- HealthVent Project -

HEALTH AND VENTILATION:
review of the scientific literature

Report WP4

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HEALTHVENT PROJECT

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Executive summary

A multidisciplinary group of European scientists with expertise in medicine, engineering, epidemiology and toxicology reviewed scientific literature concerning the health effects of ventilation in non-industrial indoor environments. The objective was to collect scientific evidence that can assist setting of the ventilation guidelines based on health, which is an overarching aim of the HealthVent project supporting present work.

The scientific literature was collected and evaluated which provided information on the association between diseases and ventilation, as well as between exposures to indoor air pollutants and ventilation. The literature was collected by searching through the following databases: MEDLINE by National Library of Medicine, Toxnet and Web of Science. Additionally the proceedings of major congresses related to indoor air such as Indoor Air and Healthy Building series were surveyed. There have been several comprehensive reviews performed with similar objective in the past. Consequently only papers published since the publication of the last comprehensive review were included in the present review to find the data published afterwards. This period ranged from the onset of 2001 until mid-2011 when the group reviewing the papers had the last meeting.

The papers found through the literature search were grouped separately for different health end-points, as follows: allergy and asthma; respiratory symptoms; airborne respiratory infections; and sick building syndrome (SBS) symptoms (called sometimes also building related (BR) symptoms).

The papers dealing with other end-points such as perceived air quality, sick-leave and performance and productivity were also included in the review and grouped separately. Finally a subset of articles reporting modelling attempts examining exposure control by ventilation was also identified and included in the review. The papers were also classified based on the type of the building where the study was carried out as follows: homes; offices; schools; and other non-industrial indoor environments excluding hospitals.

Finally, the papers were grouped depending on whether they provided information on the association of ventilation rates or ventilation system type and its maintenance with the indicated endpoints. The former contains the quantitative aspect and thus should be considered when defining the ventilation requirements dealing with rates of air which need to be supplied indoors, while the latter contains the qualitative aspect of ventilation buildings and is thus more relevant for recommendations regarding type of the system, its operation and maintenance.

The scientists agreed that among all papers identified through the literature search only 48 articles were relevant for the objective of the present work. Still the majority of these relevant papers have considerable weakness. They lack the important details describing ventilation rates, their measurements (either with direct methods or using carbon dioxide as the proxy) and/or exposures conditions. The have also very poor description of actual exposures occurring in buildings where the studies were carried out; nearly all lack the measurements of pollutants potentially responsible for the effects observed. No information is given whether there were any special measures undertaken to reduce emission rates from building materials, furnishing and equipment; in many of these buildings smoking was still possible. Nearly no study provided information on the quality of outdoor air and/or the air supplied by the ventilation system downstream the air handling unit explicitly assuming that outdoor air is clean. Numerous epidemiological studies show associations between pollutants in outdoor air (primarily PM10, PM2.5 and ozone) with morbidity and mortality. Since outdoor air is used for ventilation its quality is thus an important parameter modifying the exposures indoors either due to direct effects of pollutants brought indoors or pollutants generated due to transformations or reactions (e.g. with ozone) with substances in the indoor air.

Despite these drawbacks the reviewed studies consistently showed that there is an association between ventilation and health manifested by increased prevalence of SBS symptoms, infectious diseases, allergic diseases and asthma symptoms. Additionally they showed that there is the relationship between ventilation and the increased short-term sick leave, perceived air quality (comfort) and cognitive performance in form of effects on office work by adults and schoolwork by children. Improper maintenance, design, and functioning of ventilation systems and in particular systems with air-conditioning (cooling and humidification) were also shown in the reviewed papers to contribute to health problems manifested by increased prevalence of SBS symptoms. None of the reviewed papers provided information on the effects of ventilation rates and/or type of the ventilation system and its maintenance on the chronic health effects, such as respiratory and cardiovascular diseases or cancer.

The scientific evidence in the papers can be used to find the levels of ventilation rates at which there were no negative effects observed on health. Either the minimum ventilation rates can be defined at which at least in some studies there were no negative effects on health or maximum ventilation rates at which in all studies reviewed there were no negative effects on health.

In the present project the former approach was selected to acknowledge that health is related to exposures and that ventilation is the ultimate measure to reduce negative effects of exposures occurring indoors on health and to promote other means of controlling exposures indoors namely source control as the first advocated priority. The latter has been selected to define the ventilation rates protecting from health in some of the previous reviews performed similarly as in the present work.

Among the relevant papers the studies judged to be conclusive, i.e. providing satisfactory information on health and ventilation and in which the data were adequately analysed and reported, show that ventilation rates can be kept as low as 7 L/s per person and no elevated risk of asthma and allergic symptoms is identified (data from Scandinavian homes), and that ventilation rates can be kept as low as 8 L/s per person (in homes) and 9 L/s per person (in offices) and no increase in the onset of SBS symptoms is identified. Although these numbers are not perfectly accurate they form at present the best available tentative estimate of the minimum rates with no observable adverse health effect.

It is however not possible to generalize these rates and use them to define health-based ventilation rates. One reason is the lack of proper characterization of exposures in the reviewed studies, not only regarding indoor but also outdoor air quality; in fact, none of the studies provided information on the potential pollutants transported from outdoors, explicitly assuming that the outdoor air was clean. Besides, apart from carbon dioxide, only a few studies measured the pollutants produced indoors. A further reason is that the reviewed studies examined only the effects of ventilation on the short-term (acute) health effects, and therefore potentially important long-term health effects or the exposure to pollutants causing long-term health effects were not assessed. Another reason is that most of the studies lacked proper ventilation measurements, either with direct methods or using proxies. Finally it is likely that in the investigated buildings not all potential methods were in place to further reduce the emissions and subsequent exposures.

So it is likely that the actual ventilation rates could have been even lower than these indicated above and no negative health effects could have been observed should proper source control been in place.

There is no clear distinction in the reviewed scientific papers whether ventilation supplied using natural or mechanical forces (by natural or mechanical ventilation systems) are optimal for health. These are ventilation rates that ascertain that exposures are kept at the levels not harmful for health rather than how ventilation is achieved. However to reduce indoor pollution levels the proper source control and design and maintenance of ventilation systems must be implemented. The literature shows that improper maintenance, design, and functioning of HVAC systems contribute to an increased prevalence of SBS symptoms. This indicates a need for safety factors and proper maintenance of ventilation systems, including such aspects as appropriate distance separating the inlet and exhaust, replacing dirty filters, cleaning ducts, and the prevention of water reservoirs and water in the systems.

The present review clearly indicates gaps in knowledge regarding the associations between ventilation and health. It shows that further research is needed. The recommended approach to study the association between ventilation and health need to be multidisciplinary and should try to establish correlations between indoor air pollution and ventilation.

The first need is to assess indoor safe pollutant levels. Majority of the studies report data for acute not chronic health effects whereas most of the guidelines regarding the pollutants are based on the data for chronic exposures. The short-term exposure limits allow higher levels of pollutants than the long-term chronic exposures.

A better characterization of exposures is needed. Ventilation measurements made using different techniques in different seasons and different averaging times, sometimes using concentration of CO2 to estimate ventilation rates. Future research should better document which ventilation measurements are valid in the context of health.

Outdoor air contains contaminants that can affect health whether inhaled outdoors or indoors and ventilation can serve as a means of introducing these contaminants into indoor spaces. Better characterization of outdoor air quality is needed.

In conclusion, because of complex relationships between contaminant levels, ventilation rates, and building-related health effects, ventilation should not be used as the only but as the ultimate means to deal with pollution when all other means failed. Source control and other strategies should first be entertained rather than ventilation increased.

1. Introduction

Every European citizen has right to indoor air quality (IAQ) that does not endanger the health. The 2008-estimated annual burden of disease related to inadequate IAQ is 2 million disability adjusted life years (DALY) in EU27. Reducing this burden is a high priority in the European health policies and a proper exposure control through ventilation is one of the key steps to achieve this aim.

Ventilation is the process of exchanging indoor (polluted) air with outdoor (presumably fresh and clean) air. Its main purpose is to create optimal conditions for humans in indoor environments, taking into account their health, comfort, and productivity by providing air for breathing and for removing and diluting indoor pollutants; ventilation is also used as a means for controlling humidity (adding or removing moisture) and thermal environment (for heating or cooling); these two processes can influence exposures and therefore are named here but they are not the main focus of this report; these two processes should not be confused with the general purpose of ventilation being the provision of clean air for breathing and the exposure control.

The European project HealthVent is targeting on demonstrated adverse health effects of inadequate indoor air quality to provide tangible health benefits for the building occupants and European populations. The purpose is to create health-based ventilation guidelines for Europe. This is a different approach to define ventilation guidelines which at present are mainly based on comfort requirements, specifically the perception of air quality and odour.

To achieve these goals one of the tasks of HealthVent is to define the link between ventilation and health in non-industrial indoor environments. This task is performed in WorkPackage 4 (WP4) on “Health and Ventilation” and achieved by reviewing the existing literature on this issue; no new and/or additional experimental work on this issue is carried out.

The review is performed by a multidisciplinary group of scientists with an expertise in medicine, epidemiology, toxicology, and engineering, members of the HealthVent project. The review builds upon the previous reviews of a similar type, and supplements them rather than duplicates the previous work. The results of this review are described in this document which constitutes the Deliverable 4 “Report on the association between health and ventilation, and on the scientific basis for health based guidelines” of the HealthVent project and is at the same time the Final Report of WP4.

2. Objective

The objective of the present work is to collect and evaluate published studies reporting the relationship between health (health indicators) and ventilation (rates, systems, strategies and technologies) in order to provide evidence that can be used to define the health-based ventilation guidelines.

3. Materials and methods

A multidisciplinary group of European scientists with expertise in medicine, engineering, epidemiology, toxicology reviewed scientific literature concerning the health effects of ventilation in non-industrial indoor environments.

The scientific literature was collected and evaluated providing information on the correlations between health (diseases) and ventilation, as well as between exposures to indoor air pollutants and ventilation if a connection to health was made. The literature was searched for in the following databases: MEDLINE by National Library of Medicine, Toxnet and Web of Science. Additionally the search was carried out through the proceedings of major congresses related to indoor air such as Indoor Air and Healthy Building series. The Papers published between the onset of 2001 until mid-2011 were included to match the period not covered by the reviews published in the past on the very same topic.

The following categories of search profiles and search terms were deemed important:

- *Indoor environments*. Indoor environments included non-industrial indoor settings, represented by all kinds of indoor environments: homes, offices, schools, day-care centres, dorm-rooms, etc., excluding hospitals.
- *Health*. Health was considered broadly, according to WHO definition (1948) which states that health is a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity. Consequently, health effects were searched both in term of diseases caused or aggravated or prevented by ventilation as well as end-points describing comfort and wellness. The list of diseases linked to ventilation included the following illnesses or symptoms referred to as diseases: allergy and asthma; respiratory and cardiovascular diseases, airborne respiratory infections, cancer. Additionally sick building syndrome (SBS) symptoms called also building related (BR) symptoms were also considered as precursors of the potential health problems and diseases. Perceived air quality was considered as an indicator of comfort. Additionally performance, productivity and absenteeism were included in the search as indicators of aggravated life quality and working conditions and potentially being also a “warning signal” of an likely negative effects of exposures which can potentially lead to aggravated health conditions.
- *Ventilation*. The term referred both to the volume of air delivered to indoor space as well as the means by which the air was delivered (a system to transport the air). Natural ventilation was defined as an airflow caused by pressure from wind and/or indoor–outdoor temperature differences. Mechanical ventilation was defined as an airflow caused by a fan through intake and/or exhaust vents specifically installed for ventilation (ASHRAE, 1993). Mechanical ventilation without air-conditioning was defined as a mechanical ventilation system in which the supply air is filtered and heated, or in which the air is exhausted by a fan. Mechanical ventilation with air-conditioning was defined as a mechanical ventilation system in which the supply air is filtered and heated, and is

additionally cooled and/or humidified and/or dehumidified. The search considered thus ventilation expressed both in qualitative and quantitative terms. Qualitative aspects of ventilation refer to the type of ventilation system, in term of natural or mechanical ventilation system, with or without air-conditioning. Qualitative aspects of ventilation systems also included their maintenance. Quantitative aspects of ventilation refer to ventilation rate, i.e. the amount of outdoor air supplied to indoor spaces.

- *Indoor related health risk exposure factors*. This category included search records describing different pollutants such as allergens, dampness, moulds, dust mites, bioaerosols, bacteria, viruses, combustion particles, NOx, PM, CO, VOCs, indoor chemistry products, mineral fibres, noise and microclimate parameters (temperature, humidity); Radon was not included as it is dealt with in another project RADPAR, carried out in parallel to HealthVent project.

In addition to the papers that reported original research studies on ventilation and health, the review papers on this issue published from 2001 were identified. The included the following five papers: Wargocki et al. (2002); Seppänen et al. (2004); Sundell et al. (2011); Fisk et al. (2011); Dimitroulopoulu et al. (2011). The literature reviewed by these review papers was checked to find out any omissions in the literature search carried out by the HealthVent project. The conclusions formed by these review papers were considered when discussing the outcomes of the present work.

The literature search identified altogether 168 articles published in peer-reviewed scientific journals or proceedings of the premier international congresses. These papers were screened to exclude articles that did not match the objective of the work (see Section 2). The screening was carried out by examining titles and abstracts of the papers. This selection identified 68 articles. These article were subsequently assigned to eight scientists, who thoroughly reviewed them, collected information included in the papers and assessed the quality of the paper and its conclusions. Two scientists were assigned by random to each paper and each scientist reviewed about 25 papers. The papers in which the scientists were either the main authors or co-authors were not assigned to them.

Reviews were conducted according to a specially prepared assessment scheme and included assessment and examination of and/or collection of information on the following aspects:

- general environment and milieu such as type of building, country, climate;
- health aspects: type of health outcomes (including whether the perceived air quality and comfort as well as performance and productivity were measured), method and quality of diagnosis and measurement (e.g., medical/objective or self-reported);
- ventilation aspects: ventilation system type, presence of moisture (in the system), type of filters, maintenance, air recirculation, duct system, problems with ventilation systems as well as measurements of ventilation rates including method and quality of their measurements;
- exposure assessment: type of pollutants measurements including both pollutants having indoor and outdoor origin and methods of the measurement (self-reported, inspections, measurements); these data included also information on hygrothermal conditions which can potentially influence the exposures;
- statistical analysis: type of study, main outcomes, statistical methods used and quality of analysis, limitations of the study;
- consistency assessment: assessment of the direction and size of the effect for evaluated outcomes and the assessment of similarity of estimates of the effect across different end-points and different studies.

Each article was first classified separately by each reviewer and then jointly classified during consensus meeting when eight scientists participated. The papers were classified as follows:

- relevant for the objective of the present work and general aim of HealthVent project, when adequate information on ventilation, health effects, data processing, and reporting was provided;
- non-informative, when essential information concerning ventilation and/or health effects was missing;
- inconclusive, if data processing and/or reporting was incomplete so that no reliable conclusions could be drawn;
- basic background, if background information dealing with the scope of the present work was provided;
- irrelevant, when not dealing with the project scope.

During consensus meeting, when the author of the evaluated paper was a main author and/or co-author he/she did not participate in the classification process in order to have an unbiased evaluation.

The scientists selected 48 papers as relevant. They are summarized in the Results section while detailed information on these papers collected during evaluation process can be found in Annex 1. The selected 48 relevant papers articles were grouped depending on different end-points, as follows:

- allergy and asthma;
- respiratory symptoms;
- airborne respiratory infections;
- sick building syndrome (SBS) (called sometimes also building related (BR) symptoms);
- perceived air quality;
- sick leave;
- and cognitive performance and productivity.

Papers were also grouped based on the type of building studied, as follows: homes and dwellings, offices and schools.

The papers judged as relevant were grouped according to whether they provided information on ventilation rates, or on ventilation systems and their maintenance. As the former contains the quantitative aspect these data are relevant in the context of setting the actual ventilation requirements whereas the latter provides information useful in the context of selection of the ventilation system type, its operation and maintenance.

Finally a subset of articles not dealing directly with the end-points but with the exposure control by ventilation was grouped separately. To create the context to the information provided by these papers as well as to other papers in which exposures were characterized the summary was made of the WHO air quality guidelines, both for outdoor and indoor contaminants (references), as well as INDEX project **(**Kotzias et al. 2005) also dealing with the contaminants being potentially harmful for health.

4. Results

4.1 Reviews on ventilation and health

In the following the major published reviews on ventilation and health are shortly summarized.

4.1.1. Major reviews prior to 2002

Mendell (1993)

This paper reviewed the findings of 32 studies of 37 factors potentially related to office worker symptoms. Among environmental factors assessed, there were generally consistent findings associating increased symptoms with air-conditioning, carpets, more workers in a space, VDT use, and ventilation rates at or below 10 L/s per person. Studies with particularly strong designs found decreased symptoms associated with low ventilation rate, short-term humidification, negative ionization, and improved office cleaning, although studies reviewed showed little consistency of findings for humidification and ionization. Relatively strong studies associated high temperature and low relative humidity with increased symptoms, whereas less strong studies were not consistent. Among personal factors assessed, there were generally consistent findings associating increased symptoms with female gender, job stress/dissatisfaction, and allergies/asthma. For other environmental or personal factors assessed, findings were too inconsistent or sparse for current interpretation, and there were no findings from strong studies. Overall evidence suggested that work related symptoms among office workers were relatively common, and that some of these symptoms represented preventable physiologic effects of environmental exposures or conditions.

Godish and Spengler (1996)

In this paper the Authors discussed that the adjustment of ventilation rates in buildings is widely practised, both to provide good air quality on a proactive basis and to mitigate air quality problems associated with occupant complaints. However, both cross-sectional and experimental epidemiological studies have reported mixed results and have for the most part failed to establish definitive relationships between ventilation rates and symptom prevalence or dissatisfaction with air quality. The difficulties involved in establishing such relationships may be due to a variety of confounding factors which include limitations in study design and interaction effects; difficulties in controlling ventilation rates in experimental studies; inadequate mixing of supply air in occupied spaces; high source strengths for some contaminants; dynamic interactions between sources and ventilation rates that result in increased contaminant emissions; contaminant dose-response sensory effects which are log-linear; potential contaminant generation within ventilation systems themselves; and multifactorial genesis of sick building symptoms.

In particular they concluded that there is limited evidence to suggest that ventilation rate increases up to 10 L/s per person may be effective in reducing symptom prevalence and occupant dissatisfaction with air quality and that higher ventilation rates are not effective. Because of complex relationships between ventilation rates, contaminant levels, and building-related health complaints, dissatisfaction with air quality, the use of ventilation as a mitigation measure for air quality problems should be tempered with an understanding of factors which may limit its effectiveness.

Seppänen et al. (1999)

This paper reviewed the literature on the associations of ventilation rates and carbon dioxide concentrations in non-residential and non-industrial buildings (primarily offices) with health and other human outcomes. Twenty studies, with close to 30,000 subjects, investigated the association of ventilation rates with human responses, and 21 studies, with over 30,000 subjects, investigated the association of carbon dioxide concentration with these responses. Almost all studies found that ventilation rates below 10 L/s per person in all building types were associated with statistically significant worsening in one or more health or perceived air quality outcomes. Some studies determined that increases in ventilation rates above 10 L/s per person, up to approximately 20 L/s per person, were associated with further significant decreases in the prevalence of sick building syndrome (SBS) symptoms or with further significant improvements in perceived air quality.

In particular the Authors stated that the carbon dioxide studies support these findings. About half of the carbon dioxide studies suggested that the risk of sick building syndrome symptoms continued to decrease significantly with decreasing carbon dioxide concentrations below 800 ppm. The ventilation studies reported relative risks of 1.5–2 for respiratory illnesses and 1.1–6 for sick building syndrome symptoms for low compared to high low ventilation rates.

Seppänen and Fisk (2002)

This paper provides a summary of knowledge about the associations of ventilation system types in office buildings with sick building syndrome symptoms. Most studies have indicated that relative to natural ventilation, air conditioning, with or without humidification, were consistently associated with a statistically significant increase in the prevalence of one or more SBS symptoms, by approximately 30% to 200%. In two of three analyses from a single study (assessments), symptom prevalence was also significantly higher in air-conditioned buildings than in buildings with simple mechanical ventilation and no humidification. The available data also suggested, with less consistency, an increase in risk of symptoms with simple mechanical ventilation relative to natural ventilation. The statistically significant associations of mechanical ventilation and air conditioning with SBS symptoms were much more frequent than expected from chance and also not likely to be a consequence of confounding by several potential personal, job, or building-related confounders. Multiple deficiencies in HVAC system design, construction, operation, or maintenance, including some of which cause pollutant emissions from HVAC systems, may contribute to the increases in symptom prevalence but other possible reasons remain unclear.

Wargocki et al. (2002)

Wargocki et al. (2002) reported the review made by the multidisciplinary group of scientists. They reviewed 105 papers published in peer-reviewed scientific journals. The review was performed in similar way as in the present work, i.e. each paper was reviewed by two scientists especially invited to join the review work and the decisions on the quality of information presented in each paper were made during the plenary meeting. The only marginal difference compared to the present work was that Wargocki et al. (2002) selected only papers published in peer-reviewed journals which had already undergone the independent peer-review.

They judged 30 papers as conclusive, i.e. providing sufficient information on ventilation, health effects, data processing, and reporting, 14 papers as providing relevant background information on the issue of ventilation and health but not sufficient for forming positions and statements, 43 papers as relevant but non-informative or inconclusive, i.e. lacking essential information to draw sound conclusions, and 18 papers as irrelevant for the issue discussed.

Based on the data included in the papers judged conclusive, the scientists agreed that ventilation is strongly associated with comfort (perceived air quality) and health (Sick Building Syndrome (SBS) symptoms, inflammation, infections, asthma, allergy, short-term sick leave), and that the scientific data indicate an association between ventilation and productivity (performance of office work).

The scientists also concluded that increasing outdoor air supply rates in non-industrial environments improves perceived air quality, but no formal cut-off point or recommendation regarding rate for control of perceived air quality was given; that outdoor air supply rates below 25 L/s per person were considered to increase the risk of SBS symptoms and the short-term sick leave, and to decrease productivity among occupants of office buildings. The ventilation rates above 0.5 air changes per hour (h-1) in homes were considered to reduce infestation of house dust mites in Nordic countries.

The scientists concluded additionally that the literature indicates that in buildings with air-conditioning systems there may be an increased risk of SBS symptoms compared with buildings which are naturally or mechanically ventilated, and that improper maintenance, design, and functioning of air-conditioning systems contributes to the increased prevalence of SBS symptoms.

4.1.2. Major reviews after 2002

Mendell and Heath (2005)

Authors reviewed the scientific evidence relating indoor pollutants and thermal conditions, in schools or other indoor environments, to human performance or attendance. Regarding direct associations, little strongly designed research was available. Persuasive evidence links higher indoor concentrations of NO2 to reduced school attendance, and suggestive evidence links low ventilation rates to reduced performance. Regarding indirect associations, many studies link indoor dampness and microbiologic pollutants (primarily in homes) to asthma exacerbations and respiratory infections, which in turn have been related to reduced performance and attendance. Also, much evidence links poor IEQ (e.g. low ventilation rate, excess moisture, or formaldehyde) with adverse health effects in children and adults and documents dampness problems and inadequate ventilation as common in schools.

Overall, evidence suggests that poor IEQ in schools is common and adversely influences the performance and attendance of students, primarily through health effects from indoor pollutants. Evidence is available to justify (i) immediate actions to assess and improve IEQ in schools and (ii) focused research to guide IEQ improvements in schools.

Seppänen et al. (2006)

Seppänen et al. (2006) reviewed literature reporting studies on the effects of ventilation and performance of office and school work. They performed metanalysis of the collected data and correlated the performance against the ventilation rates adjusting for the number of observations, while disregarding the descriptors of the quality of the study or the potential differences in exposures. Their analysis indicated that almost all studies included in their review suggested that increased ventilation rates increase cognitive performance. The studies indicated typically a 1-3% improvement in average performance per 10 L/s-person increase in outdoor air supply rate. The performance increase per unit increase in ventilation was bigger with ventilation rates below 20 L/s-person and almost negligible with ventilation rates over 45 L/s-person. The performance increase was statistically significant with increased ventilation rates up to 15 L/s-person (when 95% confidence interval of the modelled data was applied) and up to 17 L/s-person when confidence interval was set to 90%. This suggests that when ventilation rates are above 15-17 L/s per person there are no further significant effects on performance.

Fisk et al. (2009)

Fisk et al. (2009) attempted to create the association between ventilation and the prevalence of SBS symptoms, and in this sense it is particularly relevant when the health-based ventilation guidelines are developed and/or the impact of different ventilation rates in the existing buildings on health is discussed. They performed the metanalysis of the data from all studies which quantified the effects of ventilation on risk of SBS symptoms. In case the risk was not estimated in the original papers the authors attempted to estimate the risk themselves based on available data. They accepted all available data without their qualitative assessment.

The modeling showed that when ventilation rates are reduced from 10 to 5 L/s per person then the risk of the prevalence of SBS symptoms is increased by ca. 23% and when ventilation rates increase from 10 to 25 L/s per person the risk decreases by ca. 29%. Their results suggest when ventilation rates are above 22-25 L/s per person there will be no significant reduction in risk of symptoms, which is basically similar to what was concluded by Wargocki et al. (2002) as the same set of studies was used. The model developed had quite large confidence interval which could be caused by many factors which were not adjusted for. No discussion is made on which risk level and/or which, prevalence or intensity of symptoms should be selected when setting ventilation requirements based on health.

Sundell et al. (2011)

Sundell et al. (2011) reviewed the papers on the effects of ventilation rates on health in indoor environments published until 2005, supplementing thus the review by Wargocki et al. (2002) by the peer-reviewed studies published between 2001 and 2005. They used the same methodological approach to review the papers as proposed by Wargocki et al. (2002); they invited multidisciplinary panel of scientists to judge the papers which had already undergone the peer-review process. A total number of 27 papers published in the peer-reviewed scientific journals were judged as providing sufficient information on both ventilation rates and health effects and used for forming the conclusions. They concluded that multiple health endpoints show similar relationships with ventilation rate and that there is biological plausibility for an association of health outcomes with ventilation rates, although the literature does not provide clear evidence on particular agent(s) for the effects.

They also agreed that the data provided by the papers judged conclusive suggested that above 25 L/s per person no negative effect on health was observed and thus this rate (and the rates above this level) could be selected as a cut-off point (safe level). The papers also indicated that the limited available data suggest that inflammation, respiratory infections, asthma symptoms and short-term sick leave increase with lower ventilation rates. They also concluded that the reviewed papers showed that ventilation rates in homes above 0.5 air changes per hour are associated with the reduced risk of allergic manifestations among children in Nordic climates.

Dimitropolou (2011)

Dimitroulopoulou (2011) provided information on the current status of residential ventilation standards and regulations in Europe as well as reviewed the information on the measurements of ventilation rates in European dwellings and examined their compatibility with the European ventilation standards/regulations.

The review concluded that ventilation in European homes is poor if the measured ventilation rates are used as the classifying criterion. The ventilation rates are frequently lower than 0.5 h-1 which is the recommended level of ventilation in the current ventilation standards in many European countries. She also reported that there are increased concentrations of indoor pollutants (environmental tobacco smoke, traffic related pollutants that penetrate indoors, dampness in homes with visible moulds, volatile and semi-volatile organic compounds, phthalates and chlorine) reported in the literature which may elevate the risk for health.

Although the reviewed papers indicate that people generally think that ventilation in residences is important, they also show that people have often very little control over ventilation in their homes. As a result homes and dwellings are underventilated. This finding emphasize the importance of human factor in achieving the required ventilation rates and implies that the guidelines should be developed instructing when and how the ventilation should be achieved and how to maintain the ventilation in a good operational conditions.

The following table summarized the previous reviews.

Table 4.1. Summary of review papers providing information on the association between ventilation, health and performance

Study	Main results
Mendell (1993)	Symptoms in office workers were associated with air-conditioning, carpets, more workers in a space, VDT use, and ventilation rates at or below 10 L/s per person.
Godish and Spengler (1996)	Limited evidence suggests that ventilation rate increased up to 10 L/s per person may be effective in reducing symptom prevalence and occupant dissatisfaction with air quality. Because of complex relationships between ventilation rates, contaminant levels, and building-related health complaints, dissatisfaction with air quality, the use of ventilation as a mitigation measure for air quality problems should be tempered with an understanding of factors which may limit its effectiveness.
Seppänen et al. (1999)	Ventilation rates below 10 L/s per person in all building types were associated with statistically significant worsening in one or more health or perceived air quality outcomes. Some studies determined that increases in ventilation rates above 10 L/s per person, up to approximately 20 L/s per person, were associated with further significant decreases in the prevalence of SBS symptoms or with further significant improvements in perceived air quality. The risk of sick building syndrome symptoms continued to decrease significantly with decreasing carbon dioxide concentrations below 800 ppm.
Seppänen and Fisk (2002)	Increase in risk of SBS symptoms was observed with simple mechanical ventilation compared to natural ventilation. Multiple deficiencies in HVAC system design, construction, operation, or maintenance, including some of which cause pollutant emissions from HVAC systems, may have contributed to the increases in symptom prevalence.
Wargocki et al. (2002)	Outdoor air supply rates below 25 L/s per person increase the risk of SBS symptoms, increase short-term sick leave, and decrease productivity.
Mendell and Health (2005)	No identification of a set of findings sufficiently persuasive to establish specific causal relationships between indoor pollutants or thermal conditions in schools and the performance of students. Overall, evidence suggests that poor IEQ in schools is common and adversely influences the performance and attendance of students, primarily through health effects from indoor pollutants. Persuasive evidence links higher indoor concentrations of NO_2 to reduced school attendance. Suggestive (although not fully consistent) evidence links low outdoor air ventilation rates in buildings to decreased performance in children and adults.
Seppänen (2006)	A 1-3% improvement in average performance was associated with a 10 L/s-person increase in outdoor air ventilation rate. The performance increase was statistically significant with increased ventilation rates up to 15 l/s-person with 95% CI and up to 17 L/s-person. The performance increase per unit increase in ventilation was bigger with ventilation rates

	below 20 L/s-person and almost negligible with ventilation rates over 45 L/s-person.
Fisk (2009)	As the ventilation rate drops from 10 to 5 L/s x person, relative SBS symptom prevalence increases approximately by 23% (12% to 32%), and as ventilation rate increases from 10 to 25 L/s x person, relative prevalence decreases approximately 29% (15% to 42%).
Sundell (2011)	Higher ventilation rates in offices, up to about 25 L/s per person, were associated with reduced prevalence of sick building syndrome (SBS) symptoms. Ventilation rates in homes above 0.5 air changes per hour are associated with the reduced risk of allergic manifestations among children in Nordic climates.

4.2 Current review on ventilation and health

The information in 48 papers judged relevant is summarized below; more detailed information included in these papers can be found in Annex 1 to the present report.

4.2.1 Asthma and allergy symptoms

Among the papers judged as relevant some indicated that there is an association between ventilation rate and health effects, and some that there is an effect between the ventilation system, and asthma and allergy symptoms. Table 4.1 summarizes the papers reporting the association between ventilation rates and allergy. As regards effect between the ventilation system and asthma and allergy symptoms data generally showed that mechanical ventilation system reduced allergic symptoms. Use of heat recovery ventilation, compared with placebo, was associated with a progressive fall in the odds ratio for the reported wheeze (Kovesi et al. 2009). Also Xu et al. (2010) reported that installation of ventilation units effectively reduced asthma symptoms and indicators of airway inflammation though the effect was confounded with parallel operation of an air cleaner. Domestic mechanical heat recovery ventilation system (MHRV) expected to increase ventilation rate by 0.5 h^{-1}, in addition to allergen avoidance measures, improved asthma control by attenuating recolonisation rates (Wright et al. 2009). Howieson et al. (2003) also reported that installation of MHRV reduced asthmatic symptoms and improved lung functions and in parallel reduced house dust mites and the levels of relative humidity. However in one study a large amount of pollen could enter dwellings through air ducts when the windows were closed and when the ventilation fans were in operation and thus the ventilation system could be responsible for the allergic effects observed (Takahashi et al. 2008). Also Ezratty et al. (2003) showed that self-estimated asthma and allergy symptoms were increased with poor ventilation, although many other factors could also contribute to the observed effect.

As indicated in Table 4.1 a direct beneficial effect of increased ventilation on asthma and allergy symptoms was basically observed. A low-ventilation rate was associated with increased asthma symptoms: lower ventilation rates in homes might be a risk factor for allergies among children (0.31 ach vs 0.37 ach) (Bornehag et al. 2005), while increasing ventilation rate in dorm rooms was associated with a decreased prevalence of allergic symptoms among students (Sun et al. 2011). Kovesi et al. (2009) reported reduced odds for the reported wheeze when ventilation rates were increased after installing heat-recovery ventilator. In the study by Emenius et al. (2004) no benefit of increasing air change rate nor from the type of ventilation system could be seen for the risk of recurrent wheeze in children up to the second year of their lives. However in their study the risk was increased with the increased humidity and dampness, which both can be affected by ventilation. Also in the study by Clausen et al. (2012) carried out using similar measuring protocol as the study of Bornehag et al. (2005) there was no difference in the estimated ventilation rates in homes of children with asthma and allergic symptoms (cases) and the population of children with and without asthma and allergy symptoms (bases).

Table 4.2. Summary of papers identified as providing adequate information on the association between asthma and allergy symptoms and ventilation rates

Study	Building type	Study type	Main result
Emenius et al. (2004)	Homes	Cross-sectional	Ventilation rate > 0.4 - 0.5 h^{-1} is not associated with decreased wheezing (corresponding to 8-10 L/s per person).
Bornehag et al. (2005)	Homes	Case-control	The measured air change rate in the 390 buildings was generally low (about 80% of the single-family houses and 60% of the multifamily houses did not fulfil the minimum requirements for homes according to the Swedish building code is 0.5 ach). There is an association between home ventilation and the health effects studied as cases with rhinitis had ventilation of 0.32 h^{-1} while controls w/o rhinitis 0.37 h^{-1}; many associations did not reach statistical significance.
Kovesi et al. (2009)	Homes	Intervention	Mean CO_2 concentration without and with heat recovery ventilators (HRV): 915 and 1359 ppm. Decrease in wheezing and rhinitis with HRV.
Xu et al. (2010)	Homes	Intervention	Mean CO_2 concentration with and without ventilation units with an air cleaner were: 800-900 ppm and 1500 ppm. Improvement in the exhaled breath condensate and peak expiratory flow.
Clausen et al. (2011)	Homes	Case-base	Cases and bases had similar ventilation rate estimated to be about 0.46 h^{-1} based on the measurements of CO_2
Sun et al. (2011)	Dorm rooms	Case-control	Below 2.0 h^{-1} there is a presence of wheezing and dry cough; no rhinitis or eczema symptoms.
Synthesis of the evidence			No effects on asthma and allergy in homes (dorms) when ventilation rates in the range from 0.37 to 2 h^{-1} or $CO_2 \leq 900$ ppm (above outdoors)

4.2.2 Respiratory symptoms

Only one study reported the relationship between ventilation rate and the respiratory systems. Simoni et al. (2010) showed that upper respiratory tract symptoms were more prevalent in poorly ventilated classrooms; children exposed in classrooms having CO_2 levels >1,000 ppm had higher risk for dry cough and rhinitis.

Many reviewed studies showed an association between ventilation system type and the respiratory systems. They showed that improperly maintained and operated ventilation system can increase the risk of symptoms by becoming the source of pollutants and thus elevating the exposures indoors.

Improper maintenance of ventilation systems possibly supporting the microbiologic growth was suspected to be the reason for increased negative effects on the respiratory tract particularly among asthmatics (Mendell et al. 2003). An increased risk for lower respiratory symptoms was indicated to be due to lack of cleaning of drip pans, while an increased risk for mucous membrane symptoms was modelled to be the result of the lack of cleaning of cooling coils (Mendell et al. 2006). The age of the ventilation system represented a risk factor for respiratory symptoms development (Graudenz et al., 2002): increase in upper respiratory symptoms was associated with age of the ventilation system in an office building (Graudenz et al. 2002). Cleaning of ducting and exchange of the air-conditioning system for the new one improved the building-related respiratory symptoms, naso-ocular symptoms, and reduced the persistent cough (Graudenz et al. 2004). When compared with the building with natural ventilation system, the presence of air-conditioning increased respiratory symptoms even in office buildings in cities with hot and humid climate (Graudenz et al. 2005).

Increase of respiratory symptoms due to operation of mechanical ventilation system or air conditioning system was also reported in day care centres (Zuraimi et al. 2007). The current rhinitis among children was significantly higher if they attend mechanically ventilated child care centres compared to naturally ventilated child care centres. Higher adjusted prevalence ratio of severe phlegm and cough symptoms and lower respiratory illness was observed in the air-conditioned child care centres. Also child care centres with hybrid ventilation were at high risk for almost all the respiratory symptoms studied.

4.2.3 Airborne infectious diseases

Myatt et al. (2004) found that lower ventilation rates are potentially associated with the increased risk of exposure to infectious droplet nuclei by showing an association between the probability of detecting airborne rhinovirus in filters and a weekly average CO_2 concentration. Whether these droplet nuclei are important vectors of infection remained uncertain.

There are no studies identified on the ventilation systems type and the spread and transmission of airborne infectious diseases except for the study of Pantelic et al. (2009) who suggested that using personal ventilation may protect against infectious diseases. They carried out experimental study and measured droplets generated by coughing machine inhaled by the manikin.

Li et al. (2007) performed a systematic review of the role of the built environment in the transmission of airborne infectious agents, in general. Specifically, they examined whether there was sufficiently strong evidence in the contemporary scientific literature to substantiate a contributory role of ventilation rates and airflow patterns in the airborne transmission of infectious agents in different indoor settings. They searched the major literature databases between 1960 and 2005, and then screened titles and abstracts, and finally selected 40 original studies based on a set of criteria. A review panel was established, comprising medical and engineering experts in the fields of microbiology, medicine, epidemiology, indoor air quality, building ventilation, etc., the process being similar to this exercised in HealthVent and by Wargocki et al. (2002). Ten of 40 reviewed studies were considered to have conclusive evidence on the association between building ventilation and the transmission of airborne infection.

The conclusion of this review was that there is strong and sufficient evidence substantiating the association between ventilation, air movements in buildings and the transmission/spread of infectious diseases such as measles, tuberculosis, chickenpox, influenza, smallpox and SARS. However, there is insufficient data to clearly define the ventilation rates that can reduce the risk of the spread of infectious diseases via the airborne route for hospitals, schools, offices, homes and isolation rooms. Very often, overcrowding is identified as a factor that may be related to ventilation of buildings. However, without details of airflow rates, it is difficult to rigorously demonstrate a direct relationship between overcrowding and the airborne transmission of infection. Moreover, overcrowding may increase the likelihood of disease transmission via direct contact.

WHO guidelines “*Mold and dampness”* (2009) concluded that persistent dampness and microbial growth on interior surfaces and in building structures should be avoided or minimized, as they may lead to adverse health effects. As the relationships between dampness, microbial exposure and health effects cannot be quantified precisely, no quantitative, health-based guideline values or thresholds can be recommended for acceptable levels of contamination by microorganisms.

The studies do not provide ventilation rate that could be useful for setting requirements in guidelines minimizing the risk of infectious diseases. Results concerning airborne infectious diseases in different settings indicate that no quantitative, ventilation values or thresholds can be recommended for acceptable levels of contamination by microorganisms.

4.2.4 SBS/BRS symptoms (and perceived air quality)

There were many studies which investigated the association between ventilation and sick building syndrome (called sometimes building related symptoms). Generally they show that increased ventilation can reduce the onset of these symptoms and that provision of sufficient per-person outdoor ventilation air could decrease prevalence of selected building related symptoms (Table 4.2). This is among others indicated by Erdmann et al. (2004) who by showing the relationship between indoor minus outdoor CO_2 concentrations and the risk of mucous membrane/lower respiratory symptoms suggests that air contaminants are implicated in the aetiology of BRS. Also Wargocki et al. (2004) showed that increased outdoor air supply rates reduced the intensity of some health symptoms though only when the filters in the ventilation system (downstream of the mixing box of outdoor and exhaust air) were new. Norbäck et al. (2008) showed that the symptoms among students in computerized classrooms somewhat increased when ventilation rate was 10-13 L/s per person compared with 7 L/s per person, though he observed that the dominant impact on symptoms should be attributed to the increased temperature. However Skyberg et al. (2003) showed that general SBS symptoms (not mucosal and skin symptoms) increased when ventilation rates were estimated (not measured) by building engineer to be ≥5 m^3/h per m^2; there are no clear explanation to this finding though neither exposures nor ventilation were measured in this study. Also Zhang et al. (2011) observed the increase in symptoms among pupils that could not be explained by the change in ventilation rate; in their study the average CO_2 levels were very high, as high as 2,650 ppm.

Engvall et al. (2005) studied if a 25–30% reduction of outdoor ventilation flow during heating season influenced sick building syndrome (SBS) and the perception of the indoor environment. This was done in a 1-year cross-over intervention study with 44 subjects in a multi-family building. They concluded that reducing the ventilation rate in dwellings to a level below the current Swedish ventilation standard (0.5 h^{-1}) may cause a perception of impaired air quality but no negative effects on SBS were observed.

Norbäck et al. (2011) showed that the type of ventilation has an impact on the perceived air quality in a school building, which is probably the result of change in ventilation efficiency that is equivalent of a change in ventilation rate at the breathing zone. Health effects were studied in three elementary school classes when changing from mixing ceiling ventilation to two types of displacement ventilation, front ventilation system and floor master system. When changing from mixing ventilation to the former, the pupils perceived better air quality and reported less dyspnoea as compared to controls; break up time, a measure of eye symptoms was improved. At desk level, mean CO_2 was reduced from 867 to 655 ppm. The study showed that displacement ventilation may reduce negative health effects among pupils as compared to conventional mixing ceiling systems. The study additionally showed that increased air flow will improve air quality perceived by children upon entering the calls as well as during class occupation, the effect being confounded with the system type (air flow at the desk level was ca. 40-50% higher with displacement ventilation as indicated by CO_2 levels).

Many studies showed that there is a clear association between ventilation system type and/or maintenance of ventilation systems and SBS symptoms. A study by Engvall et al. (2003) indicated that occupants in dwellings with a mechanical ventilation system had less ocular and nasal symptoms, but major reconstruction of the interior, direct heated electric radiators, wood heating, and multiple sealing of buildings were also associated with an increase of some symptoms. Also Leech et al. (2004) showed that occupants of houses with energy efficient mechanical ventilation and best construction practices report less SBS symptoms than matched controls in houses having the same price range some of which having and some not mechanical system. Also a personalised ventilation system, providing clean outdoor air directly to the breathing zone was shown in an experimental study with recruited subjects to reduce SBS symptoms compared to mechanical ventilation (Kaczmarczyk et al. 2004); improved perceived air quality was also observed when the air was provided by the personalized system. Mysen et al. (2005) showed that installing demand controlled ventilation system with facade supply improves some symptoms among pupils in schools and more pupils reported that they were satisfied even though CO_2 levels were quite low before and after retrofit. In another study Smedje et al. (2011) reported only small differences between symptoms and perceptions in classrooms equipped with mixing and displacement ventilation; symptoms were slightly better when there was displacement ventilation while the perceptions of air quality in the mixing mode, and the estimated ventilation rates were about 10.6 to 12.3 L/s per person.

Kishi et al. (2009) showed that mechanical ventilation system is not associated with the risk of sick building syndrome in detached houses in contrary to many studies showing that the presence of ventilation systems does increase such the risk of health symptoms defined as SBS or BRS. For example, Hummelgaard et al. (2007) showed that there is a lower prevalence of symptoms among the occupants of office buildings with natural ventilation compared with the occupants residing in the mechanically ventilated buildings; the lower symptom prevalence was accompanied with higher degree of satisfaction with the indoor environment. Wong et al. (2004) showed that the prevalence of symptoms was higher in dwellings with air conditioners (though only used to cool the air and there were no mechanical ventilation system installed) compared with naturally ventilated dwellings without air conditioner. At the same time they observed that CO_2 levels in air conditioned dwellings were about 1,600 ppm compared with 550-600 ppm in naturally ventilated ones. Coelho et al. (2005) postulated that elevated health complaints among elderly in dwellings are due to poorly maintained ventilation systems, dirty filters and blocked vents.

A potential explanation to why people can complain more often with symptoms in buildings with mechanical ventilation was provided by Buchanan et al. (2008). They found a joint risk of BR symptoms from polyester/synthetic filters and outdoor ozone above 67.6 $\mu g/m^3$ to be much higher than the risk from each one alone, suggesting that ozone and specific filter media have interactive effects increasing the risks for health symptoms. Ozone alone can also increase the risks of symptoms. Apte et al. (2008) showed a positive relationships between ambient ozone concentrations and upper respiratory, dry eyes, neurological symptoms and headaches all being a part of the definition of building related symptoms. The study suggests that ventilation air can be a carrier of outdoor pollution (ozone) which can result in health symptoms.

Few studies looked specifically on the effects of ventilation rate on the perception of air quality. One experimental study found that that poorly maintained ventilation system will be an important pollution source aggravating the perceived air quality (Bitter et al. 2002). Another experimental study showed that it may be ineffective to handle the pollution sources by increasing ventilation rate compared to reducing the pollution sources indoors (Wargocki et al. 2007); this study may indirectly suggest that in case of no or weak effects of increased ventilation rate on symptoms there could have been strong dominant sources of pollution which could not be handled by ventilation.

Table 4.3 Summary of papers identified as providing adequate information on the association between sick building syndrome symptoms (and perceived air quality) and ventilation rates

Study	Building type	Study type	Main result
Skyberg et al. (2003)	Office	Cross-sectional	Ventilation flow > 5 $m^3/h/m^2$ is associated with increased general symptoms, no association with skin and mucosal symptoms was observed.
Erdmann et al. (2004)	Office	Cross-sectional	The implied potential maximum reductions in BRS prevalence that could be achieved by reducing dCO_2 concentrations in the BASE buildings are on average roughly 64%, 75%, 64%, 74%, and 85% for dry eyes, sore throat, nose/sinus, sneeze, and wheeze, respectively. [dCO_2 mean (ppm/100): 2,6 ppm (0.40-6.1)].
Wargocki et al. (2004)	Office	Intervention	Increasing the outdoor air supply rate from 2.5 to 25 L/s per person in the system with recirculation reduced intensity of symptoms but only when particle filters were new.
Engvall et al. (2005)	Home	Cross-over intervention	Reduction of ventilation rate from 0.5-0.8 h-1 to 0.4-0.5 h-1 did not have negative effect on SBS symptoms, but air was perceived as stuffy/poor.
Wong et al. (2004)	Home	Cross-sectional	Occupants in dwellings with air conditioners where CO_2 levels were up to 1,600 ppm reported more symptoms that occupants in dwelling without air conditioners where CO_2 levels were 550-600 ppm; both types of dwelling had natural ventilation only.
Smedje et al. (2011)	School	Cross-sectional	Mixing associated with reduced eye symptoms (mean CO_2 in mixing=840 ppm vs mean CO_2 in displacement=794). No change in eyes and nose symptoms in the two different ventilation type. Eyes symptoms decreased in mixing.
Zhang et al. (2011)	School	Cross-sectional	General and mucous symptoms negatively associated with CO2. Mean CO2 concentrations (min-max): 2211(789-4170); 2560 (886-4170), 2651(965-3996).
Norbäck et al. (2008)	School	Cross-sectional	Change in ventilation from 7 to 10 L/s per person can improve thermal comfort and air quality.
Synthesis of the evidence	Office	Data are inconsistent and meagre, but according to Erdman, 450 ppm above outdoors (ca. 9 L/s per person) would correspond to a 20% decrease in prevalence of symptoms.	
	Home	Ventilation rate of 0.4 h^{-1} (corresponding 8 L/s per person) was not associated with increase in symptoms: no effects were seen at CO2 ca. 600 ppm which is ca. 21 L/s per person.	
	School	At 10 L/s per person and above SBS symptoms were observed to be lower.	

4.2.5 Sick leave

Three studies looked on the effect of ventilation on the short-term sick leave and none looked at the effect of system type. Milton et al. (2000) analyzed 1994 sick leave for 3,720 hourly employees of a large Massachusetts manufacturer, in 40 buildings with 115 independently ventilated work areas. They rated outdoor air supply rate as moderate (25 cfm/person, 12 L/s-person) or high (50 cfm/person, 24 L/s-person) based on the knowledge of ventilation systems and CO_2 measurements on a subset of work areas. Moderate ventilation rates compared to high rates were attributable to the 35% of annual sick leave (1.2-1.9 days per person per year). They concluded that benefits continue to accrue when ventilation is increased above 10 L/s-person, and that experimental study to validate and to determine mechanisms for these observational findings should be a priority for indoor air research.

Myatt et al. (2002) conducted an intervention study in which outdoor air supply rates were adjusted periodically to increase the range of CO_2 concentrations (37 to 250 ppm with a peak CO_2 concentration above background of 312 ppm). They determined the frequency of sick leave among 294 hourly workers scheduled to work approximately 49,804.2 days in the study areas using company records. In the two buildings studied with differential CO_2 concentration of 50-200 ppm (approximately 40-45 L/s-person) they found no association between sick leave and CO_2 differential.

Shendell et al. (2004) explored the association of student absence with measures of indoor minus outdoor carbon dioxide concentration (dCO_2). Absence and dCO_2 data were collected from 409 traditional and 25 portable classrooms from 22 schools located in six school districts in the states of Washington and Idaho. Study classrooms had individual heating, ventilation, and air conditioning

(HVAC) systems, except two classrooms without mechanical ventilation. Classroom attributes, student attendance and school-level ethnicity, gender, and socioeconomic status (SES) were included in multivariate modeling. Forty-five percent of classrooms studied had short-term indoor CO_2 concentrations above 1000 ppm (range 580 to 1510 with max. 4230 ppm). A 1000 ppm increase in dCO_2 was associated ($P < 0.05$) with a 0.5–0.9% decrease in annual average daily attendance (ADA), corresponding to a relative 10–20% increase in student absence. They concluded that improving classroom ventilation should be considered a practical means of reducing student absence.

Table 4.4 Summary of papers identified as providing adequate information on the association between sick-leave and ventilation rates

Study	Building type	Study type	Main result
Milton et al. (2000)	Office	Cross-sectional	At the range of moderate ventilation rates (approximately 12 L/s per person) compared to high (approximately 24 L/s per person) was attributable 35% of annual sick leave (1.2-1.9 days per person per year).
Myatt et al. (2002)	Office	intervention	In two buildings with differential CO_2 concentration of 50-200 ppm (approximately 40-45 L/s per person) there was no association between ventilation rates and sick leave.
Shendell et al. (2004)	School	Cross-sectional	A 1000 ppm increase in dCO_2 was associated with a 0.5–0.9% decrease in annual average daily attendance, corresponding to a relative 10–20% increase in student absence.
Synthesis of the evidence	School	Every 4 L/s per person corresponds to 10-20% change in school absence rates (1 L/s per person ~ 2.5-5%)	
	Office	> 12 L/s per person is associated with reduction in annual sick leave (1.2-1.9 days per person per year)	

4.2.6 Performance and productivity

Two field intervention experiments investigated the effects of increased outdoor air supply rate on the work of call centre operators. Wargocki et al. (2004) showed that increasing ventilation rate to 25 L/s per person reduced talk-time of the operators but only when new particle filters were installed. In another study (Federspiel et al., 2004) no improved performance of call-centre operators were seen until CO_2 levels above outdoors were below 75 ppm above outdoors (corresponding to 50 L/s per person); no consistent change in performance was seem with reduced CO_2 levels.

In three field experiments there was consistent relationship between increased ventilation rate and the performance of schoolwork measured using math and language tasks as well as using the standard math and reading tests developed by the educational department. This relationship shows that ventilation rates generally below 8 L/s per person will have negative effect on performance per person (Bakò-Birò et al. 2007; Wargocki et al. 2007; Haverinen-Shaughnessy et al. 2010).

No study investigated impact of the type of ventilation system on performance though it should be mentioned that the study of Wargocki et al. (2004) showed that dirty particle filters can be a source of pollutants increasing exposures which reduced the performance of office workers, while Bakò-Birò et al. (2007) retrofitted mechanical ventilation system in naturally ventilated classrooms which caused that CO_2 levels were reduced substantially.

Table 4.5 Summary of papers identified as providing adequate information on the association between performance and ventilation rates

Study	Building type	Study type	Main result
Federspiel et al. (2004)	Office	Field intervention	No improved performance if CO_2 levels above outdoors are lower than 300 ppm corresponding to 15 L/s per person; significant improvement at ventilation rate >50 L/s per person.
Wargocki et al. (2004)	Office	Field intervention	Ventilation rates of 25 L/s per person improved performance of office work.
Wargocki et al. (2007)	School	Field intervention	Improved performance (reduced time for solving math and language tests) when ventilation rates increased between 3 and 8.5 L/s per person (corresponding average CO_2 levels were 900-1,300 ppm).
Bako Biro et al. (2007)	School	Field intervention	The outdoor air supply increased from 0.3-0.5 to 13-16 L/s per person and the pace at which match tests were solved was increased.
Haverinen-Shaughnessy et al. (2010)	School	Cross-sectional	The linear association between classroom ventilation rates and students' academic achievement within the range of 0.9–7.1 L/s per person. For every unit (1 L/s per person) increase in the ventilation rate within that range, the proportion of students passing standardized test (i.e., scoring satisfactory or above) was expected to increase by 2.9% for math and 2.7% for reading.
Synthesis of the evidence	Office	Performance improved in the range 25 to 50 L/s per person	
	School	Performance improved in the range from 7 to 16 L/s per person	

4.2.7 Exposure control

Two papers suggest interesting approach to connect the measurements of exposure, ventilation rates and health effects. By modelling Sherman et al. (2004) estimated which ventilation rates would be necessary to achieve current indoor safe levels of formaldehyde using data on the measured concentrations and emissions rates of formaldehyde in the U.S. housing. Results indicate that to maintain 99% of new houses below a widely accepted action level or ceiling concentration of 100 ppb of formaldehyde, the minimum long-term ventilation rate should be 0.68 $m^3/m^2/h$. For a house with a typical 8-ft ceiling this is equivalent to a ventilation rate of 0.28 h^{-1}. This would correspond to about 7 L/s per person in a 100 m^2 house with 3 people.

In the context of EXPOLIS studies, measurements of indoor and outdoor concentrations from Finland were entered as inputs into an evaluated simulation model to compare exposures in the current ventilation scenarios in residential buildings with an alternative scenario, where the distribution of ambient PM2.5 infiltration factors in all residential and occupational buildings are assumed to be similar to the subset of existing occupational buildings using supply air filters (Hänninen et al. 2005). Results provided by the study indicate that exposures to ambient PM2.5 were reduced by 27%, suggesting that indoor concentrations of ambient particles and the associated health risks, also in term of cancer risk, can be reduced by using mechanical ventilation systems with supply air filtering in buildings.

4.3. Summary of current air quality guidelines

As integration to this review, WHO air quality guidelines, both air and indoor, and INDEX report **(**Kotzias et al. 2005) that defined health based air guidelines have been summarized in table 4.6 (see details in Annex 2).

WHO Air Quality guidelines

The primary aim of the WHO guidelines is to provide a uniform basis for the protection of public health from adverse effects of exposure to air pollution, and to eliminate or reduce to a minimum exposure to those pollutants that are known or are likely to be hazardous. The guidelines are based on the scientific knowledge available at the time of their development.

The "WHO guidelines on dampness and mould" (WHO, 2009) concluded that "… persistent dampness and microbial growth on interior surfaces and in building structures should be avoided or minimized, as they may lead to adverse health effects. As the relationships between dampness, microbial exposure and health effects cannot be quantified precisely, no quantitative, health-based guideline values or thresholds can be recommended for acceptable levels of contamination by microorganisms. Instead, it is recommended that dampness and mould-related problems be prevented. When they occur, they should be remediated because they increase the risk of hazardous exposure to microbes and chemicals".

The "WHO Guidelines for Indoor Air Quality: Selected pollutants" (WHO, 2010) recommend targets for nine indoor air quality pollutants at which the health risks are significantly reduced and provide a scientific basis for legally enforceable standards in all regions of the world.

The steering group assisting WHO in designing the indoor air quality guidelines concluded that there is no convincing evidence of a difference in the hazardous nature of particulate matter (PM) from indoor sources as compared with those from outdoors and that the indoor levels of PM10 and PM2.5, in the presence of indoor sources of PM, are usually higher than the outdoor PM levels. Therefore, the air quality guidelines for particulate matter recommended by the 2005 global update are also applicable to indoor spaces and a new review of the evidence is not necessary at present.

The nine substances considered in this review are common indoor air pollutants globally and are just a few of many chemicals encountered in indoor spaces. They have been selected for the purpose of this review based on the existence of their indoor sources, availability of evidence on their health effects, and common presence in concentrations of health concern. Based on the accumulated science, the experts formulated health risk evaluations and agreed on proposing guidelines for each of the following nine pollutants: Carbon monoxide; Nitrogen dioxide; Benzene; Trichloroethylene; Tetrachloroethylene; Formaldehyde; Naphthalene; Polycyclic aromatic hydrocarbons (PAHs); Radon.

European INDEX project

The European INDEX project "Critical appraisal of the setting and implementation of indoor exposure limits in the EU" was funded by the European Commission DG SANCO and JRC and was coordinated by the JRC in collaboration with a Steering Committee of leading European experts in the area of indoor air pollution (Koistinen et al. 2008; Kotzias et al. 2005).

The project was given the assignment to identify priorities and to assess the needs for a Community strategy and action plan in the area of indoor air pollution by: 1) setting up a list of compounds to be regulated in indoor environments with priority on the basis of health impact criteria; 2) providing suggestions and recommendations on potential exposure limits for these compounds; 3) providing information on links with existing knowledge, ongoing studies, legislation, etc. at world scale.

On the basis of a literature review the Steering Committee decided to include into a detailed assessment 14 compounds (out of initial 41 candidate compounds). Finally a list of compounds, consisting of 5 chemicals, with potential of high indoor concentrations, uncontested health impacts, and effective risk management were selected to be regulated with priority. For each selected compound, guideline values and management options were suggested: Formaldehyde; Carbon Monoxide; Nitrogen Dioxide; Benzene; Naphthalene.

The second group of priority chemicals which are not considered to urgently require regulatory risk management actions specifically in indoor air included: Acetaldehyde; o-, p- and m-Xylene; Toluene; Styrene. Finally the third group of Additional chemicals of interest which are considered to require further research with regard to human exposure or dose response before recommendations can be made included: Ammonia; delta-Limonene; and alpha-Pinene.

Knowledge gaps, key issues, research priorities

Available toxicological data are very limited for firm conclusions for many pollutants and so specific air quality guideline values for general indoor settings have been established for only a few air contaminants. Very limited are the studies on the risks of serious chronic health effects, such as cancer. Difficulties are also related to the fact that many pollutants contribute to annoyance, irritation, and to perception of poor indoor air quality; relationships between indoor office building conditions and wellbeing of occupants are complex.

Many indoor stressors can exert their effects additively or through complex interactions. Many pollutants may contribute to the so called “cocktail effects” (presumably observable adverse effect of a complex chemical mixture in which each individual component exists clearly below its LOEL concentration).

Table 4.6. Indoor and air guidelines (WHO – INDEX project)

Pollutant	IAQ Guidelines			Air Guidelines	
	IAQ WHO (2010)	INDEX (2005)		AQ WHO (2000)	AQ WHO (2005)
CO (mg/m^3)	100 (15 m)	100 (15 m)		100 (15 m)	
	60 (30 m)	60 (30 m)		60 (30 m)	
	30 (1 h)	30 (1 h)		30 (1 h)	
	10 (8 h)	10 (8 h)		10 (8 h)	
	7 (24 h)				
NO_2 ($\mu g/m^3$)	200 (1 h)	200 (1 h)		200 (1 h)	200 (1 h)
	40 (1 y)	40 (1 w)		40 (1 y)	40 (1 y)
SO_2 ($\mu g/m^3$)				500 (10 m)	500 (10 m)
				125 (24 h)	20 (24 h)
PM10 ($\mu g/m^3$)					50 (24 h)
					20 (1 y)
PM2.5 ($\mu g/m^3$)					25 (24 h)
					10 (1 y)
OZONE ($\mu g/m^3$)					100 (8 h)
RADON (Bq/m^3)	No safe level Reference level: 100 Not more than: 300				

Table 4.6 continued. Indoor and air guidelines: organic compounds (WHO – INDEX project)

Pollutant	**IAQ Guidelines**			**Air Guidelines**	
	IAQ WHO (2010)	**INDEX (2005)**		**AQ WHO (2000)**	**AQ WHO (2005)**
Benzene ($\mu g/m^3$)	No safe level	No safe level Not more than outdoor level		UR 6×10^{-6}	
Trichloroethylene	No safe level			UR 4.3×10^{-7}	
Tetrachloroethylene ($\mu g/m^3$)	250 (1 y)			250 (1 y) 8000 (30 m)	
Toluene ($\mu g/m^3$)		300		260 (1 w) 1000 (30 m)	
Styrene ($\mu g/m^3$)		250		260 (1 w) 70 (30 m)	
Xylenes ($\mu g/m^3$)		200			
Naphtalene ($\mu g/m^3$)	10 (1 y)				
Formaldehyde ($\mu g/m^3$)	100 (30 m)	30 (30 m)		100 (30 m)	
Polycyclic aromatic hydrocarbons (PAHs)	No safe level			8.7×10^{-5} per ng/m^3 of B[a]P.	

5. Discussion

Asthma and allergy symptoms

The prevalence of asthma and allergies has increased rapidly in the last few decades and the estimates say of about 300 million or more worldwide affected. This is why there is such a great interest in this health endpoint. Several studies, in some cases with large cohorts, have been carried out to observe whether there is an association between ventilation and self-reported asthma and allergy symptoms.

A number of papers indicated that an association existed between ventilation system and asthma and allergy symptoms (Bornehag et al. 2005; Sun et al. 2011). One of this studies indicated that a low-ventilation rate was associated with worsened asthma symptoms: lower ventilation rates in homes might be a risk factor for allergies among children (0.31 ach vs. 0.37 ach) (Bornehag et al. 2005).

However, in the study of Emenius et al. (2004), an increase of air change rate above 0.4 h-1 and different types of ventilation systems did not seem to affect the risk of recurrent wheeze in children up to the second year of their lives. In their study the negative impact of increased humidity and dampness on their condition was seen and could be regarded as indirect evidence that increasing ventilation rates could possibly reduce these influences.

In general there are few studies on the effects of ventilation on asthma and allergy, and the results are inconsistent implying that multiple exposures can be responsible for the effects observed. There are also too few and inconsistent data to determine ventilation rate required to protect against these problems though suggesting that ventilation rates below 0.4 h^{-1} are likely to elevate the risk of asthma/allergy symptoms. The data also suggest that the form of the exposure-response relationship is non-linear and that there may be no benefits if ventilation is higher than 0.7 h^{-1} and when nothing is done to amend other potentially hazardous exposures.

It is still unclear whether the effects are observed because the humidity is reduced by increased ventilation. If true, the ventilation is merely a mean for controlling moisture, and a very expensive one. Other ways of controlling moisture levels in homes should be considered instead. Whether reducing moisture will justify the reduced ventilation rates in the context of controlling risks of asthma and allergy symptoms still remains unclear and the study of this type has certainly a high priority for understanding the underlying mechanisms. In such study humidity in homes of cases should be controlled by ventilation and by other means and the impact on symptoms prevalence should be monitored in parallel. None of the studies reviewed applied this approach.

The studies reviewed can be characterized as lacking or having poor ventilation measurements or as using proxies for ventilation (such as CO_2). They used self-estimated symptoms prevalence and lacked proper characterization of buildings, sources and exposures. The future studies must much better address these important limitations.

Respiratory symptoms

The reviewed studies found an association between ventilation and respiratory systems, mainly showing that elevated exposures due to improperly maintained ventilation system can increase the risk of symptoms, indicating that ventilation system can become an important source of pollution. No clear cut-off point defining the rate of ventilation can be determined above which it can be said that the risk of respiratory problems is negligible. One reason is the nature of studies which principally were observational and the other is confounding caused by the level of pollution caused by the system. Studies in day care centres showed that air conditioning may have negative effects on respiratory symptoms not because the air conditioning system is potentially source of pollution but also due to need to saving energy in air conditioned buildings resulting in very low ventilation rates sometimes far below 10 L/s per person. As a result day care centres with natural ventilation were observed to protect against symptoms not because of natural ventilation but because the ventilation rates were significantly higher in these buildings compared with buildings with either central or de-central air conditioning.

The above observation is important in the context of findings in offices already discussed by the previous reviews as well as discussed in the present work showing that the reason why there are less symptoms observed in naturally ventilated buildings could be not because natural ventilation is superior towards mechanical systems but because exposures (due to reduced sources of pollution from the system and higher ventilation) were lower. This clearly emphasize the need for ensuring that ventilation is connected to and designed based on the actual exposures rather than according to the principle than one size fits all, i.e. that the universal recommendations can be used and applied across the entire building stock independently of the exposure. This would result in the very high requirements, higher than 25 L/s per person or even as high as 50 L/s per person as indicated in the

papers reviewed here.

The main limitations of the studies dealing with respiratory systems were as follows: (1) these were observational studies in which different buildings with different exposures were compared; (2) ventilation was measured mainly using CO_2 as a proxy or there was lack of ventilation measurements; (3) exposures were improperly characterized; and (4) as a health end-points self-assessed acute symptoms were used with a long recall period in some cases.

Infectious diseases

The burden of disease attributable to airborne respiratory infections is huge, resulting in a very high numbers of lost work among adults and days of missed school among children. In particular schools are the major source of community outbreaks of respiratory infections. The studies reviewed do not provide ventilation rate that could be useful for setting requirements in guidelines minimizing the risk of infectious diseases.

One of the difficulties in developing ventilation requirements concerns the quantification of the infectious sources and the exposure of population. In nearly all situations/outbreaks, there are a large number of factors that can contribute to the transmission of infection, and it would be very difficult to identify that ventilation is a main risk factor. Most existing studies deal with multiple co-existing factors, which makes it difficult to completely rule out the possibility of transmission by other routes. Moreover, the most inherent limitation in almost all existing investigations is the rapid disappearance of airborne evidence of infection, once the infectious period is over. It becomes very difficult then to, retrospectively, reproduces the same ventilation and airflow conditions that existed at the time of the outbreak. Many existing epidemiological studies do not include adequate airflow studies. Finally, in collocating evidence of an association between ventilation and the airborne transmission of diseases, other factors need consideration. These include the generation of infectious pathogen-containing aerosols, the survivability of infectious pathogens in air, and the infectious dose. As a consequence, studies investigating whether ventilation rates are sufficient in decreasing the risk of spread and outbreak of infectious diseases are needed.

Sick Building Syndrome symptoms (and perceived air quality)

Unspecific symptoms of irritation of eyes, nose and mucous membranes, malaise, fatigue and headaches experienced by building occupants, often referred as Sick Building Symptoms (SBS) (WHO, 1982) are often used to observe negative effects of indoor environmental quality on people. These symptoms are self-reported by building occupants who sometimes assess their intensity but most often they assess frequency of their occurrence (occasionally, weekly, and daily) in the period preceding the survey; usually the recall period being 1 to 3 months but sometimes even 6 to 12 months. During the period of more than 3 decades Sick Building Syndrome (SBS) symptoms, sometimes also called Building Related Symptoms (BRS), have been the subject of investigations in office buildings, schools, hospitals, homes and other types of non-industrial buildings.

Table 5.1 summarize main findings of these past reviews. They show a decrease of SBS symptom prevalence with increasing ventilation rates up to 25 L/s per person; airflow rates below 10 L/s per person were observed to be strongly associated with higher symptoms. However some reviews concluded that air-conditioning systems were associated with the risk for increasing SBS prevalence compared to natural ventilation; this effect was attributed to improper maintenance, design, and functioning of air-conditioning systems.

Table 5.1: Main conclusions on the effects of ventilation on SBS symptoms drawn from 5 reviews

Conclusions	Mendell 1993	Seppanen 1999	Wargocky 2002	Fisk 2009	Sundell 2011
Air conditioning vs. natural ventilation increases symptoms	x	x	x		
Use of carpets increases symptoms	x				
Higher density of occupants in the space increases symptoms	x				
Use VDTs increases symptoms	x				
Significant decrease of symptoms for the increase of ventilation rate from 0 to 10 L/s x person	x	x			
Airflow rates up to 25 L/s x person are associated with reduced prevalence or SBS symptoms		x	x	x	x
Improper maintenance, design, and functioning of air-conditioning systems contributes to the increase prevalence of SBS symptoms		x	x		

Table 5.2 compares the studies on SBS symptoms included in the previous reviews and in the current work. It shows that in total there were 41 publications discussing ventilation and SBS symptoms, of which 19 show that a higher ventilation rate increases SBS; as many as 16 studies show no association. This may suggest

multifactorial origin of SBS, though the relationship between indoor minus outdoor CO_2 concentrations and mucous membrane/lower respiratory symptoms suggests that air contaminants are implicated in the aetiology of BRS. The results shown in Table 5.2 but may be a sign of a quality of the studies.

The general weakness of the past research on this topic is well articulated by Mendell et al. (1993) who said that "*Future research on the relationship between IEQ and SBS symptoms should include blind experimental and case-control studies, using improved measurements of both environmental exposures and health outcomes*". Additionally, health effects were determined by self-administrated questionnaires and not – at least to some extent – by clinical examinations, there was no adequate and/or generally not present exposure measurement; the studies did not have proper confounding, an essential whenever investigating sick building symptoms, especially for cross-sectional studies; and finally there were generally lack of well designed, blinded experimental studies, and if existing they had too low sample sizes.

The studies examining the effect on perceived air quality used different techniques to assess the perceived air quality from the rating made by untrained panel using the continuous acceptability scale (Wargocki et al. 2007), and by trained panel using the reference scale of 2-Propanone (Bitter et al. 2002) to self-administered questionnaires indicating the degree of quality of air, odour and/or stuffiness of air (Engvall et al. 2005; Norbäck et al. 2011). These different measuring scales are not directly comparable and are all just good for indicating trends.

Table 5.2: Summary of primary publications used by the 5 reviews on ventilation and SBS and used in the present work

Author	Year	Mendell 1993	Seppänen 1999 (2004)	Wargocki 2002	Fisk, 2009	Sundell 2011	CURRENT WORK	total	High VR / High SBS	High VR / Low SBS	No association
TOTAL		**15**	**14**	**16**	**8**	**11**	**4**	**69**	**6**	**19**	**16**
Gamble	1986		x					1		1	
Burge	1990	x						1			1
Jaakkola	1990	x						1			1
Norbäck	1990	x		x				2			1
Skov	1990	x		x				2			1
Skov	1990a	x						1			1
Hodgson	1991	x						1			1
Nagda	1991	x						1		1	
Jaakkola	1991a	x	x	x	x	x		5		1	1
Jaakkola	1991b		x	x		x		4		1	1
Hill	1992	x		x				2			1
Hodgson	1992	x						1			1
Mendell	1992	x						1			1
Sundell	1992	x						1		1	
Wyon	1992	x	x	x				3	1		
Zweers	1992	x		x				2		1	
Menzies	1993a	x	x	x	x	x		5			1

Jaakkola	1994		x	x	x	x		4	1	1	1
Ruotsalainen	1994		x	x				2		1	
Stenberg	1994		x	x	x	x		4		1	
Sundell	1994		x	x		x		3		1	
Sundell	1994a		x	x		x		3		1	
Cochet	1995		x					1		1	
Groes	1995		x					1		1	
Jaakkola	1995		x	x	x	x		4	1	1	
Nordström	1995a		x	x				2	1		
Wu	1996		x					1			1
Wargocki	2000			x		x		2		1	
Skyberg	2003						x	1	1		
Erdmann	2004					x	x	2		1	
Tham	2004				x			1		1	
Wargocki	2004				x	x		2		1	
Mendell	2005				x			1		1	
Norbäck	2008						x	1			1
Smedje	2011						x	1			1
Zhang	2011						x	1	1		

Performance and sick leave

The results in the reviewed papers show that increased ventilation rate can improve performance of office work. Although the figures should be used cautiously as the actual benefits can be smaller there is a clear consistency of findings. Even if productivity would be increased by 1% the economic benefits would be significant in the developed countries. The economic consequences of insufficient ventilation rates were discussed by Fisk et al. (2011). They estimated some of the benefits and costs of among others increasing ventilation rates in the US office buildings when they are below 10 or 15 L/s per person, and as well as adding outdoor air economizers and controls when absent; they also tested scenarios in which winter indoor temperatures >23°C were eliminated, and dampness and mold problems were reduced. The estimated benefits of the scenarios analyzed were shown to be substantial in magnitude, including increased work performance, reduced sick building syndrome (SBS) symptoms, reduced absence, and improved thermal comfort for millions of office workers. The combined potential economic benefit of a set of no overlapping scenarios was estimated to be approximately $20 billion per year; of this number $ 5.6-13.5 billion can be attributed to increased ventilation rate, $11.8 billion to providing economizers with outdoor air.

The studies also showed that increased ventilation rate would have positive effect on learning progress. In this case the economic estimates are difficult to predict but it is fair assumption that better education can lead to the wealthier society as implied by the results of OECD study on the high cost of low educational performance showing that better score on the tests used in the Programme for International Student Assessment (PISA) correlates well with higher GDP.

Outdoor and indoor pollutant control

The entry of outdoor air into indoor environments poses some problems. Outdoor air contains contaminants that can affect health whether inhaled outdoors or indoors. Ventilation can serve as a means of introducing these contaminants into indoor spaces. However, the outdoor air quality is not very much discussed and neither quantified nor characterized in the reviews.

When evaluating the effects of ventilation rates on health, it is important to be mindful of the quality of the outdoor air used to provide ventilation. Numerous epidemiological studies showed associations between pollutants in outdoor air (primarily PM10, PM2.5 and ozone) and both morbidity and mortality (Pope and Dockery, 2006). The studies reviewed generally did not consider the potential for adverse health outcomes to be associated with higher exposure to outdoor air pollutant concentrations. Increased ventilation means increase outdoor-to-indoor transport of outdoor pollutants (Weschler, 2006). Then it may be expected that the effects observed due to exposures indoors can be confounded with the quality of ambient air which is supplied indoors by ventilation. In areas with good outdoor air quality the effects of increasing ventilation can be much more dominant and in the polluted areas the effect may be smaller as the outdoor air quality can itself elevate the risk. In locations with polluted outdoor air, there may be ventilation-rate-mediated trade-offs between health risks from outdoor pollutants and those from indoor sources. Any recommendations to increase ventilation must address the issue of poor ambient air quality and not just assume that more outdoor air will necessarily improve indoor environmental quality.

Health based ventilation guidelines

Available literature show that there is an association between ventilation and health, in term of SBS symptoms, infectious diseases, allergic disease and asthma symptoms, short-term sick leave and comfort as indicated by perceived air quality; it also indicates that there is an association between ventilation rate and productivity (as indicated by performance of office work). The data are summarized in Table 5.3. They provide the minimum ventilation rates at which no negative effects were observed satisfying the condition of primary prevention, i.e. acknowledging that ventilation is not a primary mean to control exposure and that there can be other methods to reduce negative impacts.

Improper maintenance, design, and functioning of air-conditioning systems contributes to the increase prevalence of SBS symptoms. When evaluating the effects of ventilation rates on health, it is important to be mindful of the quality of the outdoor air used to provide ventilation. Numerous epidemiological studies have demonstrated associations between pollutants in outdoor air (primarily PM10, PM2.5 and ozone) and both morbidity and mortality (Pope and Dockery, 2006).

Table 5.3. Summary of the findings on the association between health and ventilation rates

Health endpoint	Home	Office	School
Asthma and allergic symptoms	0,37 - 0,32 ach (corresponding to 7 L/s per person)	-	-
Airborne infectious diseases	No quantitative, health-based guideline values or thresholds can be recommended for acceptable levels of contamination by microorganisms. Association between a weekly average CO_2 differential concentration greater than approximately 100 ppm and the probability of detecting airborne rhinovirus (Office)		
SBS symptoms	> 0,4 ACH protect (> 8 L/s x p)	> 9 L/s per person (< 20% of prevalence of SBS symptoms)	From 7 L/s per person to 10 L/s per person no change on SBS symptoms but increased perceived air quality
Annual sick leave	-	> 12 L/s per person reduction annual sick leave (1.2-1.9 days per person per year)	Every 4 L/s per person corresponds to 10-20% change in school absence rates (1 L/s per person ~ 2.5-5%)
Performance	-	≥ 15 L/s per person are likely to reduce potentially negative effects on performance	≥ 7 L/s x p are likely to reduce potentially negative effects on performance

It has to be underlined that none of the reviewed studies assessed the impact of building ventilation rates on the risks of serious chronic health effects, such as respiratory, cardiovascular diseases, and cancer. In most of the reviewed studies, important details describing the ventilation levels, measurement method and/or conditions are not reported. Generally the studies reviewed can be also characterized as having poor description of exposures. These considerations apply both as regards quite simple measurements of ventilation rates using CO_2 as a proxy and secondly nearly lack of measurements of other pollutants. Also no information is often present as regards outdoor air pollutants and their level. One study showed that increased ventilation rate increased SBS symptoms, which probably was caused by transport of pollutants from outdoors. Few studies showed clearly that this process, here as regards ozone brought indoors from outdoors either per se or due to reactions on ventilation filters (or other surfaces) can increase the risk of SBS symptoms. Many of the previous studies are quite old and the buildings in which they were performed did not implement special measures of reducing emission rates from building materials, furnishing and equipment, as well as in many buildings smoking was still possible.

The usefulness of the present results summarized in Table 5.3 for setting the ventilation guidelines based on health can be discussed. The relevant question would be whether they can be used to set ventilation requirements. The answer is negative. Since these figures do reflect specific exposures it is unlikely that they could be used universally in any building and would protect against negative health effects. There are also other reasons why the answer to this question is negative.

Firstly, the dependence of indoor pollutant levels on ventilation rates varies among pollutants and, although understood in principle, has not been completely characterized. Some pollutants can be affected to a large extent and some only moderately and not at all.

Secondly, some knowledge is insufficient to derive adequate ventilation rates to control exposure. There is basically absence of limit values for most indoor pollutants. It is consequently impossible to determine the required ventilation rates to guarantee safe indoor pollutant levels. Even if existing there is no sufficient knowledge on emissions of pollutants as well the combined effects of low-dose mixture of pollutants which occur normally indoors are not well understood.

Thirdly, health effects are related to exposures and it should be acknowledged that there are other methods that should be used to control exposures. Adopting the primary prevention approach reducing strength of pollution sources, and/or controlling humidity should be used at first.

Considering that effects on health and comfort are related to the exposures to the pollutants that are potentially harmful to humans it is difficult to set the ventilation rate that would meet ventilation requirements for health in all kinds of indoor environment. The reason is that indoor spaces will always include pollutants of different types, with one exception. In all indoor spaces there will always be pollutants emitted by humans (bioeffluents). Hypothetically if all sources of pollutants are controlled/reduced the only pollutants left would always be human bioeffluents. Consequently, if universally applicable ventilation guidelines for health were to be proposed they would only address the dilution of bioeffluents and would be thus minimum basic ventilation requirements in indoor spaces.

Any future recommendations regarding ventilation requirements need to always address two aspects: maintenance of systems and outdoor air quality. The reviewed literature shows that improper maintenance, design, and functioning of HVAC systems contribute to an increased prevalence of SBS symptoms. This indicates a need for safety factors and proper maintenance of ventilation systems, including such aspects as appropriate distance separating the inlet and exhaust, replacing dirty filters, cleaning ducts, and the prevention of water reservoirs and water in the systems. The entry of outdoor air into indoor environments poses some problems. Outdoor air contains contaminants that can affect health whether inhaled outdoors or indoors. Ventilation can serve as a means of introducing these contaminants into indoor spaces. Any recommendations to increase ventilation must address the issue of poor ambient air quality and not just assume that more outdoor air will necessarily improve indoor environmental quality.

Future research

The present review clearly indicates gaps in knowledge regarding the associations between ventilation and health. It shows that further research is needed. The recommended approach to study the association between ventilation and health need to be multidisciplinary and should try to establish correlations between indoor air pollution and ventilation rates.

The first need is to assess indoor safe pollutant levels. Most of the experimental data show the results for acute not chronic effects whereas most of the guidelines regarding the pollutants are based on the data for chronic exposures.

Exposure assessment of indoor generated pollutants, generally not existing at present, can be based on pollutants indicated by the authoritative regulative bodies, as well as it can also be based on a “simple” sensory evaluation not differentiating between 15% and 30% dissatisfied as done at present but assuming certain degree of accuracy (i.e. ±20%) checking whether the air quality is adequate. In future this can also be achieved by sensors. This implies also that the ventilation guidelines would only indicate the level of ventilation which should then be verified and/or adjusted under building use under the principle of compliance.

A better characterization of exposures is hence needed. Ventilation measurements made using different techniques in different seasons and different averaging times, sometimes using concentration of CO_2 to estimate ventilation rates. Future research should better document which ventilation measurements are valid in the context of health.

6. Conclusions

Present review shows that ventilation rates are associated with the acute health symptoms, perceived air quality, short-term sick leave and performance of office work and schoolwork. The literature indicates that ventilation rates above 7 L/s per person reduced the risk of asthma and allergic symptoms. As to SBS symptoms, they show that a ventilation rate as high as 8 L/s per person in homes and 9 L/s per person offices was associated with a decreased onset of the symptoms or percentage of people complaining. Similar results indicate that ventilation rates in the range 8-10 L/s per person in school buildings improved perceived air quality. Outdoor air rates above 12 L/s per person in office buildings were seen to reduce the risk of short-term sick. Ventilation rates higher than 15 L/s x p in offices were shown to reduce potentially negative effects on performance, while ventilation rate in schools should be kept at least at 7 l/s per person to ensure no negative effects on learning.

Many of these studies reviewed are quite old and were carried out in buildings in which they were performed did not implement special measures of reducing emission rates from building materials, furnishing and equipment, as well as in many buildings smoking was still possible. The studies lack also proper characterization of exposures, outdoor air quality and sometimes proper ventilation measurements. Therefore the rates should be considered cautiously.

No clear distinction in the scientific data was seen whether natural or mechanical ventilation is optimal for health. The differences observed between the two systems can be attributed to differences in ventilation rates. They can also be due to improper maintenance of mechanical systems as data show that systems can become a significant source of pollution. Measures should be adopted to reduce indoor pollution refer to proper source control and design and maintenance of adequate ventilation systems. These measures also apply to control of outdoor air quality as outdoor air contains contaminants that can affect health whether inhaled outdoors or indoors. To this end ventilation can serve as a means of introducing these contaminants into indoor spaces.

The present review clearly indicates gaps in knowledge regarding the associations between ventilation and health. The recommended approach to study the association between ventilation and health need to be multidisciplinary and should try to establish much better the connection between indoor air pollution (exposures), ventilation rates (mediator of exposures) and health. The present results show that there are recommendations regarding safe health levels for only few pollutants. Even though it would be strongly recommended that the exposure measurements in future always address these pollutants and that the design of future buildings makes sure that these recommendations are always met.

7. References

Apte M.G., Buchanan I.S.H., Mendell M. J. Outdoor ozone and building-related symptoms in the BASE study. Indoor Air 2008; 18: 156–170.

Bakó-Biró Zs., Kochhar N., Clements-Croome D.J.,. Awbi H.B., Williams M. Ventilation Rates in Schools and Learning Performance. Proceedings of Clima 2007 WellBeing Indoors.

Bitter F., Fitzner K. Odour emissions from an HVAC-system. Energy and Buildings 2002; 34: 809–816.

Bornehag C.G., Sundell J., Hägerhed-Engman L., Sigsgaard T. Association between ventilation rates in 390 Swedish homes and allergic symptoms in children. Indoor Air 2005; 15: 275–280.

Buchanan I.S.H., Mendell M.J., Mirer A.G., Apte M.G. Air filter materials, outdoor ozone and building-related symptoms in the BASE study. Indoor Air 2008; 18: 144–155.

Chao H.J., Schwartz J., Milton D.K., Burge H.A. The Work Environment and Workers' Health in Four Large Office Buildings. Environ. Health Perspect. 2003; 111: 1242–1248.

Coelho C., Steers M., Lutzler P., Schriver -Mazzuoli L. Indoor air pollution in old people's homes related to some health problems: a survey study. Indoor Air 2005; 15: 267–274.

Clausen G., Høst A., Toftum J., Bekç1 G., Weschler C., Callesen M., Buhl S., Ladegaard M.B., Langer S., Andersen B., Sundell J., Bornehag C.G., Sigsgaard T. Children's health and its association with indoor environments in Danish homes and daycare centres – methods. Indoor Air 2012

Dimitroulopoulou C. Ventilation in European dwellings: A review. Building and Environment 2011; 47: 109-125.

Emenius G., Svartengren M., Korsgaard J., 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.

Engvall K., Norrby C., Norbäck D. Ocular, nasal, dermal and respiratory symptoms in relation to heating, ventilation, energy conservation, and reconstruction of older multi-family houses. Indoor Air 2003; 13: 206–211.

Engvall K., Wickman P., Norback 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: 120–126.

Erdmann C.A., Apte M.G. Mucous membrane and lower respiratory building related symptoms in relation to indoor carbon dioxide concentrations in the 100-building BASE dataset. Indoor Air 2004; 14 (Suppl 8): 127–134.

Ezratty V., Duburcq A., Corinne E., Lambrozo J. Residential Thermal Comfort, Weather-Tightness and Ventilation: Links With Health in a European Study (Lares).

Fisk W.J., Mirer A.G., Mendell M.J. Quantitative relationship of sick building syndrome symptoms with ventilation rates. Indoor Air 2009; 19: 159–165.

Fisk W.J., Black D., Brunner G. Benefits and costs of improved IEQ in U.S. offices Indoor Air 2011; 21: 357–367.

Federspiel C.C., Fisk W.J., Price P.N., Liu G., Faulkner D., Dibartolomeo D.L., Sullivan D.P., Lahiff M. Worker performance and ventilation in a call center: analyses of work performance data for registered nurses. Indoor Air 2004; 14 (Suppl 8): 41–50.

Godish T. and Spengler J.D. Relationships Between Ventilation and Indoor Air Quality: A Review. Indoor Air 1996; 6: 135-145

Graudenz G.S., Kalil J., Saldiva P.H., Latorre Mdo R., Morato-Castro FF. Upper respiratory symptoms associated with aging of the ventilation system in artificially ventilated offices in São Paulo, Brazil. Chest 2002; 122: 729-735.

Graudenz G.S., Kalil J., Saldiva P.H., Latorre Mdo R., Morato-Castro F.F. Decreased respiratory symptoms after intervention in artificially ventilated offices in São Paulo, Brazil. Chest 2004; 125: 326-329.

Graudenz G.S., Oliveira C.H., Tribess A., Mendes C.Jr, Latorre Mdo R., Kalil J. Association of air-conditioning with respiratory symptoms in office workers in tropical climate. Indoor Air 2005; 15: 62–66.

Hänninen O.O., Palonen J., Tuomisto J.T., Yli-Tuomi T., Seppänen O., Jantunen M. J. Reduction potential of urban PM2.5 mortality risk using modern ventilation systems in buildings. Indoor Air 2005; 15: 246–256.

Haverinen-Shaughnessy U., Moschandreas D.J., Shaughnessy R.J. Association between substandard classroom ventilation rates and students'academic achievement. Indoor Air 2010; 21(2): 121-131.

Howieson S.G.,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 (3): 137-147

Hummelgaard J., Juhl P., Sæbjornsson K.O., Clausen G., Toftum J., Langkilde G. Indoor air quality and occupant satisfaction in five mechanically and four naturally ventilated open-plan office buildings. Building and Environment 2007; 42: 4051–4058.

Kaczmarczyk J., Melikov A., Ranger P.O. Human response to personalized ventilation and mixing ventilation. Indoor Air 2004; 14 (Suppl 8): 17–29.

Kishi R., Saijo Y., Kanazawa A., Tanaka M., Yoshimura T., Chikara H., Takigawa T., Morimoto K., Nakayama K., Shibata E. Regional differences in residential environments and the association of dwellings and residential factors with the sick house syndrome: a nationwide cross-sectional questionnaire study in Japan. Indoor Air 2009; 19: 243–254.

Koistinen K., Kotzias D., Kephalopoulos S., Schlitt C., Carrer P., Jantunen M., Kirchner S., McLaughlin J., Molhave L., Fernandes E.dO., Seifert B. (2008): The INDEX project: executive summary of a European Union project on indoor air pollutants. Allergy, 63(7): 810-9.

Kotzias D., Koistinen K., Kephalopoulos S., Schlitt C., Carrer P., Maroni M., Jantunen M., Cochet C., Kirchner S., Lindvall T., McLaughlin J., Mølhave L., Fernandes E.dO., Seifert B. (2005): The INDEX project. Critical Appraisal of the Setting and Implementation of Indoor Exposure Limits in the EU. Final Report. EUR 21590 EN. European Commission, Directorate General, Joint Research Centre.

Kovesi T., Zaloum C., Stocco C., Fugler D., Dales R.E., Ni A., Barrowman N., Gilbert N.L., Miller J.D. Heat recovery ventilators prevent respiratory disorders in Inuit children. Indoor Air 2009; 19: 489–499.

Lan L., Wargocki P., Wyon D.P., Lian Z. Effects of thermal discomfort in an office on perceived air quality, SBS symptoms, physiological responses, and human performance. Indoor Air 2011; 21: 376–390.

Li Y., Leung G.M., Tang J.W., Yang X., Chao C.Y.H., Lin J.Z., Lu J.W., Nielsen P.V., Niu J., Qian H., Sleigh A.C., Su H.-J.J., Sundell J., Wong T.W., Yuen P.L. Role of ventilation in airborne transmission of infectious agents in the built environment – a multidisciplinary systematic review. Indoor Air 2007; 17: 2–18.

Leech J.A., Raizenne M., Gusdorf J. Health in occupants of energy efficient new homes. Indoor Air 2004; 14: 169–173.

Mendell M.J. Non-specific symptoms in office workers: a review and summary of the epidemiologic literature. Indoor Air 1993; 3: 227-36.

Mendell M.J., Naco G.M., Wilcox T.G., Sieber W.K. Environmental Risk Factors and Work-Related Lower Respiratory Symptoms in 80 Office Buildings: An Exploratory Analysis of Niosh Data. American Journal of Industrial Medicine 2003; 43: 630–641.

Mendell M.J. and Heath G.A. Do indoor pollutants and thermal conditions in schools influence student performance? A critical review of the literature. Indoor Air 2005; 15: 27–52

Mendell M.J., Cozen M., Lei-Gomez Q., Brightman H.S., Erdmann C.A., Girman J.R., Womble S.E. Indicators of moisture and ventilation system contamination in U.S. office buildings as risk factors for respiratory and mucous membrane symptoms: analyses of the EPA BASE Data. Journal of Occupational and Environmental Hygiene 2006; 3: 225–233.

Milton D.K., Glencross P.M., Walters M.D. Risk of Sick Leave Associated with Outdoor Air Supply Rate, Humidification, and Occupant Complaints. Indoor Air 2000; 10: 212–221.

Myatt T.A., Staudenmayer J., Adams K., Walters M., Rudnick S.N., Milton D.K. A study of indoor carbon dioxide levels and sick leave among office Workers. Environmental Health: A Global Access Science Source 2002; 1: 3.

Myatt T.A., Johnston S.L., Zuo Z., Wand M., Kebadze T., Rudnick S., Milton D.K. Detection of airborne rhinovirus and its relation to outdoor air supply in office environments. Am J Respir Crit Care Med 2004; 169: 1187–1190.

Mysen M., Schild P.G., Hellstrand V., Thunshelle K. Evaluation of simplified ventilation system with direct air supply through the facade in a school in a cold climate. Energy and Buildings 2005; 37: 157–166.

Nagda N.L., Rector H.E.. Instruments and methods for measuring indoor air quality. In: Indoor Air Quality Handbook. 2000: 51.2-51.4.

Norbäck D., Wieslander G., Zhang X., Zhao Z. Respiratory symptoms, perceived air quality and physiological signs in elementary school pupils in relation to displacement and mixing ventilation system: an intervention study. Indoor Air 2011; 21: 427–437.

Norbäck D., Nordstrom K. Sick building syndrome in relation to air exchange rate, CO_2, room temperature and relative air humidity in university computer classrooms: an experimental study. Int. Arch. Occup. Environ. Health 2008; 82: 21–30.

Pantelic J., Sze-To G.N., Tham K. W., Chao C.Y.H., Khoo Y.C.M. Personalized ventilation as a control measure for airborne transmissible disease spread. J. R. Soc. Interface 2009; 6: 715-726.

Pope, C.A., and Dockery, D.W. Health effects of fine particulate air pollution: lines that connect. Journal of the Air & Waste Management Association 2006; 56(6): 709-742.

Rudnick S.N., Milton D.K. Risk of indoor airborne infection transmission estimated from carbon dioxide concentration. Indoor Air 2003; 13: 237–245

Seppänen O.A., Fisk W.J., Mendell M.J. Association of Ventilation Rates and CO_2 Concentrations with Health and Other Responses in Commercial and Institutional Buildings. Indoor Air 1999; 9: 226–252.

Seppänen O.A., Fisk W.J. Relationship of SBS-symptoms and ventilation system type in office buildings. Indoor Air 2002, 12 (2): 98-112.

Seppänen O.A., Fisk W.J. Summary of human responses to ventilation. Indoor Air 2004; 14 (Suppl 7): 102–118.

Seppänen O.A., Fisk W.J., Lei Q.H.. Ventilation and performance in office work. Indoor Air 2006; 16: 28–36.

Shendell D.G., Prill R., Fisk W.J., Apte M.G., Blake D., Faulkner D. Associations between classroom CO2 concentrations and student attendance in Washington and Idaho. Indoor Air 2004; 14: 333–341.

Sherman M.H., Hodgson A.T. Formaldehyde as a basis for residential ventilation rates. Indoor Air 2004; 14: 2–8.

Skyberg K., Skulberg K.R., Eduard W., Skaret E., Levy F., Kjuus H. Symptoms prevalence among office employees and associations to building characteristics. Indoor Air 2003; 13: 246–252.

Simoni M., Annesi-Maesano I., Sigsgaard T., Norback D., Wieslander G., Nystad W., Cancianie M., Sestini P., Viegi G. School air quality related to dry cough, rhinitis and nasal patency in children. Eur. Respir. J. 2010; 35: 742–749.

Simons E., Hwang Syni-An, Fitzgerald E.F., Christine K., Lin S. The Impact of School Building Conditions on Student Absenteeism in Upstate New York. J. Public Health 2010; 100: 1679–1686.

Smedje G., Mattsson M., linder R.W. Comparing mixing and displacement ventilation in classrooms: pupils'perception and health. Indoor Air 2011; 21: 454–461.

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: 277–283.

Sundell J. Levin H.W., Nazaroff W., Cain W.S., Fisk W.J., Grimsrud D.T., Gyntelberg F., Li Y., Persily A.K., Pickering A.C., Samet J.M., Spengler J.D., Taylor S.T., Weschler C.J. Ventilation rates and health: multidisciplinary review of the scientific literature. Indoor Air 2011; 21: 191–204.

Takahashi Y., Takano K., Suzuki M., Nagai S., Yokosuka M., Takeshita T., Saito A., Yasueda H., Enomoto T. Two Routes for Pollen Entering Indoors: Ventilation and Clothes. J. Investig. Allergol. Clin. Immunol. 2008; 18 (5): 382-388.

Wargocki, P., Sundell, J., Bischof, W., Brundrett, G., Fanger, P. O., Gyntelberg, F., Hanssen, S. O., Harrison, P., Pickering, A., Seppänen, O. and Wouters, P. Ventilation and Health in Nonindustrial Indoor Environments. Report from a European Multidisciplinary Scientific Consensus Meeting', Indoor Air 2002, 12, 113-128

Wargocki P., Lagercrantz L., Witterseh T., Sundell J., Wyon D.P., Fanger P.O. Subjective perceptions, symptom intensity and performance: a comparison of two independent studies, both changing similarly the pollution load in an office. Indoor Air 2002; 12 (2): 74-80.

Wargocki P., Knudsen H.N., Zuczek P. Effect of using low-polluting building materials and increasing ventilation on perceived indoor air quality. Proceedings of Clima 2007 WellBeing Indoors.

Wargocki P., Wyon D.P., Ranger P.O. The performance and subjective responses of call-center operators with new and used supply air filters at two outdoor air supply rates. Indoor Air 2004; 14 (Suppl 8): 7–16.

Weschler CJ. Ozone's impact on public health: contributions from indoor exposures to ozone and products of ozone-initiated chemistry. Environ Health Perspect. 2006;114:1489–1496.

WHO guidelines for indoor air quality: dampness and mould. Copenhagen, WHO Regional Office for Europe, 2009.

WHO (2010): WHO Guidelines for Indoor Air Quality: Selected pollutants. Copenhagen, WHO Regional Office for Europe, 2010.

Wong N.H., Huang B. Comparative study of the indoor air quality of naturally ventilated and air-conditioned bedrooms of residential buildings in Singapore. Building and Environment 2004; 39: 1115 – 1123.

Wright G.R., Howieson S., McSharry C., McMahon A.D., Chaudhuri R., Thompson J., Donnelly I., Brooks R.G., Lawson A., Jolly L., McAlpine L., King E.M., Chapman M.D., Wood S., Thomson N.C. Effect of improved home ventilation on asthma control and house dust mite allergen levels. Allergy 2009: 64: 1671–1680.

Xu Y., Raja S., Ferro A.R., Jaques P.A., Hopke P.K., Gressani C., Wetzel L.E. Effectiveness of heating, ventilation and air conditioning system with HEPA filter unit on indoor air quality and asthmatic children's health. Building and Environment 2010; 45: 330–337.

Zeiler W., Boxem G. Ventilation of Dutch schools; an integral approach to improve design. Proceedings of Clima 2007 Well Being Indoors.

Zhang X., Zhao Z., Nordquist T., Norbäck D. The prevalence and incidence of sick building syndrome in Chinese pupils in relation to the school environment: a two-year follow-up study. Indoor Air 2011; 21: 462–471.

Zuraimi M.S., Tham K.W., Chew F.T., Ooi P.L. The effect of ventilation strategies of child care centers on indoor air quality and respiratory health of children in Singapore. Science of the Total Environment 2007; 377: 1–11.

ANNEX 1 - Literature search

1.1 Asthma and allergy symptoms

Homes

First author	Year	Study characteristics	Main outcome	country	Study type	population	ventilation type	ventilation rate	Exposure assessment	Strength of observations
Emenius G	2004	A birth cohort followed during their first 2 years of life. Children with recurrent wheezing, and two age-matched controls per case, were identified and enrolled in a nested case–control study.	Living in an apartment erected after 1939, or in a private home with crawl space/concrete slab foundation were associated with an increased risk of recurrent wheezing, odds ratio (OR) 2.5 (1.3-4.8) and 2.5 (1.1-5.4), respectively. The same for living in homes with absolute indoor humidity >5.8 g/kg, OR 1.7 (1.0-2.9) and in homes where windowpane condensation was consistently reported over several years, OR 2.2 (1.1-4.5). However, air change rate and type of ventilation system did not seem to affect the	USA	Case-control study nested in a birth cohort	4089 children	Natural; exhaust, balanced inspected by health officer	4 week, PFT, accuracy 11%, mean±sd 0.68±0.32h-1; in 69% >0.5h-1	Ventilation rate, humidity, temperature. NO_2 in and out (Palmes tubes) (HDM as well); NO_2 <25 (in) <40 (out) µg/m3	Strong (but not as regards ventilation but other exposures approximated by building age humidity and windowpane condensation.

			risk.							
Comments: The study may suggest that even high ventilation rates (on average measured at 0.69 h-1 and in 70% of investigated homes above 0.5h-1) cannot protect against asthma and allergy symptoms when other exposures are likely (approximated here as elevated levels of humidity).This result can be interpreted as follows: 1. Ventilation rates higher than 0.69 h-1 would be needed to control asthma and allergy; 2. There is no need to increase ventilation above the minimum of 0.5 h-1 as this may not give benefits; 3. Before increasing ventilation rates exposures are to be amended.										
Bornehag CG	2005	The effect of higher ventilation was investigated with respect to allergy symptoms	Cases with allergic disease had significantly lower ventilation rates than controls (0.31 ach vs 0.37 ach, p>0.05). A low-ventilation rate of homes may be a risk factor for allergies among children.	Sweden	case-control	Children, 198 cases with allergy and 202 healthy controls, living in 390 homes	Natural (66%) and mechanical exhaust and balanced; inspections	1 week PFT; mean±sd 0.36±0.32h-1 (single) 0.48±0.43 (multi)h-1 Effects only in single (0.34 vs 0.38 h-1) not in chain (0.37 vs. 0.32 h-1 (5% of all) and multi 0.49 vs. 0.47 h-1 (10% of all)	None	Strong (but single houses only with natural vent)
Comments: The study with strong design but few limitations namely comparison of two extremes of the studied population (only cases vs only controls) and very small difference in ventilation (0.05 h-1) between homes of cases and controls where the significant effects were observed, being probably within the measuring error though systematic. The effect of higher ventilation was basically observed in single homes at ventilation rates below 0.5 h-1, even below 0.4 h-1 suggesting thus that the negative effects of ventilation rate on asthma and allergy symptoms are likely if ventilation is below 0.4 h-1.										
Kovesi T	2009	Home heat recovery ventilators (HRV) were studied for their	Use of HRV was associated with a progressive fall in the odds ratio for reported wheeze of	Canada	Intervention study	68 Inuit children	Heat recovery ventilators installed for the purpose (filters presumably new,	7,5 L/s/pers	CO_2 levels (915±163 vs. 1359±539 ppm) with 5-	Strong (but high smoking rate)

		ability to reduce the risk of respiratory illnesses in young Inuit children by improving ventilation.	12.3 per week (95%CI 1.9–21.6, p=0.022). Rates of reported rhinitis were significantly lower in the HRV group than the placebo group in month 1 (odds ratio 0.20, 95%CI 0.058–0.69, P = 0.011) and in month 4 (odds ratio 0.24, 95%CI 0.054–0.90, P = 0.035).				counter-cross heat exchangers)		6 people in a house. (ETS not quantified but highly prevalent >80%)	
Comments: This study show clearly that doubling ventilation rates (as indicated by the measured CO_2 levels) reduced symptoms, the effect being strongly confounded by the presence of ETS. Simple estimations suggest that after installing HRV ventilation rates in homes was about 0.4-0.5 h-1 or higher (assuming ca. 100-150 m^2 house) and thus half of this prior to the intervention. Also important to mention is that the Authors show that symptoms were alleviated, but it is not clear whether a threshold exists.										
Wright GR	2009	A domestic mechanical heat recovery ventilation system (MHRV), in addition to allergen avoidance measures, was tested if it can improve asthma control by attenuating recolonisation rates	Change in mean morning peak expiratory flow (PEF) as compared with baseline, did not differ between the MHRV group and the control group. However evening mean PEF significantly improved in the MHRV group.	UK	Interve ntion	120 subjects	Heat recovery ventilators installed for the purpose (filters presumably clean at least in the beginning) supplemented with vacuum cleaning	Not measured, heat recovery units supposed to increase ventilation rate by 0.5 h-1	Allergens, (about 20% smokers)	Weak

Clausen G	2012				Case-base study		Mechanical or no ventilation assessed by inspectors	CO_2 measurements using Vaisaala monitors used to estimate ventilation rate; no difference between cases and bases 0.46 h-1	PAH (<0.12 µg/g dust)	STRONG (no effect, estimated ventilation rate does not separate between outdoor air and make-up air from other rooms)
Comments: This study is a repetition of Bornehag et al. study described above using slightly modified protocol i.e. comparing bases and cases rather cases and controls i.e. looking at the actual population not only on extremes, as well as measuring ventilation rates using CO_2 as a marker. The results of Bornehag could not be confirmed as regards the effects of ventilation though the estimated dilution rates of CO_2 were as high as 0.46 h-1 but outdoor air supply rates measured by Bornehag with PFT method were most likely lower, but difficult to judge by how much.										
Ezratty V	2003				Cross-sectional		Forced ventilation present and absent; LARES cohort, self-administered quest.	N/A	N/A	WEAK (some association with ventilation type)
Xu Y	2010	The effect of an air cleaning /ventilating unit in the bedrooms of 30 asthmatic children was assessed over a period of 18 weeks using objective indicators of	The combination ventilation with air cleaning effectively reduce asthma symptoms and the indicators of airway inflammation	USA	Two-arm randomized cross-over	Thirty asthmatic children 5-16 years	HepaAIrx units installed and randomly operated (ventilation plus air cleaner)	1.4 to 2.3 m3/min; CO2 from about 518-1000 to 550-1344 ppm, estimated ventilation rate 15,6±5 h-1 and 0.32±0.14	PM10 (0.1-11 to 3-35 µg/m3), CO (0.3-1.2 to 0.6-1.5 ppm)	STRONG (but the effect of improved ventilation rate confounded by the operation of air cleaner – cannot be

		asthma control: pH and nitrate exhaled breath condensate and daily peak expiratory flow measurements						h-1		separated)
Comments: In the present study, intervention to ventilation conditions was made in homes, with a potentially strong design. The study cannot separate the effects caused by air cleaner and ventilation, though shows how effective exposure control can be to achieve reduction of asthma/allergy symptoms.										

Dorm rooms

Author	year	Study characteristics	Main outcome	country	Study type	population	ventilation type	ventilation rate	Exposure assessment	Strength of observations
Sun Y	2011	Dorm rooms were inspected. Measured variables were ventilation rate, air temperature, and relative humidity indoors. Allergic symptoms in the last 12 months were self-reported by occupants.	Ventilation rate is an effective modifier for moisture control and indoor pollutants. The prevalence of allergic symptoms in students in dorm rooms decreased with increasing ventilation rate. The combination of a localized mould/moisture indicator and a low air change rate significantly increased the risk of case status compared to the reference condition with no-dampness and high ventilation rate (above the median).	China	Case-control study	348 college students – in 223 dorm rooms	Inspectors; naturally ventilated	24 hours, CO_2 monitor; median 6.72 (0.29-29.55) h-1 (summer); 0.71 (0.05-6.93)h-1 (winter)	CO_2	Strong (but only winter above vs. below median; no direct comparisons of cases and controls)
Comments: The study confirms that increased ventilation rates modify exposures and subsequently that the symptoms of asthma/allergy can be reduced to some extent. At the same time, this study presents flaws/limitations similar to many other experimental studies, namely the use of questionnaires for self-estimated symptoms, a very long recall time, and the use of CO_2 as a proxy for ventilation. Although the data and analysis are strong enough to conclude that ventilation do improve health conditions, because of the limitation regarding ventilation measurements, it is difficult to set clear cut-off point and/or define ventilation rate at which the risk will be of no concern. Ventilation rates above 0.7 h-1 were shown to be effective in this respect in this study. It should though be remembered that density of people in dorms is much higher than in homes and thus these environments as regards exposures do not compare with homes.										

Experimental studies

Author	**year**	**Study characteristics**	**Main outcome**	**country**	**Study type**	**population**	**ventilation type**	**ventilation rate**	**Exposure assessment**	**Strength of observations**
Takahashi Y	2008	The amount of pollen clinging to fabrics (clothes, laundry, and futon bedding) outdoors was measured by quantification of Japanese cedar pollen antigen Cry j 1. The effect of air ventilation on the amount of pollen indoors was also investigated using several neighbouring unoccupied apartments with an identical layout while controlling the ventilation conditions.	A large amount of pollen entered dwellings through air ducts when the windows were closed and the ventilation fans working.	Japan	Experimental	Two adults. 6 unoccupied neighbouring apartments with an identical layout under controlled ventilation conditions.	Windows closed vs open		pollen antigens	weak

1.2 Respiratory symptoms

Office buildings

Author	Year	Study characteristics	Main outcome	country	Study type	population	ventilation type	ventilation rate	Exposure assessment	Strength of observations (weak vs. strong)
Graudenz GS	2002	The study analyzes the associations between air conditioning (years of use and age of ventilation ducts), allergen exposure and symptoms.	There was a higher prevalence of building-related worsening of respiratory symptoms ($p=0.004$; odds ratio [OR], 8.53) and symptoms of rhinoconjunctivitis ($p= 0.01$; OR, 8.49) in group with ventilation machinery and ducts with> 20 years of use. Upper respiratory symptoms were associated with aging of the ventilation system in artificially ventilated offices	Brazil	Cross-sectional	330 adults	AC+ ducts >20 years old; mixed ducts<2 years machinery >20 years old; mixed+ducts<2years old	N/A		Weak
Chao HJ	2003	A 1-year epidemiologic study was conducted to examine the associations between environmental factors and office	Upper respiratory symptoms were positively associated with CO_2 concentration.	USA	observational	98 subjects in 21 offices		CO_2	allergens levels	

		workers' health. Environmental sampling every 6 weeks were conducted and concurrently detailed questionnaires to collect information were administered on work-related symptoms, psychosocial factors, and perceptions of the office environments.								
Comments: This is a potentially important study, suggesting a dose-response relationship between ventilation and health, even if no information on CO_2 levels is given. After adjusting for sampling date, upper respiratory symptoms had significant relationships with CO2 concentrations, total airborne fungal concentrations, total fungal concentrations in chair dust, and the second PCA factor for chair fungi (chair factor 2), which included *Aspergillus* and *Zygomycetes* (Table 5). In the multivariate model for environmental measurements (Table 8, Model 1), CO_2 concentrations and total chair fungal concentrations remained significant predictors of upper respiratory symptoms. In the study, CO_2 concentrations in the investigated buildings (mean = 689 ppm) were within the range of typical office levels and below recommended standards (Nagda and Rector 2000).										
Mendell MJ	2003	Lower respiratory symptom-based outcomes and risk factors for potential microbiologic contamination in 80 office buildings.	Multivariate logistic regression models for selected outcomes identified adjusted odds ratios (95% confidence intervals) for ‘‘at least three of four work-related lower respiratory symptoms’’ that were, for debris in ventilation air intake, 2.0 (1.0–3.9), and for	USA	Cross-sectional	80 office buildings, 2345 subjects adults	Hygienist inspected ventilation systems	N/A	None	Strong (but not adjusted for ventilation rates)

			poor drainage in air-conditioning drip pans, 2.6 (1.3–5.2) and debris in ventilation systems, possibly by supporting microbiologic growth, may increase adverse respiratory effects, particularly among asthmatics.							
Comments: An important study showing that ventilation system can become pollution source though having significant drawbacks such as lack of ventilation measurements or not randomized selection of buildings. A limitation to the study refers to selection of buildings with problems which creates selection bias.										
Graudenz GS	2004	An air-conditioning intervention in a ventilation system with > 20 years of continuous use was investigated. The renovation of the HVAC system Hitachi; Tokyo, Japan) [self-type, 10 tons of refrigeration] consisted of exchanging the ventilation ducts, and cleaning and maintenance of the ventilation machinery. There was an internal	A protective effect on building-related worsening of respiratory symptoms was shown (odds ratio, 0.132; 95% confidence interval, 0.030 to 0.575), naso-ocular symptoms (odds ratio, 0.231; 95% confidence interval, 0.058 to 0.915), and persistent cough (odds ratio, 0.071; 95% confidence interval, 0.014 to 0.356). The air-conditioning intervention showed a protective effect on building-related worsening of	Brasil	Intervention	18 office workers	Ventilation with air conditioning, without humidification	Cleaning and maintenance of ventilation system, exchanging ducts	N/A	Weak

		rearrangement of the office desks and exchange of the carpets and coverings as well.	respiratory symptoms, naso-ocular symptoms, and persistent cough.							
Graudenz GS	2005	Self-administered questionnaires were given to 2000 individuals working in air-conditioned office buildings and to 500 control workers in naturally ventilated buildings.	A positive association of nasal symptoms (odds ratio, OR ¼ 1.59, 95% confidence interval, CI ¼ 1.11–2.28), naso-ocular symptoms (OR ¼ 1.58, 95% CI ¼ 1.05–2.38), persistent cough (OR ¼ 3.04, 95% CI ¼ 2.00–4.63) sinusitis symptoms (OR ¼ 1.85, 95% CI ¼ 1.27–2.71) and building-related worsening of the symptoms (OR ¼ 4.92, 95% CI ¼ 2.93–8.27) with working in air-conditioned buildings. Artificial air-conditioning is a matter of concern for respiratory symptoms in cities with hot and humid climate.	Brasil	Cross-sectional	1994 adults	Air conditioned vs. naturally ventilated	N/A	N/A	Weak

Schools

Author	Year	Study characteristics	Main outcome	country	Study type	population	ventilation type	ventilation measurem ent	pollutant measurem ent	Strength of observatio ns (weak vs. strong)
Simoni M	2010	Effects of IAQ on respiratory health of schoolchildren living in Norway, Sweden, Denmark, France and Italy were assessed.	Upper respiratory symptoms were more prevalent in children from poorly ventilated classrooms and were associated with higher CO_2 levels.	UE	Cross section al survey	n=654 children; sub-sample=193 (clinical tests)	N/A	CO_2 (QTrack): mean (in) 1461 (range 525-3475) PPM; using equilibrium airflow estimated, mean: 7.5 (range 1.5-35) L/sp at 18 LCO_2/hp	NO, HCHO, O_3, PM10 (TSI8520), mean (in): 112 (range 14-260) µg/m^3 (1-2h averages): guideline 20(1y) and 50 (24h) µ/m^3	Strong (CO_2 correlated but not PM10)
Comments: A potentially important study indicating that PM10 did not correlate with respiratory symptoms. However, the lack of exposure response relationship makes it difficult to use the results to define guideline requirements.										

Experimental studies

Author	Year	Study characteristics	Main outcome	country	Study type	population	ventilation type	ventilation measurement	pollutant measurement	Strength of observations (weak vs. strong)
Zuraimi MS	2007	Effects of ventilation strategies on IAQ and respiratory health of children within 104 child care centres (CCCs) in a hot and humid climate.	The risk of current rhinitis among children is significantly higher if they attend mechanically ventilated CCCs compared to NV CCCs. Air-conditioned CCCs were also associated with higher adjusted prevalence ratio of severe phlegm and cough symptoms and lower respiratory illness. Finally, children attending CCCs with hybrid ventilation (NV and AC intermittently operating) are at high risk for almost all the respiratory symptoms studied. Study shows how different ventilation and air conditioning strategies influence children health related symptoms	Singapore	Quasi-experimental	Children in 104 child care centers	Ventilation system type inspected: natural (NV), natural+AC (ACNV or HB), mechanical+AC (ACMV), AC	CO_2 (Telaire) used as a tracer; ACMV (1±1.6), AC (1.6±2), ACNV (8,9±18.9), NV (16.4±29.5) L/sp CO2: AC 1163±575, ACMV 930±175, ACNV 538±147, NV 466±72 ppm (OUT ca. 370 ppm)	CO (T15v Langan), PM2.5 TSI8520), O_3 (2B Technol), 1-day measurements during opening hrs IN AC, ACMV, ACNV, NV: CO: 1.2±1; 0.7±0.4;1.3 ±0.7;1±0.8 ppm PM2.5: 71.5±8.6; 48.1±18.1;66.8±28.3;71 ±32.5 µg/m^3 O_3: 18±12.4; 12.1±9.5; 32.3±14.8; 36.8±16.4 ppb OUT AC, ACMV, ACNV, NV:	Strong (but associate symptoms with conditions at day care centre what about homes, note PM2.5 similar independent of ventilation type

									CO: 0.9±0.7; 1.5±1.7;1.2 ±0.8; 0.8±0.6 ppm; PM2.5: 80.5±45.9; 91.2±44.6; 67.9±29.2; 70.9±33.6 µg/m3 =3: 56.3±30; 40.3±16.9; 49.1±16.9; 45.9±19.0 ppb	
Comments: An important experiment characterizing exposures, at least providing evidence that PM2.5 exposures was not affected by changing levels of ventilation.										

1.3 Airborne infectious diseases

Office buildings

Author	year	Study characteristics	Main outcome	country	Study type	population	ventilation type	ventilation measurement	pollutant measurement	Strength of observations (weak vs. strong)
Myatt A	2004	Detection of airborne rhinovirus and its relation to outdoor air supply was investigated in office buildings. Rhinovirus were investigated in the filters and from nasal lavage samples from building occupants with upper respiratory infections, by polymerase chain reaction technology.	Airborne picornavirus were detected in 32% of air sampling filters in office buildings using molecular methods. A significant positive relationship between the frequency of virus detection in air filters and degree of building ventilation with outdoor air as measured by average CO_2 concentrations greater than 100 ppm above the background.	USA	Observational study	3 office buildings, 212 adults	Mechanical ventilation without humidification	Indoor carbon dioxide (CO_2) concentrations were recorded every 10 minutes as a surrogate for outdoor air supply.	CO_2	

Experimental study

Author	year	Study characteristics	Main outcome	country	Study type	population	ventilation type	ventilation measurement	pollutant measurement	Strength of observations (weak vs. strong)

Pantelic J	2009	The protective role of personalized ventilation (PV) against plausible airborne transmissible disease was investigated using cough droplets released from a coughing machine simulating the human cough at different distances.	PV was able to both reduce the peak aerosol concentration levels and shorten the exposure time at all the examined injection distances. PV could reduce the infection risks of two diseases, influenza A and tuberculosis, by between 27 and 65 per cent. The protection offered by PV is less effective at a distance of 1.75 m than the other distances.	Singapore	Experimental study	Manikin	Personalized ventilation in the laboratory	5 L/s	Droplets generated by coughing machine	STRONG (though laboratory study with manikin and coughing machine)
Comments: This study shows that ventilation can play important positive and negative roles in spreading the infectious diseases, the importance of personal cloud of fresh air is also provided , which is also important in the context of other diseases. The study does not define the rate at which the risk can be considered as negligible, but indicates that ventilation effectiveness at which fresh air is supplied play a very important role.										

1.4 SBS/BRS

Homes

Main author	Year of publication	Study characteristics	Main outcome	country	Study type	population	ventilation type	ventilation measurement	pollutant measurement	Strength of observations (weak vs. strong)
Engvall K	2003	The relationships between symptoms compatible with the SICK building syndrome, type of heating and ventilation system, energy saving, and reconstruction in older dwellings was investigated.	Subjects in buildings with a mechanical ventilation system had less ocular and nasal symptoms (OR ¼ 0.29–0.85). Major reconstruction of the interior, direct heated electric radiators, wood heating, and multiple sealing of buildings were associated with an increase of some symptoms. Mechanical ventilation in dwellings is sometimes beneficial from a health point of view.	Sweden	Cross sectional survey	3241 inhabitants in multi-family buildings built before 1961	Information on building type and system gathered by postal questionnaire from building owners (and central building register), not inspected; no system; exhaust only and balanced	N/A	N/A	Rather weak Limitation: health effects are self-reported; Pro: high number of participants, good response rate, objective information about buildings!
Comments: This is a fairly weak study as all associations are based on data from postal questionnaire and there was lack of inspections. However the study pointed out clearly that sealing house as an energy retrofit increases the risk of SBS symptoms. Though the study shows association between mechanical ventilation and symptoms suggesting protective effect of the system, the results probably indicate that provision of outdoor air supply rate has protective effect due to control of exposures.										

Leech JA	2004	Occupants of energy efficient (mechanical ventilation by a heat recovery ventilator) new homes were compared to occupants of other new built homes with regard to self reported symptoms. A follow up took place 1 year later.	Because of the use of inadequate statistical methods the only result – improvement of health symptoms in occupants of energy efficient houses – is questionable.	Canada	Cohort study	128+149	52 homes with heat recovery ventilation / 53 homes without mechanical ventilation, additional questions about operation and maintenance of mechanical ventilation	N/A	N/A	very WEAK
Wong NH	2004	In 2 similar bedrooms, only different in ventilation, CO2, CO, RH, t, dust velocity bacteria, mould were measured. Occupants were asked for SBS-symptoms and IAQ-perception.	Air conditioning is characterized by increased CO2-levels and increased SBS-prevalence. An association is not statistically assured.	Singapore	Cross-sectional	n=105+58	Natural ventilation vs. air conditioning in residential buildings	CO_2, RH, temperature, CO, particulate level and air velocity, all measurements in the middle of bedrooms, calculation of PPD, n/a for ventilation rates	CO (Qtrack), PM (Dustrack) (8h monitoring) (40 to 80 µg/m^3 NV and 35-72 µg/m^3 AC)	WEAK, study design doesn't support the aim of the study; no statistics
Comments: This is a study indicating the presence of risks for of installing air conditioning in houses to control thermal comfort, especially if no special provisions for outdoor air supply rate are made simultaneously health (namely for SBS symptoms after sleeping in rooms with AC). Many studies in offices do show that buildings with air conditioning increase risks of SBS symptoms, where the mechanism is likely to be the pollution from AC system. This study shows that installing AC causes substantial reduction of the outdoor air supply rate and subsequently most likely elevated exposures which cause elevated risks of SBS symptoms. It should be noted that the levels of PM were measured in these studies and were not much different between the two studied conditions, being generally below 80 µg/m^3. The study do										

not show a protective effect of AC against symptoms related with particle exposure (due to reduced outdoor air supply rate and reduced transport of outdoor particles indoors).										
Kishi R	2009	The distribution of Sick House Syndrome (SHS) in Japan and the association between dampness/mould and symptoms is considered in a questionnaire study.	An elevated damp index, stuffiness and odour and an increasing age of the house are significant impacts on SHS in an adjusted logistic model. An insignificant protective effect of ventilation was shown (univariate).	Japan	Cross-sectional	n=2297	Airing (windows opening) 62,3% / natural ventilation 13,3% / mechanical ventilation 22,7% / not ventilated 1,7% additional questions about existence (in how many rooms) and operation of mechanical ventilation	N/A	N/A	WEAK Mech.vent. not associated with symptoms. Information on dampness only via questionnaire, no expert rating or measurements)

Office buildings

Main Author	**Year of publication**	**Study characteristics**	**Main outcome**	**country**	**Study type**	**population**	**ventilation type**	**ventilation measurement**	**pollutant measurement**	**Strength of observations (weak vs. strong)**
Skyberg K	2003	A cross-sectional study was performed in buildings without previously recognized indoor air problems.	A high ventilation flow or central ventilation unit filter EU7 vs. EU8 seemed to be associated with an increased risk of general symptoms. Risk for higher	Norway	Cross sectional survey	n=3562 occupants in 32 buildings of 8 companies	Non problem buildings; balanced; VAV and induction balanced data from building engineer (no inspection?)	< and ≥5 m3/h/m2 assessed (not measured?) by building engineer	N/A	WEAK

		Engineers filled in a technical questionnaire on building characteristics, floor surface materials, ventilation, cleaning procedures, heating and cooling.	general symptoms associated with ventilation flow >5 m3 air/h/m2 floor) was found (1.3, $p>0.05$, CI 1-1.6). No association with skin and mucosal symptoms was observed.							
Comments: This study is incomplete as regards many important details and presents a weak design; it does show a protective effect of reduced ventilation on SBS symptoms. The likely explanation is that increased ventilation may increase transport of outdoor pollutants and subsequently increased exposure to these pollutants. This hypothesis cannot be verified because the authors did not characterize exposures in the buildings										
Hummelgaard J	2007	Occupant responses and indoor environment characteristics were recorded and compared in five mechanically and four naturally ventilated open-plan office buildings.	The temperature and the CO_2 concentration varied more and were in some cases higher in the naturally ventilated buildings, but occupant responses in terms of symptoms and adverse perceptions differed only modestly between the two building types. Although rarely supported by statistical significance, the results indicated a somewhat higher	Denmark	Cross sectional survey	Office workers: 92 in non-ventilated and 160 in mechanically ventilated office buildings	Mechanically and naturally ventilated inspected	CO_2, Vaisala; NV 640 (425-1000) ppm and MV 480 (405-555) ppm	Temperature	WEAK

			degree of satisfaction with the indoor environment and a lower prevalence/intensity of symptoms among the occupants in the naturally ventilated buildings							
Comments: This study shows basically no significant differences between perceptions of comfort and SBS symptoms among of occupants of naturally ventilated buildings and mechanically ventilated buildings. At the same time the measurements of ventilation indicated no differences in outdoor air supply rates with slight tendency for higher ventilation in naturally ventilated buildings where there also were tendencies of less symptoms. The study is in line with other studies and implies that the differences observed between naturally and mechanically ventilated buildings can be caused by the, often not measured, differences in outdoor air supply rate. Also other causes are likely, namely the intrinsic characteristics of studied buildings or pollution from the system. The study indirectly shows association between health and ventilation though does not give any indication at which rates the risks are negligible.										
Buchanan ISH	2008	Data from the US EPA Building Assessment Survey and Evaluation (BASE) study were investigated to determine if ozone and specific filter media have interactive effects on building-related symptoms (BRS). A subset of 34 buildings was analysed to determine the separate and joint associations of filter medium	A joint risk of BRS from Polyester/synthetic filters and outdoor ozone above 67.6 µg/m^3 was much greater than the risk from each one alone suggesting that ozone and specific filter media have interactive effects on building-related symptoms (BRS).	USA	cross sectional survey	34 office buildings	98 with AC, 2 w/o AC, 64 without operable windows; maintenance and condition of ventilation system assessed by the inspector; filter type: fiberglass and polyester or synthetic	ΔCO_2 indoor-outdoor, mean 254 ppm, 40-608 ppm	O_3 (estimated from local measuring station); cut off point 67.6 µg/m3 (32 ppb)	STRONG

		and outdoor ozone concentration (above/below the median, 67.6 microg/m^3) with BRS.								
Comments: This study does not contribute to the knowledge regarding association between ventilation and health. It does show that air used for ventilating the rooms can contain pollutants, namely ozone, which under certain conditions can react with surfaces or other pollutants and creating contaminants otherwise not present indoors which affect exposures. In particular such reaction can occur on surfaces of dirty filters which are used to remove particles.										
Apte MG	2008	The U.S. EPA Building Assessment Survey and Evaluation (BASE) study data were analyzed for associations between ambient ozone concentrations and building-related symptom (BRS) prevalence.	A positive relationships ($p< 0.05$) between ambient ozone concentrations and upper respiratory (UR), dry eyes, neurological and headache BRS (odds ratios ranged from 1.03 to 1.04 per 10 µg/m^3 increase in ambient ozone concentrations). A linear dose–response in UR symptoms was observed with increasing ambient ozone ($P = 0.03$). A clear relationship between ambient ozone concentrations and building-related health symptoms was identified. An association between	USA	Cross sectional survey	Office buildings, around 4300 subjects	98 with AC, 2 w/o AC, 64 without operable windows; maintenance and condition of ventilation system assessed by the inspector; filter type: fiberglass and polyester or synthetic	ΔCO_2 indoor-outdoor, mean 254 ppm, 40-608 ppm	O_3 (estimated from local measuring station); 4.9 to 166 ug/m^3 (2-78.5 ppb); formaldehyde, benzene, o-xylene measured not reported	STRONG

			maintenance (debris in ventilation, poor drainage) and respiratory effects was found.							
Comments: The study does not provide new evidence in the context of the association between ventilation and health. It does however point out that ventilation air is a carrier of outdoor pollution which can elevate the risks of acute SBS symptoms.										
Fisk WJ	2009	Data from published studies were combined and analyzed to develop best-fit equations and curves quantifying the change in SBS symptom prevalence in office workers with ventilation rate.	As the ventilation rate drops from 10 to 5 L/s-person, relative SBS symptom prevalence increases approximately 23% (12% to 32%), and as ventilation rate increases from 10 to 25 L/s-person, relative prevalence decreases approximately 29% (15% to 42%).	USA	Meta-analysis	office workers	Office buildings, ventilation systems n/a	Modelling of previous data ca. 5 to 35 L/s p, miscellaneous ventilation measurements flow hoods or similar methods to measure supply airflow rates to rooms or zones of buildings with HVAC systems that supply 100% outdoor air or; measurement of carbon dioxide concentrations in occupied spaces and use of mass	N/A	STRONG, uncertainty about quality of primary studies

								balance equations to calculate ventilation rates or; use of tracer gas decay methods or other tracer methods or; Use of anemometers to measure airflow rates through the outdoor-air intake sections of HVAC systems with 100% outdoor air supply		
Comments: This study shows that there is an association between ventilation and SBS symptoms. Metanalysis was performed from all studies which quantified the effects of ventilation on risk of SBS symptoms without their qualitative assessment. The limitation of this approach is the presence of meagre data and results in large confidence interval and inaccuracies of the created model.										
Erdmann CA	2004	Multivariate logistic regression analyses of 100 office-building BASE Study dataset, to quantify the relationship between indoor CO_2 concentrations and mucous membrane and lower	Provision of sufficient per-person outdoor ventilation air could decrease prevalence of selected building related symptoms. Relationship between indoor minus outdoor CO_2 concentrations and	USA	Cross-sectional study	Office workers, 100 office buildings	98 with AC, 2 w/o AC, 64 without operable windows; maintenance and condition of ventilation system assessed by the inspector	ΔCO_2 indoor-outdoor, mean 254 ppm, 40-608 ppm	VOCs	STRONG

		respiratory system building related symptoms, adjusting for age, sex, smoking status, presence of carpet in workspace, thermal exposure, relative humidity, and a marker for entrained automobile exhaust.	mucous membrane/lower respiratory symptoms with 100 ppm. increases in dCO_2 ranged from 1.1 to 1.2., suggests that air contaminants are implicated in the aetiology of BRS.							
Comments: This is one of the few existing studies trying to quantify the effect of ventilation on SBS symptoms. It is based on a large randomized set of buildings in the US, though using CO_2 as a marker of ventilation. It clearly shows that SBS symptoms can be reduced when CO_2 levels are lower which means that outdoor air supply rates are presumably higher. A limitation of the study include quite small differences between outdoor and indoor CO_2 levels, suggesting that ventilation rates were quite high in the studied office buildings, on average can be estimated to about 15 L/s per person. The other limitation is that these data stem from the study performed in the 1990s when in the U.S. smoking was still prevalent and no specific measures to control pollution emitted from building materials was implemented,. Thus although the study clearly shows the association between ventilation and risk of SBS symptoms, the magnitude of ventilation (or the exposures in the buildings) may not be representative for today's building stock.										
Wargocki	2004	The performance and subjective responses of call centre operators with new and used supply filters at two outdoor air supply rates were investigated.	Increasing outdoor air supply rate from about 2.5 L/s p to 25 L/s p improved the performance /reduced talk time) of the call centre operators (number directory) but only when new filter was installed; with used filter the performance was actually reduced; change of the filter	Denmark	Interventi on study with repetition each condition lasting 1 week/ performa nce of call center operators (talk-time)	Adults, 26 operators	Mechanical ventilation with recirculation, filter new and old	Tracer gas and CO_2: 230 to 830 ppm; 2.5 L/sp to 25 L/sp	PM and UFP (but only counts, not absolute levels), O_3 (out) ca. 30 ppb	STRONG (interactions with filter condition, only better when new and increased ventilation, reverse when used)

			also improved the performance; some effects on SBS symptoms were observed							
Comments: The study showed that some symptoms were affected by increasing ventilation rates but the effects were quite meager. The thresholds at which symptoms are negligible are not set. Also it shows that increasing ventilation rates can improve performance, but only if there are no sources of pollution brought by the ventilation system (in this case filters were used). The study is quite important as it is one of the few showing impact of recirculation of air in non-smoking office. The conclusion suggested is to avoid recirculation unless controlling/removing pollution in the recirculated air. Removal of pollution from recirculated air should not be causing its accumulation on e.g. surface of the filters.										

School buildings

Main author	Year of publication	Study characteristics	Main outcome	country	Study type	population	ventilation type	ventilation measurement	pollutant measurement	Strength of observations (weak vs. strong)
Mysen M	2005	Comfort evaluation in a school with a simplified ventilation system	On cold days, thermal comfort in the classroom deteriorated due to cold downdraught from the supply outlet. In addition, moist and fertile conditions for microbiological growth were observed in the air supply ductwork. On the other hand the same pupils are more satisfied with the school and have less SICK building syndrome (SBS)	Norway	Field experiment	50 pupils in 2 classrooms	Installed DCV with facade supply	CO_2 measured not reported kept <800 ppm	Microbiological assays of airborne particles, Air temperature	WEAK

			symptoms during winter than summer. An improved control strategy with a temperature-compensated CO_2 set-point for controlling the airflow is suggested. The study shows that the pupils are generally satisfied with unfiltered air quality; the sedimentation of organic material in the air supply duct, in combination with the presence of moisture, provides fertile conditions for microbiological growth that is potentially harmful.							
Norbäck D	2008	The effects of ventilation in computer classrooms were studied with university students in a blinded study.	Ocular (OR = 1.52 per 1℃), nasal (OR = 1.62 per 1℃) and throat symptoms (OR = 1.53 per 1℃), headache (OR = 1.51 per 1℃) and tiredness (OR = 1.54 per 1℃) were significantly associated with temperature;	Sweden	Field experiment	355 students	Mechanical ventilation	7 and 10-13 L/s per person; tracer gas N_2O; CO_2 (Qtrack) (830-1200 ppn)	Ultrafine particles (P-Track), PM10 (Dusttrack) (1 hour) (in 15 and 20 µg/m^3 at high and low	STRONG (but only headache associated, mainly with temperature in narrow range 21.8-24.3C)

			headache was associated only with CO_2 (OR = 1.19 per 100 ppm CO_2). Longitudinal analysis demonstrated that increased room temperature was related to tiredness (P < 0.05). There were fewer medical symptoms among university students in computer classroom at lower air temperatures and lower CO_2 levels, with temperature as dominant factor. After mutual adjustment (temperature, RH, CO_2, air exchange), measured temperature was associated with a perception of higher temperature (P < 0.001), lower air movement (P < 0.001), and poorer air quality (P < 0.001). Higher air exchange was associated with a perception of lower temperature (P < 0.001), higher air						VR) HCHO (2-4 µg/m^3), NO_2 (in 11µg/m^3, out 10 µg/m^3) and O_3 (in 22 µg/m^3 (10 ppb) and out 68 µg/m^3 (32 ppb) (weekly)	

			movement (P = 0.001), and better air quality ($P < 0.001$). In the longitudinal analysis (n = 83), increased air exchange caused a perception of lower temperature (P = 0.002), higher air movement ($P <$ 0.001), better air quality (P = 0.001), and less odour (P = 0.02). Computer classrooms have CO_2 levels above 1000 ppm and temperatures above 22℃. Increased ventilation from 7 l/s per person to 10–13 l/s per person can improve thermal comfort and air quality.							

Comments: The study suggests the association between health and ventilation but in fact a quite modest change in ventilation from 7 to 10 L/s per person does not have significant effects on symptoms. It is worth to note that this study characterized exposures as regards some pollutants and they were not very much affected by ventilation which may to some extents explain the lack of the effect of increased ventilation. Another explanation could be that the level of SBS symptoms could already be low and thus increasing ventilation rates did not have considerable effects.

Smedje G	2011	Displacement ventilation was compared to mixing ventilation in a cross-over experimental design with regard to pupils perception of IAQ and self-reported and examined health symptoms	Minor differences between the both ventilation types; only the prevalence of self-reported eye symptoms (significant) and of self-reported respiratory symptoms (tendency) is increased in displacement mode. IAQ is perceived as slightly better in mixing mode.	Sweden	Field experime nt	111 pupils in 4 class rooms	1 school with 4 classrooms, experimental comparison of mixing and displacement ventilation	Supply air temperature 19.3 ℃ +- 0.2 K, CO_2, RH, temperature, air flow 10.6-12.3 l/(s*pers.)	CO_2, t, RH, cat allergens	STRONG (no differences, more eye symptoms at DV)
Comments. This study is investigating the solution for providing ventilation in classrooms and shows that if the levels of CO_2 are not affected by different solutions there are no effects on symptoms. Both solutions used mechanical ventilation with presumably filters installed so although not measured it is likely that concentration of outdoor particles was low and quite similar under both conditions.										
Zhang X	2011	Indoor and outdoor measurements of t, RH, CO_2 and NO_2 were carried out in classrooms in two waves 2004 and 2006. Pupils were asked for SBS- and atopic symptoms.	Although in 2006 more symptoms were reported, results of measurements do not explain the increase in multivariate model.	China	Field experime nt	1143 pupils from 10 schools	Only windows opening	temperature, RH, CO_2 (average level 2651 ppm, range 965 – 3996 ppm) indoors and outdoors, calculation of supply air flow (min –mean – max: 1.0 - 2.1 - 9.3 ach) from CO_2-difference between indoor and outdoor	SO_2 (264.8 µg/m^3 IN, 2-3 times higher OUT), NO_2 (39.4 µg/m^3 IN1-1.5 times higher OUT), 7 days averagin g time	STRONG (CO_2 negatively associated with SBS NO_2 and SO_2 also associated but no incidence)

Experimental study

Main author	Year of publication	Study characteristics	Main outcome	country	Study type	population	ventilation type	ventilation measurement	pollutant measurement	Strength of observations (weak vs. strong)
Kaczmarczyk J	2004	The response (perceived air quality, thermal comfort, intensity of Sick Building Syndrome symptoms and performance) of 60 human subjects to a personalized ventilation system (PVS), providing control of positioning of the air terminal device and the airflow rate, was compared with the response to mixing ventilation (MV) during 3 h 45 min exposures.	The PVS providing outdoor air improved perceived air quality and decreased SBS symptoms compared to MV alone and when the room air was re-circulated through the PVS. The percentage dissatisfied with air quality, 3 min after initial occupancy, decreased from 22% with MV to 7% with PVS; and from 49% to 20%, at room temperatures 23℃ and 26℃, respectively. Over time, these differences in percentage dissatisfied decreased markedly.	Denmark	Experimental study	60 subjects adults	Mechanical (mixing) and personalized ventilation	15L/s x p with 20 and 23℃	N/A (laboratory)	weak statistic unknown (not adjusted)

			Headache and decreased ability to think clearly were reported as least intense when the PVS supplied outdoor air at 20 ℃, while the most intense symptoms occurred with MV. PVS increased self-estimated performance.							
Comments: Though indirectly and in the experimental setting, this study shows the importance of clean ventilation air for symptoms intensity. When the unpolluted air is directly provided to the breathing zone the intensity of SBS symptoms is reduced The study shows that symptoms are related to exposure and ventilation is only the means to modify the exposure.										

1.5 Perceived air quality

Homes

Main author	Year of publication	Study characteristics	Main outcome	country	Study type/end point	population	ventilation type	ventilation measurement	pollutant measurement	Strength of observations (weak vs. strong)
Engvall K	2005	The aim was to study if a 25–30% reduction of outdoor ventilation flow during heating season influenced sick building syndrome and the perception of the indoor environment in a 1-year cross-over intervention study in a multi-family building.	Reducing the ventilation flow in dwellings to a level below the current Swedish ventilation standard (0.5 ACH) may cause a perception of impaired air quality (stuffy odour and air quality perceived most likely by occupant (not by visitor as prescribed by the present standard) but did not have significant effects on symptoms; strong cross-over design though small population; the measurements of CO_2 and ventilation rate showed much smaller reduction in ventilation than	Sweden	Cross-over intervention study; self-administered questionnaire sent by post; no details when the actual assessment was taking place; no further details; 3 months recall period for symptoms	44 subjects living in 45 apartments adults	Mechanical	0.5-0.8 vs 0.4-0.5 h-1 CO_2 920 to 980 ppm (night (720-760 ppm daily average), estimated to 8.6 to 7.8 L/sp	N/A	STRONG (but changes in VR very small to observe measureable effects)

			indicated by the air exchange rate from 8.6 to 7.8 L/s p.; the results suggest that reducing to 0.4/0.5 h-1 will not elevate prevalence of symptoms but may aggravate air quality perceived by residents							
Comments. This study shows interaction of the ventilation with perceived air quality. Though no effects on symptoms could be shown when ventilation rates in dwellings were reduced to about 0.4-0.5 h-1, the comfort of occupants in the building was affected as demonstrated by lower perceived air quality compared with higher ventilation rate, the effect being only relative.										

Office buildings

Main author	**Year of publication**	**Study characteristics**	**Main outcome**	**country**	**Study type/end point**	**population**	**ventilation type**	**ventilation measurement**	**pollutant measurement**	**Strength of observations (weak vs. strong)**
Bitter F	2002	The odour emission of a new HVAC-system in an office building was investigated.	The tests have been carried out with and without mechanical ventilation. Since the other pollution sources in the rooms emitted from building materials and furnishings did not change significantly during the measurement period, the	Germany	Intervention study; perceived air quality in decipol compared with the reference created by 2-propanone with	Trained human panel	Mechanical	ACH rates rooms were reduced from 2,5 to 1,6 for 5 days.	N/A (laboratory)	WEAK

			differences in the assessments are considered to be mainly caused by the HVAC system, though increasing ventilation rates did not show to systematically improve the perceived air quality; so-called trained panel of visitors was used to assess the air quality using acetone as a reference exposure		known decipol levels; the assessments made by subjects (5 to 12) trained to make these assessments					

Schools

Author	year	Study characteristics	Main outcome	country	Study type/end point	population	ventilation type	ventilation measurement	pollutant measurement	Strength of observations (weak vs. strong)
Norbäck D	2011	Health effects were studied in three elementary school classes when changing from mixing ceiling ventilation to two types of displacement ventilation, front ventilation system	When changing from mixing ventilation to FVS, the pupils perceived better air quality and less dyspnoea as compared to controls, and BUT was improved. At desk level, mean CO_2 was reduced	Sweden	Intervention study; questionnaire indicating whether the air quality was extremely poor or	61 pupils in three elementary school classes	displacement ventilation	mean CO_2 was reduced from 867 to 655 ppm.	CO_2	

		(FVS) and floor master system (FMS).	from 867 to 655 ppm. Displacement ventilation may have certain positive health effects among pupils, as compared to conventional mixing ceiling systems. The study shows that having sufficient flow of air some improvements of the air quality as perceived by children (as occupants and visitors) can be expected; though, as indicated by lower co2 level in the displacement ventilation condition the effect of using the different system type (and thus presumably much higher ventilation efficiency) are confounded with increased airflowrate at the desk level (ca. 40-50% higher as indicated by CO_2 levels)		extremely good (7 point scale) assessed by children as in the class (occupants, last hour perception) and upon entering the class (immediate perception)						

Comments. The study showed that using different principle of ventilation the perceived air quality can be improved as well as some health effects such as dyspnoea. The effects observed though weak are probably associated with the increased supply of ventilation rather than the system per se as the positive effects were associated with slightly though measurably lower ventilation rates. Thus the study contributes to the evidence on the association between ventilation rates however it is difficult to say from the results which levels would be needed to reduce the symptoms so that the effects are negligible.

Experimental studies

Main author	**Year of publication**	**Study characteristics**	**Main outcome**	**country**	**Study type/end point**	**population**	**ventilation type**	**ventilation measurement**	**pollutant measurement**	**Strength of observations (weak vs. strong)**
Wargocki P	2007	The relationship between ventilation rate and the perceived indoor air quality was studied. A sensory panel assessed the air quality in test rooms ventilated with realistic outdoor air supply rates, where combinations of high- and low-polluting wall, floor and ceiling materials were set up.	Substituting materials ranked as high-polluting with materials ranked as lower-polluting improved the air quality in the test rooms perceived by visitors to rooms (immediate perception). This improvement was greater than what was achieved by a realistic increase of the ventilation rate in the test rooms. Thus reducing pollution emitted from building materials that affects the perceived air quality	Denmark	Experimental; acceptability of air quality assesses on a continuous scale by a panel of untrained subjects (taught only to use acceptability scale); the size of a panel was 38 subjects;	sensory panel	mechanical	1.3±0.1, 2.8±0.1, 6.4±0.2h-1		

			has a considerable potential of limiting the energy for ventilation without compromising indoor air quality. The study clearly shows that increasing ventilation rate may not be that effective in handling pollution		the assessments taken immediately upon entering the rooms (as visitors)					
Comments: This study shows in the experimental setting that controlling exposures (in this case created by emissions from building materials) by ventilation will improve air quality. The results can also be interpreted that though not confirmed by chemical measurements increased ventilation rates reduce concentration of pollutants in air which is a useful mitigating means also suggesting that there is a relationship between pollutants and ventilation.										

1.6 Performance/absenteeism

Schools

Author	year	Study characteristics	Main outcome	country	Study type/end point	population	ventilation type	ventilation measurement	pollutant measurement	Strength of observations (weak vs. strong)
Shendell DG	2004	Association of student absenteeism with measures of indoor minus outdoor carbon dioxide concentration (dCO_2).	A 1000 ppm increase in dCO2 concentrations was associated with a 0.5 to 0.9% decrease in annual average daily attendance corresponding to 10-20% increase in students' absence	USA	Cross sectional survey; average attendance on school (or class level, unclear in the paper) for the entire school year was calculated on the year of the measurements, for the year prior to measurements and after the	22 schools located in six school districts in the states of Washington and Idaho; 409 traditional and 25 portable classrooms	22 schools, 436 classrooms served by own HVAC system, wall heater or no system	CO_2 (Qtrack) 2 5-minute measurements; CO_2 average from 580-1510 ppm (max. up to 4230 ppm)		WEAK (10-20% increase for 1,000 ppm increase) (although adjusted for ethnicity, gender, free-lunch programme there are many other reasons for absence rate; poor ventilation measurements)

					measurements; adjusted for socioeconomic factors, ethnicity, gender					
Comments: Despite the relevance, the data presented in this paper are only indicative of the potential association between absenteeism and CO2 levels in schools.										
Bakò-Birò Z	2007	Associations between classroom ventilation and pupils' performance were investigated in a primary school. A direct air supply system through the windows was used to alter the ventilation rates in the classrooms. The system was set either to provide outdoor air or to re-circulate the classroom air while all other physical parameters were left unchanged.	Intervention in term of fresh air supply increase from 0.3-0.5 to as high as 13-16 L/s per person increased pupils' work rate by ~7% in addition ($p<0.036$) and subtraction ($p<0.052$), and had positive effect on range of cognitive tests	UK	Cross-over Intervention study of 1 week duration/ pen and pencil tests of maths and reading and the battery of psychological tests presented on a PC	Around 25 pupils per class	Especially installed AHU recirculating or providing fresh air	CO_2 (Vaisaala) and tracer gas measurements; 0.6 to 4 h-1; 0.6-4 L/sp to 5.1-9.6 L/sp, CO_2 average 644 to 2833 ppm	N/A	STRONG

Comments: The study shows presumably no effects of increases ventilation rate in classrooms on intensity of the acute SBS symptoms though significant effects on performance of tests typical of schoolwork and cognitive psychological tasks were observed. No aetiology is discussed though it may be expected that increased ventilation rate modified exposures and thus affected performance. Performance here is thus indicative of the potential underlying physiological responses (chronic because acute effects were not seen). The study shows that increased ventilation affected CO_2 levels and human bioeffluents, most likely the dominant pollutant in school classrooms with high occupancy level per volume and m2 compared with the potential other sources of pollution per m^2 and volume. Whether the observed effects on performance have aetiology in CO_2 is unknown.										
Wargocki P	2007	The effect of outdoor air supply rate on school performance of students in elementary classrooms was investigated	Increased outdoor air supply rate significantly improved the performance of many tasks, mainly in terms of how quickly each pupil performed the task. The pupils indicated that the air was significantly fresher in classrooms when the outdoor air supply rate was increased; no effect on intensity of SBS symptoms reported by students; in subsequent paper dose-response relationship indicated 8% to 14% increase in performance of schoolwork for doubling the ventilation rate	Denmark	Cross-over intervention with 1 week duration per condition/ performance of schoolwork measured by pencil and paper tests of maths and language (reading, comprehension)	1 school, 4 classrooms, 2 in winter and 2 in summer, about 23 students per class	Mechanical ventilation with filter new and old	CO_2 1300 to 900 ppm, ventilation rate 3-8.5 L/sp	PM different size and UFP (counts only not mass)	STRONG

Comments: The study showed no effects on intensity of acute SBS symptoms though clear effects on performance of typical school tasks and perceived air quality (assessed by children and recruited assessors)were observed when ventilation rates were increased above the minimum of 3.5 L/s per person.										
Haverinen-Shaughnessy U	2010	One hundred elementary schools were studied. Ventilation rates were estimated using CO_2 concentrations measured during occupied school days. In addition, standardized test scores and background data related to students in the classrooms studied were obtained from the districts.	A dose-response relationship was found between CO_2 (transformed into ventilation rate) and performance on standardized tests up to the ventilation rate of about 7L/sec per person indicating increased performance with increased ventilation rate; 1L/s person increase correspond to ca. 2.9% increase in math and 2.7% in reading	USA	Cross-sectional/ performance measured using standardized math and reading tests by counting those who passed/not passed the test rather than grade adjusted for mobility rate, percent limited English, free-lunch programme (socio-	100 elementary school children	Mechanical ventilation, windows closed	1-day measurements using Vaisaala CO_2 monitor ±3% reading or ±50 ppm; 661 to 6,000 ppm estimated ventilation rate 0.7 to 7.1L/sp	N/A	STRONG

					economic status), and gifted enrolment					
Comments: This study does not provide evidence on the effects of ventilation on health endpoints. By monitoring CO_2 concentrations it shows that more students pass standard tests examining progress in math and reading. No mechanisms of causation are proposed though assuming that poor educational performance is an indicator of physiological effects/symptoms of ill-health after controlling for potential confounders this study shows that ventilation rates below 7 L/s per student may have negative consequences above which the effects seem to be negligible.										
Simons E	2010	Upstate New York school building conditions and the associations between school absenteeism and building condition problems were investigated	Student absenteeism was associated with visible mould, humidity, poor ventilation (OR=3.10 (95%CI:1.79-5.37), vermin, 6 or more individual building condition problems, and building system or structural problems related to these conditions. Schools in lower socioeconomic districts and schools attended by younger students showed the strongest associations between poor building conditions and absenteeism. An associations between student	USA	Cross sectional survey/ absenteeism on a school level adjusted for free-lunch, urbanity, attendance by high school students, students-to-teacher ratio, school density and pupil expenditure	New York public schools serving students from kindergarten to grade 12 Children; after necessary adjustments: 2751 schools with over 1.6 mil pupils	Hired inspectors and engineers assessed condition of HVAC system (blocked, dirty, inadequate ventilation rate (how measured?)		N/A	WEAK (no measurements, just observations, though large sample n=2,751 attended by 1.6 mil students)

			absenteeism and adverse school building conditions, also in term of poor ventilation, was found in all analyses based on the data from the school districts and no verification of conditions in schools were made.							

Office buildings

Main author	Year of publication	Study characteristics	Main outcome	country	Study type/end point	population	ventilation type	ventilation measurement	pollutant measurement	Strength of observations (weak vs. strong)
Federspiel CC	2004	The relationship between ventilation rates and individual work performance in a call centre was studied.	Performance at low and high ventilation rates was statistically the same, performance at intermediate ventilation rates was worse by about 2%, and that the increased talk time (decreased work speed) was statistically significant. The productivity benefits of ventilation rates that exceed common standards such as ASHRAE Standard may be small (0–2%). The results show that performance (talk-time) improved only at the highest ventilation rate (0-75 ppm bin above background) while it is actually reduced	USA	Intervention study of different duration per condition/ call-centre performance in form of talk-time and wrap-up time	Call centre operators; max 119 registered nurses and 179 tele-service representatives	4 VAV units with economizer though disabled; filters presumably new	Pitot tubes (av 2.07 L/sm^2, 0.26 to 10 L/sm2) and CO_2 (253 ppm av above out (13-611ppm)	N/A	STRONG (talk time improved at the very high ventilation rate but not monotonic)

			when CO_2 was reduced from >300 ppm to 225-300ppm bin, 150-225ppm bin and 75-150 ppm bin. The relationship between CO_2 and talk-time is not strong and not monotonic. No effect of ventilation rate on wrap-up time was seen.							
Comments: This study does not show any result on the association between ventilation and health. It does show that performance can be somewhat affected by ventilation but the results on one hand show that there is no or even negative effect of elevated ventilation rate on performance and only at extremely high ventilation rates the effect can be expected. The results are thus not monotonic as could be expected if changes in exposure were to suspected. It may suggest that the effects are observed by chance or that elevated ventilation rates actually promoted emissions which could not be handled by ventilation until the very high levels (e.g. by promoting reactions with ozone). There are no data to support this observation but the results are quite important as they show that elevated ventilation rates may not always be a solution to the problem.										

1.7 Exposure control

Author	year	Study characteristics	Main outcome	country	Study type	population	ventilation type	ventilation measurement	pollutant measurement	Strength of observations (weak vs. strong)
Sherman MH	2004	Modelling approach applied to derive ventilation rates to guarantee IA formaldehyde safe levels	To maintain 99% of new houses below a widely accepted action level or ceiling concentration of 100 ppb, the minimum long-term ventilation rate should be 0.68 $m^3/m^2/h$. For a house with a typical 8-ft ceiling this is equivalent to a ventilation rate of 0.28/h.	USA	Modelling				formaldehyde	STRONG
Hänninen	2005	EXPOLIS measurements of indoor and outdoor concentrations were entered as inputs into an evaluated simulation model to compare exposures in the current scenario with an alternative scenario, where	In the alternative scenario hypothesised, exposures to ambient PM2.5 were reduced by 27%. Indoor concentrations of ambient particles and the associated health risks can be reduced by using mechanical	Finland	Modelling				PM2.5	STRONG

		the distribution of ambient PM2.5 infiltration factors in all residential and occupational buildings are assumed to be similar to the subset of existing occupational buildings using supply air filters.	ventilation systems with supply air filtering in buildings.							
Zeiler W	2007		IAQ in the evaluated schools did not meet the requirements and more ventilation was essential for better IAQ.	Netherla nds	Observati onal	5 schools	exhaust-only ventilation systems		CO_2	

ANNEX 2. OVERVIEW OF CURRENT INDOOR AIR QUALITY REGULATIONS REGARDING HEALTH: WHO GUIDELINES AND INDEX PROJECT

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INTRODUCTION

The sources of information to be included in this approach refer to WHO air quality guidelines, both outdoor and indoor, and INDEX report that defined health based guidelines

WHO Air Quality guidelines

The primary aim of the WHO guidelines is to provide a uniform basis for the protection of public health from adverse effects of exposure to air pollution, and to eliminate or reduce to a minimum exposure to those pollutants that are known or are likely to be hazardous. The guidelines are based on the scientific knowledge available at the time of their development.

In 1987 the WHO Regional Office for Europe published the first edition of "Air quality guidelines for Europe", containing health risk assessments of 28 chemical air contaminants. In 2000, WHO published a second edition of the guidelines and a "global update" was published in 2006. The second edition focused on the pollutants considered in the first edition. The global update focused on a small group of pollutants (particulate matter, ozone, nitrogen dioxide and sulfur dioxide) but also included chapters that addressed some health-related general subjects of importance to the air pollution field, including a chapter on indoor air quality.

As concerning indoor air, the first edition of the Air quality guidelines for Europe (1987) included a chapter on radon and an annex on tobacco smoke and indoor air pollutants with significant adverse public health impacts. The second edition published in 2000 provided a section on indoor air pollutants and added manmade vitreous fibres to radon and tobacco smoke. The 2005 global update of the air quality guidelines drew attention to the large impact on health of indoor air pollution in developing countries. This is in line with the recommendations of an earlier WHO working group formulating a set of statements on “The right to healthy indoor air” and in particular with Principle 6, which states that “Under the principle of accountability, all relevant organizations should establish explicit criteria for evaluating and assessing building air quality and its impact on the health of the population and on the environment.” (WHO, 2000b) .

Acknowledging that indoor air has a special role as a health determinant and that the management of indoor air quality requires approaches different from those used for outdoor air, the WHO working group in October 2006 confirmed the applicability of the existing WHO guidelines for air quality to indoor air and identified a number of chemical substances for which specific indoor air guidelines should be recommended. The working group also recommended developing guidelines for two additional categories of risk factor of particular importance for health in indoor environments: biological agents and indoor combustion.

Following these recommendations, the “WHO guidelines on dampness and mould” and the “WHO Guidelines for Indoor Air Quality: Selected pollutants” were published in 2009 and 2010. A third volume concerning “Household fuels combustion” is in preparation.

The “WHO guidelines on dampness and mould” (WHO, 2009) concluded that “ … persistent dampness and microbial growth on interior surfaces and in building structures should be avoided or minimized, as they may lead to adverse health effects. As the relationships between dampness, microbial exposure and health effects cannot be quantified precisely, no quantitative, health-based guideline values or thresholds can be recommended for acceptable levels of contamination by microorganisms. Instead, it is recommended that dampness and mould-related problems be prevented. When they occur, they should be remediated because they increase the risk of hazardous exposure to microbes and chemicals”.

The “WHO Guidelines for Indoor Air Quality: Selected pollutants” (WHO, 2010) recommend targets for nine indoor air quality pollutants at which the health risks are significantly reduced and provide a scientific basis for legally enforceable standards in all regions of the world.

The working group defined the following criteria for selecting compounds for which the development of WHO guidelines for indoor air could be recommended:

- existence of indoor sources
- availability of toxicological and epidemiological data
- indoor levels exceeding the levels of health concern (no observed adverse effect level (NOAEL) and/or lowest observed adverse effect level (LOAEL).

Based on these criteria, pollutants considered were divided into two categories: Group 1 included pollutants for which WHO guidelines for indoor air were needed and WHO was requested to plan their development; Group 2 included pollutants of potential interest, but the group concluded that further investigation would be needed before it was clear whether there was sufficient evidence to warrant their inclusion in the guidelines at present.

The steering group assisting WHO in designing the indoor air quality guidelines concluded that there is no convincing evidence of a difference in the hazardous nature of particulate matter (PM) from indoor sources as compared with those from outdoors and that the indoor levels of PM10 and PM2.5, in the presence of indoor sources of PM, are usually higher than the outdoor PM levels. Therefore, the air quality guidelines for particulate matter recommended by the 2005 global update are also applicable to indoor spaces and a new review of the evidence is not necessary at present.

The nine substances considered in this review are common indoor air pollutants globally and are just a few of many chemicals encountered in indoor spaces. They have been selected for the purpose of this review based on the existence of their indoor sources, availability of evidence on their health effects, and common presence in concentrations of health concern.

The general approach and terminology used in setting air quality guidelines is based on a careful review and interpretation of globally accumulated scientific evidence linking exposure to a selected pollutant in the air with the health outcomes of that exposure. For each of the selected substances, a search of bibliographic databases was conducted to identify relevant studies. The review of the evidence focuses on the papers considered to be most relevant for development of the guidelines, and in particular on the studies providing quantitative links between health outcomes and the exposures (as determined by the concentrations of pollutants and the duration of exposure) encountered in indoor environments.

The background material on each of the nine pollutants reviewed contained sections on:

- general description of the compound;
- indoor sources and pathways of exposure;
- current indoor levels and relationship with outdoor levels;
- kinetics and metabolism (including experimental evidence on pathogenic
- mechanisms from animal and in vitro studies); and
- health effects.

In addition to the sections listed above, a first draft of the “Health risk evaluation” section. The working group meeting was convened to agree on the risk evaluation for each of the pollutants and to formulate WHO guidelines for protecting public health from these risks.

Based on the accumulated science, the experts formulated health risk evaluations and agreed on the following guidelines for each of the pollutants.

Carbon monoxide - Exposure to high levels of carbon monoxide is a frequent cause of fatal accidents. At lower levels, exposure leads to reduced exercise ability and increased risk of ischaemic heart disease. A series of guidelines is recommended to prevent effects of short peaks of exposure. New guideline value of 7 mg/m3 is defined for 24-hour mean CO concentration to prevent effects of chronic exposures.

Nitrogen dioxide - An annual average indoor nitrogen dioxide guideline of 40 µg/m3 is recommended. This guideline intends to reduce the risk of a broad range of respiratory symptoms associated with the exposure.

Benzene - Indoor air is a significant source of benzene and inhalation is the main pathway of human exposure. Benzene is a genotoxic carcinogen in humans and no safe level of exposure can be recommended. Life-long exposure to benzene at concentrations commonly observed in houses in European cities are associated with up to 10 excess cases of leukaemia per 100 000 people.

Trichloroethylene - The plausibility of a human cancer risk (including liver, kidney and testicular cancer as well as non-Hodgkin’s lymphoma) leads to the recommendation of a non-threshold approach.

Tetrachloroethylene - The recommended guideline for year-long exposure is 0.25 mg/m^3. At higher exposures, effects can appear in the kidney indicative of early renal disease and impaired neurobehavioural performance.

Formaldehyde - Indoor sources are the dominant contributor of exposure to formaldehyde. A 30-minute guideline of 0.1 mg/m^3 is recommended to prevent sensory irritation in the general population. This guideline, valid for any 30 minutes period, prevents also effects of long term exposures on lung function or on risk of nasopharyngeal cancer and myeloid leukaemia.

Naphthalene - The main health concerns of exposure to naphthalene are respiratory tract lesions, including tumors in the upper respiratory tract. A guideline value of 0.01 mg/m3 is established as an annual average to prevent these risks.

Polycyclic aromatic hydrocarbons (PAHs) - Lung cancer is the most serious health risk from exposure to PAHs in indoor air. Benzo[a]pyrene is one of the most potent carcinogens among the known PAHs. No safe level of exposure can be recommended. Life-long exposure to PAHs at concentrations commonly observed in European or North American cities are associated with excess up to 50 cases of lung cancer per 1 000 000 people. Markedly higher risks have been estimated for houses with smokers or poorly ventilated indoor combustion sources.

Radon - There is evidence from residential epidemiological studies of the lung cancer risk from radon, with no safe exposure level. Continuing smokers have 20-25 times higher risk of lung cancer than nonsmoker at radon mean concentrations commonly observed in houses in various regions of the world.

European INDEX project

The European INDEX project “Critical appraisal of the setting and implementation of indoor exposure limits in the EU” was funded by the European Commission DG SANCO and JRC and was coordinated by the JRC in collaboration with a Steering Committee of leading European experts in the area of indoor air pollution (Koistinen et al. 2008; Kotzias et al. 2005).

The project was given the assignment to identify priorities and to assess the needs for a Community strategy and action plan in the area of indoor air pollution by: 1) setting up a list of compounds to be regulated in indoor environments with priority on the basis of health impact criteria; 2) providing suggestions and recommendations on potential exposure limits for these compounds; 3) providing information on links with existing knowledge, ongoing studies, legislation, etc. at world scale.

On the basis of a literature review the Steering Committee decided to include into a detailed assessment 14 compounds (out of initial 41 candidate compounds). Finally a list of compounds, consisting of 5 chemicals, with potential of high indoor concentrations, uncontested health impacts, and effective risk management were selected to be regulated with priority. For each selected compound, guideline values and management options were suggested, as reported below.

Formaldehyde: The non-carcinogenic no-effect level is 30 µg/m^3. Based on IARC revision of formaldehyde carcinogenicity, a guideline should be as low as reasonably achievable. Management options are to restrict and avoid the use of formaldehyde containing materials and products in buildings. In the INDEX 2009 Update (not yet published) the exposure limit (acute) was suggested to be 90-120 µg/m^3 as short-term exposure (30 min).

Carbon Monoxide: Proposed guideline values are 10 µg/m^3 (8-hour) and 30 µg/m^3 (1-hour). Management options are to connect each combustion equipment /appliance to chimney or vented hood, to ensure sufficient local extract ventilation in kitchens with gas stove, mandatory inspection and maintenance of indoor combustion devices, and CO alarms.

Nitrogen Dioxide: Proposed guideline values are 40 µg/m^3 (1-week) and 200 µg/m^3 (1-hour). Management options are to connect each indoor combustion device/appliance to chimney or vented hood, and to ensure sufficient local extract ventilation in kitchens with gas stove.

Benzene: Benzene is a carcinogen therefore its indoor air concentration should be kept as low as reasonably achievable and not exceed outdoor concentrations. Management options are to ban benzene sources indoors, and lower the permissible benzene content in any building material and consumer product.

Naphthalene: Proposed long term guideline value is 10 µg/m^3. Management option is to restrict the use of naphthalene containing household products.

The second group of priority chemicals which are not considered to urgently require regulatory risk management actions specifically in indoor air included: Acetaldehyde; o-, p- and m-Xylene; Toluene; Styrene. Finally the third group of Additional chemicals of interest which are considered to require further research with regard to human exposure or dose response before recommendations can be made included: Ammonia; delta-Limonene; and alpha-Pinene.

Knowledge gaps, key issues, research priorities

In table 1 Indoor and ambient guidelines (WHO – INDEX project) are summarized.

Available toxicological data are very limited for firm conclusions for many pollutants and so specific air quality guideline values for general indoor settings have been established for only a few air contaminants.

In indoor environments many indoor sources may be present and occupants may be exposed to many outdoor and indoor pollutants. New materials, equipment and other consumer products are used and there is interest about reactive indoor air chemistry.

Most studies have limited or no information about indoor pollutant sources or about outdoor air quality. In contrast to ambient air, any indoor air monitoring data represent for short periods of time, usually non-representative fractions of indoor spaces.

For pollutants with significant sources and concentrations both indoors and outdoors, indoor concentration limits cannot be managed without acknowledging the outdoor concentrations as an unavoidable and variable background.

Very limited are the studies on the risks of serious chronic health effects, such as cancer.

Difficulties are also related to the fact that many pollutants contribute to annoyance, irritation, and to perception of poor indoor air quality; relationships between indoor office building conditions and wellbeing of occupants are complex.

Many indoor stressors can exert their effects additively or through complex interactions. Many pollutants may contribute to the so called “ cocktail effects” (presumably observable adverse effect of a complex chemical mixture in which each individual component exists clearly below its LOEL concentration).

Finally, different conditions (e.g. age, sex, disease) and agents (e.g. psychosocial stressors) have been hypothesized to make individuals more susceptible to environmental exposures and their role need to be further investigated.

References

Koistinen K, Kotzias D, Kephalopoulos S, Schlitt C, Carrer P, Jantunen M, Kirchner S, McLaughlin J, Molhave L, Fernandes EO, Seifert B (2008): The INDEX project: executive summary of a European Union project on indoor air pollutants. Allergy, 63(7): 810-9.

Kotzias D, Koistinen K, Kephalopoulos S, Schlitt C, Carrer P, Maroni M, Jantunen M, Cochet C, Kirchner S, Lindvall T, McLaughlin J, Mølhave L, Fernandes EdO and Seifert B (2005): The INDEX project. Critical Appraisal of the Setting and Implementation of Indoor Exposure Limits in the EU. Final Report. EUR 21590 EN. European Commission, Directorate General, Joint Research Centre.

WHO (1987): Air quality guidelines for Europe. Copenhagen, WHO Regional Office for Europe, 1987 (WHO Regional Publications, European Series, No. 23.

WHO (2000): Air quality guidelines for Europe, 2nd ed. Copenhagen, WHO Regional Office for Europe, 2000 (WHO Regional Publications, European Series, No. 91.

WHO (2000b): The right to healthy indoor air. Report on a WHO meeting, Bilthoven, Netherlands, 15–17 May 2000. Copenhagen, WHO Regional Office for Europe, 2000.

WHO (2006): Air quality guidelines. Global update 2005. Particulate matter, ozone, nitrogen dioxide and sulfur dioxide. Copenhagen, WHO Regional Office for Europe, 2006.

WHO (2009): WHO guidelines for indoor air quality: dampness and mould. Copenhagen, WHO Regional Office for Europe, 2009.

WHO (2010): WHO Guidelines for Indoor Air Quality: Selected pollutants. Copenhagen, WHO Regional Office for Europe, 2010.

Table 1. Indoor and ambient guidelines (WHO – INDEX project)

Pollutant	IAQ Guidelines			Ambient Air Guidelines	
	IAQ WHO (2010)	**INDEX (2005)**		**AQ WHO (2000)**	**AQ WHO (2005)**
CO (mg/m^3)	100 (15 m)	100 (15 m)		100 (15 m)	
	60 (30 m)	60 (30 m)		60 (30 m)	
	30 (1 h)	30 (1 h)		30 (1 h)	
	10 (8 h)	10 (8 h)		10 (8 h)	
	7 (24 h)				
NO_2 ($\mu g/m^3$)	200 (1 h)	200 (1 h)		200 (1 h)	200 (1 h)
	40 (1 y)	40 (1 w)		40 (1 y)	40 (1 y)
SO_2 ($\mu g/m^3$)				500 (10 m)	500 (10 m)
				125 (24 h)	20 (24 h)
PM10 ($\mu g/m^3$)					50 (24 h)
					20 (1 y)
PM2.5 ($\mu g/m^3$)					25 (24 h)
					10 (1 y)
OZONE ($\mu g/m^3$)					100 (8 h)
RADON (Bq/m^3)	No safe level Reference level: 100 Not more than: 300				

Table 1 continued. Indoor and ambient guidelines: organic compounds (WHO – INDEX project)

Pollutant	IAQ Guidelines			Ambient Air Guidelines	
	IAQ WHO (2010)	**INDEX (2005)**		**AQ WHO (2000)**	**AQ WHO (2005)**
Benzene ($\mu g/m^3$)	No safe level	No safe level Not more than outdoor level		UR 6×10^{-6}	
Trichloroethylene	No safe level			UR 4.3×10^{-7}	
Tetrachloroethylene ($\mu g/m^3$)	250 (1 y)			250 (1 y) 8000 (30 m)	
Toluene ($\mu g/m^3$)		300		260 (1 w) 1000 (30 m)	
Styrene ($\mu g/m^3$)		250		260 (1 w) 70 (30 m)	
Xylenes ($\mu g/m^3$)		200			
Naphtalene ($\mu g/m^3$)	10 (1 y)				
Formaldehyde ($\mu g/m^3$)	100 (30 m)	30 (30 m)		100 (30 m)	
Polycyclic aromatic hydrocarbons (PAHs)	No safe level			8.7×10^{-5} per ng/m^3 of B[a]P.	