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4 **A longitudinal study of ventilation rates**
5 **in California office buildings and self-reported occupant outcomes including respiratory**
6 **illness absence**
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List of Abbreviations

ASHRAE American Society of Heating, Refrigerating
and Air-Conditioning Engineers

BA Bay Area

CO₂ carbon dioxide

CV Central Valley

cfm cubic feet per minute

GEE generalized estimating equation

HZEB Healthy Zero Energy Building;

HVAC heating, ventilating, and air-conditioning

IRR incident rate ratio

IAQ indoor air quality

MERV Minimum Efficiency Reporting Value

1	OR	odds ratio
2	parts per million	ppm
3	T	temperature
4	RH	relative humidity
5	SBS	sick building syndrome
6	SC	South Coast
7	VR	ventilation rate

Abstract

248 words vs.250 max

Background – Limited evidence has associated lower ventilation rates (VRs) in offices with higher illness-related absence rates.

Methods – We studied spaces in office buildings, selected without knowledge of their VRs, in three California climate zones. In each study space, real-time logging sensors measured carbon dioxide and thermal parameters for one year. Web-based surveys every three months collected data on occupants' health outcomes. Using multivariate models, relationships were assessed between CO₂ concentrations, or VRs estimated from CO₂, and adverse occupant outcomes including respiratory infections and illness absences. For all outcomes, positive associations were hypothesized with higher CO₂ levels (and negative associations with higher VRs).

Results – Low survey response limited sample size and study power. In the 16 study spaces, CO₂ concentrations were uniformly low over the year, and most estimated VRs ranged from twice to nine times the California office minimum VR standard (7 L/s or 15 cfm per person). Primary CO₂ and VR metrics had no statistically significant relationships with occupant outcomes.

Conclusions–Within the observed range of uniformly low CO₂ and high VRs (mostly 16-42 L/s per person), little variation in contaminant concentrations would be expected, which would explain lack of relationships with occupant outcomes. These high VRs resulted partly from frequently used energy-saving “economizer” cycles in moderate California climates, but VRs at other times also substantially exceeded required VRs. These findings suggest, consistent

1 with theory, that within a higher VR range, increased VRs do not reduce respiratory illness.

2 Further studies are needed to better characterize such relationships.

3

4

5 **Keywords**

6 ventilation rate; indoor air quality; illness absence; respiratory illness

7

1.0 Background

Indoor air pollutants in office buildings, which may cause adverse effects in occupants, can be emitted by the buildings and their contents, including furniture, equipment, and the occupants themselves [1]. Outdoor air brought into offices by mechanical ventilation systems is the primary means used to control levels of indoor-generated pollutants. (Source control or air cleaning can also be used to control indoor air pollutants, some of which are best removed by means other than outdoor air ventilation.) Heating or cooling the introduced outdoor air to comfortable indoor levels requires increased energy as VRs increase. Adverse human outcomes of current potential concern in setting minimum standards for commercial VRs include building-related symptoms, infectious respiratory disease, asthma exacerbations, illness-related work absence, reduced work performance, and poor perceived air quality [1], although most of these are not considered in current standards.

Standards for minimum VRs in commercial buildings historically have been based on subjective acceptability of air quality, assessed in laboratory studies that considered occupants to be the only pollutant sources. More recently, standards have considered, to a limited extent, research on how VRs affect prevalence of “sick building syndrome” (SBS) symptoms. SBS symptoms, including symptoms that may be irritant or allergic in origin, have been used extensively as a measure of health-related outcomes in offices. Chemical and non-infectious biological pollutants indoors may cause irritation, allergies, or dissatisfaction with indoor air quality. Lower VRs have been associated with elevated prevalence and intensity of SBS symptoms [2, 3]. Research now suggests that VRs elevated above the current commercial ventilation standards would further

1 reduce SBS symptoms [1, 3, 4], and that satisfaction with perceived air quality in most office
2 buildings is lower than desired, even with VRs at the current standard [5, 6]. It is not known if
3 SBS symptoms can be severe enough to contribute to illness-related absence.

4
5 Additional evidence suggests that VRs are associated with other effects in occupants, including
6 communicable respiratory disease and illness-related absence [1]. Illness absence from work may
7 be related to respiratory infections, asthma, allergies, gastrointestinal infections, or other disease,
8 and can serve as an indicator of health effects sufficiently severe to miss work. Building
9 occupants can emit infectious respiratory agents that cause illness in other occupants [7]. The
10 primary hypothesis underlying this study is that lower VRs in office buildings, as indicated by
11 higher measured carbon dioxide (CO₂) concentrations, would lead to greater indoor air
12 concentrations of agents causing infectious respiratory disease, which would lead to higher rates
13 of illness absence in the occupants. This hypothesis is supported by prior findings in a variety of
14 indoor settings, as summarized by Li et al. [7] and Sundell et al. [1]. Various findings are
15 consistent with this hypothesis, in offices [8] [9] and other indoor settings [10-12][13-15].

16
17 Some studies, however, have found no changes in health effects with changes in VR within a
18 high range of VRs; e.g., for respiratory infections, [16] and for symptoms [17]. This fits with
19 theoretical predictions that at higher VRs, concentrations of indoor-generated pollutants are not
20 much reduced by further increased VR [3]. A range of high ventilation rates within which further
21 increases would not be expected to provide further health benefits for occupants has not been
22 defined, and such a range would vary by indoor contaminant sources and specific occupant
23 endpoints.

1
2 This project was part of the Healthy Zero Energy Building (HZEB) Study, intended to provide
3 data on costs and benefits of decreasing or increasing minimum VR standards, to help support
4 evidence-based and energy efficient but health-protective ventilation standards for commercial
5 buildings in California. In setting energy-conscious VR standards, adverse effects on occupants
6 from inadequate ventilation can be considered as costs to be weighed against the benefits of
7 reduced energy use and energy costs.

8
9 The primary goal of this study was to quantify the associations between measured CO₂
10 concentrations or estimated ventilation rates (VRs) in offices and adverse effects among building
11 occupants – primarily respiratory illnesses and illness-related absences from work, but also acute
12 health symptoms at work and dissatisfaction with air quality at work. Since CO₂ is a product of
13 human respiration, indoor CO₂ concentrations can be used as a proxy to evaluate the
14 effectiveness of ventilation in controlling airborne concentrations of human-produced infectious
15 respiratory agents, which could contribute to illness and absence. Exposure variables analyzed in
16 this study thus included daily *mean indoor CO₂* as an indicator of bioeffluent exposures.
17 However, since ventilation standards specify minimum VRs, this study also included daily
18 *maximum indoor CO₂*, which with some assumptions can be used to estimate VRs, and also the
19 estimated VRs based on maximum CO₂ concentrations.

20 21 **2.0 Methods** 22

2.1 Building recruitment

Buildings in California were solicited for participation by emails, flyers, and phone calls to the employers. Eligible office buildings were from the public or private sector in three distinct climatic regions of California – Bay Area, Central Valley, and South Coast. In each participating building, at least one study space was selected, each with if possible at least 30 occupants. The study space was either a subset of the building and its workers, or the full building, within which relatively uniform VRs were anticipated (e.g., contiguous spaces or spaces with shared air recirculation from air handling systems). A single building could contain multiple separate study spaces. If multiple study spaces in a building were available, spaces with the most occupants were selected for inclusion, with the number of spaces included depending on willingness of the building owner or employer to allow employee participation. Buildings or study spaces containing unusual contaminant sources were excluded. The target size of the study was a total of 30-40 study spaces, including 30 or more workers in each.

Given the high expected refusal rate during building recruitment (based on our prior experience), the sample was not intended to be representative of California commercial buildings, but was a sample of convenience. Recruitment, enrollment, and data collection were conducted in a rolling manner, with data collection beginning in the earliest recruited buildings while other buildings were being recruited. Data were collected for at least a full year within each building, but study periods were not simultaneous across all study buildings.

2.2 Environmental Data

Several types of environmental data were collected: measurements of indoor CO₂ concentration, temperature (T), and relative humidity (RH), along with information on selected characteristics of the buildings and ventilation systems. Other indoor air pollutants were not measured. CO₂ was monitored by the Vaisala CARBOCAP™ #GMW110 sensors (Vaisala Inc., Boulder CO).

HOBO T & RH loggers (Onset Computer Corporation, Cape Code, MA) were used to measure T and RH and to log the CO₂ sensor data.

CO₂, T, and RH were measured at continuous 10-minute intervals at 2-4 indoor locations (most had 3) per study area. In an initial visit at each building, the sensor packages (CO₂ sensor plus T and RH data loggers) were installed at suitable locations --e.g. attached to the top of space partitions or in common areas such as hallways – away from likely direct occupant exhalation. A contact at each building was queried about which 2-hour period in the morning in each study space was most likely to have a stable number of occupants. Every three months, in-place sensor packages were replaced with sensor packages containing newly-calibrated CO₂ sensors. Sensor replacement across the set of study buildings were not simultaneous, but determined by date of original installation. The 3-month survey periods in the study spaces did not correspond to specific calendar seasons. Data collected from the two to four sensors within each study space were first averaged at each time point to provide more stable real-time estimates for the whole study space (i.e., single sensor values were not paired with nearby workers).

Metrics of both daily peak 60-minute-averaged CO₂ concentrations and daily time-averaged mean CO₂ (referred to as daily peak and daily mean CO₂) were used in analyses. The 60-minute

average was used to reduce influence of irrelevant peaks from occupants breathing on sensors, or other brief incidents. These two metrics were intended for use in two ways: (1) prior 3-month medians of daily peak and daily mean CO₂, for the primary analyses with occupant outcomes that involved occupant recall over the prior 3 months (respiratory infections and illness absences), and (2) daily values, as indicators of peak and mean exposure to human bioeffluents, for the secondary analyses with occupant outcomes linked to the day of the occupant survey (symptoms and perceived air quality).

CO₂ data were also used to estimate daily VRs for each study space, which were then used to calculate prior 3-month medians of time-averaged daily VRs, for analyses with the prior 3-month respiratory infections and illness absences. Real-time spatially averaged CO₂ data from 8 a.m. to 5:30 p.m. on workdays were used to estimate the daily workday VRs (as outdoor airflow rates in L/s per person) using the equilibrium CO₂ method; i.e., from observed peak moving 60-minute-averaged CO₂ concentrations, per ASTM D6245-12 [18]. These calculations assumed that daily VRs in each office were stable and CO₂ reached equilibrium daily in each. The outdoor air flow Q (m³/h) was estimated from the maximum indoor CO₂ concentration as follows:

$$\frac{Q}{N} = \frac{S}{(C_{\max} - C_o)} \times \frac{h}{3600 \text{ s}} \quad (1)$$

where Q/N (L/s-person) is the per-person outdoor airflow rate, C_o (g/m³) is the outdoor CO₂ concentration (estimated as 380 ppm), $C_{\max}$ (g/m³) is the maximum moving 60-minute averaged

CO₂ concentration measured indoors between 8:00 a.m. and 5:30 p.m., and S is the CO₂ generation rate, set at 18.6 L/h-person [19] for sedentary persons with an activity level of 1.2 met units. (The estimated daily VR daily is thus essentially a transformed version of the maximum CO₂ metric, C_{max}.)

An alternative method was also used for estimating VRs (VR Method 2), based on the build-up of indoor CO₂; this required no assumption about equilibrium but assumed stable ventilation rates and stable occupancy during selected periods. This method uses CO₂ data from a 2-hour period when the number of office workers is roughly stable. This occurs typically in the morning, when most workers have already arrived at work and before lunchtime, but may occur in the afternoon. During this stable period, the rate of increase in indoor CO₂ is reflective of the ventilation rate per occupant, and also the air change per hour Q/V (h⁻¹), where Q is the outdoor air flow and V is the building volume. Additional information about the CO₂ measurements and about both VR estimation methods is available in Supplementary file 1.

Many commercial buildings with air-conditioning have “economizer” control systems that increase VRs above the minimum setting during times of cool-to-moderate outdoor air temperatures by increasing outdoor air flow rates, thus reducing use of building energy for air-conditioning. In general, minimum VRs in a building are provided when the outdoor temperature is either above the desired indoor temperature or below approximately 10° C; however, control strategies vary somewhat from building to building. In much of California, economizers increase VRs above the set minimum VR most of the time. Dutton and Fisk [20] estimated that overall, for California offices with economizers, VRs will exceed the set minimum VR approximately

80% of the time. Use of economizer cycles in the HVAC was determined by interviews with building managers.

The particle filtration efficiencies in the heating, ventilating, and air-conditioning (HVAC) systems in the study buildings were determined via interviews with building managers to obtain filter make and model, and corresponding data obtained from filter manufacturers.

2.3 Human outcomes data

Initial development of tools and procedures for data collection from occupants included a human subjects consent form, a web-based survey tool developed for administration via the Internet, and data-handling protocols to ensure the confidentiality of personal information. Before collecting human subjects data, a human subjects protocol was approved by the Lawrence Berkeley National Laboratory Human Subjects Committee.

Data on occupants and their outcomes were obtained from web-based surveys of occupants every three months during the study, starting three months after initial sensor installation in the building. See Figure 1 for a schedule of sensor installation and survey administration. In the initial survey for each participant only, data were obtained on personal/demographic variables that could influence risk of respiratory illness (age, gender, smoking status, asthma status), home variables (young children at home), and work factors (job type, office space sharing, hours per week worked in building). See Supplementary file 2 for questions in the initial and recurring surveys.

Months	1	2	3	4	5	6	7	8	9	10	11	12	13
Period for ventilation rate averaging	1			2			3			4			
Sensor installation ^a	•			•			•			•			
Survey administration				#1			#2			#3			#4

^a in period 1, initial installation of calibrated sensors; in later periods, replacement by newly calibrated sensors

Figure 1. Schedule for sensor installation and survey administration in each building during the year of study (*1-column figure*)

In the initial and in each recurring survey, data (self-reported) were obtained on the number of episodes of infectious respiratory illnesses and the number of days of work absence caused by respiratory illnesses, during the prior three months. The specific questions were:

- “In the last 3 months, how many *episodes* have you had of infectious respiratory illness, like a cold (common cold) or flu (influenza), either mild or severe? If *one* illness lasted multiple days, count that as *one* episode.”
- “In the last 3 months, on how many days were you absent from work (for a whole day) *because of these respiratory illnesses*? Please report as well as you can remember.”

1 These surveys also included questions on acceptability of perceived air quality (for air quality
2 and for odors) and on severity of four symptoms on the day of the survey (dry, itching, or
3 irritated eyes; headaches; unusual tiredness or fatigue; and congested nose). (For details, see
4 Supplementary file 3.)

5
6 To improve survey response rate, a small financial incentive was provided: upon submission of
7 each survey, a \$4 gift certificate was provided in an email as a numeric code for online
8 redemption, except that for the fourth survey among those also completing the prior three
9 surveys, an \$8 incentive was provided. In several buildings, administrative restrictions did not
10 allow use of financial incentives for surveys. In one of these buildings, however, the facility
11 manager instituted a competition between the two study spaces in the buildings on their survey
12 response rate throughout the study, to encourage participation.

14 *2.4 Data analysis*

15 Survey data were excluded from analyses from occupants who either reported working less than
16 20 hours per week in their building or failed to complete an initial questionnaire providing
17 background information. Environmental data, collected in real time during the study period, were
18 excluded from analyses outside the weekday hours of 8:00 a.m. – 5:30 p.m., on U.S. federal
19 holidays, and during periods of local shutdown at university buildings. Also, any day in a study
20 space with no apparent elevation of indoor CO₂ above approximately 400 ppm was excluded as a
21 non-work day in that space.

1 Data collected were analyzed to assess relationships between estimated ventilation rates or CO₂
2 concentrations, either daily or averaged over the prior 3-month periods, and occupant outcomes
3 assessed in the survey at the end of each quarter (Figure 1). Data analyses were performed using
4 Stata v. 11 (StataCorp LP, College Station, TX, USA; www.stata.com). Analyses were at the
5 individual (subject) level, and included unadjusted and adjusted models accounting for study
6 spaces and repeated measurements on individuals.

7
8 Analyses provided point estimates and confidence intervals for the estimated relationships.
9 Appropriate statistical models were selected for analysis of each type of human outcome, all
10 using “bootstrap” procedures to estimate variance of the model estimates, to account for
11 clustering on individuals and study spaces. For respiratory illness episodes and illness absence
12 days, zero inflated negative binomial, zero inflated Poisson, negative binomial, or Poisson
13 models were used, all producing point estimates as incident rate ratios (IRRs). All adjusted
14 models included covariates for potential confounding as appropriate. For repeated measures
15 analyses within individual subjects and study spaces, adjustment for unchanging personal
16 variables as potential confounding was not necessary. For analyses of respiratory illness episodes
17 and related absences, a covariate was included in models for a “respiratory illness season.” (Plots
18 of prior respiratory illness by month showed higher numbers reported on surveys in the months
19 of January through April for illness in the prior three months, corresponding to a season of
20 increased respiratory illness spanning October-April; this was used to define the respiratory
21 illness season.) Table 1 provides details about the models used, along with the specific types of
22 exposure variables (e.g., estimated CO₂ concentrations or VRs) and the covariates included in
23 models for respiratory illness-related outcomes.

Table 1. Description of analysis models for respiratory illness-related outcomes, with exposure variables and covariates

Outcomes	Statistical Model	Exposure Variables	Covariates in Adjusted Models ^a
Number of respiratory illness episodes in prior 3 months; Number of days of respiratory illness-related work absence in prior 3 months	Zero-inflated negative binomial, zero inflated Poisson, negative binomial, or Poisson models; clustered on person and space	Median over prior 3 months of daily VR ^b (before the day of individual's survey)	Smoking, young children in home, respiratory illness season ^c , number of people sharing workspace
“	“	Median over prior 3 months of daily mean indoor CO ₂	“

Outcomes	Statistical Model	Exposure Variables	Covariates in Adjusted Models ^a
“	“	Median over prior 3 months of daily maximum indoor CO ₂ ^d	“
“	Secondary model: logistic regression, with outcome dichotomized as 0 and >0	(same three exposure variables as above)	“

^a in negative binomial model component; zero-inflated model component included only CO₂, season, number of people in work area, and hours worked per week

^b Primary models estimate VR from peak daily CO₂; secondary models estimate VR from curve-fitting algorithm; both described in Supplementary file 1.

^c if illness reporting period (3-month period prior to survey) within October—April

^d maximum sliding 60-minute average CO₂ over the workday hours of 830 a.m.-530 p.m.

3.0 Results

Building recruitment was challenging: only a small proportion of contacted buildings agreed to participate. A total of 17 separate study areas within 10 office buildings were successfully recruited for participation. Due to loss of environmental data, 16 study spaces

in nine buildings were included in analyses (Table 2). One included space contained fewer than 30 office workers. All the included buildings but two were in the public sector (state or municipal government, higher education, research). The efficiency of particle filters in the study spaces, expressed as a Minimum Efficiency Reporting Value (MERV) rating ranging from 1-16, was clustered at only two values, 8 and 14 MERV, with the higher efficiency present in the study spaces in only two Bay Area buildings. All study spaces had air-conditioning and were reported to have economizers. Data collection from sensors in the first participating building began in May 2012, and the first occupant survey was conducted in that building 3 months later, in August 2012. (Data collection was continuous except in study spaces 2a and 2b, where a major furniture move after the third period required a 3-month suspension of the study before proceeding with the fourth 3-month period.) Completed data collection from sensors and surveys was concluded in all study spaces by October, 2013, except in space 9, which was enrolled so late that data from the fourth survey (with few responses) was not available in time for analysis deadlines.

Table 2. Buildings participating in the HZEB Office Building Ventilation Rate Study

Study Space	Sector	Study	Study		Density	Date		Particulate
		Area	N of	of Occu-	Initial	End Date of	Filter	
		Area	Occs	pancy	Sensors	4th survey	Efficiency	
		(m²)		(/100 m²)	Installed		(MERV)	
Bay Area								
1a	Public	Fl 2	920	53	5.7	2/29/2012	6/14/2013	8

(north)								
1b	Public	Fl 2	830	41	4.9	2/29/2012	6/14/2013	8
(south)								
2a	Private	Fl 6	2,310	140	6.1	3/15/2012	11/1/2013	14
2b	Private	Fl 7	2,310	127	5.5	3/15/2012	11/1/2013	14
3a	Public	Fl 7	1,860	71	3.8	4/18/2012	8/6/2013	14
3b	Public	Fl 12	1,860	68	3.7	4/18/2012	8/6/2013	14
3c	Public	Fl 13	1,860	100	5.4	4/18/2012	8/6/2013	14
3d	Public	Fl 15	1,860	33	1.8	4/18/2012	8/6/2013	14
6	Public	Fl 2 +	1,370	64	4.7	5/24/2012	6/14/2013	8
part 3								
<i>Central</i>								
<i>Valley</i>								
4	Public	Fl 3	1,070	74	6.9	5/3/2012	6/14/2013	8
(part)								
9	Public	Fl 2+3	1,370	21	1.5	12/12/2012	8/30/13 ^a	8
(1 wing)								
<i>South</i>								
<i>Coast</i>								
5a	Private	Fl 1	1,440	61	4.2	5/15/2012	6/14/2013	8
5b	Private	Fl 2	1,630	115	7.1	5/15/2012	6/14/2013	8
7	Public	Fl 1, 2,	4,170	86	2.1	10/03/2012	11/1/2013	8
3, 4								
8b	Public	Fl 1	2,240	114	5.1	10/3/2012	11/1/2013	8
8c	Public	Fl 3	2,240	50	2.2	10/3/2012	11/1/2013	8
(part)								

1 ^a end date of 3rd survey, 4th survey not included in this space

Abbreviations: FL, floor; HZEB, Healthy Zero Energy Building; MERV, Minimum Efficiency Reporting Value; N, number; Occs, occupants.

3.1 Occupant data

Response rates for the occupant survey were lower than expected, despite the financial incentives (Supplementary file 4, Table S4-1). The 1,297 valid surveys received represented an overall 27% response on the four surveys, varying from 16 to 41% across study spaces. However, the incentives, of \$4-\$8 for each 5-minute survey, did increase response over the non-incentive study spaces by 50% (from 18% to 27%). The competition set up between two non-incentive study spaces within one building (1a and 1b), with no prize other than pride in winning, produced a response rate 78% higher than other non-incentive spaces, and even 18% higher than the spaces with financial incentives.

Table 3 provides information on the study respondents. No data were available to allow comparison of survey participants to nonparticipants. Respondents included slightly more males (53%), included a broad range of ages from under 30 (17%) to over 50 (29%), and were highly educated (98% with at least a college degree, 45% with a graduate degree). Most (78%) reported never smoking. Half (50%) reported some history of allergy or asthma, including 25% for hay fever and 16% for asthma, and 11% reported current asthma. Most participants (75%) worked in open office spaces, with 70% sharing their workspace with at least 7 others; only 18% had private offices. Most (68%) reported high levels of job stress, but only 26% reported high levels of job dissatisfaction.

1

2 Table 3. Characteristics of survey respondents^a

3

	n (%) ^b	Categories used in adjusted models
Hours worked each week in building: ^c		
21-40	182 (46%)	21-40
>40	216 (54%)	>40
Number of others sharing workspace: ^c		
0	73 (18%)	0
1-2	25 (6%)	1 or more
3-6	19 (5%)	
7 or more	279 (70%)	
Job stress (1=not at all, 7=extremely): ^c		
1-2	17 (4%)	(not included)
3-4	110 (28%)	
5-7	270 (68%)	
Job dissatisfaction (1=very satisfied, 7=very dissatisfied): ^c		
1-2	152 (39%)	1-2
3-4	133 (34%)	3-4
5-7	102 (26%)	5-7
Number of children up to age 3 years at home:		
0	321 (81%)	0
1-2	68 (17%)	1 or more
3 or more	7 (2%)	

Smoking status:			
Never	302 (78%)	Never	
Former	66 (17%)	Former/current	
Current	17 (4%)		
Age			
Under 30	67 (17%)	Under 30	
30-39	113 (29%)	30 or over	
40-49	99 (25%)		
50 or over	113 (29%)		
Gender			
Female	185 (47%)	Female	
Male	208 (53%)	Male	
Education completed			
High school	9 (2%)		
College degree	210 (53%)	No graduate degree	
Graduate degree	176 (45%)	Graduate degree	
Prior medical diagnoses: ^c			
Asthma	62 (16%)		
Current asthma	45 (11%)		
Eczema	43 (11%)		
Hay fever (pollen allergy)	100 (25%)		
Dust allergy	84 (21%)		
Mold allergy	53 (13%)		
Any prior allergy	183 (46%)	Any prior allergy	
No prior allergy	201 (50%)	No prior allergy	

^a after exclusion of surveys from workers who worked <21 hours/week in the building and from those not completing an initial survey with background data

^b proportions are calculated using total of non-missing answers

^c from initial survey response to a question repeated on each survey

Table 4 shows the distributions, in each study space and overall, of the numbers of respiratory infection episodes reported in the prior three months and respiratory illness-related absences in the prior three months. For the number of respiratory infection episodes in the prior 3 months, the overall mean was 0.92, with means across study spaces ranging from 0.67 to 1.32. The 95th percentile value overall was 3, ranging in specific study spaces from 2 to 4. For the number of respiratory illness-related work absences in the prior 3 months, the overall mean was 0.78, with means across study spaces ranging from 0.10 to 1.38. The 95th percentile value overall was 4, ranging in specific study spaces from 1 to 6.

Table 4. Respiratory illness outcomes among respondents*

Study Space	Number of respiratory infection episodes in prior 3 months				Number of days of respiratory illness-related work absences in prior 3 months			
	percentiles				percentiles			
	mean	50%	75%	95%	mean	50%	75%	95%
<i>Bay Area</i>								
1a	0.71	0	1	3	0.57	0	1	4
1b	0.85	1	1	3	0.37	0	0	1

2a	0.92	1	1	3	0.67	0	1	3
2b	0.98	1	2	3	0.80	0	1	3
3a	0.94	1	1	4	1.34	0	2	6
3b	1.32	1	2	4	1.38	1	2	5
3c	1.00	1	2	3	1.17	.5	2	4
3d	0.70	0	1	2	0.70	0	1	4
6	0.92	1	1	2.5	0.65	0	1	4.5
<i>Central Valley</i>								
4	0.71	1	1	2	0.61	0	1	3
9	1.10	1	2	3	0.10	0	0	1
<i>South Coast</i>								
5a	0.94	1	1	3	0.42	0	0	3
5b	1.01	1	1	3	0.49	0	1	2
7	0.91	1	2	3	0.96	0	2	4
8b	0.67	1	1	2	0.60	0	0	4
8c	1.00	1	1	4	0.90	0	2	4
<i>TOTAL</i>	0.93	1	1	3	0.78	0	1	4

* after all exclusions (see Table 3 footnote)

Supplementary file 3 summarizes the reported symptoms and the reported acceptability of indoor air quality and odor on the days of the surveys. The most commonly reported symptoms were eye, fatigue, and nose symptoms, at 65%, 61%, and 51% of surveys; among those reporting these symptoms, mean severity scores were 4.4, 4.4, and 4.0, respectively. Prior symptoms before work on the survey day were common, ranging from 38% to 65%. Unacceptability of perceived

air quality was low, averaging 10.2%, with only two of 156 spaces failing to provide acceptable air quality for at least 80%. Only 3.7% of surveys rated odors as unacceptable.

3.2 Environmental data

Based on recalibration of CO₂ sensors after deployment in the field for 3-month periods, sensor drift was small, approximately $\pm 5\%$ (see Supplementary file 1). Temperature sensors were determined to have read fairly consistently 1 °C high, due to an internal heat source in monitoring modules, and temperature values used in modeling were adjusted accordingly.

Table 5 summarizes, by study space and specific survey periods for each, median values during the prior three months of daily mean CO₂, daily maximum CO₂, and daily VRs. Three-month medians of daily mean CO₂ in study spaces ranged from 425-957 ppm, medians of daily maximum CO₂ from 494-1230 ppm, and median VRs from 6.9 to 65.8 L/s per person. VRs were uniformly high relative to the current minimum VR standards for office space: 7 L/s (15 cfm) per person from California Title 24, and 8.5 L/s (17 cfm) per person from ASHRAE 62.1, at the default density of occupancy. Other than one median quarterly VR of 6.9 L/s-person in space 4, all other quarterly medians exceeded 13 L/s per person, or almost double the California standard.

1 Table 5. Prior three-month^a median of daily mean CO₂, daily maximum CO₂, and daily ventilation rates (VRs)^b by study space

2

Study Space	Three-Month Median of				Three-Month Median of				Three-Month Median of			
	Daily Mean CO ₂ :				Daily Maximum CO ₂ :				Daily VRs:			
	(ppm)				(ppm)				(L/s-person)			
	S1	S2	S3	S4	S1	S2	S3	S4	S1	S2	S3	S4
<i>Bay Area</i>												
1a	571	605	607	580	669	703	702	679	21.2	19.2	19.7	20.9
1b	573	603	603	579	723	731	749	729	18.8	17.1	17.1	17.6
2a	569	615	660	587	661	713	803	678	21.3	17.9	13.9	19.6
2b	570	602	657	566	660	699	803	660	21.5	18.4	13.8	22.0
3a	550	534	513	533	713	628	664	672	17.8	25.2	22.1	19.8
3b	470	482	481	463	538	547	578	541	38.9	36.4	31.3	39.4
3c	587	532	526	534	873	652	704	843	13.7	24.4	19.6	15.4
3d	480	496	475	483	588	571	566	602	29.8	34.9	31.9	28.6
6	432	471	492	477	500	547	580	567	65.8	41.9	32.6	38.2
<i>Central Valley</i>												
4	602	663	957	656	720	825	1230	822	18.8	13.1	6.9	14.0

9	563	529	577	NA	733	699	703	NA	20.7	25.6	20.3	NA
<i>South Coast</i>												
5a	646	605	647	653	759	732	777	764	15.4	17.5	16.0	15.8
5b	555	572	580	569	711	682	752	673	17.6	20.1	17.2	20.9
7	574	530	538	541	659	594	618	629	23.1	28.4	27.0	27.1
8b	512	507	446	441	726	835	568	584	27.9	23.4	58.1	52.6
8c	525	471	448	425	581	528	501	494	30.8	41.6	58.8	64.9

1 ^a prior three-month period ending on the first day of each survey period in each space

2 ^b VR Method 1

3

Figure 2 shows distributions of daily *maximum* CO₂ measurements, over the entire study, by study space. Figure 2 shows that the study spaces had generally low maximum CO₂ concentrations and thus high VRs, except space 4, which had a slightly higher CO₂ distribution. Patterns of CO₂ level differences across buildings were similar for daily maximum and mean CO₂. Distributions of daily *mean* CO₂ values are provided in Supplementary file 5 (Figure S5-1). Figure 3 shows daily *maximum* CO₂ values over time in each study space. Most study spaces had relatively uniform maximum CO₂ throughout the study, with the exception of spaces 4 and, to a lesser extent, 8b. Patterns for daily maximum and mean CO₂ over time were similar. Space 4, Survey 3, had the most high CO₂ levels and low VRs; otherwise the ranges across buildings and surveys were narrower. Distributions of daily mean values over time are provided in Supplementary file 5 (Figure S5-2).

Figure 2. Distributions of daily maximum indoor CO₂ measurements, by study space grouped by climate zone (boxes show median, 25th and 75th percentiles; whiskers, 75th percentile plus 1.5 times the interquartile distance, and 25th percentile minus 1.5 times the interquartile distance) (*1-column figure*)

Figure 3. Daily CO₂ maximum indoor values over time (y-axis, in ppm, per study space grouped by climate zone (BA, CV, and SC) (*1-column figure*)

Inspection of daily CO₂ plots for the study spaces (not shown) showed that an underlying assumption of equation (1), daily peak CO₂ equaling an equilibrium concentration, often was not

met, causing likely overestimation of VRs on those days. Daily maximum CO₂ values were highly variable within study spaces. The alternative VR method (method 2) produced unacceptable estimates on many days (see Supplementary file 1). Analyses of the daily symptom and air quality outcomes (for up to four survey days for each respondent) used as independent variables the two daily CO₂ metrics but not the daily VR estimates. Analyses of the prior-3-month recalled outcomes from occupant surveys used as independent variables the prior 3-month medians for the two CO₂ metrics and the estimated VRs based on Method 1 and, secondarily, Method 2.

Figure 4 shows the distributions of estimated VRs in each study space, and the 5th percentile values used to indicate minimum supplied VRs, potentially representing periods of non-economizer use. Minimum supplied VRs based on the 2.5th percentile were similar. The estimated minimum supplied VRs substantially exceeded the 7 L/s per person requirement in most study spaces, with an average estimated minimum of 15 L/s per person. In 13 of 16 study spaces, the estimated minimum VR exceeded 10 L/s per person.

Because economizer systems were present in all study spaces it was not possible to include economizer presence as a variable in models. Because the efficiency of particle filters clustered at only two values, 8 and 14 MERV, with the higher efficiency present in the study spaces in only two Bay Area buildings, it was also not possible to include this in models.

Space	5th Percentile
B1S1	15.7
B1S2	12.1
B2S1	9.2
B2S2	9.3
B3S1	13.2
B3S2	20.8
B3S3	11.1
B3S4	18.0
B4S1	5.4
B5S1	11.7
B5S2	11.9
B6S1	27.9
B7S1	21.0
B8S2	15.4
B8S3	27.6
B9S1	16.2
Average	15.4

- 1 Figure 4. Distributions of ventilation rates calculated via method 1, and estimated minimum ventilation rates from 5th percentile values
- 2 (*2-column figure*)

3.3 Environment and outcome results

Supplementary file 6 (Table S6-1) provides summaries of occupant outcomes by categories of various demographic and personal variables of occupants. Workers in private offices had the lowest proportions of respiratory infections and days of respiratory illness-related work absence, but these outcomes did not worsen consistently with increased numbers of others sharing the workspace. Very low job stress and low job dissatisfaction were associated with unusually low levels of respiratory illness-related absence. Smokers reported relatively low levels of respiratory illness episodes and related work absence. Females reported many more respiratory illness-related work absences.

Table 6 summarizes the associations, unadjusted and adjusted, between CO₂ and VRs in the prior three months and the two respiratory illness outcomes, estimated from zero-inflated negative binomial models. (Covariates and their categories used in these adjusted models are described in Table 3.) None of the unadjusted or adjusted estimates were significantly associated with CO₂ or VR. All estimates not equal to 1.0 were in directions opposite those hypothesized (below rather than above 1.0 for the CO₂ metrics, and above rather than below 1.0 for VR). For analyses using VR method 2, results (in Supplementary file 7) were similar to those using method 1, with all outcomes in the direction opposite that hypothesized. Furthermore, for VR method 2, with increased VR, the unexpected increase in respiratory illness-related absence was statistically significant – OR (95% CI) 1.015 (1.0005-1.03), p=0.04, but not the smaller increase for respiratory illness episodes – 1.001 (0.90-1.01), p=0.78.

Table 6. Unadjusted and adjusted associations, as incident rate ratios (IRRs) and 95% CIs,^a between CO₂ or ventilation rates (VRs) in the prior three months, and respiratory illness outcomes, estimated from zero inflated negative binomial (or, as noted, negative binomial or zero-inflated Poisson) models

	Number of respiratory infection episodes in prior 3 months				Number of days of respiratory illness- related work absences in prior 3 months			
	unadjusted		adjusted ^b		unadjusted		adjusted ^b	
	IRR	(95% CI)	IRR	(95% CI)	IRR	(95% CI)	IRR	(95% CI)
Median of daily CO ₂ mean, prior 3 months	0.98 ^c	(0.87, 1.10)	0.93 ^d	(0.83, 1.05)	0.87	(0.74, 1.03)	0.86	(0.69, 1.07)
Median of daily CO ₂ maximum, prior 3 months	0.98 ^c	(0.91, 1.06)	0.94 ^d	(0.86, 1.02)	0.97	(0.88, 1.08)	0.97	(0.84, 1.12)
Median of daily estimated VR, prior 3 months	1.00 ^c	(0.996, 1.02)	1.00 ^d	(0.99, 1.02)	1.01	(0.997, 1.02)	1.01	(0.99, 1.03)

^a The IRR is interpreted as the multiplicative change in estimated rate of outcomes for each increase of 100 ppm CO₂ or 1 L/s per person of VR. Estimates for VR models were hypothesized to be in the opposite direction as CO₂ models.

^b Models adjusted for: smoking, young children in home, people sharing workspace, respiratory illness season (illness reporting period in October—April); see Table 3 for details on covariate variables.

^c Negative binomial model

^d Zero-inflated Poisson model

Table 7 summarizes associations between the same primary variables but estimated from logistic regression models. All adjusted estimates were still in directions opposite those hypothesized, although no associations were statistically significant. The directions of all adjusted estimates, and the magnitudes for the respiratory illness episodes, were similar to (or showed smaller effects than) those from the models in Table 6.

Table 7. Adjusted and unadjusted associations between CO₂ and ventilation rates in the prior three months and respiratory illness outcomes, estimated from logistic regression models

	Number of respiratory infection episodes in prior 3 months				Number of respiratory illness-related work absences in prior 3 months			
	unadjusted		adjusted ^a		unadjusted		adjusted ^a	
	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Median of								
daily CO ₂		(0.91,		(0.79,		(0.95,		(0.79,
mean, prior	1.08	1.30)	0.97	1.18)	1.14	1.35)	0.97	1.19)
3 months								

Median of								
daily CO ₂								
maximum,	1.003	(0.89,	0.94	(0.82,	1.06	(0.94,	0.98	(0.85,
prior 3		1.13)		1.08)		1.19)		1.13)
months								
Median of								
daily								
estimated	0.99	(0.98,	1.001	(0.99,	0.99	(0.98,	1.003	(0.98,
VR, prior 3		1.01)		1.02)		1.01)		1.02)
months								

^a Models adjusted for: smoking, young children in home, people sharing workspace, respiratory illness season (illness reporting period in October—April); see Table 3 in main text.

Of the four other covariates in models for the two respiratory illness-related outcomes, only respiratory illness season (i.e., October through April) had strong and consistent associations, with highly significant IRRs of about 1.5 and, from logistic regression models, ORs of 2.0, for both illness episodes and days of illness absence. Shared workspace had significant positive associations only in the logistic models, with ORs of 1.6 for illness episodes and 2.0 for days of illness absence. Young children at home had significantly elevated associations only in logistic models for illness episodes, with ORs of 1.7. Ever smoking had no consistent associations with either outcome.

Results from models for same-day CO₂ metrics and outcomes of symptoms (as continuous outcomes) and perceived air quality (as dichotomous and as continuous outcomes) are provided in Supplementary file 3, Tables S3-5, S3-6, and S3-7. No associations were statistically significant, magnitudes of effects were generally small, and directions were mixed, with exactly half of the nonsignificant estimates in a direction opposite of expected.

4.0 Discussion

The objective of this study was to quantify the relationships between CO₂ or VRs in California office buildings and occupant outcomes that were hypothesized, based on prior research, to be increased at lower VRs: respiratory illnesses and respiratory illness-related absences, and also building-related symptoms and dissatisfaction with indoor air quality and odors. No statistically significant relationships with primary environmental metrics were found. In this study, VRs were uniformly high over time in almost all study spaces. For the three-month median VRs in each study space that were used in illness absence analyses, most (between the tenth and ninetieth percentiles) were between 16 and 42 L/s per person, which is over twice to over nine times the California minimum VR standard. Thus this study was unable to assess relationships with VRs considered substandard, and could only compare high with very high VRs, a range throughout which indoor contaminant levels are highly diluted and little VR-related variation in contaminant concentration would occur. The findings might be interpreted as additional evidence for a high range of VRs within which increased VRs will not substantially reduce illness absence, as suggested in prior reviews [1, 3, 4]. Myatt et al. [16], for instance, also found no associations with respiratory infections within a range of very high VRs. However, it would be premature to

1 consider findings for the specific VR range studied here to be generalizable: this study included
2 only a convenience sample of buildings in California, health effects studied were self-reported,
3 VRs in this study were likely to be overestimated, and VR effects in any building would depend
4 on the specific mix and source strengths of indoor air pollutants there.

5
6 The findings for respiratory infection-related effects suggest that, within the high range of VRs
7 included in this study, actual relationships with VR were absent (or possibly with tendencies in
8 the direction opposite that expected). Relationships between the primary metrics of CO₂ and VR
9 and the illness absence-related outcomes were almost entirely (11 of 12 estimates from two types
10 of models) in directions opposite those hypothesized, although not statistically significant.

11 Interestingly, two adjusted estimates using an alternate VR metric were also in the direction
12 opposite that expected, and one was statistically significant; however, one or two statistically
13 significant associations might have been expected simply by chance, of the many estimated,
14 without reflecting true underlying relationships. One possible explanation for an actual
15 unexpected relationship like this would be that very high VRs might bring outdoor urban air
16 pollutants indoors sufficiently to influence respiratory infections (but apparently not acute
17 symptoms) relative to more moderate VRs. Any explanatory outdoor pollutants would not
18 include infectious respiratory agents, but could possibly influence susceptibility to such agents
19 indoors. Because this study measured no outdoor pollutants, this speculative explanation for a
20 mere tendency in these findings would require further research to validate or dismiss. If such an
21 effect were documented, it would add, to energy-efficiency, another reason to avoid higher VRs
22 in buildings, or, given that high VRs during use of economizers actually saves energy, a reason
23 for better cleaning of outdoor air introduced into buildings.

1
2 Many reviews have concluded that lower VRs are associated with adverse human outcomes,
3 including respiratory infections or illness absence as well as SBS symptoms [1-4, 21, 22].
4 Theoretical considerations suggest that lower VRs in buildings could increase airborne
5 transmission of infectious respiratory disease between occupants [7, 23-25]. VR is not expected
6 to influence exposure to disease agents occurring by direct or indirect contact or by short-range
7 large aerosols such as from nearby sneezing. The finding by Pejtersen et al. [26] of a nearly
8 monotonic relationship between numbers of others sharing an office and annual days of self-
9 reported sickness absence, although not replicated here, could have been due to long-range or
10 other means of disease transmission. Specific studies have reported associations of lower VRs
11 (or higher CO₂ concentrations) with increased respiratory infections in densely occupied group
12 domiciles, including respiratory infections in dormitories [12], febrile respiratory illness in
13 barracks [13], and pneumococcal disease in a jail [14].

14
15 Two studies have reported findings consistent with lower office VRs being associated with
16 respiratory infections, but one found no association at varying higher VR levels. Milton et al. [8]
17 reported a 35% reduction in short-term illness absence among office workers with VRs of 24 L/s
18 per person compared to those with 12 L/s per person, with VRs estimated from CO₂ data. Myatt
19 et al. [9] found an association between building ventilation and the occurrence of airborne
20 rhinovirus (i.e., without studying human health) with weekly average CO₂ concentrations over
21 100 ppm greater than outdoors. The authors suggested that “occupants in buildings with low
22 outdoor air supply may have an increased risk of exposure to infectious droplet nuclei emanating
23 from a fellow building occupant.” In contrast, Myatt et al.[16] found no difference in illness

1 absence in offices at varying high levels of VR (estimated mean 40 to 45 L/s-person). The
2 weekly mean, workday, CO₂ concentration differential ranged from 350-560 ppm (37 to 250
3 ppm above a background of 312 ppm); that study [16] was unable to obtain data on low VRs, as
4 was ours. In fact, Myatt et al. [9] also estimated that below a mean CO₂ differential of 450 ppm
5 (an indoor CO₂ of approximately 760 ppm, above most values in the present study), indoor
6 airborne person-to-person transmission of rhinovirus was unlikely, although this might differ for
7 more contagious agents such as influenza.

8
9 Two studies reported that higher classroom VRs were associated with increased school absences.
10 Mendell et al. [10] found that lower VRs within the range of approximately 2-20 L/s per person
11 (650-2500 ppm CO₂ indoors), estimated from indoor real time CO₂ measurements taken daily,
12 were associated with significantly increased illness absence in primary school students. For each
13 additional 1 l/s-person of VR, IA was reduced significantly ($p < 0.05$) in models for combined
14 districts (by 1.6%). Shendell et al. [11] reported that higher classroom ventilation rates as
15 estimated by indoor CO₂ measurements taken on one day in the school year were associated with
16 a substantial reduction in overall student absence. A decrease of 1000 ppm in indoor minus
17 outdoor CO₂ concentrations within the observed range of 10–4200 ppm was associated with a
18 10–20% relative decrease (0.5–0.9% absolute decrease) in total student absence.

19
20 There are multiple differences between the present study and those that found relationships
21 between lower VRs and increased illness absence or respiratory infections. This study included a
22 range of almost entirely very high VRs (3-month means ranging from approximately 450-650
23 ppm CO₂, or from approximately 16-42 L/s per person), unlike [8], which compared

1 approximately 12 to 24 L/sec per person. In addition, the self-reported illness-related outcomes
2 used here are likely to be less accurate than the other studies, and thus would create a bias toward
3 null results. However, this study was more like that of Myatt et al. [16], which reported a weekly
4 mean indoor CO₂ range of 350-560 ppm. In the current study, among all 3-month median values
5 of indoor CO₂ in the 18 studied spaces, only one of these 64 values exceeded 760 or even 660
6 ppm. Per Myatt [9], this suggests that airborne person-to person transmission of at least
7 rhinovirus was unlikely in these studied spaces, and thus would not be reduced at the lower VRs
8 observed.

9
10 This study was also unlike the two school VR studies that found clear associations: Mendell et
11 al. [10] included an indoor CO₂ range of roughly 650-4150 ppm, and Shendell et al. [11] a range
12 of approximately 350- 4500 ppm. For the school studies as well as the studies of densely
13 occupied domiciles [12-14], the low VRs were combined with much higher occupant densities,
14 which might lead to greater presence of infectious agents and thus a greater ability to see
15 differences with differing removal by ventilation; e.g., Sun et al. [12] reported differences in
16 occurrence of common colds between VRs of 1 and 5 L/sec per person, with 90% of VRs below
17 8.3 L/s per person. Also, subjects in the school studies were in primary school, and may be more
18 susceptible to respiratory infections.

19
20 Similarly, prior studies have found increased SBS symptoms and worsened perceived air quality
21 associated with lower VRs, but not in higher VR ranges, such as above 20 or 25 Ls⁻¹ per person
22 [1, 3, 4]. Still, as Sundell et al. [1] has said, a threshold ventilation rate above which increases do

not further improve SBS symptoms is poorly defined; this may be in part because the related indoor pollutant sources vary across buildings.

4.1 Strengths and limitations

Strengths of this study include the prospective design, following office workers over four seasons during a full year, which allowed within-person analyses and reduced statistical confounding by personal factors; use of CO₂ data from each study space based on real-time CO₂ measurements every day over a year instead of the usual short-term measurements over one or several days; and use of frequently recalibrated CO₂ sensors, successfully keeping sensor drift within 5% over a year. While buildings were not all studied at the same time, collecting data from each over a full year considered illness through all seasons. Adjustment in models for a winter respiratory illness season prevented or reduced confounding from seasonal effect. One-time illness outbreaks are unlikely to have distorted findings unless they were highly correlated with very high or low VRs across multiple buildings in the study.

The study had multiple limitations which may have contributed to the lack of associations seen, the most important of which were limited power, inaccuracies in estimation of VRs, and the use of subjective recall for prior health outcomes. The insufficient statistical power resulted in part from a study size too small to detect the small differences in exposure and effects expected within the observed range of VR. The sample size was smaller than planned, a combined result of the inability to recruit the desired number of buildings (due to the unwillingness to participate of management in most buildings contacted), and the very low survey participation rates of occupants in participating buildings, despite financial incentives. Findings may apply only to

1 public-sector buildings, as most contacted in the private sector declined to participate, and to the
2 minority of study space occupants (averaging 27%) who participated in the surveys.

3
4 Estimation of VRs involved many potential sources of error, as assumptions underlying use of
5 equation 1 are often invalid: peak CO₂ levels in each space not reaching true equilibrium during
6 many work days (resulting in overestimation of true VRs as well as random error); potential
7 errors in measuring and estimating indoor CO₂ levels in each study space, such as from poor air
8 mixing (we did not evaluate air mixing within each space) or nearby occupant exhalation
9 (resulting in underestimation of VRs; this is why we used a 60-minute averages to estimate peak
10 indoor CO₂ although this may have underestimated actual peaks and thus overestimated VRs);
11 the use of a fixed rather than measured outdoor CO₂ levels, which would have varied by location
12 and time of day, in calculating VRs (resulting in random VR errors); possibly inaccurate
13 assumptions about CO₂ generation rate by occupants; and the assumption of unchanging VR per
14 person during each day in each space, ignoring varying occupancy and part-day use of
15 economizers. VRs calculated from the alternative metric rely on different assumptions, but only
16 represent VRs during selected short time periods, and failed to produce acceptable estimates on
17 many days.

18
19 Respiratory illness episodes and respiratory illness-related work absence were self-reported and
20 assessed by questionnaire, and retrospectively for the prior three month period, resulting in
21 potential nonsystematic inaccuracies and findings biased toward the null. Density of occupancy,
22 as a factor separate from VR per person, may influence indoor transmission of respiratory
23 illness; however, we did not have sufficiently accurate data to assess this. Prospective gathering

of data from occupants, or more frequent data gathering, would have been more accurate, but also more onerous and susceptible to nonresponse. Data on symptoms and perceived air quality, assessed for the day of occupant surveys, should not have been susceptible to recall bias.

4.2 Implications

Ventilation rate standards are still largely based on decades-old studies of the amount of ventilation needed to provide satisfactory air quality for 80% of visitors to a space, with the occupants as the dominant pollutant source [27, 28]. There is no explicit analysis underlying the current standards that considers health risks from exposure to indoor air pollutants, potential impacts to workers' performance, or energy and other associated cost considerations. Further research is still necessary to provide scientific support for health-protective building VR standards.

The uniformly high VRs in the California office buildings in this study presumably result from the combination of generally moderate climates with the use of economizer systems that bring in large volumes of outdoor air (for "free cooling") during periods of moderate outdoor temperatures. However, even the estimated minimum supplied VRs observed in these buildings (when presumably operating without economizers) generally exceeded the minimum required in the California Title 24 standard, suggesting poor control of minimum VRs. (Some proportion of these high VR estimates was, as discussed previously, likely due to overestimation based on daily peak CO₂ levels.) Reviewed studies in mechanically ventilated European office buildings have also found VRs often far above standards, with a mean of 18 L/s per person and ranging up to 55 L/s per person [29].

1

2 The conduct and findings of the present study, and the difficulties encountered, provide lessons
3 for future studies on this topic. The prospective observational design used in the present study is
4 relatively economical and allows greater generalizability of findings than controlled chamber
5 studies, which could not study respiratory infections in office populations over extended periods.
6 However, to the extent that characterization of complex indoor exposures is not practical in
7 large, extended field studies, other study designs may be more appropriate, such as more detailed
8 observational studies, with more intensive measurements, but in smaller numbers of buildings.
9 Also, field intervention studies comparing existing low and experimentally raised VRs across
10 otherwise unchanged conditions, if done for extended periods in consideration of seasonal illness
11 patterns, in large populations to achieve sufficient power, and with crossover designs to account
12 for building differences, could provide more precise findings on VR and respiratory infections.

13

14 Future large-scale observational assessments of the relationships studied in this project, if
15 performed, need multiple improvements: inclusion of geographic areas with more severe
16 climates and lower VRs; greater time and effort to recruit a sufficiently large sample of
17 buildings; substantially increased financial incentives or other novel approaches to achieve
18 desired response rates; improved methods to estimate VRs (e.g., existing tracer gas methods
19 measure VRs more accurately, but are not practical for year-long studies in multiple buildings);
20 consideration of outdoor air pollutants and higher VRs, especially in urban locations; and if
21 feasible, prospectively collected diary data from occupants on respiratory infections, or even
22 more objectively, employer-provided illness absence data. To the extent that specific indoor
23 office pollutants that might vary with VR or even independently of VR could influence

1 respiratory illness, measurement of these over time would reduce statistical noise and allow
2 greater power in smaller studies; however, such measurements could be quite costly. Data
3 collection and analyses of VRs and respiratory illness or related absence should include variables
4 shown in this study to be clearly or possibly associated with these outcomes – e.g., respiratory
5 illness season, shared workspace, and young children at home. Respiratory illness season,
6 because related independently to both VR and respiratory illness and not included in the causal
7 pathway between VR and respiratory illness, is a classical confounding variables and thus
8 requires adjustment in statistical models on VR and respiratory illness-related outcomes.

9
10 In addition, developing increased knowledge about physical mechanisms of indoor transmission
11 of respiratory infections would help focus future field studies on determinants of transmission. It
12 is still uncertain how much of this disease transmission occurs by each of four possible modes: a
13 direct contact mode (person-to-person contact); an indirect contact mode (from physical contact
14 with surfaces contacted by those infected); a droplet mode (the impact of large droplets from
15 coughing and sneezing on others quite nearby); or by long-range airborne transmission (through
16 very small droplet aerosols produced by drying of larger aerosols expelled in coughing or
17 sneezing). VRs may influence transmission of infectious respiratory disease by changing indoor
18 concentrations of the very small aerosols associated with long-range airborne transmission or
19 possibly by changing humidity or concentrations of air pollutants that might affect either the
20 period of viability of infectious particles or people's susceptibility to infection. However, all of
21 the disease transmission mechanisms are linked; e.g., increased long-range airborne transmission
22 would result in more sick occupants who could transmit infections via other transmission
23 mechanisms. Also, a number of infectious agents are involved in the mix of infectious diseases

in an office population, and each may be primarily transmitted through different mechanisms. Improved understanding of these processes will help inform field research in buildings.

5.0 Conclusions

This study found no statistically significant relationships between primary metrics of CO₂ or VRs in these California commercial buildings and occupant outcomes hypothesized to be increased by lower VRs: respiratory illnesses and respiratory illness-related absences, building-related symptoms, and dissatisfaction with indoor air quality and odors. (One significantly positive association of an alternative VR metric with increased respiratory illness-related absence, contrary to hypotheses, may have been a chance finding among many analyses.) The overall lack of relationships presumably resulted from the almost uniformly very high VRs in the studied spaces over the year of the study. The three-month median VRs in the study spaces, with one exception, ranged from almost twice to over nine times the California minimum VR standard of 7 L/s (15 cfm) per person. Thus this study had limited contrast in exposures, and could compare only high with very high VRs, a range in which little variation in contaminant concentration and occupant effects would result. Multiple other weaknesses limit the ability of this study to draw firm conclusions; however, this study may provide additional evidence, already available from at least one prior study, for a high range of VRs within which increased outdoor air has little or no benefit for respiratory illness or related absence.

This study provided some limited data on actual minimum VRs in California office buildings (during non-use of economizers), suggesting that, to the extent the studied buildings are

1 representative, these VRs are usually substantially higher than required in the current applicable
2 standard. This conclusion is limited by potential errors of overestimation for VRs in this study.

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