

A. OVERALL COVER PAGE

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hESC: No	Inventions/Patents: No

B. OVERALL ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

Threats of bioterrorism worldwide make it incumbent for the public health community to thoroughly understand the life-course of health-related consequences (psychological, physical and behavioral) from the dual exposures to emotional trauma and environmental toxins that potentially arise from any mass disaster. Fortunately, there have been extensive studies by the World Trade Center Health Registry (WTCHR), as well as others, characterizing what turned out to be very significant physical and psychological consequences of 9/11-related exposures in adults; these studies continue to drive screening, prevention and treatment interventions. However, there has not been a similar degree of investigation or intervention for those exposed as children or adolescents, whose bodies and brains were in the process of developing and, thus, were especially vulnerable. It is crucial, therefore, that we identify and characterize the holistic health consequences of the 9/11-related traumatic and toxic exposures to these youth, including physical (airway disorders and inflammatory processes, obesity, blood pressure, etc.), psychiatric (mental health, substance abuse), behavioral health (decision anomalies and high-risk behavior), as well as educational, occupational and social functioning. We can, and should, make sure that their health status and future risks are thoroughly understood, so that they too can receive preventative and therapeutic interventions over their life course, especially as they transition into adulthood and potentially become more at-risk for cancer and other chronic diseases. As an important step in this agenda, our team, the Global Psychiatric Epidemiology Group (GPEG), conducted the Stress and Well Being Study (UO1OH010414; PI: Hoven), an in-depth mental health evaluation of N=1,000 individuals exposed to 9/11 as children under the age of 18, drawn from the WTCHR, with N=500 unexposed Controls of similar age, gender and sociodemographic distributions. That study, the largest 9/11 child study with in-person diagnostic mental health assessments, ended in August 2016, and is in the process of thoroughly characterizing this unique cohort and control group, in terms of their psychosocial, psychiatric and behavioral characteristics. It has already documented the first objective evidence linking 9/11 exposures to a wide-range of subsequent psychiatric disorders, many years later.

Currently, however, there is no in-person study of children, linking 9/11-related traumatic and toxic exposures to physical health outcomes, which we have reason to believe are significant. Our Co-Investigator, Dr. Szema, for example, found a 66% increase in new asthma diagnoses in Manhattan's Chinatown, blocks from Ground Zero, in the year after 9-11, and these problems have persisted. Moreover, the comorbidity of physical and psychiatric disorders can lead to broad negative health outcomes, such as: sinusitis, poor exercise tolerance, obesity, type II diabetes, hypertension and cancer, as well as poor psychological and functional outcomes in the educational, occupational and social domains. In this study, therefore, we aim to close this gap by collecting and characterizing key physical health indicators from our well-characterized S&W cohort, to examine interactions between physical and psychological health, and to collect and store biologicals for future investigations as these youth age.

Thus, we created an interdisciplinary collaboration across psychiatry, behavioral science, pediatric allergy/immunology, pulmonology and epidemiology, and to draw on our unique S&W cohort of 9/11 directly exposed youth, to examine the health consequences of that event. This study will enhance the largest, most comprehensive, representative study of children derived from the WTCHR, directly exposed to the attack of September 11, 2001, and thus establish the most thoroughly characterized cohort of 9/11 children to be followed for decades of ongoing health, mental health and co-morbidity research.

SPECIFIC AIMS

In a WTCHR representative sample of youth (N=1,000) under 18 years of age on September 11, 2001, who were directly exposed to 9/11, compared to unexposed Controls (N=500), we will:

- Aim 1: Characterize physical health status, focusing on pulmonary diseases and allergic/immunologic consequences.
- Aim 2: Examine gene-environment interactions, determining if genetic vulnerability modifies the relationship between 9/11 exposure in childhood and subsequent psychiatric symptoms.
- Aim 3: Examine physical and mental health comorbidities and their consequences to educational, occupational and social functioning outcomes.
- Aim 4. Collect key biologicals (e.g., blood) relevant to physical and mental health status, potentially related to 9/11 exposure, for analysis in subsequent investigation(s): 1) inflammatory/immune biologicals; 2) DNA for epigenetics, and 3) RNA for gene

expression.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

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B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

NOTHING TO REPORT

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

Not Applicable

**9/11 Trauma and Toxicity in Childhood:
Longitudinal Health and Behavioral Outcomes**

S&W2 Study

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**9/11 Trauma and Toxicity in Childhood:
Longitudinal Health and Behavioral Outcomes**

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Abstract

On 9/11, children who were residents of the World Trade Center area or students in local schools experienced a wide range of psychological traumas and toxic exposures. Yet, surprisingly, much less research has been done with those exposed to 9/11 as children than with adults. The bulk of research has focused on those who were adults on 9/11, which has furnished strong evidence linking 9/11 traumatic and toxic exposures (both on 9/11 and subsequently) to a wide range of subsequent adult psychiatric and physical disorders. Based on this research, we can, unfortunately, expect that youth who were directly exposed on 9/11, during sensitive periods in their physical and mental development, will carry even greater and ongoing lifetime risks for a variety of behavioral and physical health difficulties.

The Stress and Well-Being (S&W) study followed N=1,000 individuals exposed to 9/11 as children and N=500, age and gender matched, unexposed Controls. The study was focused on psychological trauma and psychiatric and behavioral outcomes and generated concrete evidence for the ongoing developmental psychiatric and behavioral problems in this group, a decade after 9/11. In this S&W2 Study, we expanded the scope of the baseline S&W Study by assessing these individuals for toxic exposures, objective measures of their physical health (airway disorders and inflammatory processes), as well as their ongoing psychiatric (mental health, substance abuse) and behavioral (decision anomalies and high-risk behavior) outcomes. We examined the interaction between traumatic and toxic exposures and the resulting comorbidities of physical and mental health issues. This approach was designed to fill important knowledge gaps, resulting in valuable information to guide both psychiatric and general medical care for those children exposed to 9/11, while simultaneously providing new information about the long-term comorbid mental-physical health sequelae of traumatic exposure in childhood, relevant for all youth exposed to traumatic events.

Significant (Key) Findings

The S&W2 data demonstrated that early life exposure to disasters, such as 9/11, can have a significant, negative consequence on both an individual's mental, behavioral and physical health, including pulmonary health, starting as early as adolescence and manifesting in young adulthood. Our data showed a clear association of 9/11 exposure with physiologically measured respiration function (Aims 1 & 3). Evidence was shown for increased respiratory symptoms, impact on respiratory symptoms, and total respiratory health impairment in 9/11 exposed versus unexposed participants. A strong association of measurably greater deleterious pulmonary outcomes with amount of direct exposure to the 9/11 attack also found. Energy and emotional well-being were reduced in 9/11 exposed versus unexposed subjects. These findings added biological specificity to existing findings of generic deficits in wellbeing (Aims 2 & 4).

Our findings also support the idea that those with one pre-existing condition, pulmonary or psychiatric, are more vulnerable to the other and these comorbidities need to be evaluated and addressed with future analyses of key biologicals collected in this study (Aims 1, 2, 3, & 4). We found evidence for statistically significant interaction between 9/11 exposure and internalizing disorders at 2 waves. Our analyses support the conclusion that 9/11 exposure is associated with asthma in this cohort, but only among those with internalizing disorders, and that the relationship is strongest among those with persistent internalizing disorder over 2 waves. Moreover, among the S&W2 Cohort, substance use was elevated in the 9/11 exposed group. We also found a significant interaction between level of current smoking and 9/11 exposure for airway obstruction, such that with each unit of increased level of current smoking, 9/11 exposure was associated with a decrease in FEV1-FVC.

The relationship of mental health, substance use, and COVID-related exposures of S&W youth and parent participants was also explored (Aims 1 & 3). Overall, depression, GAD, and increased alcohol or smoking/vaping among those who used alcohol or cigarettes were highest among both groups in wave 1 (early pandemic) and declined on average over time, noting, however, that youth prevalence of smoking/vaping remained elevated. Prevalence of perceived discrimination increased across waves, while parents report of anxiety remained somewhat elevated. Finally, in this S&W cohort, recent exposure to COVID-19 persisted in the range of 20-30% across waves, while the feeling of safety from COVID-19 increased over time.

Translation of Findings

The S&W2 Study has shown that the effects of exposure to mass trauma in childhood reverberate into young adulthood, and this occurs in the somatic, psychiatric, behavioral and developmental realms. The findings of the S&W2 Study reinforce the notion that the physical health status of children exposed to 9/11 is an ongoing concern. As noted, while physical health has been central to 9/11 support and studies of adults, the impact on children has been less well examined. As children mature and their lungs continue to grow throughout childhood, they are vulnerable to both emotional and environmental assault. S&W2, for the first time, supported the idea that there were long term **physiologically measurable** pulmonary effects in the Individuals with 9/11 exposure in childhood. Importantly, these effects could be manifest twenty years after 9/11.

The long-term health sequelae demonstrated here represents a substantial public health concern that demands ongoing longitudinal follow-up of this cohort, as well as a public health awareness that all children/adolescents exposed to 9/11 should be assessed, in order to truly understand the breadth and depth of these comorbid psychiatric and physical health consequences across the life span, with the goal of intervening to minimize these individuals' lifetime morbidity.

The specific physiological measures in S&W2 have also expanded our understanding of the lung-mind nexus. Our finding that individuals with specific degrees of lung dysfunction are significantly more likely to report increasingly higher rates and intensities of anxiety symptoms has both public health implications and opens basic questions regarding the physiologic connectivity of lung and brain, and its developmental significance. Because the exposures among children were more limited than those among many first responders, this finding was not predicted by many trauma and 9/11 researchers. However, the comorbidity of physical and mental health outcomes in those exposed to 9/11 in childhood may reflect the interconnectedness of physical and mental health in ways that have not previously been physiologically understood, and whose mechanism and anatomy must now be explored in earnest.

During the suspension of field activities consequent to COVID, the cohort was interviewed three times by telephone, to assess mental health, health behaviors and attitudes in the context of the pandemic. Findings from that survey will be important when planning the next S&W follow-up, as it provides additional information about the adaptive effects of exposure to yet another mass trauma.

Political and public support for victims of 9/11 has been sustained for over 20 years. The nature of 9/11, and these findings with respect to the mental and physical health and functioning of those exposed in childhood, provide more than sufficient grounds to obligate us to continue following them. Clinical support should be automatic. The question has been what are the most important issues from a public health and a scientific perspective that can be addressed. We believe that results from S&W2 have contributed to answering this question.

Outcomes/Impact

To ensure the long-term well-being of individuals exposed to 9/11 as children, it is imperative that we understand the longitudinal, lifetime effects that these traumatic and toxic exposures are having on their physical health and behavioral development, as they grow and move through adulthood. This study followed a cohort of children exposed to 9/11, assessing the longitudinal behavioral (mental health, substance abuse) and physical health (airway disorders and inflammatory processes) effects of the toxic as well as traumatic exposures they experienced, as well as examining the interactions of these factors in their development. These data will fill important knowledge gaps, resulting in valuable information to guide both psychiatric and general medical care for those children exposed to 9/11, while simultaneously providing new information relevant for youth exposed to other traumatic events. Unfortunately, due to the COVID-19 pandemic, there were serious limitations both on data collection, analysis and publications of this study's findings. The PI and researchers involved in this long-term investigation intend to address these limitations in subsequent investigations.

Scientific Report

1. Background:

Threats of bioterrorism worldwide make it incumbent for the public health community to thoroughly understand the life course of health-related consequences (mental health, physical health, and behavioral changes) of the dual exposures to emotional trauma and environmental toxins that potentially arise from any mass disaster. Fortunately, there have been extensive studies by the World Trade Center Health Registry (WTCHR) and others, characterizing what turned out to be very significant physical and psychological consequences of 9/11-related exposures in adults; these studies continue to drive screening, prevention and treatment interventions. However, there has not been a similar degree of investigation or intervention for those exposed as children or adolescents, whose bodies and brains were in the process of developing and, thus, were especially vulnerable. It is crucial, therefore, that we identify and characterize the holistic health consequences of the 9/11-related traumatic and toxic exposures to these youth, including physical (airway disorders and inflammatory processes, obesity, blood pressure, etc.), psychiatric (mental health, substance abuse), behavioral health (decision anomalies and high-risk behavior), as well as educational, occupational and social functioning in those individuals included in the S&W Investigations. We can, and should make sure that their health status and future risks are thoroughly understood, so that they too can receive preventative and therapeutic interventions over their life course, especially as they transition into and through adulthood and potentially become more at-risk for cancer and other chronic diseases. As an important step in this agenda, our team, the Global Psychiatric Epidemiology Group (GPEG), conducted the Stress and Well-Being Study (S&W) (U01OH010414; PI: Hoven), an in-depth mental health evaluation of N=1,000 individuals exposed to 9/11 as children under the age of 18, drawn from the WTCHR, with N=500 unexposed Controls of similar age, gender and sociodemographic distributions. This study, the largest 9/11 child study with in-person diagnostic mental health assessments, ended in August 2016, having thoroughly characterized this unique cohort and control group, in terms of their psychosocial, psychiatric and behavioral characteristics. It also produced the first concrete evidence linking 9/11 exposures to a wide-range of subsequent psychiatric disorders, many years later.

However, there were no in-person study of children, linking 9/11-related traumatic and toxic exposures to physical health outcomes. Our Co-Investigator, Dr. Szema, for example, found a 66% increase in new asthma diagnoses in Manhattan's Chinatown, blocks from Ground Zero, in the year after 9-11, and these problems have persisted. Moreover, the comorbidity of physical and psychiatric disorders can lead to broad health outcomes, such as: sinusitis, poor exercise tolerance, obesity, type II diabetes, hypertension and cancer, as well as poor psychological and functional outcomes in the educational, occupational and social domains. Therefore, in this S&W2 Study, we propose to close this gap by collecting and characterizing key physical health indicators from our well-characterized S&W cohort, to examine interactions between physical and psychological health, and to collect and store biologicals for future investigations as these youth age.

Thus, S&W2 created an interdisciplinary collaboration across psychiatry, behavioral science, pediatric allergy/immunology, pulmonology and epidemiology, and

drew on our unique S&W cohort of 9/11 directly exposed youth, to examine the health consequences of that event. This study enhances the largest, most comprehensive, representative study of children derived from the WTCHR, directly exposed to the attack of September 11, 2001, and thus establishes the most thoroughly characterized cohort of 9/11 children to be followed for decades of ongoing health, mental health and co-morbidity research.

SPECIFIC AIMS

In a WTCHR representative sample of youth (N=1,000) under 18 years of age on September 11, 2001, who were directly exposed to 9/11, compared to unexposed Controls (N=500), we will:

Aim 1: Characterize physical health status, focusing on pulmonary diseases and allergic/immunologic consequences.

Aim 2: Examine gene-environment interactions, determining if genetic vulnerability modifies the relationship between 9/11 exposure in childhood and subsequent psychiatric symptoms.

Aim 3: Examine physical and mental health comorbidities and their consequences to educational, occupational and social functioning outcomes.

Aim 4. Collect key biologicals (e.g., blood) relevant to physical and mental health status, potentially related to 9/11 exposure, for analysis in subsequent investigation(s): 1) inflammatory/immune biologicals; 2) DNA for epigenetics, and 3) RNA for gene expression.

2. Methodology

2.1 Samples:

2.1.1. Index Sample: The **S&W2** drew its Index sample of youth directly exposed to the 9/11 events as children (0 to 18 years of age on 9/11/2001), and at the start approximately 15-32 years of age, from the S&W study. This S&W sample (N=1,000) was originally drawn from the WTCHR Pediatric Sample, which had only been assessed by the WTCHR via brief mailed, telephone and web-based surveys. Thus the S&W study was the first time that this WTCHR Pediatric Sample experienced an in-depth, face-to-face assessment. Due to this face-to-face design, only those currently living in NYC, and within a 100-mile radius of the WTC were included. Due to COVID-19 limiting the possibility of collecting face-to-face interviews and physical parameters, such as respiratory function testing and blood draws. Of the original 1,000 Index participants, N=452 had participated in the **S&W2**, prior to the onset of COVID-19. All individuals were at least 18 years of age at the time of their assessment.

2.1.2. Control Sample: N=500 non-exposed (to 9/11) community Controls were recruited as part of the original S&W Study and provided appropriate power to make the proposed comparisons of the exposed (Index) sample with a similar, non-exposed (Control) sample. The Control Sample is comparable to the Index Sample demographically, though not designed to be specific individual level matches. A community probability sample of youth who were not directly exposed to the events were selected from the Astoria, Elmhurst, East Elmhurst, Corona and Whitestone neighborhoods of Queens, NYC. These nearly contiguous neighborhoods were selected because they have the potential to generate a sample with similar racial-ethnic and socioeconomic status distribution to that of the WTCHR Pediatric Sample and within the same age range. The Controls were sampled using community based probability sampling methods and InfoUSA^{1, 2}. A total of N=254 Controls in the **S&W2** were assessed. As with the Index sample, all participants were at least 18 years of age at the time of assessment.

2.1.3. S&W2 Recruitment: In the original S&W Study, all participants, during their interview, were asked if they would allow GPEG to contact them for future studies and consented to be contacted. All participants of the S&W Study were invited to participate in the **S&W2**. The participants were initially contacted by mail and after a waiting period of one week, by telephone or in-person. For those participants whose letters and telephone numbers were no longer accurate (e.g., letters returned or telephone numbers disconnected), new contact information was obtained from Lexis-Nexus' AccurInt database. This procedure successfully yielded new contact information for much of GPEG's other longitudinal studies^{3, 4}. In those cases where new contact information could not be obtained through an AccurInt search, GPEG recruiters visited their last known address to attempt contact with the individuals. GPEG has a proven record of maintaining an 85% retention rate or greater with its other longitudinal studies^{3, 4} using these methods.

2.1.4. Physical Health/Pulmonary Procedures: In most cases, up-to two separate meetings with the youth were scheduled: one for the psychosocial interviews and one for the physical health/pulmonary procedures and pulmonary-related assessments, if they agreed. In some cases, the participant elected to conduct the psychosocial and physical/pulmonary assessments on the same day.

The physical health/pulmonary procedures were conducted by highly trained interviewers with a medical or biology background and certified in phlebotomy, who visited the homes of the participants. At the pulmonary visit, we used a laptop to administer the St. George's Respiratory Questionnaire, Redline Asthma Questionnaire, and the SF-36 health questionnaire. We assessed vital signs: temperature with a forehead monitor, blood pressure, pulse, respiratory rate; and, conducted a straight line 6 minute walk to determine exercise capacity⁵, with results measured in distance covered and oxygen saturation (measured with pre- and post- pulse oximetry).

Jaeger Impulse Oscillometry (IOS) is a noninvasive, rapid (2 minute), effort-independent method to assess peripheral airways narrowing (D5-D20) and airway hyper-responsiveness (X5) without the need to inhale irritating chemicals as was the case in the older methacholine challenge procedure. Based on the manufacturer's (Jaeger) predicted values, we compared our control subjects to those exposed to 9/11 and to the manufacturer's percentage predicted values to determine if they exceed 250% predicted.

Spirometry for standardized measures of airway obstruction (FEV1, FVC, FEV1/FVC, FEF25-75 percentage predicted measures of large and medium sized airways for obstruction) was conducted, and compared to IOS⁶ and standardized pulmonary and allergy survey questionnaires described above (Redline Allergy/Asthma, SF-36, St. George's).

For abnormal values, the subject was notified by a member of the research team (Dr. Szema) and advised to contact their primary care physician. We (Dr. Szema) also provided referral information for those without a primary care clinician.

Blood Collection Procedures: As mentioned above, funding for this study did not permit analysis of all relevant biomarkers (immune biomarkers, VIP, psychiatric genetics, epigenetics, RNA), but it did offer a unique opportunity to collect the biomarkers from our well-characterized cohort of children exposed to 9/11, with the expectation of obtaining additional funding to conduct the analyses on these biomarkers as well.

During the visit described above, the certified phlebotomist, drew three tubes of blood: 1) PaxGene DNA tube, the DNA source for current psychiatric genetics, and for later study of epigenetics. This tube was placed in -80°C storage at the New York State Psychiatric Institute (NYSPI) on the Columbia University Medical Center Campus. 2) PaxGene RNA tube. RNA source for future gene expression analyses. 3) K2 EDTA plasma collection tube for cytokine and vasoactive intestinal peptide [VIP] analyses. These K2 EDTA tubes are best for detection of low concentrations of analytes. In a future study, we will analyze plasma Vasoactive Intestinal Peptide (VIP), IL1-b, IL-6, TNF-alpha, gamma interferon, IL-4, IL-5, IL-2, IL-8 (CXCL8), IL12p40, MIP1-apha, total IgE, and IgE to aero-allergens. As with the other tubes, they are in -80°C storage at NYSPI.

Inflammatory / Immunity Procedures: Exhaled breath condensate nitric oxide (NO) was administered with a disposable filter and mouthpiece for each individual tested. Exhaled breath condensate nitric oxide (NO) noninvasively measures a by-product of eosinophilic airway inflammation by analyzing the concentration of nitric oxide gas in parts per billion (>50 is abnormally high in an adult over age 12)⁷. The next generation NioX test is handheld, rapid (3 minutes), and does not require a laptop⁸.

2.1.5. Psychosocial Interview Procedures: Index and Control interviews were the same, and all youth interviews prior to the COVID-19 Pandemic were assessed in-person. After the initial restart of field work, several of the youth opted for a telephone interview. In-person interviews took place at the participants' residence, or at the GPEG offices at NYSPI, by trained lay interviewers. All interviews were conducted in private and were done by rigorously trained lay interviewers. All **S&W2 Study** interviews were collected on laptop computers.

2.2. Measures

2.2.1. Physical Health/Pulmonary: As described above: Impulse Oscillometry, A straight line 6 minute walk, Spirometry for standardized measures of airway obstruction, Vital signs, Redline Allergy/Asthma questionnaire, SF-36 questionnaire, St. George's Questionnaires.

2.2.2. Inflammatory / Immunity: As described above: Exhaled breath condensate nitric oxide (NO), Plasma sample for Inflammatory/ Immune bio-markers was collected for subsequent analysis, as described above.

2.2.3. Genetics: PaxGene DNA tube was collected for psychiatric genetics as described above.

2.2.4. Biomarkers for Future Analysis: DNA and RNA, as well as serum for cytokines and VIP has been stored for future analyses.

2.2.5. Youth Behaviors and Psychiatric Disorders

(a) Mental and Substance Use Disorders and Symptoms: All youth participants were at least 18 years of age or older at the time of their assessment. We therefore used the Composite International Diagnostic Interview (CIDI)^{9,10} an adult diagnostic measure. The instrument is designed to be administered by lay interviewers and diagnoses are made by computerized algorithms. The following disorders were assessed: Mood Disorders, Anxiety Disorders (Agoraphobia, panic, generalized anxiety and post-traumatic stress disorder [PTSD]); and Alcohol and Drug Use Disorders. We also used questions assessing quantity and frequency of use of alcohol and other drugs from the Center for Disease Control and Prevention (CDC) Youth Risk Behavior Survey (YRBS)¹¹.

(c) Sexual Risk Behaviors: HIV/STI risk behaviors were examined using questions from the *Adolescent-Risk Behavior Assessment (ARBA)*¹². The ARBA is a structured interview, designed specifically for use with youth to assess their self-reported sexual behavior, and has established test-retest reliability¹³. The items in this adolescent version were derived from the adult instrument, RBA, a well-established measure of sexual behavior¹⁴⁻¹⁶, which can be used in emerging adults without compromising continuity. We included ARBA questions assessing sexual behavior (e.g., lifetime sexual intercourse, frequency, condom use and high-risk sexual behavior, including sex with drug and/or alcohol use) within past 30 days and past 6 months.

Table 1. Summary Measures	
Domain	Measure Description
EXPOSURE	
Exposure to 9/11	Closeness to WTC epicenter; physically hurt; witnessed disturbing events (previously collected in S&W Study)
Exposure to other Traumatic Events	Exposure to traumatic events: Life Event Checklist (LEC) ¹⁷ fulfilling DSM PTSD criterion A (traumatic exposure) Exposure to Trauma ^{18,19} Child Abuse ²⁰⁻²²
OTHER INDIVIDUAL/ FAMILIAL FACTORS	
Demographics	Youth gender, age, race/ethnicity, socioeconomic status
LIFE DISRUPTIONS	
Family Economic Hardship	Developed for GPEG's Parent Exposed Youth Study ²³ .
PULMONARY	Impulse Oscillometry; 6 minute walk with pre and post pulse oximetry ⁵ ; spirometry ⁶ questionnaires (Redline Allergy/Asthma, SF-36, St. George's); vital signs, weight, height, BMI
INFLAMMATORY/ IMMUNITY	Exhaled breath condensate nitric oxide (NO) ⁸ ; BLOOD COLLECTION FOR LATER ANALYSIS: K2 EDTA plasma collection tube for cytokine and vasoactive intestinal peptide [VIP], lyses.
GENETICS	PaxGene DNA blood sample tube for current psychiatric genetics PaxGene RNA tube RNA tubes for RNA and microRNA, epigenetics
YOUTH BEHAVIORS	Mental and Substance Use Disorders and Symptoms (CIDI, YRBS); Sexual Risk Behaviors (ARBA); Injury Risk Behaviors (AIC, NSSI, DSHI).
CONTEXTUAL FACTORS	
Family composition, parental education	Developed for GPEG's Parent Exposed Youth Study ²³ .

(d) Injury Risk Behaviors: Unintentional injury was measured according to standard causes²⁴⁻²⁶ appropriate to youth, including being struck by or against an object, falls, motor vehicle accidents and injuries resulting from overexertion. Assessments included lifetime and the Adolescent Injury Checklist (AIC)²⁷ for the past six months, including sports activities common in youth, such as skate boarding, bicycle use, use of firearms, etc. In addition, deliberate self-harm, including suicidal and non-suicidal self-injury (NSSI) and behaviors was assessed. The CIDI assessed history of suicidal behaviors and non-suicidal self-harm was assessed by a modified version of the Deliberate Self-Harm Inventory (DSHI)²⁸.

2.3. COVID-19 Pandemic

We conducted an unplanned longitudinal telephone survey over 3 waves during the COVID-19 pandemic (Wave 1: March-August 2020, Wave 2: September 2020-February 2021, Wave 3: March-August 2021), in part, as a check-in of the sample members. Participants included a random selection of S&W participant families, including young adults and parents of young adults from the same family. Questions related to mental health and well-being during the pandemic and characterization of participants' pandemic exposure experience.

3. Results

3.1. Physical Health Status: Pulmonary Diseases and Allergic/Immunologic Consequences.

We used multivariable regression to test the association of 9/11 exposure with each physical health outcome (self-reported allergy and asthma symptom scales, spirometry, distal airway narrowing and airway hyper responsiveness, airway inflammation as measured by exhaled nitric oxide in parts per billion, 6-minute walk distance in feet, and pre-post percentage change in oxygen saturation in response to the 6-minute walk). Both binary (exposed vs. controls) and continuous (a score based on types of direct exposure such as attending a ground zero area school, exposure to the dust cloud, having to move out of one's home, seeing the planes hit or towers collapse, seeing injured persons or dead bodies, or being physically hurt in the attack) measures of 9/11 exposure were used as predictors. All models were adjusted for age, sex, and race/ethnicity.

As shown in Table 2, we found evidence for increased respiratory symptoms (beta=3.91; p=0.01); impact of respiratory symptoms (beta=1.13, p=0.02); and total respiratory health impairment (beta=1.43, p=0.01), measured by the St. George questionnaire in 9/11 exposed versus unexposed participants. The approximate 4-point increase in the symptom measure associated with 9/11 exposure corresponds to a clinically relevant differences²⁹. Moreover, energy and emotional well-being (SF-36 subscales) were reduced in 9/11 exposed versus unexposed subjects, by 6.1 points (p<0.01) and 3.3 points (p<0.01) on 0-100 scales, respectively. The relationship for energy was such that each additional type of direct 9/11 exposure was associated with a statistically significant (p=0.02) 1.2 point decrease in SF-36 Energy. Each additional type of direct 9/11 exposure was also associated with increased X5, a measure of airway hyperresponsiveness (beta=0.004, p=0.01) and decreased D5-D20, a measure of peripheral airway narrowing (beta=-1.06; p=0.02). 9/11 exposure (dichotomous or direct count) was not associated with inflammation or exercise tolerance using the assessed measures.

Table 2. Adjusted regression model estimates for association of 9/11 exposure with physical health measures

Dependent	<u>9/11 exposed vs. unexposed</u>			<u>Count of types of direct exposure</u>		
	β^a	s.e.	p-value	β^a	s.e.	p-value
<i>Asthma and allergy</i>						
Redline: asthma score	0.18	0.16	0.24	0.03	0.04	0.55
Redline: allergy score	0.07	0.07	0.32	0.01	0.02	0.55
St. George: symptoms	3.91	1.59	0.01	<i>0.80</i>	<i>0.44</i>	<i>0.07</i>
St. George: activity	0.58	0.41	0.16	0.02	0.11	0.89
St. George: impact	1.13	0.48	0.02	0.16	0.13	0.23
St. George: total	1.43	0.52	0.01	0.22	0.14	0.13
SF-36: Physical function	-0.55	1.07	0.61	-0.05	0.30	0.86
SF-36: Energy	-6.12	1.85	0.00	-1.22	0.51	0.02
SF-36: Emotional well being	-3.29	1.04	0.00	-0.31	0.29	0.28
SF-36: Social function	-1.36	1.81	0.45	0.06	0.50	0.91
SF-36: Pain	-2.45	1.66	0.14	-0.28	0.46	0.55
SF-36: General health	-1.34	1.37	0.33	-0.40	0.38	0.29
<i>Airway hyperresponsiveness</i>						
X5	0.01	0.01	0.22	0.004	0.001	0.01
<i>Peripheral airway narrowing</i>						
D5-D20	-2.25	1.57	0.15	-1.06	0.43	0.02
<i>Airway obstruction</i>						
FEV1	0.00	0.07	0.99	0.02	0.02	0.37
FVC	-0.01	0.08	0.87	0.01	0.02	0.68
FEV1/FVC	0.00	0.01	0.72	0.00	0.00	0.54
FEF25-75	0.06	0.18	0.75	-0.01	0.05	0.81
<i>Exercise capacity</i>						
6 minute walk: change in O2 saturation	0.13	0.66	0.84	-0.19	0.18	0.29
6 minute walk: distance	-11.68	87.24	0.89	-2.90	24.04	0.90
<i>Airway inflammation</i>						
Exhaled nitric oxide	-1.71	1.94	0.38	-0.55	0.53	0.30

^aAdjusted for subject's sex, race/ethnicity, and age.

3.2. Physical and Mental Health Comorbidities and their Consequences to Educational, Occupational and Social Functioning Outcomes.

To test hypothesis (3.a) that pulmonary abnormalities, as objectively measured by distal airway narrowing and airway hyper responsiveness and pulmonary inflammation as measured by exhaled nitric oxide (NO), will moderate the relationship between 9/11 exposures and anxiety disorders, we fit a series of logistic regression models for the dichotomous outcome of past year anxiety disorder at wave 2. Each model included independent terms for 9/11 exposure, for a pulmonary measure, and for 9/11 exposure X pulmonary measure interaction, as well as demographic covariates. Statistical significance was assessed based on $p < 0.05$ for the interaction term. We found evidence for interaction between 9/11 exposure and FVC ($p\text{-int}=0.037$). Specifically, direct 9/11 exposure was associated with significantly higher odds of anxiety disorder among those with FVC levels at or above the median, but not among those with FVC levels below the median (Figure 1). Other interactions were not statistically significant.

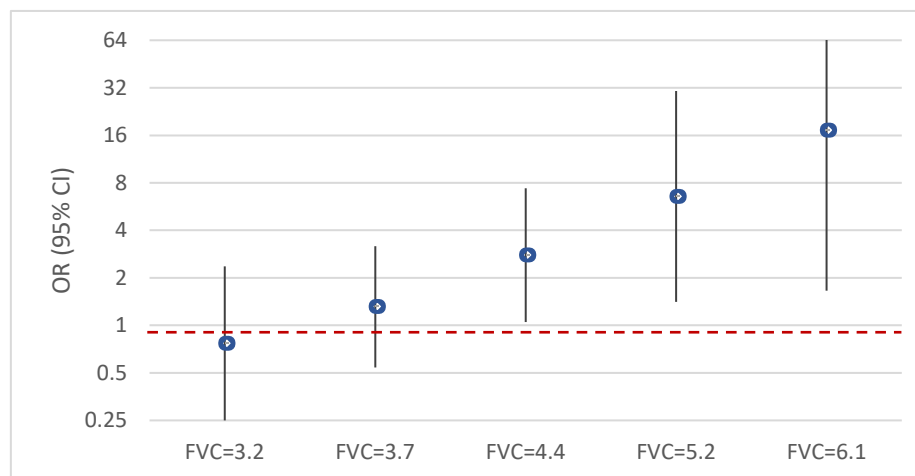


Figure 1. Odds ratios for past year anxiety disorder associated with 9/11 exposure, by FVC (10th, 25th, 50th, 75th, and 90th percentiles). ORs at FVC values at and above the median were statistically significantly greater than 1.0 ($p < 0.05$).

To test the hypothesis (3.b) that psychiatric diagnosis moderates the relationship between 9/11 exposures and asthma/allergy, self-reported allergy and asthma symptoms outcomes were modeled with linear regression, examining 9/11 exposure status, psychiatric diagnoses at two waves, and their interaction terms as predictors. We found evidence for statistically significant interaction between 9/11 exposure and internalizing disorders at 2 waves ($p\text{-int}=0.002$; $df=7$). Specifically, Redline asthma score was significantly increased among subjects who were directly exposed to 9/11 AND positive for internalizing disorders at BOTH baseline and follow-up waves versus subjects who were not directly exposed to 9/11 and did not have internalizing disorders at either baseline or follow-up ($\beta=1.22$, $s.e.=0.33$; $p=0.0002$).

Redline asthma score was also significantly increased, though to a lesser extent, among subjects who were directly exposed to 9/11 AND positive for internalizing

disorders at EITHER baseline or follow-up waves versus subjects who were not directly exposed to 9/11 and did not have internalizing disorders at either baseline or follow-up (beta=0.62, p=0.03 and beta=0.55, p=0.047 for 9/11 exposed subjects positive for internalizing disorders at only baseline and at only follow-up, respectively). Groups with 9/11 exposure but no internalizing disorder, or with internalizing disorder at one or both time points but not 9/11 exposure did not have significantly increased asthma scores relative to the unexposed/no internalizing disorder group. This finding also held when considering 9/11 direct exposure as a continuous score. Among those positive for internalizing disorders at both baseline and follow-up, each 1-unit increase in direct exposure was associated with a significant increase in Redline asthma score (beta=0.33, s.e.=0.10, p=0.0006); whereas 9/11 direct exposure level was not significantly associated with asthma score among those not positive for internalizing disorders at both assessment time points. We did not see evidence for psychiatric disorders modifying the 9/11 association with allergy, therefore this relationship appeared specific for asthma. In sum, these analyses support the conclusion that 9/11 exposure is associated with asthma in this cohort, but only among those with internalizing disorders, and that the relationship is strongest among those with persistent internalizing disorder over 2 waves.

To test the hypothesis that marijuana and/or cigarette use will be elevated in the 9/11-exposed cohort, we examined the association of 9/11 exposure (considered dichotomously and as a level based on number of different types of direct exposure) with substance use outcomes at wave 2 using logistic or linear regression adjusted for demographics. Results are shown in Table 3. Each additional type of direct exposure to 9/11 was associated with an increased odds of getting drunk at least weekly (OR=1.17, 95% CI=0.99-1.38; p=0.06).

Table 3. Association of 9/11 Exposure with Substance Use Outcomes at wave 2.

Outcome	9/11 Exposure	OR	LCL	UCL
AUD, past year	Dichotomous	1.19	0.74	1.93
	Level	1.10	0.86	1.40
SUD, past year	Dichotomous	34.5	0.00	>999
	Level	0.38	0.04	3.57
Binge drink alcohol, at least weekly	Dichotomous	0.99	0.77	1.27
	Level	1.09	0.95	1.25
Got drunk, at least weekly	Dichotomous	1.13	0.82	1.54
	Level	1.17	0.99	1.38
		beta	s.e.	p-value
Drinks alcohol/week	Dichotomous	6.39	8.94	0.47
	Level	2.70	2.43	0.27
Marijuana use/week	Dichotomous	0.07	0.19	0.70
	Level	0.03	0.05	0.63
Current level of smoking	Dichotomous	0.02	0.13	0.90
	Level	-0.02	0.04	0.52

AUD, alcohol use disorder; SUD, drug use disorder; All models adjusted for age, sex, and race/ethnicity. Italics denote p<0.1.

To test the hypothesis that marijuana and /or cigarette use will moderate the relationships of 9/11 exposure with reduction in pulmonary function, and with inflammation as measured by exhaled nitric oxide (NO), measures of pulmonary functioning and inflammation were modeled as outcomes in linear regression models with 9/11 exposure status, the substance use variables, and their interactions terms, as well as demographic covariates as predictors. Statistical significance was assessed based on $p < 0.05$ for interaction terms. A significant interaction was found between level of current smoking and 9/11 exposure for FEV1-FVC ($p\text{-int}=0.047$), such that 9/11 exposure was not associated with FEV1-FVC among non-smokers, however, with each unit increased level of current smoking, 9/11 exposure was associated with a decrease ($\beta=-0.015$) in FEV1-FVC.

3.3. COVID-19 Pandemic.

The mental health and substance use and COVID-related exposures of S&W youth and parent participants over 3 waves of this telephone survey are shown in **Table 4**. Overall, depression, GAD, and increased alcohol or smoking/vaping among those who used alcohol or cigarettes were highest among both groups in wave 1 (early pandemic) and declined on average over time. Prevalence of perceived discrimination and of testing positive for COVID-19 increased across waves. Recent exposure to COVID-19 persisted in the range of 20-30% across waves, while the feeling of safety from COVID-19 increased over time.

Table 4. Prevalence of Mental Health and COVID-Related Exposures among Youth and Parent S&W Participants over 3 Waves of the COVID-19 pandemic.

	Youth (N=278)			Parents (N=221)		
	Wave 1	Wave 2	Wave 3	Wave 1	Wave 2	Wave 3
	%	%	%	%	%	%
<i>Mental health and substance use</i>						
Depression	21.9	14.4	8.9	16.0	12.0	7.9
GAD	21.9	13.5	8.9	17.2	14.6	11.8
Increased alcohol use*	31.0	6.5	9.3	26.0	9.4	4.1
Increased smoking/vaping*	35.9	20.0	28.6	69.2	40.0	18.2
<i>COVID-related exposures</i>						
Perceived discrimination	5.4	9.2	17.2	7.2	10.7	17.1
Tested positive for COVID-19	3.2	4.8	5.2	2.7	5.0	6.6
Loss of family or friends due to COVID-19	7.2	12.6	10.8	7.2	20.8	17.6
Recent exposure to COVID-19	31.7	29.9	23.0	22.6	19.9	22.6
Concern about being victim of violent crime	2.9	0.4	2.1	6.5	2.5	4.7
	<u>mean</u>	<u>mean</u>	<u>mean</u>	<u>mean</u>	<u>mean</u>	<u>mean</u>
Household financial impact of COVID-19 (none=0 to 2=a lot)	0.79	0.75	0.76	0.91	0.90	0.74
Current feeling of safety from COVID-19 (none=0 to 2=a lot)	1.18	1.17	1.48	1.00	1.04	1.43

*Among those who use the respective substance

4. Discussion

Based on data from the S&W2 Study, exposure to the 9/11 attacks during childhood appears to substantially impact an individual's physical health, including impacting their allergic/immunologic health. While traumatic events are common in childhood and known to be related to adult psychiatric disorders, particularly anxiety and depression, these data demonstrate that exposure to a disaster, such as 9/11, early in life can have a significant, negative consequence on pulmonary health, starting as early as late adolescence and manifesting in young adulthood. Compared to the adult literature on 9/11 exposure, where toxic exposure was often very intense and lasted over weeks and months, the 9/11 exposure of our youth cohort involved less exposure to toxicants while the emotional trauma, especially because they were children and adolescents was substantial. The long-term health sequelae demonstrated here, represents a substantial public health concern that demands ongoing longitudinal follow-up of this cohort and a public health awareness of all children/ adolescents exposed to 9/11, in order to truly understand the breadth and depth of these comorbid psychiatric and physical health consequences across the life span, with the goal of intervening to minimize these individuals' lifetime morbidity. While we have been better at this with adults exposed to 9/11, this study is a call to action for the children of 9/11.

By using state-of-the-art, in-depth and in-person psychiatric and physiological assessments, an adequate sample size, and a carefully constructed control group, the S&W2 Study demonstrates, for the first time, that exposure to 9/11 in childhood or adolescence has had a broad impact not only as mentioned above on pulmonary health and psychopathology, but also continues to have an effect on broad developmental pathways, as measured by life-role functioning and social maturity. In addition, there was a demonstrable effect on health behaviors such as substance use and cigarette smoking. AS COVID-19 intervened during the conduct of this study, it brought to the country's attention the importance of individuals' health behaviors, not only for their outcomes but for the health of all. The finding of greater carelessness in personal health behaviors – thus exacerbating the already consequential impact of childhood trauma exposure, is an important and we think new understanding of the many-fold impacts that such exposures unleash and that the public needs to be aware of.

In the S&W2 Study, exposure to 9/11 showed a clear association, almost twenty years later, with physiologically measured respiratory function, and also had a clear association with measured energy physiology, adding a great deal of biological specificity to existing findings of generic deficits in wellbeing. We also observed a strong association of measurably greater deleterious pulmonary outcomes with amount of direct exposure to the 9/11 attack. This is important in two ways: (1) clinical attention to functional respiratory deficits in those exposed as children should not be conceived as being a short term or time-limited intervention, and (2) children/adolescents with “more” direct exposure should be considered most vulnerable to long-lasting pulmonary effects.

The specific physiological measures in S&W2 has expanded our understanding of lung-mind nexus, that has often been studied through questionnaires or frequency of clinical visits. Our finding that individuals with specific degrees of lung dysfunction are significantly more likely to report increasingly higher rates and intensities of anxiety symptoms has both public health implications and opens basic questions regarding the

physiologic connectivity of lung and brain, and its developmental significance. While pediatricians are anecdotally familiar with this connection, this work adds further support to a need for a research program that explores this connectivity more intensely. In terms of public health response, our results confirm the need to simultaneously address impacted intervals physical and mental health need concomitantly. Our findings also support the idea that those with one pre-existing condition, pulmonary or psychiatric, are more vulnerable to the other and these comorbidities needs to be evaluated and addressed.

The S&W2 finding that substance use was elevated in the 9/11 exposed group, now takes on a possible further clinical complication. Substance use could possibly have been used as a form of self-soothing or self-medication for those with greater anxiety. In the case of cigarette smoking this would further impact poor lung function setting up a vicious circle – which needs to be a prime area of prevention.

As mentioned, when COVID-19 interfered with the face-to-face visits required by the physiological measures and blood draws in S&W2. We chose to make lemonade and took the opportunity to use telephonic interviews to examine the impact of important aspects of the COVID-19 pandemic on our cohorts longitudinally, and to compare the S&W2 cohort with a parent's cohort. While measures of psychopathology decrease over waves of data collection, and we have observed some differences between our youth and parent cohorts, most notably related to perceived discrimination and concern about being a victim of violent. Parents report of anxiety remained somewhat elevated while we observed a decrease overtime among youth. In contrasts to parents, youth prevalence of smoking/vaping remained elevated (in agreement with a NIDA MTF report). The takeaway is socioeconomic concerns and perceived discrimination measures, which until now have not traditionally been included in trauma studies, should be.

5 Conclusion

In the most general sense, the S&W2 Study has shown that the effects of exposure to mass trauma in childhood reverberate through, at least, to young adulthood, and this occurs in the somatic, psychiatric behavioral and developmental realms. As with many mass traumatic events, the exposures are both mental and physical; the S&W2 Study demonstrates that the outcomes are likewise a mix of comorbidities – some surprising. What has not been previously examined are the impairments in function in significant areas during the transition to adulthood.

The findings of S&W2 Study reinforce an ongoing concern that the physical health status of children exposed to 9/11 should be assessed longitudinally. While physical health has been central to 9/11 support and studies of adults, the impact on children has been less well examined. As children's lungs grow throughout childhood, they are a group vulnerable to both emotional and environmental assault. That there were long term **physiologically measurable** pulmonary effects is supported in the S&W2, for the first time. Individuals with 9/11 exposure in childhood were at greater risk of respiratory dysfunction and manifesting symptoms, as well as airway hyperresponsiveness almost twenty years after exposure. Moreover, they had heightened risk of having low energy. Because the exposures among children were more limited than those among many first

responders, this finding was not predicted by many trauma and 9/11 researchers. It obligates 9/11 service and research groups to continue follow-up of these young people.

During the suspension of field activities consequent to COVID, the cohort was interviewed three times by telephone, to assess mental health, health behaviors and attitudes in the context of the pandemic. Findings from this survey will be important when planning the next SW follow-up, as it establishes exposure to yet another mass trauma.

Political and public support for victims of 9/11 has been sustained for over 20 years. The nature of 9/11, and the findings with respect to the mental and physical health and functioning of those exposed in childhood provide more than sufficient grounds to obligate us to continue following them. Clinical support should be automatic. The question has been what are the most important issues from a public health and from a scientific perspective that can be addressed, we believe that results from S&W2 have contributed to answering this question.

Finally, the comorbidity of physical and mental health outcomes in those exposed to 9/11 in childhood may reflect the interconnectedness of physical and mental health in ways that have not been physiologically understood, and whose mechanism and anatomy must now be explored in earnest. These interconnections were viewed from various angles, demonstrating the complexity of these interactions. Taking anxiety disorders as the outcome, heightened risk in the relationship between direct, 9/11 exposure and anxiety disorders was significant for those w/o pulmonary impairment as measured by FVC, whereas the association between 9/11 and anxiety was nonsignificant among those with pulmonary impairment. Taking asthma/allergy as the outcome, the association between direct 9/11 exposure and asthma/allergy was modified by persistent internalizing disorders. Asthma scores increased among the 9/11 exposed who exhibited internalizing disorders at baseline and follow-up, versus subjects who were not directly exposed to 9/11 and did not have persistent internalizing disorders. If verified, we anticipate that these kinds of associations and risk structures will make their way into clinical practice. This level of associative specificity would not have been exposed without the specific research design and measures of S&W2.

**9/11 Trauma and Toxicity in Childhood:
Longitudinal Health and Behavioral Outcomes**

S&W2 Study

Grant/Cooperative Agreement # U01OH011308
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C. OVERALL PRODUCTS**C.1 PUBLICATIONS**

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

No

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

NOTHING TO REPORT

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period? No

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization? No

C.5 OTHER PRODUCTS AND RESOURCE SHARING

NOTHING TO REPORT

D. OVERALL PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
HOVENC	Y	Hoven, Christina W.	MPH,MOTH,MS,DRPH	PD/PI	2.4	0.0	0.0			NA
BRESNAHANM	Y	BRESNAHAN, MICHEALINE A	BA,PHD,MPH	Co-Investigator	1.2	0.0	0.0			NA
ASZEMA	Y	SZEMA, ANTHONY M	MD,BS	Co-Investigator	1.2	0.0	0.0			NA
DR2097	N	Rodriguez Moreno, Diana	PHD	Project Director	1.4	0.0	0.0			NA
GERONAZZO	Y	Geronazzo-Alman, Lupo		Co-Investigator	3.8	0.0	0.0			NA
	N	Hsu, Yi Ju		Non-Student Research Assistant	2.3	0.0	0.0			NA
	N	Buffetta, Jacqueline		Non-Student Research Assistant	1.3	0.0	0.0			NA
	N	Duque-Villa, Yuly		Non-Student Research Assistant	2.4	0.0	0.0			NA
	N	Rizk, Zalpha		Non-Student Research Assistant	4.5	0.0	0.0			NA
	N	Khan, Aziza		Non-Student Research Assistant	3.8	0.0	0.0			NA
	N	Wasserman, Camilla		Non-Student Research Assistant	2.4	0.0	0.0			NA
	N	Ouyang, Bensheng		Assistant Data Manager	1.5	0.0	0.0			NA
	N	Cole, Hugh		Non-Student Research Assistant	3.1	0.0	0.0			NA
	N	Tang, Huilan		Non-Student Research Assistant	1.9	0.0	0.0			NA
	N	Zemeck, Heather		Non-Student Research Assistant	1.5	0.0	0.0			NA
	N	Ryan, Megan		Field Director	1.5	0.0	0.0			NA
	N	Harp, Derek		Non-Student Research Assistant	3.3	0.0	0.0			NA

	N	Sun, Xiaoxiao		Non-Student Research Assistant	1.2	0.0	0.0			NA
	N	Mahan, Janice		Non-Student Research Assistant	2.0	0.0	0.0			NA
	N	Bravo, Benjamin		Non-Student Research Assistant	3.6	0.0	0.0			NA
	N	Keating, William		Non-Student Research Assistant	3.0	0.0	0.0			NA
	N	Ananthasayan, Mythili		Non-Student Research Assistant	1.7	0.0	0.0			NA
	N	Cuchacovich, Sharon		Non-Student Research Assistant	2.0	0.0	0.0			NA

Glossary of acronyms:

S/K - Senior/Key

Cal - Person Months (Calendar)

Aca - Person Months (Academic)

Sum - Person Months (Summer)

Foreign Org - Foreign Organization Affiliation

SS - Supplement Support

RS - Reentry Supplement

DS - Diversity Supplement

OT - Other

NA - Not Applicable

D.2 PERSONNEL UPDATES**D.2.a Level of Effort**

Not Applicable

D.2.b New Senior/Key Personnel

Not Applicable

D.2.c Changes in Other Support

Not Applicable

D.2.d New Other Significant Contributors

Not Applicable

D.2.e Multi-PI (MPI) Leadership Plan

Not Applicable

E. OVERALL IMPACT**E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?**

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

NOTHING TO REPORT

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

NOTHING TO REPORT

G. OVERALL SPECIAL REPORTING REQUIREMENTS SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

NOTHING TO REPORT

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

Not Applicable

G.4.b Inclusion Enrollment Data

File(s) uploaded:

SnW2_CumulativeInclusionEnrollmentReport.pdf

G.4.c ClinicalTrials.gov

Does this project include one or more applicable clinical trials that must be registered in ClinicalTrials.gov under FDAAA?

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

NOT APPLICABLE

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT No foreign component
G.10 ESTIMATED UNOBLIGATED BALANCE Not Applicable
G.11 PROGRAM INCOME Not Applicable
G.12 F&A COSTS Not Applicable

Cumulative Inclusion Enrollment Report

This report format should NOT be used for collecting data from study participants.

Study Title:

Comments:

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/ Alaska Native										
Asian										
Native Hawaiian or Other Pacific Islander										
Black or African American										
White										
More Than One Race										
Unknown or Not Reported										
Total										

I. OVERALL OUTCOMES

I.1 What were the outcomes of the award?

To ensure the long-term well-being of individuals exposed to 9/11 as children, it is imperative that we understand the longitudinal, lifetime effects that these traumatic and toxic exposures are having on their physical health and behavioral development, as they grow and move through adulthood. This study followed a cohort of children exposed to 9/11, assessing the longitudinal behavioral (mental health, substance abuse) and physical health (airway disorders and inflammatory processes) effects of the toxic as well as traumatic exposures they experienced, as well as examining the interactions of these factors in their development. These data will fill important knowledge gaps, resulting in valuable information to guide both psychiatric and general medical care for those children exposed to 9/11, while simultaneously providing new information relevant for youth exposed to other traumatic events. Unfortunately, due to the COVID-19 pandemic, there were serious limitations both on data collection, analysis and publications of this study's findings. The PI and researchers involved in this long-term investigation intend to address these limitations in subsequent investigations.