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Asthma-COPD overlap in World Trade Center Health Registry enrollees, 2015–2016

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Abstract

Introduction: Asthma-chronic obstructive pulmonary disease (COPD) overlap (ACO) is a newly redefined form of chronic airway disease and has not been well studied among 9/11-exposed populations with increased prevalence of asthma. We assessed the prevalence and risk factors associated with ACO in an exposure cohort of World Trade Center Health Registry (WTCHR) enrollees.

Methods: This is a longitudinal study, including enrollees with complete data on 9/11/01 exposure at enrollment (2003–2004, Wave 1), asthma and COPD diagnoses and at least 25 years of age at the time of the 2015–2016 (Wave 4) WTCHR survey. Probable ACO was defined as self-reported post-9/11 physician-diagnosed asthma and either emphysema, chronic bronchitis, or COPD. We evaluated whether probable ACO was associated with World Trade Center (WTC)-related exposures, using multivariable logistic regression.

Results: Of 36,864 Wave 4 participants, 29,911 were eligible for this analysis, and 1,495 (5.0%) had self-reported post-9/11 probable ACO. After adjusting for demographics and smoking status, we found 38% increased odds of having ACO in enrollees with exposure to the dust cloud, and up to 3.39 times the odds in those with ≥3 injuries sustained on 9/11. Among rescue/recovery workers, ever working on the pile, on the pile on 9/11 or 9/12/01, or working on the WTC site for >7 days showed increased odds ratios of having ACO.

Conclusion: Probable ACO is associated with WTC exposures. Further study of ACO is needed to understand the development of this and other environmentally or occupationally-related airway diseases, and how to prevent these in disasters like 9/11.

Keywords

Epidemiology; phenotypes

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Declaration of interest

The authors declare no other relevant conflict of interest.

Introduction

Persons exposed to the 9/11/2001 World Trade Center (WTC) disaster have experienced multiple adverse health outcomes associated with the complex mixture of dust, combustion products, other chemical substances and stressful events that occurred during and subsequent to the building collapses (1–4). Asthma and chronic obstructive pulmonary disease (COPD) (5,6), as well as a heterogeneous group of lower airway diseases (7) are conditions reported among WTC-exposed populations. The Asthma-COPD overlap (ACO) is a well-recognized (8) but re-defined chronic lower respiratory disease (9). In 2014, the Global Initiative for Asthma and the Global Initiative for Chronic Obstructive Lung Disease jointly published a consensus description of ACO for clinical use. Asthma-COPD Overlap was defined as a condition "characterized by persistent airflow limitation with several features usually associated with asthma and several features usually associated with COPD" (8,10). Patients with ACO experience more frequent exacerbations with dyspnea and respiratory distress, have a worse health-related quality of life, have a more rapid decline in lung function and use more health services than patients with asthma or COPD alone (11). In a study of 2137 New York City firefighters exposed to the WTC 9/11/01 disaster with clinically indicated post bronchodilator pulmonary function testing, ACO was diagnosed in 99 subjects (4.6%), and was predicted by an elevated early post-9/11 blood eosinophil concentration (12).

ACO shares many of the same disease risk factors as COPD, including smoking, advancing age and history of asthma (13). Exposure to air pollution has been linked to the development of asthma and COPD, but its effect on ACO is not well studied. One recent Canadian study found that patients with higher cumulative exposure to fine particulate matter and ozone had nearly threefold greater odds of developing ACO (14). Occupational exposures were associated with ACO in unadjusted but not adjusted analyses in a French study (15), but COPD was more prevalent among workers with current work- vs. non-work-related asthma (16).

The epidemiology of ACO has recently been summarized (13,17–19). The prevalence of ACO depends on which population or age group is studied, and which definition is used. In the United States, the prevalence of self-reported/physician diagnosed asthma and COPD in the third phase of the National Health and Nutrition Examination Survey (NHANES III) among those aged at least 25 years was reported as 2.7% (20). The estimate based on Behavioral Risk Factor Surveillance System (BRFSS) data on subjects aged at least 35 years was 3.2% (17).

In the current study of World Trade Center Health Registry enrollees, we examined whether there may be an association between WTC disaster exposure and ACO. We hypothesized that 9/11 exposures, may be risk factors for having ACO.

Materials and methods

Study sample and data source

The WTC Health Registry was designed as a longitudinal closed cohort study involving rescue/recovery workers and volunteers (hereinafter referred to as "RRW"), as well as

local-residents, passersby, area workers, students and teachers (hereinafter referred as "survivors"). Enrollees were recruited through lower Manhattan area building or employer lists, visits to firehouse and police precincts, outreach through local merchant displays or through a toll-free telephone number or website. In 2003–2004, 71,431 persons enrolled in the Registry and completed a baseline survey (Wave 1, W1) by phone (95%) or in-person interview (5%). Enrollees have been re-surveyed every three to four years subsequently. The most recent follow-up survey (Wave 4, W4) was carried out in 2015–2016. We used data from W1 on WTC exposures, sex, race/ethnicity, and W4 for data on health conditions, age, marital status, smoking status, education and income. We included all active Wave 4 participants at least 25 years of age at the time of the W4 survey. Participants were excluded if (1) they had a pre-2001 asthma diagnosis (n = 2,201), (2) missing responses at W4 on asthma (n = 2,683), chronic bronchitis (n = 481), emphysema/COPD (n = 309), (3) missing responses at W1 on injury count (n = 201), or dust exposure (n = 131), or (4) W4 survey form either filled out by proxy or missing proxy information (n = 607) (Figure 1).

Outcome variable

Asthma was defined as present if participants reported on the Wave 4 survey having a physician diagnosis of asthma between 2001 and 2016. COPD was defined as present if participants reported on the Wave 4 survey having a physician diagnosis of emphysema, chronic bronchitis or COPD between 2001 and 2016. ACO was then defined as present if both post-9/11 diagnoses of asthma and COPD were reported on the W4 survey.

World Trade Center exposures and covariates

Information on WTC exposure were self-reported at W1. They included being caught in the dust or debris cloud on 9/11, and number of physical injuries (0 to 5) other than eye injuries sustained on 9/11. Specific WTC exposures limited to RRW included working on the 16-acre pile of rubble ("the pile") within the first 48 h, working on the pile any time during 9/11/2001 – 6/30/2002, and cumulative days worked at the WTC site (categorized as 1 to 7 days, ≥7 to 30 days, >30 to 90 days and >90 days). The boundaries of the World Trade Center site include Chambers Street to the North, Rector Street or Rector Place on the South, Broadway on the East, and the Hudson River on the West.

Covariates included information reported at W4: sex, smoking status (current, former, never), age (25–44 years, 45–64 years, 65+ years), marital status (married, never married, not married – living with a partner, widowed, divorced or separated), race/ethnicity, annual income, and educational level.

Statistical analysis

Unconditional logistic regression models were used to assess the associations between probable ACO (compared to enrollees without asthma and/or COPD) at W4 and WTC exposures, for the entire group, and for RRW and subgroups. All covariates above were included in all models.

All analyses were performed using SAS software (SAS Institute, Cary, NC. v9.4). Significance level was set at two-sided $p < 0.05$. This study received Institutional Review

Board (IRB) exemption from the Icahn School of Medicine and was approved by the IRB for the NYC Department of Health and Mental Hygiene.

Results

A total of 29 911 Wave 4 participants met the inclusion criteria. Probable ACO following 9/11/01 was reported by 1495 (5.00%), asthma alone by 2172 (7.26%), and COPD alone by 1508 (5.04%) subjects. Table 1 shows the prevalence of post-9/11 ACO, asthma and COPD by socio-demographic characteristics of the study population. Those who were widowed or divorced/separated, had lower education or income level, of older age, or were current smokers had a higher prevalence of ACO than those without either asthma or COPD.

Table 2 shows the prevalence of ACO status by WTC exposure among both survivors and RRW, and by specific WTC exposures among the latter. The prevalence of ACO was 3.22% among survivors, and 6.97% among RRW. Increased prevalence of ACO was seen among both survivors and RRW who were exposed to the dust cloud, those who reported increased number of injuries on 9/11/01, and among RRW who ever worked on the pile, who worked on the pile on 9/11/01 or 9/12/01, and who worked more days on the WTC site. There were also consistently higher prevalence of both asthma alone and COPD alone among those with more WTC-related exposures, and among RRW than survivors.

Table 3 shows results of multivariable logistic regression modeling of the association between probable post-9/11/01 ACO versus those without asthma or COPD, assessing reported work on the pile, duration of work at WTC site, arrival to work in the first 48 h, number of injuries on 9/11 and dust cloud exposure reported at W1, adjusting for age, sex, income, marital status, education and smoking reported at W4. Among both rescue and recovery workers and survivors, ACO was significantly associated with dust cloud exposure (adjusted OR, AOR = 1.38, 95% CI = 1.29–1.47) and the number of physical injuries reported (One injury vs. None: AOR = 1.68, 95% CI = 1.53–1.84, two injuries: AOR= 2.28, 95% CI = 1.95–2.66, three or more injuries: AOR = 3.39, 95% CI = 2.57–4.46). Among rescue and recovery workers, ACO was significantly associated with work on the pile anytime during the nine months of rescue/recovery operations (AOR = 1.74, 95% CI = 1.58–1.92), working on the pile on 9/11/01 and/or 9/12/01 (AOR = 2.48, 95% CI = 2.27–2.71), and duration of work on the pile from ≥7 to 30 days (AOR = 1.33, 95% CI = 1.19–1.49), >30–90 days (AOR = 1.77, 95% CI = 1.56–2.01), >90 days (AOR = 1.89, 95% CI = 1.66–2.16), compared to <7 days of work on WTC site. There were no significant interactions between smoking and WTC exposures (data not presented).

Discussion

In this large study population of WTCHR enrollees who participated in the Registry's Wave 4 (2015–2016) survey we identified cases of probable ACO based on self-reported post-9/11 physician diagnosed asthma and COPD. Our results suggest a high prevalence of ACO particularly among those who had higher levels of WTC-related environmental and occupational exposures following the 9/11 attacks.

A previous study of NYC firefighters (12) did not find a significant association between high exposure to the 9/11 attacks and ACO. The authors suggested that an intense brief irritant exposure did not increase the risk of airway remodeling. However, our current study involved a much larger sample, with a broader range of participants, including both rescue and non-rescue and recovery survivors, with differing types of exposures, including longer exposure duration, and not selected on the basis of disease status. Additionally, that study included a nonrandom subgroup of their cohort (2137/9958) who underwent clinically indicated bronchodilator response testing, and was subject to further misclassification by defining asthma by the presence of such response (which COPD patients can have), and COPD by at least one test with fixed obstruction (which can be unstable as a means to diagnose COPD) (21). These factors likely explain the differences between the two studies.

Exposures to the WTC building collapses, with their resulting high levels of dust and acute injuries, as well as high levels of emotional stress, have resulted in multiple health problems, particularly adverse respiratory outcomes, primarily asthma (22), but also other chronic lower airway diseases (7). Thus, it is not surprising that ACO is emerging as a health concern among those most highly exposed. The resulting public health impacts include the likelihood of a more severe spectrum of disease among those affected, compared to those with asthma or COPD alone (11).

In the United States, the prevalence of self-reported physician-diagnosed ACO has been reported to be 2.7–3.4% (17,20,23–25). A review of international studies of prevalence found a pooled prevalence of ACO in the general population was 2.0% (95% CI: 1.4–2.6%) (19). The prevalence of post-9/11 self-reported and concurrent physician-diagnosed asthma and COPD found in our study is higher (3.22% among survivors, 6.97% among RRW). The age distribution of ACO patients found in our study was similar to previous studies, in that people with asthma were younger than those with ACO and the latter younger than those with COPD (11,20).

Besides age, smoking is well known to impact ACO prevalence. A study among primary care patients in Finland found a high prevalence of ACO (27%) among older asthmatics with a positive smoking history, but no previous diagnosis of COPD (26). In another study, ACO and COPD alone included a substantial proportion of older persons and exhibited similarly high rates of current smoking (27). In our study, smoking status at W4 was positively associated with both COPD and ACO; however, the strength of the association was much higher for COPD than for ACO.

In contrast to general demographic characteristics, the potential impact of occupational exposures on ACO prevalence has received less attention. Importantly, a recent study based on the BRFSS survey suggested higher prevalence ratios of COPD among subjects with work- vs. non-work-related asthma (16). Other than etiology, few pathophysiological features differentiate work-related from -unrelated asthma (4), so they would not be expected to differ in their ability to overlap with COPD. Analyses of mortality have indeed identified higher risks in a number of industries and occupations (28). Many of these industries and occupations had exposure to vapors, gas, dust, or fumes at work (29) suggesting that irritant or toxic exposures may be associated with an increased risk of ACO.

Overall, the results of Table 2 show that ACO, asthma, and COPD are all associated with WTC-related occupational exposures, with somewhat stronger associations noted for ACO.

While we have a relatively large study sample of 9/11 exposed populations, our study has several limitations. The definitions of asthma and COPD were based on self-reported physician-diagnoses of the disease and were not validated with lung function testing or medical record review. As such, the results may be subject to recall, surveillance, and reporting bias. However, these definitions have been widely used in large national (15,17,23) and international population-based surveys (19) and have proved to be reasonably reliable, and comparable to those of our study. Our definition of COPD was based on the physician diagnosis of at least one of three conditions (COPD, emphysema, or chronic bronchitis), e.g. as a diagnosis of chronic bronchitis, or a finding of emphysema by themselves do not meet present diagnostic criteria for COPD. This might have resulted in an overestimation of the actual prevalence of COPD. It is also likely that our definition of diseases based on physician diagnoses could have led to under-diagnoses of a certain proportion of the population. This study was unable to control for obesity and weight gain, a risk factor for poorer respiratory health (15,17,30,31), smoking intensity, and smoking status at any time other than W4, and for pre-9/11 occupational exposures, a risk factor for both asthma and COPD (32). In an individual enrollee the clinical assessment of obstructive airway disease requiring objective confirmation by spirometry criteria may have not been available to their treating physicians, and which were not available in our study. However, ACO studies based on spirometry may have limited generalizability too. Primary care providers frequently lack access to spirometry to establish obstructive airway disease diagnoses, and older patients who are weak and cognitively impaired may have difficulty performing spirometry (33,34). Importantly, the predominant spirometric abnormality in WTC RRW has been nonobstructive low forced vital capacity (3,4,7,35,36), which is not clearly diagnostic of either asthma or COPD, and can be a transitional state to and from COPD (37). As the recognition of ACO is experiencing a resurgence, future research should consider validating a health administrative definition of ACO that can be used globally to identify individuals with ACO and link them to other health administrative data. Data on treatment differences between those with ACO compared with asthma or COPD alone were not available for WTCHR Enrollees.

Probable Posttraumatic Stress Disorder (PTSD) has been found to be a precursor of both clinically significant bronchodilator response and incident asthma among WTC rescue and recovery workers and volunteers (38). The question whether PTSD is associated with the later development of ACO was not examined in the current study.

Selection bias is a consideration in this study due to attrition inherent in the longitudinal study design. This has been evaluated in prior Registry studies, where response rates to the W2 survey did not vary by type of exposure (29), and none of the disaster exposure measures measured at the W1 survey were associated with W3 nonparticipation (23).

To improve patient classification, more research is needed to develop more objective criteria, including biomarkers that are generalizable (39,40), and to better understand the molecular mechanisms of ACO and its related phenotypes. ACO is presently diagnosed by clinicians

in longstanding/aging and/or smoking asthmatics (13). Recent investigations also suggest that ACO occurs in COPD with eosinophilia/TH2 dominant inflammatory markers, and in steroid-resistant asthmatics with neutrophilic inflammation (41,42). Another study suggests that there may be different genetic involvement in ACO than in typical COPD or in asthma (43). If confirmed by further studies, these biomarkers may allow for more precise ACO diagnoses in the future.

This study found that those exposed to the dust cloud resulting from the collapse of the WTC towers, those reporting higher number of injuries, and work as rescue and recovery worker at the WTC site had greater odds ratios of developing ACO, adjusting for risk factors of sex, race/ethnicity, marital status, income, age, education, and current smoking. Future research using clinical evidence to define ACO may provide additional insight into the effect of 9/11 exposure on ACO. This research provides further evidence on the association of ACO with exposure to toxins or irritants. Better knowledge of the risk of environmental exposures in the development of ACO may help us better understand and prevent the progressive deterioration of lung function that may lead to ACO following large irritant exposures such as that what occurred at the WTC disaster site, or, more broadly, in high-risk occupational settings.

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References

1. Lioy PJ, Weisel CP, Millette JR, Eisenreich S, Vallero D, Offenberg J, Buckley B, Turpin B, Zhong M, Cohen MD, et al. Characterization of the dust/smoke aerosol that settled east of the World Trade Center (WTC) in lower Manhattan after the collapse of the WTC 11 September 2001. Environ Health Perspect. 2002;110(7):703–714. doi:10.1289/ehp.02110703. [PubMed: 12117648]
2. Perlman SE, Friedman S, Galea S, Nair HP, Eros-Sarnyai M, Stellman SD, Hon J, Greene CM. Short-term and medium-term health effects of 9/11. Lancet. 2011;378(9794):925–934. doi:10.1016/S0140-6736(11)60967-7. [PubMed: 21890057]
3. Prezant DJ, Weiden M, Banauch GI, McGuinness G, Rom WN, Aldrich TK, Kelly KJ. Cough and bronchial responsiveness in firefighters at the World Trade Center site. N Engl J Med. 2002;347(11):806–815. doi: 10.1056/NEJMoa021300. [PubMed: 12226151]
4. de la Hoz RE, Shohet MR, Chasan R, Bienenfeld LA, Afilaka AA, Levin SM, Herbert R. Occupational toxicant inhalation injury: the World Trade Center (WTC) experience. Int Arch Occup Environ Health. 2008;81(4):479–485. doi:10.1007/s00420-007-0240-x. [PubMed: 17786467]
5. Prezant DJ, Levin S, Kelly KJ, Aldrich TK. Upper and lower respiratory diseases after occupational and environmental disasters. Mt Sinai J Med. 2008;75(2): 89–100. doi:10.1002/msj.20028. [PubMed: 18500710]
6. Bello GA, Teitelbaum SL, Lucchini RG, Dasaro CR, Shapiro M, Kaplan JR, Crane MA, Harrison DJ, Luft BJ, Moline JM, et al. Assessment of cumulative health risk in the World Trade Center general responder cohort. Am J Ind Med. 2018;61(1):63–76. doi:10.1002/ajim.22786. [PubMed: 29148090]
7. de la Hoz RE. Occupational lower airway disease in relation to World Trade Center inhalation exposure. Curr Opin Allergy Clin Immunol. 2011;11(2):97–102. doi:10.1097/ACI.0b013e3283449063. [PubMed: 21325944]
8. Fletcher C, Gilson JG, Hugh-Jones P, Scadding JG. Terminology, definitions and classification of chronic pulmonary emphysema and related conditions. Thorax. 1959;14:286–299.

9. Gina-Gold GIfA. Diagnosis of diseases of chronic airflow limitation: asthma, COPD and asthma-COPD overlap syndrome (ACOS), 2015.
10. Kendzerska T, Sadatsafavi M, Aaron SD, To TM, Lougheed MD, FitzGerald JM, Gershon AS, Concurrent physician-diagnosed asthma and chronic obstructive pulmonary disease: a population study of prevalence, incidence and mortality. PLoS One. 2017; 12(3):e0173830. doi:10.1371/journal.pone.0173830. [PubMed: 28301574]
11. Menezes AMB, Montes de Oca M, Pérez-Padilla R, Nadeau G, Wehrmeister FC, Lopez-Varela MV, Muiño A, Jardim JRB, Valdivia G, Tálamo C, et al. Increased risk of exacerbation and hospitalization in subjects with an overlap phenotype: COPD-asthma. Chest. 2014;145(2):297–304. doi:10.1378/chest.13-0622. [PubMed: 24114498]
12. Singh A, Liu C, Putman B, Zeig-Owens R, Hall CB, Schwartz T, Webber MP, Cohen HW, Berger KI, Nolan A, et al. Predictors of asthma/COPD overlap in FDNY firefighters with World Trade Center dust exposure: a longitudinal study. Chest. 2018;154(6): 1301–1310. doi:10.1016/j.chest.2018.07.002. [PubMed: 30028968]
13. Putcha N, Wise RA. Asthma-chronic obstructive pulmonary disease overlap syndrome: nothing new under the sun. Immunol Allergy Clin North Am. 2016;36(3): 515–528. doi:10.1016/j.iac.2016.03.003. [PubMed: 27401623]
14. To T, Zhu J, Larsen K, Simatovic J, Feldman L, Ryckman K, Gershon A, Lougheed MD, Licskai C, Chen H, et al. Progression from asthma to chronic obstructive pulmonary disease. is air pollution a risk factor? Am J Respir Crit Care Med. 2016;194(4): 429–438. doi:10.1164/rccm.201510-1932OC. [PubMed: 26950751]
15. Caillaud D, Chanez P, Escamilla R, Burgel P-R, Court-Fortune I, Nesme-Meyer P, Deslee G, Perez T, Paillasseur J-L, Pinet C, et al. Asthma-COPD overlap syndrome (ACOS) vs 'pure' COPD: a distinct phenotype? Allergy. 2017;72(1):137–145. doi:10.1111/all.13004. [PubMed: 27501862]
16. Dodd K, Mazurek J. Prevalence of COPD among workers with work-related asthma. J Asthma. 2019:58; 1–9. doi:10.1080/02770903.2019.1640733. [PubMed: 31448976]
17. Kumbhare S, Pleasants R, Ohar JA, Strange C. Characteristics and prevalence of asthma COPD overlap in the US. Annals ATS. 2016;13(6):803–810. doi: 10.1513/AnnalsATS.201508-554OC.
18. Bateman ED, Reddel HK, van Zyl-Smit RN, Agusti A. The asthma-COPD overlap syndrome: towards a revised taxonomy of chronic airways diseases? Lancet Respir Med. 2015;3(9):719–728. doi:10.1016/S2213-2600(15)00254-4. [PubMed: 26255108]
19. Hosseini M, Almasi-Hashiani A, Sepidarkish M, Maroufizadeh S. Global prevalence of asthma-COPD overlap (ACO) in the general population - a systematic review and meta-analysis. Respir Res. 2019;20(1): 229. doi:10.1186/s12931-019-1198-4. [PubMed: 31647021]
20. Diaz-Guzman E, Khosravi M, Mannino DM. Asthma, chronic obstructive pulmonary disease, and mortality in the U.S. population. COPD. 2011;8(6):400–407. doi:10.3109/15412555.2011.611200. [PubMed: 22149399]
21. Aaron SD, Tan WC, Bourbeau J, Sin DD, Loves RH, MacNeil J, Whitmore GA, Diagnostic instability and reversals of chronic obstructive pulmonary disease diagnosis in individuals with mild to moderate airflow obstruction. Am J Respir Crit Care Med. 2017;196(3): 306–314. doi:10.1164/rccm.201612-2531OC. [PubMed: 28267373]
22. Wheeler K, McKelvey W, Thorpe L, Perrin M, Cone J, Kass D, Farfel M, Thomas P, Brackbill R. Asthma diagnosed after 11 September 2001 among rescue and recovery workers: findings from the World Trade Center Health Registry. Environ Health Perspect. 2007;115(11):1584–1590. doi:10.1289/ehp.10248. [PubMed: 18007989]
23. Pleasants R, et al. Chronic obstructive pulmonary disease and asthma–patient characteristics and health impairment. COPD. 2014;11(3):256–266. [PubMed: 24152212]
24. Mannino D, et al. Asthma and chronic obstructive pulmonary disease overlap: the effect of definitions on measures of burden. COPD. 2017;4(2):87–92. [PubMed: 28848917]
25. Kumbhare S, Strange C. Mortality in asthma-chronic obstructive pulmonary disease overlap in the United States. South Med J. 2018;111(5):293–298. doi:10.14423/SMJ.0000000000000807. [PubMed: 29767222]

26. Kiljander T, et al. Prevalence of asthma-COPD overlap syndrome among primary care asthmatics with a smoking history: a cross-sectional study. NPJ Prim Care Respir Med. 2015;25:15047. [PubMed: 26182124]
27. Vaz Fragoso C, Murphy T, Agogo G, Allore H, McAvay G. Asthma-COPD overlap syndrome in the US: a prospective population-based analysis of patient-reported outcomes and health care utilization. COPD. 2017;12:517–527. doi:10.2147/COPD.S121223.
28. Dodd K, Wood J, Mazurek J. Mortality among persons with both asthma and chronic obstructive pulmonary disease aged ≥25 years, by industry and occupation — United States, 1999–2016. MMWR. 2020;69(22):669–679.
29. Calvert GM, Luckhaupt SE, Sussell A, Dahlhamer JM, Ward BW. The prevalence of selected potentially hazardous workplace exposures in the US: findings from the 2010 National Health Interview Survey. Am J Ind Med. 2013;56(6):635–646. doi:10.1002/ajim.22089. [PubMed: 22821700]
30. de la Hoz RE, Liu X, Doucette JT, Reeves AP, Bienenfeld LA, Wisnivesky JP, Celedón JC, Lynch DA, San José Estépar R. Increased airway wall thickness is associated with adverse longitudinal first-second forced expiratory volume trajectories of Former World Trade Center workers. Lung. 2018; 196(4):481–489. doi:10.1007/s00408-018-0125-7. [PubMed: 29797069]
31. de la Hoz RE, Liu X, Celedón JC, Doucette JT, Jeon Y, Reeves AP, San José Estépar R. Association of obesity with quantitative chest CT measured airway wall thickness in WTC workers with lower airway disease. Lung. 2019;197(4):517–522. doi:10.1007/s00408-019-00246-z. [PubMed: 31254057]
32. Blanc PD, Annesi-Maesano I, Balmes JR, Cummings KJ, Fishwick D, Miedinger D, Murgia N, Naidoo RN, Reynolds CJ, Sigsgaard T, et al. The occupational burden of nonmalignant respiratory diseases. Am J Respir Crit Care Med. 2019;199(11):1312–1334. doi: 10.1164/rccm.201904-0717ST. [PubMed: 31149852]
33. Allen SC, Yeung P. Inability to draw intersecting pentagons as a predictor of unsatisfactory spirometry technique in elderly hospital inpatients. Age Ageing. 2006;35(3):304–306. doi:10.1093/ageing/afj090. [PubMed: 16638772]
34. Ferguson GT, Enright PL, Buist AS, Higgins MW. Office spirometry for lung health assessment in adults: a consensus statement from the National Lung Health Education Program. Chest. 2000;117(4): 1146–1161. doi:10.1378/chest.117.4.1146. [PubMed: 10767253]
35. Weber J, Reeves AP, Doucette JT, Jeon Y, Sood A, San José Estépar R, Celedón JC, de la Hoz RE. Quantitative CT evidence of airway inflammation in WTC workers and volunteers with low FVC spirometric pattern. Lung. 2020;198(3):555–563. doi:10.1007/s00408-020-00350-5. [PubMed: 32239319]
36. de la Hoz RE, S M, Nolan A, Celedón JC, Szeinuk J, Lucchini RG. Association of low FVC spirometric pattern with WTC occupational exposures. Respir Med. 2020;170:106058. doi:10.1016/j.rmed.2020.106058. [PubMed: 32843177]
37. Sood A, Petersen H, Qualls C, Meek PM, Vazquez-Guillamet R, Celli BR, Tesfaigzi Y. Spirometric variability in smokers: transitions in COPD diagnosis in a five-year longitudinal study. Respir Res. 2016;17(1): 147. doi:10.1186/s12931-016-0468-7. [PubMed: 27832774]
38. de la Hoz RE, Jeon Y, Miller GE, Wisnivesky JP, Celedón JC. Post-traumatic stress disorder, bronchodilator response, and incident asthma in World Trade Center Rescue and Recovery Workers. Am J Respir Crit Care Med. 2016;194 (11):1383–1391. doi:10.1164/rccm.201605-1067OC. [PubMed: 27548615]
39. Soler-Cataluna JJ, et al. Consensus document on the overlap phenotype COPD-asthma in COPD. Arch Bronconeumol. 2012;48(9):331–337. [PubMed: 22341911]
40. Ghebre MA, Bafadhel M, Desai D, Cohen SE, Newbold P, Rapley L, Woods J, Rugman P, Pavord ID, Newby C, et al. Biological clustering supports both “Dutch” and “British” hypotheses of asthma and chronic obstructive pulmonary disease. J Allergy Clin Immunol. 2015;135(1):63–72. doi:10.1016/j.jaci.2014.06.035. [PubMed: 25129678]
41. Green BJ, Wiriyachaiporn S, Grainge C, Rogers GB, Kehagia V, Lau L, Carroll MP, Bruce KD, Howarth PH. Potentially pathogenic airway bacteria and neutrophilic inflammation in treatment resistant severe asthma. PLoS One. 2014;9(6):e100645. doi:10.1371/journal.pone.0100645. [PubMed: 24955983]

42. Christenson SA, Steiling K, van den Berge M, Hijazi K, Hiemstra PS, Postma DS, Lenburg ME, Spira A, Woodruff PG. Asthma-COPD overlap. Clinical relevance of genomic signatures of type 2 inflammation in chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2015;191(7):758–766. doi:10.1164/rccm.201408-1458OC. [PubMed: 25611785]

43. Hardin M, Cho M, McDonald M-L, Beaty T, Ramsdell J, Bhatt S, van Beek EJR, Make BJ, Crapo JD, Silverman EK, et al. The clinical and genetic features of COPD-asthma overlap syndrome. Eur Respir J. 2014;44(2):341–350. doi:10.1183/09031936.00216013. [PubMed: 24876173]

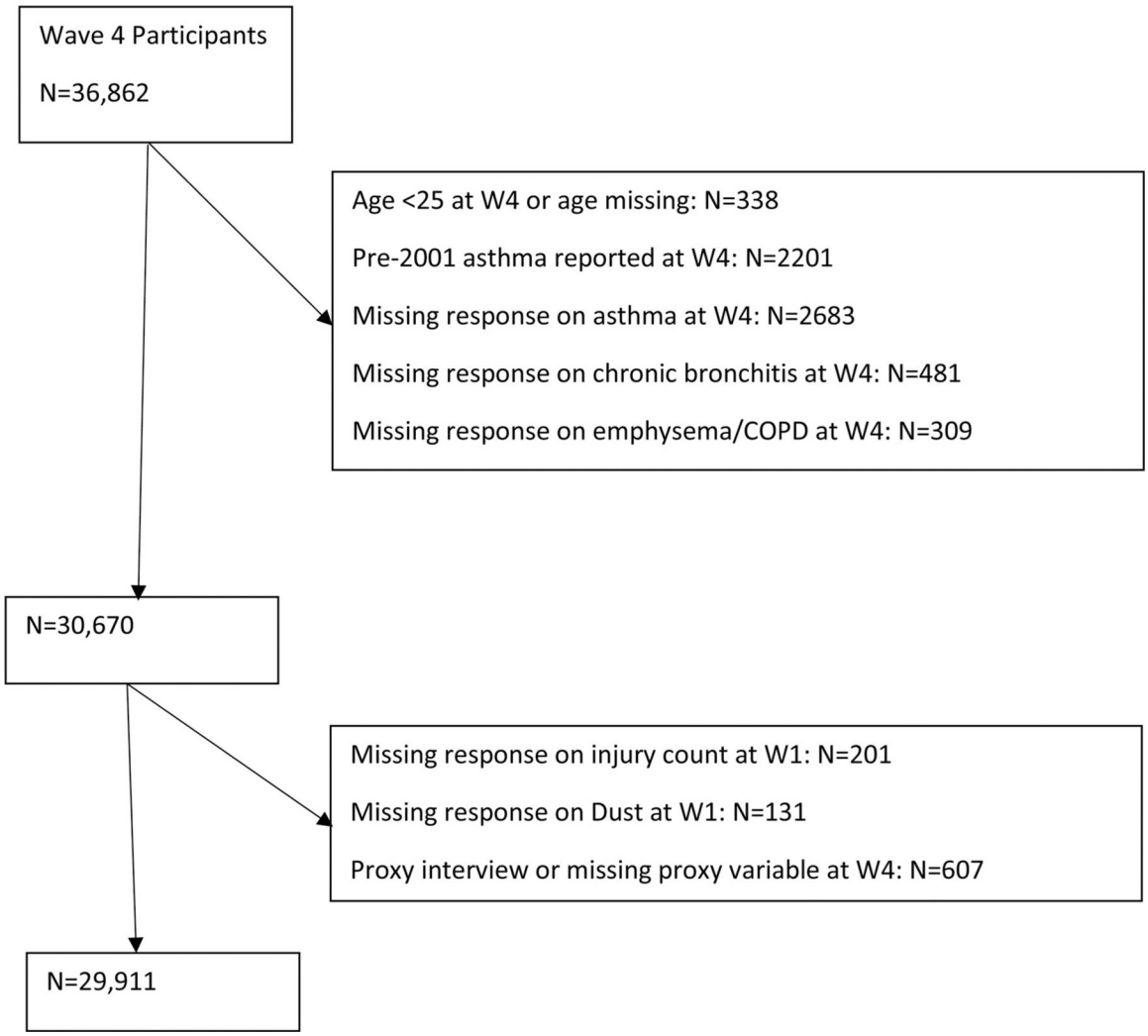

Figure 1.
Flow chart of participation - asthma-COPD overlap syndrome (ACOS).

Table 1.

Prevalence of asthma-COPD Overlap, Asthma and COPD among World Trade Center Health Registry enrollees, 2015–2016 by demographic factors.

Characteristic at Wave 4	Total sample N (col %)	ACOS (*n* = 1,495)	Asthma alone (*n* = 2,172)	COPD alone (*n* = 1,508)
Overall	29,911	5.00	7.26	5.04
Sex				
Female	11,517 (38.50)	4.59	8.93	4.53
Male	18,394 (61.50)	5.25	6.21	5.36
Age				
25–44	5,058 (16.91)	2.93	7.77	2.67
45–64	18,273 (61.10)	5.84	7.92	5.15
≥65	6,577 (21.99)	4.24	4.24	6.57
Race/ethnicity				
Non-Latino White	21,451 (71.72)	4.75	6.72	5.23
Non-Latino Black	2,799 (9.36)	4.86	7.65	5.14
Latino	3,162 (10.57)	6.64	10.56	4.65
Asian	1,515 (5.07)	4.69	7.33	3.10
Multi-racial	548 (1.83)	6.02	8.03	6.20
Other/unknown	436 (1.46)	6.19	6.19	3.44
Education				
K-8	177 (0.60)	9.04	10.73	6.78
At most 9–11 grade	485 (1.64)	5.57	7.84	7.63
High school graduate	3,783 (12.76)	6.71	7.03	6.48
Some college	8,649 (29.16)	7.13	7.90	6.67
College graduate	8,778 (29.60)	3.92	6.63	4.00
Postgraduate	7,785 (26.25)	2.89	7.33	3.42
Marital status				
Never married	4,082 (13.73)	4.36	8.23	4.56
Married	19,484 (65.55)	4.74	6.99	4.75
Live with partner	1,161 (3.91)	4.31	7.15	5.00
Widowed	1,061 (3.57)	5.66	5.18	6.79
Divorced/Separated	3,936 (13.24)	6.91	8.18	6.45

Characteristic at Wave 4	Total sample N (col %)	ACOS (*n* = 1,495)	Asthma alone (*n* = 2,172)	COPD alone (*n* = 1,508)
Annual household income				
<$25,000	2,150 (7.64)	9.26	10.82	6.51
$25,000–49,999	3,245 (11.54)	6.63	8.01	6.32
$50,000–74,999	4,154 (14.77)	5.42	7.39	6.23
$75,000–99,999	4,137 (14.71)	5.85	7.32	5.83
$100,000–149,000	6,537 (23.24)	4.79	7.63	5.06
$150,000+	7,906 (28.11)	2.82	6.56	3.02
Smoking status				
Current	2,439 (8.32)	7.18	4.55	11.28
Former	8,776 (29.92)	7.02	7.02	6.29
Never	18,112 (61.76)	4.71	7.80	3.61

Table 2.

Prevalence of post-9/11 asthma, COPD, and overlap (ACOS) by WTC exposure, WTCHR, 2015–2016.

		Prevalence, %		
Characteristic at Wave 4	**Total sample N (col %)**	**ACOS (*n* = 1,495)**	**Asthma alone (*n* = 2,172)**	**COPD alone (*n* = 1,508)**
Among survivors (N = 15,743)		3.22	6.76	4.24
Dust cloud exposure on 9/11/01				
Yes	10,043 (63.79)	3.81	7.24	4.83
No	5,700 (36.21)	2.18	5.93	3.19
Number of injuries on 9/11/01				
0	13,919 (88.41)	2.74	6.49	3.97
1	1,411 (8.96)	5.10	9.21	5.88
2	315 (2.00)	12.70	6.98	6.35
3 or more	98 (0.62)	13.27	9.18	11.22
Among all RRW (N = 14,168)		6.97	7.81	5.94
Dust cloud exposure on 9/11/01				
Yes	5,384 (38.00)	9.55	9.94	6.91
No	8,784 (62.00)	5.40	6.51	5.34
Number of injuries on 9/11/01				
0	12,018 (84.82)	5.94	7.19	5.73
1	1,499 (10.58)	11.61	10.41	7.00
2	535 (3.78)	13.83	12.71	6.92
3	116 (0.82)	22.41	16.38	8.62
Ever worked on the pile				
Yes	6,279 (45.81)	9.33	9.01	6.67
No	7,427 (54.19)	5.22	6.95	5.33
Worked on the pile on 9/11/01 or 9/12/01				
Yes	3,788 (12.66)	11.46	10.35	6.71
No	26,123 (87.34)	4.06	6.81	4.80
Days worked on the WTC site				
≤7	4,531 (34.16)	4.81	6.84	4.57
>7 to 30	4,349 (32.79)	6.76	7.52	6.69

Characteristic at Wave 4	Total sample N (col %)	Prevalence, %		
		ACOS (*n* = 1,495)	Asthma alone (*n* = 2,172)	COPD alone (*n* = 1,508)
>30 to 90	2,322 (17.51)	9.91	9.09	6.37
>90	2,062 (15.55)	9.99	9.65	6.94

Table 3.

Adjusted odds ratio for World Trade Center exposures and ACO in WTCHR enrollees, 2015–16.

	ACO	
	AOR	**(95% CI)**
Among all (N = 29,911)		
Dust cloud exposure on 9/11		
No	1.00	
Yes	1.38	(1.29–1.47)
Number of injuries on 9/11	1.00	
None		
1 injury	1.68	(1.53–1.84)
2 injuries	2.28	(1.95–2.66)
3 or more injuries	3.39	(2.57–4.46)
Among RRW (N = 14,168)		
Ever worked on the pile during 9/11–6/30/02		
No	1.00	
Yes	1.74	(1.58–1.92)
Worked on WTC pile on 9/11 or 9/12		
No	1.00	
Yes	2.48	(2.27–2.71)
Days worked on the WTC pile		
≤7	1.00	
>7 to 30	1.33	(1.19–1.49)
>30 to 90	1.77	(1.56–2.01)
>90	1.89	(1.66–2.16)

Separate multivariable logistic regression models were run for each of the exposure variables listed in this table, adjusting for gender, age group, educational level, race/ethnicity, marital status, income and current smoking status at W4.