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Air filter materials, outdoor ozone and building-related symptoms in the BASE study

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Abstract Used ventilation air filters have been shown to reduce indoor environmental quality and worker performance and increase symptoms, with effects stronger after reaction of filters with ozone. We analyzed data from the US EPA Building Assessment Survey and Evaluation (BASE) study to determine if ozone and specific filter media have interactive effects on building-related symptoms (BRS). We analyzed a subset of 34 buildings from the BASE study of 100 US office buildings to determine the separate and joint associations of filter medium [polyester/synthetic (PS) or fiberglass (FG)] and outdoor ozone concentration (above/below the median, 67.6 μg/m^3) with BRS. Using logistic regression models and general estimating equations, we estimated odds ratios (ORs) and 95% confidence intervals for the association of filter medium, ozone, and filter medium × ozone with BRS. Relative to FG + low ozone, PS alone or high ozone alone, were each significantly ($P < 0.05$) associated only with fatigue/difficulty concentrating (ORs = 1.93 and 1.54, respectively). However, joint exposure to both PS + high ozone, relative to FG + low ozone, had significant associations with lower and upper respiratory, cough, eye, fatigue, and headache BRS (ORs ranged from 2.26 to 5.90). Joint ORs for PS + high ozone for lower and upper respiratory and headache BRS were much greater than multiplicative, with interaction P-values < 0.10. Attributable risk proportion (ARP) estimates indicate that removing both risk factors might, given certain assumptions, reduce BRS by 26–62%. These findings suggest possible adverse health consequences from chemical interactions between outdoor ozone and PS filters in buildings. Results need confirmation before recommending changes in building operation. However, if additional research confirms causal relationships, ARP estimates indicate that appropriate filter selection may substantially reduce BRS in buildings, especially in high-ozone areas.

Key words: Building-related Symptoms; Sick Building Syndrome; Ozone; Air Filters; Risk Factor Interaction.

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Practical Implications

The results indicate that a better understanding of how filters interact with their environment is needed. While the mechanism is unknown and these findings need to be replicated, they indicate that the joint risk of BRS from polyester/synthetic filters and outdoor ozone above 67.6 μg/m^3 is much greater than the risk from each alone. These findings suggest potential reductions in BRS from appropriate selection of ventilation filter media or implementing strategies to reduce ozone entrained in building ventilation systems. If the relationships were found to be causal, filter replacement and ozone abatement should be undertaken.

Introduction

Building-related symptoms (BRS), more commonly known as sick building syndrome (SBS), describe a set of health symptoms with unknown etiology that office workers report experiencing at work, but that improve away from the work environment. These symptoms, which have not been clearly linked to specific causal environmental exposures, can include irritation of the eyes, nose, throat, respiratory tract and skin, and headaches and fatigue (WHO, 1983). Although the severity or clinical significance of these symptoms is unknown, they affect and may reduce the productivity of a large portion of the working population. Analyses suggest that BRS are responsible for a 2% reduction in productivity, which translates to an economic loss on the order of $60 billion per year in the United States alone (Fisk, 2000, Mendell et al., 2002).

Studies have investigated links between BRS and specific building characteristics, e.g. construction materials, configurations of heating, ventilation and air conditioning (HVAC) systems, and aspects of indoor environmental quality (e.g. ventilation rates, light quality) (Fisk, 2000; Mendell, 1993). A review of 11 BRS studies (Seppänen and Fisk, 2002), comprising 467 buildings and approximately 24,000 subjects found great consistency in the association between increased prevalence of BRS and presence of air conditioning systems, compared with natural ventilation (a 30–200% increase). Findings from several studies suggest that HVAC air filters can diminish perceived indoor environmental quality, contribute to BRS, and decrease work performance (Clausen et al., 2002; Wargocki et al., 2004).

In another area of research in indoor environments, indoor chemical reactions between strong oxidizing agents, such as ozone, and other volatile organic compounds (VOCs) have been shown to produce highly irritating by-products (Weschler et al., 2006; Wolkoff et al., 2006). Such 'indoor chemistry' may help explain some causes of BRS. New attention has been focused on indoor ozone's ability, in the presence of VOCs and other compounds indoors, to produce by-products such as formaldehyde, low-molecular-weight VOCs, and submicron particulate matter, suggestive of causing decrements in perceived air quality and/or adverse health effects (Weschler et al., 2006). Studies published in recent years have shown that the products of these reactions are often more irritating than their chemical precursors (Klenø and Wolkoff, 2004; Knudsen et al., 2003; Mølhave et al., 2005; Nøjgaard et al., 2005; Tamas et al., 2006a; Wolkoff et al., 2006, Weschler and Shields 2000). It is now believed that ozone is responsible for the majority of highly reactive and irritating compounds created indoors (Weschler, 2000, 2004; Weschler et al., 2006). A recent analysis of data from the US EPA Building Assessment Survey and Evaluation (BASE) study demonstrated a relationship between higher outdoor ozone concentrations and increased BRS within office buildings. In addition, indoor concentrations of certain VOCs known to be formed from ozone reactions, such as formaldehyde and acetaldehyde, were positively correlated with outdoor ozone concentrations (Apte et al., 2008).

Several laboratory studies of different air filter types have shown that reactions in filters consume ozone and may produce chemical by-products that then flow into the building, exposing occupants to odorous and potentially irritating chemicals (Beko et al., 2006; Clausen, 2004; Hyttinen et al., 2003, 2006, 2007; Weschler et al., 2006). In addition, the loss of ozone as it passes through ventilation air filters suggests the possibility of an interaction between the air filter matrix and trapped particulate matter, and ozone that increases BRS prevalence within a building. Ozone reactions on surfaces are not confined to filters, but are likely to occur in HVAC ducts, indoor building surfaces and furnishings, as well as on occupants themselves (Tamas et al., 2006b; Weschler, 2004).

Recent studies have examined specific components of a building's mechanical ventilation systems (e.g. air filters) as causes of poor indoor air quality and occupant discomfort. Several laboratory studies have shown that ventilation air filters can affect occupants' perception of indoor air quality and act as sources of perceived pollution (Bluyssen, 1993; Clausen et al., 2002; Pasanen et al., 1994; Pejtersen, 1996). Of particular interest are two studies that examined the effects of used air filters in the ventilation systems on human comfort and performance. Clausen et al. (2002) demonstrated that human subjects could detect the presence of a used filter in the study environment and that certain health symptoms (intensity of headaches and dizziness) increased in subjects exposed to air passing through a used filter. Wargocki et al. (2004) studied the effects of used ventilation filters on performance of call-center employees. They discovered that performance increased (i.e. average talk time decreased) when a new filter replaced a used filter, and that irritation of the nose and eyes decreased in the presence of a new filter relative to an old filter.

The impacts of outdoor ozone exposure on human health have been known and studied for a long time; acute effects include reduced lung function and respiratory symptoms (cough, chest pain, or throat irritation), with severity increasing with exposure to higher concentrations of ozone (Höppe et al., 2003; Lippmann, 1989; Lippmann and Schlesinger, 2000; Mckee, 1994). However, as ozone concentrations are usually lower indoors than outdoors (Weschler et al., 1994, 2006), it is unlikely that ozone exposures have a direct impact on BRS in the workforce (Weschler, 2006). Thus, ozone is considered to be responsible for much of the highly reactive odorous and irritating compounds created indoors (Weschler, 2000, 2004; Wolkoff et al., 2006), although the number of possible reactions and by-products that could be formed is immense and not well understood.

A recent analysis of data from the US EPA BASE study demonstrated a relationship between outdoor ozone concentrations and BRS within the office building environment (Apte et al., 2008). Results from the study indicated that occupants experienced 3–4% increased odds of BRS per 10 $\mu g/m^3$ increase in outdoor late workday (15:00–18:00 hours) ozone concentrations. In addition, this analysis found that indoor concentrations of certain VOCs known to be formed from ozone reactions, such as formaldehyde and acetaldehyde, were positively correlated with outdoor ozone concentrations. These findings suggest that ozone plays an important role in the health and quality of the indoor environment.

Several laboratory studies (Beko et al., 2006; Clausen, 2004; Hyttinen et al., 2003, 2006, 2007; Zhao et al., 2007) have examined different air filter types as possible sites for ozone reactions and their impact on indoor air quality (IAQ). These studies showed consistently that ozone concentrations downstream of the filter are less than those upstream of the filter, suggesting that reactions on filters consume ozone and may produce by-products that then flow into the building, exposing occupants to potentially harmful chemicals, and may contribute to BRS within the workplace. These findings also showed that increased humidity was found to increase the ozone reaction rates and decrease downstream ozone levels.

Based on the informed hypothesis that supply air filters can act as a sink for ozone and as possible sources of chemical products that may increase occupant BRS, the purpose of this analysis was to determine if certain materials used in the ventilation air filters themselves increase occupants' risk of BRS. Using data gathered by the US EPA during the BASE study, we examined the relationship between BRS, filter materials, outdoor ozone, and the combination of filter materials and outdoor ozone. The final analysis incorporated data from the 34 BASE Study buildings that used only one or the other of the two most common filter material types: polyester/synthetic or fiberglass. This analysis was designed to determine the separate and joint associations of polyester or synthetic filters (relative to fiberglass filters) and higher outdoor ozone concentration (relative to concentrations below the median of 67.6 $\mu g/m^3$) with a variety of BRS symptom outcomes.

Methods

The data

The data used in these analyses were obtained from the US EPA's BASE study. The BASE study, conducted between 1994 and 1998, examined a representative set of 100 US office buildings for 1 week, each in either the summer or winter (Girman et al., 1995; Womble et al., 1996). During the week in which each building was studied, the BASE study collected data on environmental factors (e.g. indoor and outdoor temperatures, relative humidities, CO_2 concentrations, and selected VOC concentrations), study space ventilation rates, building characteristics (e.g. HVAC configuration and maintenance), and workplace factors (e.g. cleaning schedules, cleanliness, occupant density). Confidential self-administered questionnaires were used to collect personal information (e.g. age, sex, health symptoms, pre-existing medical conditions, smoking status, and self-reported environmental sensitivities) from building occupants. The medical conditions included doctor-diagnosed asthma, allergies, migraine, eczema, and hay fever, and environmental sensitivities included tobacco smoke or chemicals in the air. The full BASE protocol including the building selection protocol has been described elsewhere in more detail (EPA, US, 2003; Womble et al., 1993).

Study variables

The self-reporting of several specific health symptoms, including symptom frequency and location (i.e. at work or away from work) were used to define BRS. This analysis uses the same definition of BRS used in previous analyses of the BASE data (Apte et al., 2000; Erdmann and Apte, 2004). A health symptom was classified as building-related if (a) it occurred at least 1–3 days per week during the preceding 4 weeks and (b) the symptom improved when the occupant was away from the building.

Using the above three-part definition of BRS, this analysis focused on four individual BRS and three aggregate BRS categories. Individual symptoms included cough, dry eyes, dry skin, and headache. Aggregate symptom categories were defined as the presence of at least one of the category's respective symptoms: lower respiratory (LR: wheeze, shortness of breath, or chest tightness), upper respiratory (UR: nose/sinus congestion, sore throat, or sneeze), and neurological (FTCN: fatigue or difficulty concentrating).

The main independent variable of interest in the existing BASE data was filter materials. Filter material data were collected during an inspection of each air handler serving the study space. The BASE study noted details about each filter, such as its condition, fit in the frame, and material. Filter-related variables used in this analysis were all based upon the data gathered during this inspection. The majority of filters were described as being composed of fiberglass, polyester, synthetic, cotton, or cellulose materials. The two most common types of single filter material categories were fiberglass and polyester or synthetic, while the most common blends of filter materials were cotton–polyester and cotton–synthetic. By grouping the buildings based on these recorded filter materials we created categories to investigate the possible influence of filter materials on BRS. Categories that we examined included buildings with filters containing any fiberglass vs. none, any polyester or synthetic material vs. none, and any polyester or synthetic material vs. any fiberglass but no polyester or synthetic material. The 'any polyester or synthetic material' filters included 100% polyester or synthetic filters as well as blended filters containing polyester or synthetic, such as cotton–polyester and cotton–synthetic filters.

These categories, reflecting any presence of specific materials, allowed inclusion of most or all buildings in analyses. We also constructed a dichotomous variable using 'pure' categories of filter medium, restricted to buildings concordant on filter materials, although these included smaller numbers of buildings. For this variable, the reference group was 'concordant fiberglass filter' (CFF) buildings (buildings with *only* fiberglass filters), while the comparison group was 'concordant polyester or synthetic filter' (CPSF) buildings (buildings with *only* polyester or synthetic filters). There are two reasons for selecting the CFF and CPSF materials for study. First, these are by far the most common filter material types, and second, the materials are very different, with fiberglass being rather inert chemically, and the synthetic polymers being more susceptible to oxidative degradation by ozone.

The BASE study did not measure indoor or outdoor ozone concentrations. Therefore ozone data were obtained from the EPA (blindly through a third-party contractor) after data collection for the BASE study was completed. Contemporaneous outdoor ozone concentration data were obtained from the historical records of ambient air quality-monitoring stations nearest to the study buildings. Correlations between workday average ozone concentration for BASE Study survey administration days and those for single or 2 weeks were very high, indicating that ozone variability from the event day to previous days was low and that the event-day metrics were suitable for use in regression models against the symptoms reported with a 4-week recall period (Apte et al., 2008). The ozone variable used in this analysis is a two-part ordinal divided at the median (67.6 $\mu g/m^3$) of the outdoor ozone concentrations for the late workday (13:00–18:00 hours). This time period was chosen because it had the strongest association with BRS in previous analyses. The distance from each BASE building to the corresponding ambient ozone-monitoring station varied from less than 0.5 to over 300 km. This was because many of the buildings studied in the winter season were very near to ozone-monitoring sites that did not record hourly ozone concentrations in the winter. In this case the next nearest hourly monitoring site that was collecting data was used. The geometric mean (geometric standard deviation) distance from the ambient monitoring site to BASE building was 5.8 (5.5) km (mean 28 ± 56 km). All buildings studied in the summer were located between 0.3 and 10.2 km while the distance for those studied in the winter ranged from 0.3 to 204 km.

Other filter-related variables were constructed from the BASE study inspection of building ventilation systems, in one case augmented by additional information. The panel filter replacement frequency (PFRF) was classified into three categories based on the reported replacement schedule (annually or less, and quarterly to semi-annually vs. semi-quarterly or more). The filter condition (COND), based on visual inspection, was analyzed as a dichotomous variable (fair or poor vs. good condition). The filter shape (SHAPE) was analyzed as flat or pleated vs. other. The fit of the filter in the frames (FIT) was assessed using a two-part variable (fair or poor vs. good condition). We created a two-part variable for the overall filtration efficiency of all the filters in each study space. Filtration efficiency was measured on the 'minimum efficiency reporting value' scale (MERV) as MERV ≤ 7 vs. MERV > 7. MERV values for filters were obtained from the manufacturer after the completion of the BASE study, or estimated based on data provided by the manufacturer. In study spaces that were serviced by more than one air handler or by more than one filter, an overall study space MERV value was estimated.

Data collected in the self-administered questionnaires were used to create personal covariates. Personal variables included gender (female vs. male), age (greater than 40 years vs. less than 40 years), smoking status (current smoker vs. non-current smoker), and an environmental sensitivity variable defined as having one or more of a sensitivity to chemicals or tobacco smoke or pre-existing asthma or allergies.

Environmental variables included indoor minus outdoor CO_2 concentrations per 100 ppm (dCO_2, per 100 ppm), relative humidity [RH: less than 20% (expected humidity-mediated symptoms) vs. greater than 20%], season during which the building was studied (winter vs. summer), thermal exposure (ThermExp: per 10°C-hours above 20°C), heating degree-days and cooling degree-days (HDD and CDD: °C-days) and indoor 1,2,4-trimetheylbenzene [1,2,4-TMB (ppb): a proxy for indoor penetration of automobile exhaust, Apte et al., 2000]. Details on the construction of the personal and environmental variables have been reported previously (Apte et al., 2000; Erdmann and Apte, 2004).

Occupants were assigned their respective building-level variables, i.e. all occupants in CFF buildings were considered to be the reference group for occupants in CPSF buildings. This was necessary to include individual-level risk factors (e.g. age, gender, smoking status) and building-level risk factors (e.g. filter material and ventilation) in the same models.

Statistical analyses

Statistical analyses were conducted using SAS version 8.2 for Windows PC (SAS Institute Inc, 1999). Using Proc Genmod, logistic regression models, and general estimating equations (GEEs), we estimated odds ratios (OR) and 95% confidence intervals (CI) for the association with BRS of filter medium, ozone, and the joint effect of filter medium and ozone. GEEs assuming an exchangeable variance were used to account for possible clustering effects of occupants within each study building. Crude (bivariate) and adjusted (multivariate) models were constructed for each of the four individual symptoms and the three symptom categories. Primary risk factors of interest were filter material, ozone and filter material × ozone (interaction term). Covariates in adjusted models included MERV, PFRF, COND, SHAPE, FIT, occupant age, sex, smoking status, sensitivities, dCO_2, RH, season, ThermExp, HDD, CDD, and 1,2,4-TMB. The interaction of filter materials with ozone was assessed by including an interaction term (the product of the filter materials variable and the ozone variable) in adjusted logistic regression models. Using the 'estimates' option in SAS Proc Genmod, the joint exposure to polyester/synthetic filters and high ozone relative to fiberglass filters and low ozone was calculated from the estimates of the association between filter material, ozone, and their interaction term. Adjusted interaction models were constructed for comparisons of any polyester or synthetic filter material vs. none, and, in a smaller set of buildings, for CPSF material vs. CFF.

For selected risk factors and outcomes, we roughly estimated the attributable risk proportion (ARP), which is the proportion of the risk seen in the total population that is attributable to the specific risk factor, and that would be prevented if the risk factor were removed. Our procedure is based on assumptions that estimated ORs in models are unbiased and represent directly causal relationships, that estimating adjusted ARP from adjusted ORs does not introduce substantial additional bias, and that there are no competing risks operating for the same outcomes.

We first estimated adjusted relative risks (RRs) from adjusted ORs, using the formula of Zhang and Yu (1998):

$$RR = \frac{OR}{(1 - P_0) + (P_0 \times OR)} \tag{1}$$

where P_0 is the proportion with disease in the exposed population. Values for RR were then included in the following formula for ARP (Rothman, 1986):

$$ARP = \frac{RR - 1}{P_e^{-1} + (RR - 1)} \tag{2}$$

where P_e is the proportion with exposure in the total population.

Results

Three of the BASE study buildings were naturally ventilated and thus lacking ventilation systems and filters, and were excluded from this analysis, leaving 97 buildings. Six additional buildings had values for filter material that were either missing or did not identify a specific type of filter material. Thus the maximum set of buildings available for analyses on filter material was 91.

Table 1 Initial risk factor categories in entire and selected BASE datasets

Risk factor categories	Number (%) of buildings	Total number of buildings
Any fiberglass filter	41 (45)	91
No fiberglass filter	50 (55)	
Outdoor ozone <67.6 μg/m^3	42 (46)	91
Outdoor ozone ≥67.6 μg/m^3	49 (54)	
Any poly/synthetic filter	47 (52)	91
No poly/synthetic filter	44 (48)	
Any poly/synthetic filter	47 (62)	76
Any fiberglass, no poly/synthetic filter	29 (38)	
Only poly/synthetic filter (CPSF)	16	42
Only fiberglass filter (CFF)	26	
Outdoor ozone <67.6 μg/m^3	22 (52)	42
Outdoor ozone ≥67.6 μg/m^3	20 (48)	
Outdoor ozone <67.6 μg/m^3	15 (44)	34[a]
Outdoor ozone ≥67.6 μg/m^3	19 (56)	

[a]Eight of the observed CPSF or CFF buildings had covariate values missing, reducing the number of usable observations for multiple logistic regression from 42 to 34.

Table 1 shows the numbers of buildings for specific filter material categories and ozone levels included in analyses. These included any fiberglass filters vs. none, any polyester/other synthetic filter materials vs. none, and any polyester/other synthetic filter material vs. any fiberglass filter but no polyester/other synthetic filter materials. Logistic regression models were constructed for successively more restrictive filter variable criteria with the purpose of comparing the effects of the two classes of filter materials. In the case of the 42 building set, CPSF buildings had no know fiberglass filters, while the CFF buildings had no known polyester/synthetic filters.

Two filter criteria definitions containing 91 buildings were analyzed (any vs. no fiberglass filter; and any vs. no polyester/synthetic filter). The buildings with any polyester/synthetic filter vs. those that had any fiberglass filter but no polyester filter numbered 76. Forty-two buildings had the most restrictive with either CPSF or CFF. Eight of the observed CPSF or CFF buildings had covariate values missing, reducing the number of usable observations from 42 to 34 for multiple logistic regression (MLR). The relative proportions of buildings with lower (<67.6 μg/m^3) and higher (≥67.6 μg/m^3) late afternoon average outdoor ozone concentrations for the different-sized building sets are also included in Table 1.

Results from the crude logistic regression models for filter medium in the 91 and 76 building datasets are presented in Table 2. The presence of any fiberglass filter vs. none had a significant positive association ($P < 0.05$) only for dry skin. All other symptoms had

Table 2 Results from crude logistic models for the relationship of BRS with any fiberglass filter (91 BASE buildings), any polyester/synthetic filters (91 BASE buildings) and any polyester/synthetic filters (76 BASE buildings) relative to no fiberglass filter

	Filter material					
	Any fiberglass vs. no fiberglass		Any poly/syn vs. no poly/syn		Any poly/syn vs. any fiberglass	
BRS	OR	95% CI	OR	95% CI	OR	95% CI
LR	0.91	0.63-1.31	**1.66**	**1.17–2.37**	**1.56**	**1.08–2.25**
Cough	0.88	0.61–1.28	**1.65**	**1.16–2.35**	**1.51**	**1.08–2.11**
UR	0.96	0.75–1.23	**1.41**	**1.12–1.77**	**1.43**	**1.2–1.71**
Dry Eyes	0.83	0.66–1.05	**1.29**	**1.04–1.6**	**1.38**	**1.14–1.67**
FTCN	0.91	0.72–1.15	**1.31**	**1.05–1.63**	**1.42**	**1.16–1.73**
Dry Skin	**1.48**	**1.03–2.13**	1.22	0.84–1.77	1.04	0.75–1.44
Headache	0.90	0.73–1.12	**1.24**	**1.01–1.52**	**1.31**	**1.07–1.61**

Statistically significant associations ($P < 0.05$) are highlighted in bold.

ORs <1 but with broad confidence intervals. In contrast, the presence of any polyester or synthetic filter material vs. none had significant ($P < 0.05$) positive associations for all symptoms excluding skin, with ORs ranging from 1.24 to 1.66. This pattern of increased risk was the same for comparison of any polyester/other synthetic filter material vs. any fiberglass filter but no polyester/other synthetic filter material, with significant ORs ranging from 1.31 to 1.56.

Table 3 provides results from crude logistic regression models assessing the associations with BRS in 42 buildings of CPSF vs. CFF, and of higher vs. lower outdoor ozone. Significant ORs ($P < 0.05$) for polyester/other synthetic filters relative to fiberglass filters ranged from 1.45 to 1.79 for LR, UR, dry eyes, and FTCN. Cough was marginally significant with a P-value of 0.07. No significant ($P < 0.05$) ORs were found for relationships between late workday outdoor ozone concentrations above 67.6 $\mu g/m^3$, although all ORs exceeded 1 except headache and dry skin. A visual comparison of the BRS ORs in Tables 2 and 3 provides convincing support that the crude effects seen in the 91-building dataset are also evident in the 34-building set with more restrictive filter material criteria, and that the associations between filter type and BRS become clearer as the criteria are more precisely defined. The value of the narrow filter definition appeared to be greater than the benefit of having a larger, less stringently defined filter criterion. For this reason the subsequent analyses focused on the 34-building dataset.

Table 4 provides summary statistics for the other covariates included in the adjusted models and for the BRS outcome variables, within the 34 buildings included in final multivariate models. Prevalence of the four individual BRS outcomes in these 34 buildings ranged from 5% to 20%, while in all 97 air-conditioned BASE buildings the same symptoms ranged from 5% to 19%. For the aggregate symptom categories, prevalence in the 34 buildings ranged from 5% to 22% while in the 97 buildings the range was 4–21%. The

Table 3 Results from crude logistic models, in 42 BASE buildings, for BRS vs. concordant filter materials (SPSF relative to CFF) and BRS vs. ambient ozone (above BASE average concentration relative to below average)

	Filter medium: concordant poly/synthetic vs. concordant fiberglass		Ambient ozone >67.6 $\mu g/m^3$	
BRS	OR	95% CI	OR	95% CI
LR	**1.79**	**1.06–3.02**	1.07	0.74–1.55
Cough	1.61	0.97–2.67	1.01	0.71–1.44
UR	**1.55**	**1.07–2.24**	1.16	0.91–1.47
Dry Eyes	**1.45**	**1.04–2.00**	1.08	0.87–1.35
FTCN	**1.49**	**1.06–2.11**	1.08	0.87–1.36
Dry Skin	0.93	0.57–1.54	0.99	0.69–1.43
Headache	1.30	0.91–1.87	0.99	0.81–1.22

Statistically significant associations ($P < 0.05$) are highlighted in bold.

Table 4 Summary statistics for individual-level and building-level variables in the 34-building subset of the BASE study

Variable	Percent	Mean	SD	Min	Max
Individual-level variables (n = 1406–1447)					
BRS outcomes					
LR	5				
Cough	5				
UR	22				
Dry Eyes	20				
FTCN	16				
Dry Skin	5				
Headache	15				
Covariates					
Female	66				
At least one sensitivity	80				
Age ≥40	54				
Current smoker	15				
Risk factors					
CPSF Buildings	32				
Ozone >67.6 $\mu g/m^3$	44				
Other covariates					
MERV >7 vs. MERV ≤ 7	50				
Filter shape: flat or pleated	41				
Filter fit: good	79				
Filter condition: good	44				
Panel filter replacement freq.					
Semi-quarterly or more	32				
Qrtrly. or Semi-annually	41				
Annually or less	26				
dCO_2 (ppm/100)		2.4	1.4	0.4	6.1
Heating degree-days (°C-days)/100		23.9	11.7	1.1	46.2
Cooling degree-days (°C-days)/100		6.9	5.6	0.2	22.4
ThermExp (°C-hours >20°C)		26.6	5.4	13.8	37.1
RH <20%	18				
Season: Winter	41				
1,2,4-TMB (ppb)		1.2	1.4	0.1	6.7

n, number of observations at the building or occupant level.
Proportion is given for categorical variables, and the mean, standard deviation (SD), minimum (min) and maximum (max) values are given for continuous variables.

Table 5 Adjusted interaction model estimates, from the 34-building subset, for the effect of filter materials, ozone, and filter materials + ozone

	Concordant Fibreglass Filters			Concordant Polyester/Synthetic Filters		
	BRS	OR		BRS	OR	95% CI
Low Ambient O_3	LR	1.00		LR	1.45	0.56–3.77
	Cough	1.00		Cough	2.97	0.83–10.61
	UR	1.00		UR	1.15	0.53–2.49
	Dry Eyes	1.00		Dry Eyes	2.07	0.88–4.87
	FT/CN	1.00		FT/CN	**1.93**	**1.01–3.71**
	Dry Skin	1.00		Dry Skin	0.79	0.25–2.45
	Headache	1.00		Headache	1.16	0.65–2.06
	BRS	OR	95% CI	BRS	OR	95% CI
High Ambient O_3	LR	1.47	0.58–3.71	LR	**5.90**	**1.73–20.08**
	Cough	1.33	0.56–3.16	Cough	**2.67**	**1.00–7.10**
	UR	1.10	0.65–1.88	UR	**2.63**	**1.36–5.08**
	Dry Eyes	1.37	0.79–2.36	Dry Eyes	**2.26**	**1.17–4.38**
	FT/CN	**1.54**	**1.02–2.35**	FT/CN	**2.76**	**1.60–4.76**
	Dry Skin	1.15	0.50–2.62	Dry Skin	0.37	0.14–1.02
	Headache	1.15	0.69–1.91	Headache	**2.54**	**1.25–5.15**

All ORs are relative to fiberglass and low ozone.
Statistically significant associations ($P < 0.05$) are highlighted in bold.

Table 6 Results of adjusted interaction model, from the 34-building subset, for the relationship of ozone to BRS in CPSF buildings and for the risk in high ozone areas to occupants in CPSF buildings relative to occupants in CFF buildings

Ozone risk in CPSF buildings			CPSF building risk (rel. to CFF building) in high ozone		Test for interaction between ozone level and CPSF
BRS	OR	95% CI	OR	95% CI	*P*-value
LR	**4.08**	**1.24–13.4**	**4.01**	**1.94–8.31**	0.03
Cough	0.90	0.35–2.28	2.00	0.90–4.48	0.55
UR	**2.29**	**1.24–4.22**	**2.38**	**1.59–3.58**	0.07
Dry Eyes	1.09	0.58–2.05	**1.66**	**1.12–2.44**	0.61
FT/CN	1.43	0.75–2.71	**1.79**	**1.29–2.47**	0.82
Dry Skin	0.47	0.18–1.26	0.32	0.14–0.78	0.12
Headache	**2.19**	**1.18–4.07**	**2.21**	**1.50–3.26**	0.03

Statistically significant associations ($P < 0.05$) are highlighted in bold.

results of a pooled *t*-test indicated that there were no statistically significant differences between the BRS prevalences of the 34 building subset and the 97-building BASE population. In addition, no statistical differences were detected between the values for the covariates in the 34-building subset and the larger BASE population.

Tables 5 and 6 show estimates from the adjusted logistic interaction models employing GEE. Because of missing values in building-level covariates, adjusted models contained a total of only 34 buildings: 11 CPSF and 23 CFF. In Table 5, all ORs are relative to occupants of CFF building in low-ozone areas. In low-ozone areas, ORs for occupants in CPSF buildings relative to CFF buildings ranged from 0.79 to 2.97, but only FTCN had a significant relationship at $P < 0.05$ and only dry skin had an OR <1. ORs for high vs. low ozone in CFF buildings ranged from 1.10 to 1.54, but again, only FTCN had a significant relationship, with $P < 0.05$. The joint risk for occupants in CPSF buildings with high ozone, relative to occupants in CFF buildings with low ozone, included ORs ranging from 2.26 to 5.90. All symptoms were significant at the $P < 0.05$ level except dry skin, with the only OR <1.

Table 6 provides the ORs for high- vs. low-ozone levels within the set of CPSF buildings, and for polyester/synthetic filter risk (relative to fiberglass filter) within the set of high ozone buildings. For high vs. low ozone in CPSF buildings, the significant ORs for LR, UR and headache ranged from 2.19 to 4.08. For polyester/synthetic filters (relative to fiberglass filters) in high ozone buildings, significant ORs for LR, UR, dry eyes, FTCN, and headache ORs ranged from 1.66 to 4.01 ($P < 0.05$) and all ORs exceeded unity except dry skin, which was significantly reduced. *P*-values for the interaction terms (the product of the filter material variable and the ozone variable) were <0.10 for LR, UR, and headache.

Covariates in MLR models

The relationships between BRS and the filtration-related covariates in the adjusted models are presented in Table 7 and discussed here. Increased filtration efficiency (MERV) was associated with increased risk for most of the BRS, with significant increases for cough and eye. Bag or roll filter shapes, relative to flat or pleated, were associated with significant decrease in headache. Fair or poor filter condition, relative to good condition, was associated with significant increases in LR and UR, but significant decrease in dry skin. Fair or poor filter fit, relative to good fit, was associated with general decreases, not significant except for LR and headache, in most BRS. Less frequent filter replacement at the quarterly to semi-annual level was associated with increases in all BRS except skin, including significant increases for LR and UR, but at the level of annual or less showed less consistent patterns, including a significant increase for LR and a significant decrease for skin symptoms.

Regarding other environmental covariates, dCO_2 had small positive or negative associations with specific BRS (not shown), including a significant increase in LR (OR = 1.24). 1,2,4-TMB was associated with at least some increase in all BRS relationships with many of the symptoms (not shown), including significantly elevated ORs per ppb ranging from 1.23 to 1.52 for LR, cough, eye, FTCN, and skin.

Table 7 Associations between filter-related covariates and BRS symptoms in the adjusted interaction models for the 34-building subset

Filter efficiency rating		Filter shape	Filter condition	Filter fit	Panel filter replacement frequency	
Symptom Group	MERV >7[a] OR (95% CI)	Other[b] OR (95% CI)	Fair or poor[c] OR (95% CI)	Fair or poor[c] OR (95% CI)	Quarterly to semi-annually[d] OR (95% CI)	Annually or less OR (95% CI)
LR	1.35 (0.78–2.33)	0.71 (0.38–1.34)	**4.12 (1.61–10.6)**	**0.39 (0.15–0.99)**	**9.26 (1.70–50.5)**	**3.10 (1.14–8.45)**
Cough	**1.98 (1.04–3.78)**	1.40 (0.79–2.46)	1.14 (0.53–2.45)	1.03 (0.51–2.06)	1.27 (0.58–2.77)	0.63 (0.36–1.10)
UR	1.10 (0.73–1.66)	0.72 (0.51–1.02)	**1.58 (1.04–2.41)**	0.64 (0.31–1.34)	**2.19 (1.09–4.38)**	1.12 (0.56–2.23)
Dry Eyes	**1.47 (1.10–1.96)**	0.93 (0.67–1.30)	1.10 (0.70–1.73)	0.86 (0.46–1.58)	1.30 (0.55–3.08)	0.88 (0.50–1.54)
FT/CN	1.14 (0.78–1.66)	1.00 (0.70–1.45)	0.88 (0.60–1.29)	0.75 (0.44–1.29)	1.29 (0.71–2.34)	0.79 (0.47–1.32)
Dry Skin	1.76 (0.84–3.70)	0.75 (0.37–1.52)	**0.29 (0.13–0.65)**	1.47 (0.63–3.44)	0.40 (0.16–1.04)	**0.22 (0.09–0.55)**
Headache	0.88 (0.63–1.25)	**0.57 (0.37– 0.88)**	1.50 (0.95–2.36)	**0.57 (0.35–0.94)**	2.18 (0.93–5.14)	1.19 (0.93–5.14)

Statistically significant associations ($P < 0.05$) are highlighted in bold.
Reference Category: [a]MERV ≤ 7; [b]flat or pleated; [c]good; [d]semi-quarterly or more.

Attributable risk proportions

Given the limitations described in the *Methods* section, we estimated, from the interaction models for CPSF/CFF, the proportion of symptoms that would be prevented (assuming that estimated ORs from GEE models were unbiased and represented directly causal relationships in the absence of competing risks), if all entrained outdoor ozone concentrations were lowered to below the 67.6 μg/m^3 level and fiberglass filters were substituted for all polyester/synthetic filters. The proportional reductions were 62%, 38%, 29%, 26%, 33%, and 30%, for LR, cough, UR, dry eyes, FTCN and headache BRS, respectively. For skin BRS, which had a nearly significant OR = 0.37, the same formula would estimate a 31% increase in prevalence.

Discussion

It is important to recognize the relative nature of the statistical analysis conducted here; the observed CPSF effects are relative to the CFF, but the analyses say nothing about the absolute risks from using any HVAC filter, as mentioned in the *Introduction*. These analyses showed, in a representative sample of US office buildings, that relative to the use of fiberglass air filters, polyester or synthetic air filters alone, or the presence of slightly elevated ambient ozone levels alone, were associated with increases in one or more BRS in occupants, but the joint presence of these two risk factors had a substantially increased risk for several symptoms. CPSF alone was associated with increase in FTCN, and possibly in cough and dry eyes also, in either low or high ozone environments. Higher ambient ozone alone was associated with an increase in FTCN in CFF buildings. Buildings with both risk factors, CPSF and high ozone, relative to those with neither, were associated with substantial and significant increases in all symptoms except skin. To what extent can these latter risks be attributed to either risk factor alone or their joint presence? In high-ozone areas, increased risk of LR, UR, and headache BRS associated with CPSF relative to CFF was much greater than the product of the risks associated with CPSF or high ozone alone (i.e. the joint risk was greater than multiplicative). *P*-values for the interaction term for LR, UR, and headache were 0.03, 0.07, and 0.03, respectively. Thus for these BRS, one cannot consider the risks of polyester/synthetic filters and high ozone separately without considering the joint risks. These statistical interactions suggest an underlying physical interaction between polyester/synthetic filters and ozone with generally adverse health consequences. (There is, however, a suggestion of a negative or protective interaction for skin symptoms.)

Contrary to expectations, occupants in buildings with more efficient air filters (MERV >7) had increased odds of some BRS (cough, eye, and possibly skin and LR) relative to occupants in buildings with less efficient filtration (MERV ≤ 7). More efficient filters remove from the indoor air a greater proportion of the smallest airborne particles, which are known to cause a variety of health effects from epidemiologic studies of ambient air pollutants (Fisk et al., 2002; USEPA 2004). One hypothesis, needing further investigation, is that higher efficiency filters provide greater filter surface area (and greater contact with trapped particulate matter) on which ozone-initiated surface reactions can occur, and thus increased release into the indoor environment of known or heretofore unidentified irritating compounds produced from such reactions.

A possible alternative explanation for the unexpected association found between more efficient particle filters and increase in many symptoms would be that these filters tend to have extended surface area, to be expensive, and thus to be changed infrequently. Then, if infrequent filter change, because of airflow through long-accumulated dust between changes, directly caused increase in symptoms, increased symptoms might be associated with highly efficient filters simply as a proxy for infrequently changed filters. This is not a plausible explanation, however; as MERV and filter change frequency are included in all multivariate models, adjusting for this potential confounding. Furthermore, less frequent change of panel filters was associated with lower, and not higher risks for most symptoms, with reductions of up to 40–50%. Therefore, we do not think that the proposed correlation with filter shape or frequency of filter change explains the multivariate-adjusted associations of higher filter efficiency with increase in some symptoms. By the same token, the multivariate adjustment of the estimates reported is also not consistent with a hypothesis that the increased risks observed for polyester/synthetic filters are really due to correlation of these materials with higher efficiency filters, which for some reason cause higher symptoms. Note that some of the very large ORs and very broad CIs for LR with filter condition (4.12) and filter replacement frequency (9.26) presumably result from small cell sizes.

Regarding other environmental covariates, 1,2,4-TMB had significant increases with many of the symptoms. 1,2,4-TMB is a pollutant generated by automobile engine combustion and therefore indicates outdoor to indoor transportation of air pollutants. The ORs, from 1.2 to 1.5 per ppb, indicate a large impact over the observed range of 0.1–6.7 ppb of 1,2,4-TMB. Associations of higher dCO_2, a surrogate for per-person ventilation rate, with increased BRS in adjusted models were weaker than in the bivariate models and in prior multivariate analyses focused on dCO_2 (Apte et al., 2000; Erdmann and Apte, 2004). This is similar to results from an analysis examining only the effect of ozone on BRS (Apte et al., 2008) which found that the addition of ozone into a multivariate model reduced the strength of relationship between dCO_2 and BRS.

Limitations

These analyses have all the limitations of cross-sectional studies, in which temporal sequence of risk factors and outcomes is unknown, making causal interpretations of any correlations found inappropriate. Estimates may be biased by prior loss of potential participants, non-random lack of participation by buildings or occupants, and errors in assessing occupant or environmental data. Errors in measuring occupant or environmental data, if not systematically related to the outcomes, are likely to obscure any true relationships by biasing estimates toward the null. Ambient ozone data, for instance, were available only for larger areas and were imperfect measures of ambient ozone precisely at the study buildings. Information on filter materials was imprecise, and many buildings contained multiple filter materials. Although analyses containing most study buildings were possible, we chose to focus on a subgroup of buildings with entirely concordant filter materials. We focused on comparison between concordant polyester/synthetic filters and fiberglass filters because this contrast, even in preliminary models with mixed filter materials present, showed the strongest associations. Buildings with mixes of different filters, or buildings with blended filters (such as cotton-polyester or cotton-synthetic) were excluded. The final analyses, with more specific metrics and less misclassification of exposure by filter material, showed strong associations between filter material and BRS. Power, however, was substantially reduced, with only 34 of the 100 BASE buildings and 1400 of 4237 respondents included in models. The power reduction may have lowered the significance of findings for some true relationships. Filter materials other than polyester/synthetic or fiberglass may have different risk for BRS relative to polyester, synthetic or fiberglass filters, but were not sufficiently present in the data to assess.

Because building-wide values, such as filter types or ozone concentrations, were applied to each individual occupant, and thus observations in the logistic models were not truly independent of each other, there may be clustering of observations within buildings that leads to overestimation of true precision. We used generalized estimating equations to adjust for the clustering effects within study buildings. Use of GEE actually increased the significance of most of the estimates for associations of filter material and ozone with BRS.

Implications

Causality of the relationship between polyester/synthetic filters and increased BRS needs to be confirmed by intervention studies before recommending changes to building maintenance practices, but such studies would be relatively simple and inexpensive. If the findings were confirmed, it would offer a surprisingly simple intervention to reduce BRS. From the interaction models, there are two pathways for reducing BRS. One is to lower outdoor ozone concentration and the other is to replace polyester or synthetic ventilation filters with fiberglass filters. Based on the results of the ARP analysis, the best case would be to reduce both risk factors by lowering outdoor ozone concentrations to below 67.6 $\mu g/m^3$ (or even lower) and replacing polyester/synthetic filters with fiberglass ones. However, filter replacement seems simpler and more practical, and possible within any building. The PRR analysis indicated that replacement of ventilation filters alone could have a major impact, reducing BRS prevalence by up to 75% in buildings with outdoor ozone concentrations above 67.6 $\mu g/m^3$ and by up to 39% in lower ozone environments. A third option would be to use adsorbing or catalytic media downstream to remove odorous and irritating VOCs. However, source control is typically a more prudent approach than pollutant removal, where possible.

These findings also indicate a need for research to identify mechanisms by which polyester/synthetic filters react with higher levels of ozone in ways that increase respiratory symptoms and headache in occupants. Understanding the mechanism of interaction is especially important because the higher ozone levels in this analysis, in absolute concentrations, were rather low. In this analysis the dividing value between low and high ozone levels was 67.6 $\mu g/m^3$ (about 34 ppb), which can be typical of urban cities. This level is far below the National Ambient Air Quality Standards of 80 ppb over an 8-h period, indicating that effects of ozone on morbidity may occur well below the current safety standards. This finding is consistent with recent studies that have found increased morbidity and mortality at low ozone concentrations (Bell et al., 2004, 2006) and is suggestive that ozone-initiated reactions may be a source of exposures to pollutants, currently known or unknown, that mediate human health responses.

Studies of the physical properties of polyester/synthetic filters may lead to a mechanistic explanation for interaction of ozone with these filter materials. The chemical composition of the filters and how they react and interact with gas and particulate air contaminants may prove valuable. Determination of the inertial and electrostatic conditions affecting loading patterns on different filter materials may also be important. Quantification of the types of surface chemical reactions that take place on and in filters, and identifying the by-products that are released by such reactions will also be an important component towards understanding the plausible causal mechanism.

Finally, future studies need to include and improve sampling for ozone and ozone reaction by-products. Ozone concentrations should be measured both upstream and downstream of the air filters in ventilation systems, in order to assess losses of ozone at or in the filter. Because ozone was not measured as part of the BASE study, we had to rely on centrally measured ambient ozone data that may have poorly characterized concentrations closer to the study buildings. To better understand the exact relationship between filter medium and ozone, measurements upstream and downstream of the HVAC filters are necessary. Measurements of possible filter-ozone surface chemistry by-products need to be quantified as well to accurately estimate occupant exposure and more precisely model BRS.

While the results presented here are only a first step toward understanding the complex relationship between air filters and ozone, it is apparent that future studies of BRS or building-related health concerns involving ventilation or ventilation systems need to consider both the filter material present and the ozone concentrations at the building site. Further research is needed to identify why and how ozone modifies the effect of filters on BRS or vice versa.

The relationships found in these analyses are only correlations and do not justify conclusions about causation. Before a conclusion is made regarding these findings, replication in additional studies is necessary, preferably in blinded, controlled intervention studies. If confirmed, it would also be important to understand the mechanism by which polyester and synthetic filters in combination with ozone and other environmental factors (e.g. humidity, oxides of nitrogen) increase BRS in building occupants. However, the results of these analyses indicate that there exists an interaction between polyester and synthetic filters and outdoor ozone and that this interaction may contribute to BRS in occupants.

Conclusions

A clear relationship between polyester/synthetic filters relative to fiberglass filters, and increased building-related symptoms have been observed in this analysis. In addition, ozone appears to modify this effect leading to large increases in occupants' odds of having BRS if they work in buildings with all polyester or synthetic filters, in areas where the median late workday ambient ozone concentration is greater than 67.6 $\mu g/m^3$ (about 34 ppb). The observed effects are not likely to explain all BRS risk from HVAC filters, as the analysis compares the odds of BRS from the CPSF only relative to the CFF, and relative to ambient ozone concentration. However, the strong and large relative increase in prevalence of selected BRS identified for the CPSF is of concern. Nonetheless, before changes to building equipment configurations and maintenance practices occur, the findings presented here need to be replicated and the mechanism by which polyester/synthetic filters increases BRS needs to be better understood. If the relationship is causal, ARP analyses indicate that replacing all polyester/synthetic filters with fiberglass filters and reductions in the amount of ozone allowed to enter a building's ventilation system would help to reduce BRS.

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