi.org/10.1037/0033-2909.131.6.925

Pressman, S. D., Cohen, S., Miller, G. E., Barkin, A., Rabin, B. S., & Treanor, J. J. (2005). Loneliness, social network size, and immune response to influenza vaccination in college freshmen. *Health Psychology, 24*, 297-306. https://doi.org/10.1037/0278-6133.24.3.297

Repetti, R. L., Taylor, S. E., & Seeman, T. E. (2002). Risky families: Family social environments and the mental and physical health of offspring. *Psychological Bulletin, 128*, 330-366. https://doi.org/10.1037//0033-2909.128.2.330

Reis, H. T., & Patrick, B. C. (1996). Attachment and intimacy: Component processes. In E. T. Higgins & A. W. Kruglanski (Eds.), Social psychology: Handbook of basic principles (pp. 523-563). The Guilford Press.

Reuben, A., Moffitt, T. E., Caspi, A., Belsky, D. W., Harrington, H., Schroeder, F., Hogan, S., Ramrakha, S., Poulton, R., & Danese, A. (2016). Lest we forget: Comparing retrospective and prospective assessments of adverse childhood experiences in the prediction of adult health. *Journal of Child Psychology and Psychiatry, 57*, 1103-1112. https://doi.org/10.1111/jcpp.12621

Ross, K. M., Liu, S., Tomfohr, L. M., & Miller, G. E. (2013). Self-esteem variability predicts arterial stiffness trajectories in healthy adolescent females. *Health Psychology, 32*, 869-876. https://doi.org/10.1037/a0031458

Ruiz, F. S., Rosa, D. S., Zimberg, I. Z., Dos Santos Quaresma, M. V., Nunes, J. O., Apostolico, J. S., Weckx, L. Y., Souza, A. R., Narciso, F. V., Fernandes-Junior, S. A., Goncalves, B., Folkard, S., Bittencourt, L., Tufik, S., & Tulio de Mello, M. (2020). Night shift work and immune response to the meningococcal conjugate vaccine in healthy workers: A proof of concept study. *Sleep Medicine, 75*, 263-275. https://doi.org/10.1016/j.sleep.2020.05.032

Sacadura-Leite, E., Sousa-Uva, A., Rebelo-de-Andrade, H., Ferreira, S., & Rocha, R. (2014). Association between chronic stress and immune response to influenza

vaccine in healthcare workers. *Revista Portuguesa de Saúde Pública, 32*, 18-26. https://doi.org/10.1016/j.rpsp.2013.09.002

Schleifer, S. J., Bartlett, J. A., Keller, S. E., Eckholdt, H. M., Shiflett, S. C., & Delaney, B. R. (2002). Immunity in adolescents with major depression. *Journal of the American Academy of Child and Adolescent Psychiatry, 41*, 1054-1060. https://doi.org/10.1097/01.CHI.0000020271.43550.85

Segerstrom, S. C., Hardy, J. K., Evans, D. R., & Greenberg, R. N. (2012). Vulnerability, distress, and immune response to vaccination in older adults. *Brain, Behavior, and Immunity, 26*, 747-753. https://doi.org/10.1016/j.bbi.2011.10.009

Segerstrom, S. C., & Miller, G. E. (2004). Psychological stress and the human immune system: A meta-analytic study of 30 years of inquiry. *Psychological Bulletin, 130*, 601-630.

Segerstrom, S. C., Schipper, L. J., & Greenberg, R. N. (2008). Caregiving, repetitive thought, and immune response to vaccination in older adults. *Brain, Behavior, and Immunity, 22*, 744–752. https://doi.org/doi.org/10.1016/j.bbi.2007.11.004

Shadur, J. M., Hussong, A. M., & Haroon, M. (2015). Negative affect variability and adolescent self-medication: The role of the peer context. *Drug and Alcohol Review, 34*, 571-580. https://doi.org/10.1111/dar.12260

Shattuck, E. C. (2021). Networks, cultures, and institutions: Toward a social immunology. *Brain, Behavior, and Immunity - Health, 18*, 100367. https://doi.org/10.1016/j.bbih.2021.100367

Shonkoff, J. P., Garner, A. S., The Committee on Psychosocial Aspects of Child and Family Health, Committee on Early Childhood, Adoption, and Dependent Care, and Section on Developmental and Behavioral Pediatrics, Siegel, B. S., Dobbins, M. I., Earls, M. F., Garner, A. S., McGuinn, L., Pascoe, J., Wood, D. L. (2012). The lifelong effects of early childhood adversity and toxic stress. *Pediatrics, 129*, e232-246. https://doi.org/10.1542/peds.2011-2663

Sin, N. L., Rush, J., Buxton, O. M., & Almeida, D. M. (2021). Emotional vulnerability to short sleep predicts increases in chronic health conditions across 8 Years. *Annals of Behavioral Medicine, 55*, 1231-1240. https://doi.org/10.1093/abm/kaab018

Slatcher, R. B., Selcuk, E., & Ong, A. D. (2015). Perceived partner responsiveness predicts diurnal cortisol profiles 10 years later. *Psychological Science, 26*, 972-982. https://doi.org/10.1177/0956797615575022

Spiegel, K., Sheridan, J., & Van Cauter, E. (2002). Effect of sleep deprivation on response to immunization. *The Journal of the American Medical Association, 288*, 1471-1472.

Stanton, S. C. E., Selcuk, E., Farrell, A. K., Slatcher, R. B., & Ong, A. D. (2019). Perceived partner responsiveness, daily negative affect reactivity, and all-cause mortality: A 20-year longitudinal study. *Psychosomatic Medicine, 81*, 7-15. https://doi.org/10.1097/PSY.0000000000000618

Stanton, S. C., Slatcher, R. B., & Reis, H. T. (2019). Relationships, health, and well-being: The role of responsiveness. In *New directions in the psychology of close relationships* (pp. 118-135). Routledge.

Stawski, R. S., Sliwinski, M. J., Almeida, D. M., & Smyth, J. M. (2008). Reported exposure and emotional reactivity to daily stressors: The roles of adult age and global perceived stress. *Psychology and Aging, 23*, 52-61. https://doi.org/10.1037/0882-7974.23.1.52

Stetler, C., Chen, E., & Miller, G. E. (2006). Written disclosure of experiences with racial discrimination and antibody response to an influenza vaccine*. International Journal of Behavioral Medicine, 13*, 60-68.

Talbot, H. K., Coleman, L. A., Zhu, Y., Spencer, S., Thompson, M., Cheng, P. Y., Sundaram, M. E., Belongia, E. A., & Griffin, M. R. (2015). Factors associated with maintenance of antibody responses to influenza vaccine in older, community-dwelling adults. *BMC Infectious Diseases, 15*, 195. https://doi.org/10.1186/s12879-015-0926-8

Taylor, D. J., Kelly, K., Kohut, M. L., & Song, K. S. (2017). Is insomnia a risk factor for decreased influenza vaccine response? *Behavioral Sleep Medicine, 15*, 270-287. https://doi.org/10.1080/15402002.2015.1126596

Taylor, S. E., & Repetti, R. L. (1997). Health psychology: What is an unhealthy environment and how does it get under the skin? *Annual Review of Psychology, 48*, 411-447.

Trzonkowski, P., Myśliwska, J., Godlewska, B., Szmit, E., Łukaszuk, K., Więckiewicz, J., Brydak, L., Machała, M., Landowski, J., & Myśliwski, A. (2004). Immune consequences of the spontaneous pro-inflammatory status in depressed elderly

patients. *Brain, Behavior, and Immunity, 18*, 135-148. https://doi.org/10.1016/s0889-1591(03)00111-9

Uchino, B. N., Landvatter, J., Zee, K., & Bolger, N. (2020). Social support and antibody responses to vaccination: A meta-analysis. *Annals of Behavioral Medicine, 54*, 567-574. https://doi.org/10.1093/abm/kaaa029

Vedhara, K., Ayling, K., Sunger, K., Caldwell, D. M., Halliday, V., Fairclough, L., Avery, A., Robles, L., Garibaldi, J., Welton, N. J., & Royal, S. (2019). Psychological interventions as vaccine adjuvants: A systematic review. *Vaccine, 37*, 3255-3266. https://doi.org/10.1016/j.vaccine.2019.04.091

Vedhara, K., Cox, N. K. M., Wilcock, G. K., Perks, P., Hunt, M., Anderson, S., Lightman, S. L., & Shanks, N. M. (1999). Chronic stress in elderly carers of dementia patients and antibody response to influenza vaccination. *The Lancet, 353*, 627-631. https://doi.org/doi.org/10.1016/S0140-6736(98)06098-X

Vedhara, K., McDermott, M. P., Evans, T. G., Treanor, J. J., Plummer, S., Tallon, D., Cruttenden, K. A., & Schifitto, G. (2002). Chronic stress in nonelderly caregivers psychological, endocrine and immune implications. *Journal of Psychosomatic Research, 53*, 1153-1161.

Watson, D. (1988). Intraindividual and interindividual analyses of positive and negative affect: Their relation to health complaints, perceived stress, and daily activities. *Journal of Personality and Social Psychology, 54*, 1020-1030.

Watson, D., Clark, L. A., & Carey, G. (1988). Positive and negative affectivity and their relation to anxiety and depressive disorders. *Journal of Psychopathology and Clinical Science, 97*, 346-353. https://doi.org/10.1037/0021-843X.97.3.346

Wong, S. Y., Wong, C. K., Chan, F. W., Chan, P. K., Ngai, K., Mercer, S., & Woo, J. (2013). Chronic psychosocial stress: Does it modulate immunity to the influenza vaccine in Hong Kong Chinese elderly caregivers? *Age, 35*, 1479-1493. https://doi.org/10.1007/s11357-012-9449-z

Wu, R. F., Zimmerman, R. K., & Lin, C. J. (2017). The effect of perceived psychological stress on the immunogenicity of the quadrivalent human papillomavirus vaccine in males*. Human Vaccines & Immunotherapeutics, 13*, 676-679. https://doi.org/10.1080/21645515.2016.1236880

Zimmerman, P., & Curtis, N. (2019). Factors that influence the immune response to vaccination. Clinical Microbiology reviews, 32, e00084-18. https://doi.org/10.1128/CMR.00084-18

APPENDIX A

Institutional Review Board Approval Letter

Tucker Hall, Room 212
310 E. Campus Rd.
Athens, Georgia 30602
TEL 706-542-3199 | FAX 706-542-5638
IRB@uga.edu
http://research.uga.edu/hso/irb/

Human Research Protection Program

APPROVAL OF PROTOCOL

August 12, 2021

Dear Katherine Ehrlich:

On 8/12/2021, the IRB reviewed the following submission:

Title of Study:	2021 Daily Experiences Study (Daily Diary): Adult and Teen
Investigator:	Katherine Ehrlich
IRB ID:	PROJECT00004076
Funding:	NATIONAL INSTITUTES OF HEALTH
Grant ID:	(FP00012295/1DP2MD013947-01)
Review Category:	Expedited 7

Materials Reviewed: IRB submission; NEW_2021DS_Child Assent Letter;NEW_2021DS_ Parent Consent Letter; NEW_2021DS_Adult Consent Letter; 2021Daily Diary_Mental Health Resources; Depressive Symptoms (CESD-10); Loneliness (UCLA Loneliness-8); 2021Daily Diary_ Evening Questionnaires; 2021DailyDiary_ Morning Questionnaires; Home Demographics; Personality (BIG5-10); Open_Response 7.19.21; Religious & Spiritual Background (PMBC-5); Anxiety Symptoms (GAD-7); Social Network Size (SNS-4); Shift and Persist (SAPQ-8); Altruism (SRAS-20); 2021 Daily Diary_Daily Morning Survey Email; 2021 Daily Diary_Daily Evening Survey Text; 2021 Daily Diary_Daily Morning Survey Text; 2021 Daily Diary_Daily Evening Survey Email; 2021 Daily Diary_Reminder Email; NEW_2021 Daily Diary_Parent Initial Email; NEW_2021 Daily Diary_Parent Follow-Up Email; NEW_2021 Daily Diary_Child Follow-Up Email copy; NEW_2021 Daily Diary_Adult Follow-Up Email; NEW_2021 Daily Diary_Adult Initial Email; NEW_2021 Daily Diary_Child Initial Email.

This research is eligible for expedited review under 45 CFR.46.110.

A request to waive documentation of consent, parental permission, and assent (i.e. signature) has been approved under 45 CFR 46.117 (c)(1)(ii). Please note that you are

Commit to Georgia | give.uga.edu
An Equal Opportunity, Affirmative Action, Veteran, Disability Institution

required to obtain consent, permission, and assent with the letters approved with this submission and document this process. Consent, parental permission, and assent have not been waived; only the requirement for signature has been waived.

This study meets the criteria for permissible research with children as set forth at 45 CFR 46.404. One parent or guardians' permission is sufficient to enroll minor subjects. Parent or guardian permission must be obtained, as well as assent of the child, as per 45 CFR 46.408.

A request to waive informed consent has been reviewed and approved under 45 CFR 46.116 (f)(1). Criteria have been met for a waiver of consent for minors who turn 18 while the researchers are still analyzing individually-identifiable data.

The IRB approved the protocol beginning 8/12/2021. A progress report will be requested prior to 8/12/2024. Before or within 30 days of the progress report due date, please submit a progress report or study closure request. Submit a progress report by navigating to the active study and selecting Progress Report. The study may be closed by selecting Create Version and choosing Close Study as the submission purpose.

Please close this study when all human subject research activities and data analysis of identifiable information is complete.

In conducting this study, you are required to follow the requirements listed in the Investigator Manual (HRP-103).

Sincerely,
Kate Pavich, IRB Analyst
Institutional Review Board
University of Georgia

APPENDIX B

Daily Stress Inventory

Thought about the future	Performed poorly at task
Ran out of food/personal article	Performed poorly due to others
Argued with spouse/boyfriend/girlfriend[6]	Thought about unfinished work
Argued with another person	Hurried to meet deadline
Waited longer than you wanted	Interrupted during task/activity
Interrupted while thinking/relaxing	Someone spoiled your completed task
Someone "cut" ahead of you in a line	Did something you are unskilled at
Performed poorly at sport/game	Unable to complete a task
Did something that you did not want to do	Was disorganized
Unable to complete all plans for today	Criticized or verbally attached
Had car trouble	Ignored by others
Had difficulty in traffic	Spoke or performed in public
Money problems	Dealt with rude waiter/waitress/salesperson
A store lacked a desired item	Interrupted while talking
Misplaced something	Was forced to socialize
Bad weather	Someone broke a promise/appointment
Unexpected expenses (fines, traffic ticket, etc.)	Competed with someone
Had confrontation with an authority figure	Was stared at
Heard some bad news	Did not hear from someone you expected to hear from
Concerned over personal appearance	Experienced unwanted physical contact (crowded, pushed)
Exposed to feared situation or object	Was misunderstood
Exposed to upsetting TV show, movie, book	Was embarrassed
"Pet Peeve" violated[7]	Had your sleep disturbed
Failed to understand something	Forgot something
Worried about another person's problems	Feared illness/pregnancy
Experienced narrow escape from danger	Experienced illness/physical discomfort[8]
Your property was damaged	Someone borrowed something without your permission
Had problem with kids	Had minor accident (broke something, tore clothing)
Was late for work/Appointment	Stopped unwanted personal habit (overeating, smoking, nail-biting)

Note. Yellow highlights indicate the items we selected.

[6] Changed to: Confrontation with a friend (e.g., school peer, coworker, sibling, spouse, girl/boyfriend, etc.

[7] Changed to: Someone did something that got on your nerves

[8] Changed to: Feared illness/physical discomfort

APPENDIX C

List of Models

Models 1 & 2: Number of Stressors and Perceived Stress

- **Number of Stressors**
  - Model 1A: Mean number of stressors predicting vaccine response
  - Model 1B: Mean number of stressors and variability in number of stressors predicting vaccine response
- **Perceived Stress**
  - Model 2A: Mean perceived stress predicting vaccine response
  - Model 2B: Mean perceived stress and variability in perceived stress predicting vaccine response

Models 3 & 4: Amount Disclosed and Perceived Responsiveness

- **Amount Disclosed**
  - Model 3A: Mean level of disclosure predicting vaccine response
  - Model 3B: Mean level of disclosure and variability in disclosure predicting vaccine response
- **Perceived Responsiveness**
  - Model 4A: Mean perceived responsiveness predicting vaccine response
  - Model 4B: Mean perceived responsiveness and variability in perceived responsiveness predicting vaccine response

Models 5 & 6: Positive and Negative Mood

- **Positive Mood**
  - Model 5A: Mean level of disclosure predicting vaccine response
  - Model 5B: Mean level of disclosure and variability in disclosure predicting vaccine response.
- **Negative Mood**
  - Model 6A: Mean perceived responsiveness predicting vaccine response
  - Model 6B: Mean perceived responsiveness and variability in perceived responsiveness predicting vaccine response

Models 7 & 8: Sleep Duration and Sleep Quality

- **Sleep Duration**
  - Model 7A: Mean sleep duration predicting vaccine response
  - Model 7B: Mean sleep duration and variability in sleep duration predicting vaccine response
- **Sleep Quality**
  - Model 6A: Mean sleep quality predicting vaccine response
  - Model 6B: Mean sleep quality and variability in sleep quality predicting vaccine response

APPENDIX D

Protocol of Power Analysis

F tests - Linear multiple regression: Fixed model, R^2 deviation from zero

Analysis:	Sensitivity: Compute required effect size		
Input:	α err prob	=	0.05
	Power (1-β err prob)	=	.8
	Total sample size	=	100
	Number of predictors	=	10
Output:	Noncentrality parameter λ	=	17.9462730
	Critical F	=	1.9387913
	Numerator df	=	10
	Denominator df	=	89
	Effect size f^2	=	0.1794627

F tests - Linear multiple regression: Fixed model, R^2 deviation from zero

Analysis:	Sensitivity: Compute required effect size		
Input:	α err prob	=	0.05
	Power (1-β err prob)	=	0.8
	Total sample size	=	100
	Number of predictors	=	24
Output:	Noncentrality parameter λ	=	27.9669297
	Critical F	=	1.6633378
	Numerator df	=	24
	Denominator df	=	75
	Effect size f^2	=	0.2796693