LBNL 63370

ERNEST ORLANDO LAWRENCE **BERKELEY NATIONAL LABORATORY**

 Contaminants in Buildings and Occupied Spaces as Risk Factors for Occupant Symptoms in U.S. Office Buildings: Findings from the U.S. EPA BASE Study

M.J. Mendell1, A. Mirer1, Q. Lei-Gomez2

1Lawrence Berkeley National Laboratory Environmental Energy Technologies Division Indoor Environment Department Berkeley, CA 94720

2 Harvard University School of Public Health Boston, MA

 August 2007

 This work was supported by the Indoor Environments Division, Office of Radiation and Indoor Air, Office of Air and Radiation of the U.S. Environmental Protection Agency through interagency agreement DW8992169501-1 with the U.S. Department of Energy under Contract Agreement No. DE-AC02-05CH11231.

Disclaimer

This document was prepared as an account of work sponsored by the United States Government. While this document is believed to contain correct information, neither the United States Government nor any agency thereof, nor The Regents of the University of California, nor any of their employees, makes any warranty, express or implied, or assumes any legal responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by its trade name, trademark, manufacturer, or otherwise, does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or any agency thereof, or The Regents of the University of California. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or any agency thereof, or The Regents of the University of California.

Ernest Orlando Lawrence Berkeley National Laboratory is an equal opportunity employer.

Contaminants in Buildings and Occupied Spaces as Risk Factors for Occupant Symptoms in U.S. Office Buildings: Findings from the U.S. EPA BASE Study

M.J. Mendell¹, A. Mirer¹, Q. Lei-Gomez²

¹ Lawrence Berkeley National Laboratory, Indoor Environment Dept., Berkeley; ² Harvard University School of Public Health, Boston

Corresponding author: Mark J. Mendell Lawrence Berkeley National Laboratory Indoor Environment Department 1 Cyclotron Rd., MS 90-3058 Berkeley, CA 94720, USA Phone: 1-510-486-5762 email: mjmendell@lbl.gov

Keywords:

indoor air quality; building-related symptoms; sick building syndrome; cleaning; sources

Acknowledgements

This work was supported by the Indoor Environments Division, Office of Radiation and Indoor Air, Office of Air and Radiation of the U.S. Environmental Protection Agency through interagency agreement DW8992169501-1 with the U.S. Department of Energy. Conclusions in this paper are those of the authors and not necessarily those of the U.S. Environmental Protection Agency. We thank Michael Bates and David Lorenzetti for review of the draft manuscript.

Contaminants in Buildings and Occupied Spaces as Risk Factors for Occupant Symptoms in U.S. Office Buildings: Findings from the U.S. EPA BASE Study

Abstract

Background: Nonspecific building-related symptoms among occupants of modern office buildings worldwide are common and may be associated with important reductions in work performance, but their etiology remains uncertain. Most reported research into environmental risk factors for these symptoms has focused on ventilation system-related factors, dampness, and particle removal through filtration and cleaning, with relatively few studies of other potential sources of indoor contaminants.

Methods: We analyzed data collected by the U.S. Environmental Protection Agency (EPA) from a representative sample of 100 large U.S. office buildings – the Building Assessment and Survey Evaluation (BASE) study – using multivariate-adjusted logistic regression models with generalized estimating equations. We estimated odds ratios (ORs) and 95% confidence intervals (CIs) for associations between seven building-related symptom outcomes and a diverse set of potential indoor and outdoor sources for indoor pollutants.

Results: Although most of the investigated risk factors showed no apparent association with building-related symptoms, some interesting associations resulted. Increased prevalence of symptoms was associated with carpets older than one year (lower respiratory symptoms), noncarpeted floors (upper and lower respiratory symptoms), older furniture (eye and skin symptoms), infrequent vacuuming (upper respiratory, eye, and skin symptoms and headache), and masonry exterior walls (cough, eye symptoms, and fatigue/concentration difficulty).

 Discussion: For the many potential risk factors assessed, almost none had been investigated previously, and many associations found here may have been by chance. Additional confirmatory research focused on risk factors initially identified here is needed, using more objective measures of health outcomes and risk factors or exposures.

Background

Complaints of respiratory, eye, and skin symptoms, headache, and fatigue have been reported by occupants of office buildings in many countries since the 1970s. Explaining or preventing these problems has been difficult. Although indoor exposures causing these symptoms have not been identified, researchers have identified environmental "risk factors" that are correlated with higher prevalences of symptoms in buildings, and thus may be proxies for unidentified causal exposures. These risk factors include the presence of air-conditioning systems (Seppanen and Fisk 2002), contaminated components of heating, ventilating, and air-conditioning (HVAC) systems (Mendell, Naco et al. 2003), low ventilation rates (Seppanen, Fisk et al. 1999), and dampness or visible mold in buildings (Park, Schleiff et al. 2004; Mendell, Cozen et al. 2006).

The Building Assessment and Survey Evaluation (BASE) study, conducted by the U.S. Environmental Protection Agency, is the largest available study of building environments and occupant symptoms in a representative set of U.S. office buildings. This paper presents findings from an analysis of risk factors in the BASE data involving potential contaminant sources, related to either the buildings, the occupied spaces, or the contents, that had been determined by inspection or interview. Risk variables in the BASE data assessed in this analysis include those related to the building envelope, indoor surface materials, furnishings and equipment, and practices of housekeeping, building maintenance, and building operation. Most of these risk factors have not been assessed in prior analyses of indoor contaminants in the BASE data, which focused primarily on moisture-related contamination (Mendell, Cozen et al. 2006).

The analyses reported here primarily explored previously untested hypotheses about specific sources of indoor contaminants as causing various irritant, allergic, or toxic responses in occupants. We therefore investigated correlations of risk variables with increased prevalence of work-related symptoms, including lower and upper respiratory symptoms, cough, eye symptoms, fatigue/ difficulty concentrating, headache, and skin symptoms. Because many of these risk factors were correlated with each other, and because many other environmental and nonenvironmental factors in office buildings are known to be associated with symptom reporting, we used multivariate models to estimate the independent associations with building-related symptoms (BRS) of these risk factors for indoor sources of contaminants.

Methods

The study has been described by Brightman and Moss (2000), and full details of the study protocol published elsewhere (U.S. Environmental Protection Agency 2003). Briefly, data in the BASE study were collected by the U.S. EPA from 100 representative office buildings selected from geographic regions throughout the U.S. during 1994-1998. Within each of the 100 buildings, the study randomly selected a "study space" with, if possible, at least 50 occupants and served by no more than two ventilation air-handling units. As only one study space was selected per building, the terms "building" and "study space" are used here interchangeably. Environmental data were collected using standardized procedures including building inspections, interviews with facility managers, and a broad range of environmental measurements. Personal data were collected from questionnaires distributed to all occupants of each study space. Each building was studied once, in either summer or winter.

Outcomes

The questionnaire asked each respondent about the frequency of occurrence of various symptoms during the last four weeks at work, and also whether each symptom was better or worse on days when the respondent was away from the building. A specific symptom was considered "weekly, building-related" for a respondent if the symptom was reported as having occurred in the building at least one day per week over the four weeks prior to the survey, and as having improved away from the building. For analyses, we used seven types of weekly, BRS outcomes, some defined as the presence of *at least one* of several specific weekly, building-related symptoms: lower respiratory (wheeze, shortness of breath, or chest tightness), cough, upper respiratory (stuffy or runny nose, sneezing, or sore or dry throat), eye symptoms (dryness, irritation, or itching), fatigue or difficulty concentrating, headache, and skin symptoms (dryness, irritation, or itching).

Risk Factors

These analyses investigated potential risks associated with exposure to contaminants from a variety of sources related to the indoor workplace, including building characteristics, cleaning materials and practices, indoor materials and renovation, outdoor pollutants, pesticide application, and "special uses" (i.e., specific unusual uses of office space that might produce unusual contaminants, such as graphics shops or kitchens). Potential risk factors of interest are listed in Table 1. We will use the term "risk factor" here to indicate factors that may *potentially* be markers for increased risk of health outcomes (rather than, as it is sometimes used, to indicate factors already identified as markers for increased risk). Some of the original variables were combined into composite or index variables, or omitted, due to missing, inconsistent, or illogical data values, insufficient variation, or strong intercorrelations. Continuous variables were converted to categorical variables for the analyses, as using a continuous independent variable forces an assumption of a linear relationship. Some variables described sources related to entire study buildings, and some related to specific spaces in the buildings. We considered either or both of these as seemed most appropriate.

Some variable categories were combined when too few buildings had a particular characteristic. For example, neighboring land uses were classified as *agricultural* or *industrial* for so few buildings that we combined these into the category *other*. Variables describing materials for each specific type of indoor surface or furnishing were complex: for each type of surface/furnishing (e.g., walls, partitions, movable furniture) perhaps five or more specific materials (e.g., wood, painted wallboard, cloth, metal, glass, other) could each be specified as *primary*, *secondary*, or *other.* We generally considered only materials described as primary for each surface or furnishing. When appropriate based on prior hypotheses, primary materials were grouped on the basis of relevant properties (such as level/type of potential emissions). As an example of a variable created for analyses, the variable on carpet combined information on primary floor coverings with a variable on carpet renovation.

Confounding Variables

Many factors were considered as potential confounders of the associations between contaminant exposure and weekly building-related symptoms. Potential environmental confounders included temperature (the product of number of degrees over 20°C and number of hours at each level, in quartiles (Apte, Fisk et al. 2000)), mean humidity ratio (a measure of absolute humidity, in

quartiles), ventilation rate (as estimated from volumetric flow measures (Mendell, Lei et al. 2005)), floor area in study space per operable window, average hours of ventilation per weekday, and season during which each building was studied. Personal variables considered as potential confounders included subject's age, gender, smoking status, job category, level of education, job satisfaction, job demand, job conflict, hours worked weekly, years worked in the building, workstation location, hours worked at a computer daily, photocopier use, comfort of chair, comfort of desk, and histories of hay fever, dust allergy, mold allergy, eczema, and asthma.

Analysis Methods

All analyses were performed using SAS version 8 (SAS Institute Inc. 2002). Appendix 1 provides details of the analytic procedures. In brief, descriptive univariate analysis was performed first, and variables lacking sufficient variation or completeness were re-categorized or excluded. Next, the crude association of each of the seven symptom outcomes with each of the remaining risk factor variables was estimated. Those with even moderate associations were retained for each outcome, and subjected as a group to "backward" selection (see (3) in Appendix 1). Potential confounders were then chosen for inclusion in these models containing selected risk factors based on changes of at least 10% in any risk estimate. The resulting models produced the initial multivariate adjusted estimates. This was followed by reconsideration for inclusion, in models including the chosen confounders, of any risk factors excluded during prior stages of modeling. Finally, for each outcome, the chosen risk factors and confounders were included in a logistic regression model with generalized estimating equations (GEE) to account for potential clustering of subjects within the same building.

Estimates from bivariate analyses and final multivariate adjusted models with GEE are presented as odds ratios (ORs) and 95% confidence intervals (CIs). An odds ratio greater than one indicates a greater prevalence in the group of subjects with the risk factor than in those without the risk factor, while an odds ratio less than one indicates the reverse. An odds ratio of 1.0 indicates approximately equal prevalences in both groups, that is, no association between the risk factor and the symptom outcome. Estimates from multivariate models may be interpreted as the relationship of the prevalences in subjects with and without the risk factor, independent of all other risk factors and confounding factors present in the model.

Results

BASE data were available from 4,326 building occupants in 100 study spaces/buildings. The overall response rate for the occupant questionnaire was 85%. Overall prevalence of the seven symptom outcome definitions in the entire survey population ranged from 4.2% for lower respiratory symptoms to 20.9% for upper respiratory symptoms. Prevalence of each outcome varied substantially among the 100 buildings.

The study population has been described elsewhere in more detail (Brightman and Moss 2000). Among the respondents, 66% were female, 61% were between the ages of 30 and 49, and 15% were current smokers. Respondents' job categories were: 35% professionals, 34% clerical, 17% managers, and 14% technical. Approximately 46% of respondents had less than a college degree, and 54% had at least an undergraduate degree.

Descriptive (univariate) analysis

We organized the risk factors at the building and study space levels into two categories: physical characteristics and pollutant sources. Table 1 lists the risk factors of initial interest.

Table 2 shows the risk factor variables after initial exclusion, combination, and recategorization, along with the number of buildings or study spaces in each category of the risk factor variables. The 50 risk variables are organized under the following headings (all pertain to test spaces unless noted): indoor materials (7 variables), cleaning (17 variables), pesticides (5 variables), special uses in study spaces (6 variables), special uses in buildings (4 variables), building characteristics (5 variables), and outdoor sources near buildings (6 variables). Almost all variable categories contained at least five buildings. Numbers for each variable may not add to 100 due to missing values.

Unadjusted (bivariate) analyses

Table 2 also shows bivariate associations with outcomes for the risk factor variables selected or created after univariate analyses, unadjusted for any confounding involving correlation with each other or with personal variables. We observed two primary patterns among some of the 50 risk factors assessed: 1) generally lower prevalence of most symptoms, or 2) generally higher prevalence of most symptoms, both including varying numbers of statistically significant differences. Other risk factors showed small associations in both directions with occasional significant changes in at most one symptom. We will not mention patterns of change that were generally around 10% or less.

Factors that were associated in unadjusted models to generally higher prevalence of most symptoms included: carpet greater than one year old as primary flooring, or no primary carpet, relative to carpet replaced within the prior year; cloth partitions, furniture, or paint greater than one year old, relative to these materials renovated within the prior year; office cleaning or dry mopping during occupied hours; vacuuming less frequently (weekly-to-monthly vs. daily); dry mopping more frequently; relatively infrequent application of interior pesticide, or especially with no available information on frequency, relative to no application; exterior pesticide application four or more months prior, relative to no application; any past interior pesticide applications, relative to no past applications, especially if four or more months prior; interior pesticide applications that include the test space; presence of a computer room; presence of loading docks; study spaces whose buildings contained smoking lounges elsewhere within the building (relative to spaces with no smoking allowed in the buildings); nearby heavy vehicular traffic or nearby emergency generators; and buildings constructed between 1946 and 1975 (relative to the oldest buildings, constructed before 1946).

Factors that were associated in unadjusted models to generally lower prevalence of most symptoms included: presence of systems furniture; less frequent wet mopping (weekly-tomonthly relative to none); exterior pesticide application daily to monthly, relative to no application; presence of a kitchenette in the study space; buildings in "other" neighborhoods, including industrial and agricultural neighborhoods, relative to those in residential neighborhoods; buildings with glass/metal curtain or "other" kinds of exterior walls, relative to masonry exterior walls; and the most recently constructed buildings (1976-1996, relative to the oldest buildings, constructed before 1946).

For each symptom outcome model, bivariate model outcomes determined which variables were included in initial risk selection models (not shown), using criteria described in Appendix 1. All risk factors then retained in each risk selection model were kept throughout the construction of final models for that outcome.

Adjusted analyses

Table 3 provides estimates from the final multivariate logistic regression/GEE models, along with the number of individuals and buildings included in each final model. The Hosmer-Lemeshow goodness-of-fit p-values for all final models produced by the basic algorithm had pvalues >0.05, without requiring additional alteration to improve fit.

Spaces with carpet older than one year as primary flooring, relative to those with carpets replaced during the prior year, had significantly increased prevalence of lower respiratory symptoms, with OR=1.87. Spaces with only primary flooring materials other than carpet, relative to spaces with newer carpet, had significantly increased prevalence of lower and upper respiratory symptoms, with ORs= 2.34 and 2.24, respectively. Spaces with furniture older than one year, relative to those with furniture replaced within the prior year, were associated with significant increases in eye and skin symptoms, with ORs of 1.42 and 2.06, respectively. Cloth partitions were not substantially associated with any symptom, and recent painting was not included in any final symptom model.

Any scheduled wet mopping was associated with some reduction in headache, including a significant reduction for weekly-to-monthly frequency, with OR=0.46. Weekly-to-monthly vacuuming, relative to daily, was associated with significantly increased prevalence of upper respiratory symptoms, eye symptoms, and headache, and marginally with skin symptoms, with ORs of 1.38, 1.30, 1.42, and 1.37, respectively. Use of window cleaner was associated with a significant reduction in upper respiratory symptoms, OR=0.72, and use of bathroom cleaner was associated with increased lower respiratory symptoms, OR=2.29. Application of exterior pesticide semiquarterly to annually, relative to none, was associated with a significant increase in upper respiratory symptoms, OR=1.44, but daily to monthly, or unscheduled applications, were not. Application of interior pesticides four or more months prior, relative to no past application, was associated with significant increases in upper respiratory symptoms, fatigue/difficulty concentrating, and headache, with ORs of 1.79, 1.70, and 1.57 respectively. Applications up to three months prior were associated with smaller increases in the same symptoms.

Among special uses, presence of a kitchenette was associated with significantly reduced fatigue/difficulty concentrating and marginally significantly reduced cough, with ORs of 0.70 and 0.75 respectively. Relative to masonry exterior walls, other exterior wall materials were mostly associated with substantial decreases in cough, eye symptoms, and fatigue/difficulty concentrating. For instance, glass/metal curtain walls were associated with significantly reduced ORs for cough and eye symptoms of 0.47 and 0.64. Relative to buildings in which smoking was completely prohibited, study spaces in which smoking was permitted in the test space were associated with increased skin symptoms, OR=1.84.

Discussion

The EPA BASE data allow the first broad assessment in U.S. office buildings of the associations between suspected indoor environmental risk factors and nonspecific symptoms in office workers. The present analysis primarily investigated factors not previously assessed for associations with symptoms: features or practices, not related to the ventilation system, that can be determined by inspection or interview and that may indicate contaminant sources correlated with symptoms.

. These exploratory analyses were intended to investigate associations between symptoms and a wide variety of potential sources, indoor or outdoor, of pollutants in the office environment, that could be ascertained from inspection or interview. Little prior investigation has been reported on associations between acute symptoms and this set of potential contaminant sources. While unadjusted estimates showed many of the investigated risk factors to have associations with most of the symptoms assessed, multivariate adjusted estimates showed many fewer associations. This was presumably because unadjusted estimates included associations better explained by other correlated risk factors. Still, several risk factors had statistically significant or nonsignificant but substantial associations with multiple symptoms. Others had associations with one symptom, which may have been due to chance. We consider ORs associated with categories containing five or fewer buildings, even if significant or large, to be too unstable for interpretation.

Carpets are sometimes considered potential sources for exposure to accumulated or amplified dust mites, microorganisms, and particles (Allermann, Wilkins et al. 2006), but they may also be "sinks" for these contaminants and, by collecting and retaining them, reduce related exposures. Prior studies have been inconsistent about whether carpets are risk factors for adverse health. For instance, studies have shown carpets to be associated with increased risk of asthma (Mohamed, Ng'ang'a et al. 1995; Jaakkola, Ieromnimon et al. 2006); decreased risk of asthma (Zock, Jarvis et al. 2002), respiratory symptoms (Skorge, Eagan et al. 2005; Trevillian, Ponsonby et al. 2005), and eczema (Palmer, Valinsky et al. 1999); or no effects on asthma (Voute, Zock et al. 1994). The BASE study is not ideal for investigating risks associated with carpet, as 91 of 100 study spaces had carpet as a primary floor covering. The reduced prevalence of lower and upper respiratory symptoms associated in the BASE study with presence of carpet, especially newer carpet, suggests a protective effect (if other unknown confounding factors do not explain this). This does not agree with some prior reports (Jaakkola, Parise et al. 2004). On the other hand, the findings suggest that any benefit may diminish over time, perhaps as the carpet inevitably accumulates particles, including fungi and allergens, with normal use and maintenance (Dybendal, Vik et al. 1989; Dybendal, Vik et al. 1990; Dybendal and Elsayed 1992; Cho, Reponen et al. 2006; Giovannangelo, Gehring et al. 2007). Unfortunately, the data did not include specific age of carpets older than one year.

We saw little other association between symptoms and different types of office furnishings or surface materials in multivariate models, except that the presence of older furniture was associated with increased prevalence of eye and skin symptoms. The different symptoms associated with less recently replaced carpets and furniture suggests a lack of a common underlying exposure or biologic mechanism. Findings here did not corroborate findings in some, but not all, prior studies by others of increased risk of symptoms or respiratory health effects

from presence of fleecy or high-surface-area materials such as carpets or cloth partitions (e.g., (Skov, Valbjorn et al. 1990; Jaakkola, Tuomaala et al. 1994; Jaakkola, Oie et al. 1999; Zock, Jarvis et al. 2002; Skorge, Eagan et al. 2005; Jaakkola, Ieromnimon et al. 2006)).

Office cleaning activities are intended to improve cleanliness and appearance of indoor surfaces; however, they may increase, immediately and for some time after cleaning, indoor levels of volatile organic compounds and airborne dust (Wolkoff, Schneider et al. 1998). We found no evidence in the BASE data that any specific kind of cleaning activity during work hours resulted in consistent increase in exposures causing any building-related symptoms. Regarding scheduled frequencies for specific types of cleaning, only two were associated with changes in prevalence of any symptom. Less frequently scheduled vacuuming was associated with increased upper respiratory, eye, headache, and skin symptoms. While the category of vacuuming "as needed or missing" was not associated with similar increases, this is not necessarily inconsistent, as the category included only a small number of buildings, including several with no information. The association found between any scheduled wet mopping and significant reductions in headache is difficult to interpret. Ninety-one BASE study spaces had carpet as the primary floor covering, which could not be wet-mopped. Only eight study spaces, however, were reported to have no wet mopping, presumably because bathroom floors were generally wet-mopped, as well as any secondary hard surfaces such as hallways. While the estimates might suggest that performing wet mopping of hard-surface floors in office spaces reduces risk of headache, perhaps due to removal of some contaminants, it is unclear whether this association with an activity in secondary spaces is meaningful.

Only one kind of cleaning product was associated in the BASE data with a symptom increase among office workers: bathroom cleaner was associated with increased lower respiratory symptoms. While this would be consistent with an irritant effect of a repeatedly used cleaning product in spaces that all workers are likely to enter, high average exposures would not be expected from repeated but short-term presence in a room in which a cleaning product had been previously applied. Moreover, it seems likely that all office buildings use some kind of bathroom cleaning products, whether or not reported in this study. Still, there is evidence that professional cleaners are at increased risk for asthma from exposure to cleaning products they use, especially bleach (Zock, Kogevinas et al. 2001; Jaakkola and Jaakkola 2006; Macaira, Algranti et al. 2007). The association of window cleaner with reduced prevalence of headache but not other symptoms may be a chance association.

The evidence for adverse acute effects on occupants of exterior pesticide application is not persuasive, as only relatively infrequent application was associated with some increase in just upper respiratory symptoms, and more frequent application had little association with that symptom. Frequency of interior pesticide application was not associated with symptoms in multivariate models. Although previous interior pesticide application, four or more months prior, was associated with increase in three symptoms, including upper respiratory, relative to no prior application, a more recent application was not associated with as large an increase. The evidence for symptoms resulting from exterior or interior pesticide applications in these office buildings is apparently inconsistent.

It is not clear why masonry exterior walls were associated with higher prevalence of cough, eye symptoms, and fatigue/concentration relative to glass/metal curtain walls and some other wall materials. One possible explanation might be a greater probability of water incursion through masonry walls into indoor spaces, due to the high permeability of masonry materials or the presence of cracks or deteriorated mortar. (For discussions of moisture problems related to masonry exterior walls, see http://epdweb.engr.wisc.edu/aecarticles/rsrc04.lasso and http://irc.nrccnrc.gc.ca/pubs/cp/wall_e.html.) That office spaces in which smoking was permitted had an increase only in skin symptoms is not consistent with current knowledge of the effects of secondhand smoke. We assume the finding is a result of confounding or chance (see discussion below). This finding also has limited practical implications, as tobacco smoking is allowed in increasingly fewer U.S. office buildings.

Limitations

The BASE study, although a large and unusually comprehensive collection of data from a representative set of U.S. office buildings, has many limitations for epidemiologic analyses aimed at understanding causes of building-related health effects. The study, designed around 1990, was conducted primarily to obtain normative data rather than to test specific *a priori* hypotheses. Many building features of current research interest cannot be investigated in these data because of insufficient representation or variation in the study buildings. In addition, the BASE study collected limited information on a large number of environmental characteristics of the study buildings, so the data often lack sufficient detail to answer current hypothetical questions. It is also inherently difficult to study environments as complex as large buildings. Although the BASE study contained responses from over 4,000 individual occupants of the study spaces, most environmental data can be analyzed only at the level of the 100 study spaces or buildings, providing limited variation for analysis of the environmental factors. Perhaps most important, the environmental reports from inspection, as well as the self-reported health outcome assessments used, are subjective and imprecise, and the resulting inaccuracies are likely to have biased estimates for any true risk factors toward the null (i.e., toward showing no association), obscuring true associations.

With respect to limitations in the analyses, many environmental factors of interest were too highly correlated to include in the same models, making it impossible to assess risks for some factors of interest while holding other closely related factors constant. Many factors of interest did not have sufficient variation in the study buildings to include in analyses. Finally, this analysis assessed many risk factor/symptom combinations, leading to the possibility of false positive associations occurring by chance alone (Rothman 1990). We consider the risk factor variables used in the analyses to be the 72 terms for potential risk factors included in initial bivariate models for seven outcomes. If no true underlying associations existed and all estimates were independent, chance alone would predict approximately 25 associations with p<0.05 (e. g, 72 x 7/20) in final models. Thus, given the 21 associations with p-values <0.05 in the final multivariate models, at least that many false positives would be expected. While this does not provide confidence in meaningful associations among the findings here, we suggest that the associations least likely to be false positives are those where a single risk factor is associated with a very large or small OR in adjusted models or with multiple biologically related symptom outcomes (e.g., upper respiratory symptoms with lower respiratory symptoms or cough, rather than, say, fatigue with skin symptoms), or where prior findings or biologic plausibility exist.

Many or all of the findings in this analysis, given the large number of risk factors and symptom outcomes investigated, may be due to chance. Findings from this study of most potential interest include: the increased prevalence of lower respiratory symptoms associated with older carpets relative to newer ones, and the increased prevalence of upper and lower respiratory symptoms associated with non-carpeted floors; increased eye and skin symptoms associated with older furniture; increased upper respiratory, eye, and skin symptoms and headache associated with less frequent vacuuming; and increased cough, eye symptoms, and fatigue/concentration difficulty associated with masonry exterior walls. These are all suggestive but preliminary findings. Replication of these results in other settings, with more precise measurements of exposure and response, would be necessary to confirm any of the associations reported initially in these analyses.

Appendix 1. Modeling procedures

All analyses were performed using SAS version 8 (SAS Institute Inc. 2002). We first identified all variables in the BASE data corresponding to risk factors of interest for this analysis: features or practices in buildings hypothesized to be sources of contamination. We used data from the specific test space studied in each building where available and appropriate; otherwise we used data applicable to each building. Additional steps in the analyses were as follows:

- (1) From univariate/descriptive analyses of potential risk variables, we excluded those with too many missing values (>10%), or insufficient variation in the key contrast (less than 5% of observations in any key category). We collapsed categories where appropriate, and in some cases created combined variables or indices that summarized risks from closely related or highly correlated variables, to create the initial set of risk factor variables. All risk variables used in models were dichotomous or categorical.
- (2) For each of the seven symptom outcomes, we performed bivariate analyses with the initial risk factor variables, retaining for further analyses those with at least moderate associations. For this we required an overall p-value ≤ 0.25 , or for multicategorical variables, either an overall p-value <0.25, a p-value <0.15 for any single term or category, or a Mantel-Haenzsel trend p-value of <0.15. The set of retained risk factors varied across the different outcome models.
- (3) For each symptom outcome, we then examined all risk variables remaining after step (2) together in a "risk selection" model, in order to identify and omit variables with no association with the outcomes when adjusted for other risk factors. We sequentially excluded the variable with the highest p-value, stopping when all p-values were <0.20. We also identified highly correlated risk variables, and combined, revised, or eliminated them as necessary.
- (4) To the reduced set of risk variables in each outcome model, we added potential confounding variables, personal or environmental. Potential confounders were added sequentially to the model, and retained if an addition changed the point estimate for any risk factor by at least 10%. Selection of confounding variables was not based on hypothetically predicted potential for confounding (e.g., gender is included as a confounder, although unlikely to be systematically related to sources of contamination).
- (5) We then reconsidered previously rejected risk variables, one at a time, for contribution to these expanded models, retaining any with a p-value ≤ 0.05 .
- (6) At this point, we examined the Hosmer-Lemeshow Goodness-of-Fit statistic. All pvalues were >0.05 in final models. (For any models with p-values ≤ 0.05 , we would have sequentially omitted the confounder with the highest p-value until the Goodness-of-Fit pvalue >0.05 .) The final models provide adjusted estimates, as odds ratios and 95% confidence intervals, for the strength of association between the risk variables and the symptom outcomes.
- (7) Using the set of final logistic regression models for each of the seven outcomes, we then imputed missing values on personal variables (but not environmental or building variables) using SAS Proc MI (4 iterations), and re-ran the final logistic regression models. Finally, we used General Estimating Equations (GEE) in SAS Proc Genmod to adjust for potential correlation of observations within each building.

References

- Allermann, L., C. K. Wilkins, et al. (2006). "Inflammatory potency of dust from the indoor environment and correlation to content of NAGase and fungi." Toxicol In Vitro **20**(8): 1522-31.
- Apte, M. G., W. J. Fisk, et al. (2000). "Associations between indoor CO2 concentrations and sick building syndrome symptoms in U.S. office buildings: an analysis of the 1994-1996 BASE study data." Indoor Air **10**(4): 246-57.
- Brightman, H. S. and N. Moss (2000). Sick building syndrome studies and the compilation of normative and comparative values. Indoor Air Quality Handbook. J. Spengler, J. M. Samet and J. F. McCarthy. New York, McGraw-Hill**:** 3.1-3.32.
- Cho, S.-H., T. Reponen, et al. (2006). "The effect of home characteristics on dust antigen concentrations and loads in homes." Science of The Total Environment **371**(1-3): 31-43.
- Dybendal, T. and S. Elsayed (1992). "Dust from carpeted and smooth floors. V. Cat (Fel d I) and mite (Der p I and Der f I) allergen levels in school dust. Demonstration of the basophil histamine release induced by dust from classrooms." Clin Exp Allergy **22**(12): 1100-6.
- Dybendal, T., H. Vik, et al. (1989). "Dust from carpeted and smooth floors. II. Antigenic and allergenic content of dust vacuumed from carpeted and smooth floors in schools under routine cleaning schedules." Allergy **44**(6): 401-11.
- Dybendal, T., H. Vik, et al. (1990). "Dust from carpeted and smooth floors--III. Trials on denaturation of allergenic proteins by household cleaning solutions and chemical detergents." Ann Occup Hyg **34**(2): 215-29.
- Giovannangelo, M., U. Gehring, et al. (2007). "Levels and determinants of [beta](1 --> 3) glucans and fungal extracellular polysaccharides in house dust of (pre-)schoolchildren in three European countries." Environment International **33**(1): 9-16.
- Jaakkola, J. J. and M. S. Jaakkola (2006). "Professional cleaning and asthma." Curr Opin Allergy Clin Immunol **6**(2): 85-90.
- Jaakkola, J. J., L. Oie, et al. (1999). "Interior surface materials in the home and the development of bronchial obstruction in young children in Oslo, Norway." Am J Public Health **89**(2): 188-92.
- Jaakkola, J. J., H. Parise, et al. (2004). "Asthma, wheezing, and allergies in Russian schoolchildren in relation to new surface materials in the home." Am J Public Health **94**(4): 560-2.
- Jaakkola, J. J., P. Tuomaala, et al. (1994). "Textile wall materials and sick building syndrome." Arch Environ Health **49**(3): 175-81.
- Jaakkola, J. J. K., A. Ieromnimon, et al. (2006). "Interior Surface Materials and Asthma in Adults: A Population-based Incident Case-Control Study." Am. J. Epidemiol. **164**(8): 742-9.
- Macaira, E. D., E. Algranti, et al. (2007). "Rhinitis and asthma symptoms in non-domestic cleaners from the Sao Paulo Metropolitan Area, Brazil." Occup Environ Med.
- Mendell, M. J., M. Cozen, et al. (2006). "Indicators of moisture and ventilation system contamination in U.S. office buildings as risk factors for respiratory and mucous membrane symptoms: analyses of the EPA BASE data." J Occup Environ Hyg **3**(5): 225- 33.
- Mendell, M. J., Q. Lei, et al. (2005). Estimated ventilation rates and work-related symptoms in U.S. office buildings -- the BASE Study. Indoor Air 2005: Proceedings of the 10th

International Conference on Indoor Air Quality and Climate, Beijing, China, Tsinghua University Press.

- Mendell, M. J., G. M. Naco, et al. (2003). "Environmental risk factors and work-related lower respiratory symptoms in 80 office buildings: an exploratory analysis of NIOSH data." Am J Ind Med **43**(6): 630-41.
- Mohamed, N., L. Ng'ang'a, et al. (1995). "Home environment and asthma in Kenyan schoolchildren: a case-control study." Thorax **50**(1): 74-8.
- Palmer, L. J., I. J. Valinsky, et al. (1999). "Environmental factors and asthma and allergy in schoolchildren from Western Australia." Eur Respir J **14**(6): 1351-7.
- Park, J. H., P. L. Schleiff, et al. (2004). "Building-related respiratory symptoms can be predicted with semi-quantitative indices of exposure to dampness and mold." Indoor Air **14**(6): 425-33.
- Rothman, K. J. (1990). "No adjustments are needed for multiple comparisons." Epidemiology **1**(1): 43-6.
- Seppanen, O. and W. J. Fisk (2002). "Association of ventilation system type with SBS symptoms in office workers." Indoor Air **12**(2): 98-112.
- Seppanen, O., W. J. Fisk, et al. (1999). "Association of ventilation rates and CO2 concentrations with health and other responses in commercial and institutional buildings." Indoor Air **9**(4): 226-252.
- Skorge, T. D., T. M. Eagan, et al. (2005). "Indoor exposures and respiratory symptoms in a Norwegian community sample." Thorax **60**(11): 937-42.
- Skov, P., O. Valbjorn, et al. (1990). "Influence of indoor climate on the sick building syndrome in an office environment." Scand J Work Environ Health **16**(5): 363-71.
- Trevillian, L. F., A. L. Ponsonby, et al. (2005). "Infant sleeping environment and asthma at 7 years: a prospective cohort study." Am J Public Health **95**(12): 2238-45.
- U.S. Environmental Protection Agency (2003). A standardized EPA protocol for characterizing indoor air quality in large office buildings. Washington, D.C., U.S. Environmental Protection Agency.
- Voute, P. D., J. P. Zock, et al. (1994). "Peak-flow variability in asthmatic children is not related to wall-to-wall carpeting on classroom floors." Allergy **49**(9): 724-9.
- Wolkoff, P., T. Schneider, et al. (1998). "Risk in cleaning: chemical and physical exposure." Sci Total Environ **215**(1-2): 135-56.
- Zock, J. P., D. Jarvis, et al. (2002). "Housing characteristics, reported mold exposure, and asthma in the European Community Respiratory Health Survey." J Allergy Clin Immunol **110**(2 Pt 1): 285-92.
- Zock, J. P., M. Kogevinas, et al. (2001). "Asthma risk, cleaning activities and use of specific cleaning products among Spanish indoor cleaners." Scand J Work Environ Health **27**(1): 76-81.

Table 1. Risk factors initially considered for analyses related to contaminants from buildings and occupied spaces

Risk Factors of Initial Interest	
Test Space-Level Factors	Building-Level Factors
Test Space Physical Characteristics: Floor area per workstation Distribution of workstations (e.g., open, partitioned, etc.) Primary wall finish (e.g., wallpaper, fabric, wallboard, wood paneling, etc.) Primary partition finishes	Building Physical Characterization: Age of building Location - urban/suburban/rural Neighboring land uses (e.g., agricultural, industrial, etc.) Exterior wall construction
Primary floor finishes (e.g., carpet, wood, other, etc.) Primary material of furniture workstations Primary material of moveable furniture workstations	Building-Level Pollutant Sources: Outdoor contaminant sources Smoking policy Renovation frequency Cleaning materials and storage location Trash storage ¹
Test Space-Level Pollutant Sources: Smoking policy Recent renovations ¹ Cleaning frequencies (e.g., general cleaning, dry mopping, wet mopping, vacuuming, $etc.$) ¹ Time of cleaning 2 ٠ Cleaning materials and storage ² Trash storage ¹ Special use areas (e.g., with special processes such as print shops, graphic arts, labs, etc.) ^{1,2}	Pesticide use ¹ - internal and external Pesticide use - days since last application Pesticide use - location of application Special use areas (e.g., with special processes such as print shops, graphic arts, labs, $etc.$) ¹

¹ The following risk factors were excluded before bivariate models because of missing data, inadequate variation, or inconsistent information, and thus were never evaluated for associations with symptoms: trash storage, pesticide storage, type of pesticide used, special use: restrooms, presence of dedicated vents or exhausts in special use areas, recent roof renovation, type of vacuum (standard/HEPA).

² The following variables were excluded from all outcome models after bivariate analyses: Vending room in test space, storage of cleaning materials in test space.

Table 2. Unadjusted odds ratios (OR) and 95% confidence intervals (CI) for associations between occupant symptoms and contaminants related to the building or indoor space, in U.S. office buildings in the BASE study, 1994-1998

* P-value <0.05 1 schedule for typical office cleaning such as straightening, tidying, and dusting

² "Other" neighboring land uses included agricultural and industrial.

³ "Other" exterior wall materials included exterior insulation finish; siding on frame; metal building system; stucco exterior; aluminum panels over honeycomb insulation; steel frame, styrofoam and stucco; and quartzite blocks.

Table 3. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs), from logistic regression models¹ with generalized estimating equations, for associations between occupant symptoms and risk factors for contaminants from buildings or indoor spaces in U.S. office buildings in the BASE study, 1994-1998

* P-value ≤ 0.05

 1 For each of the seven symptom outcomes, all potential risk factors in this Table were included simultaneously in one model, along with confounding variables selected during model construction. Potential confounding variables included environmental variables (temperature, humidity, ventilation rate, occupant density, area per operable window, season of study) and personal variables (gender, age, education, smoking status, asthma, mold allergy, dust allergy, eczema, hay fever, type of workstation, comfort of chair, satisfaction with work station, job satisfaction, job demand, job conflict, hours worked per week, photocopier use, hours working at a computer, and years worked in building).