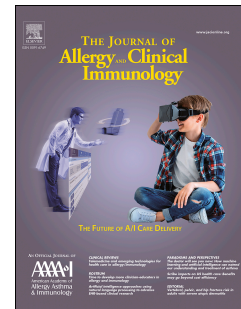


Journal Pre-proof

Impact of a pollution breach at a coke oven factory on asthma control in nearby vulnerable adults

Brandy M. Byrwa-Hill, MS, Albert A. Presto, PhD, Sally Wenzel, MD, James P. Fabisiak, PhD



PII: S0091-6749(21)00649-7

DOI: <https://doi.org/10.1016/j.jaci.2021.04.011>

Reference: YMAI 15079

To appear in: *Journal of Allergy and Clinical Immunology*

Received Date: 9 December 2020

Revised Date: 29 March 2021

Accepted Date: 8 April 2021

Please cite this article as: Byrwa-Hill BM, Presto AA, Wenzel S, Fabisiak JP, Impact of a pollution breach at a coke oven factory on asthma control in nearby vulnerable adults, *Journal of Allergy and Clinical Immunology* (2021), doi: <https://doi.org/10.1016/j.jaci.2021.04.011>.

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2021 Published by Elsevier Inc. on behalf of the American Academy of Allergy, Asthma & Immunology.

Impact of a pollution breach at a coke oven factory on asthma control in nearby vulnerable adults

Brandy M. Byrwa-Hill¹ MS, Albert A. Presto² PhD, Sally Wenzel^{1, 3*} MD, and James P. Fabisiak^{1*} PhD

¹Department of Environmental and Occupational Health, University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA

²Center for Atmospheric Particle Studies, Department of Mechanical Engineering, Carnegie Mellon University, Pittsburgh, PA

³University of Pittsburgh Asthma Institute @UPMC, Pittsburgh, PA

*Indicates co-senior and corresponding authorship

Correspondence should be addressed to: S Wenzel swenzel@pitt.edu, 412-624-9345 and JP Fabisiak fabs@pitt.edu, 412-624-7335

103 De Soto Street

Department of Environmental and Occupational Health

University of Pittsburgh Graduate School of Public Health

Pittsburgh, PA 15261 USA

Competing Interests: No financial or competing interests to declare

Key Words: Bronchial Asthma, Air Quality, Cohort Analysis, Sulfur Dioxide, Adults

Clinical Implications: Our data confirm an association between adverse asthma outcomes and acute increases in ambient SO₂. Clinicians should be aware of the potential for environmental pollutants like SO₂ to influence asthma control.

Abbreviations used: ACHD (Allegheny County Health Department), (Asthma control questionnaire) ACQ, (Air Quality Index) AQI, (Coke Works fire) CWF, (Emergency Department) ED (Environmental health survey) EHS, (Environmental Protection Agency) EPA, (Exhaled nitric oxide) FeNO50, (Hydrogen sulfide) H₂S, (Nitrogen dioxide) NO₂, (Ozone) O₃, (Particulate matter) PM₁₀, PM_{2.5}, Parts per billion (ppb), (Pulmonary function testing) PFT, (Standard deviation) SD, (The University of Pittsburgh Asthma Institute Registry) AIR, (Sulfuric and Sulfurous acid) (H₂SO₄) and (H₂SO₃), (Sulfur dioxide) SO₂

Capsule Summary:

This study identified a worsening of asthma related outcomes in adults living in closer proximity to a coke works plant during an acute environmental exposure to increased atmospheric SO₂.

Abstract

Background: Previous studies relate sulfur dioxide (SO₂) exposure with asthma exacerbations. We utilized the University of Pittsburgh Asthma Institute registry (AIR) to study associations of asthma exacerbations between two geographically distinct adult asthma populations.

Objective: The objective was to examine if asthma symptoms worsened following a significant fire event that destroyed pollution control equipment at the largest Coke Works in the United States.

Methods: Two groups of asthma patients 1) those residing within 10 miles of the Coke Works Fire (CWF) “proximal group” (n=39), and 2) those beyond that range “control group” (n=44) were geocoded by residential address. Concentrations of ambient air SO₂ were generated using local AIR monitor data. Factory emissions were also evaluated. Patient historical, acute exposure survey and in-person follow-up data were evaluated. Inferential statistics were used to compare groups.

Results: In the immediate post-fire period (6-8 weeks), there was increase in SO₂ factory emissions of 25 times above typical emissions. Following the pollution control breach, the proximal cohort self-reported an increase in medication usage (RR: 1.76, 95% CI 1.1-2.8, p<0.01) and more exacerbations. In a small subset of the follow-up cohort of those who completed the acute survey only, asthma control metrics improved.

Conclusions: A real world exposure to a marked increase in ambient levels of SO₂ from a pollution control breach associated with worsened asthma control in patients proximal to the event, which improved following repair of the controls. Improved spatial resolution of air pollutant measurements would enable better examination of exposures and subsequent health impacts.

Introduction

Patients with asthma tend to be more sensitive to development of symptoms from poor air quality as compared with healthy populations. Overwhelming evidence has accumulated that particulate matter (PM₁₀, PM_{2.5})^{1,2} and gases like nitrogen dioxide (NO₂)^{3,4} and ozone (O₃)^{5,6} can worsen asthma control and lead to exacerbations. While mechanisms remain inadequately defined, experimental exposure to various air pollutants increases oxidative stress which can contribute to greater airway reactivity and bronchial inflammation^{7,8,9}. While much recent work has focused on traffic-related emissions common in urban settings^{10,11} major industrial point sources remain in this country, including coal-fired power plants and various manufacturing plants, as well as those related to the steel industry.

Significant industrial point sources of emissions continue to exist in Allegheny County PA (home to Pittsburgh), related to its legacy as a steel industry center. Steel manufacturing requires the use of highly refined coal, or “coke”, as fuel used in blast furnaces to produce steel. Coke is generated from extreme heating of coal under anaerobic conditions to volatilize and remove impurities of which hydrogen sulfide (H₂S) and, and to a lesser extent, sulfur dioxide (SO₂) are major components^{12,13}. While the primary form of sulfur is in the reduced form as H₂S, fugitive emissions of H₂S can

spontaneously oxidize to SO_2 in the air, or following deliberate flaring of coke oven gas, contributing to the release of SO_2 into the atmosphere. While pollution control equipment collects and eliminates most H_2S emissions, disruption of these controls, as was seen following a catastrophic fire at the US Steel Clairton Coke Works plant (the largest in the United States) can (and did) render the equipment inoperable. The Coke Works consequently burned a large volume of coke oven gas to eliminate the noxious H_2S and released an unprecedented amount of SO_2 into the environment over 102 days before repairs to the damaged pollution control equipment were completed.

SO_2 is a recognized air pollutant, which is monitored and regulated by the Environmental Protection Agency (EPA). SO_2 is biochemically transformed in the atmosphere and on the airway mucosa SO_2 can oxidize to sulfurous (H_2SO_3) and sulfuric acid (H_2SO_4), which act as powerful lung irritants^{14,15,16,17}. In addition, sulfites and bisulfites are formed, which have been reported to increase mucus production in bronchial airways¹⁸. These known toxic effects led to studies which associated SO_2 with both asthma exacerbations and worsened lung function, including lower lung function in children^{19,20,21}. However, other studies have failed to show such an effect²².

Based on this convergence of acute large scale increases in a known toxicant in a defined locale, prior controversies of SO_2 and asthma, and our Institute's ability to rapidly engage asthma patients in the regions affected by the fire, we hypothesized that patients living within close proximity to the Coke Works would demonstrate a measurably higher asthma symptomology acutely, as compared to those living further away. We correlated these results with local air quality measures, in particular SO_2 , during and after the fire.

Methods

Participants (n=83) were recruited from The University of Pittsburgh Asthma Institute registry (AIR). This registry was established in 2007 and contains ~2200 patients with physician-diagnosed asthma. All registrants had asthma questionnaire data, agreed to be contacted in the future for additional studies, and most had baseline pulmonary function testing (PFT) from time of enrollment. Immediately after the fire, a 13-question Environmental Health Survey (EHS) survey (see Data File E1 in the online data supplement) was developed for distribution to existing AIR patients recruited to the study. Figure 1 is a CONSORT diagram outlining recruitment, while (Figure E1, supplement) maps the study area and patient locations within that area. The buffer was set to reflect the municipalities listed as “potentially impacted” by the health department, in addition to the natural break in the distribution of AIR patients around the Pittsburgh area. Recruitment began with the identification of all “Proximal” AIR patients (10-mile radius from CWF, n=177). Secondly, AIR participants (n=1920) were identified as potential controls if they lived “distal” (>10 miles from CWF). Participants were ordered based on their most recent participation with the AI, then contacted. Due to the time-sensitive nature of the event, recruitment was stopped after slightly more than 200 people were contacted, leading to over 40 rapidly consented participants with completed phone surveys in both the proximal and distal groups. Asthma patients were asked to recall information specific to the four weeks immediately prior to the date of the CWF to obtain a snapshot of their health during the *immediate* aftermath of the CWF.

Following recruitment, baseline demographic, clinical and physiologic data were pulled from the historical AIR. An asthma severity designation of mild or moderate-severe was assigned to each participant, using a combination of Fev1% predicted,

prescribed inhaled corticosteroid (ICS) dosage and/or oral steroids, and symptom type and frequency. Initial cohort recruitment and questionnaire administration occurred between February 1-20 of 2019, representing the time-period corresponding to the pollution control failure and high emissions.

After pollution control equipment was operational, participants were then invited to return to the Asthma Institute in person two months later to repeat the EHS, complete an updated asthma control questionnaire (ACQ), and undergo additional PFT and exhaled nitric oxide (FeNO50) testing to assess severity, control and inflammation²³. The University of Pittsburgh Institutional Review Board (IRB) approved all studies.

SO₂ Emission and Regulatory Air Monitor Data

Daily SO₂ emission estimates from the Coke Works corresponding to the first six months of 2019 were obtained from the Allegheny County Health Department (ACHD). The emission data are reported as tons/day and include the amount of SO₂ released into the atmosphere directly through a variety of processes (fugitive, flaring of coke gas, etc.) as well as secondary conversion from reduced H₂S. To determine if elevated emissions during the time of the CWF translated into changes in ambient air quality, we compared readings at EPA-regulatory air monitors proximal and distal to the CWF (Data file E2, supplement).

Statistical Analysis

Daily ACHD air monitor data were analyzed using non-parametric Kruskal-Wallis test followed by Dunn's multiple comparisons test. EHS responses were set up into contingency tables and Risk Ratios (RR) were calculated. $RR = \text{Rate [1]} / \text{Rate [2]}$ where "Rate" equals the proportion in group with the condition present, while confidence

intervals accompanied the ratios. Chi-square tests of association along with the Fisher exact probability test were used in combination with RR to determine statistical significance between group responses. Continuous data (emission, age, lung function) are reported as means $\pm$ standard deviation (SD). Mann Whitney tests were performed on continuous, non-parametric data. Acute survey results (pre-control room repair) were compared to follow-up responses (post control room repair) using the paired t-tests. P values < 0.05 were considered significant. Data analysis and graphs were generated using JMP Pro 14 software and Graph pad Prism 8.

Results

In the immediate aftermath of the fire, SO₂ emissions from the Coke Works averaged between 40 and 50 tons per day. At times, especially in the months of March and April, daily emissions exceeded 50 tons per day (25 times higher than typical levels). Immediately following the repair of the pollution control room, daily emissions of SO₂ dramatically declined to levels that were less than 5% of those reported during the breach (Figure 2).

In 2019, coinciding with the large emissions of SO₂ from the Coke Works during the pollution control breach, daily maximal SO₂ readings and SO₂-dependent Air Quality Index (AQI) values were elevated at monitor 1 (closest to the Coke Works) as compared to the previous 2 years (Figure 3). In contrast, time-dependent changes in measurements of SO₂ in ambient air were not observed at either of the two other monitors (Table E1, supplement). Thus, enhanced emission(s) of SO₂ during the pollution control breach were associated with measurable changes of SO₂ in ambient air in close proximity to the Coke Works.

Impact during the acute exposure (during loss of pollution control system)

To determine the impact of these increased emissions on asthma control, we recruited and surveyed a proximal and distal (control) cohort of asthma patients both before and after the pollution controls were repaired. Historical registry data (collected 1 to 8 years prior to the fire), indicated both proximal and distal groups were generally well matched over a variety of demographic factors including age, race, sex and type of health insurance (Table 1). Both educational attainment and marital status either tended to or statistically differed across the groups ($p=.07$ for education, $.04$ for marital status), supporting higher SES in the distal/control group. Despite this, the groups were well matched on known confounders of asthma such as exposure to or history of smoking and BMI. Notably, there was a significant difference in historical FEV₁% predicted and asthma related emergency department (ED) visits compared with the control group (Table 1).

Given the need for rapid assessment of a potentially “at risk” population, the first patient questionnaires to these two cohorts were administered by telephone. Not surprisingly, and consistent with the SO₂ data, more proximal group patients reported the presence of rotten egg smells near their home compared to controls and more were aware of the CWF event compared to those living further away (Figure 4). During the time-period corresponding to the pollution control breach, the proximal group also self-reported an increase in asthma exacerbations (Q5) compared to distal controls (RR: 1.7, 95% CI 1.1-2.8, $p<0.01$), and increased medication usage (RR 1.4, 95% CI 1.0-2.0, $p<0.05$) (Figure 4). Nearly all proximal group patients (77%), reported that their asthma worsened and perceived the worsening to be a result of air pollution, compared to only 48% of distal controls.

To account for boundary effects of potential “edge bias”²⁴ to our 10 mile buffer zone which defined the proximal group, we determined whether there were differences in those < 5 miles (n=13, 33%) from CWF and those 5-10 miles (n=26, 67%) away. As expected those living closer to the factory (< 5 miles) were more likely to notice industry smells (Q5 p=0.01, Q6 p=0.009) and were more aware of the CWF (Q8, p=0.0002) compared to the 5 –10 mile group (Supplemental Table E2). However, there were no differences in asthma control between the near vs far proximal groups in the aftermath of the fire.

Lastly, because general news coverage of the CWF may have selectively influenced survey responses, we compared responses within the proximal group based on their expressed knowledge of the CWF (54% aware and 46% unaware). No differences in survey responses to medication and/or asthma related exacerbations were observed based on stated awareness. Of note, those reporting less awareness of the CWF tended to be more likely to report Medicaid (53%, p=0.16) as their primary insurance and were less likely to have a college degree (71% p=0.07) as compared to those who were aware, suggesting lower SES.

Follow up (post repair)

To assess the potential impact of changing exposure to SO₂ more directly on measures of asthma control and to determine the relationship of location to current pulmonary function and airway inflammation, those patients who completed the initial survey were re-contacted 2 months post-pollution control repair to arrange an in-person visit. Of the original cohort, 57% (22 from the proximal group and 25 from the distal control group) returned to the AI after resolution of the breach for an in-person evaluation. There were baseline differences between those who only completed the

phone survey and those who completed both phone and in-person surveys, particularly within the proximal cohort (Supplemental Tables E4 and E4). Those in the proximal group agreeing to the follow-up visit tended to report better asthma control at the time of the phone survey than those who answered only the initial phone survey (Supplemental Table E3). Although there were no differences in asthma severity or FEV1, those who returned reported a higher percentage of being employed outside the home and a lower percentage of Medicaid insurance than those who did not return for the in-person survey, consistent with potential differences in SES. In contrast, within the distal/control group initial only and follow-up groups differed only in regards 2nd hand smoke exposure (Supplemental Table E4).

Paired testing on those with both the phone and in-person questionnaires performed initial and follow-up comparisons of questionnaire responses. Our analysis of the proximal group indicated persistent industry smells (Q6) and improved asthma control (Q9, Q11), (Figure 5A) which coincided with improved factory emissions. There were no longitudinal changes in asthma control questions in the distal/control group. However, a heightened perception that adverse air quality may sometimes affect their asthma control was observed in the distal/control group (Q7), perhaps due to the repeat nature of the survey (Figure 5B). Lastly, all participants who came into the AI were evaluated with FeNO50, spirometry and ACQ tests. Overall, the proximal group had worse asthma control and more inflammation compared to distal controls, although the small sample size limited significance (Table 2). A paired analysis of historical and follow-up mean FEV1% predicted over a 2.5 year period revealed no change in the control group ($p=0.7$) and 73.7 vs. 76.1 ($p=0.2$) within the proximal group.

Discussion

This study provided the opportunity to examine short-term asthma outcomes relative to an individual's proximity to a major industrial event that emitted 20 times more SO₂ than what is typically discharged per day over a several month period. Key findings include the measurable differences detected in self-reported asthma control between those living proximal and distal from the CWF that corresponded to large changes in factory emissions and air quality. Despite persistently poor air quality in this region, historical air monitor data support our assertion that air quality during our study period was exceptionally poor and likely contributed to acute negative effects on asthma outcomes in our small cohort of asthmatics. To our knowledge, this study is the first of its kind to describe the short-term impact on well-characterized asthma patients from real world factory emissions at this plant and to decrements in air quality health outcomes within an adult asthmatic population.

Short term controlled (chamber) SO₂ exposures have been shown to augment bronchoconstriction in asthma patients²⁵. While the mechanisms for the effects are unclear, SO₂ can act as both an oxidizing and reducing agent, depending on its environment. It has been reported to increase mucus production and lead to bronchoconstriction through unclear molecular pathways²⁶. Exposure has also been linked to exacerbations and reductions in pulmonary function, in particular (FEV₁).^{26, 27} In adults, higher SO₂ exposure during the winter months was associated with lower lung function in poorly controlled asthmatics.²⁸ Similarly, SO₂ levels were high in the winter months of our study and may have affected lung function. Other studies however, failed to demonstrate consistent associations.²⁹ This may be attributable to the spectrum of study designs in the literature, combined with different outcomes.

Furthermore, some asthmatics may respond to SO₂ and others may not³⁰. This suggests a rationale for deeper phenotyping of these patients to identify potential SO₂ hyper-reactive asthma patients. Lastly, a recent study has implicated SO₂ ambient exposure with increased ED visits over extended lag periods.³¹ These studies suggest a multifaceted approach is needed to create a holistic picture of the impact SO₂ has on adults with asthma.

Though a direct measure of sulfur dioxide was not obtained at the homes of the participants, data from regulatory grade air monitors in close proximity to the plant where the CWF occurred were publicly available. Despite persistently high levels of factory SO₂ emissions (over 102 days); the most proximal monitor reported exceedances of the EPA threshold (75 ppb) on only 9 days. This is likely due to a combination of meteorological and topographical factors that, in addition to emissions, influence ground-level SO₂ concentrations. The highest SO₂ concentrations occur during meteorological inversions, which are periods when vertical mixing in the atmosphere is limited and emissions are concentrated near the surface. The net result is that the actual ground-level SO₂ concentrations are a complex function of multiple factors influenced by both emissions and meteorology, which may not be reflected in monitor measurements.

Five of the exceedance days occurred during the acute survey timeframe following the CWF from January 1, through February 20, 2019 (baseline survey period) (Supplemental Figure E2). Importantly, these exceedances were only reported at the most proximal monitor, suggesting that location of monitoring equipment is very important. Communities which rely on a few citywide air monitors are likely unable to

model a population's true exposure. This is especially true in communities with varying topography and/or with major point sources that can have disproportionate impacts on immediate downwind areas. In home monitoring may be needed to better reflect the more localized impact of point source pollution.

Acute health effects measured throughout this study trended with air quality and emission changes. First, those living close to CWF reported worse outcomes compared to those who lived further away during the same period corresponding to elevated emissions. This minimizes the chance that weather or prevalence of seasonal respiratory infections contributed the differences. Supporting this, longitudinal data on patients who completed both phases of the study indicated asthma control improved from the immediate post-fire period in the proximal group, when pollution controls were operational and air quality improved.

To control for information bias, we examined whether participants who knew about the CWF answered their questions differently from those that did not know. Responses did not differ in those with or without knowledge of the fire. However, those less likely to be aware (nearly 50% of the proximal group) of the CWF also reported lower SES.

This study demonstrates the benefits of having a pre-existing interactive asthma registry of well-characterized asthma patients. Participant consent allowed us the ability to quickly gain access to patients following an environmental disaster. This study also revealed some potential reasons why some patients may be more likely to follow up or participate in environmental health research than others. Patients with poorer SES indicators and less education may have transportation issues or work in occupations that have limited paid time off and therefore patients are less likely to visit the Asthma

Institute. Because participant dropout is an unfortunate reality of research studies, our aim was to better understand the population that did not complete our study. The asthma registry data allowed us to compare various SES and other metrics between groups. Participants that did not return to the AI for the follow-up visit tended to have poorer asthma control according to the baseline survey, these participants were more likely to report a clinic, ER, or ambulance visit because of their asthma. Additionally, this subgroup tended to have poorer SES indicators. These factors may have influenced communication and transportation efforts within this sub group. Unfortunately, since this subgroup did not complete the follow up questionnaire we are unable to discern how their asthma control may have changed with improved air quality.

Some incidental findings of our study alluded to the potential for more chronic asthma related issues within this cohort based on their residential proximity to the Coke Works. When considering the historical registry data, we identified significant baseline differences in mean lung function between those proximal compared to those distal to the Coke Works. While multiple factors could contribute to these differences, in general, the 2 groups were well matched for baseline demographics, as well as smoking status and SES. This suggests chronic exposures may adversely affect lung health, and warrants further study in larger patient surveys.

This study focuses specifically on emissions associated with an operational failure at a single point source near Pittsburgh. Excess emissions after the CWF, modified by meteorology and topography, impacted ground-level air pollution and the resultant exposure and health impacts catalogued here. Exposure assessment was limited because the sparse network of air pollutant monitors does not enable neighborhood-level air quality assessment. Communities in other cities are also

impacted by nearby point sources, and exposure estimates in those locations may be similarly impacted by a lack of nearby monitors.

Study Limitations

As with all human and environmental studies, the potential for confounders exist. The largest concern is the small cohort where confounders may have influenced the observed differences. However, overall the 2 groups were well matched and in the proximal group, differences improved in concert with improved air quality when other factors were constant. This was not a random population, but one derived from an existing asthma registry. However, given the historical information on these patients, including standard lung function testing, it is very likely these patients indeed had asthma, as compared to random dialing approaches.³² Importantly, only 50% of patients returned to the AI for full evaluation after repairs were completed, and consequently in a different season (winter vs. spring). There were substantial differences in those who returned and those who did not, which may explain the resolution of all clinical differences between the two groups at the later follow up.

Conclusion

Data from this study reveals an association between acute exposures to increased ambient levels of SO₂ to worsened asthma control, in a potentially vulnerable population living close to the source of the pollution. However, it also supports the loss of acute effects when EPA established air-quality levels are re-established. While our data additionally suggest that chronic long-term exposure may negatively influence lung function, further study is needed.

Acknowledgments: Special thanks to the Allegheny Health Department for their collaboration with this project. This project was supported by Dr. Sally Wenzel NIH grants P01 AI106684-01A1, R01 AI145406-01A1 in addition to Dellenback Funds and Dr. Jim Fabisiak grant from Heinz Endowments (#E4820).

Author Contributions: BMBH developed study design and questionnaires, collected and analyzed the data, and drafted initial manuscript. AP assisted with air quality data review and manuscript editing. SW and JF assisted in study design and questionnaire development and provided oversight of data analysis and manuscript editing.

References

1. Lim H, Kwon H-J, Lim J-A, Choi JH, Ha M, Hwang S-S, et al. Short-term Effect of Fine Particulate Matter on Children's Hospital Admissions and Emergency Department Visits for Asthma: A Systematic Review and Meta-analysis. *Journal of Preventive Medicine and Public Health*. 2016; 49(4):205–19.
2. Mann JK, Balmes JR, Bruckner TA, Mortimer KM, Margolis HG, Pratt B, et al. Short-Term Effects of Air Pollution on Wheeze in Asthmatic Children in Fresno, California. *Environmental Health Perspectives*. 2010; 118(10):1497–502.

3. Brown JS. Nitrogen dioxide exposure and airway responsiveness in individuals with asthma. *Inhalation Toxicology*. 2014; 27(1):1–14.
4. Takenoue Y, Kaneko T, miyamae T, Mori M, Yokota S. Influence of outdoor NO₂ exposure on asthma in childhood: Meta-analysis. *Pediatrics International*. 2012; 54(6):762–9.
5. Cody RP, Weisel CP, Birnbaum G, Lioy PJ. The effect of ozone associated with summertime photochemical smog on the frequency of asthma visits to hospital emergency departments. *Environmental Research*. 1992; 58(1-2):184–94.
6. Thurston GD, Lippmann M, Scott MB, Fine JM. Summertime haze air pollution and children with asthma. *American Journal of Respiratory and Critical Care Medicine*. 1997; 155(2):654–60.
7. Delfino RJ, Staimer N, Gillen D, Tjoa T, Sioutas C, Fung K, et al. Personal and Ambient Air Pollution is Associated with Increased Exhaled Nitric Oxide in Children with Asthma. *Environmental Health Perspectives*. 2006; 114(11):1736–43.
8. Liu, L, Poon, R, Chen, L, Frescura, A. M, Montuschi, P, Ciabattini, et al. Acute Effects of Air Pollution on Pulmonary Function, Airway Inflammation, and Oxidative Stress in Asthmatic Children. *Environ Health Perspect*. 2009;117(4):668-674. doi:10.1289/ehp11813
9. Poynter ME, Persinger RL, Irvin CG, Butnor KJ, van Hirtum H, Blay W, et al. Nitrogen dioxide enhances allergic airway inflammation and hyperresponsiveness in the mouse. *Am J Physiol - Lung Cell Mol Physiol*. 2006;290(1).

doi:10.1152/ajplung.00131.2005

10. Rusconi F, Catelan D, Accetta G, Peluso M, Pistelli R, Barbone F, et al. Asthma Symptoms, Lung Function, and Markers of Oxidative Stress and Inflammation in Children Exposed to Oil Refinery Pollution. *Journal of Asthma*. 2010; 48(1):84–90.
11. Perez L, Declercq C, Iñiguez C, Aguilera I, Badaloni C, Ballester F, et al. Chronic burden of near-roadway traffic pollution in 10 European cities (APHEKOM network). *European Respiratory Journal*. 2013; 42(3):594–605.
12. Ghosh. Desulfurization in Secondary Steelmaking. *Secondary Steelmaking: Principles and Applications*. 2000.
13. EPA. Environmental Protection Agency; [cited 2021Apr9]. Available from: <https://www.epa.gov/>
14. Samoli E, Nastos PT, Paliatsos AG, Katsouyanni K, Priftis KN. Acute effects of air pollution on pediatric asthma exacerbation: Evidence of association and effect modification. *Environmental Research*. 2011; 111(3):418–24.
15. Liu Y, Pan J, Zhang H, Shi C, Li G, Peng Z, et al. Short-Term Exposure to Ambient Air Pollution and Asthma Mortality. *American Journal of Respiratory and Critical Care Medicine*. 2019; 200(1):24–32.
16. He B, Huang JV, Kwok MK, Au Yeung SL, Hui LL, Li AM, et al. The association of early-life exposure to air pollution with lung function at ~17.5 years in the “Children

of 1997” Hong Kong Chinese Birth Cohort. *Environment International*. 2019;
123:444–50.

17. Fernandez R, Ariza M, Iscar M, Martinez C, Rubinos G, Gagatek S, et al. Impact of
Environmental Air Pollutants on Disease Control in Asmathic Patients. *Lung*. 2015;
193(2):195–8.

18. Li R, Meng Z. Effects of SO₂ derivatives on expressions of MUC5AC and IL-13 in
human bronchial epithelial cells. *Archives of Toxicology*. 2007; 81(12):867–74.

19. Barbone F, Catelan D, Pistelli R, Accetta G, Grechi D, Rusconi F, et al. A Panel
Study on Lung Function and Bronchial Inflammation among Children Exposed to
Ambient SO₂ from an Oil Refinery. *International Journal of Environmental
Research and Public Health*. 2019; 16(6):1057.

20. Rusconi F, Catelan D, Accetta G, Peluso M, Pistelli R, Barbone F, et al. Asthma
Symptoms, Lung Function, and Markers of Oxidative Stress and Inflammation in
Children Exposed to Oil Refinery Pollution. *Journal of Asthma*. 2010; 48(1):84–90.

21. Chen C-H, Chan C-C, Chen B-Y, Cheng T-J, Leon Guo Y. Effects of particulate air
pollution and ozone on lung function in non-asthmatic children. *Environmental
Research*. 2015; 137:40–8.

22. Shutt RH, Kauri LM, Weichenthal S, Kumarathasan P, Vincent R, Thomson EM, et
al. Exposure to air pollution near a steel plant is associated with reduced heart rate
variability: a randomised crossover study. *Environmental Health*. 2017; 16(1).

23. Dweik RA, Boggs PB, Erzurum SC, Irvin CG, Leigh MW, Lundberg JO, et al. An Official ATS Clinical Practice Guideline: Interpretation of Exhaled Nitric Oxide Levels (FeNO) for Clinical Applications. *American Journal of Respiratory and Critical Care Medicine*. 2011; 184(5):602–15.
24. Griffith DA, Amrhein CG. An Evaluation of Correction Techniques for Boundary Effects in Spatial Statistical Analysis: Traditional Methods. *Geographical Analysis*. 2010; 15(4):352–60.
25. Johns DO, Svendsgaard D, Linn WS. Analysis of the concentration–respiratory response among asthmatics following controlled short-term exposures to sulfur dioxide. *Inhalation Toxicology*. 2010; 22(14):1184–93.
26. Bonser L, Erle D. Airway Mucus and Asthma: The Role of MUC5AC and MUC5B. *Journal of Clinical Medicine*. 2017; 6(12):112.
27. Trenga CA, Koenig JQ, Williams PV. Sulphur dioxide sensitivity and plasma antioxidants in adult subjects with asthma. *Occupational and Environmental Medicine*. 1999; 56(8):544–7.
28. Yu S, Park S, Park C-S, Kim S. Association between the Ratio of FEV1 to FVC and the Exposure Level to Air Pollution in Never-smoking Adult Refractory Asthmatics Using Data Clustered by Patient in the Soonchunhyang Asthma Cohort Database. *International Journal of Environmental Research and Public Health*. 2018; 15(11):2349.

29. Shepherd MA, Haynatzki G, Rautiainen R, Achutan C. Estimates of community exposure and health risk to sulfur dioxide from power plant emissions using short-term mobile and stationary ambient air monitoring. *Journal of the Air & Waste Management Association*. 2015; 65(10):1239–46.
31. Lu P, Zhang Y, Lin J, Xia G, Zhang W, Knibbs LD et al. Multi-city study on air pollution and hospital outpatient visits for asthma in China. *Environmental Pollution*. 2020 Jan; 257. 113638. <https://doi.org/10.1016/j.envpol.2019.113638>
32. Aaron SD, Boulet LP, Reddel HK, Gershon AS. Underdiagnosis and Overdiagnosis of Asthma. *American Journal of Respiratory and Critical Care Medicine*. 2018; 198(8):1012–20.

Figure Legends:

Figure 1. CONSORT flow diagram outlines study recruitment.

Figure 2. Each point represents a single day of Coke Works factory emissions. The larger black dot indicates the date pollution control equipment was damaged and inoperable. The grey triangle indicates a second fire that damaged pollution controls for a single day. The horizontal error bars indicate the initial baseline study and follow-up periods.

Figure 3. Figures A and B depict two proximal regulatory air monitors located within 10 miles of the CWF and one distal control monitor beyond the 10-mile range and their relative location from the Clairton Coke Works. Figures compare daily ambient SO₂ expressed as median maximum and AQI values for 2019, and after the CWF compared with historical data in 2017 and 2018 for reference.

Figure 4. Graph depicts difference by percentage of respondents (N=83) who answered "yes" between both control and proximal groups. *Definition of abbreviations.* * = P-value < 0.05, ** = P-value < 0.005, *** = P-value < 0.0005; Rate= proportion in-group with response "yes" to "no", Risk Ratio= Rate [1]/Rate [2]; CI= Confidence Interval. Survey questions (ID) are listed above and correspond with the question number on the y-axis.

Figure 5. Figure A and B compare responses of "yes" to our survey at baseline following the CWF relative to their follow-up responses post factory repair. Reference Figure 4 for survey questions. Definition of abbreviations * = P-value < 0.05.

Table 1. Baseline comparison of the control and proximal cohorts using Asthma Institute Registry data. Data represents registry metrics at time of enrollment into AIR (N=83).

Characteristics	Distal Control N=44 n (%) or Mean $\pm$ SD	Proximal Group N=39 n (%) or Mean $\pm$ SD	P-Value
Age	45.1 $\pm$ 14.6	45.6 $\pm$ 14.6	0.41
Female	39 (84.0)	32 (86.0)	0.76
Non-White	16 (36)	16 (41)	0.82
Body Mass Index (BMI)	31.9 $\pm$ 11	33.1 $\pm$ 10.5	0.41
Asthma Indicators			
Mean Fev ₁ % predicted (SEM)	84.8 (7.1)	77.2 (12.1)	0.04*
Moderate-Severe Asthma	18 (41)	19 (49)	0.51
Health Insurance			
Medicaid	12 (27)	14 (36)	0.47
Other	32 (72)	25 (64)	
Employment Status			
Outside of Home	31 (70)	24 (62)	0.36
Education			
High School Graduate or Less	4 (9)	10 (26)	0.04
Partial or College Graduate	40 (90)	29 (74)	
Marital Status			
Single or Other	22 (50)	27 (69)	0.07
Married	22 (50)	11 (28)	
Smoking Status			
History of Smoking	13 (29)	9 (23)	0.62
Second Hand Smoke	8 (18)	11 (28)	0.31

Definition of abbreviations: * = P-value <0.05

Table 2. Physiologic results at follow-up visit between control and proximal groups (n = 17) after the bone marrow pollution controls were repaired.

Patient Characteristics	Distal Control n (%) or Mean $\pm$ SD	Proximal Group n (%) or Mean $\pm$ SD	P-Value
Post Factory Repair			
Exhaled Nitric Oxide (FeNO)	20.3 $\pm$ 12.6	27.1 $\pm$ 19	0.2
Asthma Control (ACQ)	1.32 $\pm$.95	1.61 $\pm$ 1.2	0.3
Mean Fev ₁ % predicted (SEM)	82.4 (16.7)	76.1 (19.6)	0.3

Definition of abbreviations: * = P-value < 0.05; Rate = proportion in groups with response "yes" to "no", Risk Ratio = Rate [1]/Rate [2], CI = Confidence Interval.

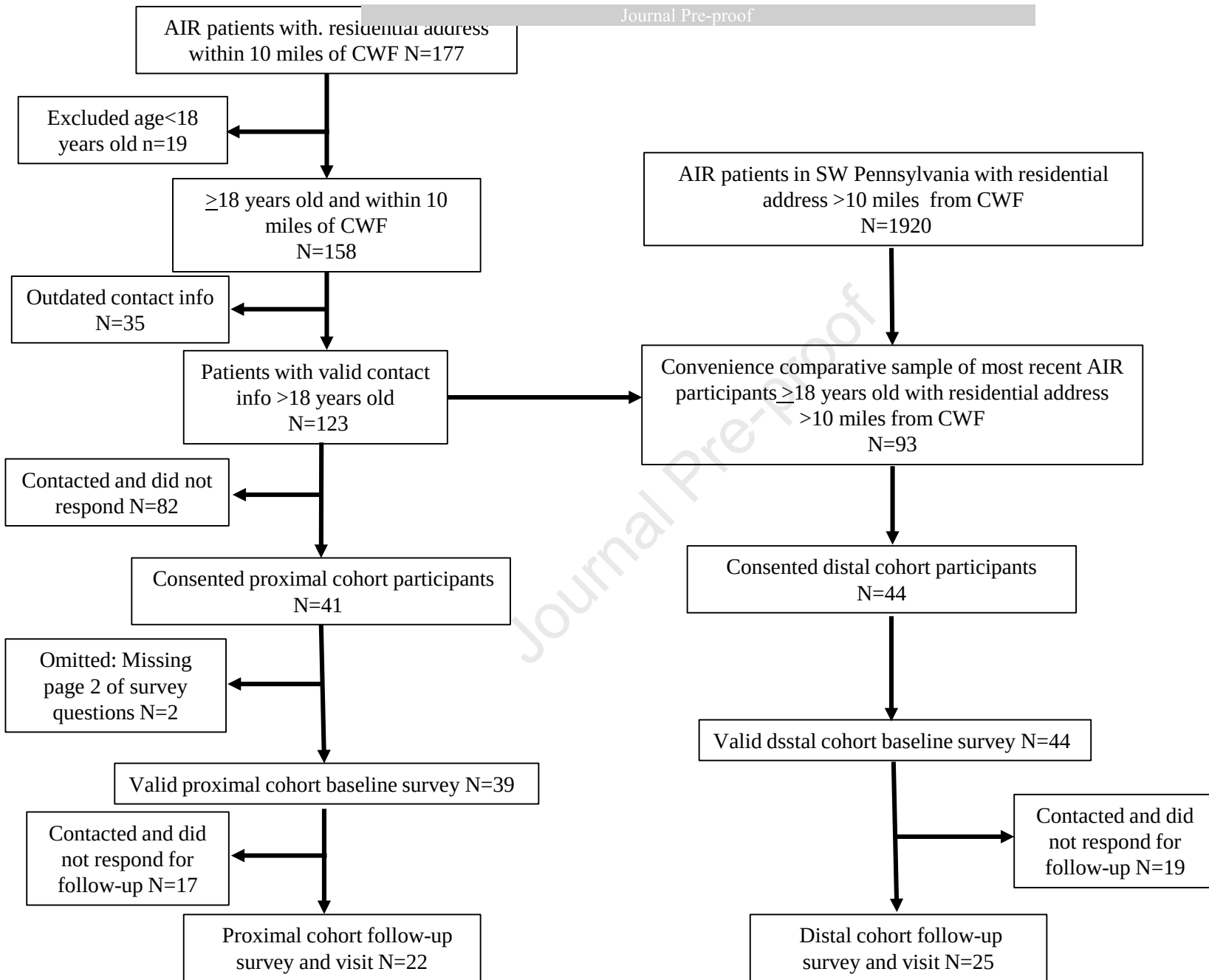


Figure 1.

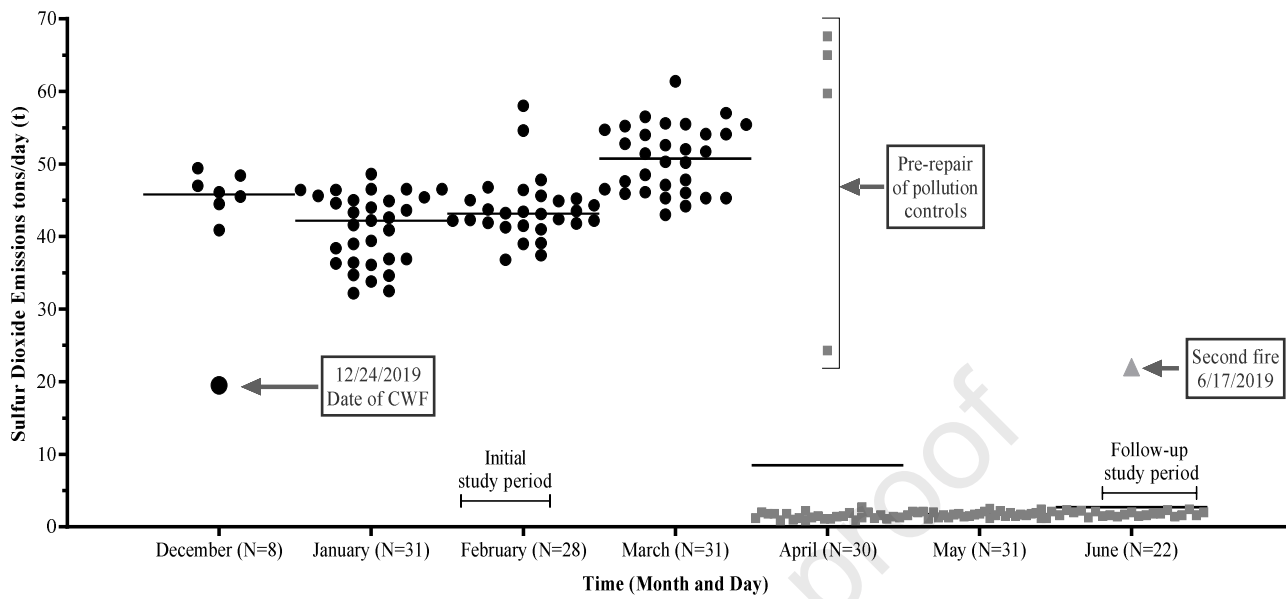


Figure 2.

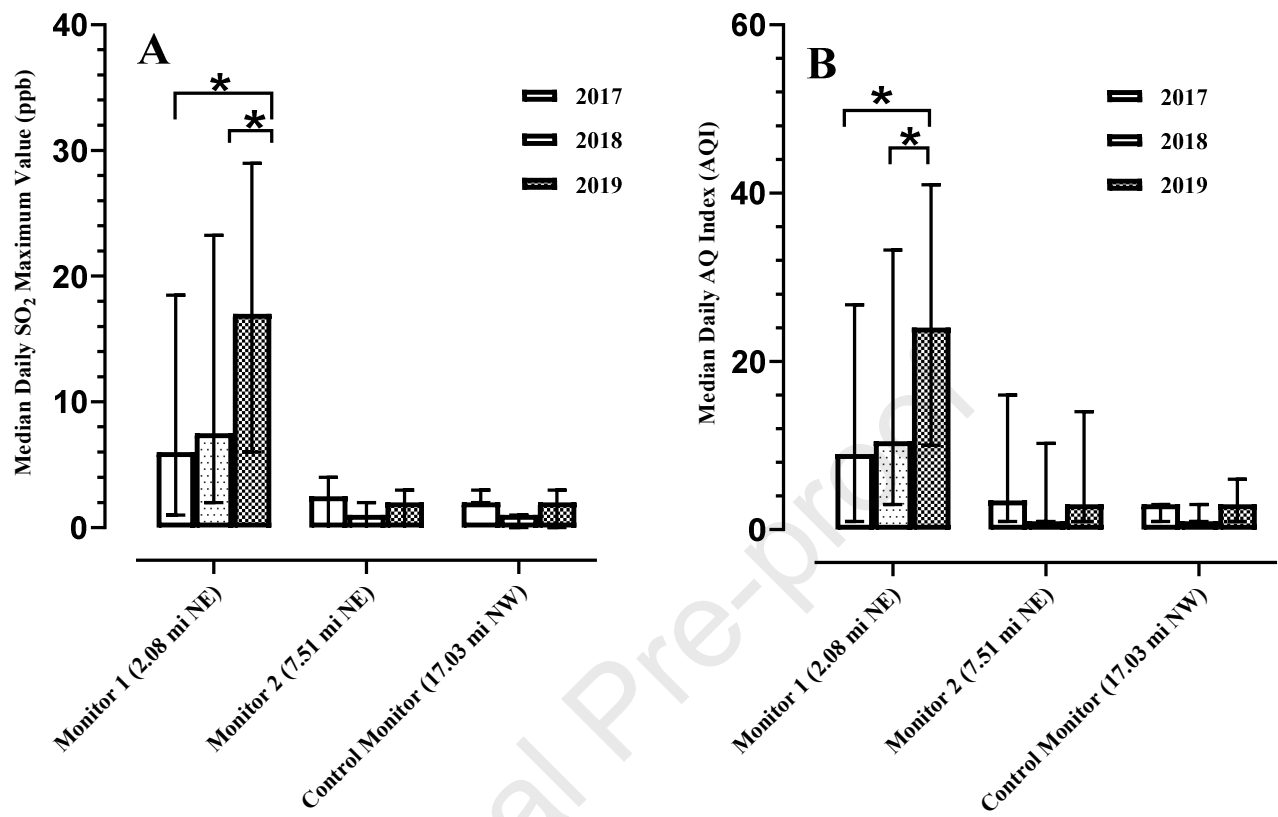
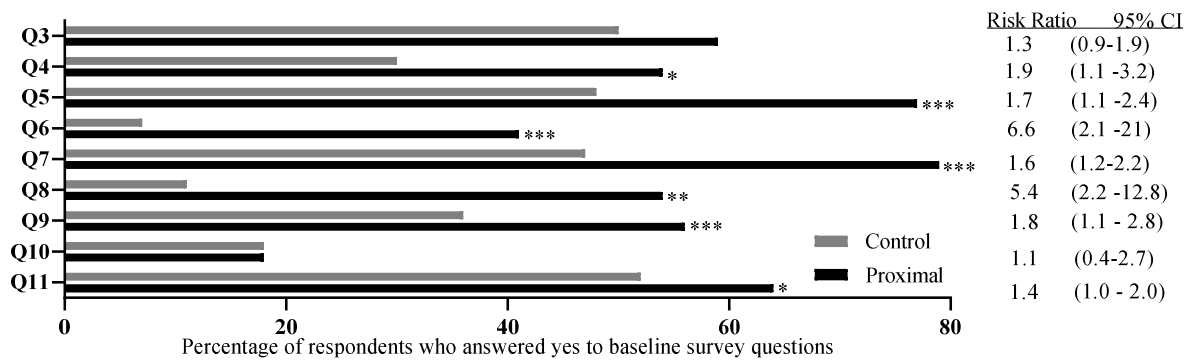


Figure 3.



ID Questions

Q3 Over the past 30 days: Have your asthma symptoms worsened WHILE OUTDOORS

Q4 Over the past 30 days: Have your asthma symptoms worsened WHILE INDOORS

Q5 Over the past 30 days: Have you noticed a 'rotten egg' smell in the outside air near your home

Q6 Over the past 30 days: Have you noticed any other smell in the outside air near your home

Q7 Do you think air pollution in your area sometimes worsens your asthma symptoms

Q8 Are you aware of any recent events (within the last 30-60 days) that may have affected the outside air near your home (events like gas explosion, factory accidents, or fires)

Q9 Over the past 30 days: Did you have an asthma attack (coughing, wheezing, trouble breathing) that required you to take more asthma medicines than usual for you

Q10 Over the last 30 days: Did you seek medical attention (clinic visit, ER, or ambulance) for your asthma

Q11 Over the last 30 days: Have you needed to use more of your asthma medications

Figure 4.

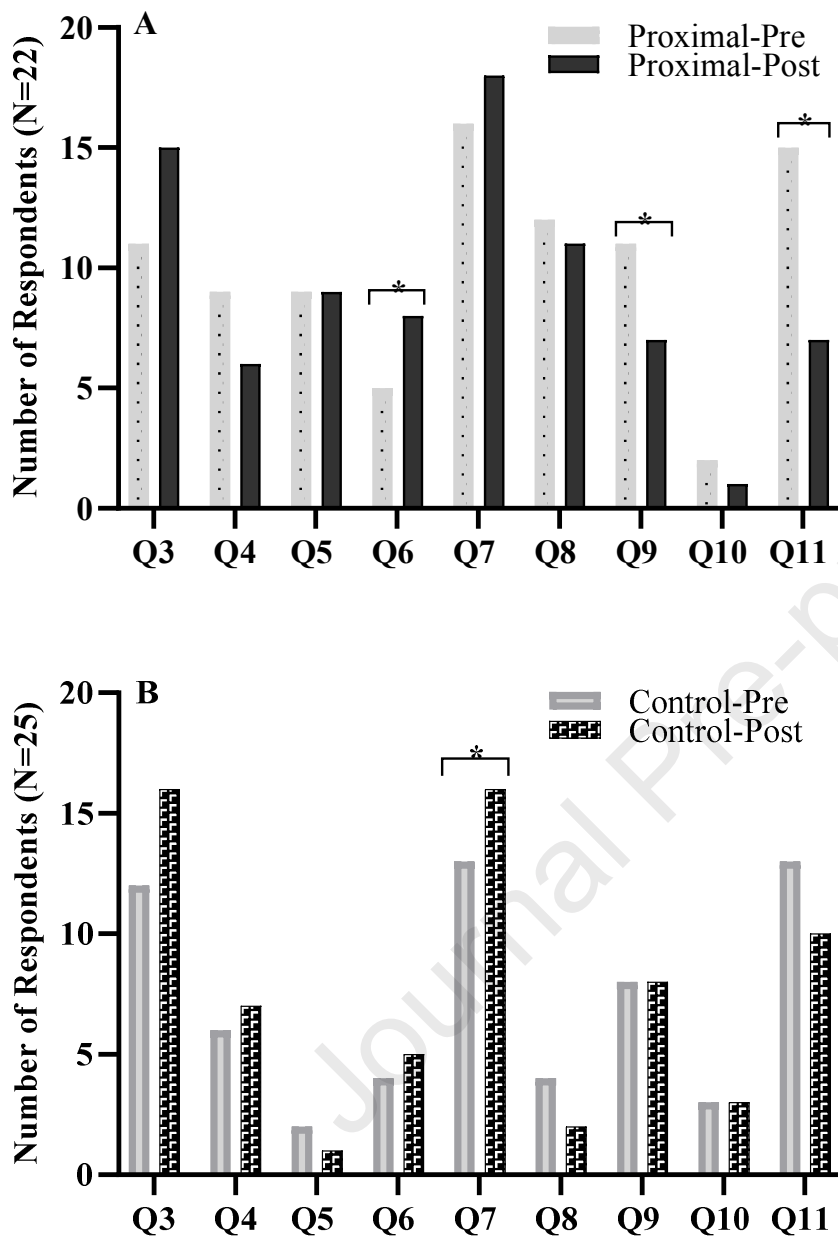


Figure 5.