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Spokane, Washington 99207
Office (509) 489-3860
Fax (509) 489-6140

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Andrews Mechanical, Inc.

March 5, 2025

Here is supporting Documentation for 24-GP1-288 Code section C403.4.13.1.
If you read the Title 1 from the attachment. (**Infection Microorganism Don't Care About Your Existing Policies.)** This is very telling in the title alone. If you look at Figure 2 on page 44 from the article it shows that Low RH droplets are transmitted in the air over great distances. Whereas RH at 40% to 60% don't, as in figure 3. This is the same truth in all our buildings. In Title 3 from the attachment, this is shown in a chart for **(Criteria for Human Exposure to Humidity in Occupied Buildings)** the optimum range for humidity is 40% to 60% in a graph chart where 50% is the optimum humidity where viruses don't grow. This is one of the reasons why Covid ran so rampant. Title 4 from the attachment, the (**Cochrane Library)** on page 9 shows this same chart about Humidity, **I hope you take time and read these reports as I have**. It is time that we take a hard look about how we are doing things for IAQ. Like air changes and humidity. I can remember when this code years ago had in code to tighten these homes up airtight, and we did what the code said and we all kinds of Mold issues. We still need to listen to experts that lower humidity level is not good for us like 30% and less. A lot of doctor bills could be avoided by proper humidity in our buildings. I think back to an early proposal about not requiring window space around the windows not being required to be insulated. This too doesn't make sense due to the fact mold could start in those spaces. Worse IAQ again. Yes, more energy will be required for this humidity. Humidity is cheap instead of dryness symptoms, upper respiratory infections, overall sickness, plagues, deaths and doctor bills. Most controls for humidity now have outdoor senser to reset humidity when it gets colder outside so condensation doesn't happen on the wall or windows.

One of the respondents on the 2-28-2025 commercial energy code respondents said that all we need to do is increase air flow for more heat. That is so wrong by these studies. 1st it is always' s cost less to increase temperature in the air stream for these reasons, 1. you don't want turbulent air in your room, 2. the duct size most time will not allow for such an increase of 3. The cost to run the fan at a higher rate of speed is always' s using more energy than just raising the temperature of the air stream to get the required BTU'S for the spaces. That is why most people don't sleep on the floor, your bacteria and viruses settle on the floor, you don't want to stir them up and hopefully they are clean up or die.
If we follow these practices from these articles, this world would be a healthier place in our buildings.

Larry Andrews

ANDREWS MECHANICAL, INC.

2727 North Madelia Unit 8 **(**Shop & ship to address**)**
1503 East Wabash (Mailing address)
Spokane, Washington 99207
Office (509) 489-3860
Fax (509) 489-6140

March 25, 2025

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Articles about Proper Humidification Health Benefits

Featuring:

Dr. Stephanie Taylor

ASHRAE

Cochrane Library

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Section 1:

Infectious microorganisms do not care about your existing policies - By Dr. Stephanie Taylor

INFECTIOUS MICROORGANISMS DO NOT CARE ABOUT YOUR EXISTING POLICIES

Personnel, common practices, and pathogen behavior all complicate the battle against hospital-acquired infections (HAIs). An overly narrow definition of "airborne" and a habit of confusing comfort with safety may be making things worse, too. Understand the enemy — why less may be more when it comes to room changes, and more may be more regarding relative humidity — to get beyond "business as usual" and knock down the risk to patients.

By Stephanie Taylor, M.D.

The transmission of infections is once again in the forefront of worldwide concerns. The current Ebola virus outbreak which started in Africa has killed many people and the future of this epidemic is unknown.

When studying infectious disease transmission and prevention, the hospital as a building is a virtual guinea pig. The high rates of patient deaths due to healthcare-associated infections (HAIs) indicate that this guinea pig is very sick indeed. Why is the hospital physical environment a place where infections flourish?

Hospitals are shelters and enclosures for:

- A human population very susceptible to infections — patients;
- The most aggressive pathogens — multi-drug resistant organisms such as Methicillin Resistant Staph Aureus (MRSA) and opportunistic pathogens such as Clostridium Difficile;
- Difficult-to-access and -clean "nooks and crannies" in the walls and ceilings where medical gas lines, electrical wires, and HVAC ducts reside — interstitial spaces where pathogens can hide and reproduce.

In addition to these components, hospital administrative and organizational dynamics make understanding and preventing HAIs very difficult. Without a full understanding of the current situation, verifying the benefits of change is impossible. What are some of the components of this impetus to open communication? The facility managers and engineers who run the hospital have very different professional training and educational backgrounds from the doctors and nurses who care for patients. Each group has years of education on subjects that do not intersect, creating silos of knowledge and unspoken hierarchies that can make communication extremely difficult. In addition to knowledge silos there are:

- Clinical staff who are usually rushed and often tired, making

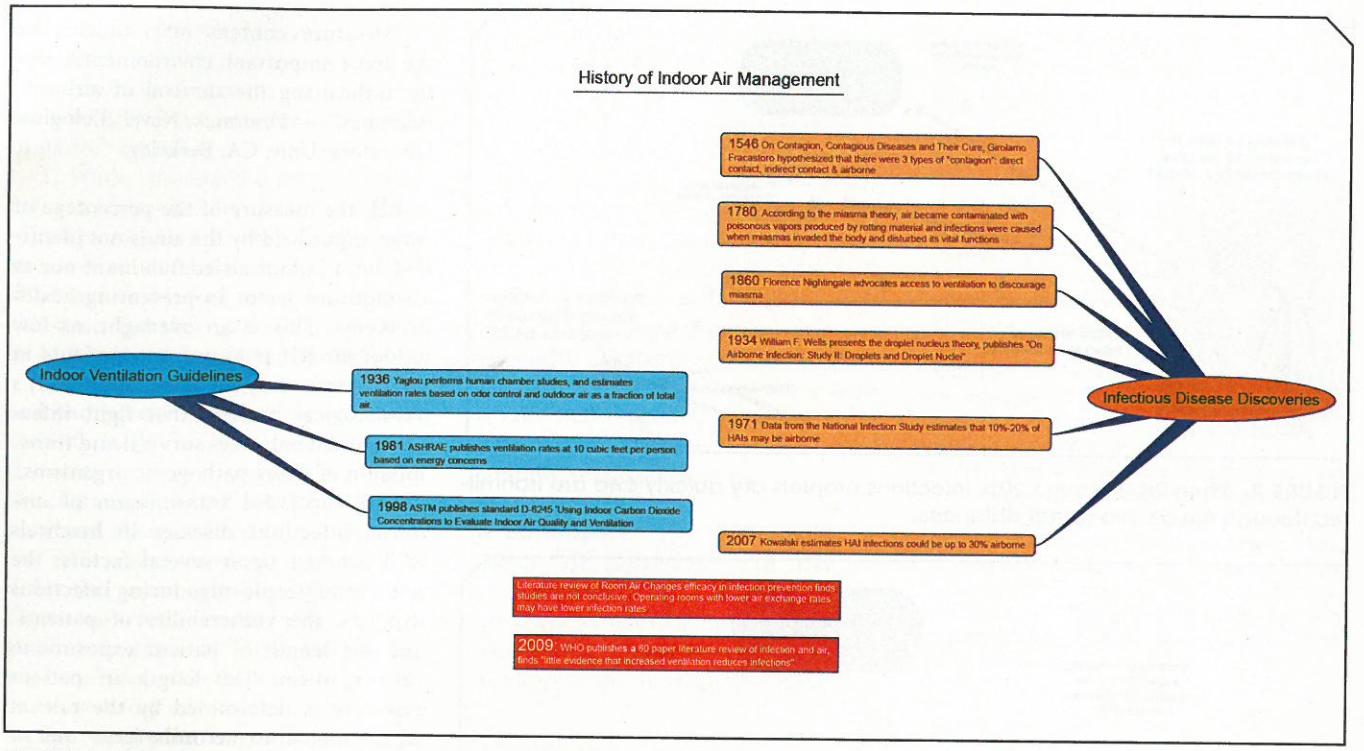

FIGURE 1. The history of infectious diseases and IAQ guidelines are largely divergent fields.

cutting corners a likelihood;

- Housekeeping workers who are among the lowest paid, yet who have the essential job of cleaning rooms between patient admissions;
- Administrative and clinical staff who regulations onerous;
- Layers upon layers of internal and external guidelines;
- Recently, government financial penalties for open disclosure of HAIs.

Even though challenging existing regulations and guidelines seems like an almost insurmountable obstacle when communication and teamwork is strained, statistics on the incidence of patient deaths due to hospitalization show that it is imperative to take new approaches to improve patient safety. The non-disruptive route of following existing policies without researching their efficacy is no longer acceptable. Infectious disease transmission and HAIs need to be interrupted!

THE CURRENT SITUATION IN HOSPITALS

There is scientific evidence that many infectious microorganisms are transmitted through the air on fomite carriers of tiny droplets, particles, skin flakes, or dust. Despite this evidence, airborne transmission is currently minimized in hospital infection control strategies, which are dominated by interruption of direct transmission routes such as unwashed hands. While rules on hand hygiene are essential, they are not sufficient.

Why is airborne transmission not adequately addressed? There are many reasons, most of which are beyond the scope of this article. One, however, will be addressed here. Many researchers use the term "airborne" to describe only "obligate airborne organisms," or pathogens that ONLY travel through the air and initiate infection in the lungs. This definition excludes pathogens that are spread by direct contact, but can also be spread over long distances through the air on fomites and instigate infection through the lungs, nasopharynx, gastrointestinal tract, or breaks in the skin.

A definition of airborne transmission that looks beyond a microbiologist's view of the organism would include all air transmission of the pathogen to the patient becoming infected. Most pathogens that can be spread by direct contact can also be carried through the air on fomites. This expanded definition of airborne transmission emphasizes the criticality of hospital indoor air management as an infection control step.

FOCUSING ON IAQ

IAQ guidelines are historically based on comfort measures — primarily odor and smoke clearance. At some point in time, probably with the advent of tuberculosis, airborne infection control became more obviously a problem in hospitals, so air pressurization and turbulence control were introduced to direct "dirty" air away from clean areas. To date, however, there are few controlled studies proving that these air-handling strategies improve patient outcome.

Review of the research reveals that the current IAQ recommendations for air handling in patient rooms are still largely based on comfort studies (ASHRAE Transactions, 2012) with little scientific data to correlate a particular number of room air changes with improved patient outcome. Historically, IAQ studies on controlling occupant comfort and odor control use smoke and other carbon based molecules as the test material. Infectious particles found in hospitals, however, are made up of lipids, polysaccharides, and

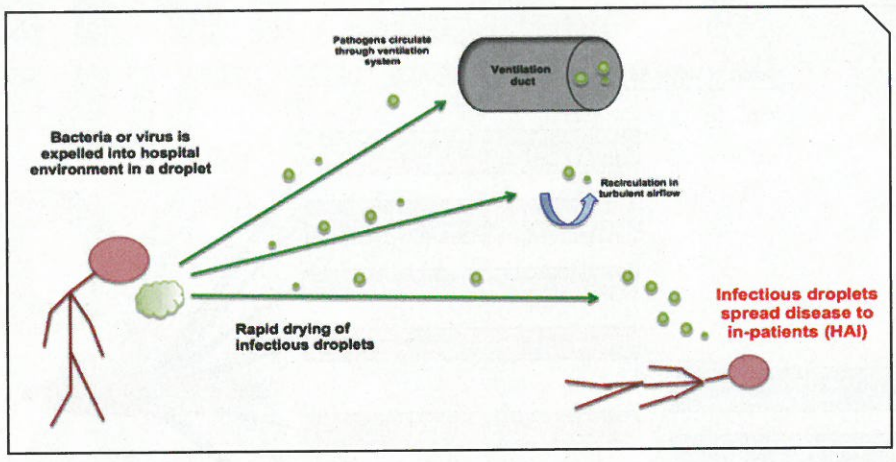

FIGURE 2. When RH is around 20%, infectious droplets dry quickly and are tranmitted through the air over great distances.

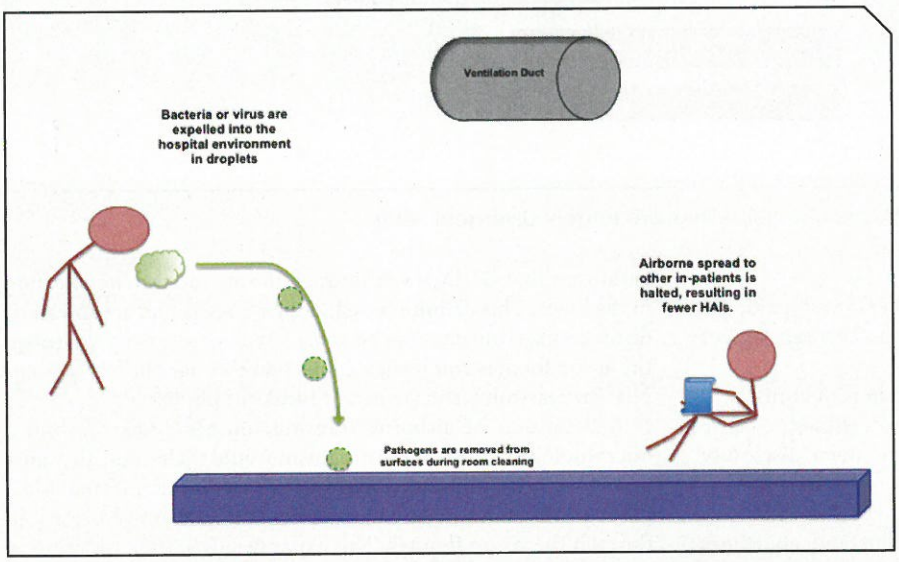

FIGURE 3. When the patient room RH is maintained at comfortable RH of 40%-60%, infectious droplets settle quickly and are removed by effective room cleaning, greatly decreasing airborne spread to other patients and mechanical systems.

proteins. The movement and infectivity of bacterial, viral, and fungal organisms vary with the RH of the air, whereas carbon based molecules do not respond in the same way. Because of these differences, comfort and odor studies are not an accurate basis for preventing airborne transmission of pathogens.

Regulations currently state that increased ventilation rates yield increased patient safety; however, infection control studies show that this is not necessarily the case. Excessive turbulent air movement can actually decrease patient safety as well as cause unneeded energy expenditure. Controlling air physical characteristics such as RH and turbulence to support the health of patients is underutilized as an infection control precaution.

BUT: Biology knows no silos, and it doesn't care about regulations! What indoor air parameters can improve the health of the occupants of a hospital?

"Moisture content may, indeed, be the most important environmental factor influencing the survival of airborne microbes." — Dimmick, Naval Biological laboratory, Univ. CA, Berkeley

RH, the measure of the percentage of water vapor held by the air, is not identified as an indoor air contaminant nor as a significant factor in preventing health problems. This is an oversight, as low indoor air RH is harmful to patients in several ways. Dry air harms our body's physiological barriers that fight infections, and it enhances survival and transmission of many pathogenic organisms.

The successful transmission of airborne infectious diseases in hospitals is dependent upon several factors: the number of people introducing infectious droplets, the vulnerability of patients, and the length of patient exposure to the organism. The length of patient exposure is determined by the rate at which infectious aerosols settle out of the air, and by the survival of pathogens in aerosols during transmission. Maintaining the relative humidity of hospital indoor air between 40% and 60% can significantly decrease HAIs by the following mechanisms.

1) The patient physiological barriers in passages from the nose to the depths of the lungs are most functional at room RH of 40% to 60%. Mucus-lined passages prevent pathogens from invading into deeper body tissues by continually washing particles away. This critical defense mechanism is impaired by dry air, enabling harmful organisms to reach deep lung tissue and the blood stream.

2) When indoor air is dry, the size of droplets carrying infectious particles shrink quickly, enabling the pathogen to be carried on air currents over great distances. When the RH is maintained from 40% to 60%, these infectious droplets settle within 4 ft to 6 ft of their source (a person sneezing, toilet flushing). In 1934, Wells observed the evaporation of droplets in dry air and concluded that large droplets strike the floor, while smaller droplets evaporate to create tiny droplet nuclei with significantly extended residence time in the air.

Humans shed roughly a billion skin cells daily with each square centimeter of skin having a concentration between 100 to 10,000,000 bacteria. Results from studies demonstrate that many airborne bacterial organisms originate from human skin, hair, nostrils, and the mouth through shedding and are subsequently circulated in droplet aerosols. When the RH is 40% to 60%, these infectious droplets settle quickly onto the floor

and horizontal surfaces, re-suspension is prevented, and effective room cleaning with surface disinfectants eradicates the pathogens, thereby decreasing the length of patient exposure.

3) While suspended during airborne transmission in dry air, infectious microorganisms are often temporarily in "travel mode," behaving as if they are dead and non-infectious if collected at this time. But these same microbes can be highly infectious when inhaled.

4) Studies show that many viruses and pathogenic bacteria have decreased viability in RH between 40% and 70%. Reducing pathogen survival decreases direct transmission of infections as well as related allergic illnesses such as asthma. Many respiratory viruses such as influenza, severe acute respiratory syndrome-associated coronavirus (SARS), respiratory syncytial virus, Para influenza, measles, rubella, varicella zoster, and respiratory adenoviruses and rhinoviruses survive the longest at low RH of 15% to 30% and the most briefly at 40% to 60% RH.

Clearly, monitoring and controlling RH to limit the airborne spread of HAIs is essential to patient safety and hospital cost containment. Unfortunately, healthcare facility guidelines are moving toward lowering the allowed minimum RH in operating rooms. This could further promote airborne transmission of infectious diseases such as MRSA, Acinetobacter spp. and Pseudomonas spp., Clostridium difficile, and Vancomycin Resistant Enterococci (VRE). In addition, there are no regulations for monitoring relative humidity in patient rooms and clinical spaces.

DECREASE ROOM AIR CHANGES (RAC)

There is strong evidence associating building air movement via ventilation with increased spread of measles, tuberculosis, chickenpox, influenza, smallpox, and SARS. In addition, there is insufficient data to support increased RACs and the prevention of infectious disease spread via the airborne route in hospitals, schools, offices, and homes.

Turbulent airflow also plays an important role in airborne transmission. While turbulent airflow can dilute airborne contaminants, it can also cause cross-infection to other patients. Pathogens emitted in droplets via coughing, sneezing, talking, and breathing or the direct shedding of skin-associated pathogens initially settle on surfaces, only to become re-suspended in dry, turbulent airflow. Genetic pieces of bacteria found on human skin have been recovered in indoor floor dust, suggesting that re-suspension of this dust may carry human-associated bacteria. These findings highlight the importance of fully understanding the influence of both RAC and turbulence in forced and naturally ventilated systems.

IN SUMMARY

Indoor air movement and RH are important building components that can affect patient healing through both maintenance of the patient's physiological barriers and through the movement of many pathogens, whether or not these pathogens are currently classified as "obligate airborne organisms." **ES**

Dr. Stephanie Taylor is the CEO of Taylor Healthcare Commissioning, Inc. After working as a physician for many decades, Dr. Taylor obtained a Masters in Architecture as well as Infection Control certification. Her lifelong commitment to patient care includes focusing on improving the health care physical environment and clinical work processes to help patients heal quickly and save hospitals valuable dollars. Dr. Taylor is a graduate of Harvard Medical School (MD) and Norwich University (Masters Architecture). She has numerous research publications in *Nature, Science,* and other peer-reviewed journals.

Section 2:

Meeting/Event Information:
October 2023 Nashville ASHRAE Meeting
– Stephanie Taylor, M.D., M. Arch

Meeting Information

(meetinginfo.php)

- **Future Meetings (meetinginfo.php?p_or_f=f)**
- **Previous Meetings (meetinginfo.php?p_or_f=p)**

Meeting/Event Information

October 2023 Nashville ASHRAE Meeting - Stephanie Taylor, M.D., M. Arch

October 10, 2023
11:30 AM - 1:00 PM
Add to Calendar (https://nashvilleashrae.org/vcs/meeting23.vcs)

Adventure Science Center
800 Fort Negley Boulevard
Nashville, TN 37203-4833
Venue website (http://www.adventuresci.org/)
Directions (http://maps.google.com/maps?q=800+Fort+Negley+Boulevard+Nashville+TN&btnG=Search)

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Presentation Description:

The indoor environment, specifically exposure to airborne compounds and thermal metrics, are powerful determinants of health or disease. Despite this influence of indoor exposures on almost all aspects of our health, productivity and ability to learn new information, current building standards primarily focus on aesthetics, energy and dramatic failures such as fire and earthquakes. COVID-19 has shifted this emphasis; however, we are still missing a health standard to guide IAQ management specifically for occupant health.

While understanding the interrelationships between indoor environments and human physiology is complex because of multiple contributing factors, we still need to tackle these questions. Without a medically-bases health standard for IAQ, we do not know if ventilation, filtration, humidity management and air cleaning interventions are benefiting occupants.

This presentation will reveal a framework for quantifying the effect of indoor exposures on our immune system, metabolism, risk of inflammation and on our microbiome. This data-based approach allows us to manage buildings behave as true shelters.

About the Speaker:

Dr. Stephanie Taylor received her MD from Harvard Medical School, Boston, Massachusetts in 1984. For the next several decades, she practiced clinical medicine and did academic research in cellular growth mechanisms.

During this time, she became increasingly concerned about patients who were harmed by new infection during their in-patient treatment. Determined to gain a better understanding of the impact of the built environment on patient well-being, she returned to school and obtained her Master's Degree I Architecture and Engineering from Norwich University in Northfield, Vermont. After working for several years in a healthcare design architecture firm, she founded Taylor Healthcare Consulting, Inc., in order to focus on designing, building and maintaining hospitals to better support patient healing. She quickly learned that many of the building and indoor air characteristics that affect people in hospitals also influenced the health of all people in buildings.

Dr. Taylor is currently working at the intersection of architectural design, indoor air management, the microbiome of the built environment and occupant health. She finds the impact of buildings on our health startling! Managing the built environment and indoor air with the goal of decreasing diseases from acute infections to chronic inflammation to cognitive impairment, is a very underutilized yet powerful approach to disease prevention. She finds that her physician insights and biological research helps her understand the science behind the interaction of buildings, human physiology and energy consumption.

Dr. Taylor has designed hospitals globally, from the United States to Papua New Guinea to Vietnam. In addition to her Taylor Healthcare Consulting work, she is a member of the Harvard Medical School Incite Health Fellowship. This program brings together multidisciplinary teams from across the US, trains them in design thinking and entrepreneurship, and gives them the tools and resources to guide the future of medical care.

To communicate her work and understanding about the fascinating convergence of human health, microbiology and architecture, Dr. Taylor writes monthly columns and bi-annual feature articles for Engineered Systems Magazine and publishes in other healthcare journals. She is an active member of ASHRAE, ASHE and national and international medical associations. When not working elsewhere, Dr. Taylor lives in beautiful Stowe, Vermont with her husband and eight dogs. One of her favorite activities is skydiving, which she finds is great practice for staying outside of her comfort zone!

Thanks to our meeting sponsor Tom Barrow Company for their support of this meeting and the Nashville ASHRAE Chapter.

(https://www.tombarrow.com/)

Section 3:

Criteria for Human Exposure to Humidity in Occupied Buildings

Published: 1985 | ASHRAE Transactions, Vol. 91, Part 1, CH85-13 No. 1, 1985 (http://sterlingiaq.com/photos/1044922973.pdf)

Criteria for Human Exposure to Humidity in Occupied Buildings

Sterling EM, Arundel A, Sterling TD

Abstract

Authors reviewed scientific literature that focused on humidity effects on biological contaminants (viruses, bacteria and fungi) causing respiratory disease, chemical interactions and the possible impacts on human health and comfort. 74 references are listed in the paper.

Analysis of the selected literature revealed that preferences of viruses and bacteria for low and high humidity are known, while fungi prefer humidity's above 80%RH for optimal survival on surfaces. For airborne microbes, literature revealed, that midrange humidity was least favourable for survival. Interventional clinical trials by use of humidifiers were analysed for rates for respiratory infections and absenteeism.

While off-gassing of formaldehyde and chemical interactions increases above 40%RH, the concentration of irritating ozone decreases.

Conclusion

The authors conclude that the optimal humidity range for minimizing risks to human health by biological contaminants and chemical interactions, is in the narrow range between 40-60%RH, at normal room temperatures.

Scientific studies main menu ***(/humidity-health-wellbeing/scientific-studies/)***

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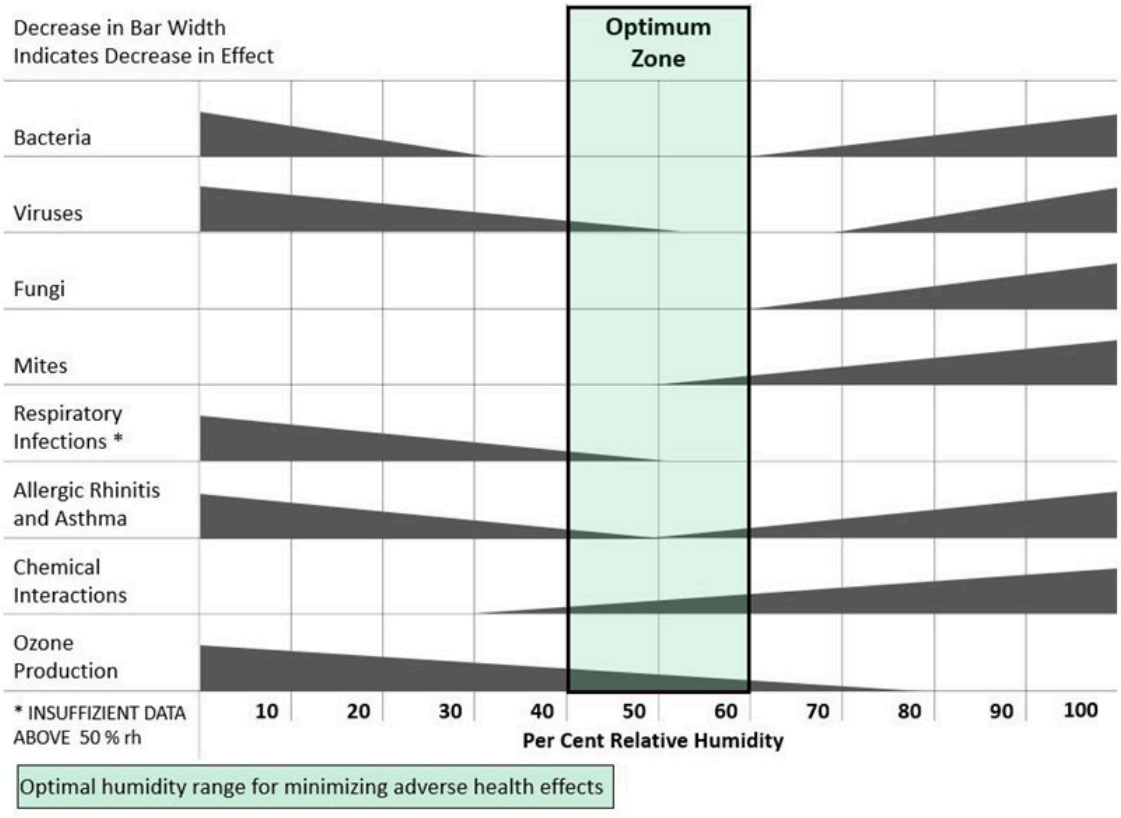

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(/humidity-health-wellbeing/dry-air-and-airborne-infection)

Dry air and airborne infection

(/humidity-health-

Doc's view...

by Dr.med. Walter Hugentobler

“The review provides good evidence that the optimal indoor humidity level for human health is 40-60%RH.

To the present day, Sterling’s and Arundel’s publications are the only reviews that are based on interventional clinical studies (seven successful studies) providing evidence for the preventive effect of humidification on respiratory infections and absenteeism.

This paper was the precursor for Arundel’s publication one year later which presented even more in-depth analysis of adverse and health supportive humidity effects.”

Download our humidity, health and wellbeing booklet

Section 4:

Humidification of indoor air for preventing or reducing dryness symptoms or upper respiratory infections in educational settings and at the workplace

Cochrane Library

Cochrane Database of Systematic Reviews

Humidification of indoor air for preventing or reducing dryness symptoms or upper respiratory infections in educational settings and at the workplace (Review)

Byber K, Radtke T, Norbäck D, Hitzke C, Imo D, Schwenkglenks M, Puhan MA, Dressel H, Mutsch M

Byber K, Radtke T, Norbäck D, Hitzke C, Imo D, Schwenkglenks M, Puhan MA, Dressel H, Mutsch M.
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Cochrane Database of Systematic Reviews 2021, Issue 12. Art. No.: CD012219.
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[Intervention Review]

Humidification of indoor air for preventing or reducing dryness symptoms or upper respiratory infections in educational settings and at the workplace

Katarzyna Byber[1], Thomas Radtke[2], Dan Norbäck[3], Christine Hitzke[1], David Imo[4], Matthias Schwenkglenks[2], Milo A Puhan[2], Holger Dressel[1a], Margot Mutsch[2b]

[1]Division of Occupational and Environmental Medicine, University of Zurich and University Hospital Zurich, Zurich, Switzerland. [2]Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Zurich, Switzerland. [3]Department of Medical Science, Uppsala University, Uppsala, Sweden. [4]Division of Occupational and Environmental Medicine, University of Zurich, Zurich, Switzerland

[a]These authors contributed equally to this work and share the last authorship.. [b]These authors contributed equally to this review and share the last authorship.

Contact: Katarzyna Byber, katarzyna.byber@usz.ch.

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ABSTRACT

Background

Indoor exposure to dry air during heating periods has been associated with dryness and irritation symptoms of the upper respiratory airways and the skin. The irritated or damaged mucous membrane poses an important entry port for pathogens causing respiratory infections.

Objectives

To determine the effectiveness of interventions that increase indoor air humidity in order to reduce or prevent dryness symptoms of the eyes, the skin and the upper respiratory tract (URT) or URT infections, at work and in educational settings.

Search methods

The last search for all databases was done in December 2020. We searched Ovid MEDLINE, Embase, CENTRAL (Cochrane Library), PsycINFO, Web of Science, Scopus and in the field of occupational safety and health: NIOSHTIC-2, HSELINE, CISDOC and the In-house database of the Division of Occupational and Environmental Medicine, University of Zurich. We also contacted experts, screened reference lists of included trials, relevant reviews and consulted the WHO International Clinical Trials Registry Platform (ICTRP).

Selection criteria

We included controlled studies with a parallel group or cross-over design, quasi-randomised studies, controlled before-and-after and interrupted time-series studies on the effects of indoor air humidification in reducing or preventing dryness symptoms and upper respiratory tract infections as primary outcomes at workplace and in the educational setting. As secondary outcomes we considered perceived air quality, other adverse events, sick leave, task performance, productivity and attendance and costs of the intervention.

Data collection and analysis

Two review authors independently screened titles, abstracts and full texts for eligibility, extracted data and assessed the risks of bias of included studies. We synthesised the evidence for the primary outcomes 'dry eye', 'dry nose', 'dry skin', for the secondary outcome

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'absenteeism', as well as for 'perception of stuffiness' as the harm-related measure. We assessed the certainty of evidence using the GRADE system.

Main results

We included 13 studies with at least 4551 participants, and extracted the data of 12 studies with at least 4447 participants. Seven studies targeted the occupational setting, with three studies comprising office workers and four hospital staff. Three of them were clustered cross-over studies with 846 participants (one cRCT), one parallel-group controlled trial (2395 participants) and three controlled before-and-after studies with 181 participants. Five studies, all CTs, with at least 1025 participants, addressing the educational setting, were reported between 1963 and 1975, and in 2018. In total, at least 3933 (88%) participants were included in the data analyses.

Due to the lack of information, the results of the risk of bias assessment remained mainly unclear and the assessable risks of bias of included studies were considered as predominantly high.

Primary outcomes in occupational setting:

We found that indoor air humidification at the workplace may have little to no effect on dryness symptoms of the eye and nose (URT). The only cRCT showed a significant decrease in dry eye symptoms among working adults (odds ratio (OR) 0.54, 95% confidence interval (CI) 0.37 to 0.79) with a low certainty of the evidence. The only cluster non-randomised cross-over study showed a non-significant positive effect of humidification on dryness nose symptoms (OR 0.87, 95% CI 0.53 to 1.42) with a low certainty of evidence.

We found that indoor air humidification at the workplace may have little and non-significant effect on dryness skin symptoms. The pooled results of two cluster non-RCTs showed a non-significant alleviation of skin dryness following indoor air humidification (OR 0.66, 95% CI 0.33 to 1.32) with a low certainty of evidence. Similarly, the pooled results of two before-after studies yielded no statistically significant result (OR 0.69, 95% CI 0.33 to 1.47) with very low certainty of evidence

No studies reported on the outcome of upper respiratory tract infections.

No studies conducted in educational settings investigated our primary outcomes.

Secondary outcomes in occupational setting:

Perceived stuffiness of the air was increased during the humidification in the two cross-over studies (OR 2.18, 95% CI 1.47 to 3.23); (OR 1.70, 95% CI 1.10 to 2.61) with low certainty of evidence.

Secondary outcomes in educational setting:

Based on different measures and settings of absenteeism, four of the six controlled studies found a reduction in absenteeism following indoor air humidification (OR 0.54, 95% CI 0.45 to 0.65; OR 0.38, 95% CI 0.15 to 0.96; proportion 4.63% versus 5.08%).

Authors' conclusions

Indoor air humidification at the workplace may have little to no effect on dryness symptoms of the eyes, the skin and the URT. Studies investigating illness-related absenteeism from work or school could only be summarised narratively, due to different outcome measures assessed. The evidence suggests that increasing humidification may reduce the absenteeism, but the evidence is very uncertain. Future RCTs involving larger sample sizes, assessing dryness symptoms more technically or rigorously defining absenteeism and controlling for potential confounders are therefore needed to determine whether increasing indoor air humidity can reduce or prevent dryness symptoms of the eyes, the skin, the URT or URT infections at work and in educational settings over time.

PLAIN LANGUAGE SUMMARY

Interventions for preventing or reducing dryness symptoms or upper respiratory infections in educational settings and at the workplace

Our aim was to find out if humidification of indoor air can prevent or reduce dryness symptoms or upper respiratory infections in the educational setting and at the workplace.

During the heating period, the humidity of indoor air is low, which can lead to complaints such as dryness of eyes, nose, throat and skin. Furthermore, the dry and irritated mucosa can in turn lead to susceptibility to upper airways infections. These conditions could also be associated with not going to work and to schools. Increasing indoor air humidity by setting up humidifiers might prevent or reduce dryness symptoms or upper respiratory infections.

Studies found:

We included 13 studies with 4551 participants. Seven studies were conducted at the workplace (in hospitals and in offices) and five studies were set in educational settings (kindergarten and schools). The data from one study could not be analysed for the purpose of this review.

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Humidification of indoor air versus no humidification

The included studies showed that increasing indoor air humidity by installing humidifiers at the workplaces had no effect, and other studies showed a decrease in symptoms of dryness of the eye, skin and upper airways. However, the certainty of evidence was low to very low.

Regarding non-attendance, the results of the studies (most of them conducted in the educational setting) are also not consistent. The evidence was of very low certainty.

Quality of evidence

We judged the certainty of the evidence to be low to very low, because of limitations in the studies. This means that we cannot be confident of the overall findings.

What do we still need to find out?

We need studies of higher certainty, with accurate definitions and measurement of the symptoms.

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SUMMARY OF FINDINGS

Summary of findings 1. Summary of findings table 'dryness symptoms'

Indoor air humidification compared with no indoor air humidification for prevention or reducing dryness symptoms of the eyes, skin and nose (URT)

Population: Adults
Setting: Occupational
Intervention: Indoor air humidification
Comparison: No indoor air humidification

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)#	Quality of the evidence (GRADE)	Comments
	Risk with no humidification	Risk with humidification				
Dry eye Cross-over study (cluster-RCT) after 6 weeks	Study population 359 per 1000	232 per 1000 (172 to 307)	OR 0.54 (0.37 to 0.79)	211 (1 cross-over cluster-RCT)	⊕⊕⊖⊖ LOW[a]	The cluster-randomised cross-over study reported a significant reduction in eye dryness following indoor air humidification over a study period of 6 weeks
Dry eye Cross-over studies (cluster non-RCT) after 6 – 12 weeks	Study population 359 per 1000	245 per 1000 (131 to 412)	OR 0.58 (0.27 to 1.25)	407 (2 cross-over cluster non-RCTs)	⊕⊕⊖⊖ LOW	2 cluster non-randomised cross-over studies reported non-significant positive effects on eye dryness following indoor air humidification over a study period of 1 - 3 months
Dry eye Before-and-after studies after 6 weeks - 4 months	Study population 359 per 1000	242 per 1000 (114 to 441)	OR 0.57 (0.23 to 1.41)	102 (2 before-and-after studies)	⊕⊖⊖⊖ VERY LOW[b, c]	2 before-and-after studies showed non-significant positive effect of indoor air humidification on dry eye symptoms over a study period of 6 weeks to 4 months
Dry skin Cross-over studies (cluster non-RCT) after 6 - 12 weeks	Study population 380 per 1'000	288 per 1000 (168 to 447)	OR 0.66 (0.33 to 1.32)	407 (2 non-RCT)	⊕⊕⊖⊖ LOW	Both cluster non-randomised cross-over studies showed an alleviation of skin dryness following indoor air humidification over a study period of 1 - 3 months
Dry skin	Study population		OR 0.69 (0.33 to 1.47)		⊕⊖⊖⊖ VERY LOW[d]	

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Before-and-after Studies after 12 weeks to 4 months	380 per 1000	297 per 1000 (168 to 474)		121 (2 before-and-after studies)		1 before-and-after study yielded a positive effect of indoor air humidification on skin dryness over a study period of 12 weeks. 1 before-and-after study showed no effect following indoor air humidification over a study period of 4 months
Dry nose (dry upper respiratory tract) Cross-over study (cluster non-RCT) after 6 weeks	Study population		OR 0.87 (0.53 to 1.42)	368 (1 non-RCT)	⊕⊕⊖⊖ LOW	The cluster non-randomised cross-over study reported an alleviation of nose dryness following indoor air humidification over a study period of 6 weeks. Hence, the result was not statistically significant
	246 per 1000	221 per 1000 (147 to 317)				
Dry nose (dry upper respiratory tract) Cross-over study (cluster-RCT) after 6 weeks	Study population		OR 1.08 (0.73 to 1.60)	211 (1 RCT)	⊕⊕⊖⊖ LOW[d]	The cluster-randomised cross-over study revealed no effect of indoor air humidification on nose dryness over a study period of 6 weeks
	246 per 1000	259 per 1000 (194 to 337)				
No studies were identified for URT (Upper respiratory infections)						

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).
#Number of participants included in the analysis were reported, See Characteristics of included studies for number of recruited and included participants.
CI: Confidence interval; **OR:** Odds ratio; **RCT:** randomised controlled trial

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[a]Downgraded twice due to high risk of bias: there were missing outcome data (the reason was not stated); the items: randomisation, allocation concealment, blinding unclear, selective outcome reporting were unclear.
[b]Downgraded twice due to high risk of bias: in one study the percentage of withdrawals and dropouts exceeds 20% for short-term follow-up and the results are presented for a dynamic population.
[c]Downgraded once due to imprecision: small sample sizes.
[d]Downgraded once due to high risk of bias: lack of control for confounding and other source of bias (dynamic population).

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We did not upgrade any of the individual studies.

Summary of findings 2. Summary of findings table 'adverse effects'

Humidification compared to no humidification for preventing or reducing of perception of stuffiness

Population: Adults
Setting: Occupational
Intervention: Indoor air humidification
Comparison: No indoor air humidification

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)#	Certainty of the evidence (GRADE)	Comments
	Risk with no humidification	Risk with humidification				
Perception of stuffiness: Cross-over study (cluster-RCT) after 6 weeks	246 per 1000	416 per 1000 (324 to 513)	OR 2.18 (1.47 to 3.23)	211 (1 cross-over cluster-RCT)	⊕⊕⊖⊖ LOW[a]	The clustered randomised cross-over study reported more frequent perception of stuffiness over a study period of 6 weeks
Perception of stuffiness: Cross-over study (cluster non-RCT) after 6 weeks	246 per 1000	357 per 1000 (264 to 460)	OR 1.70 (1.10 to 2.61)	368 (1 non-RCT)	⊕⊕⊖⊖ LOW	The cluster-non-randomised cross-over study reported more frequent perception of stuffiness over a study period of 6 weeks
Perception of stuffiness: 2 Before-and-after studies after 1-4 months	246 per 1000	148 per 1000 (-74 to 192)	St. Mean Diff. 0.24 (−0.30 to 0.78)	102 (2 before-and-after studies)	⊕⊖⊖⊖ VERY LOW[b, c]	2 before-and-after studies showed a non-significant positive effect of indoor air humidification for the perception of stuffy air over a study period of 6 weeks to 4 months

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).
Number of participants included in the analysis were reported, See Characteristics of included studies for number of recruited and included participants.
CI: Confidence interval; **OR:** Odds ratio; **RCT:** randomised controlled trial

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

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[a]Downgraded twice due to high risk of bias: there were missing outcome data (the reason was not stated); the items: randomisation, allocation concealment, blinding unclear, selective outcome reporting were unclear.
[b]Downgraded twice due to high risk of bias: in one study the percentage of withdrawals and dropouts exceeds 20% for short-term follow-up and the results are presented for a dynamic population.
[c]Downgraded once due to imprecision: small sample sizes.

Summary of findings 3. Summary of findings 'absenteeism'

Indoor air humidification compared with no indoor air humidification for prevention or reducing absenteeism

Patient or population: Children

Settings: Educational

Intervention: Indoor air humidification

Comparison: No indoor air humidification

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)#	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	No indoor air humidification	Indoor air humidification			
In total 6 non-randomised, parallel-group controlled studies were included, 5 in educational and one in an occupational setting. Different outcomes were assessed.					
Absenteeism due to cold symptoms	1 study showed a statistically significant reduction in absenteeism due to cold symptoms following indoor air humidification		OR 0.54 (0.45 to 0.65)	232 1 study	⊕⊖⊖⊖ VERY LOW[a]
Average days of absence per child	No reduction in respiratory illness could be demonstrated following indoor air humidification in 1 study.			162 1 study	⊕⊖⊖⊖ VERY LOW[a, b]
Average weekly absence	1 study revealed a statistically significant decrease in average weekly absence following indoor air humidification.		OR 0.38 (0.15 to 0.96)	263 1 study	⊕⊖⊖⊖ VERY LOW[a, c]
Average total absenteeism	10-year-average of total absenteeism: under humidified condition 4.63% and under non-humidified condition 5.08%, statistical significance at 95% CI level reported, data not shown			N unknown (12 schools, grades 1 - 8)	⊕⊖⊖⊖ VERY LOW[a]
Absenteeism due to sickness	In the humidified group the absenteeism due to sickness was the same as in the control group.			116	⊕⊖⊖⊖ VERY LOW[a]

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			1 study	
Absenteeism due to influenza-like illness	The percentage of students with influenza-like illness absences was lower under the humidified vs. the non-humidified condition		116 1 study	⊕⊖⊖⊖ VERY LOW[a]

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

#Number of participants included in the analysis were reported, See Characteristics of included studies for number of recruited and included participants.
CI: Confidence interval; **OR**: Odds Ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[a]Downgraded once due to high risk of bias: lack of control for confounding.
[b]Downgraded once due to high risk of bias: Lack of blinding.
[c]Downgraded once due to high risk of bias: Other source of bias.

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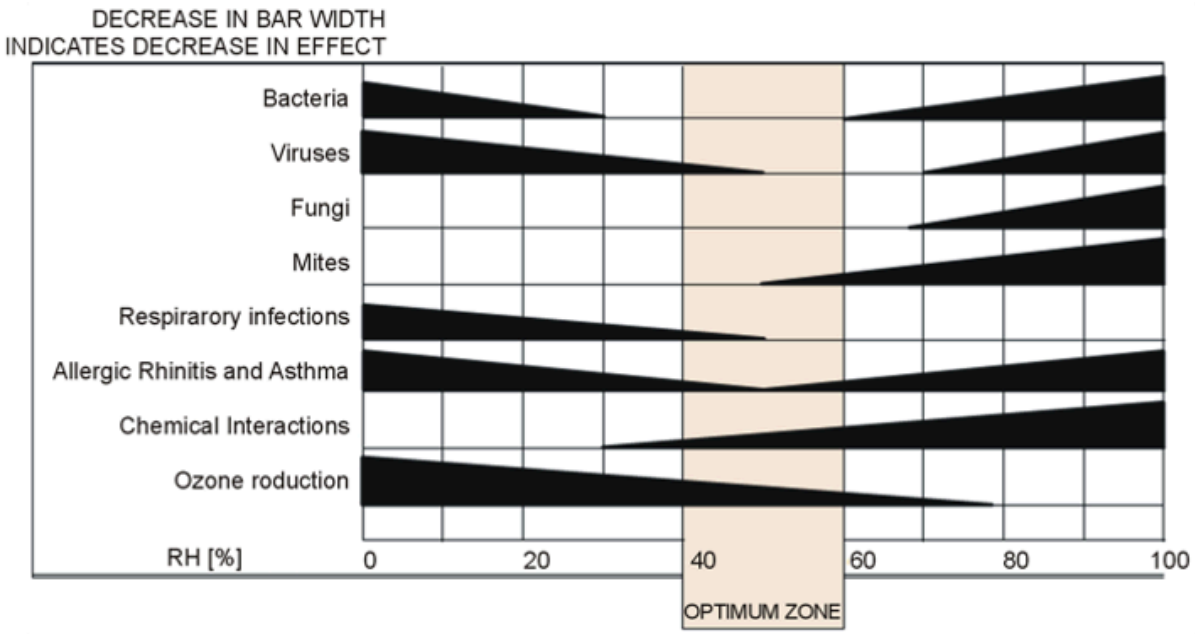
BACKGROUND

Following the progress of industrialisation, workplaces have increasingly moved from outdoor to indoor locations. This shift has changed the spectrum of conditions to which workers are exposed. This fact is not only relevant to the adult working population, but also to children and young adults, as they stay indoors for a significant part of the day throughout their education (Angelon-Gaetz 2014; Jaakkola 1991; Seppanen 2002). At most workplaces, indoor air is a predefined condition. Its components vary considerably among different occupational and educational settings. Emissions from indoor sources like building materials, furnishings, office equipment and human activities result in the release of dust as well as chemical and biological compounds. Following natural ventilation, outdoor factors, such as pollen and particulate matters, may also contribute to indoor air quality (Alsmo 2014). Indoor air climate results from a combination of four physical parameters: temperature, radiation temperature, air velocity, and humidity. Humidity is defined as absolute humidity (water vapour content of the air) whilst relative humidity (RH) is the ratio of vapour pressure and saturation vapour pressure. RH, expressed as a percentage, increases relative to a decrease in temperature. A humidity level of 100% means that the air is completely saturated with water vapour. The influence of different humidity levels on pathogens, allergens and chemical factors is presented in Figure 1 (Alsmo 2014).

Figure 1. Association of indoor relative humidity and exposure factors related to adverse health effects (Alsmo 2014)



Description of the condition

The context of indoor air humidity and health is not a new issue, with the concept of dry air being associated with poor air quality since the early 20th century (Watt 1910). Currently, there is no universal definition of dry air. It is in fact difficult to ascertain how and to what extent human beings perceive air humidity (Von Hahn 2007), as we do not have any specific receptors to trace it directly. As the perception of dry air is strongly affected by climatic parameters (particularly temperature) and environmental factors (e.g. dust), even RH levels of 50% can be experienced as dry air under certain conditions (Von Hahn 2007). Nevertheless, many recommend avoiding conditions below a lower limit of RH of 30% to 40%, as such conditions would commonly be perceived as uncomfortable (Von Hahn 2007).

Naturally-ventilated places have substantially lower levels of RH in winter than in summer. The colder it is outside and the better a building is naturally ventilated, the drier the indoor air becomes.

In cold seasons, building occupants increasingly complain about dryness of the eyes, throat and skin in close temporal relation to exposure to dry air at the workplace (Von Hahn 2007). These symptoms lack specificity and it is therefore difficult to attribute them to clearly-defined triggers. Furthermore, they can emerge through various pathways and, for instance, it may remain difficult to distinguish between symptoms due to immunological and inflammatory mechanisms. Some of these complaints are assumed to be directly associated with low levels of RH. However, most of them seem to be multifactorial in origin. In addition, they could also be the result of an indirect influence of RH due to interactions, for example with chronic illness. Individuals with certain pre-existing medical conditions and predisposed individuals appear to be more affected.

Ocular symptoms such as burning, itching, and sensations of dryness and stinging are summarised as eye irritation (Wolkoff 2008). These complaints occur commonly at the workplace, especially in women (Wolkoff 2010). The prevalence of discomfort varies considerably and ranges from 5.5% to 33.7% across studies, depending on the investigated population and the diagnostic criteria (Lin 2003). Overall, office workers suffer more frequently from eye irritation than the general population (Wolkoff 2008). A low humidity level (5% to 30%) is an environmental risk factor

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that contributes to an increased prevalence of dry eyes in office environments (Wolkoff 2008). However, there is a wide range of individual and external risk factors associated with eye irritation in the office environment (Wolkoff 2008). Age, medication and hormonal changes represent personal risk factors for developing ocular symptoms (Wolkoff 2010). Exposure to ambient irritants such as formaldehyde and ozone can cause sensory irritation in the eyes by trigeminal stimulation (Wolkoff 2010). The impact of concomitant exposure to sensory irritants (e.g. volatile organic compounds (VOCs) and ozone) and dry air on the eye has been shown to be greater at a relative humidity level of 20% compared to 50% (Wolkoff 2005). Furthermore, irritated eye symptoms resulting from exposure to low humidity levels might be exacerbated by computer screen work (Wolkoff 2007).

The mucous membrane of the airways poses a natural barrier protecting against irritants, microbes and unfavourable climatic conditions. The interaction of ciliary activity and viscosity of mucosal fluid is crucial for its self-cleaning properties (Guggenbichler 2007). This mechanism is called mucociliary clearance, and can be assessed using different methods. In the airways, the air is conditioned to 37 °C and 100% relative humidity, regardless of the ambient conditions (Pfluger 2013). However, despite this compensatory mechanism, exposure to dry air seems to induce dryness and irritation symptoms, as has been shown in several epidemiological studies (Ghaved 2005; Reinikainen 1991; Reinikainen 1992). Alongside age, air humidity and hydration status, there are many other internal and external risk factors affecting mucous membrane function.

Among occupants of buildings, the baseline prevalence of nasal symptoms is often 20% (Bascom 1991). Building occupants exposed to chemical and microbiological VOCs can develop symptoms of mucosal irritation in the eyes and upper airways by trigeminal stimulation, even at levels below threshold values (Wolkoff 2013). Concomitant exposure to low humidity may lead to instability of the mucous membrane and consequently to lowering the threshold of sensory irritation (Wolkoff 2013).

Occupants permanently exposed to low humidity commonly complain of dry, brittle and cracked skin (Pfluger 2013). Rycroft 1980 describes two outbreaks of dermatosis (pruritus, urticaria, erythema, oedema and scaling of the skin) relating to working environments with low RH (35%). Exposure to allergens and irritants at the workplace or at home may also lead to dryness or irritation symptoms of the skin and the development of dermatitis.

Several, mostly older, epidemiological studies have evaluated the effect of humidity on the incidence of respiratory infections (Arundel 1986). Most found a lower rate of respiratory infections in rooms with higher humidity compared to those with lower humidity. Most of these studies were conducted among preschool or school children, with only two studies conducted in adult workers. These latter two studies (Gubéran 1978; Serati 1969) found non-significant differences in absenteeism due to respiratory tract infections between humidified and non-humidified offices.

Experimental studies have shown that low humidity and low temperature promote the spread of the influenza virus. The winter time in temperate countries associated with exposure to cold air outdoors and its relationship with dry air indoors may therefore explain the seasonality of influenza (Lowen 2014). Humidification of a building is often coupled with airflow and ventilation, which have also been found to influence the rate of transmission of respiratory tract viruses (Pica 2012).

Dryness of the eye, skin and URT, as well as fatigue and headache, are used to describe the term 'sick building syndrome' (SBS) (Joshi 2008; Norbäck 2009). These complaints seem to be directly linked to the time spent in a particular building. According to Burge 2004, air-conditioned buildings generally have a higher prevalence of symptomatic workers than those which are naturally ventilated. Although affected individuals perceive the sensation of dryness in enclosed spaces, it has been shown that they are not exposed to dry air (Burge 2004).

Description of the intervention

The humidity level of indoor air can be increased by:

- Central or building-level interventions that increase air humidity with air conditioning systems or whole-house humidifiers;
- Local or room-level interventions, such as separate air humidifiers that can be activated on demand; or
- Other interventions, such as putting plants around the workplace or placing a container of water or wet cloths in proximity to a radiator or a heating system.

Technically, air humidity can be regulated with different types of humidifiers: steam humidifiers produce vapour by thermal evaporation; cold atomisers atomise water with a high-frequency ventilator; and the so-called ultrasound-atomisers create vapour by ultrasound waves (Fidler 1989). Re-circulated water can be used, except for steam humidifiers. Overall, these different types of humidifiers use different techniques to increase air humidity. When aiming to humidify indoor air, we also need to consider the effects of natural ventilation and seasonal variations, as well as the influence on other factors of the indoor environment.

How the intervention might work

In order to achieve the recommended level of RH indoors and to prevent consequent dryness and irritation symptoms, workplaces and schools are being artificially humidified in some countries. There is, however, currently no clear evidence to advocate indoor air humidification.

The use of air humidifiers is often suggested to decrease the symptoms of dryness and irritation attributed to heating during winter, such as dry lips or eyes. This is a current opinion, but it has not been supported by all epidemiological and laboratory studies.

Various studies, predominantly conducted under controlled laboratory conditions, have evaluated the subjective symptoms related to different humidity levels, including objectively-assessed signs and measurements of physiological parameters. Exposure to dry air may lead to ocular dryness due to deficient tear secretion and altered tear film (Lang 2014). According to Pfluger 2013, independent studies have shown that exposure to dry air causes deterioration in the quality and stability of the tear film of the eyes. These changes consequently result in an increase in eye blink frequency, which is one of the objective parameters measured in studies to assess the impact of dry air on ocular mucosa (Wolkoff 2008). Furthermore, there is a clear negative relationship between air humidity and evaporation (Pfluger 2013). A high evaporation rate reduces the quality of the tear film. These physiological changes in exposure to dry air may lead to

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ocular dryness symptoms which can be alleviated by an increase in the humidity level. There is experimental evidence that skin exposure to a low-humidity environment affects the superficial skin layers and decreases their water content (Egawa 2002). Increasing humidity levels can mitigate skin dryness. Wyon 2006 concludes that the water content of the skin measured with a corneometer was significantly higher at a humidity level of 35% than at 15%.

Dehydration of the respiratory mucous membrane causes an increase in viscosity of the mucosal fluid and, as a consequence, ciliary clearance becomes less effective (Munkholm 2014). Elderly people, especially those living in nursing homes and staying in hospitals, seem to be more affected, since they cannot regulate their water fluid balance by themselves.

When looking at experimental evidence, studies in young populations have found that low humidity did not influence the mucociliary clearance (Andersen 1972; Andersen 1974).

According to the findings of his experimental and clinical investigations, Guggenbichler 2007 concluded that mucociliary clearance seems to be more efficient when the humidity level is at least 30%. A relative humidity of 45% is even better for the self-cleaning function of the airways. Water mist produced by several types of humidifiers reduces mucus viscosity (Arundel 1986).

Mucociliary clearance protects against bacterial and viral infection (Sahin-Yilmaz 2011). Exposure to dry air results in the impairment of mucociliary clearance and leads to irritation of the mucous membrane, and as a consequence the susceptibility to infections may be increased. This hypothesis is controversial, since only a few studies with objective measurements have revealed pathophysiological damage to mucous membranes in the upper respiratory tract (URT) as a result of exposure to dry air. Alongside this direct effect of RH, the survival and transmission capacity of some respiratory viruses may be increased at a low level of absolute air humidity (Koep 2013; Makinen 2009; Shaman 2010). Overall, humidity and temperature affect host behaviour (more time spent indoors during winter time), host defences (airways mucosal function is optimal at core temperature and high humidity) (Williams 1996) and the stability and infectivity of the viruses. Furthermore, humidity also affects the respiratory droplet size, which in turn influences the time infectious particles remain airborne and can thus be inhaled.

Koep 2013 has shown that an increase in absolute humidity after humidification of the indoor environment resulted in a decreasing survival and transmission rate of the influenza virus. At a humidity level of more than 40% the influenza virus infectivity decayed (Tellier 2006). The surface of lipid-containing viruses is supposedly inactivated at high atmospheric humidity levels (Shaman 2010). At high RH, large water-laden droplets settle on the ground, which favours removal of infectious particles (Pica 2012).

During the recent pandemic of Covid-19 (coronavirus disease 2019), there has been a concern of potential exposure to SARS-Cov-2 (severe acute respiratory syndrome coronavirus type 2) via airborne droplets, aerosols and contaminated surfaces (fomites) in workplaces and schools.There are various studies on the influence of the ambient temperature and relative humidity of coronavirus persistence in the air and on surfaces (Biryukov 2020; Cheng 2020; Moriyama 2020; Otter 2016). Further research is needed to better understand these relationships.

Humidifiers and air conditioning systems can be a source of microbial spread, such as bacteria, fungi and amoebae, which can be disseminated into the air and cause health problems, such as infections and allergic reactions. In particular, facilities that are not sufficiently cleaned and maintained (Suva 2012) can be colonised with microorganisms. Furthermore, stagnant water in some humidifiers is linked to the so-called 'humidifier lung' (a type of hypersensitivity pneumonitis) and so-called 'humidifier fever' (a type of organic dust toxic syndrome).

In order to prevent pathogen growth, biocides are sometimes added to the water used for humidification. These substances may cause irritation or allergic reactions (Burge 2004) and even severe lung injuries, as presented in a number of papers (Won-Young 2017).

As stated by the World Health Organisation (WHO), RH between 60% and 90% is favourable to the growth of mould, which is dependent on the growth medium, the mould species, the length of time in high relative air humidity and the measure of growth (WHO 2009).

The results from experimental and epidemiological studies are partially consistent. Conflicting findings among studies can be explained by the use of different clinical scores to assess the outcomes, by diverse study populations being exposed to different ranges of RH, different exposure assessments and different study designs (Pfluger 2013). The variability of the study results may also be explained by the absence (in most laboratory studies) or the presence (in studies conducted under real-life conditions) of a wide range of different indoor air factors affecting skin and mucosal membranes. Some intervention studies have shown positive health effects of air humidification, like an increase in the percentage of people without dry and itchy skin (Hashiguchi 2008), alleviation of skin, pharyngeal, nasal dryness and congestion (Reinikainen 2003), significantly lower dryness symptom scores for skin and mucosa (Reinikainen 1992) and a reduction in the number and frequency of skin and mucosa symptoms (Ghaved 2005).

In summary, the effect of air humidity has been found to be dichotomised with a U-shaped association. Both low and high RH levels (above 60%) are associated with respiratory symptoms, highlighting that adverse health outcomes may occur at both extremes of the relative air humidity scale. Whereas the latter might result in dryness and irritation of the mucosa and the skin (Reinikainen 2003), the former might be related to infections associated with airborne microbial contamination (Wolkoff 2007).

See Figure 1 for an explanation of the association of indoor RH with exposure to adverse health-related factors by Alsmo 2014.

Why it is important to do this review

In Europe, recommendations on indoor relative air humidity differ between countries. In Switzerland, health authorities recommend at least 30% and a maximum of 65% RH to maintain a comfortable room climate (SECO 2011). However, there is no clear consensus on an optimal RH value, which may differ according to the working environment and the symptoms addressed. Concurrently, recommendations relating to the room temperature should be considered, since raising temperature leads to a decrease in RH. However, during heating periods, it is often not possible to achieve the recommended humidity range without active humidification.

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Further, acceptability of humidification may be of concern, because humidified air may be perceived to be of lower quality (Reinikainen 1997).

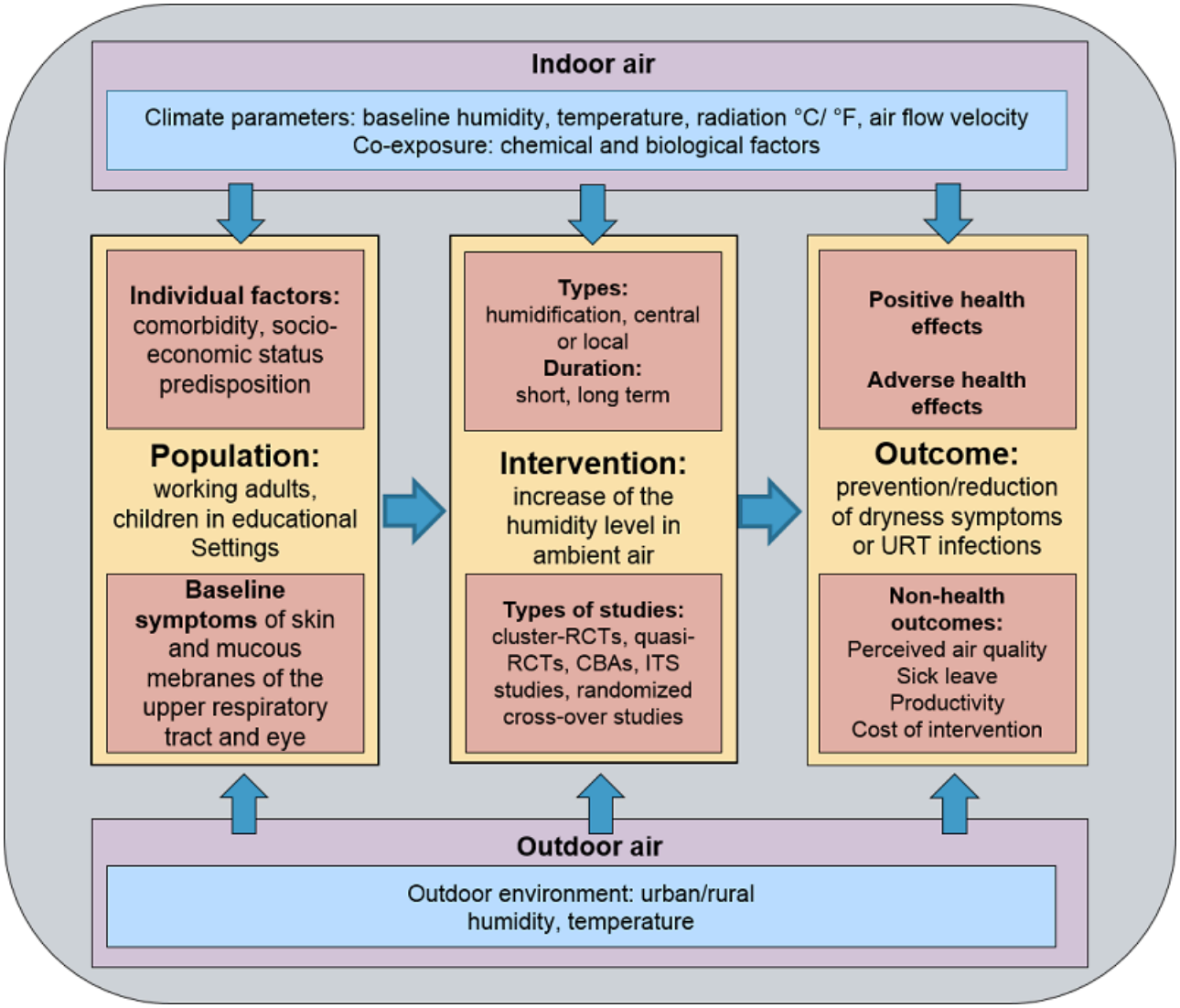
The question arises whether there is medical evidence behind the recommended RH range. In this context, Figure 1 is often shown, although its evidence base remains partially unknown. It seems questionable if it is generally possible to define a threshold at which physiological impairments occur, resulting in dryness and irritation symptoms of the skin and the mucous membranes that may consequently result in URT infections.

In countries with temperate or cold climates, air humidification is needed to reach an RH of 30% or more during the heating season. The use of air humidifiers is associated with significant costs, notably of electricity. However, if low humidity is associated with adverse health outcomes, this itself would generate direct and indirect costs, such as healthcare visits, absenteeism and reduced productivity.

A number of literature reviews have assessed the influence of humidity on human health (Arundel 1986; Green 1979; Guggenbichler 2007; Mendell 1993; Nagda 2001; Pfluger 2013; Pica 2012; Von Hahn 2007; Wolkoff 2007; Wolkoff 2008; Wolkoff 2018a; Wolkoff 2018b) whilst to date no systematic review on this topic has been published. Furthermore, we are not aware of any previous Cochrane Review that overlaps with this review. There is consequently an urgent need to compile the available evidence about health effects associated with air humidification amongst workers and in educational settings. Evidence has been accumulated over the past decades, and it is important to integrate evidence originating from epidemiological (field) studies. One challenge may be to include older evidence, generated decades ago, as well as to target different populations and settings, including children.

See Figure 2 for an explanation of the structure of our systematic review and relevant factors for the indoor environment.

Figure 2. Description of this Cochrane review. URT = upper respiratory tract.



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OBJECTIVES

To evaluate the effectiveness of interventions that increase indoor air humidity to prevent or reduce dryness symptoms of the eyes, the skin and the upper respiratory tract (URT) or URT infections at work and in educational settings.

METHODS

Criteria for considering studies for this review

Types of studies

Because we expected that the effect of indoor air humidification on symptoms would be rapid and would also disappear quickly after the intervention has stopped, we included cluster-randomised and cluster non-randomised cross-over studies.

Because humidification of the air is an intervention that usually takes place at a group level and is provided outside the clinical setting, randomisation at the individual level is scarcely possible.

We therefore included the following study types:

- Cluster-randomised and cluster non-randomised cross-over studies
- Controlled before-after studies, where the outcome is measured in both the intervention and the control group twice, once before and once after the intervention
- Interrupted time-series studies, where outcomes are measured at least three times before the intervention and three times after the intervention
- Controlled studies with parallel-group design (referred to as 'quasi-randomised studies, where the method of randomisation is not truly random, such as alternation' in the study protocol)

Types of participants

We included studies conducted in:

- Adults (18 years or older) working in buildings in any occupational sector and in any professional activity
- Children (preschool and school-age children in an educational setting (kindergarten/pre-school/nursery school, daycare centres, primary school)) and adolescents and young adults (up to a maximum age of 30) in an educational setting (college, high school/university)

If only a subset of relevant participants were included in a study, we included this study in the review if minimal data for this group could be extracted, including data about the intervention and the control group. We made it clear to the reader that the included data were only a subset of the study. We included both studies that could be considered preventive because participants were free of symptoms at the start of the study and had not requested any intervention, and studies that could be considered as remediation because participants complained of symptoms and had requested measures to improve their symptoms.

Types of interventions

We included studies evaluating the effectiveness of any type of intervention aiming to increase indoor air humidity. We categorised interventions as follows:

- Central or local indoor air humidification, i.e. air conditioning with humidification at building level (central), or stand-alone humidifying devices at room level (local)
- Other interventions, such as putting plants around the workplace

We included studies that compared the effects of indoor air humidification to no intervention or an alternative intervention.

Technically, air humidity could be regulated with different types of humidifiers: steam humidifiers produce vapour by thermal evaporation, cold atomisers atomise water with a high-frequency ventilator and the so-called ultrasound atomisers that create vapour by ultrasound waves (Fidler 1989).

To be included in this review, a study had to specify absolute or relative air humidity estimates of the intervention and the control areas or settings.

Types of outcome measures

We included studies that reported at least on one of our primary outcomes. We used data from additional outcomes reported in included studies if they were part of our secondary outcomes.

Primary outcomes

- Eye symptoms: self-reported eye symptoms, such as dry eyes, itching eyes, other physical symptoms of the eye, or objectively-measured outcomes such as the blinking rate
- Skin symptoms: self-reported skin symptoms such as a dry or itching skin or objectively-measured by e.g. a corneometer
- Upper respiratory tract (URT) symptoms and health conditions related to the quality of the mucosa, such as dry nose, nose symptoms, dry mouth, dry throat, pharyngeal dryness, and health impairments, such as rhinitis, rhinosinusitis, the common cold, sore throat, hoarseness, cough, throat inflammation or irritation, laryngitis, tonsillitis and otitis media, as self-reported or physician-diagnosed conditions or objectively-measured physiological signs (by means of acoustic rhinometry and nasal lavage)

Secondary outcomes

- Perceived air quality: air dryness, stuffy air, or a general assessment of air quality
- Sick leave or absence from work, school or education, measured as episodes or duration
- Task performance, productivity and attendance
- Costs of the intervention to increase indoor air humidity
- Adverse effects

Since effects of indoor air humidity on symptoms and infections might be observed after very short (days) as well as longer time periods (months), we intended to consider the following time scales:

- Up to one month;
- Between one month and three months (one season); and
- Longer than three months, covering several seasons.

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Exclusion criteria

This focus allowed us to detect specific seasonal patterns with indoor heating and non-heating periods that could also impact and contribute to dryness symptoms of the mucosa. We therefore excluded studies conducted in buildings situated in tropical and subtropical climates, to avoid mixed climatic patterns.

If data were available, we distinguished between allergic and non-allergic symptoms and illness, and excluded the former.

Search methods for identification of studies

Electronic searches

In order to identify all published and unpublished trials that could be considered eligible for inclusion in this review, we conducted a systematic literature search. We adapted the Ovid MEDLINE search strategy proposed in Appendix 1 to the additional databases: Embase (Appendix 2), CENTRAL (Appendix 3), PsycINFO (Appendix 4), Web of Science (Appendix 5), Scopus (Appendix 6), NIOSHTIC-2 (Appendix 7), HSELINE and CISDOC (Appendix 8). Sensitivity and precision of the search strategy had to be balanced. Our approach was based on sensitivity in order to be able to identify the relevant information. Our search included: a) the intervention and application methods used; b) targeted physiological systems and related symptoms, syndromes, infections and illness; c) effects on occupational or educational attendance; and d) workplace and educational settings in general and specific ones. We did not include the study design in our search strategy, as we expected different terminologies to be used during the past decades. We targeted this aspect within the screening process.

We included studies published as full text, abstracts as well as unpublished results, and we considered studies in all languages.

Our most recent searches were performed in 2020, and we conducted electronic searches within the following databases:

Health/biomedical

- Ovid MEDLINE with available non-indexed citations (1946 to 04 December 2020)
- Embase (1947 to 04 December 2020)
- CENTRAL (Cochrane Library up to 04 December 2020)
- PsycINFO (1806 to 04 December 2020)

We did not perform searches in PsycArticles or Psyndex.

Occupational safety and health

- NIOSHTIC-2 (from inception to 09 December 2020)
- HSELINE (from inception to 15 November 2016)
- CISDOC (from inception to 15 November 2016)
- In-house database of the Division of Occupational and Environmental Medicine, University of Zurich and University Hospital Zurich. This database results from a manual search in the Current Contents Life Sciences and the main journals of occupational and environmental health. It includes more than 50 journals related to occupational and environmental health, internal medicine, epidemiology, nephrology, and toxicology, and covers the period from 1986 to December 2013)

Interdisciplinary

- Web of Science (1988 to 04 December 2020)
- Scopus (1960 to 04 December 2020)

Searching other resources

We conducted a search of unpublished or ongoing trials in the WHO trials portal (www.who.int/ictrp/en/; up to 31 October 2019) as it collated data on trials from different countries including the USA CDC. In addition, we carefully checked the reference lists of included studies and of relevant reviews for additional eligible studies.

We searched publications from the websites of governmental agencies, such as the Centers for Disease Control, the National Institute for Occupational Safety and Health (NIOSH), and the American Society of Heating, Refrigerating and Air-Conditioning Engineers (ASHRAE).

We contacted occupational medicine and health specialists for additional references and grey literature. Where necessary, we asked for data from authors.

Data collection and analysis

Selection of studies

After removal of duplicates, two review authors (from KB, DI, MM, MS, MP or TR) independently screened titles and abstracts for inclusion. If necessary for the decision process, we read full texts, e.g.in cases where no abstracts were available. We resolved inconsistencies or disagreements through discussion and by consultation with other review authors (MP, MM, HD) where necessary. We carefully recorded the study selection process in order to complete the PRISMA flow diagram and the Characteristics of excluded studies table (Liberati 2009). Data included covered the study design, the participants, the type and technique of the intervention, the outcome measures and a final assessment for inclusion. We used Covidence for study screening and data extraction.

The screening and assessment of studies identified through systematic searches that were conducted by authors of this review was done by review authors who were not involved in the study.

Data extraction and management

We used a data collection form for study characteristics and outcome data, shown in Appendix 9, which had been piloted on two studies. Two review authors (KB, DI) extracted study characteristics from included studies. A second author (from HD, MM or TR) reviewed a random selection of data collection forms for accuracy and completeness.

We extracted the following study characteristics if available:

- General and context information: study identifier (ID), report ID, citation, year of publication, first author, contact author, affiliation, country, funding information, conflict of interest (declared and if appropriate, suspected (e.g. coworker of a relevant company)), environmental factors: season, urban or rural, type of the building, facility type.
- Methods: aim(s) and objective(s) of the study, study design, total study duration, study location, date of study, sample

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size considerations and power calculation, statistical analyses, withdrawals, and dealing with missing data.
- Participants: number of people included, selection procedure, participation, representativeness, inclusion criteria, exclusion criteria, study setting, professional activity, mean age or age range (median, percentiles), sex/gender, sociodemographic characteristics (e.g. smoking status, alcohol intake, socio-economic level, comorbidities, medication, atopy, family history).
- Interventions: types/description/content of intervention and comparison (including type of humidification), time period of intervention and comparison, duration of intervention and comparison, intensity of intervention and comparison, co-interventions, economic information. Assessment of air humidity level, control humidity level, recorded outdoor and indoor climatic parameters (e.g. temperature).
- Outcomes: definition/criteria and description of primary and secondary outcomes specified and collected, and at which time points reported or measured or both, source of outcome criteria, person measuring/reporting, outcome measurement (subjective: self-reported questionnaire (scales), interview (explanation to the participants), objective: physiologic measurements), severity of condition, diagnostic criteria if applicable, validation of outcome tools.
- Results: humidity effects (self-reported, results of scales and/or measured by physiological tests), adjusting for potential confounders.

Two review authors (from KB, DI or KB, TR) independently extracted outcome data from included studies. We noted in the Characteristics of included studies table if outcome data were not reported in a usable way. We resolved disagreements by consensus or by involving a third review author (from HD, MM, MS, MP, TR). One review author (from KB, DI, TR) transferred data into Covidence and then transferred them to the Review Manager 5 (RevMan 2020) file. We double-checked that data were entered correctly by comparing the data presented in the systematic review with the study reports. A second review author (from HD, MM, TR) spot-checked study characteristics for accuracy against the trial report. Following the decision to include studies in any language, we asked a native speaker to provide translations in case our author team was not proficient.

Assessment of risk of bias in included studies

Following pilot-testing to calibrate the assessments by KB, TR, DI, HD, MM, MP, MS, two review authors (from KB, DI or TR) independently assessed the risks of bias of all included studies. We resolved disagreements through discussion and consulted another author (from MM, MS, MP, HD) where necessary.

We used the Cochrane standard risk of bias (RoB) tool to assess the risks of bias in controlled studies.

We used the following items to assess the risk of bias in randomised controlled studies:

- Sequence generation
- Allocation concealment
- Blinding of participants or organisations if applicable, and outcome assessors
- Incomplete outcome data
- Selective outcome reporting
- Control for confounders

We have decided to use an additional item: 'Other source of bias'.

We assessed non-randomised controlled studies according to the following items:

- Blinding of participants or organisations if applicable, and outcome assessors
- Incomplete outcome data
- Selective outcome reporting
- Other source of bias
- Control for confounders

In the case that self-reported questionnaires were used in original studies, judgement on blinding of participants or organisations, and outcome assessors is not applicable.

For cross-over studies, we additionally applied the questions suggested for assessing the risk of bias from the *Cochrane Handbook for Systematic Reviews of Interventions* (Chapter 23):

- Was use of a cross-over design appropriate?
- Is it clear that the order of receiving treatments was randomised?
- Can it be assumed that the trial was not biased from carry-over effects?
- Are unbiased data available?

For each of these items, we provided one of the following summary assessments:

- Low risk of bias: plausible bias unlikely to alter the results.
- Unclear risk of bias: plausible bias that raises some doubt about the results.
- High risk of bias: plausible bias that seriously weakens our confidence in the results.

To judge risk of bias in randomised controlled studies as well as interrupted time series, we used the criteria proposed by EPOC 2015, as well as criteria from the *Cochrane Handbook.* For the additional item 'control for confounders', we first judged if there were important differences between groups prior to the intervention according to predefined confounders. If yes, we assessed whether these relevant confounders were controlled by means of study design (e.g. randomisation, restriction, matching) or as part of data analysis (e.g. stratification, statistical modelling). We considered the risk of bias to be low if there were no important differences between groups or if 60% or more of the relevant confounders were controlled in the assessed study. Otherwise, we classified the domain as 'high risk of bias'. We applied a rating of 'unclear risk' if the information was insufficient or lacking. The relevant confounders that we considered for this review included season (outdoor air), personal characteristics (e.g. age, gender), co-morbidities, atopic conditions and co-exposure in the workplace or in the educational setting.

We summarised the risk of bias within and across studies for the primary outcomes and for absenteeism.

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We considered confounding, blinding of participants and outcome assessors and incomplete outcome data to be key domains. We judged a study to have a high risk of bias when one or more key domains were rated as being at high risk of bias. Conversely, we judged a study to have a low risk of bias when we judged low risk of bias for all key domains. We summarised the risk of bias judgments across different studies for each of the domains listed.

We summarised and presented data in a risk of bias summary together with a risk of bias graph, as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Assessment of bias in conducting the systematic review

We conducted the review according to the published protocol and reported any deviations from it in the Differences between protocol and review section.

Measures of treatment effect

We analysed data separately from studies involving working populations and from studies involving children.

We reported the absolute or relative indoor air humidity as continuous variables.

We entered the outcome data for each study into the data tables in RevMan (RevMan 2020) to calculate the intervention effects. We used odds ratios (ORs) for dichotomous outcomes, mean differences (MDs) or standardised mean differences (SMDs) for continuous outcomes, and other types of data as reported by the authors of the studies. The reported outcome data were presented as percentages of participants affected and were transformed into the number of events. For the cross-over trials with dichotomous data, we computed the pooled logarithm of the OR (lnOR) based on the usual weighted average of trial lnOR where weights are the inverse of the lnOR variance. This method is described by Elbourne 2002. The lnORs were transformed to ORs in RevMan. Furthermore, we included statistical approaches available which re-expressed odds ratios as standardised mean differences (and vice versa), allowing dichotomous and continuous data to be pooled together. We did this as proposed in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) and after consultation with a biostatistician. In the case that multiple analyses were conducted in a study, review authors agreed on which of these were most relevant for the review.

Unit of analysis issues

If in future versions of this review we come across studies that use a cluster-randomised design and that report sufficient data to be included in the meta-analysis but do not make an allowance for the design effect, we will calculate the design effect based on a fairly large assumed intra-cluster correlation of 0.10, as described in the protocol (Byber 2016).

Dealing with missing data

We contacted investigators in order to verify key study characteristics and obtain missing numerical outcome data where possible (e.g. when a study was identified as abstract only). If in future updates of this review we come upon studies where this is not possible, and the missing data are thought to introduce serious bias, we will explore the impact of including such studies in the overall assessment of results by a sensitivity analysis.

We could not extract data from one study (Enomoto-Koshimizu 2002). The authors conducted a controlled before-after study, but they reported data for the intervention and control groups together. In order to gather details for the two groups separately, we contacted the authors. They made great efforts, but in the light of the elapsed time since the study was conducted, study data could not be extracted. Hence, we included this study, but study data could not be reported and assessed in this review.

The data from Gavhed 2005, a cross-over study design, were analysed as a parallel design. We asked the authors for primary data and could extract the effects for the first study period only. In a subsequent assessment we modelled all possible paired tables comparing questionnaires 2 and 3. The odds ratios were based on McNemar's test. We then chose the option close to the one calculated in the first study period and reported these data.

Similarly, if in future updates of this review we come upon studies where numerical outcome data, such as standard deviations or correlation coefficients are missing, and cannot be obtained from the authors, we will calculate them from other available statistics such as P values, according to the methods described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Assessment of heterogeneity

We assessed the clinical homogeneity of the results of included studies based on the similarity of the population, intervention, outcome and follow-up.

We considered populations as similar when they belong to the same subgroup (working adults or children in education).

We considered outcome measurements as similar enough to combine when:

- Subjective symptoms were assessed (stratified by symptom group: eye, skin, URT, combined), and when
- Objective measurements were performed (stratified by target organ: eye, skin, URT, combined).

We considered interventions as similar when they included indoor air humidification with:

- An air conditioning system (centrally-located system), or
- Local, office-based humidifiers, or
- Other measures to increase indoor air humidity, such as for instance putting plants around the workplace, or placing a container of water or wet cloths in proximity to a radiator or a heating system.

Following the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011), we used the I^2 statistic to measure heterogeneity among the trials in each analysis. As we pooled up to a maximum of two studies, after identification of substantial heterogeneity we could not explore possible causes by prespecified subgroup analysis. We narratively described the heterogeneity related to the different methods used. If future updates allow measuring of heterogeneity we will proceed and interpret as described in the protocol (Byber 2016).

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Assessment of reporting biases

We were unable to pool more than five trials in a single meta-analysis. Hence, we did not create a funnel plot to explore possible small-study biases.

Data synthesis

We present the characteristics and methods of included studies in the summary tables. We pooled data from studies with the same study design related to the same outcome. As the evidence was considered to be too heterogeneous to conduct meta-analyses, we synthesised evidence narratively.

Subgroup analysis and investigation of heterogeneity

If future versions of this review find a sufficient number of studies, we plan to undertake subgroup analyses by professional activity (office workers compared to non-office workers, e.g. healthcare workers in hospitals), and by gender as described in the protocol (Byber 2016).

Sensitivity analysis

We did not perform sensitivity analysis because there were not a sufficient number of studies. If future versions of this review find a sufficient number of studies, we will perform sensitivity analysis defined a priori to assess the robustness of our conclusions, as described in the protocol (Byber 2016).

Reaching conclusions

We based our conclusions only on findings from the quantitative or narrative synthesis of included studies for this review. We avoided making recommendations for practice based on more than just the evidence, such as values and available resources. Our implications for research suggest priorities for future research and outline what the remaining uncertainties are in the area.

Summary of findings and assessment of the certainty of the evidence

We created summary of findings tables using the outcomes of eye, skin and upper respiratory tract (URT) (nose) symptoms, measured as self-reported symptoms or conditions. We used the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to assess the quality of the body of evidence as it relates to the studies which contribute data to the meta-analyses for the prespecified outcomes. We used methods and recommendations described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). All decisions to down- or upgrade the quality of studies were justified using footnotes, and we added comments to support readers' understanding of the review decision where necessary.

We present the data for the two subgroups separately: working adults and children in education.

We graded the evidence yielded by each comparison as one of the following:

- High quality — further research is very unlikely to change our confidence in the estimate of effect;
- Moderate quality — further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate;
- Low quality — further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate;
- Very low quality — any estimate of effect is uncertain

RESULTS

Description of studies

See Figure 3, Characteristics of included studies, and Characteristics of excluded studies. No studies await classification, and no or ongoing studies were identified.

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Figure 3. Study flow diagram.

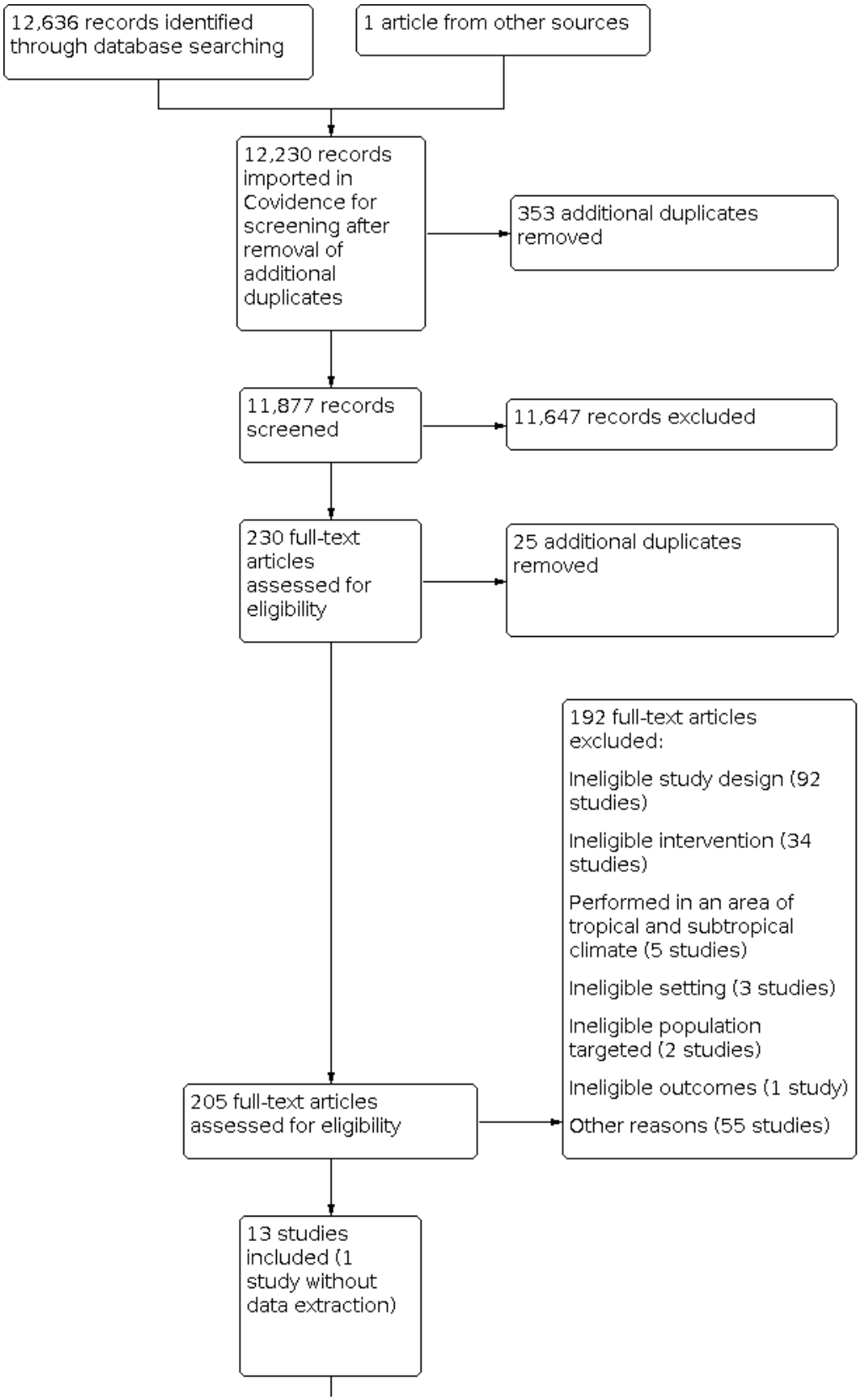

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Figure 3. (Continued)

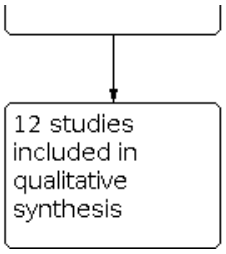

Figure 3

Results of the search

Based on our searches, we screened 12,230 references from electronic databases, and one study from other sources. The last search was run in December 2020, which updated previous searches in June 2016 and 2017 and August 2019. Based on title and abstract and, if unavailable, referring to the full text, a total of 230 references entered the full-text screening. This resulted in 13 studies to be included in the data extraction process and 192 studies were excluded after removing of duplicates (see Excluded studies). Handsearching of the reference lists did not yield additional studies.

Included studies

Study types

Occupational setting

We initially found eight studies conducted in the occupational setting and comprising office (three studies), factory (one study) and hospital workers (four studies). The data for one study (factory study) could not be extracted, as the data reported did not match our data extraction requirements (Enomoto-Koshimizu 2002).

Findings of seven studies were therefore reported, with three controlled before-after studies (Hashiguchi 2008; Norbäck 2000; Nordström 1994) and three controlled cross-over studies (Gavhed 2005; Reinikainen 2003; with one cluster-randomised cross-over design (Reinikainen 1992)). Here, the unit of randomisation was the office section (in two wings) of the building, randomly assigned at the beginning of the study (Reinikainen 1992). One study used a non-randomised controlled parallel-group design (Green 1981).

Educational setting

Five studies targeted an educational setting and were designed as non-randomised controlled parallel-group studies (Green 1975; Reiman 2018; Ritzel 1966; Sale 1972; Sataloff 1963).

Participants

Occupational setting

A total of 3422 office and hospital workers were reported as participants, of whom 3160 (92%) were included in the data analyses. No age-related information was given in the studies of Green 1981 and Reinikainen 2003. The ages of the study populations of Hashiguchi 2008; Norbäck 2000 and Nordström 1994 were as follows: Hashiguchi 2008: mean 40.1 years (± 10 standard deviation (SD)) in the intervention and mean 38.7 (± 11.5 SD) in the control group; Norbäck 2000: mean 39 (± 10 SD) in the intervention group and mean 44 (± 12 SD) in the control group; Nordström 1994: mean 40 years (± 13 SD) in the intervention and mean 38 (± 9 SD) in the control group (at the end of the study). Regarding Gavhed 2005 and Reinikainen 1992, a wider age range was described (see Characteristics of included studies). The population in the studies of Hashiguchi 2008; Norbäck 2000; and Nordström 1994 included predominantly women, whereas in Reinikainen 1992 there were almost half women and men. No gender-related information was presented in Gavhed 2005; Green 1981, and Reinikainen 2003.

Educational setting

Studies conducted in the educational setting included kindergarten and school children. No study mentioned the number of participants in the intervention and the control groups. Three studies did not report the number of individuals that entered the analyses (Green 1975; Ritzel 1966; Reiman 2018), but indicated the total school days per group (Ritzel 1966; Reiman 2018). The two remaining studies included 222 children in the intervention and 203 in the control group in the analyses (Sataloff 1963; Sale 1972). Sataloff 1963 provided no age information for the participants. Reiman 2018; Ritzel 1966 and Sale 1972 included children at preschool age (2 - 5, 4 - 6, 2½ - 6 years of age, respectively) and the pupils in the study of Green 1975 were aged between six and 14 years. None of the studies reported the gender distribution.

Sample size

Occupational setting

Three studies (Gavhed 2005; Norbäck 2000; Hashiguchi 2008) conducted in the occupational setting had very small sample sizes, below 50 participants (39, 32, 45) and a further three studies (Nordström 1994; Reinikainen 1992; Reinikainen 2003) reported fewer than 550 participants (104 (dynamic population), 290, 517). In Green 1981 the number of participants exceeded 2000 (2395), but with only 185 participants in the intervention group. The data for participants entering the data analysis are provided in Characteristics of included studies and the summary of findings tables. No sample size or power calculations were reported.

Educational setting

The number of study participants ranged between 116 and 515 (116, 232, 515, 162) (Reiman 2018; Ritzel 1966; Sale 1972; Sataloff 1963) and one study only reported that 12 schools with children of grades 1 to 8 were included (Green 1975). The number of participants entering the data analysis is provided in Characteristics of included

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studies and the summary of findings tables. No sample size or power calculations were reported.

Year of publication and geographical location

Occupational setting:

These studies were published between 1981 and 2008, with three articles before 2000 and four between 2000 and 2008. They were conducted in Canada (1), Finland (2), Japan (1), and Sweden (3).

Educational setting:

These articles were published between 1963 and 1975 and in 2018. The studies were performed in Canada (1), Switzerland (1), and the USA (3). The Swiss study was published in German.

Exposure and co-exposure

All the included studies assessed relative indoor air humidity as an indicator for dry air. In most studies, humidity was recorded continuously during the whole or parts of the study period. In one study (Gavhed 2005), the method of exposure assessment was not reported, and values of absolute humidity were mentioned in three studies (Reiman 2018; Reinikainen 2003; Hashiguchi 2008). The levels of relative humidity in the included studies varied considerably and the measured values were stated as a range, a mean value with or without standard deviation or as an unspecified value. The differences between humidity levels in the control and intervention groups were also heterogeneous. In most of the studies there were only small differences (less than 10% in humidity levels between humidified and un-humidified conditions) or the relative humidity in both conditions overlapped (Nordström 1994; Reinikainen 1992; Reinikainen 2003; Reiman 2018; Sale 1972; Sataloff 1963). The differences between humidity levels were analysed in one study and there were important differences in humidity levels between groups (Nordström 1994). An obvious difference (more than 10% difference in humidity levels) was reported in Gavhed 2005 and Reiman 2018. In all studies temperatures for both conditions were stated, and in 10 of the 12 studies the temperature levels were almost the same in the intervention and control setting (Gavhed 2005; Green 1975; Hashiguchi 2008; Norbäck 2000; Nordström 1994; Reiman 2018; Reinikainen 1992; Ritzel 1966; Sale 1972; Sataloff 1963). All studies were conducted during the heating period.

Occupational setting

In some occupational studies co-exposure was assessed. In Norbäck 2000 and Nordström 1994 volatile organic compounds were measured, and Reinikainen 2003 assessed the formaldehyde concentration. Nordström 1994 and Reinikainen 2003 additionally assessed particle concentration. Biological exposure to bacteria and fungal spores was measured in Reinikainen 2003 and Reinikainen 1992, and they also mentioned the ventilation rates. In all these studies the co-exposure seemed to be at low levels or within reference ranges and therefore an influence on developing or increasing dryness symptoms of the skin, eye and upper respiratory tract was not considered.

Educational setting

The most recent study conducted in the educational setting (Reiman 2018) assessed particles as co-exposure. The average concentration and size of particles in both conditions were measured, with 96% of the particles provided by humidification less than 1 µm. Humidified rooms showed a near doubling of both 1 - 4 µm, and > 4 µm air particles. There was a significant increase in the population of larger-sized particles (1 – 4 µm and > 4 µm) in the humidified versus control rooms. The other studies in the educational setting did not assess further co-exposure factors, except for temperature (Green 1975; Ritzel 1966; Sale 1972; Sataloff 1963).

Interventions and comparisons

Each study evaluated one intervention: the effect of indoor air humidification.

Intervention in the occupational setting

In four studies (Gavhed 2005; Green 1981; Norbäck 2000; Nordström 1994) central humidification was conducted, and in three trials (Hashiguchi 2008; Reinikainen 1992; Reinikainen 2003) local humidification. Mostly, steam humidifiers were used. No study was dealing with other interventions (such as putting plants around the workplace or placing a container of water or wet cloths in proximity to a radiator or a heating system).

Intervention in the educational setting

Most studies used only local humidification (Reiman 2018; Ritzel 1966; Sataloff 1963), and one study reported central humidification (Sale 1972). Various types, such as steam humidifiers, water atomizers, spray cold humidifiers, air washers and boilers were used in one study involving 12 different schools (Green 1975). No study was using other interventions.

Study duration

Occupational setting

In the occupational setting, the study duration ranged from six weeks (Norbäck 2000; Reinikainen 1992; Reinikainen 2003) to seven months (Green 1981), including eight weeks (Gavhed 2005), 12 weeks (Hashiguchi 2008) and five months (Nordström 1994). Green 1981 was conducted during three seasons. In order to investigate effects of indoor air humidity on symptoms and infections after very short (days) and longer time periods, we initially intended to establish three groups using three time scales (up to one month, between one and three months, longer than three months). Our data did not allow us to undertake such subgroup analyses.

Educational setting

In the educational setting, the study duration ranged from seven weeks (Reiman 2018) to six months (Green 1975). One study (Green 1975) presented additional data over a time period of 10 years.

Control

Occupational setting

Three studies (Gavhed 2005; Reinikainen 1992; Reinikainen 2003), all comprising office workers, described a cross-over design with a control group.

In the remaining four studies (Green 1981; Hashiguchi 2008; Norbäck 2000; Nordström 1994), the control group consisted of

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hospital employees. Green 1981 used two control groups, which worked in two different non-humidified hospitals. In this trial, the number of participants in the control site was disproportionate higher than in the intervention site (n = 650 in one control group, n = 1560 in the second control group versus 185 in the intervention group). The intervention group was stationed in the third hospital building, which was humidified. In Hashiguchi 2008 and Norbäck 2000, the control and intervention group participants worked in the same building, but in different stations and units, respectively. Nordström 1994 was conducted in four units in two hospitals. Two randomly-selected units, one per hospital, served as intervention and control sites, respectively.

Educational setting

Green 1975 was conducted in 12 primary schools. The control group included four non-humidified buildings and also non-humidified classes in another school. The control group of Ritzel 1966 were located in five non-humidified kindergartens, and the intervention group in five nearby kindergartens. In Sale 1972, there was no clear control group. For the purposes of the analysis, we combined a group consisting of children who were not exposed to humidified air with the group of children exposed to humidified air at home only. Reiman 2018 and Sataloff 1963 were conducted in one building, where some classes were humidified and others were not.

Outcomes and outcome assessment

Occupational setting

Primary outcomes

Primary outcomes were investigated in only six of the seven studies in the occupational setting (Gavhed 2005; Hashiguchi 2008; Norbäck 2000; Nordström 1994; Reinikainen 1992; Reinikainen 2003). Different outcome definitions were used for the assessment of symptoms related to the location. We established groups of similar symptoms according to the targeted location.

Almost all studies used self-administered questionnaires to survey symptoms. In Hashiguchi 2008 interviews with staff members about their symptoms were carried out once a week. In all studies, the symptoms and conditions were not assessed or diagnosed by a physician.

Two studies, (Norbäck 2000; Nordström 1994) referred to a standardised questionnaire for assessing symptoms, the MM-040-NA questionnaire. This validated instrument was developed at the Department of Occupational and Environmental Medicine, Örebro University Hospital in Sweden. As it was established as an exploratory questionnaire aiming to assess the sick building syndrome and no test statistics were mentioned, we left it unconsidered as a reference questionnaire for assessing work-related dryness symptoms. Furthermore, there were indications that Nordström 1994 and Norbäck 2000 used modified versions of MM-040-NA (different number of questions, different scoring).

The questionnaire used by Norbäck 2000 comprised seven questions about eye irritation (one question), airway symptoms (three questions) and dermal symptoms (three questions). The prevalence of participants with at least one weekly symptom of the eyes, airway, and skin was determined. Raw ORs were adjusted for age, sex, atopy, smoking habits, employment time, type of occupation, and psychosocial work climate. We entered the number of events into RevMan and computed unadjusted ORs for comparability. The prevalence of participants with at least one weekly symptom of the eyes, airway, and skin was calculated in Nordström 1994.

Reinikainen 1992 used one weekly symptom diary, in order to record symptoms in the humidified and non-humidified conditions. For data collection, Reinikainen 2003 used a structured diary which the participants filled in every afternoon. Strong symptoms were coded as 3 and no symptoms as 0. Gavhed 2005 used a self-administered questionnaire with a five-point Likert scale which was filled in once a week. For the analysis, we pooled the frequency responses 'seldom and never'; 'daily, many times a week', 'few times a week'. The data were transformed to ORs in RevMan.

In Norbäck 2000, there was an additional objective measurement of the outcomes (see below).

Eye symptoms

Five studies evaluated the effect of humidification on eye symptoms: three cross-over studies (one RCT: Reinikainen 1992 and two non-RCTs: Reinikainen 2003; Gavhed 2005) and two before-after studies (Nordström 1994; Norbäck 2000). Reinikainen 1992 investigated eye symptoms described as 'dryness, irritation and itching'. Reinikainen 2003 used the term 'eye dryness', without listing more details, and Gavhed 2005 additionally used the terms 'itching' and 'burning' for describing dry eyes. Nordström 1994 defined eye symptoms as 'itching, burning, or irritation in the eyes' and Norbäck 2000 evaluated eye symptoms summarised as 'burning, dry, sore eyes, eye redness, swollen eyelids'.

Objective measurements were applied in one study (Norbäck 2000). Clinical signs of the eyes were rated by assessing tear-film stability: “a standardised method, measuring the time (tear film breakup time) the subject could keep the eyes open without pain, when watching a fixed point at the wall”.

Skin symptoms

Two cluster non-randomised cross-over studies (Reinikainen 2003; Gavhed 2005) and two before-after studies (Hashiguchi 2008; Nordström 1994) investigated 'dry skin' as an outcome (Summary of findings 1). Norbäck 2000 evaluated the following skin symptoms: facial itching, facial rash, itching on the hands, rash on the hands, or eczema, whereas Reinikainen 1992 defined skin symptoms as dryness, irritation and itching.

Gavhed 2005 used a self-administered questionnaire assessing the frequency of 'dry skin' symptoms once a week on a five-point Likert scale. For the analysis, we pooled the answers 'seldom' and 'never'; 'daily', 'many times a week', 'few times a week'.

Hashiguchi 2008 used a four-point scale for reporting the frequency of dry and itchy skin: 'none', 'rarely', 'sometimes' and 'frequently'. We pooled the responses for 'rarely', 'sometimes' and 'frequently' for the purposes of our review, and treated the group 'none' separately.

Upper respiratory tract (URT) symptoms

Five studies evaluated the effect of humidification on upper respiratory tract symptoms: three cross-over studies (one RCT: Reinikainen 1992 and two non-RCTs: Reinikainen 2003;

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Gavhed 2005) and two before-after studies (Nordström 1994; Norbäck 2000). Different symptoms and location of the symptoms were investigated: Reinikainen 2003 and Reinikainen 1992 evaluated dry nose and pharyngeal dryness. Gavhed 2005 used 'dry mouth and throat' as an outcome with a five-point Likert scale for the frequency of symptoms ('never', 'seldom', 'daily', 'few times a week', 'many times a week'). For this review, the points 'seldom' and 'never' as well as 'daily', 'many times a week', 'few times a week' were put together. In Norbäck 2000 the throat symptoms were defined as dryness in the throat, sore throat, irritative cough (not shown), and nose symptoms such as runny nose, nasal itching, sneezing, or nasal obstruction. Nordström 1994 summarised the airway symptoms as irritated, stuffy or running nose, hoarse or dry throat, or cough.
In addition, Norbäck 2000 measured nasal signs by acoustic rhinometry. As parameters, the minimum cross-sectional areas (MCA) and the volumes of the nasal cavity (VOL) on each side of the nose were measured. The mean of three subsequent measurements was calculated. Furthermore, the concentrations of the following biomarkers: eosinophilic cationic protein (ECP), myeloperoxidase (MPO), albumin, and lysozyme were measured in the nasal lavage.

Upper respiratory tract (URT) infections

Symptoms of irritation, infection and allergy in the upper respiratory tract might overlap, which made their differentiation challenging. No studies investigated upper respiratory tract infections directly, which means that the diagnosis of this condition was not assessed as an outcome. Symptoms related to airway infection were investigated in Gavhed 2005; Norbäck 2000; Nordström 1994; Reinikainen 1992; Reinikainen 2003 (see above).

Of these studies, only Reinikainen 2003 mentioned an assessment of symptoms of upper respiratory infection. They stated that the applied diary comprised questions about symptoms of upper respiratory infection. These symptoms were analysed separately and no conclusion was drawn on the effect of indoor air humidification on upper airway infections.

Secondary outcomes

Perceived air quality

Perceived air quality was investigated in the following studies: Hashiguchi 2008; Norbäck 2000; Nordström 1994; Reinikainen 1992; Reinikainen 2003. Perception of dryness was assessed in five studies: one non-RCT cross-over study (Gavhed 2005), one RCT cross-over study (Reinikainen 1992) and three before-after studies (Hashiguchi 2008; Norbäck 2000; Nordström 1994). Perception of stuffiness was analysed in four studies: one non-RCT cross-over study (Reinikainen 2003), one RCT cross-over study (Reinikainen 1992) and two before-after studies (Norbäck 2000; Nordström 1994).

Nordström 1994 calculated changes in dryness perception and perception of stuffiness for each individual (range of the scale −2 to 2) at the beginning and end of the study period. The results were presented as incidence of decreased and increased perception. The changes after four months were presented, but the baseline data were unavailable. To achieve a comparison to Norbäck 2000, we recoded the reported levels of changes in participants' perceptions (i.e. increased, unchanged, decreased) into numerical variables (i.e. 0 = decreased, 1 = unchanged, 2 = increased). We transformed these data into means with standard deviations, and computed standardised mean differences in order to express the size of the intervention effect. The participants in Norbäck 2000 subjectively rated air quality (air dryness and stuffy air) on a scale between 0% to 100% at the beginning and the end of the study period in the humidified group and controls. We took the values at the study end in order to calculate the standardised mean difference. We pooled the computed values of Norbäck 2000 and Nordström 1994.

Gavhed 2005 used a self-administered questionnaire with a five-point frequency scale including 'too dry', 'slightly dry', 'neutral', 'slightly moist' and 'too moist'. For the analysis, we pooled the levels 'too dry, slightly dry', 'neutral' and 'slightly moist, 'too moist', respectively.

Hashiguchi 2008 used a seven-point frequency scale for reporting the perception of dryness, with 'very dry', 'dry', 'slightly dry', 'neutral', 'slightly damp', 'damp' and 'very damp'. We pooled the results into two categories. The responses to 'very dry', 'dry' and 'slightly dry' were than compared with those of 'neutral', 'slightly damp', 'damp' and 'very damp'.

Absence from work

In the occupational setting only Green 1981 assessed absenteeism.

Educational setting

Primary outcomes

No studies conducted in educational settings investigated our primary outcomes.

Secondary outcomes

Absence from school

Five studies investigated absenteeism, but using different outcome definitions. Some studies assessed absenteeism related to sickness in general or to upper respiratory tract illnesses, whereas others presented results for absenteeism in general without presenting reasons: Ritzel 1966 assessed absenteeism due to cold symptoms (total number of absence days). Reiman 2018 evaluated absenteeism due to sickness and influenza-like illness (with symptoms: fever + cough or fever + sore throat) and for all reasons (sickness, influenza-like illness and vacation). Green 1975 investigated total absenteeism and absenteeism due to illness, e.g. due to cold, in 12 public schools. As the data for absenteeism due to cold were only presented for a subsample, total absenteeism during the heating periods between 1960 and 1970 were presented here.

In Sale 1972, four participant groups were established: group I (humidification at school and at home), group II (humidification at school only), group III (humidification at home only) and group IV (no humidification). In order to assign an intervention group, we pooled groups I and II, and groups III and IV were considered as the control group. Retrospectively, paediatricians of the children in groups I to III reviewed their records about the frequency and severity of illnesses. The results for group IV remain unreported, and we therefore present here the average weekly absence due to all causes.

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Sataloff 1963 reported the average days of absence and the average number of illnesses of included children. As absences due to respiratory infections were not specifically assessed but only suggested, we refer to the average days of absence ("average number of school days missed") in this review.

Excluded studies

At the full-text screening, we excluded 192 studies as outlined in Figure 3, as they did not meet our inclusion criteria for study design (n = 92), intervention (n = 34), setting (n= 3), population targeted (n = 2), or outcome (n = 1). In total, five excluded studies were performed in tropical or subtropical climate zones and 55 were excluded for other reasons (e.g. reviews, book chapters, letters, studies dealing with other topics). The excluded studies with the reasons for exclusion are presented in the Characteristics of excluded studies. We removed the duplicates from the list of excluded studies. For some studies, there were several reasons for exclusion. We therefore decided to prioritise the exclusion criteria according to the sequence in the PICOS-scheme (participants, intervention, comparator, outcome, study design).

Risk of bias in included studies

See Figure 4 and Figure 5 for an overview of our judgement of the risk of bias by study. Since the figures contain the risk of bias assessments for randomised, non-randomised and cross-over studies, cells that were not applicable to a study design remain empty.

Figure 4. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

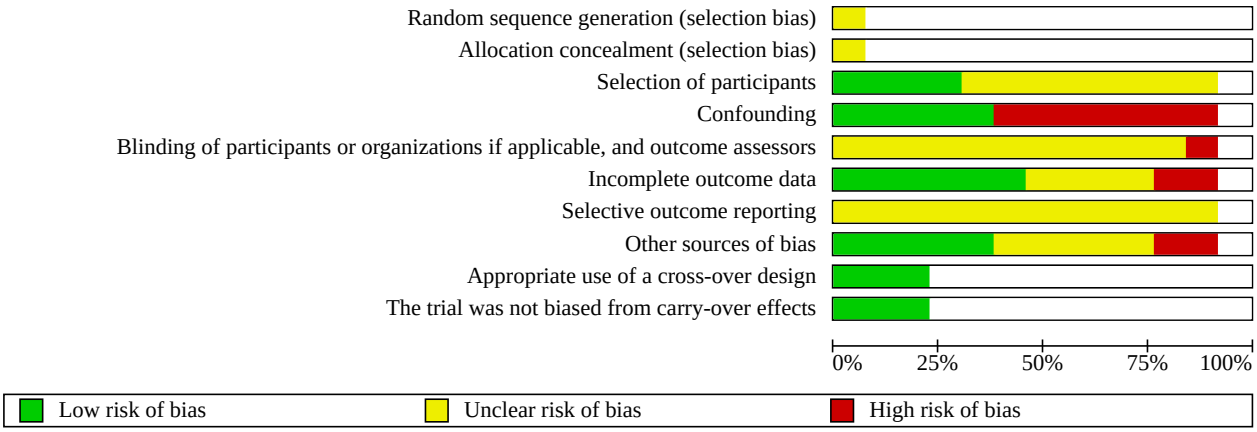

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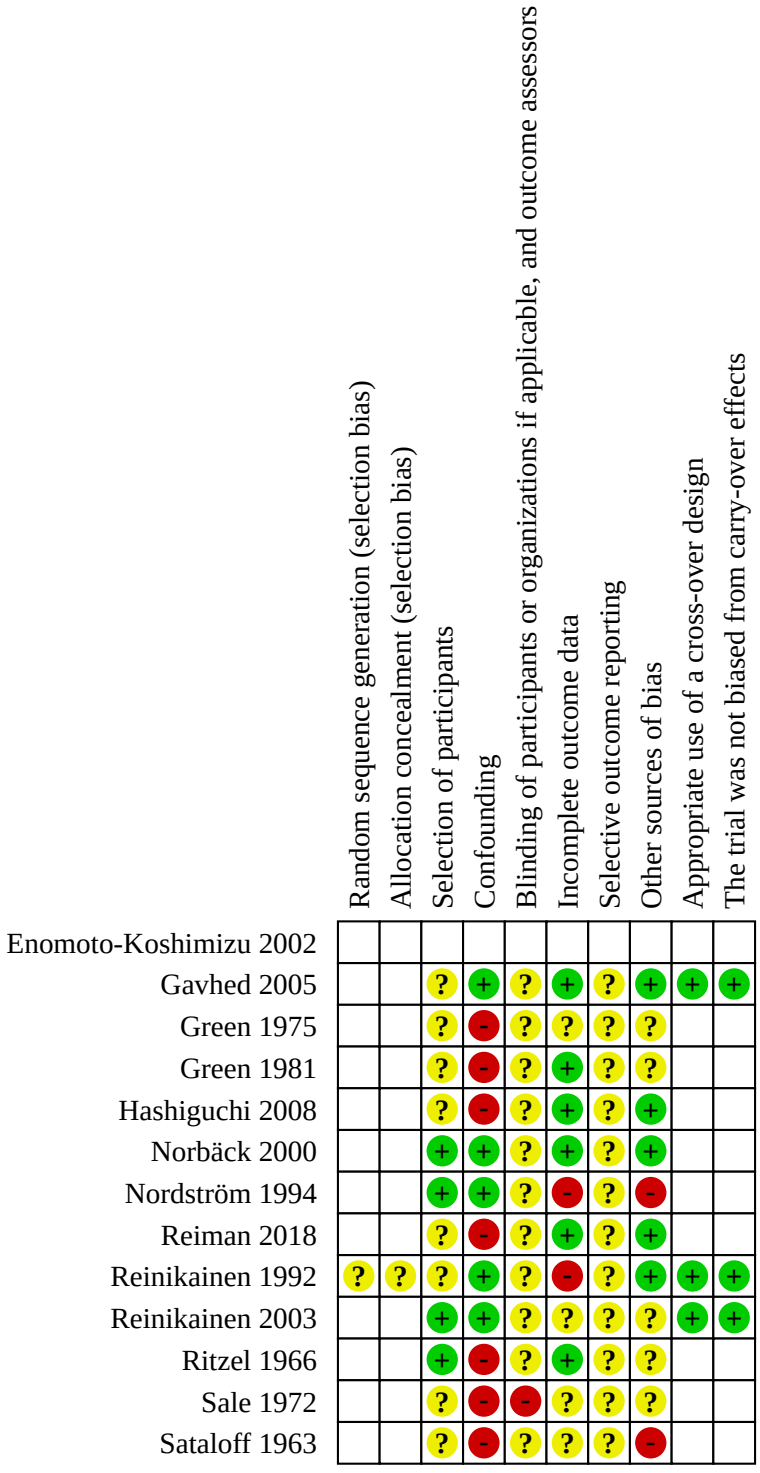
Figure 5. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



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We did not extract the data and did not conduct the risk of bias assessment for the study of Enomoto-Koshimizu 2002, as it presented results for the intervention and control groups together. As we could not analyse the results of this study, we did not assess its quality.

Allocation

As one study (Reinikainen 1992) was randomised at a group level, the bias criteria: random sequence generation and allocation concealment were assessed for this study only. However, the method of randomisation was not stated, and we therefore assessed it as having an unclear risk of bias. Allocation concealment was not reported and was therefore rated as unclear.

Blinding

We assessed blinding of participants or organisations and, if applicable, outcome assessors. In the case of self-reported questionnaires, blinding is not applicable for the outcome assessment tool. Due to lack of information on blinding, most of the studies had unclear risk of bias. For one study (Sale 1972), we rated the risk of performance bias as high, because parents of each child were informed in advance about the purpose of the study and the harmful effects of dry heated air with a booklet, and were encouraged to co-operate.

Incomplete outcome data

We judged the risk of attrition bias to be low in six studies (Gavhed 2005; Green 1981; Hashiguchi 2008; Norbäck 2000; Reiman 2018; Ritzel 1966) and unclear in four studies (Green 1975; Reinikainen 2003; Sale 1972; Sataloff 1963). As the percentage of withdrawals and dropouts exceeded 20% for short-term follow-up, Nordström 1994 was classified as having a high risk of bias. In Reinikainen 1992 missing outcome data were observed without presenting the reasons for it.

Selective reporting

Selective reporting was difficult to judge because none of the included studies had published a protocol. As we therefore had insufficient information to permit a judgement of low risk or high risk, we assigned all studies as having an unclear risk of bias. We did not find any indications in the included studies that prespecified outcomes were not reported.

Other potential sources of bias

As other potential sources of bias, we considered seasonality for the conduct of the study and exposure conditions before the start of the study. For five studies (Green 1975; Green 1981; Reinikainen 2003; Ritzel 1966; Sale 1972) we had insufficient information to assess this domain, and therefore classified these studies as having some concerns. Five studies appeared to be free of other sources of bias (Gavhed 2005; Hashiguchi 2008; Norbäck 2000; Reiman 2018; Reinikainen 1992). Furthermore, these trials were seasonally conducted during the heating period and in the study setting, the participants were exposed to the same indoor air condition before the start of the study. Because of the dynamic population in Nordström 1994, we judged it to be at high risk of bias. As due to technical problems there was virtually no difference between humidity levels in the control and the intervention groups, Sataloff 1963 was classified as having a high risk of bias.

Bias due to confounding

All studies were assessed for confounding. Age, gender, season, comorbidities, atopic conditions and co-exposures (especially temperature) were considered as relevant confounders. If at least 60% or more of the relevant confounders were considered in the statistical analysis and studies also used either restriction, matching/pre-stratification, and/or adjustment for confounding in the statistical models, we rated studies at low risk of bias. According to these criteria, Green 1975; Green 1981; Hashiguchi 2008; Reiman 2018; Ritzel 1966; Sale 1972; Sataloff 1963 were classified as high risk of bias. Due to a cross-over study design where each participant served as its own control, all three cross-over studies (Gavhed 2005; Reinikainen 1992; Reinikainen 2003) had low risk of bias. Norbäck 2000 and Nordström 1994 considered at least 60% of the relevant confounders in the statistical analysis and were therefore judged to have a low risk of bias.

Bias due to selection of participants into the study (non-randomised studies)

In the non-randomised studies we judged selection of participants due to the inclusion and exclusion criteria as reported in the articles. Most of the included studies had insufficient information to permit judgement of low risk or high risk of bias. Hence, the selection was classified as having some concerns. In Norbäck 2000; Nordström 1994; Reinikainen 2003; Ritzel 1966 there were no indications of bias resulting from inclusion and exclusion criteria.

Bias due to inappropriate use of the cross-over design and carry-over effects (cross-over studies)

All three cross-over studies (Gavhed 2005; Reinikainen 1992; Reinikainen 2003) were considered as having a low risk of bias.

Overall risk of bias by study

We judged studies to have a low overall risk of bias if we assessed them to have a low risk of bias in the following domains: confounding, blinding of participants, incomplete outcome data. This left us with no studies at low risk of bias, but all at either unclear (Gavhed 2005; Reinikainen 2003) or high risk of bias (Green 1975; Green 1981; Hashiguchi 2008; Norbäck 2000; Nordström 1994; Reiman 2018; Reinikainen 1992; Ritzel 1966; Sale 1972; Sataloff 1963).

Effects of interventions

See: **Summary of findings 1** Summary of findings table 'dryness symptoms'; **Summary of findings 2** Summary of findings table 'adverse effects' ; **Summary of findings 3** Summary of findings 'absenteeism'

See: Summary of findings 1; Summary of findings 2; Summary of findings 3.

There is one comparison: central or local indoor air humidification versus no humidification. Studies did not measure effects of other interventions. Due to the heterogeneity of follow-up times and differences in outcomes and outcome definitions, it was impossible to draw conclusions about the effects of humidification versus no humidification for different follow-up times. We are therefore uncertain about the effects, if any, of humidification on outcomes after a month, a season or several seasons.

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Primary outcomes

Outcome 'dry eye'

Summary of findings 1 outlines details about the effectiveness of humidification on dryness symptoms of the eye. This outcome was assessed in five studies (data analysed of 720 participants): three cross-over studies (one RCT: (Reinikainen 1992) and two non-RCTs: (Reinikainen 2003; Gavhed 2005)) and two before-after studies (Nordström 1994; Norbäck 2000).

The cluster randomised cross-over study Reinikainen 1992, conducted over six weeks, showed a significant reduction in eye dryness following indoor air humidification. The study reported a risk ratio for dry eye symptoms of 0.64 (95% CI 0.44 to 0.93), which indicated that people were 36% less likely to experience dryness symptoms during the humidified phase compared to the non-humidified phase. After the transformation of the results according to Elbourne 2002, the calculated OR was 0.54 (95% CI 0.37 to 0.79) (low-certainty evidence) (Analysis 1.1).

We combined the results of two cluster non-randomised cross-over trials (Reinikainen 2003; Gavhed 2005) and revealed non-significant positive effects on eye dryness following indoor air humidification over a study duration of six and eight weeks, respectively (OR 0.58, 95% CI 0.27 to 1.25) (low-certainty evidence) (Analysis 1.2). SImilarly, two before-after studies (Norbäck 2000; Nordström 1994) showed a non-significant positive effect of indoor air humidification on dry-eye symptoms over a study period of six weeks and four months, respectively (OR 0.57, 95% CI 0.23 to 1.41) (very low-certainty evidence) (Analysis 1.3).

In the before-after study of Norbäck 2000, the tear breakup times were similar in both the intervention and control groups (Analysis 1.5).

Outcome 'dry skin'

This outcome was investigated in four trials (two cluster non-RCT cross-over and two before-after studies) (data of 528 participants entered analysis). Gavhed 2005 (cluster non-RCT cross-over study) showed a significant effect of humidification on dryness of the skin: OR 0.43 (95% CI 0.19 to 0.96). In Reinikainen 2003, humidification decreased skin dryness, but the result was not statistical significant: OR 0.89 (95% CI 0.52 to 1.51). Both these cross-over studies showed a non-significant alleviation of skin dryness following indoor air humidification over a study period of one to three months: OR 0.66 (95% CI 0.33 to 1.32) (low-certainty evidence) (Analysis 1.6). One before-after study yielded a positive effect of indoor air humidification on skin dryness over a study period of 12 weeks (Hashiguchi 2008), whereas the other before-after study showed no effect following indoor air humidification over a study period of four months. The pooled analysis of these two trials provided no statistically significant result (OR 0.69, 95% CI 0.33 to 1.47) (Analysis 1.9).

Outcome 'skin symptoms'

Office workers in Reinikainen 1992 reported fewer skin symptoms of dryness, irritation or itching during the humidification phase than under non-humidified conditions: OR 0.59 (95% CI 0.39 to 0.89) (Analysis 1.7). This difference in dermal symptoms reached statistical significance.

Skin results for Norbäck 2000 are not included here, as the symptoms were not unequivocally considered as dryness symptoms (“facial itching, facial rash, itching on the hands, rash on the hands, or eczema”).

Outcome 'dry nose'

The results are summarised in Summary of findings 1. This outcome was reported in two cross-over studies (data analysed of 579 participants): one RCT: Reinikainen 1992 and one non-RCT: Reinikainen 2003. The cluster non-randomised cross-over study (Reinikainen 2003) reported an alleviation of nose dryness following indoor air humidification over a study period of six weeks. Hence, the result did not reach statistical significance: OR 0.87 (95% CI 0.53 to 1.42), and was of low-certainty evidence (Analysis 1.11). The cluster-randomised cross-over study (Reinikainen 1992) revealed no effect of indoor air humidification on nose dryness over a study period of six weeks: OR 1.08 (95% CI 0.73 to 1.60) (low-certainty evidence) (Analysis 1.12).

Outcome 'nose symptoms'

The outcome 'nose symptoms' in Norbäck 2000 comprised runny nose, nasal itching, sneezing or nasal obstruction. No effect of air humidification on nose symptoms was found (Analysis 1.13). Furthermore, no significant effects of humidification on any of the measured physiological signs during the study period of six weeks in exposed participants and controls were observed (Analysis 1.14).

Outcome 'airway symptoms'

Nordström 1994 investigated airway symptoms such as 'irritated, stuffy or running nose, hoarse or dry throat, or cough'. No significant differences between intervention and control participants were found (Analysis 1.15).

Outcome 'dry mouth and throat'

The five categories of the symptoms' frequency were pooled to two categories, as described earlier (Gavhed 2005). The air humidification had a positive effect on 'dry mouth and throat': OR 0.25 (95% CI 0.11 to 0.57) (Analysis 1.16). More specifically, under humidified conditions dry-mouth-and-throat-symptoms were less frequently reported than under non-humidified conditions.

Outcome 'pharyngeal dryness'

Humidification increased pharyngeal dryness: OR 1.15 (95% CI 0.63 to 2.11) in Reinikainen 2003 (Analysis 1.17). In Reinikainen 1992 the intervention led to an alleviation of pharyngeal irritation: OR 0.73 (95% CI 0.49 to 1.07) (Analysis 1.18). Neither result was statistically significant.

Secondary outcomes

Outcome 'perception of dryness'

Perception of dryness was assessed in five studies: one cluster non-RCT cross-over study (Gavhed 2005), one cluster RCT cross-over study (Reinikainen 1992) and three before-after studies (Hashiguchi 2008; Norbäck 2000; Nordström 1994).

Norbäck 2000 showed that air dryness was reduced after the six-week period of humidification (Analysis 1.21) and Nordström 1994 presented the same effect after four months (Analysis

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1.23 and Analysis 1.24). Following pooling of the data, the pooled standardised mean difference was −0.48 (CI 95% −3.49 to 2.54) (Analysis 1.25). The heterogeneity between the studies was considerable (I^2 value of 97%).

Hashiguchi 2008 found a statistically significant reduction in the perception of dryness following air humidification (Analysis 1.22). We pooled the two before-after studies of Norbäck 2000 and Hashiguchi 2008, and the result showed a statistically significant effect of air humidification on the perception of dryness: OR 0.05, CI 95% 0.01 to 0.22 (Analysis 1.26). The heterogeneity between the studies was considerable (I^2 value of 99%).

The only cluster-randomised cross-over study (Reinikainen 1992) reported that the sensation of dryness was significantly increased during the non-humidified phase compare with during humidification (Analysis 1.19). Similarly, Gavhed 2005 revealed a significant effect of humidification on the perception of dryness (Analysis 1.20).

Outcome 'absenteeism'

Green 1981 had investigated absenteeism in three hospitals during three winter seasons (October to April) in the years 1973 to 1974, 1974 to 1975, 1975 to 1976, and concluded that increasing the relative humidity had reduced absenteeism (pooled mean difference over three seasons −0.57 (CI 95% −0.61 to −0.53) (Analysis 1.33).

Five studies in the educational setting investigated effects of air humidification on absenteeism; see Summary of findings 3.

Ritzel 1966 showed a reduction in absenteeism due to cold symptoms in the humidified versus non-humidified kindergartens: OR 0.54, CI 95% 0.45 to 0.65 (Analysis 2.1). Sataloff 1963 revealed no reduction in the average days of absence under humidified conditions in a public school when compared to the non-humidified condition (Analysis 2.2). According to Sale 1972, the average weekly absence due to all causes was reduced in the humidified schools versus the non-humidified ones: OR 0.38, CI 95% 0.15 to 0.96 (Analysis 2.3).

The average 10-year absenteeism rate in the non-humidified schools was found to be 5.08%, and 4.63% in the humidified schools, which was reported to be statistically significant at a 95% confidence level (Green 1975) (Analysis 2.4).

The number of absences due to illness was the same in the humidified and the control rooms (Reiman 2018) (Analysis 2.5). The percentage of students with influenza-like illness absences was lower under the humidified versus the non-humidified condition (no statistical testing) (Analysis 2.6). These results were supported by the distribution of the positive influenza virus samples investigated by PCR under both conditions: in the humidified rooms, the genome copies per cubic meter of the influenza A virus were lower than in the non-humidified rooms.

Adverse events

Four studies investigated 'perception of stuffiness', which was considered to be an adverse effect of humidification (one cluster-RCT cross-over trial, one cluster non-RCT cross-over trial and two before-after studies) (Summary of findings 2). Both cross-over studies (Reinikainen 1992; Reinikainen 2003) showed that the perception of stuffiness was more common during humidification than in the non-humidified phase after six weeks (Analysis 1.27; Analysis 1.28) which was found to be statistically significant: OR 2.18, CI 95% 1.47 to 3.23 and OR 1.70, CI 95% 1.10 to 2.61. In both before-after studies (Norbäck 2000; Nordström 1994) no statistically significant effects of air humidification were observed for the perception of stuffy air after one and four months (pooled standardised mean difference 0.24 (−0.30 to 0.78)) (Analysis 1.29; Analysis 1.30; Analysis 1.31; Analysis 1.32).

DISCUSSION

Summary of main results

This systematic review aimed to assess the effectiveness of interventions in reducing or preventing dryness symptoms and upper respiratory infections following humidification of indoor air. Given the heterogeneity across study methods, types of interventions, outcome definitions, and outcome assessments, it was difficult to comprehensively interpret the studies. We did not perform sensitivity analysis because there was not a sufficient number of studies that could be combined. The outcome 'upper respiratory tract infections' was not investigated in the included studies.

The data from 12 studies were included, which were all conducted in high-income countries and were performed over a time span of more than 50 years. The effects of indoor air humidification were targeted to address adults and children and were therefore assessed in two settings, occupational and educational. Available studies covered workplaces such as offices and hospitals in the occupational setting, and kindergarten and schools in the educational setting.

This systematic review shows inconsistent findings, with low to very low-certainty evidence that indoor air humidification compared to no indoor air humidification in the workplace decreases dryness symptoms of the eye (Summary of findings 1), of the skin (Summary of findings 1) and of the upper respiratory tract (Summary of findings 1).

Furthermore, there is very low-certainty evidence about the causal relationship between increasing indoor air humidity and reduction in absenteeism (Summary of findings 3). Improvements in dryness symptoms and perception were not consistent between studies, and ranged from no effects to clearly positive effects. Perception of dryness, such as dry air, was assessed in five studies and was the only (secondary) outcome that was consistently reduced following air humidification across all studies.

Overall completeness and applicability of evidence

There are a wide range of factors contributing to indoor air quality and in turn, affecting the well-being and health of occupants. The indoor conditions vary considerably and are related to the complex interplay of exposure to ventilation characteristics, chemicals and microbial contamination. Further, the indoor air climate resulting from a combination of temperature, radiation temperature, air velocity and humidity differs between workplaces, as well as between schools. The conditions at one particular location might change continuously within a day, days, weeks and seasons. As well as these external factors, there are various individual factors contributing to the physiological response to the particular environmental conditions (Wolkoff 2018a; Wolkoff 2018b). This

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complexity poses a challenge for the evaluation of the effect of a single indoor factor, air humidification, on dryness symptoms and perception under field conditions. Hence, the appropriate method used for the assessment is of major significance.

The 12 studies described in this review covered the effectiveness of the single intervention we aimed to address, i.e. whether indoor air humidification reduces or prevents dryness symptoms of the eyes, the skin and the upper respiratory tract or URT infections, and included both settings, the occupational and the educational.

All studies were performed in high-income countries. On the one hand, this is not surprising, as we excluded subtropical and tropical climatic regions. On the other, this selection of studies from few countries might not paint the whole picture, as other geographic and cultural regions might contribute further perspectives.

Occupational setting

We presented data from seven studies. The analysed studies are related to two different working populations: office workers and hospital staff, who were exposed to humidifiers at their workplaces. Only one study (Green 1975) assessed the secondary outcome of absenteeism.

Most of the studies included (daytime) employees at the target workplace, without any restriction by age, gender or other factors. However, due to limited information about the personal characteristics (age, gender and other factors), a few studies with a limited number of participants and only two types of workplaces, the results have limited applicability to the general working population.

Although office workers and hospital staff present a major part of the indoor work force, we did not find studies including other types of workplaces, and might add more and different results if they existed. The various types of factory workers, workers in the food industry or in sales present different occupational sectors with their own environmental conditions. It is notable that one study targeting factory workers could not be extracted due to the method of data reporting.

All studies compared humidification using humidifiers to no use of humidifiers. No studies of other measures to potentially increase air humidity, such as putting plants around work places, met our inclusion criteria. Apart from the humidification technologies, more basic humidification measures might also be difficult to standardise and maintain.

The primary outcomes were at least partially targeted by the included studies, but sick leave, absenteeism and perceived air quality were the only secondary outcomes assessed. Task performance and productivity associated with indoor air humidity, as well as the costs of the intervention to increase indoor air humidity, might be important factors to be investigated. These might be key considerations to inform policy and practice and to evaluate and implement (new) measures.

Educational settings

In the educational setting we included five studies, which investigated young children aged between two and six years, and (mainly) primary school children. All of these studies considered only the secondary outcome 'absenteeism', including limited data on sick leave attributed to upper respiratory tract infections. As various outcome definitions were used, all studies were interpreted separately. Hence, conclusions about the applicability to the general child population cannot be made.

In one study, school children of grades 1 to 8 were considered, whereas all other studies included children up to grade 3 at maximum. No studies were therefore eligible which included older teenagers or young adults. This meant that we could not identify interventions targeting secondary or tertiary (higher) education.

Quality of the evidence

Overall, there was very low- to low-certainty evidence that humidification prevented or reduced dryness symptoms of the eyes, upper respiratory tract and skin. Furthermore, we judged the certainty of evidence as very low for absenteeism. We made this judgement due to a high risk of bias. Most of the included studies had substantial methodological shortcomings based on the Cochrane risk of bias tool that we used for the risk of bias assessment (Higgins 2011).

It is very challenging to study the effects of humidification on dryness symptoms, upper respiratory infections and absenteeism. On the one hand, there are many different environmental factors in the indoor air, with personal factors influencing the condition of the skin and mucosa. On the other hand, the symptoms caused by these factors are similar, and it is therefore difficult to link them causally. Hence, the use of appropriate study designs and adjustment for confounding factors are essential in order to assess the effectiveness of humidification on dryness symptoms. Only three studies had a controlled cross-over study design, where participants serve as their own control, reducing the influence of confounding covariates. Among these three trials, only one used randomisation, contributing to additionally controlling for confounding. Mostly, controlled before-after and non-randomised parallel-group controlled studies did not consider relevant confounders or did not adjust for them.

Except for four studies (two in each setting), most studies reported blinding of participants. Blinding of outcome assessors was not described.

Most studies evaluated a wide range of different symptoms, using different outcome definitions. Various self-administered questionnaires with different scoring systems were used to assess the effect of humidification. In two studies (Norbäck 2000; Nordström 1994), a modified version of a validated questionnaire for recording symptoms of the 'sick building syndrome' were used. As this questionnaire was exploratory and without test statistics, we could not consider it as a reference tool for assessing work-related dryness symptoms. The other studies did not use standardised questionnaires, so the outcome assessment in the included studies for primary outcomes was of unknown reliability, validity, and sensitivity, and was not objectively assessed. In only one study were the effects investigated by objective measurements of physiological signs.

Various outcome definitions were used for the secondary outcome 'absenteeism'. It was self-reported or reported by parents, and some studies assessed absenteeism attributed to sickness in general or to upper respiratory illnesses. Furthermore, studies

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presented results for absenteeism in general, without stating the reasons.

Most studies suffered from small sample sizes, which put them at risk of imprecision and lack of power, which could lead to under- or overestimation of intervention effects.

In order to evaluate the sustainability of the humidification impacts on dryness symptoms, we intended to distinguish three time scales for the study duration: up to one month, between one month and three months (one season) and longer than three months. As the number of studies was small and very heterogeneous, we dropped these subgroup analyses and could not evaluate the impact of exposure time on the symptoms.

This review addressed one type of intervention, which aimed to increase the indoor air humidity level. Central and local humidification using different devices were described in order to humidify the indoor air. Due to the limited number of studies and their considerable heterogeneity, we could not explore the effect of using different types of humidifiers on symptoms and absenteeism.

Potential biases in the review process

We performed searches in general medicine, health and interdisciplinary databases as well as in occupational ones, and consulted websites of appropriate societies and reference lists of included studies. We did not search for specific upper respiratory infectious disease entities, such as, for example, adenovirus or rhinovirus infections or influenza. We assumed we had covered specific infections by searching for upper respiratory symptoms in titles and abstracts. Furthermore, we combined the variables targeting humidity with the variables describing the indoor setting in the title and abstract screening. This prevented us from detecting an article combining e.g. influenza and humidity and not referring to the indoor setting. We found one such article by searching for influenza for other reasons (Reiman 2018).

One cross-over study (Gavhed 2005) was analysed and reported as a parallel-group design. Based on the data provided by the author, we calculated first the outcome results for the first phase of the cross-over study considering it as a parallel-group step (questionnaire two). We then considered all possible paired tables comparing the outcomes of the questionnaires two and three. We calculated odds ratios based on McNemar's test. We then chose the option as close as possible to the first phase result as our outcome result and entered it into Revman.

Based on the studies identified, we could not perform sensitivity analyses or assess a publication bias using funnel plots.

Agreements and disagreements with other studies or reviews

A variety of reviews have assessed the effect of indoor air humidity on human health (Arundel 1986; Green 1979; Guggenbichler 2007; Mendell 1993; Nagda 2001; Pfluger 2013; ; Von Hahn 2007; Wolkoff 2007; Wolkoff 2008; Wolkoff 2018a; Wolkoff 2018b). To the best of our knowledge, there were no other published systematic reviews on the effect of indoor air humidification on dryness symptoms and absenteeism. The previous published reviews were not conducted according to the requirements of a systematic review. Previous reviews included studies with different study designs and settings (e.g. chamber studies) (Arundel 1986; Mendell 1993; Nagda 2001; Pfluger 2013; Von Hahn 2007), and diverse populations including cabin crew personnel (Lindgren 2005), army recruits (Gelperin 1973), and factory workers (Milton 2000). The quality of the included studies was not assessed in most of these reviews, so that the evidence level was not stated. It is also important to note that most of them did not define a specific research question, but rather narratively summarised the literature on different effects of indoor air on health (Pfluger 2013; Von Hahn 2007; Wolkoff 2006; Wolkoff 2008; Wolkoff 2018b). For these reasons, a direct comparison between the findings of our review and the other reviews was not possible.

It is noteworthy that most of the reviews found positive effects of air humidification (Arundel 1986; Green 1979; Guggenbichler 2007; Nagda 2001; Pfluger 2013; Wolkoff 2006; Wolkoff 2008; Wolkoff 2018a; Wolkoff 2018b). Arundel 1986 suggested that relative humidity (RH) could influence the incidence of respiratory infections. The incidence of absenteeism or respiratory infections was found to be lower among people working or living in environments with mid-range RH (50% to 70%) as opposed to low or high RH. Green 1979 concluded that an increase in indoor relative humidity by humidification in winter significantly decreased the occurrence or absenteeism, or both, due to colds. It was recommended that winter indoor humidity should be kept as high as possible without causing building damage by condensation, but should not exceed 50% RH. Pfluger 2013 analysed the physiological effects of low indoor air humidity on mucous membranes, skin and perception of air humidity. The authors concluded that there is a need for a lower limit in the range of long-term indoor air humidity. Wolkoff 2006 and Wolkoff 2008 stated that the humidity level plays an important role in the development of eye irritation symptoms, which is related to its influence on the exposure factors in indoor environments. However, it is not clear whether low relative humidity is a direct cause of eye symptomatology. Dry-air conditions exacerbate the development of eye irritation symptoms, which can be explained by changes in physiological signs. An Increase in humidity level contributes to the decreasing perception of dry air and eye.

In contrast, Mendell 1993 showed inconsistent effects of increasing in air humidification on dryness symptoms, which is in agreement with our review. This review summarised the literature about the relationship between work-related non-specific symptoms and the variety of workplace environmental factors, and also discussed methodological issues important for the interpretation of epidemiologic studies. A total of 32 studies with different study design were included, whereas studies performed in laboratories were excluded. The included studies were categorised as experimental or observational. Of these, 12 trials investigated the influence of low humidity on work-related symptoms. In this review, the internal study validity was evaluated and interpreted. Mendell 1993 concluded that short-term humidification reduced symptoms by eliminating the negative health effects of excessively low humidity and that long-term humidification might reduce some symptoms, but more substantially, might increase the risk of symptoms from microbiologic contamination. More long-term studies were suggested for future research.

Von Hahn 2007 summarises various aspects of the effects of relative humidity on human health. This narrative review includes 29 studies with different study designs and assesses different outcomes, including smell perception, perception of

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comfort, incidence of colds, occurrence of 'sick building syndrome', symptoms of eye, upper respiratory tract and skin. The quality of the studies was not assessed. The studies included in this review showed contradictory findings. The assertion that a relative humidity of at least 30% is beneficial for a number of self-reported symptoms, incidence of colds and occurrence of 'sick building syndrome' could not be supported by the data.

The impacts of indoor plants on air quality and microclimate are highlighted in the systematic review by Han 2020, which summarised information from 88 studies. Primary effects like air purification were followed by secondary effects like increased humidity and reduced room temperature. In turn, the indoor environment was perceived as more comfortable. However, most of the results were mainly obtained in laboratory settings. Some studies were field experiments (18 studies), conducted at work places (hospitals, offices) and in classrooms. The exposure duration was between four hours and nine months. The effects of indoor plants on dryness symptoms were not investigated in the included studies.

AUTHORS' CONCLUSIONS

Implications for practice

The question of whether humidification of indoor air prevents or alleviates dryness symptoms of the skin and mucosal membranes and reduces upper respiratory tract infections in workplaces and in kindergarten or at schools is important from a public health and occupational health perspective. The prevention of symptoms and upper airway infections has a positive impact on well-being, performance and health. It therefore contributes, together with the reduction in absenteeism, to a positive socio-economic impact.

During the heating period, humidification is commonly used in current practice in some countries in many buildings. Various studies have shown that low humidity at different levels causes dryness symptoms of the eye, upper respiratory system and skin in the form of itching or burning, and humidification may alleviate these complaints. According to the results from the included studies in our review, it was not possible to define a comfort zone for the humidity level in indoor spaces in wintertime. Hence, we could not assess whether the current praxis for optimal humidity level is justified. The number of available studies was too small, and they were too heterogeneous. The investigated populations were exposed to different ranges of RH in the control and intervention groups.

It should be borne in mind that active humidification can lead to adverse events, as exemplified in many studies.

Implications for research

We found inconsistent and low to very low-certainty evidence that indoor air humidification in the workplace decreased dryness symptoms of the eye, upper respiratory tract and the skin. Studies investigating illness-related absenteeism from work or school could only be summarised narratively, due to different assessments of the outcomes. They were of very low-certainty evidence. However, they might be indicative of an intervention effect. Future studies involving larger sample sizes (according to the power calculations), assessing dryness symptoms more technically or rigorously defining absenteeism and controlling for potential confounders are therefore needed to determine whether increasing indoor air humidity can reduce or prevent dryness symptoms of the eyes, the skin, the upper respiratory tract (URT) or URT infections at work and in educational settings over time.

Outcomes should be better defined (according to medical definitions) and consistent definitions should be used in future studies. Using validated questionnaires for symptom assessment will contribute to better measurement accuracy, reliability and sensitivity. Researchers should conduct objective measurements of physiological changes in the upper respiratory airways, skin and eyes due to humidification, alongside subjective outcome assessments. This will enable better comparability of the studies and improve their informative value.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Enomoto-Koshimizu 2002

Study characteristics	
Methods	**Study design:** Controlled before-and-after study
Participants	Factory workers, manufacturing foodstuff use plastic and expanded polystyrene vessels and products, n = 104 Characteristics of participants: 55 men and 49 women No Information was available for age, smoking status, alcohol intake, socioeconomic level, comorbidities, medication, atopy, family history **Inclusion criteria:** employed workers of the production factory **Exclusion criteria:** N/A
Interventions	Category of intervention: local Intervention duration: 77 days Time period: 20 December 1995 to 19 March 1996 Type of humidification: Local water atomizer Humidification level (indoor relative humidity in %) for both conditions: between 16% and 45%

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Enomoto-Koshimizu 2002 *(Continued)*

	Temperature level (degrees Celsius): 20 - 26 ° in the non-humidified conditions, 19 - 25 ° in the humidified conditions Outdoor temperature: not measured *Exposure assessment (measurement of humidity)*: Room A has 5 locations where temperature and relative humidity were measured every 20 minutes by a data logger (thermo-recorder RS-10 manufactured by Tabai Espec Corporation)
Outcomes	Primary outcomes Eye symptoms: dry, itchy eyes; upper respiratory tract symptoms: common cold, coughing and sputum, sore throat, runny nose, dry nose, dry throat; skin symptoms: dry, itchy skin Secondary outcomes: perceived air quality: feeling or sensation of dryness
Identification	**Sponsorship source:** N/A **Country:** Japan **Setting:** Factory manufacturing foodstuff using plastic and expanded polystyrene vessels and products **Authors name:** Hikaru Enomoto-Koshimizu **Institution:** National Institute of Industrial Safety **Email:** enomoto_hikaru@isc.sagami-wu.ac.jp **Address:** Sagami Women's Univesity 2-1-1 Bunkyo, Minami-ku, Sagamihara, Kanagawa, 252-0383 JAPAN
Notes	**Study fulfilled inclusion criteria, but outcome reporting did not match the data extraction requirements of this review**

Gavhed 2005

Study characteristics	
Methods	**Study design:** Cluster non-randomised cross-over trial
Participants	Office workers in a military installation, n = 39 Characteristics of participants: 25 - 60 years old office workers. The computer-based office work was performed for 50 - 100% of the working day No information was available for: gender, smoking status, alcohol intake, socioeconomic level, comorbidities, medication, atopy, family history and employment **Inclusion criteria:** all office workers in the building **Exclusion criteria:** Not reported.
Interventions	**Intervention characteristics** Category of intervention: central humidification Intervention duration: 8 weeks

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Gavhed 2005 *(Continued)*

	Time period: January - February Type of humidification: N/A Humidification level (indoor relative humidity in %): HR 15% (± 5%) vs. HR 43% (± 3%) Temperature level (degrees Celsius): 20 - 22 ° in intervention and control conditions Outdoor temperature: between −15 °C and 0 °C *Exposure assessment (measurement of humidity)*: N/A
Outcomes	Primary outcomes: Eye symptoms: dry eyes; upper respiratory tract symptoms: running nose, dry mouth/throat; skin symptoms: red skin/heat sensation, itching/burning skin, dry lips, dry skin. Secondary outcomes: Perceived air quality: dryness of air, temperature, draught
Identification	**Sponsorship source:** No information **Country:** Sweden **Setting:** Office at a military installation in rock shelter, without windows with very clean air **Authors name:** Désirée Gavhed **Institution:** National Institute for Working Life, Thermal Climate Group, Stockholm, Sweden **Email:** desireegavhed@hotmail.com **Address:** National Institute for Working Life, Thermal Climate Group, Stockholm, Sweden
Notes	**Outcomes** Outcome assessment: Questionnaire (no information about the validation of the questionnaire, no further information about the outcome assessment tool) Conditions: The supplied air passed 3 filters of different porosities, before it was conditioned and pumped into the offices

Risk of bias

Bias	Authors' judgement	Support for judgement
Selection of participants	Unclear risk	Insufficient information to permit judgement
Confounding	Low risk	Due to the study design participants served as their own control
Blinding of participants or organizations if applicable, and outcome assessors	Unclear risk	Single-blind cross-over study
Incomplete outcome data	Low risk	No indications for missing data
Selective outcome reporting	Unclear risk	Insufficient information to permit judgement

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Gavhed 2005 *(Continued)*

Other sources of bias	Low risk	The intervention was seasonally conducted during the heating period. In the study setting, the participants were exposed to the same indoor air humidity conditions before the start of the study
Appropriate use of a cross-over design	Low risk	This study was a 2-period 2-treatment cross-over study
The trial was not biased from carry-over effects	Low risk	Washout period 1 week. Appropriate: at least 2 days

Green 1975

Study characteristics	
Methods	**Study design:** Non-randomised, parallel-group controlled study
Participants	12 primary schools in Saskatoon, Canada, grades 1 - 8, pupils n = N/A Characteristics of participants: Ages between 6 - 14 years. The pupils came from a slightly lower socioeconomic level. No information was available for: gender, comorbidities, medication, atopy, family history **Inclusion criteria:** Pupils from 12 primary schools (grades 1 - 8; ages 6 - 14) (Saskatoon) **Exclusion criteria:** N/A **Pretreatment:** N/A
Interventions	**Intervention characteristics** Category of intervention: probably local and central humidification Intervention duration: About 6 months. Time period: October 1960 to April 1961 (a total of 6 schools); October 1971 to April 1972 (a total of 12 schools); longitudinal data 1960 - 1971 Type of humidification: School number 1: steam radiators, air washer, School number 5: air washer, School number 6: humidifier and air washer, School number 7 humidified sprayed coil, School number 8: steam radiators, air washer, School number 9: boiler, sprayed coil humidifier, School number 11: gas furnace, air washer, School number 12: boilers with central ventilation. Humidification level (average indoor relative humidity in %): 1960/61: 23.1%, 1971/72: 24.1% in the non-humidified condition vs. 1960/61: 33.8%, 1971/72: 29.7% with humidification. (for the calculation, school number 7 was counted half in each condition) Temperature level (degrees Celsius): between 20 - 22.7 °C in both conditions Outdoor temperature: −17.2 °C *Exposure assessment (measurement of humidity)*: The original data were obtained with a relative humidity-temperature chart recorder. The recorder charts were replaced weekly and were calibrated at

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Green 1975 *(Continued)*

	the same time with an aspirating Psychrometer. Relative humidity for each school was averaged for the occupied period
Outcomes	Secondary outcomes: Total absenteeism %, absenteeism % colds, average total % absenteeism
Identification	**Sponsorship source:** The work was carried out with N.R.C. Grant-in- Aid A-878 **Country:** Canada **Setting:** Educational setting/ 12 Saskatoon public primary schools **Comments:** This paper presented data from 12 Saskatoon schools in the time period: 1960 - 61 and 1971 - 72 and data from 6 Halifax schools. Only data from Saskatoon Schools could be extracted **Authors name:** George H. Green **Institution:** Department of Mechanical Engineering, University of Saskatchewan, Saskatoon, Canada **Address:** Department of Mechanical Engineering, University of Saskatchewan, Saskatoon, Saskatchewan, Canada **Notes:** The author is a member of the American Society of Heating, Refrigerating and Air-Conditioning Engineers (ASHRAE)
Notes	**Interventions** Humidification 1960/61: School number 1,5,6 and 1971/72: School number 1,5,6,7,8,9,11,12. No humidification 1960/61: School number 2,3,4 and 1971/72: School number 2,3,4,7,10. School number 7: This was the only school, where pupils were exposed to both conditions: humidified and non-humidified air, but these data was not included in the longitudinal data reported. Total absenteeism was recorded and absenteeism due to illness was not obtainable

Risk of bias

Bias	Authors' judgement	Support for judgement
Selection of participants	Unclear risk	Selection of schools was not described
Confounding	High risk	Information on gender and co-morbidities was unavailable. Factors like temperature and socioeconomic levels were considered as possible causes for the observed decrease in absenteeism. The temperature was found to have no influence. The non-humidified schools were typically older, and their students came from a slightly lower socioeconomic level. However, the author stated that the analysis of variance showed that the age of the school building or the socio-economic level of the children had no influence on the results. Respective data were not presented
Blinding of participants or organizations if applicable, and outcome assessors	Unclear risk	The teachers were not informed about the reason for the enquiry and were asked to record the actual statement of the parent or child about the absenteeism. There is no indication that children and parents knew about the investigation. No information on blinding of outcome assessors
Incomplete outcome data	Unclear risk	No information about dropouts was reported.
Selective outcome reporting	Unclear risk	The study protocol was unavailable. It remained unclear whether the published reports included all outcomes

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Green 1975 *(Continued)*

Other sources of bias	Unclear risk	The intervention was seasonally conducted during the heating period. The participants were probably exposed to dry air before the implementation of the intervention. The author is a member of the ASHRAE

Green 1981

Study characteristics	
Methods	**Study design:** Non-randomised, parallel-group controlled study
Participants	3 hospitals with 2395 workers: 185 in the intervention (Hospital A), 650 in 1 control group (Hospital B) and 1560 in the second control group (Hospital C) Characteristics of participants: No information was available for age, gender, smoking status, alcohol intake, socioeconomic level, comorbidities, medication, atopy, family history, job category and employment **Inclusion criteria:** Hospital staff of 3 hospitals **Exclusion criteria:** N/A **Pre-treatment:** N/A
Interventions	**Intervention characteristics** Category of intervention: Central humidification Intervention duration: 3 seasons with a duration of 5 - 7 months each Time period: 3 winter seasons, October to April 1973 - 74, 1974 - 75, 1975 - 76 Type of humidification: N/A Humidification level (indoor relative humidity in %): Hospital A: 1973 - 74: mean 23.8%, 1974 - 75: mean 34.4%, 1975 - 76: mean 31.2% Hospital B: 1973 - 74: mean 15.8%, 1974 - 75: mean 18.8%, 1975 - 76: mean 20.2% Hospital C:1973 - 74: mean 20.3%, 1974 - 75: mean 19.1%, 1975 - 76: mean 21.9% Temperature level (degrees celsius) in the both conditions: Mean 24 °C, SD: 5 °C Outdoor temperature (degree Celsius): 1973 - 1974: −12.44 °C, 1974 - 1975: −9.66 °C; 1975 - 1976: −7.5 °C *Exposure assessment (measurement of humidity)*: Relative humidity and temperature were recorded continuously at a nursing station on each of the 6 floors for hospitals A and C, and on 5 floors for hospital B during 3 winter seasons. A portable temperature and humidity recorder with a 7-day chart was placed at each location. Relative humidity was shown to be approximately equal throughout all patient rooms and corridors of the hospital. The recorder was calibrated weekly with an aspirating psychrometer
Outcomes	Secondary outcome: Absenteeism
Identification	**Sponsorship source:** Canadian Medical and Biological Engineering Society, University Hospital of Saskatoon, University of Saskatchewan, City of Saskatoon **Country:** Canada **Setting:** 3 hospitals in Saskatchewan **Authors name:** George H. Green

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Green 1981 *(Continued)*

	Institution: Department of Mechanical Engineering University of Saskatchewan, Saskatoon, Saskatchewan, Canada **Address:** Department of Mechanical Engineering University of Saskatchewan, Saskatoon, Saskatchewan, Canada S7N OWO **Notes:** The author is a member of the American Society of Heating, Refrigerating and Air-Conditioning Engineers (ASHRAE)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Selection of participants	Unclear risk	Inclusion and exclusion criteria were not stated
Confounding	High risk	No information was available for age, gender, smoking status, alcohol intake, socioeconomic level, comorbidities, medication, atopy, family history, job category, and employment. No differences in temperatures between the hospitals during the study period were observed. Information on indoor parameters (e.g. VOCs: volative organic compounds) was lacking
Blinding of participants or organizations if applicable, and outcome assessors	Unclear risk	No information on blinding
Incomplete outcome data	Low risk	No indication of missing data
Selective outcome reporting	Unclear risk	A study protocol was unavailable
Other sources of bias	Unclear risk	Insufficient information to assess whether an important risk of bias or insufficient rationale or evidence that an identified problem would introduce bias exists

Hashiguchi 2008

Study characteristics

Methods	**Study design:** Controlled before-and-after study
Participants	Hospital workers n = 45 (15 in the intervention group and 30 in the control group) Characteristics of participants: Age in the intervention group: Mean ± SD: 40.1 years (± 10.0), age in the control group: Mean ± SD: 38.7 years (± 11.5), gender in the intervention group: 2 men, 13 women, gender in the control group: 5 men, 25 women, job category: nurses and nurses' aides. No information was available for: smoking status, alcohol intake, socio-economic level, comorbidities, medication, atopy, family history or employment **Dates:** 30 November to 22 February; in total 12 weeks. Humidifiers were introduced in some rooms on the 25 January, 8 weeks after starting the survey Humidification (nurse station H) **Inclusion criteria:** N/A

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Hashiguchi 2008 *(Continued)*

	Exclusion criteria: N/A
Interventions	**Intervention characteristics** Category of intervention: Local humidification Intervention duration: 12 weeks, analysis period: 8 weeks Time period: 30 November to 22 February (year of the intervention unknown) Type of humidification: steam humidifier Humidification level (indoor relative humidity in %): The means (SD) of relative humidity in the intervention group before and after were 32.8 (6.6)% and 43.9 (7.2)%, and the means (SD) of relative humidity in the control group before and after were 33.1 (6.6)% and 36.9 (7.5)%, respectively Temperature level (degrees Celsius): 23 to 25 ° in both conditions Outdoor temperature: 0 – 12 °C *Exposure assessment (measurement of humidity)*: The temperature and relative humidity at the nurse stations on each of the 3 floors were measured every 30 mins throughout the test period by data loggers (Thermo Recorder RS-10, RS-11; Tabai Espec Co.,Ltd., Osaka, Japan) RH was measured at 1 point in each nurse station
Outcomes	Primary outcome: skin symptoms: dry and itchy skin Secondary outcome: perceived air quality: sensation of dry air
Identification	**Sponsorship source:** Grant-in Aid for the 21st Century COE program, and Grant-in Aid for the scientific research (no.16107006) from the Japan Society for the Promotion of Science **Country:** Japan **Setting:** Hospital in the Southern part of Fukuoka, Japan **Author name:** Nobuko Hashiguchi **Institution:** Department of Ergonomics, Faculty of Design, Kyushu University, 4-9-1 Shiobaru, Minami-ku, Fukuoka 815-8540, Japan **Email:** n-hashi@design.kyushu-u.ac.jp **Address:** Department of Ergonomics, Faculty of Design, Kyushu University, 4-9-1 Shiobaru, Minami-ku, Fukuoka 815-8540, Japan
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Selection of participants	Unclear risk	Inclusion and exclusion criteria were not stated
Confounding	High risk	There was only scarce information on demographic characteristics of the control and intervention groups (e.g. age, gender). Table 1: It remained unclear, whether the differences by age and gender were important. The temperatures in the rooms of both conditions were reported. No distinct differences in tem-

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Hashiguchi 2008 *(Continued)*

		perature were found in either sickrooms or nurse stations before and after installing humidifiers
Blinding of participants or organizations if applicable, and outcome assessors	Unclear risk	No information on blinding
Incomplete outcome data	Low risk	There were no missing outcome data
Selective outcome reporting	Unclear risk	Insufficient information to permit judgement
Other sources of bias	Low risk	The study was considered to be free of other sources of bias. There was no indication of other source of biases, which were not stated in the domain list. The intervention was seasonally conducted during the heating period. In the study setting, the participants were exposed to the same indoor air humidity conditions before the start of the study

Norbäck 2000

Study characteristics	
Methods	**Study design:** Controlled before-and-after study
Participants	Day shift hospital workers, n = 26: 14 in the intervention group and 12 in the control group Characteristics of participants: age, mean (SD): 39 (9) years in the intervention group, 44 (12) years in the control group, gender: 100% female in the intervention group, 92% female in the control group, smoking status: 36% current tobacco smokers, 14% ex-smokers in the intervention group, 33% current tobacco smokers, 25% ex-smokers in the control group. Medication: 18% current asthma medication in the intervention group, 11% current asthma medication in the control group, atopy: 50% with atopy in the intervention group, 36% with atopy in the control group. No information was available about: alcohol intake, socio-economic level, comorbidities, family history, job category **Inclusion criteria:** all daytime staff employed in the 2 units (n = 32). People having a current infection, fever or were on vacation in the last 7 days were asked to come to a follow-up investigation 2 weeks later **Exclusion criteria:** not reported **Pre-treatment:** No significant differences between the groups (intervention and control group) by Fisher`s exact test (for gender, current tobacco smoking, ex-smoking, atopy, current asthma medication)
Interventions	**Intervention characteristics** Category of intervention: Central humidification Intervention duration: 6 weeks Time period: January - March 1997 (6 weeks between January and March 1997) Type of humidification: steam air humidification Humidification level (indoor relative humidity in %): 43% vs 35% Temperature level (degrees Celsius): The mean room temperature (22.5 °C) was similar in both units, before and after humidification

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Norbäck 2000 *(Continued)*

	Outdoor temperature: N/A Other exposure parameters: TVOC (total volative organic compounds) concentration: 26 µg/m^3 in the intervention group, TVOC concentration: 45 µg/m^3 in the control group *Exposure assessment (measurement of humidity)*: relative air humidity was monitored by a thermohygrograph ((CASELLA T 9420, Livingston UK Ltd, UK) over a 2-week period in each unit
Outcomes	Primary outcomes: eye symptoms: at least 1 symptom like "burning, dry, sore eyes, eye redness, swollen eyelids"; upper respiratory tract symptoms: at least 1 nasal symptoms: "runny nose, nasal itching, sneezing, or nasal obstruction", at least 1 throat symptom like "dryness in the throat, sore throat, or irritative cough" skin symptoms: at least 1 dermal symptom like "facial itching, facial rash, itching on the hands, rash on the hands, or eczema". Secondary outcomes: perceived air quality: stuffy air, air dryness, dustiness. Objective measurements: acoustic rhinometry: MCA1 Minimum cross-sectional area, MCA2 Minimum cross-sectional area, VOL1 volume of nasal cavity, VOL2 volume of nasal cavity; nasal lavage: ECP eosinophilic cationic protein, MPO myeloperoxidase, Lysosyme, Albumin; breakup time
Identification	**Sponsorship source:** This study was supported by grants from the Swedish Building Research Institute and the Swedish Foundation for Health Care Sciences and Allergy Research. **Country:** Sweden **Setting:** Geriatric hospital **Author name:** Dan Norbäck **Institution:** Department of Medical Sciences/Occupational and Environmental Medicine, Uppsala University Hospital, Uppsala, Sweden **Email:** dan.norback@medsci.uu.se **Address:** Department of Medical Sciences/Occupational and Environmental Medicine, Uppsala University Hospital, S-751 85 Uppsala Sweden
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Selection of participants	Low risk	The study population consisted of all daytime staff employed in the 2 units (N = 32). There was no indication of bias resulting from inclusion criteria
Confounding	Low risk	The study was conducted in winter. No significant differences between the groups, by Fisher's exact test for gender, smoking, atopy status, current asthma medication were stated. Mean age was 39 years (SD = 9) in the exposed group, and 44 years (SD = 12) in the control group. Important confounders were assessed in the study and at least 60% or more of the relevant confounders were considered in the statistical analysis
Blinding of participants or organizations if applica-	Unclear risk	No information was given to participants on which unit was humidified and the results of the measurements or the questionnaires were not reported to

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Norbäck 2000 *(Continued)*

ble, and outcome assessors		the participants before the completion of the study. No information on blinding of outcome assessors was reported
Incomplete outcome data	Low risk	In total, 26 of 32 participants attended on both occasions and completed all assessments (81%)
Selective outcome reporting	Unclear risk	A study protocol was unavailable. Insufficient information to permit judgement
Other sources of bias	Low risk	The intervention was seasonally conducted during the heating period. In the study setting; the participants were exposed to the same indoor air humidity conditions before the start of the study

Nordström 1994

Study characteristics	
Methods	**Study design:** Controlled before-and-after study
Participants	Hospital workers, n = 104 (dynamic population). 56 people participated in both studies. The statistical analysis was conducted with 42 people in the control and 42 people in the intervention group at the beginning of the study (December 1991) and for 38 hospital workers in the control and 38 workers in the intervention group at the end of the study (April 1992) Characteristics of participants: Age mean (SD): December 1991: 39 years (12), April 1992 40 years (13) in the intervention group; December 1991: 36 years (10), April 1992 38 years (9) in the control group Gender: December 1991: 100% female, April 1992: 100% female in the intervention group; December 1991: 93% female, April 1992: 92% female in the control group Smoking status: current tobacco smokers: December 1991: 45% , April 1992: 35% in the intervention group; December 1991: 39%, April: 1992 50% in the control group Job category: nurse: December 1991: 12% , April 1992: 11%; auxiliary nurse: December 1991: 81% , April 1992: 79%, other job category: December 1991: 7%, April 1992: 10% in the intervention group; December 1991: 12% , April 1992: 13%; auxiliary nurse: December 1991: 79%, April 1992: 72%, other job category: December 1991: 9%, April 1992: 15% in the control group. Duration of employment: December 1991: 4.2 years (4.0) , April 1992: 3.9 years (2.8) in the intervention group; December 1991: 4.3 years (2.6) , April 1992: 5.6 years (5.7) in the control group No information was available for: alcohol intake, socio-economic level, comorbidities, medication, atopy and family history **Inclusion criteria:** daytime staff from the 4 newest and best-ventilated hospital units situated in 2 hospitals. Staff had to work in the same unit. Selection procedure: The study was restricted to those 90 employees who worked during the daytime and always in the same unit **Exclusion criteria:** not reported **Pre-treatment:** No significant differences by age or duration of employment were found between the units during the study period (Table 1). The prevalence of current smokers was 45% in the humidified units, and 39% in the control units in December 1991. No significant difference in the proportion of smokers, men, or job categories was found between the humidified and the control units during the study period. In the control units, but the proportion of participants with asthma or hay fever was significantly higher (P = 0·05, Table 2)
Interventions	**Intervention characteristics**

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Nordström 1994 *(Continued)*

	Category of intervention: Central humidification Intervention duration: 4 months Time period: December 1991 - April 1992 Type of humidification: Steam air humidification, it was applied in 2 randomly selected units, 1 in each hospital Humidification level (indoor relative humidity in %): RH level: 35 - 45% in the humidified condition, 28 - 38% in the non-humidified condition Temperature level (degrees Celsius): Mean 22.4 ° (21.5 - 23.5 °) in the humidified condition, mean 21.7 ° (20.5 - 23 °) in the non-humidified condition Outdoor temperature: N/A *Exposure assessment (measurement of humidity)*: Measurements of room temperature and relative air humidity were performed in 1 room in each unit during the 4-month period by a thermo-hygrograph (CASELLA T 9420). Temperature, relative humidity, volatile organic compounds, and particle concentration were measured 1 - 5 metres above the floor
Outcomes	Primary outcomes: eye symptoms: itching, burning, or irritation of the eyes; upper respiratory tract symptoms: irritated, stuffy or running nose, hoarse or dry throat, or cough; skin symptoms: dry facial skin, itch in the scalp or ears Secondary outcomes: perceived air quality: dryness of air, stuffy bad air, draught, static electricity, dustiness
Identification	**Sponsorship source:** This study was supported by grants from the National Swedish Institute for Building Research, and the County Council of Malmöhus **Country:** Sweden **Setting:** 2 geriatric hospitals in Southern Sweden, 4 geriatric hospital units (2 units: intervention and control in each hospital) **Author name:** Klas Nordström **Institution:** Department of Working Environment, Lund Institute of Technology, University of Lund **Email:** N/A **Address:** Department of Working Environment, Lund Institute of Technology, University of Lund, S- 221 00 Lund, Sweden
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Selection of participants	Low risk	Inclusion criteria were stated. Exclusion criteria were not reported
Confounding	Low risk	Important confounders were considered: temperature in the workplace/in the educational setting; the influence of other indoor conditions such as ventilation, particle concentration, concentration of volatile organic compounds which could have an important impact of the outcome; the time of the intervention (the study was conducted during the winter months); Co-morbidities. There were no differences between the control and the intervention groups regarding age, gender, duration of employment, smoking status, job categories. In the control units, however, the proportion of subjects with asthma

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Nordström 1994 *(Continued)*

		or hay fever was significantly higher. At least 60% or more of the relevant confounders were considered in the statistical analysis
Blinding of participants or organizations if applicable, and outcome assessors	Unclear risk	No information on the purpose of the study was given to the participants during the study period. The participants were invited to participate in the indoor climate investigation, but were not informed that this included air humidification in some departments. No information on blinding of outcome assessors was provided
Incomplete outcome data	High risk	The percentage of withdrawals and dropouts exceeded 20% for short-term follow-up
Selective outcome reporting	Unclear risk	A study protocol was unavailable. Insufficient information to permit judgement
Other sources of bias	High risk	Dynamic population; results were presented for a dynamic population and not for people who provided complete pre-post measurements (n = 56). It remained unclear, to which group the 56 participants with complete pre-post measurements belonged

Reiman 2018

Study characteristics	
Methods	Study design: Non-randomised, parallel-group controlled study
Participants	Nursery school, preschool children from 4 classrooms, n = 116 (65 intervention group, 51 control group) (corresponds to the maximum number of pupils) Characteristic of participants: Age between 2 - 5 years No information was available for gender, socio-economic level, comorbidities, medication, atopy, family history **Inclusion criteria:** Pre-school-age children, who attended the nursery school **Exclusion criteria:** N/A
Interventions	Category of intervention: Local humidification Intervention duration: 7 weeks (35 school days in total) Time period: 25 January 2016 - 11 March 2016 Type of humidification: electrode steam humidifier with steam blower Humidification level (indoor relative humidity in %): Mean RH level, SD (range): 40.7%, SD 3,8 (28.1 - 56%) in the humidified condition, 29.3%, SD 2.5 (18.8 - 53.60%) in the non-humidified condition. Mean AH level, SD (range): 9.89 mbar, SD 0.99 (6.13 - 12.92 mbar) (mbar = vapour pressure) in the humidified condition, 6.33 mbar, SD 0.68 (4.61 - 12.62 mbar) in the non-humidified condition Temperature level (degree Celsius): Mean 19.2 °C in the humidified condition, mean 19.9 °C in the non-humidified condition Outdoor temperature: between - 22.8 °C - 17.8 °C Outdoor AH: 1 - 5.8 mbar

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Reiman 2018 *(Continued)*

	Exposure assessment (measurement of humidity): RH was recorded every 10 minutes during the duration of the study. Absolute humidity was calculated using Excel software
Outcomes	Absence due to sickness Absence due to influenza-like illness
Identification	**Sponsorship source:** Mayo Clinic to WCH and HJF and the National Center for Advancing Translational Sciences grant no. UL1 TR002377 to CP **Country:** USA **Setting:** Educational setting **Author name:** Chris Pierett **Institution:** Center for Clinical and Translational Science, Mayo Clinic, Rochester, Minnesota, United States of America **Email:** Pierret.Christopher@mayo.edu **Address:** Mayo Clinic, 200 1st St SW, Rochester, MN 55905, USA
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Selection of participants	Unclear risk	Inclusion and exclusion criteria were not stated. The authors of the review assumed that all pupils of these 4 classes were included in the study.
Confounding	High risk	Relevant confounders such as gender, co-morbidities, atopic conditions were not considered No information was given on socio-economic level. In addition, the study used neither restriction, matching/pre-stratification nor adjustment for confounding in the statistical models
Blinding of participants or organizations if applicable, and outcome assessors	Unclear risk	No information on blinding (participants/organisations/outcome assessors). It remained unclear whether the outcome was influenced by the lack of blinding
Incomplete outcome data	Low risk	There were no indications for missing outcome data
Selective outcome reporting	Unclear risk	The study protocol was unavailable. Insufficient information to permit judgement
Other sources of bias	Low risk	The study was considered to be free of other sources of bias. There was no indication of other source of biases, which were not stated in the domain list The intervention was seasonally conducted during the heating period In the study setting, the participants were exposed to the same indoor air humidity conditions before the start of the study

Reinikainen 1992

Study characteristics

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Reinikainen 1992 *(Continued)*

Methods	**Study design:** Cluster-randomised cross-over trial
Participants	Total number of office workers n = 290 Characteristics of participants: Age: ≤ 24 y n = 9 (4.3%); 25 - 34 y n = 38 (18%); 35 - 44 y n = 74 (35.1%); 45 - 54 n = 59 (27.9%); ≥ 55 y n = 31 (14.7%) Gender: 102 men/109 women, 48.3% male and 51.7% female Smoking status: Never n = 103 (48.8%), Ex-smoker n = 64 (30.3%), current n = 44 (20.9%) Atopy: asthma n = 11 (5.6%), hay fever n = 31 (15.5%), allergic conjunctivitis n = 22 (11.0%), eczema n = 62 (30.5%) Professional activity/professional training: None n = 37 (17.5%), course n = 18 (8.5%), trade school n = 18 (8.5%), college n = 56 (26.6%), university n = 82 (38.9%) Marital status: single n = 39 (18.8%), married n = 151 (73%), divorced/widow n = 17 (8.2%) No information was available for: alcohol intake, socio-economic level, comorbidities, medication, family history, job category and employment **Inclusion criteria:** The source population - 362 workers in 2 identical wings of the building - were all considered eligible for the study, and they received a baseline questionnaire. A total of 290 workers (148 men, 142 women) completed the baseline questionnaire and indicated their willingness to participate in the study. Therefore, these individuals were included in the trial. They had to spend at least 2 hours in the office **Exclusion criteria:** N/A **Pretreatment:** This was a cluster-randomised cross-over study. Characteristics of the whole study population, the population who completed trial and on withdrawals was provided. Of 290 participants, 211 completed the trial and were included in the analysis, 79 withdrawals. We can compare the 2 populations (completed trial and withdrawals) on the basis of table 1 (there are no statistical tests): -more people over 55 in the population, who completed the trial- more current smokers among the withdrawals- more people with a University degree among the withdrawals
Interventions	**Intervention characteristics** Category of intervention: Local humidification Intervention duration: 6 weeks Time period: 02 January - 17 February 1988 Type of humidification: electrical steam humidifiers Humidification level (indoor relative humidity in %): Range 24 - 41%, mean 30.3% in the humidified condition; range 18 - 33%, mean 25.8% in the non-humidified condition Temperature level (degrees Celsius): Range 21.4 - 22.1 °C, mean 21.8 °C in the humidified condition; range 22.2 - 22.9 °C; mean 22.5% in the non-humidified condition Outdoor temperature: The mean outdoor temperature was −0.3 °C in January and 0.0 °C in February. The authors stated that the "weather in Helsinki was exceptionally warm" during the study period Other parameters: The ventilation rate was at minimum 7 litres/second per person *Exposure assessment (measurement of humidity)*: Temperature and relative humidity were measured continuously in 3 rooms in both wings. An Envirolog continuous meter, which had an accuracy of ± 0.25 °C for temperature and ± 2% for relative humidity, was used. Point measurements of temperature and humidity were conducted in a sample of offices during each period

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Reinikainen 1992 *(Continued)*

Outcomes	Primary outcomes: Dryness symptoms overall, Eye: Eye symptoms, Upper respiratory tract: Nasal dryness, Pharyngeal dryness Skin symptoms Secondary outcomes: Perception of air quality: Sensation of dryness, unpleasant odour, stuffiness, dustiness, draft
Identification	**Sponsorship source:** This study was supported by the Finnish Work Environment Fund, the Ministry of Finance, and the Department of Energy in the Ministry of Trade and lndustry. **Country:** Finland **Setting:** Office building **Comments:** Further publication(s) in the same/partly the same population: Reinikainen 1990 et al. "The effect of air humidification on symptoms and environmental complaints in office workers. A six period cross-over study" **Author name:** Leena M. Reinikainen M.D., M.Sc. **Institution:** Laboratory of Heating, Ventilating and Air Conditioning Helsinki University of Technology **Email:** - **Address:** Laboratory of Heating, Ventilating and Air Conditioning Helsinki University of Technology
Notes	**Interventions** The supply air flow was constant and was designed to provide a minimum of 7 litres/second air per person. The participants were told that the ventilation would be adjusted during the study, but neither the objective nor the phase of the study was revealed, so the trial was considered participant-blinded

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	There were indications that the study was randomised. The method of randomisation was not described
Allocation concealment (selection bias)	Unclear risk	Not reported
Selection of participants	Unclear risk	All workers were considered as eligible. Insufficient information to permit judgement
Confounding	Low risk	Due to study design each participant served as his/her own control
Blinding of participants or organizations if applicable, and outcome assessors	Unclear risk	Blinding of participants. No information on blinding of outcome assessors was available
Incomplete outcome data	High risk	There were missing outcome data. Reasons for that were not stated. In total, 211 participants (72.8%) with 102 men and 109 women were included in the final analyses

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Reinikainen 1992 *(Continued)*

Selective outcome reporting	Unclear risk	Insufficient information to permit judgement
Other sources of bias	Low risk	The study was considered to be free of other sources of bias
Appropriate use of a cross-over design	Low risk	6-period cross-over study
The trial was not biased from carry-over effects	Low risk	Weekends were used as washout periods. Carry-over effects were not expected

Reinikainen 2003

Study characteristics	
Methods	**Study design:** Cluster non-randomised cross-over trial
Participants	Total number of office workers n= 517 workers (at baseline) Characteristics of participants: No information was available for: age, gender, smoking status, alcohol intake, socio-economic level, comorbidities, medication, atopy, family history, job category, and employment **Inclusion criteria:** People working in 3 wings (A, B and C) spending at least 2 hours in their offices were considered as study population. They received a baseline questionnaire. Those who returned the questionnaire, indicating a willingness to take part in the study, were included. A total of 368 workers (71.2%) returned the baseline questionnaire and at least 1 of the diaries with information on any of the symptoms or perceptions of interest, sufficient information on the possible symptoms of respiratory infection, and had spent at least 2 hours in their offices. In total, 342 diaries were received from non-humidified and 233 from humidified conditions **Exclusion criteria:** N/A **Pretreatment:** N/A
Interventions	**Intervention characteristics** Category of intervention: Local humidification per wing Intervention duration: 6 weeks Time period: January - February 1989 Type of humidification: Steam humidification Humidification level (indoor relative humidity in %): In humidified condition in wings: mean (range): 32.7% (26.6 - 41.2%); *in offices* mean (range): 32.4% (22.2 - 49.1%) In non-humidified condition in wings: mean (range): 25.6% (20 - 31.7%); *in offices* mean (range): 24.8 % (16.6 - 39.9%) Absolute humidity gram water/kg air: in humidified conditions in wings: mean (range): 5.6 (4.2 – 7.0) g H_2O/kg air In non-humidified condition in wings mean (range): 4.2 (3.3 – 5.6) g H_2O/kg air Temperature level (degrees Celsius):

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Reinikainen 2003 *(Continued)*

	In humidified condition in wings: mean (range): 22.4 °C (21.5 - 23.7 °C) In non-humidified condition in offices: mean (range): 22.6 °C (19 - 26 °C) Outdoor temperature: N/A Other parameters: The ventilation rate was 20 - 30 litres/second in average per person. The formaldehyde concentration was below 0.1 mg/m^3 without association with humidification. Concentrations of particles, bacteria, and fungal spores in the building were low *Exposure assessment (measurement of humidity)*: humidity and temperature were measured continuously in all 3 wings in 2 or 3 offices (the method was not stated). In addition, each participant received a dry bulb thermometer whose reading was registered in the symptom diary
Outcomes	Primary outcomes: Dry Eye, dry nose, pharyngeal dryness, dry skin Secondary outcomes: Perception of stuffiness
Identification	**Sponsorship source:** This study was supported by the Finnish Work Environment Fund **Country:** Finland **Setting:** Office **Author name:** Leena M. Reinikainen M.D., M.Sc. **Institution:** Department of Public Health, Laboratory of Heating, Ventilating and Air-Conditioning, Faculty of Mechanical Engineering, Helsinki University of Technology, Institute of Occupational Health, University of Birmingham, United Kingdom **Email:** leena.reinikainen@helsinginenergia.fi **Address:** Department of Public Health, P.O. Box 41, University of Helsinki, Helsinki FIN-00014, Finland
Notes	There were 3 published studies for the same Pasila Office Center in winter 1989 (Reinikainen et al. 1997, Reinikainen et al. 2001, Reinikainen & Jaakkola 2003). They were part of the dissertation of Leena Reinikainen (Report A6: Indoor air humidification, sick building syndrome symptoms and perceived indoor air quality in the office environment). As the publication from 2003 presented the most comprehensive results, we decided to extract data from it

Risk of bias

Bias	Authors' judgement	Support for judgement
Selection of participants	Low risk	Inclusion criteria are stated
Confounding	Low risk	Due to the study design each participant serves as own control
Blinding of participants or organizations if applicable, and outcome assessors	Unclear risk	No information on blinding of participants and/or outcome assessors
Incomplete outcome data	Unclear risk	Not clear how many participants completed the study. Information on the number of study participants is only available for baseline assessments. Information on completed diaries versus number of participants is not available

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Reinikainen 2003 *(Continued)*

Selective outcome reporting	Unclear risk	Insufficient information to permit judgement
Other sources of bias	Unclear risk	Non-validated questionnaires were used. No population characteristics were provided in the original publication (Reinikainen & Jaakkola 2003). Furthermore, the range of humidity levels in humidified and non-humidified conditions overlap
Appropriate use of a cross-over design	Low risk	6-period cross-over study
The trial was not biased from carry-over effects	Low risk	Changes in humidification were conducted during the weekends ("wash-out periods"). Carry-over effects are not to be expected

Ritzel 1966

Study characteristics	
Methods	**Study design:** Non-randomised, parallel-group controlled study
Participants	5 double kindergartens, n = 232 pre-school-age children (4 - 6 yrs. old) Characteristics of participants: No information is available for: gender, socio-economic level, comorbidities, medication, atopy, family history **Inclusion criteria:** Pre-school-age children, who attend the kindergarten **Exclusion criteria:** N/A
Interventions	**Intervention characteristics** Category of intervention: Local humidification Intervention duration: 9 weeks Time period: January to the beginning of March 1965 Type of humidification: cold water atomizer (capacity 0.5 litre water per hour) Humidification level (indoor relative humidity in %): In humidified condition: Mean 49% In non-humidified condition: Mean 40% Temperature level (degrees Celsius): In humidified condition: Mean 22.2 °C In non-humidified condition: Mean 21.9 °C Outdoor temperature: N/A *Exposure assessment (measurement of humidity)*: during school attendance, humidity level was measured continuously by a hygrometer
Outcomes	Secondary outcome: Absences due to illness
Identification	**Sponsorship source:** N/A

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Ritzel 1966 *(Continued)*

	Country: Switzerland
	Setting: 5 double Kindergarten (5 kindergarten with 2 separate pavilions)
	Author name: Ritzel, Günther
	Institution: School Medical Office of the City of Basle
	Address: Schularztamt Basel-Stadt, St. Alban-Vorstadt 194000 Basel, Switzerland
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Selection of participants	Low risk	All kindergarten children were included. There were no exclusion criteria
Confounding	High risk	The study population consisted of pre-school children almost of the same age. No information on gender, socio-economic level, comorbidities, medication, atopy, family history was provided
Blinding of participants or organizations if applicable, and outcome assessors	Unclear risk	Children and their parents were not informed about the aim of the intervention. They were therefore considered as participant-blinded (unless the teachers had told them). No information on blinding of outcome assessors was available
Incomplete outcome data	Low risk	No indication of missing outcome data
Selective outcome reporting	Unclear risk	A study protocol was unavailable. Insufficient information to permit judgement
Other sources of bias	Unclear risk	Insufficient information to assess whether an important risk of bias was present or insufficient rationale or evidence that an identified problem would introduce a bias. It was unclear, whether the air humidity level was consistent between the study groups before the start of the study

Sale 1972

Study characteristics

Methods	**Study design:** Non-randomised, parallel-group controlled study
Participants	3 nursery schools with 515 participants. Data of 263 children were analysed: 140 children in the intervention group (group I and group II: humidity at school and at home, humidity at school only (school number 1)), 123 in the control group (group III and group IV: humidity at home only, no humidity at school (school number 2 and 3)) Characteristics of participants: Age between 2.5 - 6 yrs. No information was available for: gender, socio-economic level, comorbidities, medication, atopy, family history **Inclusion criteria:** Children attending 1 of the 3 nursery schools **Exclusion criteria:** N/A
Interventions	**Intervention characteristics** Category of intervention: Central humidification

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Sale 1972 *(Continued)*

	Intervention duration: approximately 131 days Time period: 01 November 1969 to 27 March 1970 Type of humidification: Aprilaire humidifier at school Humidification level (indoor relative humidity in %): In humidified condition: Mean 51 % (range 47 - 66%) In non-humidified condition: Mean 35.2 % (range 16 - 49%) Temperature level (degrees Celsius): In humidified condition: Mean 23,7 °C (range 21.1 - 25.6 °) In non-humidified condition: Mean 22.8 °C (range 20.6 - 26.7 °) Outdoor temperature: N/A *Exposure assessment (measurement of humidity)*: hygrometer, once a week
Outcomes	Secondary outcome: weekly rate of absence (non-respiratory illnesses were omitted)
Identification	**Sponsorship source:** N/A **Country:** USA **Setting:** 3 private nursery schools **Author name:** Charles S. Sale **Institution:** N/A **Email:** N/A **Address:** N/A
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Selection of participants	Unclear risk	515 children were included in 3 schools. Data of 263 children were analysed
Confounding	High risk	Some important confounders such as temperature and influence of other indoor conditions (e.g. bacteria, airborne dust) were considered in the study. However, the confounders were not considered in the statistical analysis
Blinding of participants or organizations if applicable, and outcome assessors	High risk	An orientation booklet describing the harmful effects of dry heated air and encouraging the use of increased humidity in the home was mailed to parents. A covering letter from the school director outlining the purpose of the study and requesting the parents' co-operation was enclosed. The blinding was not assured
Incomplete outcome data	Unclear risk	Source population comprised 515 pupils and analysis was based on 263 pupils. It was unclear how many pupils participated
Selective outcome reporting	Unclear risk	The study protocol was unavailable. Insufficient information to permit judgement

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Sale 1972 *(Continued)*

Other sources of bias	Unclear risk	The way of recruitment (orientation booklet describing harmful effects of dry heated air) might affect parental behaviour and their responses to humidification

Sataloff 1963

Study characteristics	
Methods	**Study design:** Non-randomised, parallel-group controlled study
Participants	Public school, 162 school-age children (82 pupils in the intervention, 80 pupils in the control group) Characteristics of participants: No information was available for age, gender, socio-economic level, co-morbidities, medication, atopy, family history **Inclusion criteria:** classrooms with children of grades 1 - 3 **Exclusion criteria:** N/A **Pretreatment:** N/A
Interventions	**Intervention characteristics** Category of intervention: Local humidification Intervention duration: 3 months Time period: Weeks of 31 October 1960 to 13 March 1961 (in total 2 + 1 months of this period) Type of humidification: Cold vapour humidification Humidification level (indoor relative humidity in %): In humidified condition: Mean 29.58 % (range 11 - 42%) In non-humidified condition: Mean 26.56% (range 11 - 40%) Temperature level (degrees Celsius): In humidified condition: Mean 24.41 °C (range 23.33 - 25.0 °) In non-humidified condition: Mean 24.2 °C (range 23.9 - 24.4 °) Outdoor temperature: N/A *Exposure assessment (measurement of humidity)*: Automatic hair hygrometer (Brown Instrument Co.) put next to the humidifiers, averaged weekly measurements
Outcomes	Secondary outcome: Average number of school days missed per child, average number of illnesses per child
Identification	**Sponsorship source:** The Foundation for Medical Research in Hearing **Country:** USA **Setting:** Public school, primary grades 1 to 3 **Author name:** Joseph Sataloff, M.D. **Institution:** Jefferson Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania

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Sataloff 1963 *(Continued)*

	Address: Jefferson Medical College, Philadelphia, Pennsylvania, USA
Notes	The experiment was hampered by the fact that the designed control areas also received water vapour through moist air leakage from the humidified rooms, thus tending to reduce the effect

Risk of bias

Bias	Authors' judgement	Support for judgement
Selection of participants	Unclear risk	Inclusion and exclusion criteria were not stated. The review authors assumed that all pupils of these 3 classes were included in the study
Confounding	High risk	Temperature was recorded. No information was available for age, gender, socio-economic level, comorbidities, medication, atopy, family history
Blinding of participants or organizations if applicable, and outcome assessors	Unclear risk	Neither parents, teachers, nor children were told the precise purpose of the experiment. No information on blinding of outcome assessors
Incomplete outcome data	Unclear risk	No indication for missing data
Selective outcome reporting	Unclear risk	A study protocol was unavailable. Insufficient information to permit judgement
Other sources of bias	High risk	The method of humidity measurement was described. Due to technical problems there were diffusion effects between humidified and non-humidified rooms resulting in mean difference in humidity of slightly above 3%. The experimental conditions could not been consistently kept

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Abbritii 1992	Ineligible study design
Abbritti 2004	Other reason: Review
Aizlewood 2006	Ineligible study design
Akimoto 2006	Ineligible study design
Akimoto 2010	Ineligible study design
Akimoto 2014	Ineligible study design
Akiyama 2011	Ineligible intervention
Almaguer 1995	Ineligible study design
Andamon 2019	Ineligible intervention
Andersen 1973	Ineligible setting

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Study	Reason for exclusion
Anderson 1989	Other reason: Another topic
Andersson 1975	Ineligible study design
Andersson 1976	Ineligible study design
Angelon-Gaetz 2016	Ineligible study design
Anon 1980	Ineligible study design
Anonymous 1999	Other reason: Review
Appleby 1996	Other reason: Review
Bachmann 1995	Ineligible intervention
Bakke 2008	Ineligible study design
Bakó Biró 2012	Ineligible intervention
Bardana 1988	Other reason: Review
Bardana 1997	Other reason: Review
Bass 2003	Ineligible study design
Berglund 1992	Ineligible intervention
Berg-Munch 1981	Ineligible study design
Bischof 1998	Other reason: Review
Bischof 2007	Ineligible study design
Boetjer 1968	Other reason: Review
Bourbeau 1993	Ineligible outcomes
Bourbeau 1996	Ineligible study design
Bourbeau 1997	Ineligible study design
Brundage 1988	Ineligible study design
Bucakova 2006	Ineligible intervention
Burge 1987	Ineligible study design
Burge 1988	Other reason: Review
Burge 1990	Other reason: Review
Burt 1997	Ineligible intervention
Burton 1991	Other reason: Review

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Study	Reason for exclusion
Caprioli 1984	Ineligible study design
Caprioli 1985	Ineligible study design
Chao 2003	Ineligible study design
Chevalier 1992	Ineligible study design
Deng 2017	Ineligible intervention
Dorgan 2000	Other reason: Book chapter
Fang 2004	Ineligible setting
Federspiel 2004	Other reason: Another topic
Fisk 2002	Other reason: Another topic
Fisk 2011	Other reason: Another topic
Fisk 2012	Ineligible study design
Franchi 2002	Other reason: Review
Gelperin 1973	Ineligible participant population
Genjo 2019	Ineligible intervention
Gou 2012a	Tropical and subtropical climates
Gou 2012b	Tropical and subtropical climates
Graves 2000a	Other reason: Letter
Graves 2000b	Other reason: Letter
Green 1974	Other reason: The results of this study are included in the publication of Green 1975
Green 1985	Ineligible study design
Griffiths 1969	Other reason: Letter
Grisoli 2012	Other reason: Another topic
Guberan 1978	Ineligible study design
Gul 2006	Ineligible study design
Gustafsson 2017	Other reason: Review
Hähn 2020	Ineligible intervention
Hall 1993	Ineligible study design
Hantani 2009	Ineligible intervention

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Study	Reason for exclusion
Harrison 2005	Other reason: Review
Hedge 1984	Ineligible study design
Hedge 1989	Ineligible intervention
Hedge 1992	Ineligible study design
Hedge 1993a	Ineligible study design
Hedge 1993b	Other reason: Another topic
Hedge 2009a	Ineligible study design
Hedge 2009b	Ineligible study design
Hedge 2010	Ineligible study design
Helmis 2009	Ineligible study design
Hiraga 1981	Ineligible participant population
Hirayama 2013	Ineligible intervention
Hodgson 2002	Other reason: Review
Holcatova 2001	Ineligible study design
Hoppe 1993	Other reason: Review
Hosseinia 2017	Tropical and subtropical climates
Iwashita 2017	Ineligible study design
Jaakkola 1994	Ineligible intervention
Jaakola 1991	Ineligible study design
Jarvi 2018	Ineligible study design
Jigang 2004	Tropical and subtropical climates
Kaczmarczyk 2010	Ineligible study design
Kalamees 2014	Ineligible study design
Kalamees 2015	Ineligible study design
Kaushal 2004	Other reason: Another topic
Kelland 1992	Ineligible study design
Kim 2016	Other reason: Ineligible purpose of the intervention study
Kosonen 2011	Ineligible study design

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Study	Reason for exclusion
Kraus 2019	Ineligible study design
Kreiss 1993	Other reason: Review
Langevin 2011	Ineligible study design
Lebowitz 1992a	Other reason: Another topic
Lebowitz 1992b	Other reason: Another topic
Leinster 1990	Ineligible intervention
Liu 2017	Ineligible study design
Loupa 2017	Ineligible study design
Lu 2018	Ineligible study design
Mandin 2017	Ineligible intervention
Manuel 2003	Ineligible study design
Manuel 2004	Other reason: Another topic
Marques 2016	Ineligible study design
Mateo-Cecilia 2018	Ineligible study design
Matsumoto 2011	Ineligible study design
Mendell 1990	Ineligible study design
Mendell 1995	Ineligible study design
Mendell 2003	Other reason: Review
Mendell 2009	Ineligible study design
Milton 2001	Ineligible study design
Milton 2003	Other reason: Abstact
Mir 2008	Other reason: Another topic
Mishra 2015	Tropical and subtropical climates
Molina 1986	Other reason: Review
Murakami 2006	Ineligible intervention
Niven 2000	Ineligible study design
Norbäck 1990a	Ineligible study design
Norbäck 1990b	Ineligible study design

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Study	Reason for exclusion
Norbäck 2008a	Ineligible intervention
Norbäck 2008b	Ineligible intervention
Norbäck 2013	Ineligible intervention
Norbäck 2019	Ineligible study design
Oancea 2012	Other reason: Another topic
Orosa 2012	Other reason: Book chapter
Paevere 2009	Ineligible study design
Pejtersen 2001	Ineligible intervention
Pereira 2014	Ineligible intervention
Persson 2019	Ineligible intervention
Pickering 1989	Other reason: Review
Proctor 1973	Other reason: Another topic
Proctor 1980	Ineligible study design
Reinikainen 1990	Other reason: The results of this study is included in the publication Reinikainen 1992
Reinikainen 1991	Ineligible study design
Reinikainen 1997	Other reason: The results of this study is included in the publication Reinikainen 2003
Reinikainen 2001	Other reason: The results of this study is included in the publication Reinikainen 2003
Rowe 1993	Ineligible study design
Schmid 1998	Ineligible study design
Schrader 1976	Ineligible study design
Seneviratne 1997	Ineligible study design
Senitkova 2015	Ineligible study design
Senkpiel 1994	Ineligible study design
Serati 1969	Ineligible study design
Several authors 1995	Other reason: Review
Singh 2010	Ineligible intervention
Skov 1987	Ineligible study design
Smedbold 2001	Ineligible study design

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Study	Reason for exclusion
Smedbold 2002	Ineligible study design
Smedje 2011	Ineligible intervention
Sommer 1994	Ineligible study design
Song 2012	Ineligible intervention
Spivey 2002	Other reason: Another topic
Stankevica 2012	Ineligible study design
Sterling 1983	Ineligible intervention
Stolze 1995	Ineligible intervention
Sun 2013	Ineligible setting
Sun 2015	Ineligible study design
Sundell 1994	Ineligible study design
Szabo 2018	Ineligible study design
Takada 2013	Ineligible study design
Takaoka 2011	Other reason: Another topic
Takaoka 2017	Ineligible study design
Tanabe 2005	Ineligible study design
Tanabe 2006	Ineligible study design
Tanabe 2009	Other reason: Review
Tanabe 2010	Ineligible intervention
Taplin 2001	Other reason: Review
Tarlo 2010	Other reason: Book
Taylor 2020	Other reason: Review
Terzi 1986	Ineligible study design
Thatcher 2014	Ineligible intervention
Tobia 2004	Ineligible study design
Tomic 2014	Ineligible intervention
Tsutsumi 2007	Ineligible study design
Vainio 2008	Other reason: Review

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Study	Reason for exclusion
Voronova 1981	Ineligible intervention
Waldman 2004	Other reason: Another topic
Walkinshaw 1992	Other reason: Review
Wang 2015	Ineligible intervention
Wargocki 2002	Ineligible intervention
White 1982	Ineligible study design
Wirsing 1985	Ineligible study design
Wolkoff 2007	Other reason: Review
Wyon 1992	Ineligible study design
Xiao 2011	Ineligible study design
Young 1998	Other reason: Review
Zhang 2011	Ineligible study design
Zhang 2014	Ineligible study design
Zweers 1992	Ineligible study design

DATA AND ANALYSES

Comparison 1. Humidification vs no humidification in occupational setting

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Dry eye: Cross-over study cluster RCT	1		Odds Ratio (IV, Random, 95% CI)	Totals not selected
1.1.1 6 weeks	1		Odds Ratio (IV, Random, 95% CI)	Totals not selected
1.2 Dry Eye: Cross-over Studies cluster non-RCT	2		Odds Ratio (IV, Random, 95% CI)	0.58 [0.27, 1.25]
1.2.1 6 -12 weeks	2		Odds Ratio (IV, Random, 95% CI)	0.58 [0.27, 1.25]
1.3 Dry Eye: Before-and-after studies	2	102	Odds Ratio (M-H, Random, 95% CI)	0.57 [0.23, 1.41]
1.3.1 After 6 weeks - 4 months	2	102	Odds Ratio (M-H, Random, 95% CI)	0.57 [0.23, 1.41]

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.4 Dry Eye: Before-and-after studies	2		Odds Ratio (M-H, Random, 95% CI)	Totals not selected
1.4.1 Before	1		Odds Ratio (M-H, Random, 95% CI)	Totals not selected
1.4.2 After 6 weeks	1		Odds Ratio (M-H, Random, 95% CI)	Totals not selected
1.4.3 Before	1		Odds Ratio (M-H, Random, 95% CI)	Totals not selected
1.4.4 After 4 months	1		Odds Ratio (M-H, Random, 95% CI)	Totals not selected
1.5 Eye: Change in breakup time of tears (s)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.6 Dry Skin: Crossover studies cluster non-RCT	2		(IV, Random, 95% CI)	0.66 [0.33, 1.32]
1.6.1 6 -12 weeks	2		(IV, Random, 95% CI)	0.66 [0.33, 1.32]
1.7 Skin Symptoms: Cross-over study cluster RCT	1		Odds Ratio (IV, Random, 95% CI)	Totals not selected
1.7.1 6 weeks	1		Odds Ratio (IV, Random, 95% CI)	Totals not selected
1.8 Dry Skin: Before-and-after studies	2		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.8.1 Before	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.8.2 After 4 months	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.8.3 Before	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.8.4 After 12 weeks	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.9 Dry skin: Before-and-after studies	2	121	Odds Ratio (M-H, Fixed, 95% CI)	0.69 [0.33, 1.47]
1.9.1 after 12 weeks to 4 months	2	121	Odds Ratio (M-H, Fixed, 95% CI)	0.69 [0.33, 1.47]
1.10 Skin Symptoms: Before-and-after studies	1		Risk Difference (M-H, Fixed, 95% CI)	Totals not selected
1.10.1 Before	1		Risk Difference (M-H, Fixed, 95% CI)	Totals not selected
1.10.2 After 6 weeks	1		Risk Difference (M-H, Fixed, 95% CI)	Totals not selected
1.11 Dry Nose: Cross-over study cluster non-RCT	1		Odds Ratio (IV, Random, 95% CI)	Totals not selected

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.11.1 6 weeks	1		Odds Ratio (IV, Random, 95% CI)	Totals not selected
1.12 Dry Nose: Cross-over study cluster RCT	1		Odds Ratio (IV, Random, 95% CI)	Totals not selected
1.12.1 6 weeks	1		Odds Ratio (IV, Random, 95% CI)	Totals not selected
1.13 Nose Symptoms: Before-and-after studies	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.13.1 Before	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.13.2 After 6 weeks	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.14 Change of nasal signs	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.14.1 MCA1 (minimum cross-sectional areas), cm^2	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.14.2 MCA2 (minimum cross-sectional areas), cm^2	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.14.3 VOL1(volume of the nasal cavity), cm^3	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.14.4 VOL2 (volume of the nasal cavity), cm^3	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.14.5 ECP (eosinophilic cationic proein), µg/l	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.14.6 MPO (myeloperoxidase), µg/l	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.14.7 Lyosozyme, mg/l	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.14.8 Albumin, mg/l	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.15 Airway Symptoms: Before-and-after studies	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.15.1 Before	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.15.2 After 4 months	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.16 Dry mouth and throat: Cross-over study cluster non-RCT	1		Odds Ratio (IV, Fixed, 95% CI)	Totals not selected
1.16.1 12 weeks	1		Odds Ratio (IV, Fixed, 95% CI)	Totals not selected

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.17 Pharyngeal Dryness: Cross-over study cluster non-RCT	1		Odds Ratio (IV, Random, 95% CI)	Totals not selected
1.17.1 6 weeks	1		Odds Ratio (IV, Random, 95% CI)	Totals not selected
1.18 Pharyngeal Dryness: Cross-over study cluster RCT	1		Odds Ratio (IV, Random, 95% CI)	Totals not selected
1.18.1 6 weeks	1		Odds Ratio (IV, Random, 95% CI)	Totals not selected
1.19 Perception of dryness: Cross-over study cluster RCT	1		Odds Ratio (IV, Random, 95% CI)	Totals not selected
1.19.1 6 weeks	1		Odds Ratio (IV, Random, 95% CI)	Totals not selected
1.20 Perception of dryness: Cross-over study cluster non-RCT	1		Odds Ratio (IV, Random, 95% CI)	Totals not selected
1.20.1 12 weeks	1		Odds Ratio (IV, Random, 95% CI)	Totals not selected
1.21 Perception of dryness: Before-and-after study	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.21.1 Before	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.21.2 After 6 weeks	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.22 Perception of dryness: Before-and-after study	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.22.1 Before	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.22.2 After 3 months	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.23 Increased perception of dryness: Before-and-after study	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.23.2 Change after 4 months	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.24 Decreased perception of dryness: Before-and-after study	1		Odds Ratio (M-H, Random, 95% CI)	Totals not selected
1.24.1 Change after 4 months	1		Odds Ratio (M-H, Random, 95% CI)	Totals not selected
1.25 Perception of dryness: Before-and-after studies	2	82	Std. Mean Difference (IV, Random, 95% CI)	-0.48 [-3.49, 2.54]
1.25.1 Change after 1-4 months	2	82	Std. Mean Difference (IV, Random, 95% CI)	-0.48 [-3.49, 2.54]

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.26 Perception of dryness: Before-and-after studies	2		Odds Ratio (IV, Fixed, 95% CI)	0.05 [0.01, 0.22]
1.26.1 After 4 to 6 weeks	2		Odds Ratio (IV, Fixed, 95% CI)	0.05 [0.01, 0.22]
1.27 Perception of stuffiness: Cross-over study cluster RCT	1		Odds Ratio (IV, Random, 95% CI)	2.18 [1.47, 3.23]
1.27.1 6 weeks	1		Odds Ratio (IV, Random, 95% CI)	2.18 [1.47, 3.23]
1.28 Perception of stuffiness: Cross-over study cluster non-RCT	1		Odds Ratio (IV, Random, 95% CI)	Totals not selected
1.28.1 6 weeks	1		Odds Ratio (IV, Random, 95% CI)	Totals not selected
1.29 Perception of stuffiness: Before-and-after studies	2	82	Std. Mean Difference (IV, Random, 95% CI)	0.24 [-0.30, 0.78]
1.29.1 Change after 1-4 months	2	82	Std. Mean Difference (IV, Random, 95% CI)	0.24 [-0.30, 0.78]
1.30 Perception of stuffiness: Before-and-after studies	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.30.1 Before	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.30.2 After 1-3 months	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.31 Increased perception of stuffiness: Before-and-after studies	1		Odds Ratio (M-H, Random, 95% CI)	Totals not selected
1.31.1 Change after 4 months	1		Odds Ratio (M-H, Random, 95% CI)	Totals not selected
1.32 Decreased perception of stuffiness: Before-and-after studies	1		Odds Ratio (M-H, Random, 95% CI)	Totals not selected
1.32.1 Change after 4 months	1		Odds Ratio (M-H, Random, 95% CI)	Totals not selected
1.33 Absenteeism: Controlled Study non-RCT	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.33.1 Time period: 1973-1974	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.33.2 Time period: 1974-1975	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

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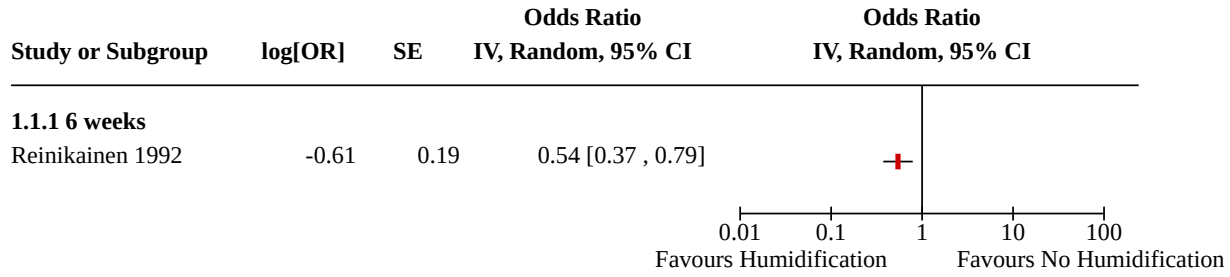
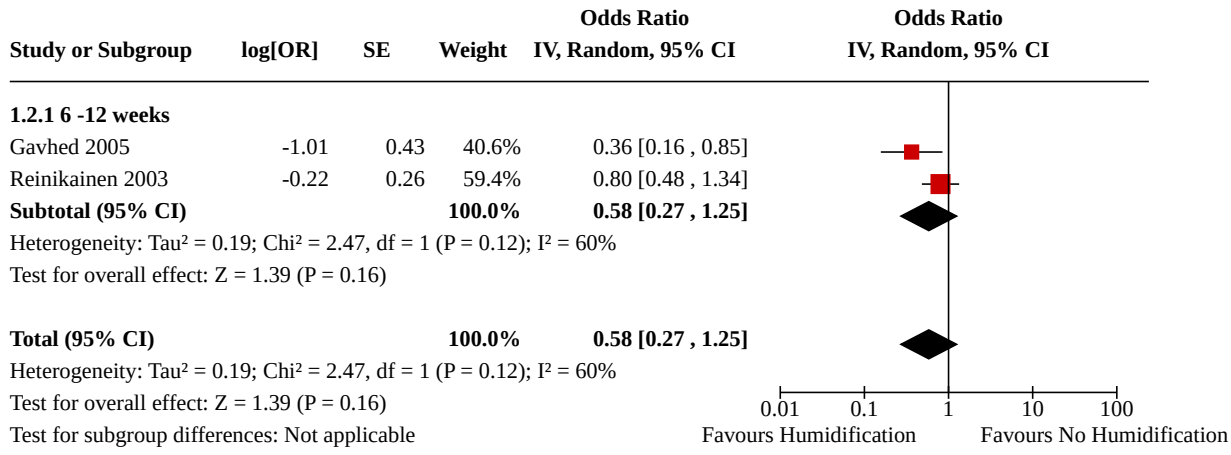
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.33.4 Time period: 1975-1976	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Analysis 1.1. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 1: Dry eye: Cross-over study cluster RCT



Analysis 1.2. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 2: Dry Eye: Cross-over Studies cluster non-RCT



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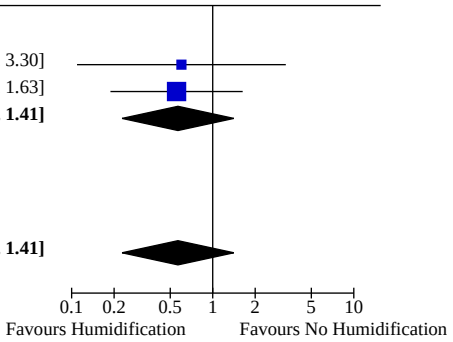
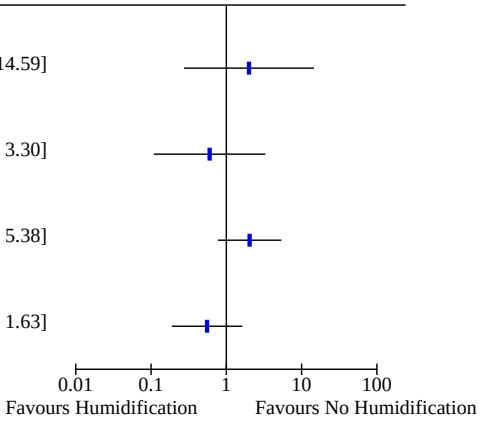
Analysis 1.3. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 3: Dry Eye: Before-and-after studies

Study or Subgroup	Humidification Events	Humidification Total	No Humidification Events	No Humidification Total	Weight	Odds Ratio M-H, Random, 95% CI
1.3.1 After 6 weeks - 4 months						
Norbäck 2000	9	14	9	12	28.6%	0.60 [0.11 , 3.30]
Nordström 1994	7	38	11	38	71.4%	0.55 [0.19 , 1.63]
Subtotal (95% CI)		**52**		**50**	**100.0%**	**0.57 [0.23 , 1.41]**
Total events:	16		20			
Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 1 (P = 0.94); I² = 0%						
Test for overall effect: Z = 1.22 (P = 0.22)						
Total (95% CI)		**52**		**50**	**100.0%**	**0.57 [0.23 , 1.41]**
Total events:	16		20			
Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 1 (P = 0.94); I² = 0%						
Test for overall effect: Z = 1.22 (P = 0.22)						
Test for subgroup differences: Not applicable						



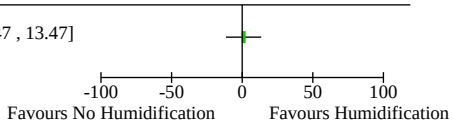
Analysis 1.4. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 4: Dry Eye: Before-and-after studies

Study or Subgroup	Humidification Events	Humidification Total	No Humidification Events	No Humidification Total	Odds Ratio M-H, Random, 95% CI
1.4.1 Before					
Norbäck 2000	12	14	9	12	2.00 [0.27 , 14.59]
1.4.2 After 6 weeks					
Norbäck 2000	9	14	9	12	0.60 [0.11 , 3.30]
1.4.3 Before					
Nordström 1994	15	42	9	42	2.04 [0.77 , 5.38]
1.4.4 After 4 months					
Nordström 1994	7	38	11	38	0.55 [0.19 , 1.63]



Analysis 1.5. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 5: Eye: Change in breakup time of tears (s)

Study or Subgroup	Humidification Mean	Humidification SD	Humidification Total	No Humidification Mean	No Humidification SD	No Humidification Total	Mean Difference IV, Fixed, 95% CI
Norbäck 2000	-6	10	14	-7	20	12	1.00 [-11.47 , 13.47]



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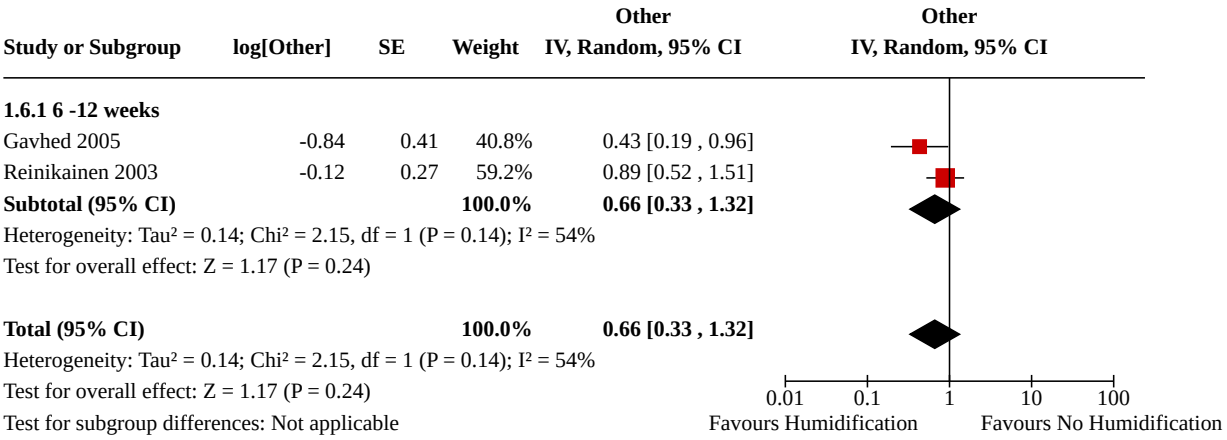
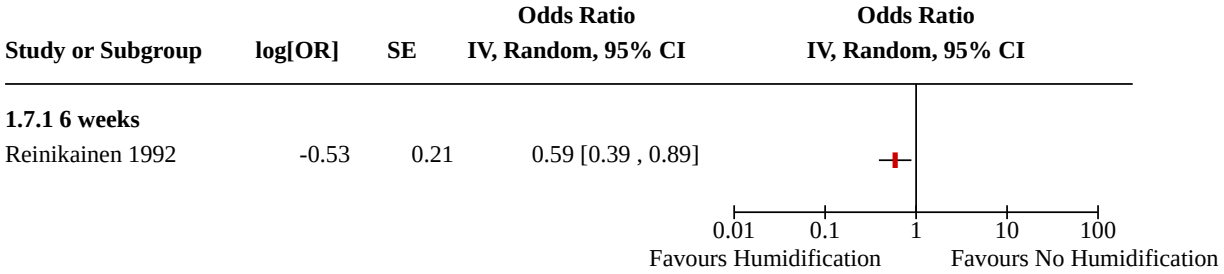
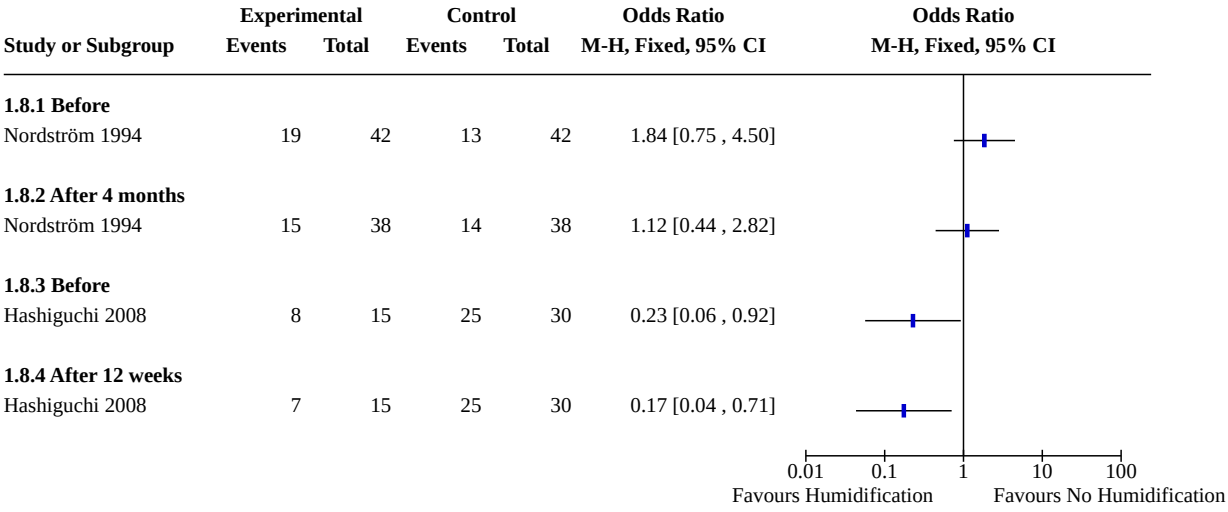
Analysis 1.6. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 6: Dry Skin: Crossover studies cluster non-RCT



Analysis 1.7. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 7: Skin Symptoms: Cross-over study cluster RCT



Analysis 1.8. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 8: Dry Skin: Before-and-after studies



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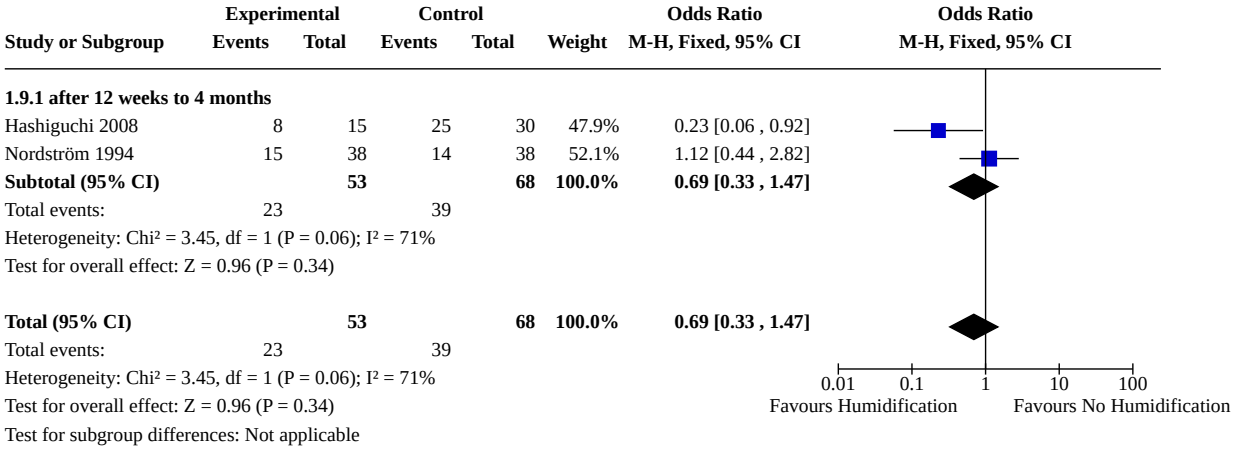
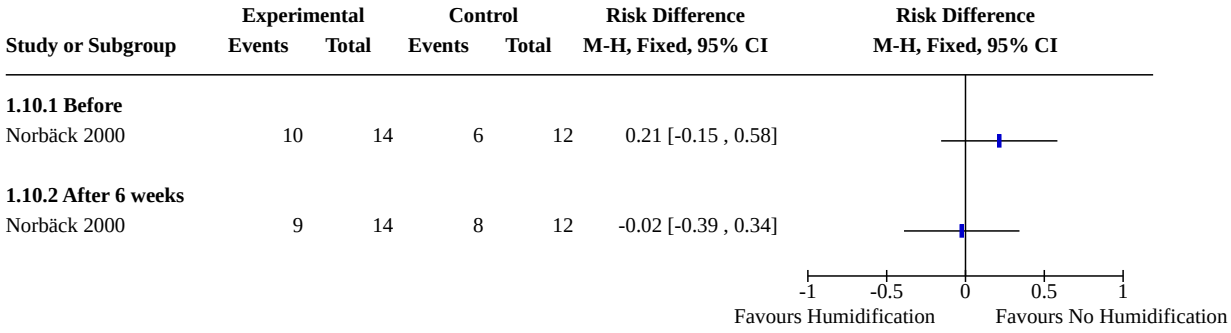
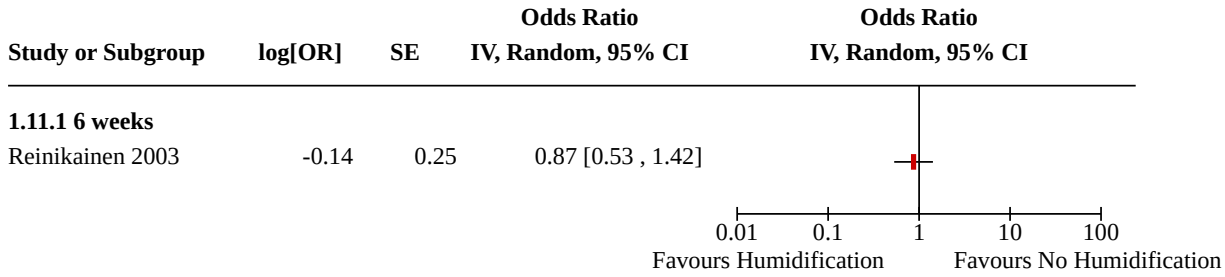
Analysis 1.9. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 9: Dry skin: Before-and-after studies



Analysis 1.10. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 10: Skin Symptoms: Before-and-after studies



Analysis 1.11. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 11: Dry Nose: Cross-over study cluster non-RCT



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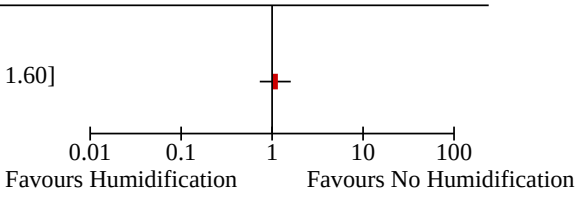
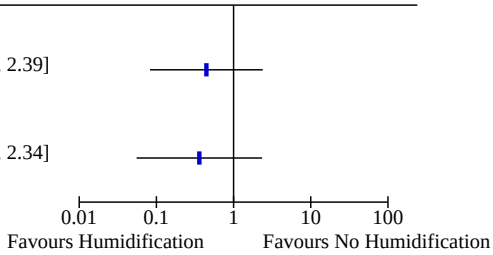
Analysis 1.12. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 12: Dry Nose: Cross-over study cluster RCT

Study or Subgroup	log[OR]	SE	Odds Ratio IV, Random, 95% CI
1.12.1 6 weeks			
Reinikainen 1992	0.08	0.2	1.08 [0.73 , 1.60]



Analysis 1.13. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 13: Nose Symptoms: Before-and-after studies

Study or Subgroup	Humidification Events	Humidification Total	No Humidification Events	No Humidification Total	Odds Ratio M-H, Fixed, 95% CI
1.13.1 Before					
Norbäck 2000	8	14	9	12	0.44 [0.08 , 2.39]
1.13.2 After 6 weeks					
Norbäck 2000	9	14	10	12	0.36 [0.06 , 2.34]



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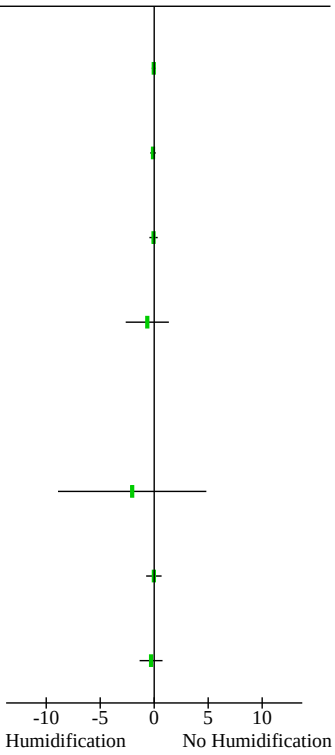
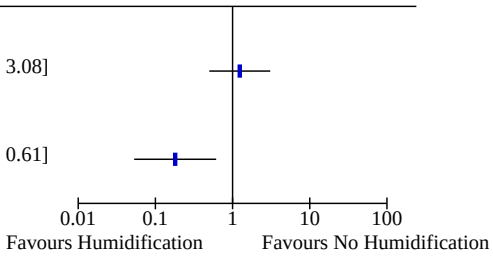
Analysis 1.14. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 14: Change of nasal signs

Study or Subgroup	Humidification Mean	SD	Total	No Humidification Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
1.14.1 MCA1 (minimum cross-sectional areas), cm2							
Norbäck 2000	0.3	0.19	14	0.34	0.27	12	-0.04 [-0.22 , 0.14]
1.14.2 MCA2 (minimum cross-sectional areas), cm2							
Norbäck 2000	0.09	0.27	14	0.2	0.38	12	-0.11 [-0.37 , 0.15]
1.14.3 VOL1(volume of the nasal cavity), cm3							
Norbäck 2000	0.35	0.34	14	0.41	0.6	12	-0.06 [-0.44 , 0.32]
1.14.4 VOL2 (volume of the nasal cavity), cm3							
Norbäck 2000	1.74	2.41	14	2.38	2.74	12	-0.64 [-2.64 , 1.36]
1.14.5 ECP (eosinophilic cationic proein), µg/l							
Norbäck 2000	-0.2	0.8	14	0	0	12	Not estimable
1.14.6 MPO (myeloperoxidase), µg/l							
Norbäck 2000	-5.15	12.1	14	-3.11	4.68	12	-2.04 [-8.91 , 4.83]
1.14.7 Lyosozyme, mg/l							
Norbäck 2000	-0.9	1.02	14	-0.87	0.84	12	-0.03 [-0.75 , 0.69]
1.14.8 Albumin, mg/l							
Norbäck 2000	-0.64	1.52	14	-0.35	1.24	12	-0.29 [-1.35 , 0.77]



Analysis 1.15. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 15: Airway Symptoms: Before-and-after studies

Study or Subgroup	Humidification Events	Total	No Humidification Events	Total	Odds Ratio M-H, Fixed, 95% CI
1.15.1 Before					
Nordström 1994	15	42	13	42	1.24 [0.50 , 3.08]
1.15.2 After 4 months					
Nordström 1994	4	38	15	38	0.18 [0.05 , 0.61]



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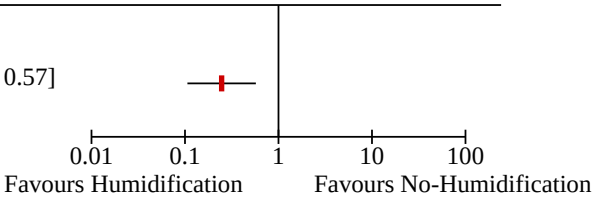
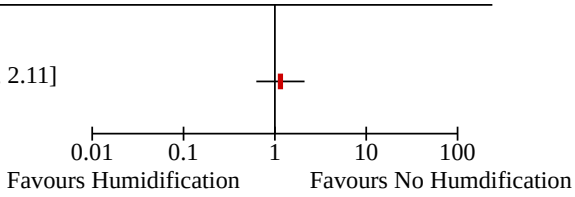
Analysis 1.16. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 16: Dry mouth and throat: Cross-over study cluster non-RCT

Study or Subgroup	log[OR]	SE	Odds Ratio IV, Fixed, 95% CI	Odds Ratio IV, Fixed, 95% CI
1.16.1 12 weeks				
Gavhed 2005	-1.4	0.43	0.25 [0.11 , 0.57]	



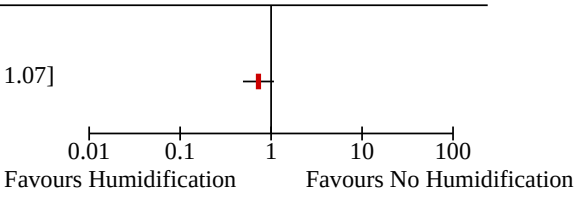
Analysis 1.17. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 17: Pharyngeal Dryness: Cross-over study cluster non-RCT

Study or Subgroup	log[OR]	SE	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI
1.17.1 6 weeks				
Reinikainen 2003	0.14	0.31	1.15 [0.63 , 2.11]	



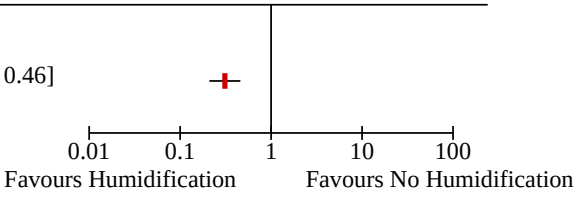
Analysis 1.18. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 18: Pharyngeal Dryness: Cross-over study cluster RCT

Study or Subgroup	log[OR]	SE	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI
1.18.1 6 weeks				
Reinikainen 1992	-0.32	0.2	0.73 [0.49 , 1.07]	



Analysis 1.19. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 19: Perception of dryness: Cross-over study cluster RCT

Study or Subgroup	log[OR]	SE	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI
1.19.1 6 weeks				
Reinikainen 1992	-1.17	0.2	0.31 [0.21 , 0.46]	



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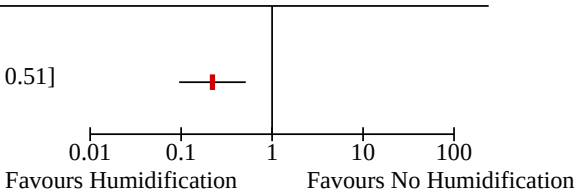
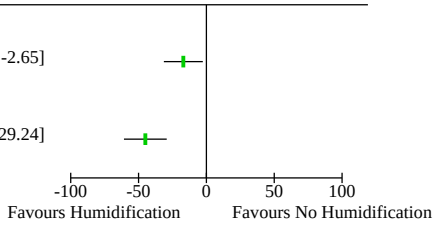
Analysis 1.20. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 20: Perception of dryness: Cross-over study cluster non-RCT

Study or Subgroup	log[OR]	SE	Odds Ratio IV, Random, 95% CI
1.20.1 12 weeks			
Gavhed 2005	-1.51	0.43	0.22 [0.10 , 0.51]



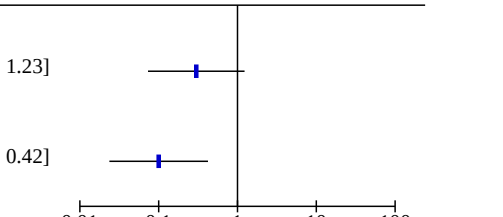
Analysis 1.21. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 21: Perception of dryness: Before-and-after study

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
1.21.1 Before							
Norbäck 2000	73	26	14	90	8	12	-17.00 [-31.35 , -2.65]
1.21.2 After 6 weeks							
Norbäck 2000	36	26	14	81	14	12	-45.00 [-60.76 , -29.24]



Analysis 1.22. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 22: Perception of dryness: Before-and-after study

Study or Subgroup	Experimental Events	Total	Control Events	Total	Odds Ratio M-H, Fixed, 95% CI
1.22.1 Before					
Hashiguchi 2008	9	15	25	30	0.30 [0.07 , 1.23]
1.22.2 After 3 months					
Hashiguchi 2008	5	15	25	30	0.10 [0.02 , 0.42]



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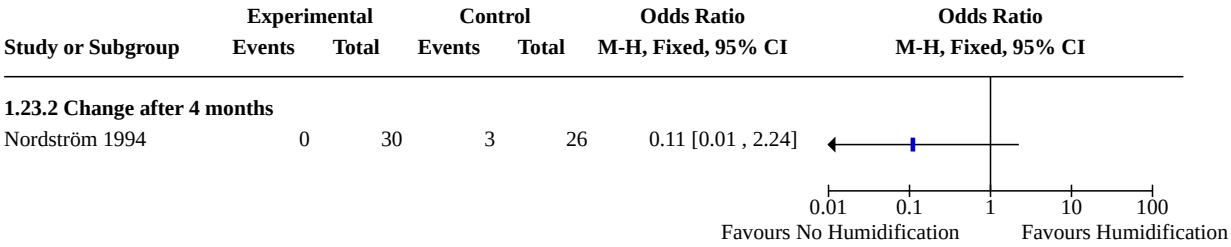
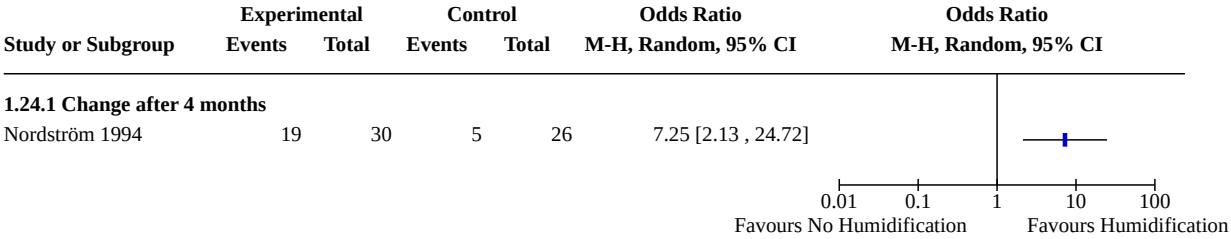
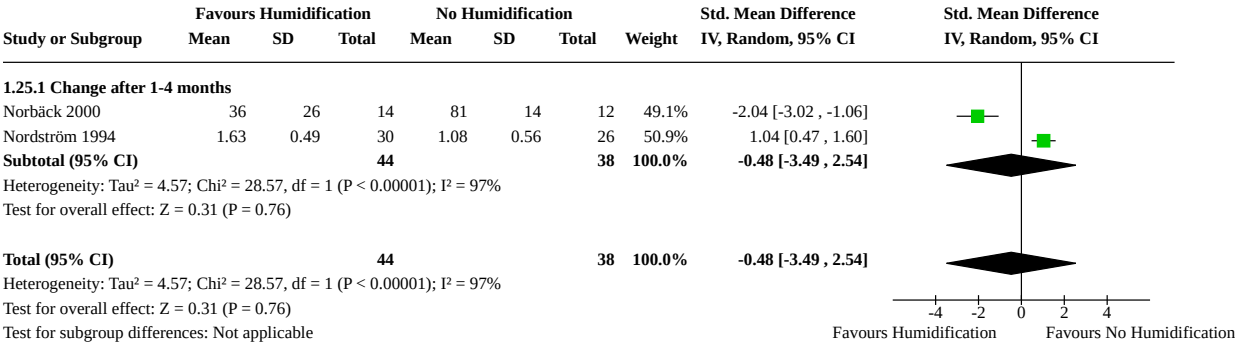
Analysis 1.23. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 23: Increased perception of dryness: Before-and-after study



Analysis 1.24. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 24: Decreased perception of dryness: Before-and-after study



Analysis 1.25. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 25: Perception of dryness: Before-and-after studies



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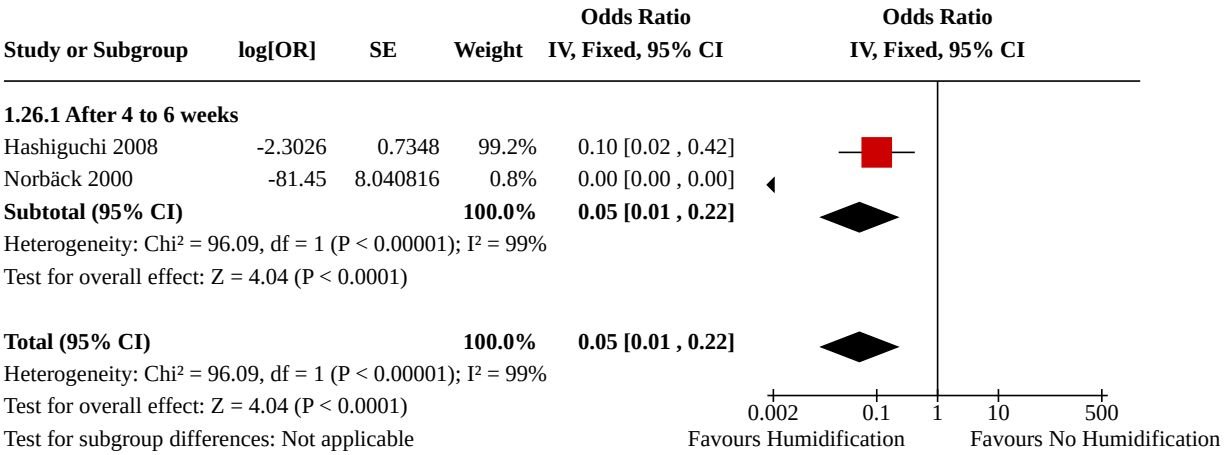
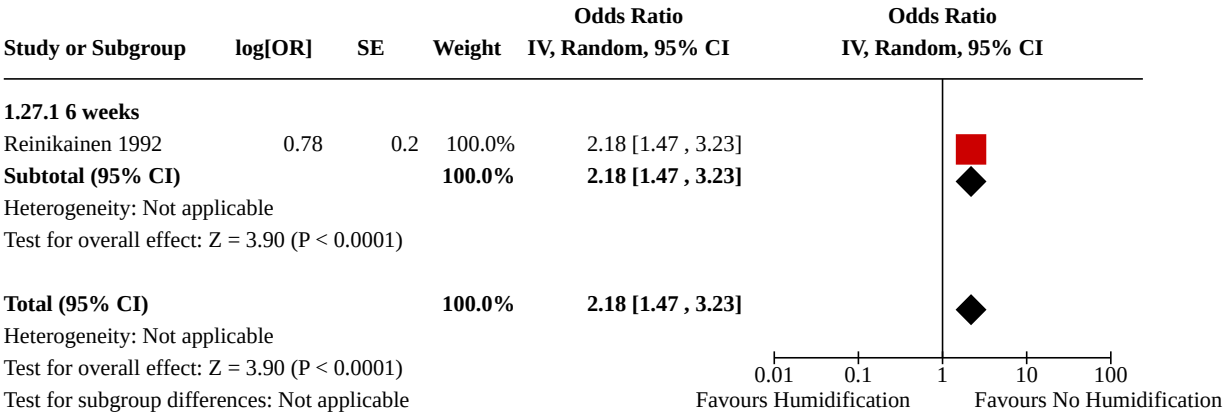
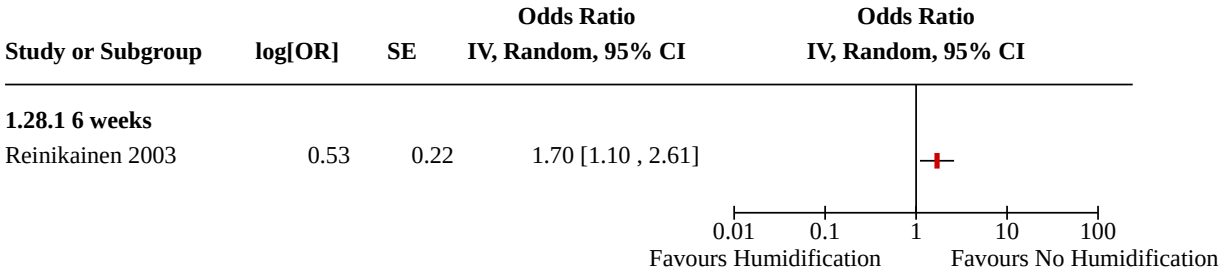
Analysis 1.26. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 26: Perception of dryness: Before-and-after studies



Analysis 1.27. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 27: Perception of stuffiness: Cross-over study cluster RCT



Analysis 1.28. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 28: Perception of stuffiness: Cross-over study cluster non-RCT



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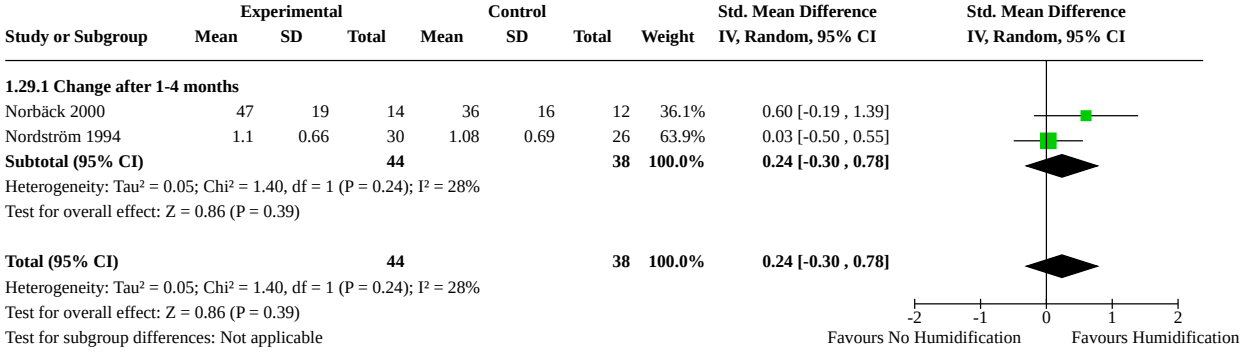
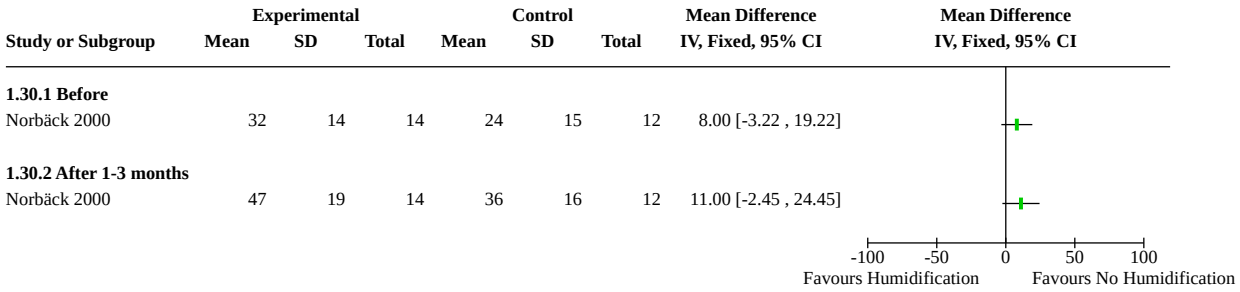
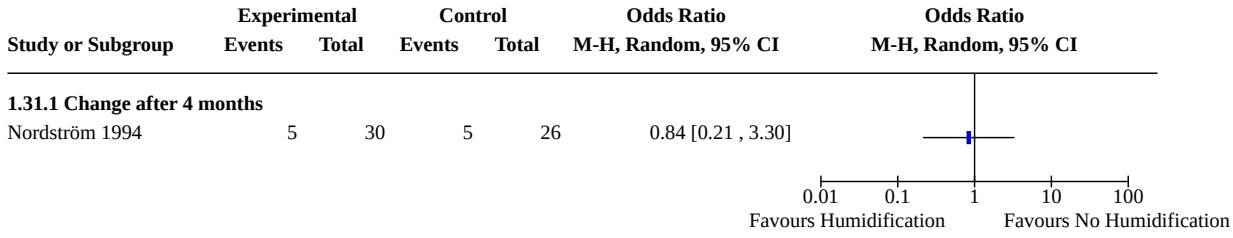
Analysis 1.29. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 29: Perception of stuffiness: Before-and-after studies



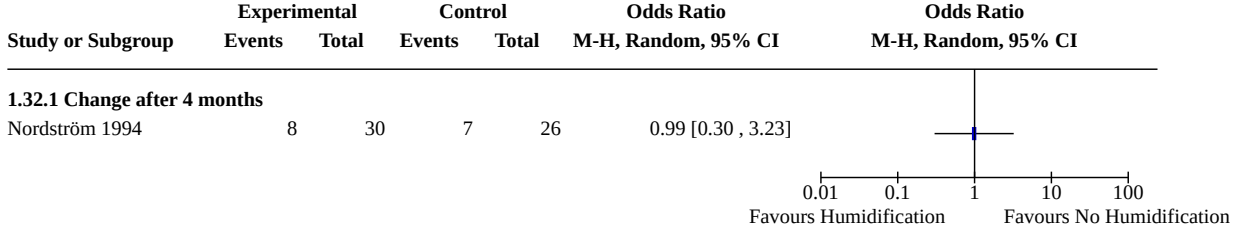
Analysis 1.30. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 30: Perception of stuffiness: Before-and-after studies



Analysis 1.31. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 31: Increased perception of stuffiness: Before-and-after studies



Analysis 1.32. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 32: Decreased perception of stuffiness: Before-and-after studies



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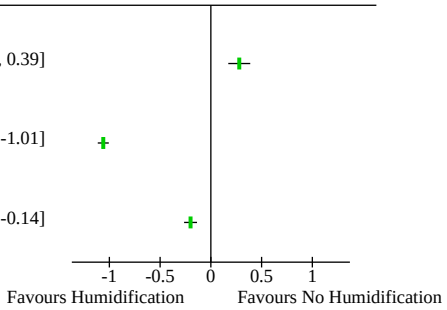
Analysis 1.33. Comparison 1: Humidification vs no humidification in occupational setting, Outcome 33: Absenteeism: Controlled Study non-RCT

Study or Subgroup	Humidification Mean	SD	Total	No Humidification Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
1.33.1 Time period: 1973-1974							
Green 1981	2.19	0.66	185	1.91	0.67	650	0.28 [0.17 , 0.39]
1.33.2 Time period: 1974-1975							
Green 1981	1.87	0.33	185	2.93	0.34	650	-1.06 [-1.11 , -1.01]
1.33.4 Time period: 1975-1976							
Green 1981	1.56	0.33	185	1.76	0.55	650	-0.20 [-0.26 , -0.14]



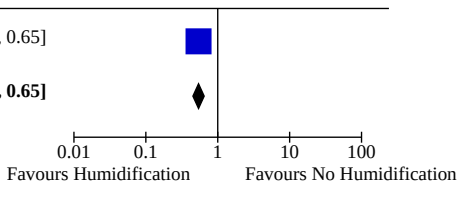
Comparison 2. Humidification vs no humidification in educational setting

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Absenteeism due to cold symptoms: Controlled Study non-RCT	1	12749	Odds Ratio (M-H, Random, 95% CI)	0.54 [0.45, 0.65]
2.2 Average days of absence per child: Controlled Study non-RCT	1		Other data	No numeric data
2.3 Average weekly absense: Controlled Study non-RCT	1	263	Odds Ratio (M-H, Random, 95% CI)	0.38 [0.15, 0.96]
2.4 Average total absenteeism: Controlled Study (1960-1971) non-RCT	1		Other data	No numeric data
2.5 Absenteeism due to sickness: Controlled Study non-RCT	1		Other data	No numeric data
2.6 Absenteeism due to influenza like illness: Controlled Study non-RCT	1		Other data	No numeric data

Analysis 2.1. Comparison 2: Humidification vs no humidification in educational setting, Outcome 1: Absenteeism due to cold symptoms: Controlled Study non-RCT

Study or Subgroup	Experimental Events	Total	Control Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Ritzel 1966	195	6501	338	6248	100.0%	0.54 [0.45 , 0.65]
Total (95% CI)		**6501**		**6248**	**100.0%**	**0.54 [0.45 , 0.65]**
Total events:	195		338			

Heterogeneity: Not applicable
Test for overall effect: Z = 6.70 (P < 0.00001)
Test for subgroup differences: Not applicable



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Analysis 2.2. Comparison 2: Humidification vs no humidification in educational setting, Outcome 2: Average days of absence per child: Controlled Study non-RCT

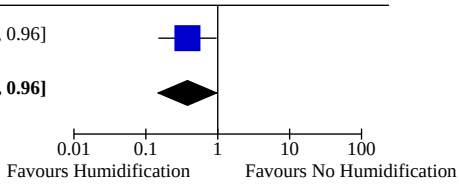
Average days of absence per child: Controlled Study non-RCT

Study	Intervention	Grade 1	Grade 2	Grade 3
Sataloff 1963	No Humidification	7.4	8.6	6.1
	Humidification	9.8	10.4	7.2

Analysis 2.3. Comparison 2: Humidification vs no humidification in educational setting, Outcome 3: Average weekly absense: Controlled Study non-RCT

	Experimental		Control			Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Sale 1972	7	140	15	123	100.0%	0.38 [0.15 , 0.96]	
Total (95% CI)		**140**		**123**	**100.0%**	**0.38 [0.15 , 0.96]**	
Total events:	7		15				

Heterogeneity: Not applicable
Test for overall effect: Z = 2.04 (P = 0.04)
Test for subgroup differences: Not applicable



Analysis 2.4. Comparison 2: Humidification vs no humidification in educational setting, Outcome 4: Average total absenteeism: Controlled Study (1960-1971) non-RCT

Average total absenteeism: Controlled Study (1960-1971) non-RCT

Study	Humidification	No Humidification
Green 1975	4.63%	5.08%

Analysis 2.5. Comparison 2: Humidification vs no humidification in educational setting, Outcome 5: Absenteeism due to sickness: Controlled Study non-RCT

Absenteeism due to sickness: Controlled Study non-RCT

Study	Non-humidification - % out	Non - humidification - Total attendance	Humidification % out	Humidification - Total attendance
Reiman 2018	1.29	1788	1.00	2293

Analysis 2.6. Comparison 2: Humidification vs no humidification in educational setting, Outcome 6: Absenteeism due to influenza like illness: Controlled Study non-RCT

Absenteeism due to influenza like illness: Controlled Study non-RCT

Study	Non humidification - % out	Non humidification - Total attendance	Humidification - % out	Humdification - Total attendance
Reiman 2018	0.39	1788	0.13	2293

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APPENDICES

Appendix 1. MEDLINE search strategy

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) 1946 to August 14.

#	Searches
1	Humidity/
2	(humid* or moist* or damp* or "water vapo?r").ti,ab.
3	(indoor* or inside or building* or room* or plant* or house* or facilit*).ti,ab.
4	(1 or 2) and 3
5	air conditioning/ or ventilation/
6	(air adj3 (condition* or cool* or ventilat* or sparg*)).ti,ab.
7	ventilat*.ti,ab.
8	4 or 5 or 6 or (7 and 3)
9	((indoor and (air or environment* or climate)) adj3 quality).mp. or ("indoor air" or "indoor climate").ti,ab.
10	(iaq or ieq).ti,ab.
11	or/8-10
12	Eye Diseases/ or exp Skin Diseases/ or Nose Diseases/ or Nasal Obstruction/ or rhinitis/ or rhinitis, atrophic/ or rhinitis, vasomotor/ or Respiration Disorders/ or exp Sinusitis/ or Cough/ or Hoarseness/ or Common Cold/ or exp Laryngitis/ or Pharyngitis/ or exp Tonsillitis/ or exp Otitis Media/ or Keratoconjunctivitis Sicca/ or exp Dry Eye Syndromes/
13	(dryness or irritation* or rhinitis or rhinosinusitis or Cough or Hoarseness or "common cold" or flu or Laryngitis or Pharyngitis or Tonsillit* or "Otitis Media" or "Keratoconjunctivitis sicca" or sneez*).ti,ab.
14	Sick Building Syndrome/ or sick building syndrome.ti,ab.
15	((nose or nasal) adj3 (disease* or symptom* or runny or running or stuffed or dry* or obstruction)).ti,ab.
16	(throat adj3 (disease* or symptom* or sore or irritat* or inflam*)).ti,ab.
17	(eye* adj3 (disease* or symptom* or red* or dry* or burning or irritat*)).ti,ab.
18	(skin adj3 (disease* or symptom* or condition* or red* or irritat* or itch* or dry* or rash)).ti,ab.
19	((sinus or respiratory) adj3 (disease* or symptom* or condition* or health)).ti,ab.
20	Absenteeism/ or Sick Leave/

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(Continued)

21	((sick or illness or disability) adj3 (leave* or day*)).ti,ab.
22	((absenteeism or attendance or attainment or productivity or performance) adj9 (job or work or office or school or preschool* or "pre-school*" or kindergar#en* or daycare or "day care")).ti,ab.
23	("mucous membrane" or mucosa or mucosal).ti,ab.
24	mucous membrane/ or exp respiratory mucosa/
25	or/12-24
26	Workplace/ or exp Schools/ or Child Day Care Centers/ or Occupational Exposure/ or Environment, Controlled/ or (office? or Work* or job? or laborator* or school* or preschool* or "pre-school*" or kindergar#en* or daycare or "day care" or classroom* or room* or education* or occupation*).ti,ab.
27	11 and 25 and 26

Appendix 2. Embase search strategy

(1947 to August 16)

#	Searches
1	('humidity'/exp OR humid*:ti,ab OR ventilation:ti,ab) AND (indoor*:ti,ab OR inside:ti,ab OR building*:ti,ab OR room*:ti,ab OR plant*:ti,ab) OR 'air conditioning'/exp OR 'room ventilation'/exp OR ((air NEAR/3 (condition*OR cooling OR ventilation OR sparging)):ti,ab) OR ((((air OR environmental) NEAR/3 quality):ab,ti) AND indoor:ab,ti) OR iaq:ti,ab OR ieq:ti,ab
2	'eye disease'/exp OR 'skin disease'/exp OR 'nose disease'/exp OR 'breathing disorder'/de OR 'coughing'/exp OR 'hoarseness'/exp OR 'laryngitis'/exp OR 'pharyngitis'/exp OR 'nose infection'/exp OR 'tonsillitis'/exp OR 'sinusitis'/exp OR dryness:ti,ab OR irritation*:ti,ab OR rhinitis:ti,ab OR rhinosinusitis:ti,ab OR cough:ti,ab OR hoarseness:ti,ab OR 'common cold':ti,ab OR laryngitis:ti,ab OR pharyngitis:ti,ab OR tonsillit*:ti,ab OR 'otitis media':ti,ab OR 'keratoconjunctivitis sicca':ti,ab OR sneezing:ti,ab OR 'sick building syndrome'/exp OR 'sick building syndrome':ti,ab OR (((nose OR nasal) NEAR/3 (disease* OR symptom* OR runny OR running OR stuffed OR dry* OR obstruction)):ti,ab) OR ((throat NEAR/3 (disease* OR symptom* OR sore OR irritat* OR inflam*)):ti,ab) OR ((eye* NEAR/3 (disease* OR symptom* OR red* OR dry* OR burning OR irritat*)):ti,ab) OR ((skin NEAR/3 (disease* OR symptom* OR condition* OR red* OR irritat* OR itch* OR dry* OR rash)):ti,ab) OR (((sinus OR respiratory) NEAR/3 (disease* OR symptom* OR condition* OR health)):ti,ab) OR 'absenteeism'/exp OR 'medical leave'/exp OR (((sick OR illness OR disability) NEAR/3 (leave* OR day*)):ti,ab) OR (((absenteeism OR attendance OR attainment OR productivity OR performance) NEAR/9 (job OR work OR office OR school OR preschool* OR 'pre-school*' OR kindergar*en* OR daycare OR 'day care')):ti,ab) OR 'mucous membrane':ti,ab OR mucosa:ti,ab OR mucosal:ti,ab OR 'mucosa'/de OR 'respiratory tract mucosa'/exp
3	'workplace'/exp OR 'school'/exp OR 'day care'/de OR 'occupational exposure'/exp OR 'microclimate'/de OR office:ti,ab OR work*:ti,ab OR job:ti,ab OR laboratory:ti,ab OR school*:ti,ab OR preschool*:ti,ab OR 'preschool*':ti,ab OR kindergar*en*:ti,ab OR daycare:ti,ab OR 'day care':ti,ab OR classroom*:ti,ab OR 'clean room':ti,ab OR education:ti,ab OR occupation*:ti,ab

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(Continued)

4	#1 AND #2 AND #3

Appendix 3. CENTRAL search strategy

Cochrane Library up to August 08

#	Searches
1	((humid* or moist* or damp* or "water vapo*r" or ventilat*) and (indoor* or inside or building* or room* or plant* or house* or facilit*)):ti,ab,kw or (air near/3 (condition* or cool* or ventilat* or sparg*)):ti,ab,kw or (((air or environment* or climate) near/3 quality) and indoor*):ti,ab,kw or (iaq or ieq):ti,ab,kw
2	(dryness or irritation* or rhinitis or rhinosinusitis or Cough or Hoarseness or "common cold" or flu or Laryngitis or Pharyngitis or Tonsillit* or "Otitis Media" or "Keratoconjunctivitis sicca" or sneez*) or "sick building syndrome" or ("mucous membrane" or mucosa or mucosal):ti,ab,kw or ((nose or nasal) near/3 (disease* or symptom* or runny or running or stuffed or dry* or obstruction)):ti,ab,kw or (throat near/3 (disease* or symptom* or sore or irritat* or inflam*)):ti,ab,kw or (eye* near/3 (disease* or symptom* or red* or dry* or burning or irritat*)):ti,ab,kw or (skin near/3 (disease* or symptom* or condition* or red* or irritat* or itch* or dry* or
3	((sinus or respiratory) near/3 (disease* or symptom* or condition* or health)):ti,ab,kw or ((sick or illness or disability) near/3 (leave* or day*)):ti,ab,kw or ((absenteeism or attendance or attainment or productivity or performance) near/9 (job or work or office or school or preschool* or "preschool*" or kindergar*en* or daycare or "day
4	#2 or #3
5	(office or Work* or job* or laborator* or school* or preschool* or "preschool*" or kindergar*en* or daycare or "day care" or classroom* or room* or education* or occupation*):ti,ab,kw
6	#1 and #4 and #5

Appendix 4. PsycINFO Search strategy

(1806 to August 08)

S	Searches
1	TX (((humid* OR moist* OR damp* OR "water vapo?r" OR ventilation) AND (indoor* OR inside OR building* OR room* OR plant* OR house* OR facilit*))) OR TX ((airN3 (condition* OR cool* OR ventilat* OR sparg*))) OR TX ((((air OR environment* OR climate) N3 quality) AND indoor) OR "indoor air" OR "indoor climate") OR TX ((iaq or ieq)))
2	(DE "Eye Disorders" DE "Skin Disorders" OR DE "Allergic Skin Disorders" OR DE "Alopecia" OR DE "Dermatitis" OR DE "Herpes Simplex" OR DE "Lupus" OR DE "Pruritus" OR DE "Respiratory Tract Disorders" OR DE "Bronchial Disorders" OR DE "Dyspnea" OR DE "Hay Fever" OR DE "Laryngeal Disorders" OR DE "Lung

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(Continued)

	Disorders" OR DE "Pharyngeal Disorders" OR DE "Mucus" OR DE "Employee Absenteeism")
3	TX (dryness or irritation* or rhinitis or rhinosinusitis or Cough or Hoarseness or "common cold" or flu or Laryngitis or Pharyngitis or Tonsillit* or "Otitis Media" or "Keratoconjunctivitis sicca" or sneez* or "sick building syndrome" OR ((nose or nasal) N3 (disease* or symptom* or runny or running or stuffed or dry* or obstruction)) OR (throat N3 (disease* or symptom* or sore or irritat* or inflam*)) OR (eye* N3 (disease* or symptom* or red* or dry* or burning or irritat*)) OR (skin N3 (disease* or symptom* or condition* or red* or irritat* or itch* or dry* or rash)) OR ((sinus or respiratory) N3 (disease* or symptom* or condition* or health)) OR ((sick or illness or disability) N3 (leave* or day*)) OR ((absenteeism or attendance or attainment or productivity or performance) N9 (job or work or office or school or preschool* or "pre-school*" or kindergar?en* or daycare or "day care")) OR ("mucous membrane" or mucosa or mucosal))
4	S2 OR S3
5	(DE "Schools" OR DE "Boarding Schools" OR DE "Charter Schools" OR DE "Colleges" OR DE "Elementary Schools" OR DE "Graduate Schools" OR DE "High Schools" OR DE "Institutional Schools" OR DE "Junior High Schools" OR DE "Kindergartens" OR DE "Middle Schools" OR DE "Military Schools" OR DE "Nongraded Schools" OR DE "Nursery Schools" OR DE "Seminaries" OR DE "Technical Schools" OR DE "Child Day Care" OR DE "Occupational Exposure")
6	(office* or Work* or job* or laborator* or school* or preschool* or "pre-school*" or kindergar?en* or daycare or "day care" or classroom* or room* or education* or occupation*)
7	S5 OR S6
8	S1 AND S4 AND S7

Appendix 5. Web of Science search strategy

(1988 to August 16)

#	Searches
1	TS=(((humid* OR ventilation) NEAR/3 (indoor* or inside or building* or room* or plant*)) OR (air NEAR/3 (condition* or cooling or ventilation or sparging)) OR (((air OR environmental) NEAR/3 quality) AND indoor) OR (iaq or ieq))
2	TS=(dryness or irritation* or rhinitis or rhinosinusitis or Cough or Hoarseness or "common cold" or Laryngitis or Pharyngitis or Tonsillit* or "Otitis Media" or "Keratoconjunctivitis sicca" or sneezing OR "sick building syndrome" OR ((nose or nasal) NEAR/3 (disease* or symptom* or runny or running or stuffed or dry* or obstruction)) OR (throat NEAR/3 (disease* or symptom* or sore or irritat* or inflam*)) OR (eye* NEAR/3 (disease* or symptom* or red* or dry* or burning or irritat*)) OR (skin NEAR/3 (disease* or symptom* or condition* or red* or irritat* or itch* or dry* or rash)) OR ((sinus or respiratory) NEAR/3 (disease* or symptom* or condition* or health)) OR ((sick or illness or disability) NEAR/3 (leave* or day*)) OR ((absenteeism or attendance or attainment or productivity or performance) NEAR/9 (job or work or office or school or preschool* or "pre-school*" or kindergar*en* or daycare or "day care")) OR "mucous membrane" or mucosa or mucosal)

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(Continued)

3	TS=(office or Work* or job or laboratory or school* or preschool* or "pre-school*" or kindergar*en* or daycare or "day care" or classroom* or "clean room" or education or occupation*)
4	#3 AND #2 AND #1

Appendix 6. Scopus search strategy

(1960 to August 16)

#	Searches
	(TITLE-ABS-KEY (((humid* OR ventilation) W/3 (indoor* OR inside OR building* OR room* OR plant*)) OR (air W/3 (condition* OR cooling OR ventilation OR sparging)) OR (((air OR environmental) W/3 quality) AND indoor) OR (iaq OR ieq))) AND (TITLE-ABS-KEY (dryness OR irritation* OR rhinitis OR rhinosinusitis OR cough OR hoarseness OR "common cold" OR laryngitis OR pharyngitis OR tonsillit* OR "Otitis Media" OR "Keratoconjunctivitis sicca" OR sneezing OR "sick building syndrome" OR ((nose OR nasal) W/3 (disease* OR symptom* OR runny OR running OR stuffed OR dry* OR obstruction)) OR(throat W/3 (disease* OR symptom* OR sore OR irritat* OR inflam*)) OR (eye* W/3 (disease* OR symptom* OR red* OR dry* OR burning OR irritat*)) OR (skin W/3 (disease* OR symptom* OR condition* OR red* OR irritat* OR itch* OR dry* OR rash)) OR ((sinus OR respiratory) W/3 (disease* OR symptom* OR condition* OR health)) OR ((sick OR illness OR disability) W/3 (leave* OR day*)) OR ((absenteeism OR attendance OR attainment OR productivity OR performance) W/9 (job OR work OR office OR school OR preschool* OR "pre-school*" OR kindergar?en* OR daycare OR "day care")) OR "mucous membrane" OR mucosa OR mucosal)) AND (TITLE-ABS-KEY (office OR work* OR job OR laboratory OR school* OR preschool* OR "pre-school*" OR kindergar?en* OR daycare OR "day care" OR classroom* OR "clean room" OR education OR occupation*))

Appendix 7. NIOSHTIC-2 search strategy

(from inception to August 08)

#	Searches
1	TW{humid* or moist* or damp* or water.1.vapor or water.1.vapour or ventilat*} and TW{indoor* or inside or building* or room* or plant* or house* or facilit*}
2	AB{humid* or moist* or damp* or water.1.vapor or water.1.vapour or ventilat*} and AB{indoor* or inside or building* or room* or plant* or house* or facilit*}
3	TW{air.-3.condition* or air.-3.cool* or air.-3.ventilat* or air.-3.sparg*} or AB{air.-3.condition* or air.-3.cool* or air.-3.ventilat* or air.-3.sparg*}
4	TW{air.-3.quality or environment*.-3.quality or climate.-3.quality} and TW{indoor*}

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(Continued)

5	AB{air.-3.quality or environment*.-3.quality or climate.-3.quality} and AB{indoor*}
6	TW{iaq or ieq} or AB{iaq or ieq}
7	#1 or #2 or #3 or #4 or #5 or #6
8	TW{dryness or irritation* or rhinitis or rhinosinusitis or Cough or Hoarseness or common.1.cold or flu or Laryngitis or Pharyngitis or Tonsillit* or Otitis.1.Media or Keratoconjunctivitis.1.sicca or sneez* or sick.1.building.1.syndrome or mucous.1.membrane or mucosa or mucosal} or AB{dryness or irritation* or rhinitis or rhinosinusitis or Cough or Hoarseness or common.1.cold or flu or Laryngitis or Pharyngitis or Tonsillit* or Otitis.1.Media or Keratoconjunctivitis.1.sicca or sneez* or sick.1.building.1.syndrome or mucous.1.membrane or mucosa or mucosal}
9	TW{nose.-3.disease* or nose.-3.symptom* or nose.-3.runny or nose.-3.running or nose.-3.stuffed or nose.-3.dry* or nose.-3.obstruction or nasal.-3.disease* or nasal.-3.symptom* or nasal.-3.runny or nasal.-3.running or nasal.-3.stuffed or nasal.-3.dry* or nasal.-3.obstruction} or AB{nose.-3.disease* or nose.-3.symptom* or nose.-3.runny or nose.-3.running or nose.-3.stuffed or nose.-3.dry* or nose.-3.obstruction or nasal.-3.disease* or nasal.-3.symptom* or nasal.-3.runny or nasal.-3.running or nasal.-3.stuffed or nasal.-3.dry* or nasal.-3.obstruction}
10	TW{throat.-3.disease* or throat.-3.symptom* or throat.-3.sore or throat.-3.irritat* or throat.-3.inflam*} or AB{throat.-3.disease* or throat.-3.symptom* or throat.-3.sore or throat.-3.irritat* or throat.-3.inflam*}
11	TW{eye*.-3.disease* or eye*.-3.symptom* or eye*.-3.red* or eye*.-3.dry* or eye*.-3.burning or eye*.-3.irritat*} or AB{eye*.-3.disease* or eye*.-3.symptom* or eye*.-3.red* or eye*.-3.dry* or eye*.-3.burning or eye*.-3.irritat*}
12	TW{skin.-3.disease* or skin.-3.symptom* or skin.-3.condition* or skin.-3.red* or skin.-3.irritat* or skin.-3.itch* or skin.-3.dry* or skin.-3.rash} or AB{skin.-3.disease* or skin.-3.symptom* or skin.-3.condition* or skin.-3.red* or skin.-3.irritat* or skin.-3.itch* or skin.-3.dry* or skin.-3.rash}
13	TW{sinus.-3.disease* or sinus.-3.symptom* or sinus.-3.condition* or sinus.-3.health OR respiratory.-3.disease* or respiratory.-3.symptom* or respiratory.-3.condition* or respiratory.-3.health} OR AB{sinus.-3.disease* or sinus.-3.symptom* or sinus.-3.condition* or sinus.-3.health OR respiratory.-3.disease* or respiratory.-3.symptom* or respiratory.-3.condition* or respiratory.-3.health}
14	TW{sick.-3.leave* or illness.-3.leave* or disability.-3.leave* or sick.-3.day* or illness.-3.day* or disability.-3.day*} or AB{sick.-3.leave* or illness.-3.leave* or disability.-3.leave* or sick.-3.day* or illness.-3.day* or disability.-3.day*}
15	TW{absenteeism.-9.job or absenteeism.-9.work or absenteeism.-9.office or absenteeism.-9.school or absenteeism.-9.preschool* or absenteeism.-9.pre.1.school* or absenteeism.-9.kindergarden* or absenteeism.-9.kindergarten* or absenteeism.-9.daycare or absenteeism.-9.day.1.care} or TW{attendance.-9.job or attendance.-9.work or attendance.-9.office or attendance.-9.school or attendance.-9.preschool* or attendance.-9.pre.1.school* or attendance.-9.kindergarden* or attendance.-9.kindergarten* or attendance.-9.daycare or attendance.-9.day.1.care} or TW{attainment.-9.job or attainment.-9.work or attainment.-9.office or attainment.-9.school or attainment.- 9.preschool* or attainment.-9.pre.1.school* or attainment.-9.kindergarden* or attainment.-9.kindergarten* or attainment.-9.daycare or attainment.-9.day.1.care}

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(Continued)

16	TW{productivity.-9.job or productivity.-9.work or productivity.-9.office or productivity.-9.school or productivity.-9.preschool* or productivity.-9.pre.1.school* or productivity.-9.kindergarden* or productivity.-9.kindergarten* or productivity.-9.daycare or productivity.-9.day.1.care} or TW{performance.-9.job or performance.-9.work or performance.- 9.office or performance.-9.school or performance.-9.preschool* or performance.-9.pre.1.school* or performance.-9.kindergarden* or performance.-9.kindergarten* or performance.-9.daycare or performance.-9.day.1.care}
17	AB{absenteeism.-9.job or absenteeism.-9.work or absenteeism.-9.office or absenteeism.-9.school or absenteeism.-9.preschool* or absenteeism.-9.pre.1.school* or absenteeism.-9.kindergarden* or absenteeism.-9.kindergarten* or absenteeism.-9.daycare or absenteeism.-9.day.1.care} or AB{attendance.-9.job or attendance.-9.work or attendance.-9.office or attendance.-9.school or attendance.-9.preschool* or attendance.-9.pre.1.school* or attendance.-9.kindergarden* or attendance.-9.kindergarten* or attendance.-9.daycare or attendance.-9.day.1.care} or AB{attainment.-9.job or attainment.-9.work or attainment.-9.office or attainment.-9.school or attainment.-9.preschool* or attainment.-9.pre.1.school* or attainment.-9.kindergarden* or attainment.-9.kindergarten* or attainment.-9.daycare or attainment.-9.day.1.care}
18	AB{productivity.-9.job or productivity.-9.work or productivity.-9.office or productivity.-9.school or productivity.-9.preschool* or productivity.-9.pre.1.school* or productivity.-9.kindergarden* or productivity.-9.kindergarten* or productivity.-9.daycare or productivity.-9.day.1.care} or AB{performance.-9.job or performance.-9.work or performance.-9. office or performance.-9.school or performance.-9.preschool* or performance.-9.pre.1.school* or performance.-9.kindergarden* or performance.-9.kindergarten* or performance.-9.daycare or performance.-9.day.1.care}
19	#8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18
20	TW{office or Work* or job* or laborator* or school* or preschool* or pre.1.school* or kindergarden* or kindergarten* or daycare or day.1.care or classroom* or room* or education* or occupation*} or AB{office or Work* or job* or laborator* or school* or preschool* or pre.1.school* or kindergarden* or kindergarten* or daycare or day.1.care or classroom* or room* or education* or occupation*}
21	#7 and #19 and #20
22	DC{OUNIOS}
23	#21 and #22

Appendix 8. HSELINE and CISDOC search strategy

#	Searches
	(mucous membrane or sick building syndrome or humid).ti, ab and humid*

Appendix 9. Study screening form

I. General information

Study screening and data extraction were performed in Covidence.

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Study ID:	Report ID:	Data form completed: Version number:
First author:	Year of study:	Data extractor:
Citation:		
Publication type (specify):		
Country of study:	Funding source of study:	Potential conflict of interest from funding? Yes – No – Unclear

II. Study eligibility

Type of study	Randomised controlled trial (RCT) Cluster randomised controlled trial (cluster-RCT) Interrupted time-series studies (ITS) - clearly defined intervention point Cross-over study - order of intervention	Controlled before-and-after study (CBA) - comparable control site Quasi-randomised studies - method of allocation Other type of controlled studies, specify:
	Does the study design meet the criteria for inclusion? Yes No: exclude Unclear	
Type of participants	Describe the participants included: They belong to which group: - Adult working population - School setting: children, young adults Do the participants meet the criteria for inclusion? Yes No: exclude Unclear	
Type of interventions	Is indoor air humidity assessed? Technique: Intervention in control group:	

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(Continued)

	Does the intervention meet the criteria for inclusion? Yes No: exclude Unclear
Type of outcome measures	List primary outcomes: List secondary outcomes: Does the study assess a single primary or secondary outcome, qualifying it for inclusion? Yes No: exclude Unclear

III. Summary of assessment for inclusion

Include in review	Exclude from review
Reason for exclusion:	
Independently assessed and then compared? Yes No	Differences resolved? Yes No
Request further details? Yes No Contact detail of authors:	
Notes:	

Do not proceed if article is excluded from review.

HISTORY

Protocol first published: Issue 6, 2016

CONTRIBUTIONS OF AUTHORS

Conceiving the protocol: CH, HD, MM, MP, MS

Designing the protocol: HD, MM, MP, MS

Co-ordinating the protocol: MM

Designing search strategies: MM, KB

Writing the protocol: KB, MM, TR, DI

Providing general advice on the protocol: MM, MP, HD

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Extracting data and conducting analysis: KB, DI, TR, MM, HD

Completing GRADE Assessments: KB, TR

Writing the review: KB, TR, MM

Contributing to writing the review and approving the final draft: DN, CH, DI, MS, MP, HD

DECLARATIONS OF INTEREST

Katarzyna Byber: none known.

Dan Norbäck: none known.

Christine Hitzke: none known.

David Imo: none known.

Matthias Schwenkglenks: none known.

Milo Puhan: none known.

Holger Dressel: none known.

Margot Mutsch: none known.

Dan Norbäck (co-)authored two of the included studies. He was not involved in the data collection, analysis and in writing the Results section.

SOURCES OF SUPPORT

Internal sources

- Internal: EBPI, University of Zurich, Switzerland

  Infrastructure, salaries and out-of-pocket expenses for Katarzyna Byber, Thomas Radtke, Christine Hitzke, David Imo, Matthias Schwenkglenks, Milo A Puhan, Holger Dressel and Margot Mutsch

External sources

- Cochrane Switzerland and Swiss School of Public Health (SSPH+), Switzerland

  Salary to Aline Flatz
- Clinic of Occupational and Environmental Medicine Department, University Hospital, Uppsala, Sweden, Sweden

  Infrastructure and salary to Dan Norbäck

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We tried to apply the a priori defined methods, as outlined in the published protocol (Byber 2016), but we decided that certain changes to the Methods were necessary. These changes are outlined in the following:

Search:

We performed the search in PsycINFO, but did not consider PsycArticles and Psyndex, as PsycINFO includes their articles, and we did not target diagnostics of psychological tests or audiovisual media.

We did not search publications from the websites of governmental agencies, such as the US Environmental Protection Agency (EPA), Canadian Centre for Occupational Health and Safety (CCOHS), Partnership for European Research in Occupational Safety and Health (PEROSH), and European Union (EU) guidelines.

Inclusion criteria:

We have considered indoor air humidification. Since there are some differences in indoor climate in aircraft cabins compared to buildings, we have decided not to include studies on this topic. Specifically, we have added to the Methods section the type of participants that we considered in occupational settings in buildings.

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Some studies conducted in occupational settings evaluated simultaneously many different effects of humidification. In such cases, we presented symptoms most likely related to indoor air humidity and omitted symptoms which could also be caused by other reasons. For example, in Reinikainen 1992, as well as dryness symptoms of the skin, eye, nose and pharynx, other symptoms like cough and nasal congestion were assessed and could not clearly be differentiated from allergic or asthma manifestations, respectively.

We intended to differentiate between central and local humidification interventions. However, the studies with local humidification included humidification at room level, but not stand-alone devices, e.g. on work desks. No differences between humidification of rooms and of several rooms or floors could therefore be identified. Hence, the local and central interventions are presented together.

Initially, we conjectured that randomisation at the individual level was impossible, as humidification of the air is an intervention that always takes place at a group level and is provided outside the clinical setting. With hindsight, we are aware that our assumption might not always apply, but we did not find any study with randomisation at the individual level.

In order to assess risks of bias of all included studies, in consultation with the Co-ordinating Editor of Cochrane Work, we decided to use an additional item: 'Other source of bias'.

Initially, we intended to summarise evidence of effectiveness for interventions graphically, using harvest plots according to Ogilvie 2008; Turley 2013. Due to the small number and size of the included studies, we synthesised the evidence only narratively.

According to the recommendation of the Co-ordinating Editor of the Cochrane Work group, for the cross-over trials with dichotomous data we computed the pooled logarithm of the OR (lnOR) based on the usual weighted average of trial lnOR, where weights are the inverse of the lnOR variance. The lnORs were then calculated to ORs in RevMan.

We limited the summary of findings tables to the primary outcomes of eye, skin and upper respiratory tract (URT) symptoms, and omitted other symptoms and physiological measurements. We also presented the outcome: 'perception of stuffiness' as an adverse effect of humidification in the SoF table.

As we grouped the studies according to the study design in order to show the evidence level, we did not perform the classification due to study periods.

NOTES

Parts of the Methods section and Appendix 1 of this review are based on a standard template established by the Cochrane Work Group.

INDEX TERMS

Medical Subject Headings (MeSH)

Absenteeism; *Air Pollution, Indoor [statistics & numerical data]; *Occupational Health; *Respiratory Tract Infections [prevention & control]; Workplace

MeSH check words

Adult; Humans

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