Respiratory Effects of Indoor Heat and the Interaction with Air Pollution in COPD

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Author Contributions: MCM, GBD, PNB, ECM, NNH provided substantial contributions to conception and design, acquisition of data, and analysis and interpretation of data. AJB, CMA, ECM, LP, DW, AS, RDP contributed to data analysis and interpretation of data. DLW contributed to data acquisition. All authors contributed to revising the manuscript critically for important intellectual content and provided final approval of the version to be published.

Sources of Support: Funding provided by the National Institutes of Health-NIEHS (R21ES024021, R21ES015781, R21ES025840, R01 ES022607, R01 ES023500), NIH-NIAID (K24AI114769), and NIH-NHLBI (R01 ES023500), NIEHS/Environmental Protection Agency (P50ES015903/RD83213901; P01ES018176/ RD83451001), NIH-NIMHD (P50 MD010431/RD83615201)

Running Title: Indoor heat and air pollution in COPD
Descriptor: 6.2 Indoor Air
Key Words: COPD, particulate matter, nitrogen dioxide, climate change, heat
Word Count: 2997

Abstract:

Rationale: There is limited evidence of the effect of exposure to heat on COPD morbidity and the interactive effect between indoor heat and air pollution has not been established.

Objectives: To determine the effect of indoor and outdoor heat exposure on COPD morbidity and to determine whether air pollution concentrations modify the effect of temperature.

Methods: Sixty-nine participants with COPD were enrolled in a longitudinal cohort study and data from the 601 participant days that occurred during the warm weather season were included in the analysis. Participants completed home environmental monitoring with measurement of temperature, relative humidity, and indoor air pollutants and simultaneous daily assessment of respiratory health with questionnaires and portable spirometry.

Measurements and Main Results: Participants had moderate to severe COPD and spent the majority of their time indoors. Increases in maximum indoor temperature were associated with worsening of daily Breathlessness, Cough, and Sputum Scores (BCSS) and increases in rescue inhaler use. The effect was detected on the same day and lags of 1 and 2 days. The detrimental effect of temperature on these outcomes increased with higher concentrations of indoor fine particulate matter and nitrogen dioxide ($p<0.05$ for interaction terms). On days that participants went outdoors, increases in maximum daily outdoor temperature were associated with increases in BCSS scores after adjusting for outdoor pollution concentrations.

Conclusions: For patients with COPD that spend the majority of their time indoors, indoor heat exposure during warmer months represents a modifiable environmental exposure that may contribute to respiratory morbidity. In the context of climate change, adaptive strategies that

include optimization of indoor environmental conditions are needed to protect this high risk group from adverse health effects of heat.

Abstract Word Count: 277

Understanding health effects of climate change has been identified as a research priority by the American Thoracic Society and other leading health organizations (1-7). The anticipated increases in temperature are one aspect of climate change that has been associated with adverse health consequences. Global average temperatures are projected to increases by 1.4-5.8% by the end of the century and heat waves are projected to be more frequent and intense and longer lasting.(8) It is critical to understand health implications of heat exposure to protect those at greatest risk.(9)

Previous population level studies have demonstrated that heat waves are associated with increases in mortality (10, 11) and that certain populations, including those with underlying respiratory and cardiac disease, are likely at increased risk (12, 13). Studies investigating impact of heat on morbidity using hospitalization and emergency visit records have also identified high risk subgroups.(14-17) To date, disease-specific indicators of morbidity have not been assessed and studies have rarely used individual-level exposure assessment(18). Very few studies have investigated the effect of indoor temperature on respiratory health and the interactive effect between indoor temperature and indoor air pollution is unknown. It is important to understand the effects of the indoor environment as individuals spend the majority of their time indoors and this is projected to increase in the context of climate change (8, 19). Further, there are actions that can reduce indoor heat exposure, such as air conditioning, cooling centers, and energy efficient building designs, and these can be deployed immediately at the individual and local level.

In order to develop strategies to protect individuals from adverse consequences of heat exposure, it is necessary to improve our understanding of specific health consequences among

high risk groups. In the present study, we sought to understand the health effects of heat among individuals with COPD, using disease-specific respiratory health outcomes. We hypothesized that 1) increases in indoor and outdoor temperature during the warmer months would be associated with increases in daily respiratory symptoms and rescue medication use and decreases in lung function among participants with COPD, and 2) increases in air pollution exposure would modify the effects of temperature, enhancing the detrimental effects of increases in temperature on these daily indicators of COPD morbidity.

Methods

Participant Recruitment and Study Design

Participants provided written informed consent and the Johns Hopkins Medical Institutional Review Board approved the protocol. Participants and methods were previously described.(20) Briefly, participants were former smokers with COPD recruited from the Baltimore area and studied at baseline, 3 and 6 months as part of the COPD and Domestic Endotoxin Study. To determine health effects of heat, we restricted analysis to the warm weather season, defined as the time between the first and last day that the maximum outdoor temperature exceeded 90 degrees Fahrenheit (F) in Baltimore for each calendar year. Sixty-nine of 84 participants had monitoring during this warm weather season. Fifty –four had one week of monitoring and fifteen had two weeks of monitoring. Participants completed health and demographic questionnaires and spirometry was performed according to American Thoracic Society (ATS) criteria (21, 22).

Environmental Monitoring of Heat and Air Quality

A home environmental assessment was completed, including a home inspection and continuous environmental monitoring over a one-week period to capture daily indoor temperature and humidity, and weekly particulate matter (PM) and nitrogen dioxide (NO_2). Participants completed a daily activity diary during the environmental monitoring period. Air sampling occurred in the main living area, identified as a room other than the bedroom where the participant reported spending the most time. Additional methods are provided in the online supplementary materials and a prior publication (21). Outdoor temperature, humidity, and pollution concentrations (PM, NO_2 and ozone) were obtained from publicly available datasets provided by National Oceanic and Atmospheric Administration (NOAA) and the Environmental Protection Agency (EPA) (Table E1).(23, 24)

COPD Daily Respiratory Health Outcomes

Participants performed daily questionnaires and spirometry during home environmental monitoring. The validated Breathlessness, Cough, and Sputum Scale (BCSS) contains three questions that each assess a symptom using a Likert-type scale ranging from 0 to 4. A change in total score of 0.3-0.4 is mild while a change of 1.0 is considered substantial (25). Handheld spirometry was also performed daily (PiKo-1, nSpire Health, Inc). Frequency of rescue inhaler medication use was captured in a daily diary as 0, 1, 2, 3 or >4 times daily.

Statistical Analysis

Descriptive statistics were analyzed using Spearman correlations, chi square tests, and t-tests. At each time point, daily maximum temperature was used as the primary exposure variables in generalized estimating equations models (22) to account for repeated measures. Models for indoor and outdoor temperature were run separately and adjusted for age, sex, education, visit (baseline, 3 or 6 months), and baseline percent predicted FEV_1. Pack years of smoking were used to account for disease severity for models in which the primary outcome was lung function.

Models were constructed to account for pollutant concentrations; models of indoor temperature included indoor daily average humidity and weekly average indoor $PM_{2.5}$ and NO_2. Models of outdoor temperature included daily average outdoor humidity, $PM_{2.5}$, NO_2, and ozone. Lag terms were created to assess same day and subsequent day health effects. To assess effect modification, interaction terms were created between pollution and temperature variables. To illustrate temperature effects at given pollution concentrations, models were used to calculate the outcomes of interest for pollutant concentrations at the 25^{th}, 50^{th}, and 75^{th} percentiles using average or mode values for other variables.

Interaction terms and stratified models were created to investigate whether time spent outdoors modified the effect of outdoor temperature on COPD. Sensitivity analyses were performed using the 95th percentile values of temperature rather than maximum values and excluding extreme outliers. Analyses were performed with Stata SE statistical software, version 11.0 (Stata Corp, College Station, TX). Statistical significance was defined as a p value less than 0.05.

Results

Study participants were older individuals with moderate and severe COPD and impaired pulmonary function (Table 1). Between 2009 and 2011, there were 601 participant study days in the warm weather season. Participants spent a substantial amount of time indoors and only went outdoors on 46% of these days. On the days that participants went outdoors, the mean (± SD) time outdoors was 2.0 (± 2.1) hours. The mean ± (SD) daily maximum indoor and outdoor temperature were 80 ± 7° F and 85 ± 9 ° F, respectively (Figure 1). There was only moderate correlation between daily indoor and outdoor maximum temperatures (Spearman's rho= 0.44, p-value <0.01).

Eighty-five percent of participants had either central air conditioning or window units. Central air conditioning was reported to have been used on 50% of study days and window air conditioning unit use was reported on 18% of days. Participants reported that they did not use air conditioning at all on 37% of study days that occurred during the warm season. The maximum indoor temperature was lower on days that participants reported using central air conditioning compared to days that they did not (mean (SD) 81.4 (6.4) versus 79.0 (7.0)° F, respectively, P<0.01)

Effect of Indoor Temperature on COPD Morbidity

Increases in maximum daily indoor temperature were associated with increases in symptoms, measured using the Breathlessness, Cough, and Sputum Scale (BCSS), and with increases in frequency of rescue inhaler use. These associations persisted even after accounting for indoor

pollutant concentrations, including indoor NO_2 and indoor $PM_{2.5}$. For example, a 10 degree F increase in indoor temperature was associated with a 0.38 (95% CI 0.01-0.67; p-value = 0.01) increase in BCSS score, even after adjustment for indoor relative humidity, $PM_{2.5}$, and NO_2. Inclusion of lag terms in these models suggested that increases in indoor temperatures had an immediate (same-day) effect and also an effect that was detectable at 1-2 days post-exposure.

We found no detectable effect of daily changes in indoor temperature on daily measurements of lung function, using either morning or evening FEV_1 (evening values shown in Table 2). Sensitivity analyses conducted excluding extreme temperature outliers (over 110° F) and using the 95^{th} percentile value of daily indoor temperature yielded similar results (Table E2). Evaluation of interaction terms and stratified models suggested an enhanced effect of indoor temperature on use of rescue inhalers among participants that had more advanced COPD (coefficient 0.27, p-value 0.06 for FEV1 $\leq$50% predicted; coefficient 0.01, p-value 0.816 among those with FEV1 $\geq$ 50% predicted; p-interaction 0.048) but did not suggest that disease severity influenced the effect of indoor heat on symptoms. Stratified models also suggested an enhanced effect of indoor temperature on symptoms and rescue inhaler use on days that participants did not go outdoors (Table E3).

Interactive Effect of Indoor Pollution and Indoor Temperature

In models investigating the effect of indoor temperature on BCSS and on rescue inhaler use, significant positive interactions were detected between $PM_{2.5}$ and temperature (interaction term p-value <0.001 in both models). Similarly, significant positive interactions were also

detected between indoor NO_2 and temperature (interaction term p-value <0.05 in BCSS model and <0.001 in rescue inhaler model).

To illustrate the positive interactive effect, Table 3 provides estimates of the effect a 10^o F increase in temperature at given percentiles of indoor pollutant concentrations and demonstrates that the effect of temperature is larger with increasing indoor pollutant concentrations. For example, a participant residing in a home that had an indoor $PM_{2.5}$ concentration at the 25th percentile of the study homes (5 μg/m^3) would experience an increased in BCSS score of 0.4 (indicative of a mild increase in symptoms) for every 10^o F degree increase in indoor temperature while an individual in a home at the 75th percentile (16 μg/m^3) would experience an increase in BCSS of 1 (indicative of a severe increase in symptoms)(25). Models investigating lung function as the outcome did not demonstrate an interactive effect between indoor temperature and pollutants.

Effect of Outdoor Temperature on COPD Morbidity

Daily maximum outdoor temperature was not significantly associated with respiratory symptoms, rescue medication use, or lung function in the overall cohort (Table 4). As participants reported going outdoors on less than half of the study days in the warm weather season, we performed analyses stratified by days that participants reported going outdoors and assessed for interaction by time outdoors. Stratified models suggested a significant association between increasing outdoor temperature and respiratory symptoms on days that participants went outdoors. There were no statistically significant interactions between outdoor temperature and outdoor air pollutants, including $PM_{2.5}$, NO_2, and ozone (data not shown).

Discussion

The present study is among the first to describe the effect of heat exposure on disease-specific morbidity outcomes among those with COPD, a group that has been identified as high risk for detrimental health effects of heat, and the first to report an interactive effect between indoor temperature and indoor pollution.

In a cohort of participants with moderate to severe COPD, we found that increases in home indoor temperature during warmer weather were associated with increases in daily indicators of COPD morbidity, including respiratory symptoms and rescue inhaler medication use. There was a positive interaction between temperature and indoor air pollution, including $PM_{2.5}$ and NO_2, such that the effect of indoor heat was greater in the presence of higher indoor air pollutant concentrations.

In this study population, participants spent a great deal of time indoors and ventured outdoors on only half of the study days. Outdoor temperature was associated with increased respiratory symptoms on these days. In the context of the anticipated increase in temperatures related to climate change, these findings suggest that adaptive strategies targeting the indoor environment provide an opportunity to minimize health risks for those with COPD.

Our results are consistent with and extend previous findings that have demonstrated adverse health consequences of heat exposure. Previous studies have largely used ambient data to assign exposure and linked this to population health effects with compelling results. Such studies have identified elderly individuals and those with underlying cardiac and respiratory diseases, including COPD, as at increased risk for adverse health effects of heat

exposure (12, 15, 26-29).

For example, a time series study across 12 US cities demonstrated increases in deaths attributable to COPD during hot weather with differences between hot and cold cities. In cold cities, hot temperatures were associated with an increase in the risk of death attributable to COPD by as much as 25% (12) with immediate, same-day effects. In hot cities, the effect of hot temperatures was attenuated and delayed with a 6% increase in COPD deaths at lags of 3 and 4 days.

A study in New York City examined COPD morbidity using hospitalization data and found that the same-day risk of COPD hospitalization increased by 7.6% for every one ºC increase above a threshold temperature of 29ºC (17) and that there was a detectable but smaller association between temperature and respiratory hospitalization when applying a 1-day lag.

Other studies have used Medicare data to provide estimates of effect that are representative of a broader portion of the U.S. population (30, 31). In a study that included 12.5 million elderly individuals in 213 urban US counties, there was a 4.7% increased risk of hospitalization for COPD for every 10^{o}F increase in ambient temperature and findings were not attributable to air pollution health effects (30). Heat and respiratory hospitalizations were most strongly associated on the day of exposure in this study but the effect was still present and significant at a lag of 1 day and no longer detectable at 2 days. The ecologic design of such studies and the potential for bias due to measurement error in exposure assignment has been a limitation that is now addressed in the present study, which provides individual level data.

Researchers who previously investigated the interactive effect of temperature and air pollution reported mixed results with little evidence for differences in COPD outcomes. For

example, in a study conducted in Brisbane Australia, PM_{10} modified the effect of temperature on respiratory hospital admissions but there was no interactive effect for respiratory emergency visits (32). Basu and colleagues examined temperature and mortality in California and did not find that pollution modified the effect of temperature (33). In a study of 9 European cities included in the EuroHEAT project, the effect of heat on overall mortality and cardiovascular mortality were increased on high PM_{10} and high ozone days but the interactive effect of these pollutants and heat on respiratory mortality was less evident (34).

Ren and colleagues analyzed data from 98 urban communities in the US National Morbidity, Mortality, and Air Pollution Study and found that ozone modified the risk for cardiovascular mortality. However, their results did not include respiratory mortality as an outcome measure. Zanobetti and coauthors studied 9 U.S. cities during the warm season and did find evidence that outdoor $PM_{2.5}$ or ozone modified the relationship between increasing outdoor temperature and risk of death (35).

In the present study, we did not find an interaction between the effects of outdoor temperature and ozone or PM. However, there was a consistent signal demonstrating that increases in indoor pollution enhanced the adverse effect of increasing indoor temperature on COPD symptoms and rescue medication use. To our knowledge, this is the first study to report interactive effects of indoor temperature and air pollution on COPD morbidity.

Previous studies linking outdoor heat with hospitalization or death have demonstrated same-day health effects of heat exposure or lag times of one day (15). Our findings suggest the health effect of indoor heat exposure is immediate and may persist for one to two days. While the mechanisms of health effects in COPD remain incompletely understood, proposed

mechanisms include both thermoregulatory responses(36) and bronchoconstrictive effects of heat.

Patients with COPD may have impaired ability to respond to heat stress. It has been proposed that heatstroke leads to increases in intravascular coagulation due to release of Il-1 or IL-6 into the systemic circulation with activation of microvascular thrombosis which may trigger a respiratory distress syndrome (37, 38). Studies in asthma suggest that breathing hot humid air may result in bronchoconstriction and increased airways resistance that is mediated via cholinergic pathways (39, 40). We did not detect an association between indoor heat and FEV_1. This may suggest that either that bronchoconstriction did not impact the airways resistance captured by the FEV_1 outcome measurement or that bronchoconstriction was not the mechanism by which participants were affected by heat.

Limitations

As this study was limited to the Baltimore region, the results may not be generalizable to other areas of the country. We used education as an indicator of socioeconomic status as household income was not reflective of socioeconomic status in our largely retired population and this approach may have resulted in some misclassification of socioeconomic status. Indoor air monitoring did not include ozone as previous studies in Baltimore city have documented that this exposure is typically low in homes (41).

While each participant had comprehensive and daily characterization of the indoor environment and COPD health outcomes, outdoor measurements of temperature and pollutant concentrations were obtained from central site monitors, which may have resulted in

measurement error in assigning outdoor exposure to each individual. This may have contributed to the weaker associations between outdoor temperature and COPD morbidity although the daily activity diary data would suggest that the small amount of time spent outdoors was also a key contributing factor.

Conclusions

Findings of the present study suggest that additional indoor cooling may improve COPD respiratory health during warmer months and that consideration should be given when traveling outdoors in warmer weather. Further, our findings that increases in indoor air pollution exaggerated adverse health effects of indoor heat exposure highlight the opportunity to improve COPD health through optimization of the indoor environment. The participants with COPD in this study spent the overwhelming majority of their time indoors during warm weather days.

Although 86% of participants had some form of air conditioning available, air conditioning was not used on 37% of study days. While we did not find that education level was associated with the use of air conditioning, we were limited in our ability to understand the extent to which use of air conditioning was influenced by financial hardship.

Addressing barriers to air conditioning use may have potential health benefit for those with COPD and future studies may be needed to fully elucidate the impact of air conditioning use on respiratory health in COPD. However, while air conditioning may provide a short-term solution for this high risk group(42), it is not without consequences. The use of air conditioning ultimately contributes to the cycle that perpetuates climate change and the steady rise in

outdoor temperatures.(43) Further, the associated costs are problematic for disadvantaged populations in the United States and around the world.

Ultimately, in addition to adaptive strategies at the individual and population level, mitigation strategies are needed at a policy level to intercept the alarming rise in outdoor temperatures. To effectively address this will require the interdisciplinary work of urban planners, public health, engineers, economists and climate scientists in addition to medical practitioners to provide the foundation for such policy.

Acknowledgements:

The authors thank the study participants and the study staff for their contributions.

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Table 1. Participant characteristics (n=69)*	
Age (years)	69 (8)
Sex, (% male)	57
White race (%)	90
Smoking (pack years)	56 (30)
Baseline post-bronchodilator FEV_1 % predicted	54 (16)
Gold Stage % II III IV	 48 40 12
Daily Health Assessment Average Values (mean (SD))*	
BCSS score	2.7 (2.2)
Inhaler use (puffs/day)	0.88 (1.3)
Morning FEV_1 (liters)	1.3 (0.6)
Evening FEV_1 (liters)	1.3 (0.6)
Environmental characteristics* N= 601 study days	
Daily maximum indoor temperature (°F)	80.1 (6.7)
Daily average indoor relative humidity (%)	40.8 (8.5)
Weekly average indoor $PM_{2.5}$ ($\mu g/m^3$)	13.1 (15.4)
Weekly average indoor NO_2 (ppb)	11.3 (11.7)
Days of reported central air conditioning use	50%
Days of reported window unit air conditioning use	18%
Days reported with no air conditioning use	37%
Days that participants went outdoors	47%
Time outdoors on days that participants went outdoors (hours)	1.95 (2.07)
Daily maximum outdoor temperature (^{o} F)	84.9 (9.9)

Daily average outdoor $PM_{2.5}$ ($\mu g/m^3$)	12.8 (6.3)
Daily average outdoor NO_2 (ppb)	27.5 (11.1)
Daily average outdoor ozone (ppb)	35.2 (8.7)
Daily average outdoor relative humidity (%)	58.3 (13.1)
* mean (standard deviation) unless otherwise indicated	

Table 2. Association between Indoor Temperature and COPD Symptoms, Rescue Medication Use, and Lung Function			
	Coefficient **	95% Confidence Interval	p-value
Breathlessness, Cough, and Sputum Scale			
Daily Temperature (limited model*)	**0.30**	0.00, 0.59	**0.048**
Daily Temperature (with humidity, NO_2, $PM_{2.5}$)	**0.38**	**0.01, 0.67**	**0.013**
Lag 0	**0.30**	**0.00, 0.59**	**0.048**
Lag 1	**0.36**	**0.01, 0.70**	**0.042**
Lag 2	**0.48**	**0.12, 0.85**	**0.010**
Lag 3	0.10	-0.27, 0.47	0.602
Rescue Inhaler Use			
Daily Temperature (limited model*)	**0.26**	0.09, 0.42	**0.002**
Daily Temperature (with humidity, NO_2, $PM_{2.5}$)	**0.23**	**0.06, 0.41**	**0.008**
Lag 0	**0.26**	0.09, 0.42	**0.002**
Lag 1	**0.17**	**-0.02, 0.36**	**0.077**
Lag 2	**0.21**	**-0.01, 0.42**	**0.058**
Lag 3	-0.02	-0.24, 0.20	0.845
Lung Function (evening FEV_1)			
Daily Temperature (limited model*)	-0.02	-0.05, 0.02	0.419
Daily Temperature (with humidity, NO_2, $PM_{2.5}$)	-0.01	-0.05, 0.02	0.439
Lag 0	-0.02	-0.05, 0.02	0.419
Lag 1	-0.01	-0.04, 0.03	0.610
Lag 2	-0.01	-0.05, 0.02	0.418
Lag 3	-0.02	-0.06, 0.02	0.262
*models include visit, age, gender, education, baseline FEV1 (pack years was used instead of baseline FEV_1 in the lung function models) ** changes are expressed per 10^{o}F increase in indoor temperature			

Table 3. Illustration of the Interactive effects between Indoor Temperature and Pollutants.
The estimated effect of a 10^{o} F increase in temperature becomes larger at with increasing indoor pollutant concentrations (NO_2 and $PM_{2.5}$), demonstrated for given percentiles

Percentile of Indoor Air Pollutant Concentrations	**Estimate effect of 10^{o} F increase in temperature at increasing indoor $PM_{2.5}$ concentrations**		**Estimated effect of 10^{o} F increase in temperature at increasing indoor NO_2 concentrations**	
	BCSS Score	**Rescue Inhaler**	**BCSS Score**	**Rescue Inhaler**
25% $PM_{2.5}$ 4.99 µg/m^3 NO_2 4.37 ppb	**0.36**	**0.25**	**0.12**	**0.05**
50% $PM_{2.5}$ 8.24 µg/m^3 NO_2 6.84 ppb	**0.54**	**0.42**	**0.20**	**0.13**
75% $PM_{2.5}$ 16.20 µg/m^3 NO_2 13.00 ppb	**0.98**	**0.85**	**0.41**	**0.34**
95% $PM_{2.5}$ 38.36 µg/m^3 NO_2 34.58 ppb	**2.21**	**2.02**	**1.12**	**1.08**

Models used to predict estimated effect included age, gender, education, baseline FEV_1, indoor humidity, and either indoor $PM_{2.5}$ or indoor NO_2.

Table 4. Daily Maximum Outdoor Temperature and COPD Health Outcomes stratified by whether the participant went outdoors on a given day *

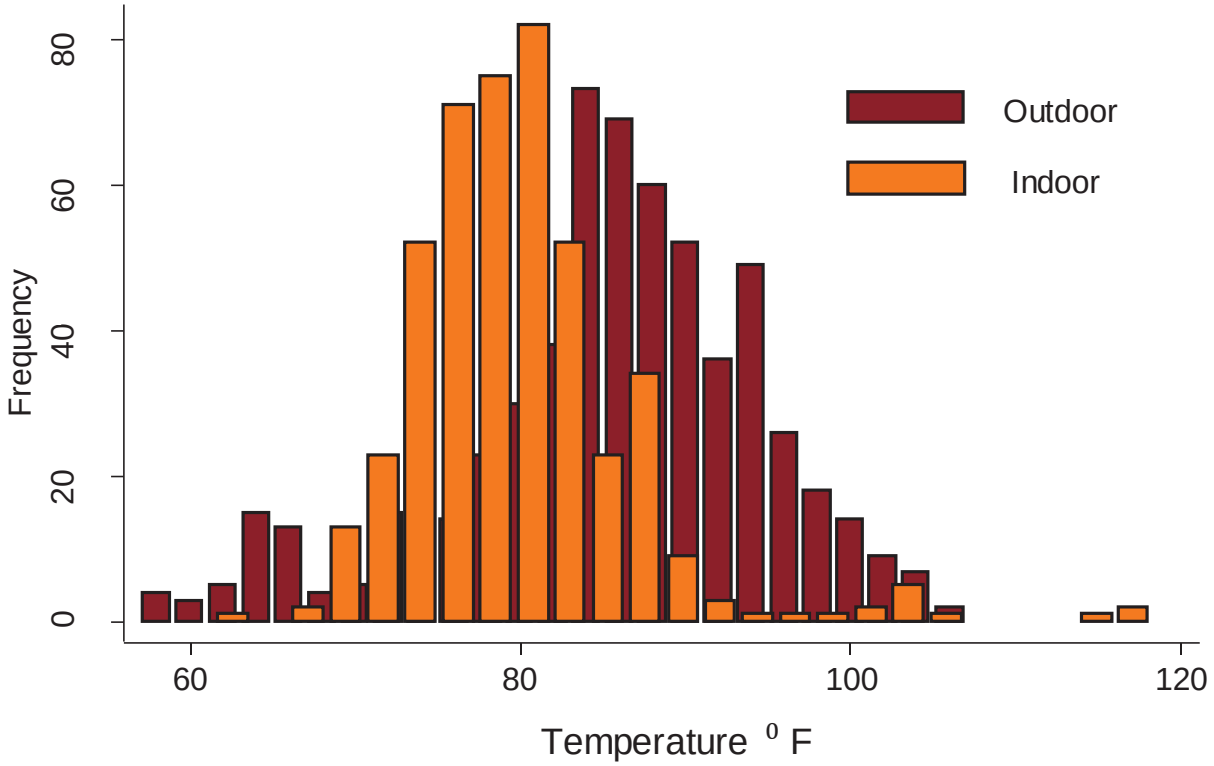
	Overall (N=485)		Days Participants stayed indoors (N=250)		Days participants went outdoors (N=229)		p-value for interaction
Outcomes	Coefficient (95% Confidence Interval)	P-Value	Coefficient (95% Confidence Interval)	P-Value	Coefficient (95% Confidence Interval)	P-Value	
BCSS	0.13 (-0.06, 0.32)	0.18	0.00 (-0.29, 0.29)	0.985	**0.38 (0.122, 0.628)**	**0.004**	**0.045**
Rescue inhaler	0.01 (-0.09, 0.10)	0.912	0.01 (-0.14, 0.16)	0.899	0.03 (-0.10, 0.17)	0.619	0.554
Evening FEV_1 **	0.00 (-0.02, 0.03)	0.830	0.01 (-0.03, 0.04)	0.749	-0.01 (-0.06, 0.03)	0.534	0.477

Multivariate analysis adjusted for age, sex, education, baseline lung function or smoking history, visit, outdoor $PM_{2.5}$, outdoor NO_2, outdoor ozone, outdoor relative humidity

**N=479 for overall, 187 for days indoors, 211 for days participants went outdoors for Evening FEV_1

Figure Legend:

Figure 1. Distribution of Maximum Indoor and Outdoor Daily Temperature Values. Distribution of daily indoor and outdoor maximum temperatures during the warm weather season. Participants spent most of their times indoors and went outside on only 47% of study days and spent about 2 hours outdoors on those days. Maximum daily indoor temperatures averaged 80^{o}F while maximum daily outdoor temperature averaged 85^{o} F.


Frequency
0
20
40
60
80
60
80
100
120
Temperature 0 F
Outdoor
Indoor

Online Data Supplement

Respiratory Effects of Indoor Heat and the Interaction with Air Pollution in COPD

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Methods:

Participant Recruitment and Study Design

Participants provided written informed consent and the Johns Hopkins Medical Institutional Review Board approved the protocol. Participants and methods were previously described.(1) Briefly, participants were former smokers with COPD recruited from the Baltimore area. Inclusion criteria included: 1) age ≥ 40 years, 2) post bronchodilator FEV_1 ≤ 80% predicted, 3) FEV_1/FVC <70%, and 4) >10 pack years smoking, but having quit >1 year prior to enrollment with an exhaled carbon monoxide level ≤6 ppm. (2)

Participants were studied at baseline, 3 and 6 months. To determine health effects of heat exposure, we defined a warm weather season as the time during each calendar year between the first and last day that the maximum outdoor temperature exceeded 90 degrees Farenheit (F) and restricted analysis to data collected during this time period. Sixty-nine of the 84 participants had monitoring during this warm weather season. Sixty-nine of 84 participants had monitoring during this warm weather season. Fifty –four had one week of monitoring and fifteen had two weeks of monitoring.

At baseline, participants completed health and demographic questionnaires and spirometry was performed according to American Thoracic Society (ATS) criteria (3, 4). Demographics included education as a surrogate for socioeconomic status as many participants were older and no longer worked, making annual household income less reliable.

Environmental monitoring of heat and air quality

Temperature and humidity were measured using HOBO (Onset, Inc. Poccosette, MA) hourly temperature and humidity loggers. Indoor air sampling for $PM_{2.5}$ (PM with aerodynamic size ≤ 2.5 μm) and NO_2 was performed as described previously (1). $PM_{2.5}$ was collected using 4 L/min

SKC personal environmental monitoring (PEM) impactors (SKC, Eighty-four, PA) loaded with 37-mm, 2.0-µm pore size, PALL Teflo PTFE membrane filters with polypropylene support rings (Pall Corp. Ann Arbor, MI). Filters were pre and post-weighed in a temperature and humidity control room using a Mettler-Toledo UP-5 microbalance (Mettler-Toledo, Columbus, OH). The limit of detection (LOD) for $PM_{2.5}$ was 0.64 µg/m^3. NO_2 was measured using a passive sampler (Ogawa badge) loaded with filters coated with triethanolamine (TEA) and detected spectrophotometrically. The LOD for NO_2 was 0.52 ppb. Indoor $PM_{2.5}$ and NO_2 values were available as week-long average values. Archived hourly (DSI 3505) temperature and humidity were accessed from the National Oceanic and Atmospheric Administration (NOAA) National Climatic Data Center website using data from the Science Center in the Inner Harbor.(5) Daily average outdoor $PM_{2.5}$, NO_2, and ozone data were obtained from the Environmental Protection Agency's (EPA) Aerometric Information Retrieval Service (now referred to as the Air Quality System database).(6) Data from the monitoring station closest to the participant's home was used and in the case of missing data, values from the next closest monitoring site were applied.

COPD daily respiratory health outcomes

Participants performed daily measurements during home environmental monitoring. The Breathlessness, Cough, and Sputum Scale (BCSS) contains three questions that each assess a symptom using a Likert-type scale ranging from 0 to 4 (higher scores indicating more severe symptoms). A change in total score of 0.3-0.4 is considered mild while a change of 1.0 is considered substantial(7). Handheld spirometry was also performed daily (PiKo-1, nSpire Health, Inc). The frequency of rescue inhaler medication use was captured in a daily diary as 0, 1, 2, 3 or >4 times daily.

Statistical Analysis

Descriptive statistics were analyzed using Spearman correlations, chi square tests, and t-tests, as appropriate. At each time point, daily maximum temperature was used as the primary exposure variables in generalized estimating equations models (8) to account for repeated measures. The GEE family was Gaussian, link was identity, and correlation was exchangeable. Models for indoor and outdoor temperature were run separately. Models were adjusted for age, sex, education, visit (baseline, 3 or 6 months), and baseline percent predicted FEV_1. Pack years of smoking was included to account for disease severity for models in which the primary outcome was lung function. Models were constructed to account for pollutant concentrations; models of indoor temperature included indoor daily average humidity and weekly average indoor $PM_{2.5}$ and NO_2. Models of outdoor temperature included daily average outdoor humidity, $PM_{2.5}$, NO_2, and ozone. Lag terms were created to assess same day and subsequent day health effects. To assess whether pollution modified the effect of heat exposure, interaction terms were created between pollution and temperature variables. To illustrate temperature effects at given pollution concentrations, the main models were used to calculate the outcomes of interest for pollutant concentrations at the 25^{th}, 50^{th}, and 75^{th} percentiles and average or mode values were applied for other variables. Interaction terms and stratified models were also created to investigate whether time spent outdoors modified the effect of outdoor temperature on COPD. Sensitivity analyses were performed using the 95^{th} percentile values of temperature rather than the maximum values. All analyses were performed with StataSE statistical software, version11.0 (Stata Corp, College Station, TX). Statistical significance was defined as a p value less than 0.05.

Table E1. Methods used to create environmental exposure variables			
Exposure Variable	Source	Method	Time interval of exposure assessment
Indoor Temperature	Participant homes	HOBO (Onset, Inc. Poccosette, MA)	Hourly average values during 24 hour period from 8 am to 8 am to create maximum and 95th percentile daily values
Indoor Humidity	Participant homes	HOBO (Onset, Inc. Poccosette, MA)	Hourly average values during 24 hour period from 8 am to 8 am to create maximum and 95th percentile daily values
Indoor $PM_{2.5}$	Participant homes	PEMS with pumps	Integrated 5- 7 day gravimetric sample
Indoor NO_2	Participant homes	Ogawa passive badges	5- 7 day average
Outdoor Temperature	NOAA(5)	available dataset	Hourly average values used to create maximum and 95th percentile values
Outdoor Humidity	NOAA(5)	available dataset	Hourly average values used to create maximum and 95th percentile values
Outdoor PM	EPA(6)	available dataset	24 hour daily average values
Outdoor NO2	EPA(6)	available dataset	24 hour daily average values
Outdoor Ozone	EPA(8)	available dataset	24 hour daily average values

Table E2. Sensitivity Analyses for Daily Indoor Temperature and COPD Health Outcomes				
	95th percentile Daily Temperature used as the exposure variable		Maximum daily temperature used as the exposure variable with extreme outliers values over 110^{o} F excluded	
Outcomes	Coefficient (95% Confidence Interval)	p-value	Coefficient (95% Confidence Interval)	p-value
BCSS	**0.40 (0.09, 0.70)**	**0.01**	**0.46 (0.15, 0.77)**	**0.004**
Rescue inhaler	**0.27 (0.10, 0.45)**	**0.003**	**0.26 (0.08, 0.44)**	**0.005**
Evening FEV_1	-0.01 (-0.05, 0.03)	0.55	0.00 (-0.04, 0.04)	0.92
**Multivariate analysis adjusted for age, sex, education, baseline lung function or smoking history, visit, indoor humidity, NO_2, $PM_{2.5}$				

Table E3. Daily Maximum Indoor Temperature and COPD Health Outcomes stratified by whether the participant went outdoors on a given day and adjusted for indoor air pollutants*

	Overall (N=333)		Days Participants stayed indoors (N=166)		Days participants went outdoors (N=161)		p-value for interaction
Outcomes	Coefficient (95% Confidence Interval)	P-Value	Coefficient (95% Confidence Interval)	P-Value	Coefficient (95% Confidence Interval)	P-Value	
BCSS	**0.38 (0.08, 0.67)**	**0.013**	**0.49 (0.06, 0.92)**	**0.026**	0.27 (-0.15, 0.68)	0.210	0.988
Rescue inhaler	**0.23 (0.06, 0.41)**	**0.008**	**0.44 (016, 0.73)**	**0.002**	0.11 (-0.09, 0.31)	0.274	**0.004**
Evening FEV_1 **	0.01 (-0.03, 0.06)	0.655	0.03 (-0.06, 0.12)	0.556	0.07 (-0.04, 0.18)	0.220	0.679

*Multivariate analysis adjusted for age, sex, education, baseline lung function or smoking history, visit, indoor $PM_{2.5}$, indoor NO_2, indoor humidity

**N=237 for overall, 120 for days indoors, 112 for days participants went outdoors for Evening FEV_1

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