Title

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Journal

Indoor Air, 28(4)

ISSN

0905-6947

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Publication Date

2018-07-01

DOI

10.1111/ina.12469

Peer reviewed

HOW HOME VENTILATION RATES AFFECT HEALTH: A LITERATURE REVIEW

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ABSTRACT

This paper reviews studies of the relationships between ventilation rates (VRs) in homes and occupant health, primarily respiratory health. Five cross-sectional studies, seven case-control studies, and eight intervention studies met inclusion criteria. Nearly all studies controlled for a range of potential confounders and most intervention studies included placebo conditions. Just over half of studies reported one or more statistically significant (SS) health benefits of increased VRs. Wheeze was most clearly associated with VR. No health outcomes had SS associations with VRs in the majority of statistical tests. Most studies that reported SS health benefits from increased VRs also had additional health outcomes that did not improve with increased VRs. Overall, the number of SS improvements in health with increased VRs exceeded the anticipated chance improvements by approximately a factor of seven. The magnitude of the improvements in health outcomes with increased VRs ranged from 20% to several fold improvements. In summary, the available research indicates a tendency for improvements in respiratory health with increased home VRs; however, health benefits do not occur consistently and other exposure control measures should be used together with ventilation. The research did not enable identification of a threshold VR below which adverse health effects occur.

Key words: carbon dioxide, health, homes, respiratory, review, ventilation rates

Practical Implications: To protect occupant health, homeowners, home builders, and developers of minimum VR standards should seek to avoid low home VRs. However, the health benefits of increased home VRs are inconsistent and other indoor exposure control measures, including avoidance of strong indoor pollutant sources, must be used together with ventilation to protect health.. To support future standards for minimum acceptable VRs in homes, it would be helpful if VR measurement methods were standardized, future studies determined and reported air exchange rates, VRs per person, and VRs per unit floor area, and indoor pollutant sources were characterized. Also, future intervention studies should measure and report initial and final VRs, not just the amount of added mechanical ventilation.

BACKGROUND

VRs may affect health indirectly by changing indoor air concentrations of contaminants or moisture that, in-turn, may affect health. The types and strengths of indoor contaminant sources and the types and concentrations of contaminants in outdoor air will mediate the relationship of VR with health. Consequently, any strategy to maintain healthful indoor air quality should include minimization of indoor contaminant sources and, when outdoor air is highly contaminated, removal of outdoor air contaminants from the air entering buildings. Nevertheless, it is important to understand the extent to which changes in VRs, in practice, indirectly influence health.

Numerous studies have investigated the associations of VRs in offices, or office like laboratory settings, with occupant health and performance. Several critical reviews and meta-analyses of the resulting published literature have been published [1-6]. These reviews indicate that increases in VRs in offices, up to approximately 25 L/s per person, are associated with decreases in prevalence rates of health symptoms at work among office workers and with increases office work performance. For schools, a recent review of published literature [7] characterized the evidence of improved student performance with increased VRs as compelling and found that the available research "suggests improvements in respiratory health with increased VRs."

Considering the evidence that VRs of offices and schools affect health, one might expect similar or even larger effects of home VRs on health. People spend more time in homes than in offices or schools [8]. Home VRs can be highly variable and bedroom ventilation rates, in particular, have sometimes been low[9,10]. Many homes contain indoor air pollutant sources such as cooking, tobacco smoking, and air fresheners that are less common in other types of buildings. Concentrations of volatile organic compounds (VOCs) in homes have tended to be higher than concentrations of VOCs in offices and schools [11,7], suggesting greater benefits of increased VRs.

Until recently, research on the associations of VRs in homes with occupant health has been very sparse. A review by an interdisciplinary team from Europe [4] identified only two "conclusive" (i.e., deemed usable) papers relating home VRs to occupant health and two more papers relating VRs to levels of dust mites in homes. This review, published in 2002, was only able to conclude that "air change rates above 0.5 h^{-1} in homes reduce the degree of infestation of house dust mites in Nordic countries" suggesting that increased VRs in Nordic homes may reduce allergies. A subsequent review[5] by a multidisciplinary group, published in 2011, considered four studies of homes, all from Scandinavia, and found that "these studies suggest an association between a low VR (<0.5 h^{-1}) and allergic symptoms, but the data are limited, and the results not fully consistent." Another paper [12] reviewed studies of the associations of health outcomes and perceptions with home ventilation characteristics more generally (VRs, ventilation system types, air conditioning, and ventilation system problems). This review included four studies published in journals that related health outcomes with measured VRs, without other simultaneous changes in building conditions. The author concluded "it seems likely that health risks may occur when VRs are below 0.4 air changes per hour in existing homes." A third multidisciplinary review [6] identified eight "conclusive" papers addressing home VRs with health, with four finding improvements in health symptoms, and one finding fewer self-reported common colds, with higher VRs.

Since these prior reviews were completed, the results of several more recent studies of the relationships of VRs in homes with health outcomes have been published. Accordingly, the present paper provides a more up-to-date review of the literature, published in refereed archival journals, addressing the association of VRs in homes with health outcomes.

METHODS

Papers were identified through searches using Google Scholar and PubMed with various combinations of the following search terms: home, dwelling, ventilation, air exchange, carbon dioxide, allergy, asthma, health, symptoms. Papers cited in the prior review articles, were also considered. The goal was to identify papers from studies relating home VRs with health outcomes, without simultaneous changes in other building conditions. However, studies were accepted that increased VRs and incorporated simultaneous exposure control measures (such as mattress covers intended to reduce risks of dust mites) if the study had control homes or control periods that also incorporated the added control measures. Excluded from this review were: 1) studies of subjects before and after a move from one home to another home; 2) studies comparing the health of occupants of "green" and conventional homes or occupants of special "healthy homes" with conventional homes; 3) studies comparing occupants of homes with different ventilation system types that did not determine VRs or indoor carbon dioxide concentrations; 4) studies with added mechanical ventilation and simultaneous addition of high efficiency particle filtration; 5) studies assessing how VRs affected perceptions, such as satisfaction with indoor air quality, but with no determination of how VRs affected health outcomes; 6) studies not published in refereed archival journals; 7) studies that only modeled health outcomes, i.e., without empirical health data. Due to the limited amount of published research, exclusion criteria did not include lack of control for specific potential confounders or, in intervention studies, lack of blinding or placebos; however, the implications of potential confounding and lack of placebos is discussed.

The key features and results of the resulting eligible studies were compiled in tables. Information tabulated included a summary of key study methods, the extent of control for confounding, whether or not intervention studies included placebos, and study findings such as odds ratios and 95% confidence intervals.

Many of the reviewed studies included several health outcomes and statistically tested for associations of each health outcome with VR. With 95% confidence limits employed to indicate statistical significance, on average for every 20 independent statistical tests where no actual association exists, one statistically significant (SS) association (5%) will be identified that is merely a chance association. Half of these chance associations would be expected to indicate an improvement in health with increased VR. It was important to determine if the number of reported SS improvements in health outcomes with increased VRs exceeded the expected number of chance improvements in health. Accordingly, the total number of statistical tests for associations of health outcomes with VRs was estimated from the data provided in the papers. The few tests of associations of VRs with injuries or learning disabilities, for which there is no a-priori reason to anticipate an association, were not included in the counts. The number of tests finding SS improvements and worsening in health with increased VR were also determined.

The reviewed studies were too diverse for a statistical meta-analysis. Consequently, observations and conclusions were judgments based on a consideration of study findings and the strengths and weaknesses of the body of research. Other considerations included the fraction of studies finding SS improvements in one or more health outcomes with increased VRs, the fraction of statistical tests indicating an improvement in health with increased VR, and the strengths of associations.

RESULTS

After exclusions based on the criteria given above, twenty studies were identified that provided data on the relationships of VRs in homes with the health of the occupants of the homes. The key study features are provided in Table 1. Tables 2 – 10 provide study results for different health outcomes or groups of health outcomes. The identified research includes five cross-sectional studies, seven case-control studies, and eight intervention studies. Twelve of the studies were performed in Europe with eight of those from Scandinavia. Five studies were performed in North America, and three in China. The health outcomes of most studies were asthma or allergy related or other respiratory health outcomes, primarily self-reported as opposed to objectively measured or doctor diagnosed, outcomes. Three studies included respiratory infection outcomes [13-15] and six studies had skin symptom outcomes [16-21]. Several studies included objectively measured health outcomes, for example measures of lung function, exhaled nitric oxide, or bronchial hyperresponsiveness. No study assessed effects of ventilation rates on premature death, cancer, or other chronic health outcomes, although those outcomes are important and might be indirectly affected by VRs.

All but one of the cross-sectional and case-control studies employed statistical models to quantify the effects of VRs on health, adjusting to the extent possible for the effects of potential confounders. Generally, as indicated in Table 1, the models considered a broad set of potential confounders.

The intervention studies assessed changes in health among the occupants of homes when VRs were intentionally changed. Some intervention studies included periods of real and placebo increases in VRs within homes, making the occupants unaware of when VRs were actually increased. Some of the intervention studies incorporated sets of control homes and control subjects with placebo increases in VRs. In these studies, changes in health among the subjects with real increases in VRs were compared to changes in health among the subjects with placebo increases in VRs. One study[19] decreased VRs provided by existing mechanical ventilation systems but occupants were unaware of the timing of the changes in VRs. Two intervention studies [22,21] had control homes with no placebo conditions, for example with no installation of non-functional mechanical ventilation systems. Relative to the cross sectional and case-control studies, the intervention study designs reduced the potential for error caused by uncontrolled confounding. However, the small number of buildings and subjects in the intervention studies reduced the power of these studies and increased the chance that the intervention study results are not representative of results expected for the larger general population.

Tables 2 – 10 provide study results grouped by health outcome. The vertical and horizontal arrows visually indicate the statistical significance of findings. An upward pointing arrow indicates a statistically significant improvement in health with increased VR or lower CO_2 concentration while a downward pointing arrow has the opposite connotation. A horizontal arrow indicates no statistically significant association of VR or CO_2 concentration with the health outcome. The coloring of arrows conveys the direction of the reported association when suitable information is available, regardless of statistical significance. A green arrow denotes an improvement in health with increased VR or lower CO_2 concentration while a red arrow has the opposite meaning.

Overall, 11 of 20 studies [23,13,24,15,21,16,25,26,22,18,17] reported a SS improvement in one or more health outcomes with increased VRs or with lower CO_2 concentrations that indicate higher VRs. Most of these studies included assessments of multiple additional health outcomes that were not statistically significantly associated with VRs. Two studies [27,28] found that low VRs increased the health risks of mold, dampness, environmental tobacco smoke or other building factors. The study by Singleton et al. [29] had a contrary finding, a SS lower prevalence of diagnosed asthma in homes with higher CO_2 concentrations. One study focusing primarily on how bedroom ventilation affected sleep [20] also reported contrary findings – SS worsenings of mouth and lip dryness when mechanical ventilation was added to bedrooms and decreased bedroom humidity.

Tables 2 – 10 contain many more green arrows than red arrows, indicating many more SS and non-SS improvements in health, than worsenings in health, with increased VR or lower CO_2 concentration. For all health outcomes except lung function, there are at least twice as many green arrows than red arrows. These findings suggest a general trend toward improved health with increased VR but due to low study power or small and inconsistent health benefits the findings of studies are often not SS.

In seven of eight intervention studies, the health effects of occupants of homes were assessed before and after, or with and without, adding a mechanical ventilation (MV) system [30,31,26,25,22,21,20]. One intervention study [19] assessed health effects before and after small reductions in the rates of ventilation provided by preexisting MV systems. Overall, four of seven intervention studies [26,25,22,21] reported SS improvements in one or more health outcomes with increased VRs, although in each of these studies there were no SS improvements in one or more additional health outcomes. One of the six studies with an added MV system [31] reported an improvement in bronchial hyperresponsiveness that was nearly SS ($p = 0.085$). In another study with a small population [30], approximately 80% of the 32 subjects with added MV plus carpet cleaning plus new bedding had improved asthma while asthma improved in 40% of the 12 subjects with placebo MV, carpet cleaning, and new bedding, but this difference was not SS. The intervention study [19] with decreases in the VRs provided by existing MV systems, reported no SS changes in health symptoms, but VRs were decreased by only a very small amount. The intent was to reduce VRs by 20% but the increases in CO_2 concentrations indicated a 9% average decrease in VRs per occupant. An intervention study with added bedroom ventilation [20] had a contrary finding -- SS worsenings of mouth and lip dryness shortly after waking when MV was provided. This study was performed during fall and winter in Denmark and the increased bedroom ventilation reduced bedroom humidity, which might explain the findings. This study did report an improvement in sleep with added bedroom ventilation, and improved sleep might be a source of future improved health.

Three of the intervention studies [30,31,25] were designed to determine whether adding MV to homes in the United Kingdom would improve health of asthmatics by reducing indoor humidity and, in turn, reducing indoor levels of house dust mites. In two of these studies[25,31], all subjects were sensitive to dust mite allergens. Only one of the three studies [25] reported a SS improvement in a health outcome with added MV, although in a second study [31] there was a nearly SS improvement in bronchial hyperresponsiveness ($p = 0.085$) and the third study [30] found large non-SS (p value not provided) improvements in asthma with added MV.

For all health outcomes except breathlessness, in the majority of statistical tests there was no SS association of the health outcome with VR. In two of four tests, breathlessness improved with an increase in VR. With an increased VR, there were SS improvements in cough symptoms in two of eight tests, SS improvements in skin symptoms in two of nine tests, and SS improvements in respiratory infections in two of seven tests. In four of 14 tests, there were SS improvements in wheeze with increased VR. For the grouping of other health outcomes, the measures of health improved with increased VR in 5 of 42 tests. Since cough, wheeze, and breathlessness are often symptoms of asthma, it was surprising that, out of 14 statistical tests, there was only one reported SS improvement in asthma diagnosis or asthma symptoms with increased VR. Also, there was one SS worsening of asthma diagnosis rate with an increased VR. There was only one SS improvement in the lung function or spirometry outcomes out of 13 tests.

When considering both the number of SS positive associations and the magnitudes of odds ratios, increased VR appeared most likely to be beneficial for wheeze. Kovesi et al.[26] reported a SS progressive 12.3% reduction per week in wheeze over 12 weeks after adding MV and Sun et al [18] reported a SS approximate doubling of wheeze with a below-median VR. Also, Bentayeb et al. [24] reported a near doubling of wheeze with above-median CO_2 concentrations, although the association was not quite SS with a lower 95% confidence limit of 0.98. The intervention study of Lajoie et al.[22] also reported non SS improvements in wheeze.

Most health outcomes were subjective. The objective (measured) outcomes included various measures of lung function with results reported in Table 8. Out of 13 statistical tests, there was only one SS improvement with increased VR. Other objective outcomes with results reported in Table 10 included bronchial responsiveness used by one study and, in two instances, markers of inflammation (eosinophil protein, exhaled nitric oxide) with no SS improvements with increased VRs. Relative to the self-reported outcomes, the objectively measured outcomes differ in both their objective status and in the types of outcomes. Therefore, from these findings one cannot draw general inferences about the effects of VRs on objectively-measured versus subjective outcomes.

Most non-objective health outcomes were self-reported outcomes. Doctor diagnosed outcomes may be considered more reliable and are identified in Tables 2- 8 by inclusion of “diagnosed” or “diagnosis” in the outcome description. In Table 5, six studies employed asthma diagnosis as an outcome. There were no SS decreases in asthma diagnosis with increased VR or lower CO_2 concentration; however, there was one SS reduction in asthma diagnosis when CO_2 concentrations exceeded 1000 ppm. In Table 6, there is one doctor diagnosed rhinoconjunctivitis outcome found not associated with VR. One of the skin symptom outcomes in Table 7 was doctor diagnosed and was not associated with VRs. In Table 10, one doctor diagnosed bronchial obstruction outcome was not associated with VR and one doctor diagnosed COPD outcome had a large increase with an above median CO_2 concentration that was nearly SS. In no case did a non-objective doctor-diagnosed health outcome have a SS improvement with increased VR. One concern with these doctor-diagnosed outcomes is that the time of diagnosis may have been far removed from the time of VR assessment and the diagnosis could have even occurred when the subject resided in a different building.

As indicated by the numerical data summarized in Tables 2 – 10, the amount by which changes in VRs in homes affected health outcomes varied widely among studies. For example, one study[23] reported, for nocturnal breathlessness, an odds ratio of 20 per 1000 ppm increase in carbon dioxide indicating a nearly 20 fold increase in nocturnal breathlessness, but the broad confidence limits for this estimate (2.7 – 146) indicate a high uncertainty. Another study [13] reported a doubling of respiratory tract infections with each 500 ppm increase in indoor CO_2 concentrations. A third study [26] reported an 80% reduction in rhinitis with addition of 25 to 30 L s^{-1} of MV. A fourth study [24] reported 40% to 100% increases in breathlessness and cough with above median indoor CO_2 concentrations. However, other studies, such as [22,21] reported SS changes in health outcomes of relatively small magnitude, about 20%, with a change in VR. In both of these studies the increases in VR were modest. One of these studies[21] estimated that VRs increased by 0.18 L s^{-1} with added MV; however, indoor CO_2 concentrations decreased by only 16%, compared to a 9% decrease in control homes. In the second of these studies[22], the VR increased by 0.17 h^{-1} in intervention homes compared to a 0.03 h^{-1} increase in control homes.

The papers for many of the studies clearly indicated the number of statistical tests and for the remaining studies the number of tests were estimated from the data provided. For every study that reported one or more SS improvements in health outcomes with increased VRs, the number of such findings appeared to have exceeded the number of improvements in health expected by chance. For wheeze, breathlessness, cough, skin symptoms, respiratory infections, the grouping of rhinitis or rhinoconjunctivitis or nasal symptoms, and the broad grouping of other outcomes in Table 10, the number of findings of improved health with increased VR exceeded the number of expected chance improvements. Overall, Tables 2 – 10 include 127 findings. With 95% confidence limits as the criterion for statistical significance, we would anticipate three chance findings (2.5% of 127 tests) of SS improvements in health with increased VR. The studies reported 22 findings of improvements in health. Also, we would anticipate three chance findings of SS worsenings in health outcomes with increased VRs which compares to three such reported findings. This analysis indicates that the reported number of improvements in health with increased VR far exceed the expected number of chance improvements.

Three of the studies took place in multi-unit residential facilities with a high occupant density [2418,14]. The findings of these three studies were similar to the findings of other studies. In these three studies, a minority (five of 23) statistical tests indicated a SS improvement in health with increased VR or lower CO_2 concentration, One study[14] reported a dose response improvement in respiratory infection with increased VR but did not report the statistical significance of the trend.. These studies did provide the only two SS improvements in cough; thus, without these studies the only evidence that increased VR improves cough was two non-SS instances of improvement.

The strength of indoor contaminant sources is expected to mediate the relationship of VR with health. Three studies[26,29,13] reported high rates of indoor tobacco smoking and one[29] reported a high rate of heating with wood which might be an indoor pollutant source. Out of 12 total statistical tests, these three studies had two SS improvements in lower respiratory infection, one SS improvement in wheeze, two SS improvements in rhinitis, and one SS worsening of asthma diagnosis with a higher VR or lower CO_2 concentration. Some of the associations were moderately strong to strong, indicating about 50% to 100% increases in health effects with lower VRs. There did seem to be a more consistent evidence of health benefits of increased VR in these three studies (5 of 12 tests), in accordance with expectations for homes with high indoor pollutant sources.

Outdoor air contaminant levels are also expected to mediate the relationship of VR with health, with high outdoor contaminant levels making increased VR less beneficial. Three studies[10,14,18] took place in urban regions of China where high levels of outdoor air contaminants are common. From these three studies, out of 14 statistical tests there are three reported SS improvements in health with increased VR or lower CO_2 concentration and one reported dose-response trend of reduced respiratory infection with increased VR for which the statistical significance is not reported. The extent to which these three studies found health benefits of increased VRs was not clearly different from the results of the full set of studies. However, two of these studies took place in dorm rooms, complicating the comparison.

For the cross sectional and case control studies, study size and the extent of control for confounding, are two indicators of study quality. Excluding studies performed in dorm rooms and nursing homes, six studies reported in eight papers[29,15,27,32,16,28,17,9] had study populations greater than 200 and controlled for a substantial range of potential confounders or found that the potential confounders were not associated with the health outcomes. The findings of this stronger subset of cross-sectional and case control studies are similar to the findings of the broader set of research. The studies provide evidence of health benefits of higher VRs, but these benefits do not occur consistently.

Among the seven intervention studies, three[30,26,25] may be considered the strongest. While all had relatively small study populations (44 to 119), each assessed health with actual and placebo addition of MV and when actual MV was added the change in VR was substantial (see Table 1). In the first of these studies[30] approximately 80% of 32 subjects with added MV had improved asthma, while 40% of subjects with placebo MV had improved asthma, but the difference was not SS. In the second study[26], MV compared to placebo MV was associated with SS reductions in rhinitis with odds ratios of 0.2 after one month and 0.24 after four months. Health center encounters were not reduced by the addition of MV. In the third study[25], with the addition of MV, peak expiratory flow in the morning improved non-significantly ($p = 0.10$), evening peak expiratory flow improved significantly ($p = 0.002$), forced expiratory volume improved non-significantly ($p = 0.5$), and there were no SS changes in an asthma control score or respiratory questionnaire score. These three studies provide evidence of health benefits of adding MV, but again the benefits do not occur consistently.

The studies employed a wide range of VR metrics in the statistical analyses of health risks. Examples included analyses of health risks: 1) with the VR or carbon dioxide above or below the median, 2) with an indoor carbon dioxide concentration above or below 1000 ppm, 3) per 500 or 1000 ppm increase in indoor carbon dioxide concentration; 4) per 0.1 h^{-1} change in VR, 5) with VRs above versus below 0.5 h^{-1}; 6) with addition, versus without addition, of ~0.17 h^{-1}, 0.4 h^{-1}, or 0.5 h^{-1} of mechanical ventilation. Three of the prior reviews [5,4,12] indicated that the published data suggest increased health risks in homes with VRs less than approximately 0.5 h^{-1}. Only two studies directly used this VR metric, above versus below 0.5 h^{-1}, in their analysis. Emenius et al.[32] found no differences in wheeze with VRs above versus below 0.5 h^{-1}. Oie et al. [27] found no direct SS association of bronchial obstruction with VRs; however, having an air exchange rate below 0.5 h^{-1} increased the risks of bronchial obstruction with exposure to environmental tobacco smoke, dampness, textile wall paper, and plasticizers. The results of other studies provide less direct evidence related to choosing 0.5 h^{-1} as a metric for adequate ventilation. Calleson et al. [17] found that asthmatic children sensitized to allergens had a median air exchange rate of 0.41 h^{-1} compared to median of 0.56 h^{-1} for non-sensitized asthmatic children. Bornehag et al. [16] reported that increased allergy symptoms were associated with small decreases in mean whole-house VRs from 0.38 to 0.34 h^{-1}, and with small decreases in mean bedroom VRs from 0.37 to 0.32 h^{-1}. They also found a dose response relationship, with the risk of being an allergy case increasing as VRs decreased below approximately 0.4 h^{-1}, although the trend was not SS. Lajoie et al. [22] reported a SS decrease in wheeze with the addition of MV, increasing the geometric mean VR from 0.17 to 0.34 h^{-1}. In a set of homes with VRs ranging from 0.07 h^{-1} to 1.14 h^{-1}, with a mean VR of 0.36 h^{-1}, Wang et al. [15] found a 14% decrease in asthma symptoms for each 0.1 h^{-1} increase in VR. This set of findings provides no clear indication of a threshold VR below which adverse health effects develop; however, a majority of studies did find improvements in health as VRs increase in the 0.07 h^{-1} to 1.14 h^{-1} range. Unfortunately, the reviewed research did not indicate whether there are health benefits of increasing VRs in the VR range of 0.5 h^{-1} and higher.

Table 1. Studies of the association of VRs in homes with occupant health*.

Study	Description	Controlled confounders
	CROSS-SECTIONAL STUDIES	
13	Cross-sectional study of 49 homes of Inuit children in Canada. VRs were measured using tracer gas methods and indoor CO_2 concentrations were measured. Lower respiratory tract infections (bronchiolitis or pneumonia) were determined with a questionnaire. 94% of homes had smokers	Gender, age, number of occupants.
14	Cross-sectional study in China estimated VRs, based on indoor CO_2 concentrations, measured temperatures, and relative humidity values in 238 dorm rooms, and used questionnaires to determine resident's incidence of common colds.	Gender, age, family allergy, environmental tobacco smoke, building age, crowdedness
24	Cross-sectional study of 600 elderly residents in 50 nursing homes in Europe. Indoor environmental conditions including CO_2 concentrations were measured, lung function was measured, exhaled NO (a marker of inflammation) was measured, and respiratory symptoms were determined with a questionnaire.	Gender, age, country, body mass index, education, smoking, season
29	Cross-sectional study of indoor CO_2 levels, other indoor pollutant levels, building conditions and respiratory health in 213 Alaska native children. 72 children had history of chronic lung disease and 141 children in the same households did not have this history. Crowded conditions, tobacco smoking, wood smoke, and dampness were common. Respiratory health was determined with interviews.	Age, crowding, presence of piped water, and, in some analyses, history of chronic lung disease
15	Cross-sectional study in Sweden of 605 single family houses with 1160 adults. Home characteristics were determined via inspections. Temperature, humidity, air exchange rate, and wood moisture content were measured. Respiratory health, symptoms and infections and demographic data were assessed with a questionnaire.	Analyses for asthma symptoms and wheeze controlled for gender, age, current smoking, outdoor temperature. Analyses for respiratory infections and rhinitis controlled for gender, age, and current smoking. Building age was shown to be not significant predictor of health.
	CASE-CONTROL STUDIES	
23	Case- control study with 88 adult subjects from Sweden. Cases had, at least one of the following: asthma attacks in the last 12 months, nocturnal breathlessness in the last 12 months, current use of asthma medication. Controls had none of those three characteristics. Health data were obtained with a questionnaire and via objective health measurements. Study included indoor air quality measurements, including measurements of Indoor CO_2 concentrations.	Age, sex, current smoking, carpets, dust mites
27	Case-control study in Norway of 172 children with bronchial obstruction and 172 control children. Home environmental conditions were assessed via inspection and measurements.	In addition to case-control pairing of subjects which controlled for age, analyses controlled for gender,

		parental atopy, breast feeding, siblings, day care attendance, ETS exposure, home dampness, birth weight, maternal age and education, income, pets and several building features
32	Case-control study in Sweden with each of the 181 case children with recurrent wheeze matched with two control children without wheeze. VRs and other home characteristics were determined from measurements and inspections.	Day of birth, gender, parental allergy or asthma, maternal smoking during pregnancy, breast feeding, building age, outdoor temperature
16 28	This study in Sweden compared measured VRs of 198 children with allergy symptoms and 202 control children without allergy symptoms	Gender, smoking in family, moisture problems in home, concentrations of a phthalate in dust
17,9,33	Case-control study of Danish children. Measured bedroom VRs were based on CO_2 concentrations Inspected homes of 200 case children with allergic disease and 242 controls without allergic disease.	Some analyses controlled for allergic predisposition, gender, breastfeeding, indoor smoking; however, the authors did not describe the controlled parameters in the analysis of associations of health with air exchange rates.
10	Case-control study with asthmatic and non-asthmatic children in 454 homes in China. Measured night time CO_2 concentrations in bedrooms were used as indicators of VR.	None described
18	Case-control study of residents of naturally-ventilated dorm rooms in China. The 143 cases had two or more symptoms of asthma, rhinitis, or eczema, the 205 controls reported no symptoms. VRs were based on the measured build-up of CO_2 concentrations at night.	Gender, age, allergy of family member, smoking, passive smoking, indoor pet, building construction period
INTERVENTION STUDIES		
30	Intervention in homes of asthmatics in UK. In homes of 32 asthmatics, ~ 0.5 h^{-1} of mechanical ventilation (MV) was added, carpets were cleaned, new bedding was provided. In homes of 12 asthmatics carpets were cleaned and new bedding was provided, and placebo MV was added. In homes of 10 asthmatics, there was placebo carpet cleaning and mechanical ventilation. IAQ measurements and health questionnaire performed every 3 months. (The present review considers only results of a comparison of the first two groups, which differed only in the addition of mechanical ventilation.)	The intervention design controlled for personal and most environmental factors
31	40 asthmatic adults and children in U.K. who were sensitive to house dust mites were divided into 4 groups: 1) 0.4 h^{-1} to 0.5 h^{-1} of MV added and received a high efficiency vacuum; 2) received only MV; 3) received only a high efficiency vacuum; and, 4) had no intervention. Humidity, mite numbers, mite allergen levels, lung function, and bronchial hyperresponsiveness were measured, health symptom scores were obtained. (The present review considers only results the comparison of group 1 with group 3, which differed only in the addition of mechanical ventilation.)	The intervention design controlled for most personal factors and building characteristics.
19	Intervention study in Sweden with 44 subjects reduced MV rates during some winter periods by a small amount (goal was 20% reduction but the carbon dioxide data indicated a 9% reduction) and assessed effects on SBS symptoms determined via a questionnaire. Subjects were blinded with respect to the changes in VRs.	The intervention design controlled for most personal factors and building characteristics. Indoor temperatures not affected by interventions.
26	Intervention study in Canada compared respiratory symptoms and health center use during active 25 to 30 L s^{-1} and placebo MV in 51 homes of Inuit children. Smoking occurred in most homes.	The intervention study design controlled for most personal and household factors
25	Intervention study in 119 homes of adult mite-allergic asthmatics in UK. 0.5 h^{-1} of MV added in 60 homes and placebo MV in 59 homes. All homes had carpets cleaned, new bedding, mattress covers. Allergen levels, temperature, humidity were measured. Symptoms were assessed via a questionnaire, asthma medication tracked, asthma medical care visits tracked, lung function measured.	The intervention design controlled for personal and household factors.
22	This intervention study in Canada measured environmental conditions, inspected homes, and tracked asthma symptoms among asthmatics in 43 homes with added MV and 40 control homes without MV. With added MV, the mean VR increased 0.17 h^{-1}. In control homes, the mean VR increased 0.03 h^{-1}. There was no placebo MV, thus, the subjects and research team were not blinded.	The intervention design controlled for personal and building factors. Analysis models controlled for year of construction, attached garage, woodstove, age, gender, parents education, eczema.
20	Intervention study with 16 adult subjects focused primarily on how bedroom ventilation affected sleep and next day performance; however, the study included several self-reported health outcomes. Considering only the main study, because bedroom noise may have affected findings of a pilot study, self-reported symptoms were recorded shortly after waking after periods with and without operation of a fan that increased the VR in bedrooms.	The intervention study design controlled for most personal and household factors.

21	VRs, aspects of indoor air quality, and occupant health symptoms of two groups of weatherized homes in the U.S. were compared. Group 1 had homes with weatherization that resulted in envelope air leakage reduction and no MV. Group 2 had homes with weatherization that resulted in envelope air leakage reduction and addition of MV. The estimated mean VR in Group 2 homes increased by 18 L s^{-1} after weatherization. The post weatherization VR was 19 L s^{-1} higher in Group 2 homes than in Group 1 homes. .However, CO2 concentrations decreased by only 16% in Group 2 homes relative to a 9% decrease in Group 1 homes.	None described, although there were no SS differences between groups in subject age, education, race, gender, income, years in the home.

*VR = ventilation rate, MV = mechanical ventilation

Table 2. Associations of ventilation rates with wheeze.

Study	Outcomes	Findings
23	wheezing or whistling in chest	↔ no association
24	wheeze	↔ OR 1.93 (0.98 – 3.85) for above median CO_2
15	current wheeze	↔ OR 0.94 (0.84 – 1.06) per 0.1 h^{-1} increase in VR
32	recurrent wheeze	↔ OR 1.3 (0.80 – 2.0) for ≥ 0.5 h^{-1} VR ↔ no association with ventilation rate per person
18	wheeze	↑ OR 2.28 (1.38 – 3.75) for winter VR below the median of 0.7 h^{-1} ↔ no association with the high summer VRs
31	wheeze last night wheeze today	↔ no association with added MV ↔ no association with added MV
26	wheeze	↑ MV compared to placebo was associated with a 12.3% (1.9% - 21.6%) reduction per week over 12 weeks
22	days with wheezing % of children with wheezing % with ≥ 4 wheeze episodes	↔ no change with added MV relative to control ↑ -22.1% (-41.8% to – 2.3%) with added MV relative to control ↑ -20% (-38.8% to – 1.1%) with added MV relative to control
29	Wheeze between colds	↔ no association with CO_2 > 1000 ppm

Key: SS = statistically significant, i.e. 95% confidence interval excludes unity or p > 0.05 ; ↔ no SS change with higher ventilation rate or lower carbon dioxide concentration; ↑ = SS improvement with higher ventilation rate or lower carbon dioxide concentration; ↓ = SS worsening with higher ventilation rate or lower carbon dioxide concentration; MV = mechanical ventilation; VR = ventilation rate; OR = odds ratio; (lower 95% confidence limit, upper 95% confidence limit)

Table 3. Associations of ventilation rates with breathlessness

Study	Outcomes	Findings
23	nocturnal breathlessness daytime breathlessness	↑ OR 20 (2.7 – 146) per 1000 ppm CO_2 ↔ no association
24	unusual breathlessness	↑ OR 1.68 (1.32 – 2.15) for above median CO_2
22	days with breathlessness	↔ -0.3 (-1.9 to 1.3) days per 14 days with added MV relative to control

Table 4. Associations of ventilation rates with cough.

Study	Outcomes	Findings
31	cough last night	↔ no association
24	unusual cough	↑ OR 2.01 (1.55 – 2.63) for above median CO_2
18	dry cough	↑ OR 2.26 (1.08 – 4.75) for winter VR below the median of 0.7 h^{-1} ↔ no association with the high summer VRs
19	cough	↔ no SS change with approximately 10% reduction in VR
22	days with cough % of children with night cough	↔ 0.6 (-1.3 to 2.5) days per 14 days with added MV relative to control ↔ -15.6% (-42.7% to 11.6%) with added MV relative to control
29	cough between colds	↔ no association with CO_2 > 1000 ppm

Table 5. Associations of ventilation rates with asthma diagnosis or symptoms

Study	Outcomes	Findings
24	ever had asthma diagnosis	↔ OR 1.09 (0.67 – 1.78) for above median CO_2
29	asthma diagnosis	↓ OR 0.32 (p= 0.032) for CO_2 > 1000 ppm ↔ OR 0.38 (p = 0.112) for CO_2 > 1000 ppm when adjusted for high risk status
15	current asthma symptoms	↑ OR 0.86 (0.75 – 0.98) per 0.1 h^{-1} increase in VR
16	asthma diagnosis	↔ no association with whole house VR ↔ no association with bedroom VR
17	asthma diagnosis	↔ no association of IgE negative asthma with VR ↔ no association of IgE positive asthma with VR
10	asthma diagnosis	↔ although more homes of cases with asthma had CO_2 > 1000 ppm in winter and summer, the differences were not SS
30	improved asthma	↔ approximately 80% of 32 subjects with added MV plus carpet cleaning plus new bedding had improved asthma versus ~ 40% of 12 subjects with placebo MV plus carpet cleaning plus new bedding, but the difference was not SS (p value not provided)
31	asthma last night	↔ no association with added mechanical ventilation (p = 0.4)
22	days with at least one of 4 asthma symptoms over 14 days months of asthma control over 4 months	↔ -0.6 (-2.0 to 0.9) days per 14 days with added MV relative to control group ↔ -0.01 (-0.6 to 0.5) months per 4 months with added MV relative to control group
21	% with asthma	↔ - 2% (p = 0.314) for added MV group versus control

Table 6. Associations of ventilation rates with rhinitis, rhinoconjunctivitis, nasal symptoms.

Study	Outcomes	Findings
15	current rhinitis without infection	↔ OR 1.01 (0.91 – 1.13) per 0.1 h^{-1} increase in VR
16	doctor-diagnosed rhinitis	↔ in single-family houses, mean whole-house VR 0.35 h^{-1} with rhinitis versus 0.38 h^{-1} without, p = 0.086 ↑ in single-family houses, mean bedroom VR 0.32 h^{-1} with rhinitis versus 0.37 h^{-1} without, p = 0.023
17	doctor diagnosed rhinoconjunctivitis	↔ no association of IgE negative rhinoconjunctivitis with VR ↔ no association of IgE positive rhinoconjunctivitis with VR
18	rhinitis	↔ OR 1.2 (0.78 – 1.86) for winter VR below the 0.7 h^{-1} median ↔ no association with the high summer VRs
19	nasal symptoms	↔ no SS change with approximately 10% reduction in VR
26	rhinitis, apart from cold air	↑ MV compared to placebo was associated with reduced rhinitis with OR 0.2 (0.058 – 0.69) after 1 month and ↑ OR 0.24 (0.054 – 0.9) after 4 months
25	rhinitis scale nasal discharge nasal blockage	↔ no association with added MV compared to placebo ↔ no association with added MV compared to placebo ↔ no association with added MV compared to placebo
22	% of children with rhinitis	↔ -0.5% (-23.4% to 22.5%) with added MV relative to control
20	nasal dryness nose blocked	↔ no SS change with added bedroom MV (p value not provided) ↔ no SS change with added bedroom MV (p value not provided)

Table 7. Associations of ventilation rates with skin symptoms.

Study	Outcomes	Findings
16	doctor-diagnosed eczema	↑ in single-family houses, mean whole-house VR 0.34 h^{-1} with eczema versus 0.38 h^{-1}

		without, p = 0.028 ↑ in single-family houses, mean bedroom VR 0.31 h^{-1} with eczema versus 0.37 h^{-1} without, p = 0.016
17	doctor diagnosed atopic dermatitis	↔ no association of IgE negative dermatitis with VR ↔ no association of IgE positive dermatitis with VR
18	eczema	↔ OR 1.44 (0.60 – 3.43) for winter VRs below the median of 0.7 h^{-1} ↔ no association with the high summer VRs
19	facial skin symptoms	↔ no SS change with approximately 10% reduction in VR
20	skin dryness	↔ no SS change with added bedroom MV
21	% with eczema or skin allergy	↔ -13% (p = 0.773) for added MV group versus control

Table 8. Associations of ventilation rates with lung function, spirometry outcomes.

Study	Outcomes	Findings
24	FEV_1 % of predicted FVC % of predicted FEV_1/FVC <70% % of predicted	↔ 1.23 (0.84, 1.81) for above median CO_2 ↔ 0.98 (0.91, 1.06) for above median CO_2 ↔ 0.60 (0.20, 1.75) for above median CO_2
31	FEV_1 PEF	↔ outcome improved with added MV with p = 0.08 ↔ no association with added MV
25	morning PEF evening PEF FEV_1	↔ morning PEF improved with added MV with p = 0.10 ↑ evening PEF improved with added MV with p = 0.002 ↔ increased by 1.8% of predicted with added MV versus by 1% of predicted in control group (p = 0.5)
22	maximum PEF (L/min) morning PEF (L/min) % daily variability in PEF days in 14 days with ≥ 15% variability in PEF % children with ≥1 day per 14 days with ≥ 15% variability in PEF	↔ 12.2 (-25.2, 49.6) with added MV relative to control group ↔ 3.3 (-22.2, 28.9) with added MV relative to control group ↔ 1.2% (-0.9%, 3.3%) with added MV relative to control group ↔ 2.8 (-1.8 – 7.5) with added MV relative to control group ↔ 14.3 (-24.3, 52.9) with added MV relative to control group

Table 9. Associations of ventilation rates with respiratory infections.

Study	Outcomes	Findings
13	lower respiratory infection	↑ OR 2.85 (1.23 – 6.59) per 500 ppm mean CO_2 ↑ OR 1.49 (1.02 – 2.20) per 500 ppm peak CO_2 ↔ OR 1.21 (0.98 – 1.50) per 1 L/s per person decrease ↔ OR 0.98 (0.86 – 1.13) for 0.1 h^{-1} decrease in air change rate
14	≥ 6 common colds per year	↔ non SS increase with decreased VR per person in winter ↔ non SS increase with decreased VR per person in summer ? dose response increase of ≥ 6 common colds with decrease in winter VR in newer buildings but statistical significance not described
15	respiratory infections	↔ OR 0.98 (0.92 – 1.05) per 0.1 h^{-1} increase in VR

Table 10. Associations of ventilation rates with groups of symptoms or other outcomes.

Study	Outcomes	Findings
27	doctor diagnosed bronchial obstruction	↔ OR 0.70 (0.39 – 1.25) for VR below 0.5 h^{-1} ↔ OR 0.93 (0.48 – 1.83) for VR (h^{-1}) continuous ↔ OR 0.98 (0.96 – 1.01) for L/s per person continuous
31	urinary eosinophil protein urinary cotinine	↔ no change with added MV ↔ no change with added MV
16	allergy symptoms (two of wheeze, rhinitis, eczema)	↑ Cases in single family houses had lower mean whole-house mean VR (0.34 h^{-1}) than controls (0.38 h^{-1}) with p = 0.014 ↑ Cases in single family houses had a lower mean bedroom VR (0.32 h^{-1}) than controls

		($0.37\ h^{-1}$) with $p = 0.011$ ↔ in single-family houses, there were dose response relationships between case status and lower whole-house and bedroom VRs that were not SS ↔ in chain houses and multi-family houses case status not associated with VRs
24	exhaled nitric oxide phlegm doctor diagnosed COP	↔ OR 0.95 (0.74 – 1.22) for above median CO_2 ↔ OR 0.87 (0.49 – 1.56) for above median CO_2 ↔ OR 2.94 (0.98 – 8.84) for above median CO_2
17	IgE sensitivity to indoor or outdoor or food allergens in asthmatics	↑ VRs were lower for IgE positive asthmatics ($0.41\ h^{-1}$), versus IgE negative asthmatics ($0.56\ h^{-1}$), $p < 0.05$
18	case status with two or more symptoms of asthma, rhinitis, eczema	↑ OR 2.00 (1.16 – 3.45) for winter VR below the median of $0.7\ h^{-1}$ ↔ no association with the high summer VRs
31	bronchial hyperresponsiveness among dust mite sensitive asthmatics	↔ outcome improved with added MV with p = 0.085
19	throat irritation headache tiredness eye symptoms	↔ no SS change with ~ 10% reduction in VR ↔ no SS change with ~ 10% reduction in VR ↔ no SS change with ~ 10% reduction in VR ↔ no SS change with ~ 10% reduction in VR
26	health center encounters	↔ no association with added MV compared to placebo
25	asthma control score respiratory questionnaire score rescue medication doctor or emergency dept. visits hospitalizations sneezing	↔ no association with added MV compared to placebo ↔ no association with added MV compared to placebo ↔ no association with added MV compared to placebo ↔ no association with added MV compared to placebo ↔ no association with added MV compared to placebo ↔ no association with added MV compared to placebo
22	% children with emergency visit % children with hospitalization days of relief medication in 14 days % of children with over 8 doses of relief medication disturbed sleep, days in 14 days	↔ 2.4% (-25.6% to 30.5%) for added MV relative to control ↔ -8.3% (-31.1% to 14.6%) for added MV relative to control ↔ -1.1 (-2.6 to 0.4) days per 14 days for added MV relative to control ↔ -18.9% (-40.7% to 2.9%) for added MV relative to control ↔ 0.4 (-0.8 to 1.5) days per 14 days for added MV relative to control
20	mouth dryness lip dryness eye dryness eye clearness headache	↓ with added bedroom MV ↓ with added bedroom MV ↔ no SS change for added bedroom MV ↔ no SS change for added bedroom MV ↔ no SS change for added bedroom MV
21	general health score % with 3 or more ear infections % with hay fever % with respiratory allergy % with headaches	↔ improvement p = 0.062 for added MV group versus control ↔ 3% increase with added MV versus 0% increase in control group (p = 0.311) ↔ 5% decrease with added MV versus 7% decrease in control group (p = 0.821) ↔ 8% decrease with added MV versus 14% decrease in control group (p = 0.447) ↑ 31% decrease with added MV versus 10% decrease in control group (p = 0.041)

DISCUSSION

As indicated in Table 1, most studies have controlled for a substantial range of potential confounders. It remains important to consider the significance of uncontrolled confounding. To influence study findings, a confounder needs to be correlated with both the risk factor; i.e., VR or CO_2 concentration, and the health outcome. The potential significance of uncontrolled confounding is discussed in the subsequent paragraphs. While more thorough control for potential confounding, particularly by socio-economic status (SES), is desirable, no source of confounding was identified that appears likely to explain the observed associations of VRs with respiratory health outcomes.

- Age, gender, pets, and indicators of predisposition to allergic or other health effects, such as parental allergy, are commonly correlated with health. However, there is little reason to expect a consistent correlation of these factors with home VRs. In individual studies, correlations of these factors with home VRs might have occurred by chance, but confounding by these factors is not likely to have systematically biased the findings of the body of research.

- Most of the cross sectional and case control studies failed to control for SES. Many of the studies were performed in Scandinavia, where variability in SES is less pronounced than in many locations. Lower SES, as a proxy for other factors, has often been associated with poorer health. Direct evidence linking SES with home VRs was not identified. One can hypothesize that lower SES and less healthy subjects reside in older more leaky houses with higher air exchange rates, thus, failure to control for SES might obscure a real relationship of VR with health. However, we might also expect lower SES subjects to live in more crowded homes with lower VRs per person and higher indoor CO_2 concentrations. Thus, failure to control for SES might lead to an apparent association of lower VRs or higher indoor CO_2 concentrations with health effects. Five of 12 cross sectional or case control studies controlled for SES, crowding, or number of occupants. Two of the five studies[29,27] reported no SS associations of VRs with health outcomes, although one of these studies[27] found that lower VRs increased the health risk of other building factors. One of the five studies[14] reported substantial but non SS increases in respiratory infections with lower VRs after controlling for crowding and also reported a dose response relationship of higher CO_2 with increased respiratory infection for which the statistical significance was not indicated. Two of the five studies found SS increases in health effects in homes with higher CO_2 concentrations. Control for SES or crowding did not eliminate the evidence of increased health effects in homes with lower VRs. In future research, increased attention should be placed on control for SES.

- Only two of the 12 case control or cross sectional studies controlled for home dampness which has often been associated with increases in respiratory health effects[34]. Direct evidence linking home dampness with home VRs was not identified. Much of home dampness is caused by water leaks and it seems unlikely that home water leaks are strongly correlated with home VRs. Indoor humidity levels are affected by VRs and high indoor humidity can lead to dampness and mold in homes. However, indoor airborne moisture can be considered another contaminant with a concentration affected by VR and a possible effect on health. The research in this review is primarily from regions with cold climates where higher VRs will tend to reduce indoor humidity levels. Controlling for home dampness might then tend to obscure real associations of VRs with health mediated by the effects of VRs on indoor humidity. One of the two studies that did control for dampness found home VRs not directly associated with bronchial hyperresponsiveness; however, lower home VRs increased the health risks of other building factors. The second of these studies that controlled for home dampness found lower home VRs associated with SS increases in rhinitis, eczema, and case status but no SS association with asthma diagnosis.

- Smoking and ETS are associated with adverse respiratory health effects. Direct evidence linking smoking or ETS with home VRs was not identified. Possibly, occupants of homes with smoking open windows more often to reduce indoor smoke levels. If so, occupants of homes with higher VRs would tend to have more smoking-caused respiratory health effects and a failure to control for smoking would tend to obscure real relationships of home VRs with health. Not counting one instance of control for maternal smoking during pregnancy, eight of 12 cross sectional or case control studies controlled for smoking and/or environmental tobacco smoke (ETS) and six of these studies[24,15,23,16-18] report SS associations of respiratory health effects with lower VRs or higher indoor CO_2 concentrations. Thus, control for smoking or ETS was common and a majority of studies that controlled for these factors found associations of respiratory health effects with lower VRs or higher indoor CO_2 concentrations.

A majority of the health outcomes were self-reported via questionnaires. If subjects were aware of the VRs in their homes and believed that lower home VRs caused adverse health effects, then the reporting of health effects might have been biased upward among subjects in homes with lower VRs. Six of eight intervention studies protected against this possible bias, for example by including periods of placebo MV; however, all of cross sectional and case control studies are subject to this potential bias. No data were identified that indicate the level of awareness of occupants of homes with home VRs. Few cues available to indicate home VRs to occupants. Odors are one possible indicator of VRs but the sources of odors vary among homes making odor levels an imprecise indicator of home VR.

Many of the studies used measured CO_2 concentrations as a proxy for home VRs and some studies estimated home VRs from the measured CO_2 concentrations. There are many potential sources of error when estimating VRs from CO_2 concentrations[35]. However, the primary focus of this paper is an assessment of whether higher VRs in homes are associated with improvements in health. For this purpose, it is only necessary that higher measured VRs correspond with actual increases in VRs and that lower indoor CO_2 concentrations are indicative of higher VRs. Thus, the errors that commonly occur when estimating VRs from CO_2 data should not affect findings related to the question of whether or not home VRs affect health. A secondary focus of this review was to determine whether the published research indicated a threshold VR, above which further increases in VR do not improve health. Errors in measurement of VR magnitudes will hinder our ability to identify a threshold. However, the primary limitation relative to the threshold question is the small amount of relevant data.

The research findings are mixed. Just over half of studies reported one or more SS health benefits from increased VRs. Among studies that reported one or more health benefits from increased VRs, most of these studies included other health outcomes that did not have a SS improvement from increased VRs. Overall, however, the number of SS improvements in health with increased VRs far exceeded the expected chance improvements in health. The magnitude of the reported SS improvements in health outcomes with increased VRs were highly variable, ranging from 20% to several-fold improvements, although the magnitude of associated changes in VR also varied among studies. Among the health outcomes assessed, increased VR appeared most likely to be beneficial for wheeze. The findings from subsets of studies considered scientifically strongest were not clearly different from the findings of the full set of studies. No source of residual confounding was identified that appears likely to explain the observed associations of VRs with respiratory health outcomes. The research did not enable identification of a threshold VR below which adverse health effects develop or above which further increases in VRs do not affect health. A threshold could be used as a basis for the minimum VRs specified in standards. However, considering that many factors other than VRs affect indoor pollutant exposure and vary among buildings and that peoples' sensitivity to pollutants also varies, it may be unreasonable to expect a threshold.

It is useful to consider why there were no SS improvements in health with increased VRs in a majority of statistical tests and in nearly half of studies. No definitive answers are provided by the available data. The large number of non-SS improvements in health, indicated by green shaded arrows in Tables 2-10, suggest that insufficient study power is a contributing factor. Most intervention studies had few homes and subjects and, in the cross sectional and intervention studies, the variability in indoor pollutant sources strengths among homes could have overwhelmed the effects of VRs on exposure and health making it hard to detect effects of VRs without a very large study. It seems likely that in most of the situations examined, the changes in VRs did not affect indoor pollutant exposures sufficiently to cause measurable changes in health.

There are many potential explanations for the variability among research findings. Factors that are expected to influence the ventilation-health relationship likely varied among study settings. These factors, in addition to study design and size, include the strength and types of indoor pollutant sources, the levels of pollutants and moisture in outdoor air, the types of health outcomes considered, the health status and susceptibility of the subjects, the magnitude of VRs, the magnitude of changes in VRs in intervention studies, and the extent to which recirculated indoor air was filtered to remove particles. The prior discussion has addressed the extent to which study findings varied with changes in many of these factors. Given the importance of these factors, we cannot expect highly consistent findings or expect ventilation alone to optimize health conditions in homes – indoor pollutant sources should be minimized and efficient filtration systems, at least for particles, should be employed.

Statistical associations do not prove causal relationships. The associations can, for example, be a consequence of confounding or chance. Also, if subjects are not blinded or subject to placebo interventions, reported improvements in subjective health outcomes may be a consequence of the subjects' expectations. However, the prior discussions suggest that the overall findings of the reviewed studies are unlikely to be largely a consequence of residual confounding, chance, or subjects' expectations of improved health when VRs are higher.

Much of the published research has investigated the influence of VRs in homes on asthma and related respiratory health outcomes. For other types of health outcomes, little is known about their dependence on home VRs. Only 20 studies met inclusion criteria, and some of the studies, particularly, the intervention studies, had small study populations. A majority of the research was performed in Europe; thus, the findings over-represent the situation in Europe. Publication bias, the more frequent publication of studies with significant findings, is always a concern. The studies used a broad range of ventilation-rate metrics, complicating comparisons among the findings of different studies. To support future standards that specify minimum acceptable VRs in homes and to help elucidate the most relevant minimum VR metrics for homes, it would be helpful if VR measurement methods were standardized and if all studies determined and reported air exchange rates, VRs per person, and VRs per unit floor area. Future intervention studies should measure and report initial and final VRs, not just the amount of added mechanical ventilation. Future research should also consider how home VRs affect sensitive segments of the population. Although challenging, future research should strive to better characterize indoor pollutant sources, outdoor pollutant levels, and other factors affecting indoor pollutant exposures because the relationship of VRs with health is expected to depend on these factors.

CONCLUSIONS

Given the inconsistency among study results, it is tempting to conclude that the available research does not support a finding of an association of home VRs with health. However, such a conclusion would be inconsistent with the following findings:

- The reported number of SS increases in health with increased VRs was about seven times higher than expected by chance; while there were few reported SS worsenings in health with increased VR.
- The number of SS and non SS improvements in health with increased VR far exceeded the number of SS and non SS worsenings of health.
- In many instances, the improvements in health with increased VR exceeded 50%.
- Most studies controlled for a broad range of confounders and no source of confounding was identified that appears likely to explain the observed associations of VRs with respiratory health outcomes.
- With the incorporation of placebos in most intervention studies and the likely ignorance about VRs of subjects of cross sectional and case control studies, study findings are unlikely to be largely a consequence of subjects' expectations of improved health when VRs are higher.

Consequently, the current evidence indicates a tendency for improvements in respiratory health with increased home VRs; however, health benefits do not occur consistently; thus, other methods of indoor exposure control must be employed together with ventilation. Wheeze was most clearly associated with VR. The research did not enable identification of a threshold VR below which adverse health effects occur or above which further increases in VRs do not affect health. Much of the published research has investigated the influence of VRs in homes on asthma and related respiratory health outcomes. For other types of health outcomes, little is known about their dependence on home VRs.

ACKNOWLEDGMENTS

This study was funded through interagency agreement DW- 89-92337001 between the Indoor Environments Division, Office of Radiation and Indoor Air of the U.S. Environmental Protection Agency (EPA) and the U. S. Department of Energy under contract DE-AC02-05CH11231. The authors thank Sean Carter and Laura Kolb for program management and Mark Mendell and Brett Singer for reviewing a draft of this paper.

REFERENCES

1 Seppänen O, Fisk WJ, Lei QH. Ventilation and performance in office work. *Indoor Air* 2006; **16**: 28-36.

2 Seppänen OA, Fisk WJ, Mendell MJ. Association of ventilation rates and CO_2 concentrations with health and other responses in commercial and institutional buildings. *Indoor Air* 1999; **9**: 226-52.

3 Fisk WJ, Mirer AG, Mendell MJ. Quantitative relationship of sick building syndrome symptoms with ventilation rates. *Indoor Air* 2009; **19**: 159-65.
4 Wargocki P, Sundell J, Bischof W, Brundrett G, Fanger PO, Gyntelberg F, Hanssen SO, Harrison P, Pickering A, Seppänen O, Wouters P. Ventilation and health in non-industrial indoor environments: report from a European multidisciplinary scientific consensus meeting (EUROVEN). *Indoor Air* 2002; **12**: 113-28.
5 Sundell J, Levin H, Nazaroff WW, Cain WS, Fisk WJ, Grimsrud DT, Gyntelberg F, Li Y, Persily AK, Pickering AC, Samet JM, Spengler JD, Taylor ST, Weschler CJ. Ventilation rates and health: multidisciplinary review of the scientific literature. *Indoor Air* 2011; **21**: 191-204.
6 Carrer P, Wargocki P, Fanetti A, Bischof W, Fernandes EDO, Hartmann T, Kephalopoulos S, Palkonen S, Seppänen O. What does the scientific literature tell us about the ventilation–health relationship in public and residential buildings? *Building and Environment* 2015; **94**: 273-86.
7 Fisk WJ. The ventilation problem in schools: literature review. *Indoor Air* 2017; **27**: 1039-51.
8 Klepeis NE, Nelson WC, Ott WR, Robinson JP, Tsang AM, Switzer P, Behar JV, Hern SC, Engelmann WH. The National Human Activity Pattern Survey (NHAPS): a resource for assessing exposure to environmental pollutants. *Journal of Exposure Analysis and Environmental Epidemiology* 2001; **11**: 231-52.
9 Bekö G, Lund T, Nors F, Toftum J, Clausen G. Ventilation rates in the bedrooms of 500 Danish children. *Building and Environment* 2010; **45**: 2289-95.
10 Liu W, Huang C, Shen L, Wang X, Cai J, Zou Z, Chang J. Associations between natural ventilation for the child's bedroom during night and childhood asthma in Shanghai, China. *Procedia Engineering* 2015; **121**: 501-5.
11 Brown S, Sim MR, Abramson MJ, Gray CN. Concentrations of volatile organic compounds in indoor air–a review. *Indoor Air* 1994; **4**: 123-34.
12 Wargocki P. The effects of ventilation in homes on health. *International Journal of Ventilation* 2013; **12**: 101-18.
13 Kovesi T, Gilbert NL, Stocco C, Fugler D, Dales RE, Guay M, Miller JD. Indoor air quality and the risk of lower respiratory tract infections in young Canadian Inuit children. *Canadian Medical Association Journal* 2007; **177**: 155-60.
14 Sun Y, Wang Z, Zhang Y, Sundell J. In China, students in crowded dormitories with a low ventilation rate have more common colds: evidence for airborne transmission. *PLoS One* 2011; **6**: e27140.
15 Wang J, Engvall K, Smedje G, Nilsson H, Norbäck D. Current wheeze, asthma, respiratory infections, and rhinitis among adults in relation to inspection data and indoor measurements in single-family houses in Sweden—The BETSI study. *Indoor Air* 2017; **27**: 725-36.
16 Bornehag CG, Sundell J, Hagerhed-Engman L, Sigsgaard T. Association between ventilation rates in 390 Swedish homes and allergic symptoms in children. *Indoor Air* 2005; **15**: 275-80.
17 Callesen M, Bekö G, Weschler CJ, Sigsgaard T, Jensen T, Clausen G, Toftum J, Norberg L, Høst A. Associations between selected allergens, phthalates, nicotine, polycyclic aromatic hydrocarbons, and bedroom ventilation and clinically confirmed asthma, rhinoconjunctivitis, and atopic dermatitis in preschool children. *Indoor Air* 2014; **24**: 136-47.

18 Sun Y, Zhang Y, Bao L, Fan Z, Sundell J. Ventilation and dampness in dorms and their associations with allergy among college students in China: a case-control study. *Indoor Air* 2011; **21**: 277-83.
19 Engvall K, Wickman P, Norbäck D. Sick building syndrome and perceived indoor environment in relation to energy saving by reduced ventilation flow during heating season: a 1 year intervention study in dwellings. *Indoor Air* 2005; **15**: 120-6.
20 Strøm-Tejsen P, Zukowska D, Wargocki P, Wyon DP. The effects of bedroom air quality on sleep and next-day performance. *Indoor Air* 2016; **26**: 679-86.
21 Francisco PW, Jacobs D, Targos L, Dixon S, Breysse J, Rose W, Cali S. Ventilation, indoor air quality, and health in homes undergoing weatherization. *Indoor Air* 2017; **27**: 463-77.
22 Lajoie P, Aubin D, Gingras V, Daigneault P, Ducharme F, Gauvin FD, Fugler D, Leclerc JM, Won D, Won D, Courteau M, Gingras S, Heroux ME, Yang W, Schleibinger H. The IVAIRE project - A randomized controlled study of the impact of ventilation on indoor air quality and the respiratory symptoms of asthmatic children in single family homes. *Indoor Air* 2015; **25**: 582-97.
23 Norbäck D, Bjornnson E, Janson C, Widstron J, Bowman G. Asthma symptoms and volatile organic compounds, formaldehyde, and carbon dioxide in dwellings. *Occupational and Environmental Medicine* 1995; **52**: 388-95.
24 Bentayeb M, Norback D, Bednarek M, Bernard A, Cai G, Cerrai S, Eleftheriou KK, Gratziou C, Holst GJ, Lavaud F. Indoor air quality, ventilation and respiratory health in elderly residents living in nursing homes in Europe. *European Respiratory Journal* 2015: ERJ-00824-2014.
25 Wright GR, Howieson S, McSharry C, McMahon AD, Chaudhuri R, Thompson J, Donnelly I, Brooks RG, Lawson A, Jolly L, McAlpine L, King EM, Chapman MD, Wood S, Thomson NC. Effect of improved home ventilation on asthma control and house dust mite allergen levels. *Allergy* 2009; **64**: 1671-80.
26 Kovesi T, Zaloum C, Stocco C, Fugler D, Dales R, Ni A, Barrowman N, Gilbert N, Miller J. Heat recovery ventilators prevent respiratory disorders in Inuit children. *Indoor Air* 2009; **19**: 489-99.
27 Oie L, Nafstad P, Botten G, Magnus P, Jaakkola JK. Ventilation in homes and bronchial obstruction in young children. *Epidemiology* 1999; **10**: 294-9.
28 Hägerhed-Engman L, Sigsgaard T, Samuelson I, Sundell J, Janson S, Bornehag CG. Low home ventilation rate in combination with moldy odor from the building structure increase the risk for allergic symptoms in children. *Indoor Air* 2009; **19**: 184-92.
29 Singleton R, Salkoski A, Bulkow L, Fish C, Dobson J, Albertson L, Skarada J, Kovesi T, McDonald C, Hennessy T. Housing characteristics and indoor air quality in households of Alaska Native children with chronic lung conditions. *Indoor Air* 2017; **27**: 478-86.
30 Howieson S, Lawson A, McSharry C, Morris G, McKenzie E, Jackson J. Domestic ventilation rates, indoor humidity and dust mite allergens: are our homes causing the asthma pandemic? *Building Services Engineering Research and Technology* 2003; **24**: 137-47.
31 Warner JA, Frederick JM, Bryant TN, Weich C, Raw GJ, Hunter C, Stephen FR, McIntyre DA, Warner JO. Mechanical ventilation and high-efficiency vacuum cleaning: A combined strategy of mite and mite allergen reduction in the control of mite-sensitive asthma. *J Allergy Clin Immunol* 2000; **105**: 75-82.
32 Emenius G, Svartengren M, J. K, Nordvall L, Pershagen G, Wickman M. Building characteristics, indoor air quality and recurrent wheezing in very young children (BAMSE). *Indoor Air* 2004; **14**: 34-42.

33 Clausen G, Høst A, Toftum J, Bekö G, Weschler C, Callesen M, Buhl S, Ladegaard M, Langer S, Andersen B. Children's health and its association with indoor environments in Danish homes and daycare centres–methods. *Indoor Air* 2012; **22**: 467-75.
34 Mendell MJ, Mirer AG, Cheung K, Tong M, Douwes J. Respiratory and allergic health effects of dampness, mold, and dampness-related agents: a review of the epidemiologic evidence. *Environ Health Perspect* 2011; **119**: 748-56.
35 ASTM. ASTM D6245-12, Standard guide for using indoor carbon dioxide concentrations to evaluate indoor air quality and ventilation. West Conshohocken, PA; 2012.