Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

Megan Warnock

Date

Identifying a PTSD resilient group based on a latent class analysis

of childhood trauma and adult PTSD symptoms

By

Megan Warnock Master of Science Biostatistics

Amita Manatunga, Ph.D. Advisor

> Ying Guo, Ph.D. Committee Member

> Limin Peng, Ph.D. Committee Member

> > Accepted:

Lisa A. Tedesco, Ph.D. Dean of the James T. Laney School of Graduate Studies

Date

Identifying a PTSD resilient group based on a latent class analysis

of childhood trauma and adult PTSD symptoms

By

Megan Warnock

B.S., Florida State University, 2012

Advisor: Amita Manatunga, Ph.D.

An abstract of

A thesis submitted to the Faculty of the

James T. Laney School of Graduate Studies of Emory University

in partial fulfillment of the requirements for the degree of

Master of Science in Biostatistics

2016

Abstract

Identifying a PTSD resilient group based on a latent class analysis of childhood trauma and adult PTSD symptoms

By Megan Warnock

Many people experience traumatic events followed by a range of reactions that subside naturally after a few weeks or months. However, for some people these adverse reactions persist and the person develops posttraumatic stress disorder (PTSD). There is no way to know for sure who will develop PTSD, making this disorder heterogeneous. The goal of this study was to investigate and better understand the structure of heterogeneity in PTSD based on reported childhood trauma and current PTSD symptoms using latent class analysis (LCA). A large sample of civilian subjects were recruited from an urban hospital in Atlanta, GA. LCA were conducted on data collected from an early cohort of participants using 25-item childhood trauma questionnaire (CTQ) and 17-item modified PTSD symptom scale (PSS) to identify classes of PTSD. Due to the large sample size, robustness of the latent classes was evaluated using a recently collected, independent group of participants. To better understand the heterogeneity between classes, resilience and affect differences between classes were analyzed.

LCA on the early cohort of 3940 subjects suggested four classes provided the best fit with meaningful, distinct classes characterized as: 1. Low childhood trauma, high PTSD symptoms; 2. High childhood trauma, high PTSD symptoms; 3. Moderate childhood trauma, low PTSD symptoms; 4. Low childhood trauma, low PTSD symptoms. LCA on the recently collected cohort of 1299 subjects replicated this finding with the same four classes suggesting these results as robust. Among the four classes, Class 3 experienced childhood trauma and yet had low PTSD symptoms, highlighting this group as psychologically resilient to PTSD. In comparison to Classes 1 and 2, who had high PTSD symptoms, Class 3 was less negative and depressed and had higher resilience measures compared to Class 2. It merits future studies to further confirm the existence of a psychologically resilient group, and to develop tools to identify such a group that implies persons at lower risk for PTSD.

Identifying a PTSD resilient group based on a latent class analysis

of childhood trauma and adult PTSD symptoms

By

Megan Warnock

B.S., Florida State University, 2012

Advisor: Amita Manatunga, Ph.D.

A thesis submitted to the Faculty of the

James T. Laney School of Graduate Studies of Emory University

in partial fulfillment of the requirements for the degree of

Master of Science in Biostatistics

2016

Acknowledgments

I would like to thank Dr. Amita Manatunga for being a wonderful advisor and mentor. Your time, encouragement, and advice has been invaluable to me and I am extremely grateful for your support. I would also like to thank my committee members, Dr. Limin Peng and Dr. Ying Guo, for their weekly contributions and guidance throughout the thesis process. I would like to thank the faculty, staff, and students of the Department of Biostatistics and Bioinformatics at Emory University for providing a supportive learning environment. I would also like to thank Dr. Tanja Jovanovic and the Grady Trauma Project for allowing me to use their data for my thesis. Finally, I would like to thank my family for their endless love, support, and encouragement.

Table of Contents

1	Intro	duction	1
2	Met	nods	4
	2.1	Participants	4
	2.2	Clinical Assessments	5
	2.3	Statistical Analysis	6
2.3.1 2.3.2		Latent Class Analysis	6
		2 Testing differences between Classes	8
3	Resu	ılts	9
	3.1	Robustness of Latent Class Analysis Results	9
	3.2	Classes of PTSD	0
	3.3	Investigating Class 3: The Resilient Group1	1
4	Disc	ussion1	2
5	Con	clusion1	4
R	eference	es1	6
A	ppendix	A: Tables2	0
A	ppendix	B: Figures	5

List of Tables

1	Descriptive statistics for early and recently collected cohort20
2	Non-standardized mean and standard deviations for five childhood trauma and21 three PTSD symptom categories by class for the early cohort
3	Comparison of LCA results between the early and recently collected cohorts22
4	Clinical assessment summary statistics and Tukey ad-hoc comparisons by class23 for the early cohort
5	Traumatic events in adulthood summary statistics and chi-square tests by class24 for the early cohort

List of Figures

1	BIC values for class sizes 2 – 8 by covariance structures	.25
2	Standardized mean scores for CTQ and PSS for the early cohort	26
3	Standardized mean scores for CTQ and PSS for the recently collected cohort	.27
4	Clinical assessment scores by class for the early cohort	28
5	Proportion of subjects that experienced adult trauma within each class for the early cohort	29

1 Introduction

Posttraumatic stress disorder (PTSD) is a heterogeneous psychiatric disorder that may develop after experiencing a traumatic event. The first criteria in order for a subject to be diagnosed with PTSD is for the subject, or someone close to the subject, to be exposed to a traumatic event such as sexual assault, sudden illness, or military combat¹. During the traumatic event, the subject must experience feelings of intense fear, helplessness, or horror. Finally, harmful cognitive, behavioral, and physiological disturbances must occur for at least one month after the event and are categorized by three symptom groups: intrusive thoughts, avoidance and numbing, and hyperarousal¹.

Subjects that suffer from PTSD may withdraw from their daily lives, become numb to their emotions, and avoid reminders of the event. The traumatic event is often re-experienced through flashbacks and nightmares. These symptoms may have a debilitating effect on the subject's personal and work lives such as occupational instability, relationship problems, and increased thoughts of suicide^{2,3}. However, the mechanism for developing PTSD if not fully understood due to the extreme heterogeneity of PTSD. For example, while over half of the US population experiences some form of trauma in their lives, only 7-8% go on to develop PTSD⁴.

Risk factors for PTSD include childhood trauma, a history of mental illness, lack of social support, and education level⁵. Discerning childhood trauma's relation to PTSD in adulthood is extremely important in understanding the development of PTSD. Exposure to multiple, previous traumatic events increases PTSD symptoms after a traumatic event. Childhood abuse is associated with an increase of traumatic experiences across the lifespan³. As a result, subjects that experience assaultive violence in childhood have been shown to be at a higher risk of developing PTSD after a traumatic event in adulthood^{6,7}. Increased cortisol levels and neurobiological changes have been found in children that experience childhood abuse, resulting in a phenotype with increased vulnerability to depression, stress, and anxiety⁸. Biological

vulnerability to PTSD symptoms has been shown to pass between mothers that experienced childhood abuse to their children, creating a devastating cycle that needs to be addressed⁹.

While childhood abuse is a risk factor for PTSD⁵, not everyone that develops PTSD experiences childhood trauma. Conversely, not everyone that experiences childhood trauma develops PTSD. There are many environmental and biological interactions that are believed to affect disease development. To our knowledge, there have been no studies assessing trends of childhood trauma categories (sexual, physical, emotional abuse and emotional and physical neglect) on PTSD symptoms in adulthood.

Understanding resilience in the face of traumatic events has become a focus in the field of resilience research¹⁰. This has led to a shift in research focus from negative consequences of traumatic events to a better understanding, evaluation, and development of teaching methods to enhance resilience¹⁰. Assessing resilience is difficult because of its subjective definition. The American Psychological Association defines resilience as the process of adapting well in the face of adversity, trauma, tragedy, threats or significant sources of stress¹¹. Previous studies have identified PTSD resilient groups in populations with high trauma¹²⁻¹⁴. A 2006 study found the prevalence of resistance to be at least one third of the study population of New York residents 6 months after the September 11th terrorist attacks¹³. In this study, resilience was measured by PTSD symptoms and defined as experiencing one or less PTSD symptom¹³. A study conducted in 2011 assessed classes of combat exposure and PTSD symptoms in a veteran population and identified a PTSD resilient group, where resilience was characterized as high combat exposure and low PTSD symptoms¹⁴. Both studies focused on populations that experienced specific types of trauma.

The goal of this study was to investigate the structure of heterogeneity in PTSD based on reported childhood trauma and current PTSD symptoms using latent class analysis (LCA), with a particular focus on identifying a PTSD resilient sub cohort. Resilience was defined as experiencing trauma but having low PTSD symptoms. We also aimed to better understand differences between subjects that were resilient to PTSD symptoms versus those that had high PTSD symptoms using clinical assessments for depression, adult trauma, resilience, and positive and negative affect.

LCA is a statistical method that studies patterns in observed measures to characterize unobserved, or latent, groups^{15, 16}. The belief is that there exists an underlying latent variable that causes the responses to the observed variables¹⁵. By studying the interrelationship among observed variables, we can understand and identify the underlying latent variable ¹⁷. LCA divides the population of subjects into classes based on the observed variables in such a way that there is heterogeneity between subjects in different classes while subjects within a class are homogeneous. For this study, the observed variables were clinical assessments measuring childhood traumas and PTSD symptoms.

This study will address a knowledge gap in PTSD research about trends in the experience of childhood trauma by type and PTSD symptoms in adulthood. Rather than looking at the overall experience or severity of trauma in childhood, we will focus on five types of childhood trauma: sexual abuse, physical abuse, emotional abuse, emotional neglect, and physical neglect.

The National Institute of Mental Health has identified one of the next steps for PTSD research to be the prevention of PTSD development soon after exposure to trauma¹⁸. Identifying a resilient group will help identify persons at lower risk for PTSD development after a traumatic event and therefore may contribute to more efficient resource allocation. Understanding differences between people that are resilient to PTSD development versus those at risk will aide in developing targeted treatments that can be implemented soon after a traumatic event with the goal being to prevent PTSD in non-resilient persons.

2 Methods

2.1 Participants

Cross-sectional data for this study were collected to assess environmental and genetic risk factors for developing PTSD in civilian, urban, low-income men and women. Screen interviews were conducted on 9807 subjects that were approached in the primary care or obstetrical-gynecological clinic waiting rooms at Grady Memorial Hospital in Atlanta, Georgia.

Historically, PTSD has been studied in relation to war veterans, trauma victims, and communities exposed to disaster¹⁹. This study population was unique due to the large sample size of a general, civilian population with high exposure to a range of traumas and rates of PTSD similar to Vietnam combat veterans²⁰.

During the screen interview process, verbal interviews were conducted for the following self-report questionnaires: Childhood Trauma Questionnaire (CTQ), modified PTSD Symptom Scale (PSS), the Beck Depression Inventory (BDI), and Traumatic Events Inventory (TEI). Approximately 49% of screened participants went to the second phase of questionnaires which included Positive and Negative Affect Schedule (PANAS), Connor-Davidson Resilience Scale 10 (CD-RISC 10), and providing DNA samples. Inclusion criteria for this study were participants having no missing data for CTQ, PSS, BDI, and TEI. 5239 subjects met the inclusion criteria.

Data collection was performed by Emory University Department of Psychiatry for the Grady Trauma project, a larger study focusing on PTSD and the clinical and psychological implications of trauma exposure²⁰. Data for this analysis were obtained from the Grady Trauma project at two time points: September 2015 (early cohort, n=5063 of which 3940 met inclusion criteria) and August 2016 (recently collected cohort, n=4744 of which 1299 met inclusion criteria). All participants provided written and verbal informed consent. Study procedures were approved by the institutional review boards of Emory University School of Medicine and Grady Memorial Hospital, Atlanta, Georgia.

2.2 Clinical Assessments

Childhood Trauma Questionnaire (CTQ)

The CTQ is a 28-item self-report inventory intended to measure childhood abuse and neglect²¹. The CTQ has been shown to be highly consistent, stable over time, and valid²¹. Responses are measured on a 5-point Likert-scale of 1 (never true) – 5 (very true). The 25-items are broken into 5-subscale scores (sexual abuse, physical abuse, emotional abuse, emotional neglect, and physical neglect) measured by 5 questions each. Overall childhood abuse can be reported as a sum of the 25-items measuring the 5-subscale scores. 3-items (10, 16, and 22) measure minimization/ denial of abuse and are not included in the overall childhood abuse score. *Modified PTSD Symptom Scale (PSS)*

The PSS is a validated 17-item self-report scale assessing PTSD symptoms over the previous two weeks^{22, 23}. Responses are measured on a 4-point Likert scale from 0 (not at all) – 3 (very much/ almost always). Higher scores indicate more severe symptoms of PTSD. Current PTSD diagnosis was based on participant's responses to the PSS and DSM-IV criteria. *The Beck Depression Inventory (BDI)*

The BDI is a 21-item self-report questionnaire measuring depression over the last 2 weeks^{24, 25}. Depressive symptoms are scored on a 4-point Likert scale from 0 to 3, with higher scores indicating more severe symptoms. The 21-items are summed to get a total score for depression severity.

Traumatic Events Inventory (TEI)

The TEI is a binary, 13-item self-report used to assess lifetime history of trauma²⁶. 13 types of traumas are listed, such as sudden illness or attacked with a weapon. Subjects report whether they experienced each type of trauma or not.

Positive and Negative Affect Schedule (PANAS)

PANAS is a 20-item self-report questionnaire used to assess subject's positive and negative affect²⁷. It contains 20 words and participants are asked to rate on a scale from 1-5 how much they relate to the feeling. 10 items measure positive affect with a high score indicating a state of higher energy, concentration, and enjoyable. Low scores indicate sadness and lethargy²⁷. The remaining 10 items measure negative affect where higher scores indicate guilt, fear, and nervousness and lower scores show a state of calmness and serenity²⁷.

Connor – Davidson Resilience Scale 10 (CD-RISC 10)

CD-RISC 10 is a 10-item self-report questionnaire used to measure a subject's resilience ^{28,29}. Scores are measured on a 1-5 point Likert scale with higher scores indicating more resilient.

2.3 Statistical Analysis

Descriptive statistics were obtained for the early and recently collected cohorts to assess differences in demographic variables between cohorts. The demographic variables assessed were age, gender, race, education, employment, and income.

2.3.1 Latent Class Analysis

The purpose of latent class analysis (LCA) is to identify unmeasured class memberships for subjects using observed variables¹⁵. In other words, to identify groups of people that are similar to others in their group but different from those not in their group. Our goal was to assess trends of childhood trauma, measured by 25-item CTQ, and current PTSD symptoms, measured by 17-item PSS, to better understand the heterogeneity of PTSD in relation to childhood trauma. In order to do this, we used the early cohort (n=3940) to identify latent classes and then the recently collected cohort (n=1299) to assess robustness of the latent classes.

R package mclust

LCA was performed using *R package mclust version* $5.0.2^{30}$. *Mclust* performs modelbased clustering based on finite Gaussian mixture modeling fitted via the EM algorithm³⁰. A unique feature of *mclust* is that it supports twelve covariance structures for EM multidimensional data. It is important to first assess which covariance structures are plausible with the data provided and then which of the plausible covariance structures is most appropriate. This can be done using the function *mclustBIC*. Next, LCA is conducted using appropriate covariance structures and specified class sizes. LCA identifies class membership based on posterior probabilities indicating the likelihood of the subject belonging to each class. Subjects are classified into the class for which the posterior probability is highest. There is not a set standard for deciding the final number of classes so a number of factors are considered including the Bayesian information criterion (BIC), bootstrap likelihood ratio test (BLRT)³¹, reproducibility, and interpretability of the classes¹⁵.

Data Analysis Steps

First, the 25-CTQ and 17-PSS items were standardized for the early and recently collected cohort. Standardized scores were computed by item for every subject by subtracting the mean item score from the subject's individual score and dividing by the standard deviation for that item. Standardized scores were calculated separately for the early and recently collected cohorts.

Then, using the early cohort data, we assessed which covariance structures were applicable for model-based clustering on standardized 25-item CTQ and 17-item PSS via *mclustBIC* for class sizes 2 - 8. *MclustBIC* returned the BIC value, where higher is better, for every possible covariance structure for each class size. BIC values by class sizes were plotted.

Next, the function *mclust* was run on the early cohort using standardized 25-item CTQ and 17-item PSS for each possible combination of covariance structure and class size (2 - 8), as indicated by *mclustBIC*. Class sizes were ordered from highest to lowest by percent of people within each class that met PTSD diagnosis, with class 1 having the highest proportion of subjects meeting PTSD diagnostic criteria. Standardized mean scores for CTQ and PSS items were plotted for each combination of covariance structure and class size to assess trends in childhood trauma

and current PTSD symptoms. The covariance structure and class size with the highest BIC that also provided distinct, clinically meaningful classes was selected.

Robustness of the results was assessed using the recently collected cohort. Model-based clustering was performed on the recently collected cohort via LCA using the standardized 25-CTQ and 17-PSS items. The covariance structure and number of classes decided upon from the early cohort were specified in *mclust*. The classes were ordered from highest percent of people meeting PTSD diagnosis within each class to lowest. Standardized mean scores for CTQ and PSS items were plotted by classes.

Percent of the total cohort included in each class and the percent within each class that met current PTSD diagnosis were calculated for the early and recently collected cohorts. Trends in childhood trauma and current PTSD symptoms, percent of cohort in each class, and percent meeting PTSD diagnosis within each class were compared for the early and recently collected cohorts. Results were considered robust if the group structures were similar between the early cohort and the independent, recently collected cohort.

2.3.2 Testing differences between Classes

Depression, adult trauma, resilience, and affect differences between classes for the early cohort were assessed using ANOVA with Tukey post-hoc comparisons. Depression and resilience were measured by summing the 21-items for BDI and 10-items for CD-RISC 10 where higher scores indicated more depressed and higher resilience measures, respectively. Negative affect was measured by summing the ten questions from PANAS that assess negative affect. Similarly, positive affect was measured by summing the ten questions from PANAS that assess positive affect. Finally, number of traumatic experiences in adulthood was measured by summing TEI scores for 11 of the 13 items. Beaten during childhood and sexual abuse before age 13 were not included in this score because those refer specifically to childhood trauma⁶ and would be confounded with the LCA results.

3 Results

In the early cohort, 3940 subjects met inclusion criteria of which the mean age was 40 years old (range 18-78), 71% were women, 92% African American, and 36% met DSM-IV PTSD diagnostic criteria. In the recently collected cohort, 1299 subjects met inclusion criteria of which the mean age was 38.4 years old (range 18-76), 90% were women, 96% African American, and 27% met DSM-IV PTSD diagnostic criteria (table 1).

Data for the early cohort (n=3940) were first analyzed using the LCA method to choose the covariance structure and number of latent classes. There were 9 covariance structures that fit our data (fig. 1). The four class model with a spherical distribution, equal volume, equal shape (EII) covariance structure was selected. While this model did not have the highest BIC, it produced the most meaningful, distinct results (fig. 2). The results indicated four unique trends for adult subjects regarding abuse in childhood and current PTSD symptoms, which are illustrated in figure 2 and described in detail in section 3.2. Non-standardized mean and standard deviations are reported in table 2 for the five types of childhood trauma: sexual abuse, physical abuse, emotional abuse, emotional neglect, and physical neglect; and three PTSD symptom categories: re-experiencing, avoidance and numbing, and hyperarousal.

3.1 Robustness of Latent Class Analysis Results

The large sample size provided the ability to assess the robustness of the LCA results using the recently collected cohort. Data for the recently collected cohort (n=1299) were analyzed using LCA method with covariance structure EII and 4 classes. The results produced 4 classes for the recently collected cohort that followed a similar trend in childhood trauma and PTSD symptoms (fig. 3) as the early cohort (fig. 2). Furthermore, the proportion of people in each class and proportion of people within each class that met PTSD diagnostic criteria were similar for the early and recently collected cohort (table 3).

3.2 Classes of PTSD

Class 1: Low Childhood Trauma, High PTSD Symptoms

Subjects in Class 1 composed 20% of the early cohort and had low trauma in childhood and high current PTSD symptoms. Of the 792 subjects in Class 1, 687 (87%) met DSM-IV diagnostic criteria for PTSD at the time of the survey. Similarly, 16% of the recently collected cohort was in Class 1, of which 85% met PTSD diagnostic criteria.

Class 2: High Childhood Trauma, High PTSD Symptoms

Subjects in Class 2 (10% of the early cohort) had high childhood trauma and high PTSD symptoms in adulthood. The average score for sexual, physical, and emotional abuse, and physical and emotional neglect were all high with sexual abuse having the largest difference from the other Classes. Of the 393 participants in Class 2, 321 (82%) met PTSD diagnostic criteria. For the recently collected cohort, 7% were in Class 2, of which 80% met PTSD diagnostic criteria.

Class 3: Moderate Childhood Trauma, Low PTSD Symptoms (Resilient Group)

Subjects in Class 3 (16% of the early cohort) had moderate childhood trauma and low current PTSD symptoms. Childhood traumas experienced in this group appeared to be predominately emotional neglect. Emotional abuse, physical abuse, and physical neglect scores were moderate. Mean scores for sexual abuse were low. 620 participants were in Class 3, of which 33% met PTSD diagnostic criteria. These results were shown to be robust in the recently collected cohort with 12% of the cohort belonging to Class 3, of which 32% met PTSD diagnostic criteria.

Class 3, despite experiencing moderate childhood trauma, had low PTSD symptoms which highlighted this group as psychologically resilient to PTSD.

Class 4: Low Childhood Trauma, Low PTSD Symptoms

Class 4 was the largest class comprised of 54% of the early cohort. Participants in Class 4 had low childhood trauma and low current PTSD symptoms. Of the 2135 subjects in Class 4, 205

(10%) met PTSD diagnostic criteria. This was also the largest class for the recently collected cohort with 65% of subjects belonging to Class 4, of which 6% met PTSD diagnostic criteria.

While a majority of the participants belonged to Class 4, since we were interested in understanding the heterogeneity of PTSD and childhood trauma we focused on Classes 1, 2, and 3 given the low incidence rate of PTSD in Class 4.

3.3 Investigating Class 3: The Resilient Group

First, we assessed differences in adult trauma for Class 3 versus Classes 1 and 2. Since Class 1 had low childhood trauma and high PTSD symptoms, we were interested in the difference in adult trauma experienced compared to the resilient group, Class 3. There was not a significant difference in total number of traumas experienced in adulthood for Class 1 versus Class 3 (d = 0.2; p = 0.17) (fig.4, table 4). Next, we were interested in the types of adult traumas experienced between the two Classes. The proportion of people that experienced serious accidents or injury, a sudden life threatening illness, witness murder of friends or family, and experiencing a traumatic event that was not listed were significantly higher for Class 1 versus Class 3 (d = 1.2, p < 0.0001).

Next, we looked at differences in depression, resilience, and affect measures (fig. 4, table 4). Class 3 was significantly less depressed than Classes 1 (d = -7.4; p < 0.0001) and 2 (d = -11.6; p < 0.0001). Class 3 had significantly lower negative affect measures than Classes 1 (d = -4.6; p < 0.0001) and 2 (d = -5.9; p < 0.0001), indicating Class 3 was more calm and serene. Interestingly, there was no difference in positive affect between Class 3 versus Classes 1 and 2 suggesting there was not a difference in energy, activity, and enjoyableness experienced between the three groups. Class 3 had significantly higher resilience measures on CD-RISC 10 compared to Class 2 (d = 2.9; p < 0.0001) although there was no difference compared to Class 1 (d = 0.8, p = 0.39). The difference in CD-RISC 10 between Class 1 and Class 2 may be the key contributing factor for their observed difference in PSS scores.

4 Discussion

Patients at the hospital in which participants were approached have high exposure to traumatic events throughout life. Approximately 80% of participants in the early cohort experienced more than one type of serious trauma throughout life (50% in recently collected cohort) of which 36% of patients met current PTSD DSM-IV diagnostic criteria (27% for the recently collected cohort), making this a strong study population for assessing childhood trauma and PTSD symptoms.

LCA on the early cohort revealed four trends between trauma in childhood and current PTSD symptoms. Our findings were robust because the LCA results produced a reproducible group structure with an independent dataset, the recently collected cohort.

Class 3 appeared to be psychologically resilient to PTSD, having experienced moderate childhood trauma but having low current PTSD symptoms. This supports previous studies findings of a PTSD resilient group in a trauma exposed population¹²⁻¹⁴. In contrast, Class 1 had low childhood trauma but high current PTSD symptoms and the highest percent of subjects meeting PTSD diagnostic criteria. The initial question that arose from this finding was if Class 1 experienced more or different types of trauma in adulthood. There was not a significant difference in the number of adult traumas experienced. The proportion of subjects in Class 1 was significantly higher than that in Class 3 for experiencing serious accidents or injury, sudden life-threatening illnesses, witnessing the murder of a friend or family member, and other traumatic experiences not included in the TEI. However, these differences did not appear to be practically meaningful. This suggests the difference between the two groups is not solely based on the type of trauma but on a difference in psychological attributes, genetics, or both.

Classes 2 and 3 both experienced childhood trauma but Class 2 had high current PTSD symptoms and Class 3 did not. While both Classes experienced childhood trauma, the largest difference was in the high scores of sexual abuse for Class 2 compared to Class 3, potentially

showing sexual abuse during childhood to be a high risk factor for PTSD in adulthood. Targeting adults who report childhood sexual abuse after a traumatic event for intervention could help reduce the risk of developing PTSD.

Class 3 had significantly lower depression and negative affect scores than Classes 1 and 2. In addition, Class 3 scored significantly higher on resilience measures than Class 2 but not Class 1. Negative affect is the way in which a person experiences negative emotions such as anger, guilt, fear, nervousness, and disgust. People with high negative affect scores generally focus on negative aspects of their lives and are more distressed²⁷. In contrast, people with low negative affect scores are more calm and serene²⁷. Focusing on negative affect to aide persons that recently experienced a trauma to cope and internalize traumatic events in a positive way may help prevent the development of PTSD or decrease the severity.

Lastly, we did an initial exploration comparing genetic differences between Classes 1, 2, and 3 by looking at 10 SNPs that have shown or are hypothesized to be associated with PTSD. We considered SNPs rs322931, rs7550394, rs9296158, rs3800373, rs1360780, rs9470080, rs2267735, rs363276, rs1800497, and rs4680. No major differences were observed for these SNPs across the classes. Future research should conduct a genome-wide association study in relation to understanding genetic differences between the resilient group and subjects that develop PTSD. Previous research showed four of the SNPs; rs9296158, rs3800373, rs1360780, rs9470080; to have a significant interaction with childhood trauma on predicting PTSD in adults³². One complication with our analysis was that we could not assess the interaction of genes with childhood trauma on PTSD outcome by class since childhood trauma was a factor for determining the class subjects were assigned.

Strengths of this study included a large number of participants that met the inclusion and exclusion criteria. One concern with LCA is that the results are specific to the subjects included in the analysis and if you were to rerun LCA on an independent set of subjects the results would be different. The large sample size allowed us to conduct LCA on two independent sets of

participants which showed the results to be robust. Another strength is that this study did not restrict the study population to people that experienced one type of traumatic event, broadening the knowledge of PTSD resilience to a range of trauma types across the lifespan.

This study had several limitations. First, participants were predominately low socioeconomic, African American women so the results may not be generalizable to the whole population. Second, this is a cross-sectional, observational study so we can only comment on the trends and states of participants at the time of the surveys. We cannot deduce that childhood traumas lead to PTSD or make inferences about risk factors. Third, childhood trauma was measured retrospectively so recall bias may have occurred. Fourth, all measures used in this study were self-report measures so recall bias, response bias, and ordinal measures may affect the results. Finally, PTSD diagnosis was based on DSM-IV criteria.

Future research may address our limitations by conducting a longitudinal study to assess the causality of childhood trauma on the development of PTSD in adulthood. Following subjects from childhood into adulthood would allow the researcher to evaluate traumas experienced throughout life and subsequent PTSD symptoms after a traumatic event. Stratified sampling is recommended to ensure enrollment of participants that do and do not experience childhood abuse. PTSD diagnosis should be assessed based on the most up-to date diagnostic criteria outlined by the Diagnostic and Statistical Manual of Mental Disorders, currently the DSM-5. Future studies should refine the definition of resilience and develop a criteria to evaluate resilience based on clinical assessments. Future research should further study genetic factors for each class to examine biological differences between the resilient class and classes with high current PTSD to help develop targeted treatments and prevent PTSD from developing in persons at higher risk.

5 Conclusion

LCA identified four robust trends of childhood trauma and current PTSD symptoms. These findings highlight Class 3 as psychologically resilient to PTSD. In future studies we would expect to see a psychologically resilient group which may help to understand the heterogeneity of PTSD and identify persons at lower risk for PTSD. Our findings indicate negative affect and resilience are important personality variables for recognizing persons at low risk of PTSD. Identifying personality variables that are unique to the resilient group could help develop therapeutic approaches targeted at harmful thought processes early after a traumatic experience.

References

- Diagnostic and statistical manual of mental disorders. 4th ed., text revision. Washington, DC: American Psychiatric Association; 2000.
- Iribarren, J., Prolo, P., Neagos, N., & Chiappelli, F. (2005). Post-traumatic stress disorder: Evidence-based research for the third millennium. *Evidence-Based Complementary and Alternative Medicine*, 2(4), 503-512.
- Kessler, R. C. (2000). Posttraumatic stress disorder: the burden to the individual and to society. *The Journal of clinical psychiatry*, 61(suppl 5), 4-12.
- Kessler, R. C., Sonnega, A., Bromet, E., Hughes, M., & Nelson, C. B. (1995).
 Posttraumatic stress disorder in the National Comorbidity Survey. *Archives of general psychiatry*, 52(12), 1048-1060.
- Brewin, C. R., Andrews, B., & Valentine, J. D. (2000). Meta-analysis of risk factors for posttraumatic stress disorder in trauma-exposed adults. *Journal of consulting and clinical psychology*, 68(5), 748.
- Binder, E. B., Bradley, R. G., Liu, W., Epstein, M. P., Deveau, T. C., Mercer, K. B., ... & Schwartz, A. C. (2008). Association of FKBP5 polymorphisms and childhood abuse with risk of posttraumatic stress disorder symptoms in adults. *Jama*, 299(11), 1291-1305.
- Breslau, N., Chilcoat, H. D., Kessler, R. C., & Davis, G. C. (1999). Previous exposure to trauma and PTSD effects of subsequent trauma: results from the Detroit Area Survey of Trauma. *American journal of Psychiatry*, 156(6), 902-907.
- Heim, C., & Nemeroff, C. B. (2001). The role of childhood trauma in the neurobiology of mood and anxiety disorders: preclinical and clinical studies. *Biological psychiatry*, 49(12), 1023-1039.

- Brand, S. R., Brennan, P. A., Newport, D. J., Smith, A. K., Weiss, T., & Stowe, Z. N. (2010). The impact of maternal childhood abuse on maternal and infant HPA axis function in the postpartum period. *Psychoneuroendocrinology*, *35*(5), 686-693.
- Southwick, S. M., Bonanno, G. A., Masten, A. S., Panter-Brick, C., & Yehuda, R. (2014). Resilience definitions, theory, and challenges: interdisciplinary perspectives. *European Journal of Psychotraumatology*, 5.
- 11. American Psychological Association (2014). The road to resilience. Washington, DC: American Psychological Association. Retrieved November 8, 2016, from http://www.apa.org/helpcenter/road-resilience.aspx.
- Lauth-Lebens, M., & Lauth, G. W. (2016). Risk and Resilience Factors of Post-Traumatic Stress Disorder: A Review of Current Research. *Clinical and Experimental Psychology*, 2016.
- Bonanno, G. A., Galea, S., Bucciarelli, A., & Vlahov, D. (2006). Psychological resilience after disaster New York city in the aftermath of the September 11th Terrorist Attack. *Psychological Science*, *17*(3), 181-186.
- Pietrzak, R. H., & Southwick, S. M. (2011). Psychological resilience in OEF–OIF Veterans: Application of a novel classification approach and examination of demographic and psychosocial correlates. *Journal of affective disorders*, *133*(3), 560-568.
- 15. McCutcheon, A. L. (1987). Latent class analysis (No. 64). Sage.
- Vermunt, J. K., & Magidson, J. (2004). Latent class analysis. The sage encyclopedia of social sciences research methods, 549-553.
- Hagenaars, J. A., & McCutcheon, A. L. (Eds.). (2002). Applied latent class analysis. Cambridge University Press.

- National Institute of Mental Health (2016). *Post-Traumatic Stress Disorder*. Retrieved November 2, 2016, from https://www.nimh.nih.gov/health/topics/post-traumaticstress-disorder-ptsd/index.shtml.
- Helzer, J. E., Robins, L. N., & McEvoy, L. (1987). Post-traumatic stress disorder in the general population. *New England Journal of Medicine*, *317*(26), 1630-1634.
- 20. The Grady Trauma Project. (2015). Retrieved November 08, 2016, from http://gradytraumaproject.com/project/project-overview/.
- Bernstein, D. P., Stein, J. A., Newcomb, M. D., Walker, E., Pogge, D., Ahluvalia, T., ...
 & Zule, W. (2003). Development and validation of a brief screening version of the Childhood Trauma Questionnaire. *Child abuse & neglect*, 27(2), 169-190.
- 22. Foa, E. B., Riggs, D. S., Dancu, C. V., & Rothbaum, B. O. (1993). Reliability and validity of a brief instrument for assessing post- traumatic stress disorder. *Journal of traumatic stress*, 6(4), 459-473.
- Breslau, N., Peterson, E. L., Kessler, R. C., & Schultz, L. R. (1999). Short screening scale for DSM-IV posttraumatic stress disorder. *American Journal of Psychiatry*, 156(6), 908-911.
- 24. Beck, A. T., Steer, R. A., & Carbin, M. G. (1988). Psychometric properties of the Beck Depression Inventory: Twenty-five years of evaluation. *Clinical psychology review*, 8(1), 77-100.
- 25. Beck, A. T., Steer, R. A., & Brown, G. K. (1996). Beck depression inventory-II. San Antonio, TX, 78204-2498.
- Sprang, G. (1997). The traumatic experiences inventory (TEI): A test of psychometric properties. *Journal of Psychopathology and Behavioral Assessment*, 19(3), 257-271.

- 27. Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: the PANAS scales. *Journal of personality and social psychology*, 54(6), 1063.
- Connor, K. M., & Davidson, J. R. (2003). Development of a new resilience scale: The Connor- Davidson resilience scale (CD- RISC). *Depression and anxiety*, 18(2), 76-82.
- Campbell- Sills, L., & Stein, M. B. (2007). Psychometric analysis and refinement of the connor–davidson resilience scale (CD- RISC): Validation of a 10- item measure of resilience. *Journal of traumatic stress*, 20(6), 1019-1028.
- 30. Fraley C, Raftery AE, Murphy TB, Scrucca L. mclust Version 4 for R: Normal mixture modeling formodel-based clustering, classification, and density estimation.
 Technical Report No. 597, Department of Statistics, University of Washington; 2012.
- 31. Nylund, K. L., Asparouhov, T., & Muthén, B. O. (2007). Deciding on the number of classes in latent class analysis and growth mixture modeling: A Monte Carlo simulation study. *Structural equation modeling*, 14(4), 535-569.
- 32. Binder, E. B., Bradley, R. G., Liu, W., Epstein, M. P., Deveau, T. C., Mercer, K. B., ... & Schwartz, A. C. (2008). Association of FKBP5 polymorphisms and childhood abuse with risk of posttraumatic stress disorder symptoms in adults. *Jama*, 299(11), 1291-1305.

Appendix A: Tables

	Early cohort (n=3940)	Recently collected cohort (n=1299)	P-value
Mean (SD)	<u> </u>	· · ·	
Age (years)	40.7 (13.6)	38.4 (14.1)	<.0001***
N (%)			
Gender (females)	2810 (71.4)	1167 (90.0)	<.0001***
Race (African American)	3588 (91.6)	1243 (95.6)	<.0001***
Education			.2855
Did not complete 12 th grade	849 (21.7)	255 (19.7)	
12 th grade or high school graduate	1348 (34.4)	487 (37.5)	
GED	185 (4.7)	66 (5.1)	
Some college/ technical school	933 (23.8)	313 (24.1)	
Technical school graduate	185 (4.7)	57 (4.4)	
College graduate	345 (8.8)	96 (7.4)	
Graduate School	70 (1.8)	23 (1.8)	
Unemployed (yes)	1199 (30.6)	441 (34.0)	.0262*
Income (\$)			.0025**
0-249	812 (21.3)	214 (17.0)	
250-499	313 (8.2)	126 (10.0)	
500-999	1018 (26.8)	329 (26.1)	
1000-1999	1046 (27.5)	357 (28.3)	
\geq 2000	615 (16.2)	236(8.7)	
$\begin{array}{l} * & p < .05 \\ ** & p < .01 \\ *** & p < .001 \end{array}$			

Table 1. Demographic characteristics for early and recently collected cohort.

Table 2. Summary statistics by class for childhood trauma types and PTSD symptoms categories. Possible range of scores for types of childhood trauma is 5 - 25, with 5 being low trauma and 25 being high trauma. Possible range for PTSD symptoms are: Re-experiencing: 0 - 15; Avoidance and numbing: 0 - 21; Hyper arousal: 0 - 15 with 0 being no symptoms.

	Class			
_	1	2	3	4
Mean (SD)	(n=792)	(n=393)	(n=620)	(n=2135)
Childhood Trauma Questionnaire (CTQ)				
Sexual Abuse	8.1 (4.6)	17.2 (6.4)	9.4 (5.3)	6.0 (2.7)
Physical Abuse	7.6 (2.6)	15.9 (5.1)	10.4 (3.9)	6.6 (1.8)
Emotional Abuse	9.0 (3.6)	18.7 (4.0)	13.1 (4.0)	6.4 (2.0)
Emotional Neglect	8.4 (3.6)	17.6 (4.9)	14.8 (3.9)	6.7 (2.4
Physical Neglect	6.4 (2.1)	12.1 (4.4)	9.0 (3.4)	5.7 (1.5
Modified PTSD Symptom Scale (PSS)				
Re-experiencing	7.9 (3.4)	7.3 (4.0)	2.5 (2.5)	1.3 (1.8
Avoidance and numbing	12.0 (3.9)	12.3 (5.0)	5.3 (4.2)	2.5 (2.9
Hyper arousal	4.0 (1.0)	4.1 (1.3)	2.2 (1.5)	1.3 (1.3

N (%)	1	2	3	4
Total in Class				
Early Cohort	792 (20.1)	393 (10.0)	620 (15.7)	2135 (54.2)
Recently Collected Cohort	206 (15.9)	92 (7.1)	161 (12.4)	840 (64.7)
PTSD Diagnosis Criteria Met				
Early Cohort	687 (86.7)	321 (81.7)	204 (32.9)	205 (9.6)
Recently Collected Cohort	175 (85.0)	74 (80.4)	52 (32.3)	54 (6.4)

Table 3. Comparing LCA results between the early (n=3940) and recently collected (n=1299) cohorts.

	Class					
	Missing	1	2	3	4	
Mean (SD)	(n=3940)	(n=792)	(n=393)	(n=620)	(n=2135)	Comparison
BDI	0	24.2 (10.5)	28.4 (13.8)	16.8 (10.7)	9.5 (8.1)	1-3***
	Ũ	2.1.2 (10.0)	2011 (1210)	1010 (1017)	<i>)</i> (0.1)	2-3***
CD-RISC 10	1574	28.7 (8.0)	26.6 (9.2)	29.5 (7.9)	33.4 (6.1)	1-3 2-3***
PANAS						
Negative	1213	26.7 (8.7)	28.0 (10.4)	22.1 (7.7)	18.3 (7.0)	1-3***
						2-3***
Positive	1215	36.1 (9.0)	34.7 (9.7)	36.1 (8.3)	41.0 (7.5)	1-3
						2-3
Adult	0	3.4 (1.7)	4.4 (2.0)	3.2 (1.7)	2.3 (1.4)	1-3
Trauma						2-3***
* p < .05						
** p < .01 *** p < .001						
P \.001						

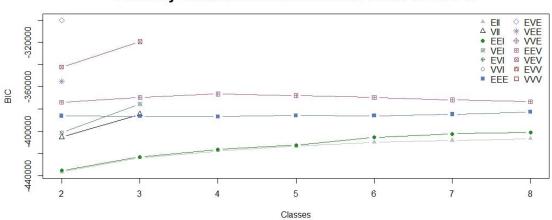
Table 4. Summary statistics and Tukey ad-hoc comparison results for comparing resilient group, Class 3, to classes with high PTSD symptoms, Classes 1 and 2.

		Cla			
N (%)	1 (n=792)	2 (n=393)	3 (n=620)	4 (n=2135)	Comparison
Traumatic event inventory (yes)					
Natural Disaster	281 (35.5)	153 (38.9)	193 (31.1)	605 (28.3)	1-3 2-3*
Serious accident or injury	475 (60.0)	256 (65.1)	330 (53.2)	1067 (50.0)	1-3* 2-3***
Sudden life- threatening illness	252 (31.8)	147 (37.4)	148 (23.9)	481 (22.5)	1-3** 2-3***
Military combat experience	13 (1.6)	8 (2.0)	13 (2.1)	51 (2.4)	1-: 2-:
Witness murder of friend or family	172 (21.7)	96 (24.4)	102 (16.5)	265 (12.4)	1-3 2-3**
Attack with gun or knife	331 (41.8)	178 (45.3)	231 (37.4)	613 (28.7)	1- 2-3
Attack without weapons	259 (32.7)	157 (39.9)	226 (36.5)	563 (26.4)	1- 2-
Witness violence of parents or caregiver	299 (37.8)	260 (66.2)	335 (54.0)	527 (24.7)	1-3** 2-3**
Sexual contact between 14-17	161 (20.3)	193 (49.1)	120 (19.4)	152 (7.1)	1- 2-3**
Sexual contact after 17	144 (18.2)	147 (37.4)	100 (16.1)	126 (5.9)	1-: 2-3**;
Other traumatic experience	312 (39.4)	136 (34.6)	207 (33.4)	563 (26.4)	1-3 ³ 2-3

Table 5. Number of people that experienced traumatic event within each class. Chi-square p-values are reported for comparing the resilient group, Class 3, to classes with high PTSD symptoms, Classes 1 and 2.

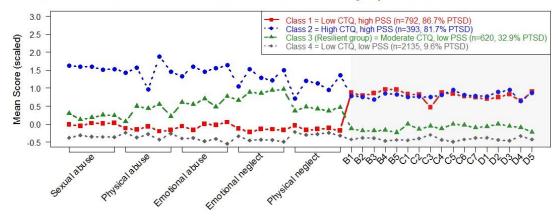
Appendix B: Figures

Figure 1. Plot of BIC values by covariance structure for each class size for early cohort (n=3940).



BIC's by covariance structures for class sizes 2-8

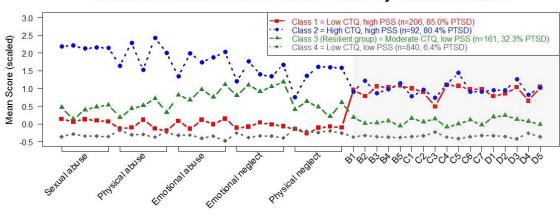
Figure 2. Standardized mean scores on CTQ and PSS questionnaires by 4-class latent model for early cohort (n=3940).



Trends in childhood trauma and adult PTSD symptoms: Four latent classes

B1: Intrusive memories, B2: Nightmares, B3: Flashbacks, B4: Psychologic reactivity, B5: Physiologic reactivity, C1: Avoid thinking, C2: Avoid activities, C3: Amnesia, C4: Diminished interest, C5: Detached, C6: Restricted affect, C7: Foreshortened future, D1: Insomnia, D2: Irritability, D3: Concentration problems, D4: Hypervigilance, D5: Exaggerated startle

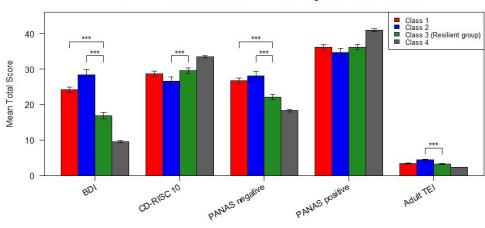
Figure 3. Standardized mean scores on CTQ and PSS questionnaires after LCA was applied to recently collected cohort (n=1299), showing results are robust. Same number of classes, 4, and covariance structure, EII, as early cohort.



Results are robust: Similar trend in recently collected cohort

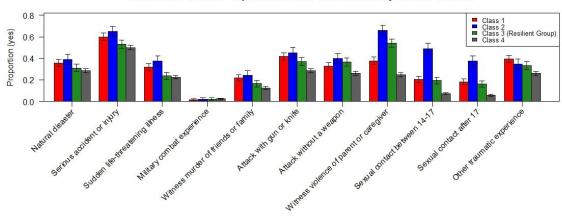
B1: Intrusive memories, B2: Nightmares, B3: Flashbacks, B4: Psychologic reactivity, B5: Physiologic reactivity, C1: Avoid thinking, C2: Avoid activities, C3: Amnesia, C4: Diminished interest, C5: Detached, C6: Restricted affect, C7: Foreshortened future, D1: Insomnia, D2: Irritability, D3: Concentration problems, D4: Hypervigilance, D5: Exaggerated startle

Figure 4. Mean total score on clinical assessments by latent classes. Illustrates differences in depression, resilience, negative affect, positive affect, and total number of adult traumas experienced. Tukey's post-hoc comparison p-values are only reported when Class 3 is significantly different from Classes 1 or 2. *** p-value<0.0001.



Clinical assessment scores by latent classes

Figure 5. Proportion of participants in each class that experienced adult traumas by traumatic event types measured by the TEI.



Traumatic events experienced in adulthood by latent classes