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## **Quantitative relationship of sick building syndrome symptoms with ventilation rates**

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### **Abstract**

Data from published studies were combined and analyzed to develop best-fit equations and curves quantifying the change in sick building syndrome (SBS) symptom prevalence in office workers with ventilation rate. For each study, slopes were calculated, representing the fractional change in SBS symptom prevalence per unit change in ventilation rate per person. Values of ventilation rate, associated with each value of slope, were also calculated. Linear regression equations were fitted to the resulting data points, after weighting by study size. Integration of the slope-ventilation rate equations yielded curves of relative SBS symptom prevalence versus ventilation rate. Based on these analyses, as the ventilation rate drops from 10 to 5 L/s-person, relative SBS symptom prevalence increases approximately 23% (12% to 32%), and as ventilation rate increases from 10 to 25 L/s-person, relative prevalence decreases approximately 29% (15% to 42%). Variations in SBS symptom types, building features, and outdoor air quality may cause the relationship of SBS symptom prevalence with ventilation rate in specific situations to differ from the average relationship predicted in this paper.

### **Keywords**

*Association, Health, Quantification, Sick building syndrome, Symptoms, Ventilation rate*

### **Practical implications**

On average, providing more outdoor air ventilation will reduce prevalence rates of SBS symptoms. However, given the costs of energy use, including increased risks of climate change, it is important to balance the benefits and risks of increased ventilation. This paper provides initial estimates of how the incremental health benefits per unit of increased ventilation diminish at higher levels of ventilation.

### **Introduction**

Sick building syndrome (SBS) symptoms are health symptoms, such as eye, nose, or throat irritation, headache, and fatigue, that are associated with occupancy in a specific building. SBS symptoms do not implicate specific diseases or exposures; however, there is considerable evidence that their prevalence and severity are affected by indoor environmental conditions as well as by psychosocial conditions (Mendell and Fisk 2007). Numerous experimental and cross-sectional studies have investigated the associations of the prevalence rates of sick building syndrome (SBS) symptoms with office building ventilation rates. Studies have typically used the

odds ratio or relative risk to indicate strength of the association of SBS symptom prevalence with ventilation rates and have generally controlled via the study design or analysis method for several potential confounding factors. Although ventilation rates, SBS symptom types, and findings have varied among studies, most studies have found that occupants of office buildings with lower rates of ventilation (outdoor air supply) per person have statistically significantly higher prevalence rates of SBS symptoms (Seppanen et al. 1999; Wargocki et al. 2002). For this paper, we have analyzed data to develop best-fit equations quantifying the change in relative SBS symptom prevalence with ventilation rate. A prior similar analysis quantified the relationship of relative work performance with ventilation rate (Seppanen et al. 2006). By quantifying these and other relationships between IAQ factors and health or performance outcomes, we seek to provide tools that better inform decisions about building design or operation.

## **Methods**

### **Overall approach**

The overall approach employed in this study is indicated by the following steps:

- establishment of criteria for input data;
- searching for and obtaining data (i.e., documents with data) satisfying the criteria;
- extraction and analyses of applicable data from each accepted source to provide slopes (changes in SBS symptom prevalence divided by the average prevalence divided by changes in ventilation rate) and corresponding central values of ventilation rate;
- statistical analyses to fit equations to the resulting data;
- integration of the best-fit equations to provide equations for the change in relative SBS symptom prevalence versus ventilation rate.

### **Selection of input data**

This analysis started with data provided in technical papers or reports from numerous specific research studies performed in office buildings. We used data from all studies that met our criteria, regardless of the findings. Useable papers must have provided the odds ratio or relative risk for the change in symptom prevalence or intensity with change in ventilation rate, the fractional change in symptom prevalence or intensity with change in ventilation rate, or symptom prevalence or intensity data at different ventilation rates. The magnitude of the change in ventilation rate per person must be provided or quantifiable from the study data. The number of study subjects must be provided to enable weighting of each study in a statistical analysis. We accepted data from articles in refereed archival journals, papers published in conference proceedings, and reports from research institutions. When multiple papers reported on the same study, the paper with results in the format best suited to our analyses was selected.

Ideally, all of the data used in our analyses would come from studies with identical methodologies and SBS symptom definitions. In practice, however, the number of studies providing suitable data was limited and these studies have used a range of research methods and SBS symptom definitions. Consequently, in order to have enough data for analyses, we accepted the results from a variety of study types and with a range of SBS outcome definitions. We accepted data from both cross sectional and experimental studies as long as the study design or analyses controlled for potential confounding by gender, HVAC type, and temperature, and the

subjects were “blinded” (not informed) with respect to ventilation rates. When the analysis did not control for temperature, we required that the temperature at the different ventilation rates be the same within 1 °C. We required that data come from studies of office buildings with office workers as the subjects and that symptom data be from questionnaires completed by the subjects. Within the available subjective data on SBS symptoms, there remained a wide range in data types including various symptom types (e.g., eye irritation, skin irritation, headache, difficulty breathing, etc.). Although the ventilation-symptom relationship might vary among symptom types, given our objective of developing an estimate of the average quantitative ventilation-symptom relationship, and given the paucity of data, all of these types of symptoms were accepted. However, we excluded environmental perception outcomes (e.g., stuffy air) which were sometimes treated as “symptoms” by authors of papers. We accepted data from analyses with symptoms grouped into categories, e.g., mucous membrane symptoms. Symptom prevalence data were accepted regardless of the recall period (e.g., past week, past month).

The methods used to measure ventilation rates varied among studies. We accepted data based on the following measurement methods:

- A. use of flow hoods or similar methods to measure supply air flow rates to rooms or zones of buildings with HVAC systems that supply 100% outdoor air;
- B. measurement of carbon dioxide concentrations in occupied spaces and use of mass balance equations to calculate ventilation rates;
- C. use of tracer gas decay methods or other tracer methods; and
- D. use of anemometers to measure air flow rates through the outdoor-air intake sections of HVAC systems with 100% outdoor air supply.

### **Data analysis procedures**

There were three basic steps to the data analysis process. First, the data in the original papers were processed to determine normalized slopes (fractional changes in SBS symptom prevalence divided by changes in ventilation rate) and the corresponding central values (i.e., midpoints) for the ventilation rate interval were calculated. Second, a statistical model was used to fit equations to the resulting pairs of numbers (symptom change slopes and midpoint ventilation rates). Third, these equations were integrated and used to calculate equations of relative SBS symptom prevalence versus ventilation rate. The protocols used in each step are described below.

The methods employed to calculate slopes, i.e., changes in SBS symptom prevalence divided by associated changes in ventilation rates, varied with the form of the original data. However, the goal was a normalized slope defined as follows

$$S = \left( \frac{P_H - P_L}{P_H} \right) / (V_H - V_L) \quad (1)$$

where  $S$  is the slope,  $P$  is SBS symptom prevalence,  $V$  is ventilation rate per person, and subscripts  $H$  and  $L$  refer to the high and low ventilation rate conditions, respectively. As defined above, the slope is positive if the SBS symptom prevalence increases with an increase in ventilation rates, although the opposite is usually true in practice.

Two studies used symptom intensity, not prevalence, as the outcome. For these two studies, the calculated normalized slope represents the normalized change in symptom intensity divided by the corresponding change in ventilation rate. Intensity outcomes were not converted to estimates of prevalence outcomes.

The slope at the midpoint ventilation rate between  $P_H$  and  $P_L$  is

$$S_{mid} = \left( \frac{P_H - P_L}{P_{mid}} \right) / (V_H - V_L) \quad (2)$$

where the subscript “*mid*” refers to a value at the midpoint ventilation rate.

The midpoint ventilation rate  $V_{mid}$  is

$$V_{mid} = (V_H + V_L) / 2 \quad (3).$$

The point estimate of  $S_{mid}$  at the midpoint of ventilation rates in each study is calculated as shown in equation 4. The equation is based on the fact that, assuming a locally approximately linear relationship between SBS symptom prevalence  $P$  and ventilation rate from  $V_L$  to  $V_H$ , the prevalence at the midpoint ( $P_{mid}$ ) equals  $P_H \cdot [1 - 0.5 \cdot (V_H - V_L) \cdot S]$ .

$$S_{mid} = \frac{S}{1 - [0.5 \cdot (V_H - V_L) \cdot S]} \quad (4)$$

Some experimental studies provided symptom prevalence data for the high and low ventilation rate conditions. In these cases, equation 1 was used directly to calculate  $S$ . Some studies provided values of relative risk for SBS symptoms. The relative risk  $RR$  is related to symptom prevalence as follows

$$RR = P_L / P_H \quad (5)$$

From algebraic manipulations

$$1 - RR = (P_H - P_L) / P_H \quad (6)$$

thus, from equation 2,

$$S = (1 - RR) / (V_H - V_L) \quad (7)$$

Some studies provided adjusted odds ratios for SBS symptoms. The odds ratio ( $OR$ ) is defined as follows

$$OR = \frac{P_L}{1 - P_L} \bigg/ \frac{P_H}{1 - P_H} \quad (8)$$

For symptom prevalence rates less than approximately 15%, the  $OR$  is numerically very close to the  $RR$ ; however, the values of these two parameters diverge as symptom prevalence increases. We used adjusted odds ratios and reported crude (unadjusted) values of SBS symptom prevalence to estimate values of  $RR$ .

$$RR = OR \frac{(1 - P_L)_C}{(1 - P_H)_C} \quad (9)$$

where the subscript  $C$  denotes the use of crude (unadjusted) symptom prevalence rates. Equation 9 is not applicable for case-control data; therefore, the odds ratios from one study (Stenberg et al. 1994) were not converted to risk ratios.

The data from experimental studies typically included values of ventilation rates  $V_H$  and  $V_L$  for direct use in equations 1, 3, 6 and 9. Cross sectional studies often provided ranges or intervals of ventilation rate associated with the values of  $OR$ . If suitable data were available, the average ventilation rate for buildings in each range was calculated. When such data were not available, we used the midpoint of the range as an estimate of the average.

After the original data were processed to produce values of  $S_{mid}$  and  $V_{mid}$ , weighted linear regressions with and without general estimating equations (GEE) were performed using SAS 9.1 for Windows to produce linear equations fitted to the data. For the linear regression fit without GEE, a 95% confidence band was determined using Stata 8.2. The original studies varied in sample size. If all of the studies had the same underlying “true” relationship, the slopes from each study should ideally be weighted by their precision, which is inversely proportional to variance. However, since variance information was not provided for many of the studies, regression weighted by sample size was chosen as the best alternative, because in general the higher the sample size, the lower the variance. However, study differences other than sample size, such as differences in study methods and types of symptoms, likely contributed to scatter among the slopes. To prevent the largest studies from having excessive influence on the regression, we also developed a fit to the data with the square root of sample size as the weighting factor. Analytic weights were used in both cases.

Most studies had multiple results, e.g., from use of multiple ventilation rate categories or symptom types. Multiple results obtained from the same study have the potential to be highly correlated. The GEE routine accounts for the possible within-study correlations of outcomes. An exchangeable covariance structure was assumed. For our base case analysis, we selected the regression using GEE with weighting of studies by square root of sample size.

To derive curves of relative SBS symptom prevalence (RP) versus ventilation rate, we used the following equation, derived in the appendix of (Seppanen et al. 2006). Setting the lower limit of the integration to 10 forces RP to unity with a ventilation rate of 10 L/s-person.

$$RP = P(V) / P(V = 10) = \exp \left[ \int_{10}^V S_{mid} dv \right] \quad (10)$$

## Results

Table 1 provides summary information on the original studies with input data in a form suitable for use in these analyses.

Figure 1 shows the normalized slopes plotted versus midpoint ventilation rates and the fits to these data. There is considerable scatter in the data, but most slopes are negative indicating a decrease in SBS symptom prevalence with increased ventilation rate. As illustrated in the figure, the results from a technical report (Mendell et al. 2005) not reported in a journal article are not distinct from other results. With one exception, the five data points (from two studies) with SBS symptom intensity rather than prevalence as the outcome (Tham 2004; Wargocki et al. 2004) fall within the bounds of other results; however, by themselves, the studies with symptom intensity outcomes indicate no clear effect of ventilation rate on symptom prevalence. The method used to weight the studies had only a modest impact on the resulting fit to the data. The 95% confidence band for our base case (without GEE) excluded a slope of zero for ventilation rates between 5 and 24 L/s-person, reflecting, in part, the relative scarcity of data at high midpoint ventilation rates. The overall mean slope weighted by root sample size (not shown) is -0.027 with 95% CI (-0.036, -0.017); thus, the mean slope is statistically significantly negative. Note that this mean slope is the weighted mean “y” value in Figure 1, not the mean slope of the line in Figure 1.

Table 1. Study characteristics

Reference	Study Type	No. of Subjects	SBS Symptom Categories	Symptom Recall Period	No. of Data Points
(Jaakkola et al. 1991)	CS	80-484	Symptom Score	1 week	9
(Jaakkola et al. 1994)	Ex	75	Al, Cn, Ey, He, Mu, Na	1 day	6
(Jaakkola and Miettinen 1995)	CS	176, 294	Cn, Ey, He, Na	1 year	8
(Mendell et al. 2005)	CS	1160-1306	Lr, Mu	4 weeks	12
(Menzies et al. 1993)	Ex	1087	An	1 day	1
(Stenberg et al. 1994)	CC	229, 233	SBS case	3 month	2
(Tham 2004)	Ex	56	He	current time	1
(Wargocki et al. 2004)	Ex	17	Ey, Na	current time	4

Study types: CS = cross sectional; Ex = experimental, CC = case-control

Symptom categories: Al = allergy, An = any; Cn = central nervous system; Ey = eye; He = headache; Mu = mucosal; Na = nasal; SBS case = subjects are SBS cases (with symptoms) versus controls without symptoms

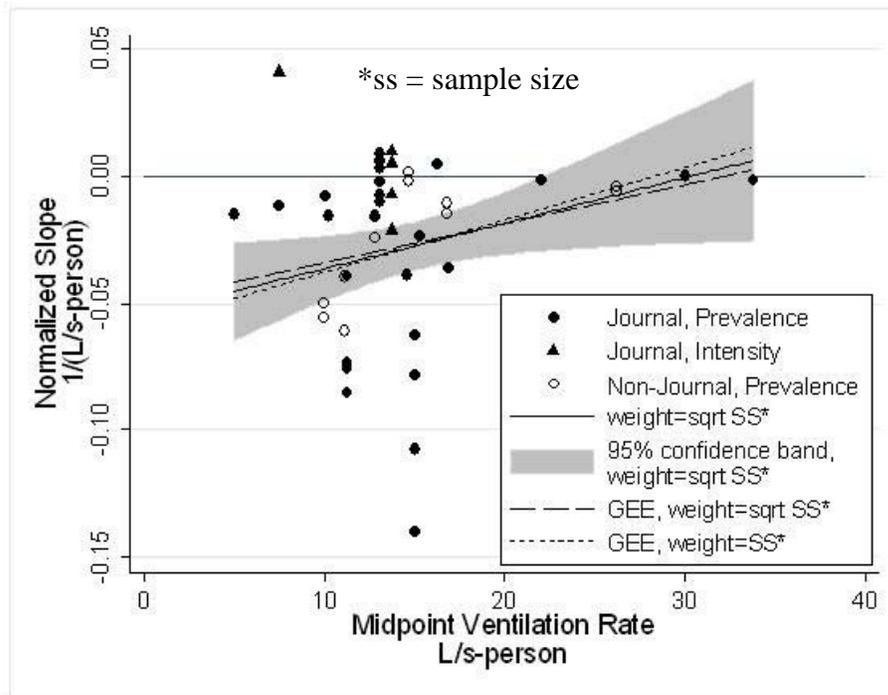


Figure 1. Normalized slopes plotted versus midpoint ventilation rates and curves fitted to the data.

Figure 2 shows the estimated curve of relative SBS symptom prevalence (RP) plotted versus ventilation rate with RP equal to unity at a ventilation rate of 10 L/s-person, which is the minimum required ventilation rate in some codes and standards. The curve determined from the GEE-based normalized slope curve is visually indistinguishable from the illustrated curve determined without GEE. The RP increases from 1.0 to approximately 1.23 (1.12 – 1.32) [95% confidence interval] as the ventilation rate drops from 10 to 5 L/s-p. RP decreases from 1.0 to approximately 0.71 (0.58 – 0.85) as ventilation rate increases from 10 to 25 L/s-person. At higher ventilation rates, the statistical uncertainty in RP becomes large relative to the estimated deviation from unity. Interpretation of Figure 2 may be facilitated by the following application example. Consider a situation in which the SBS symptom prevalence is 20% when the ventilation rate is 10 L/s-person. Based on the RP curve in Figure 2, one would predict an SBS symptom prevalence of 24.6% (20% times 1.23) with 5 L/s-person of ventilation and a symptom prevalence of 14.2% (20% times 0.71) with 25 L/s-person of ventilation.

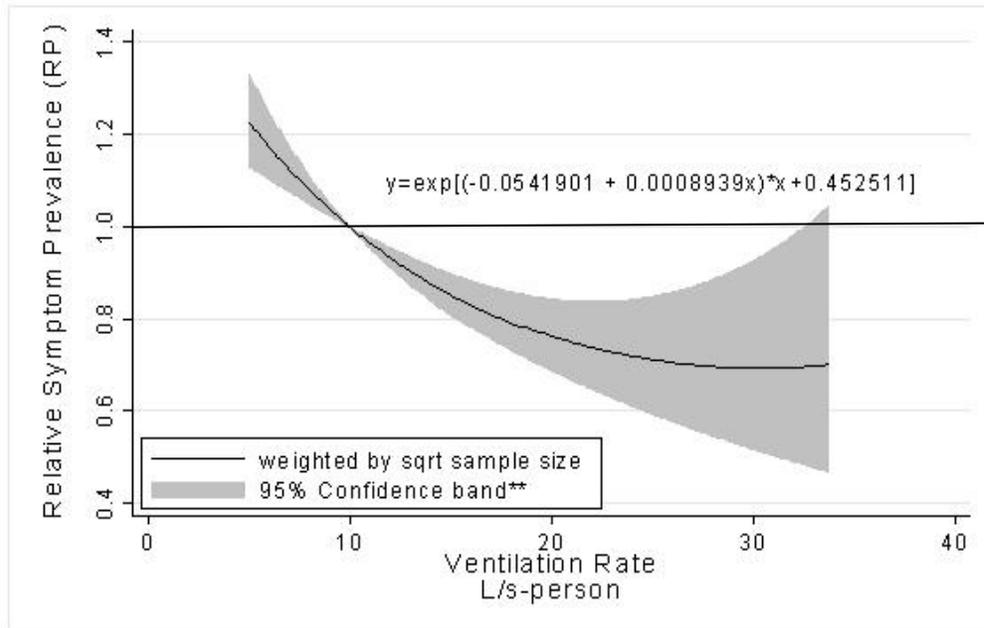


Figure 2. Estimated relative SBS symptom prevalence versus ventilation rate. \*\*The 95% confidence band is based on the definite integral of the 95% confidence bands for the curve of normalized slope versus midpoint ventilation rate.

The results depicted in Figures 1 and 2 do not differentiate among types of SBS symptoms. Figure 3 plots normalized slopes versus ventilation rates for four categories of SBS symptoms. For all symptom categories, a substantial majority of the normalized slopes are negative indicating a decrease in symptom prevalence rate with increased ventilation rate. On average, normalized slopes are smaller from the studies that used “any symptom,” “symptom score,” or “symptom case status” as the metric of symptom prevalence. The trend toward smaller normalized slopes with increased ventilation rates that is evident in Figure 1, when all symptom types are pooled, is not evident for the individual categories of symptoms except potentially for the lower respiratory symptom category. We judged the data too limited to warrant separate analyses for each category of symptoms.

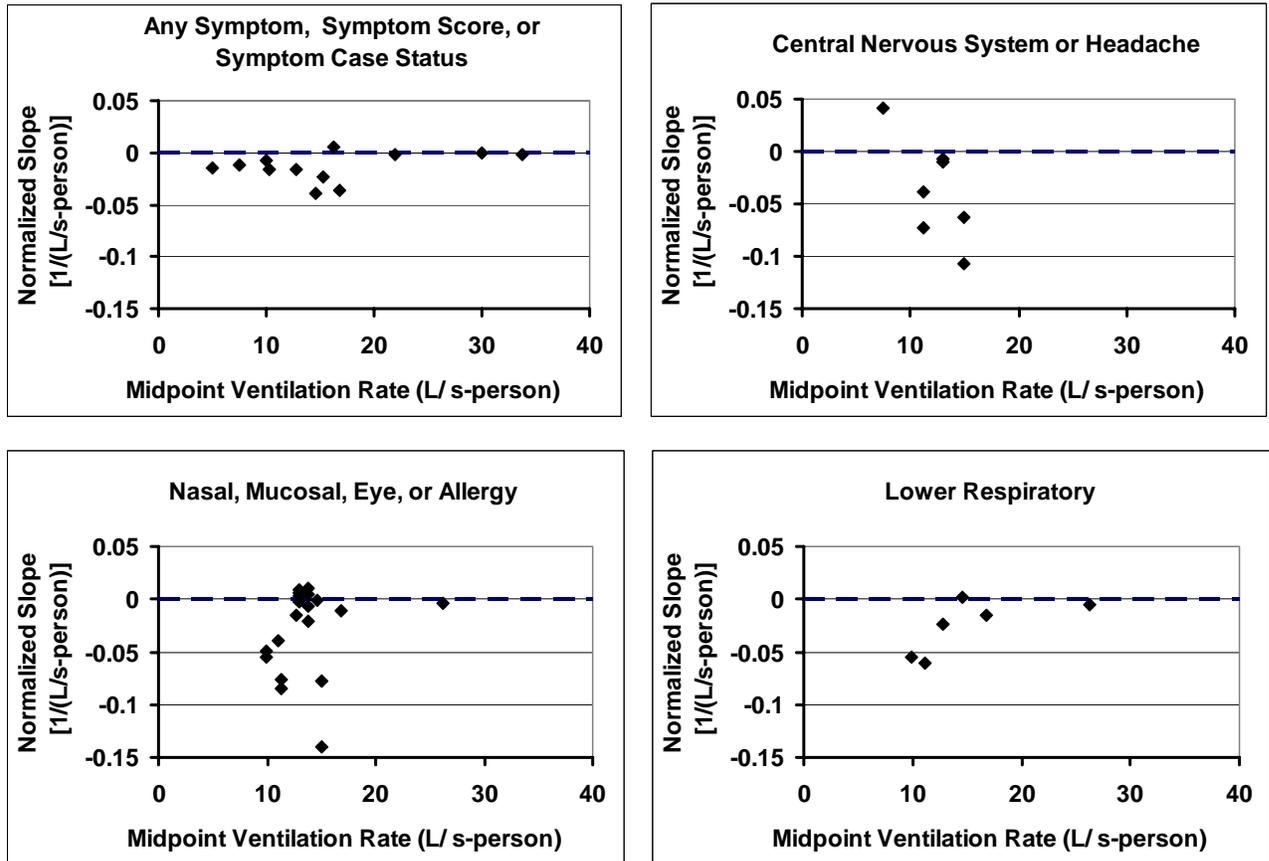


Figure 3. Normalized slopes versus midpoint ventilation rates for four symptom categories.

### Discussion

Although prior critical reviews of the literature have concluded that lower ventilation rates are associated with higher SBS symptom prevalence rates (Seppanen et al. 1999; Wargocki et al. 2002), to the best of our knowledge this paper presents the first systematic analyses of published data to produce a quantitative estimate of how SBS symptoms vary with ventilation rates. The analyses indicate that ventilation rates may have a considerable influence on symptom prevalence. For example, with a factor of two decrease in ventilation rate starting from a ventilation rate of 10 L/s-person (the minimum required value in some codes and standards), the estimated increase in symptom prevalence is approximately 23%. Similarly, with a doubling of ventilation rate from 10 to 20 L/s-person, the estimated decrease in symptom prevalence is approximately 24%. The analyses also suggest that, on average, increases in ventilation rates

above 25 L/s-person will not substantially reduce SBS symptom prevalence although the uncertainty of our estimates are high in this ventilation-rate range.

It is useful to consider whether the curves in Figures 1 and 2 have a shape consistent with general expectations. Our general hypothesis is that increased ventilation rates cause a decrease in indoor concentrations of indoor-generated air pollutants and that the decrease in pollutant concentrations causes a reduction in SBS symptoms via poorly understood mechanisms. With respect to the reduction in indoor pollutant concentrations, from mass balance calculations we know that the benefits (concentration decreases) per unit increase in ventilation rate diminish as ventilation rates get higher. We do not however, have more than a minimal understanding of how symptom prevalence is likely to vary with pollutant concentrations, e.g., is the relationship linear?, logarithmic?, is there a threshold?, etc. Given the relationship of ventilation rates with pollutant concentrations and an assumed linear or supra-linear increase in symptom prevalence with indoor pollutant concentration, one would expect larger values of  $S_{mid}$  at lower ventilation rates, which is roughly consistent with the results in Figure 2. However, with these assumptions,  $S_{mid}$  should become nearly constant, remain slightly negative, and approach zero at high ventilation rates. The linear equation fitted to the slope data is not able to match this expected behavior. With the same assumptions, one would expect the curve of  $RP$  to flatten out at high ventilation rates but always stay below unity. The curve in figure 3 has this expected shape.

The analyses presented here have several important limitations. The amount of original data available in a useable form was quite limited. We identified only eight useable studies, yielding only 43 data points. Because of the limited data, we did not perform distinct analyses for different types of SBS symptoms. In actuality, the relationship of ventilation rates with SBS symptoms may vary with symptom type as suggested by Figure 3. In addition, one would expect the relationship of SBS symptom prevalence with ventilation rate to vary depending on the strength of indoor pollutant sources, the levels of outdoor air pollution, and other factors. For example, in buildings with high indoor pollutant source strengths ventilation rates may have a larger impact on SBS symptom prevalence rates than in buildings with weak indoor pollutant sources. Thus, the present paper provides only an estimate of the average relationship.

Another limitation is that there is no *a priori* justification for using a linear equation, as opposed to any other type of equation, to fit the slope and ventilation-rate data. If we knew how SBS symptom prevalence rate was affected by indoor pollutant concentrations, a theoretical form for the best-fit equation could be derived; however, we have no strongly supported theoretical model or empirical data relating pollutant concentrations with SBS prevalence rates. If other types of equations were fitted to the data, the final curves of  $RP$  versus ventilation rate might differ significantly from those shown in figure 2.

Because precision estimates were not available from all of the original studies, we performed a weighted fit to the normalized slope data using the square root of sample size as the weighting factor. The curves in Figure 2 show that weighting by sample size and by square root of sample size resulted in very similar curves fitted to the normalized slope data. The curve shown in Figure 2 is almost unchanged when the weighting factor is changed to sample size.

A majority of the studies estimated ventilation rates in some or all buildings or spaces from measured air flow rates. These air flow rate measurements do not account for ventilation by air infiltration, thus, one would expect total ventilation rates in the study buildings to exceed the reported values. This bias is likely to have shifted the estimated curve of relative performance toward lower ventilation rates, resulting in underestimation of benefit at any specific ventilation rate. Insufficient data were available to quantify the magnitude of this effect.

The reported SBS symptom prevalence rates in the original studies ranged from 3% to 44% in the cross sectional or experimental studies and equaled 50% in the one case-control study. The RP curve in Figure 2 should not be applied to situations with symptom prevalence rates outside of these bounds.

As in most reviews and meta-analyses, our findings may also have been affected by publication bias – the tendency for studies without significant findings to less often result in publications. Publication bias would cause our predicted curve of RP versus ventilation rate to be steeper than the true curve, resulting in overestimation of symptom benefits from increased ventilation.

Given all these limitations, it is clear that considerable uncertainty remains with respect to the quantitative relationship between SBS symptoms and ventilation rates. Despite this uncertainty, we believe that our current estimates of this relationship are much preferable to having no quantitative estimates. Consequently, we hope that these quantitative estimates will be considered a valuable input for decision making about appropriate values of minimum ventilation rates in office buildings. However, decisions about minimum ventilation rates should also consider, as benefits of increased ventilation, what is known about the influence of ventilation rates on work performance (Seppanen et al. 2006), communicable respiratory disease, and perceived indoor air quality (Seppanen et al. 1999; Wargocki et al. 2002), and as costs of increased ventilation, what is known about the increased energy consumption required and the resulting greenhouse gas emissions.

## **Conclusions**

Systematic analyses of available data suggest that ventilation rates have a considerable influence on SBS symptom prevalence. The analyses indicate that the average prevalence of SBS symptoms increases by approximately 23% as the ventilation rate drops from 10 to 5 L/s-p and decreases by approximately 29% as ventilation rate increases from 10 to 25 L/s-person. These estimates should be valuable inputs for decisions about appropriate minimum ventilation rates in office buildings. Experimental studies assessing how changes in ventilation rates influence SBS symptom prevalence rates are highly desirable to enable testing and refinement of the estimates provided in this paper, and to better document a causal relationship.

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05CH11231, to support EPA's IAQ Scientific Findings Resource Bank. Conclusions in this paper are those of the authors and not necessarily those of the U.S. EPA.

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