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Non-specific Symptoms in Office Workers: A Review and Summary of the Epidemiologic Literature

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Abstract

Epidemiologic research into the causes of non-specific symptoms among office workers has produced a variety of conflicting findings which are difficult to synthesize. This paper first discusses methodologic issues important in the interpretation of epidemiologic studies, and then reviews the findings of 32 studies of 37 factors potentially related to office worker symptoms. Among environmental factors assessed, there were generally consistent findings associating increased symptoms with air-conditioning, carpets, more workers in a space, VDT use, and ventilation rates at or below 10 liters/second/person. Studies with particularly strong designs found decreased symptoms associated with low ventilation rate, short-term humidification, negative ionization, and improved office cleaning, although studies reviewed showed little consistency of findings for humidification and ionization. Relatively strong studies associated high temperature and low relative humidity with increased symptoms, whereas less strong studies were not consistent. Among personal factors assessed, there were generally consistent findings associating increased symptoms with female gender, job stress/dissatisfaction, and allergies/asthma. For other environmental or personal factors assessed, findings were too inconsistent or sparse for current interpretation, and there were no findings from strong studies. Overall evidence suggested that work-related symptoms among office workers were relatively common, and that some of these symptoms represented preventable physiologic effects of environmental exposures or conditions. Future research on this problem should include blind experimental and case-control studies, using improved measurements of both environmental exposures and health outcomes.

KEY WORDS:
Sick building syndrome, Indoor air quality, Ventilation, Health, Office buildings, Air-conditioning

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Introduction

Investigations of symptom complaints among office workers, reported increasingly in the past 20 years, have often identified neither specific illnesses nor responsible exposures. In addition to these reports of single building investigations, a sizable research literature on occurrence of such non-specific symptoms has also developed, including cross-sectional, case-control, and experimental studies, with a variety of often conflicting findings. It can be difficult, in evaluating these contradictory findings, to achieve a critical synthesis which goes beyond the numerical estimates and confidence intervals reported for various factors assessed.

This paper selects studies for review (see Methods) and summarizes their findings graphically. It also attempts to help readers interpret this literature, by discussing some study design features important for insuring study validity (i.e., lack of bias), assessing the quality and consistency of available study findings, and attempting resolution of several conflicting sets of study findings. It then summarizes other aspects of the current literature, and suggests strategies for future research.

Even one source of major bias (error which either hides, exaggerates, or even falsely creates relationships) in an otherwise excellent study can produce invalid and misleading findings. Some study features which influence potential for bias include: type of study design (e.g., various experimental or observational designs), strategies to control confounding (a distortion of apparent relationships between two factors due to another factor related to both), quality of measurements, and comparability of study populations. Larger study size, although it can improve the *precision* of findings (e.g., reduce the random error), cannot reduce bias or improve validity. These issues are discussed in detail by Rothman (1986).

Studies in the indoor air literature include both experimental and observational designs. The advantage of an experiment is that it allows changing *one* factor, while holding all others constant. The ideal experiment would randomly assign individual study participants to two groups ("randomized"), administer a single changed condition to one group and a false ("placebo") change to the other, with neither subjects nor researchers aware ("double-blind") of which group experienced the actual changed condition. A randomized, placebo-controlled, double-blind experiment can effectively minimize a variety of potential biases in evaluating causal effects, even in problematic situations; e.g., when only subjective symptom reports, sensitive to mood and psychological setting, can be used to measure health. Lack of one or more key features weakens an experiment's resistance to potential bias. An experimental study lacking individual randomization to treatment groups is vulnerable to *prior* differences between the groups (and is thus sometimes called a "quasi-experiment") (Cook and Campbell, 1979). Complete lack of a comparison group fails to control for the potent beneficial effects of being studied or for other time-related factors, and an unblinded study is vulnerable to distortion of results from subject or researcher expectations.

For a variety of reasons, however, experiments or even quasi-experiments are often not feasible in the indoor air setting: impracticality of randomizing individuals to treatments in an occupational setting; ethical constraints in administering, or even allowing, known toxic exposures; difficulty in changing only one factor in a complex environment; and so on. Instead, *observational* studies involve selection of appropriate populations to observe and compare, without interventions, so as to *simulate* the results of an experiment. Observational study designs, which include case studies, cross-sectional studies, case-control studies, and follow-up studies, are able to address a wider range of questions than experiments but are more difficult to protect against bias. Biases in observational studies, which can falsely either exaggerate or diminish true associations, can be minimized but usually not eliminated; however, a diverse body of well-designed observational studies can be persuasive.

Most of the observational studies reviewed here are cross-sectional (i.e., they collect information on health and exposures at the same time), while some are case-control studies (which compare groups with high levels of symptoms to those with low levels). The cross-sectional design is often the most practical approach in studying office worker symptoms, though it has more limitations than the case-control or follow-up designs. Cross sectional studies will underestimate disease effects if the most susceptible have left the workplace; another limitation is that they cannot assess temporal relationships (such as whether stress or symptoms occurred first). Case studies (i.e., problem building investigations performed as a public health response to worker complaints in a single building), have rarely provided scientifically useful findings due to their limited designs. Strategies for minimizing bias in epidemiological studies include: *techniques to control confounding,* such as multiple regression modelling, matching, or within-subject comparisons; use of optimally accurate measurements – e.g., *objective health measurements,* less liable to be influenced by extraneous factors than subjective ones, and *person-specific environmental measurements,* more likely to be accurate for each person than room-average measurements; and (particularly in cross-sectional and case-control studies) *selection of populations* appropriate for the comparisons of interest.

Methods

This review selected reports from the literature of epidemiologic studies on work-related symptoms (those occurring at work or improving away from work) among workers in office buildings, choosing where possible the single most complete report for each study. Articles from 1984 through December, 1992 were sought in several computerized scientific databases, and also in a number of selected journals and conference proceedings; later published updates were also considered. All reports of single "problem" building investigations, some reports of smaller studies (one or two buildings), and studies performed in laboratories were omitted for brevity.

For each study included here, reported relationships between *symptom prevalence* and a variety of *factors or environmental measurements* were reviewed. Direction of association (factor associated with higher symptom prevalence, not associated with symptom prevalence, or associated with lower symptom prevalence) was determined. Association with symptom prevalence was defined as a statistically significant association with *at least one* of the following symptoms: eye, nose, throat, or skin symptoms; breathing or lower respiratory problems; fatigue or tiredness; or headache.

Findings for each specific factor or measurement were evaluated across studies and classified as consistent, mostly consistent, or too inconsistent or sparse for simple interpretation. "Consistent" was defined as agreement by all relevant studies reviewed, with a minimum of three studies. "Mostly consistent" was defined as one discordant finding in four to six studies, one or two discordant findings in seven or more studies, and so on (e.g., less than 30% discordant). Except as noted, this classification did not consider differences between studies in measurement methods, levels of factors compared, or definitions of factors used. Inconsistent findings for several factors, including ventilation rate, were considered in more detail.

The presence of several key study features which reduce potential bias was also evaluated for each study. Findings from study designs considered to be *strong* (highly resistant to bias) were identified; as design features varied even within studies, this determination was finding-specific, not study-specific. For instance, an experimental study may have controlled ventilation rate to assess relationships with symptoms, but may also have assessed association of symptoms with variations in temperature and other variables that happened to occur (e.g., Menzies et al., 1993); the ventilation finding would be considered stronger than the temperature finding. For experimental studies, a strong study required an adequate comparison group (simultaneous, and either untreated or placebo-treated) and at least a single-blind design (e.g., subjects unaware of group treatment). Note that a single-blind study is possible for ventilation rate, but may not be for temperature. For observational studies, a strong study design required either a case-control or follow-up study design, along with control for major confounding variables, person-specific environmental measurements, and use of appropriate study populations.

Some additional research reports relevant to the interpretation of the epidemiologic studies were also reviewed but not included in the summary Table.

Results

Table 1 summarizes findings from 32 reports on associations between worker symptoms and 17 environmental measurements, 5 building factors, 7 workspace factors, and 8 job and personal factors. Studies are categorized in Table 1 as experimental or observational; one (Jaakkola et al., 1991) was both. Experimental studies were further grouped by whether or not adequate comparison groups (as defined previously) were used. All experimental studies reviewed were technically quasi-experiments, as none randomized individuals to treatments. Observational studies were grouped by the presence or absence of techniques to control confounding. Within each of these groups, studies are listed alphabetically by author. Observational studies were cross-sectional except for four case-control studies (Sundell et al., 1992; Menzies et al., 1992; Skov and Valbjørn, 1990a; Burge et al., 1990).

As shown in the Table 1 legend, symptom associations reported for factors or measurements are categorized as: associated with higher symptoms, no associations, or associated with lower symptoms. (Some factors were "reversed" for comparability across studies e.g., improved cleaning (Leinster et al., 1990) and poor cleaning (Skov et al., 1989, 1990; Skov and Valbjørn, 1990a).) Specific findings from study designs considered strong are highlighted. Some key study design features used are also indicated in the Table.

In this paper, humidification refers to the addition of moisture to air supplied by mechanical ventilation systems, using methods such as drip, spray, or steam. Ionization refers to the use of ion generators which emit negative ions and increase their concentration in indoor air. Carpets refer to the presence in the workspace of carpets of any age, not just new. More workers in the workspace refers to the number of other workers sharing a room or workspace with a study respondent; specific levels compared varied between studies.

The bottom row of Table 1 summarizes the apparent consistency of findings across studies. Consistent associations were reported between higher symptom prevalence and: air-conditioning systems (nine studies), higher job stress/dissatisfaction (seven studies), and allergies/asthma (six studies). Mostly consistent associations with higher symptoms were reported for: carpets (five of six studies), more workers in the workspace (five of seven), video display terminal (VDT) use (six of eight), and female gender (12 of 13). Consistent or mostly consistent findings of *no* association with altered symptom prevalence were reported for total viable fungi, total viable bacteria, total particles, air velocity, carbon monoxide, formaldehyde, and noise. For other factors and environmental measurements considered in the review, findings were too inconsistent or sparse for simple interpretation. Findings for

Table 1 Summary of reported associations between work-related symptoms and various environmental factors and measurements, along with summary of key design features of studies reviewed

STUDIES	STUDY FEATURES: Experimental comparison group	Blinded Experiment	Control for confounding	Objective health msmts.	Person-specific envir. msmts.	ENVIRONMENTAL MEASUREMENTS: Low ventilation rate	Carbon monoxide	Total VOCs	Formaldehyde	Total particles	Respirable particles	Floor dust (all or protein)	Total viable bacteria	Total viable fungi	Endotoxins	Beta-1,3-glucan	Low negative ions	High temperature	Low humidity	Air velocity	Light intensity or glare	Noise
EXPERIMENTAL																						
Jaakkola 90	+C	+2	+			[○]																
Jaakkola 91	+	+	+			[◒]																
Leinster 90	+	+2																				
Menzies 93	+C	+2	+			[○]												◓		◓		
Raw 91	+P	+																				
Reinikainen 92	+C	(+)	+																◓			
Wyon 92	+P/+	+/		+		[○]											(◓)	◓	◓		◓	
Finnegan 87		+2	+														(◒)					
Hawkins 84		+2															(◓)	○	○			
Nagda 91		+				◓																
Norbäck 89																						
OBSERVATIONAL																						
Hedge 89			+																			
Hodgson 91			+		+	○	○	◓			○				○			○	○	○	◓	○
Hodgson 92			+		+	○	○	◓										○	○	○	○	◓
Jaakkola 91			+			○												◓				
Mendell 92			+			○	○	○					○	○				○				
Menzies 92			+	+	+									[○]								
Norbäck 90			+			○		◓			◓							○	○			
Reinikainen 91			+																◓/◒			
Skov 89			+	(+)																		
Skov 90			+	(+)		○		○	○	○		◓	○	○				◓	○	○	○	◒
Skov 90a			+	(+)		○		○		○		○	○	○			○	◓	(◒)		○	○
Sundell 92			+			◓												○	○			
Zweers 92			+			○												○	○		○	○
Burge 90						○												○	○	○	○	○
Finnegan 87a																						
Harrison 92										○			○	◓								
Hill 92						○					◓											
Knave 85																						
Kroeling 88																						
Mendell 90																						
Robertson 89																					◓	
Rylander 92															◓	◓						
SUMMARY						↑	O	?	O	O	?	?	O	O	?	?	?	?	?	O	?	O

Table 1 (continued)

STUDIES	BUILDING FACTORS					WORKSPACE FACTORS							JOB AND PERSONAL FACTORS							
	Air conditioning	Humidification	Mechanical vent'n, no a.c.	Newer building	Poor vent'n maintenance	Ionization	Improved office cleaning	Carpets	Fleecy materials/open shelves	Photocopier in room or near	Environmental tobacco smoke	More workers in the space	Clerical job	Carbonless copy use	Photocopier use	VDT use	Job stress/dissatisfaction	Female gender	Smoker	Allergies/asthma
EXPERIMENTAL																				
Jaakkola 90																				
Jaakkola 91																				
Leinster 90							■													
Menzies 93																◓		◓		◓
Raw 91							■													
Reinikainen 92		■																		
Wyon 92		◒				■														
Finnegan 87						◓														
Hawkins 84						◒														
Nagda 91																				
Norbäck 89								◓												
OBSERVATIONAL																				
Hedge 89	◓	◓											◓			◓	◓	◓		
Hodgson 91											○	◓				○		○	○	
Hodgson 92									○			○	○				◓	◓		
Jaakkola 91											◓						◓	◓		◓
Mendell 92	◓		◓					◓		○		◓	○	◓	◓	○	◓	◓	◓	◓
Menzies 92								◓								◓			◓	◓
Norbäck 90			○	○				◓									◓		◓	
Reinikainen 91		◒/◓																		
Skov 89							○					◓	◓	◓	◓	◓	◓	◓	◓	◓
Skov 90	◓		◓	◓			○	◓	◓			◓								
Skov 90a		(◓)					◒		○			○						◓		
Sundell 92			○						○	◓										
Zweers 92	◓	◓	◓					○	○		◓	◓		○		◓	◓	◓	○	◓
Burge 90					◓													◓		
Finnegan 87a	◓	◓																◓		
Harrison 92	◓	○																		
Hill 92																		◓		
Knave 85														○		◓		◓		
Kroeling 88	◓																			
Mendell 90	◓	○																		
Robertson 89	◓																			
Rylander 92																				
SUMMARY	↑↑	?	?	?	?	?	?	↑	?	?	?	↑	?	?	?	↑	↑↑	↑	?	↑↑

LEGEND

STUDY FEATURES

- \+ Yes
- +P Yes, placebo
- +C Yes, crossover
- +2 Yes, double blind
- ( ) Indirectly applicable

ASSOCIATIONS WITH FACTORS AND MEASUREMENTS

- ◓ Higher symptoms
- ○ No associations
- ◒ Lower symptoms
- Not assessed
- ( ) Indirectly applicable
- ■ Strong design

SUMMARY

- ↑↑ Consistent higher symptoms
- ↑ Mostly consistent higher symptoms
- **O** Consistent lack of association
- ○ Mostly consistent lack of association
- ? Sparse or inconsistent findings

only four factors, however, were so inconsistent as to include associations with both higher and lower symptom prevalence: humidity, noise, humidification, and ionization. Findings for low ventilation rate are considered mostly consistent (see below).

Strong study designs found low ventilation rate (Jaakkola et al., 1991) to be related to increased symptoms; humidification (Reinikainen et al., 1992), ionization (Wyon, 1992), and improved office cleaning (Leinster et al., 1990; Raw et al., 1991) to be related to decreased symptoms; and low ventilation rate (Jaakkola et al., 1990; Menzies et al., 1993; Wyon, 1992) also to be *unrelated* to symptom frequency (an apparent inconsistency).

Figure 1 summarizes findings and study design information regarding symptom prevalence and ventilation rate. There were mostly consistent findings of statistically significant higher symptom prevalence associated with mean outside air ventilation rates at or below 10 liters/second/person (l/s/p) (21 cubic feet/minute/person) (Nagda et al., 1991; Sundell et al., 1992; Jaakkola et al., 1991), with one exception (Jaakkola et al., 1990). Statistically significant differences in symptom prevalence were not apparent in comparisons of mean ventilation rates above 10 l/s/p (Jaakkola et al., 1991; Menzies et al., 1993; Wyon, 1992). A number of additional studies which reported no relationships between symptom prevalence and CO_2 concentration (an approximate index of ventilation adequacy) were not included in Figure 1 because the volume of outside air supplied per person was not reported (Skov et al., 1990; Mendell, 1992; Hodgson et al., 1991; Burge et al., 1990).

A number of other points emerged from the literature review. Six cross-sectional studies reported data from buildings selected without regard to symptom complaints: all reported an overall prevalence greater than 20% of at least one work-related symptom (Hedge et al., 1989; Mendell, 1992; Norbäck et al., 1990; Skov et al., 1990; Zweers et al., 1992; Finnegan and Pickering, 1987a). Although these data are from subjective symptom reports only, and thus susceptible to bias from psychological influences, Franck and Skov (1991, not listed in Table 1) found subjective reports of eye irritation from questionnaires in cross-sectional building studies (Skov et al., 1990; Skov and Valbjørn, 1990a) to be significantly correlated with objective clinical measurements of eye dryness. Wyon (1992) also reported significant correlations between objective and subjective measurements of dry mouth, lips, skin, nails, and eyes, and significant improvement of some objective health measurements with blinded environmental manipulations in his experimental study.

Discussion

This paper provides a brief overview of a difficult research area in which neither disease outcomes nor relevant exposures are well defined. Although specific etiologic *exposures* for office worker symptoms have not been implicated in this review, a number

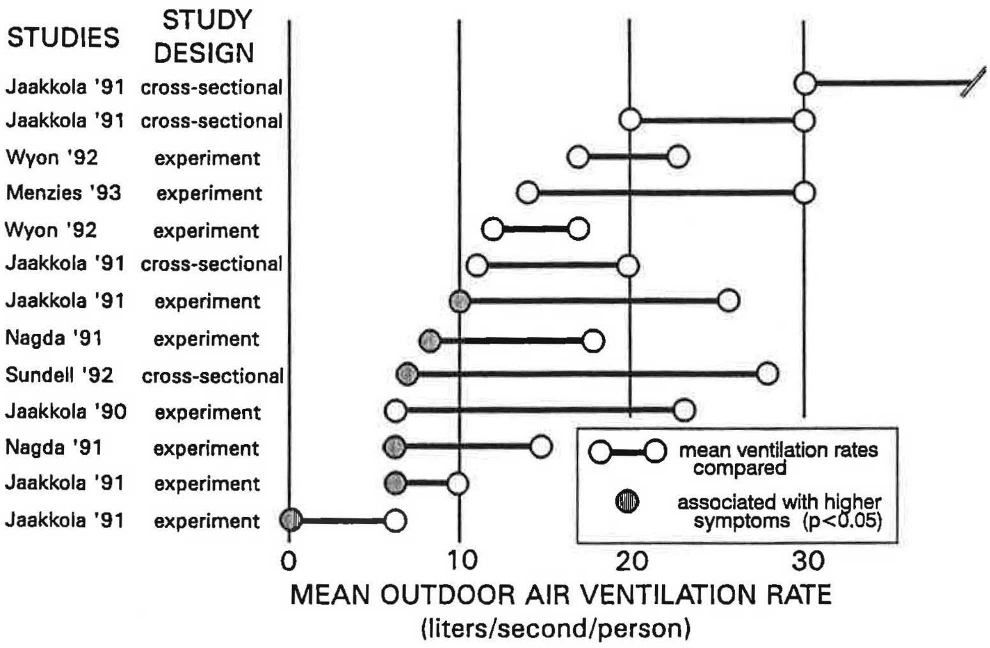

Fig. 1 Outdoor air ventilation rates and work-related symptoms: reported relationships summarized using estimated mean ventilation rates compared.

of environmental factors, possible *indicators* for etiologic exposures, have been related to symptom prevalence by consistent or strong findings. Related to increased symptoms with at least general consistency were air-conditioning, carpets, more workers in the space, VDT use, and ventilation rates at or below 10 liters/second/person. These ventilation rates were associated with increased symptoms in one study of strong design; humidification systems, negative ionization, and improved office cleaning were found in studies of strong design to be associated with decreased symptoms. Some personal factors were independently related to increased symptoms. Job stress/dissatisfaction and allergies/asthma may represent either causal factors for increased symptoms, indicators of increased susceptibility, or possibly *outcomes* of exposures which also cause symptom increases. Female gender may be associated with higher levels of exposures or stressors, or with differential susceptibility or reporting.

Reports of *no association* were considered less persuasive than positive findings, because real associations may *fail to be detected* for many reasons. False negative findings may be due to any of the sources of error possible in positive findings (chance, confounding, and various directional biases), but also from additional errors. These include several types of measurement error (e.g., inaccuracy; choice of a non-relevant exposure component, time interval, or location for measurement), as well as inadequate power to detect effects due to small sample size or limited variation in exposures (Rothman, 1986). Furthermore, the exposure range included in a study may not exceed threshold values for actual effects (e.g., viable fungi, carbon monoxide, formaldehyde, and noise were found consistently in this review to be unrelated to worker symptoms, but are known to cause health effects at high levels). Most inconsistencies found in this review, between findings of positive associations and findings of no associations, are thus not surprising.

Findings were completely consistent for only seven of the 37 factors or measurements assessed. For some factors with inconsistent findings, the stronger study designs reviewed (even if not classified here as "strong") found associations not found by many of the less strong studies, suggesting possibly biased, false negative findings in the latter. Such findings include associations of increased symptoms with high temperature (Wyon, 1992), low humidity (Reinikainen et al., 1992; Wyon, 1992), thorough cleaning (Raw et al., 1991; Leinster et al., 1990), and possibly VOC (Hodgson, 1991, 1992), and associations of decreased symptoms with humidification (Reinikainen et al., 1992; Wyon, 1992) and ionization (Wyon, 1992). For example, Hodgson et al. (1991, 1992) found relationships between VOCs assessed, with presumably greater accuracy, at each occupant's workstation and simultaneous symptom intensity, whereas other studies comparing VOCs measured in larger areas to retrospectively reported symptoms failed to find relationships (Mendell, 1992; Skov 1990; Skov and Valbjørn, 1990a). Inconsistencies may also have resulted from differences between studies in measurement methods, definitions, or ranges of factors included. Closer examination of differences between studies may reduce apparent inconsistencies, as with ventilation rate.

The apparent resolution of most inconsistencies regarding symptoms and ventilation rate (Figure 1) should, however, be interpreted cautiously. Comparisons made across studies necessitated crude estimation of some mean ventilation rates: some studies directly reported mean ventilation rates for each study area or condition (Jaakkola et al., 1990, 1991; Menzies et al., 1993; Nagda et al., 1991), while others reported multiple rates (Wyon, 1992) or ranges of rates (Sundell et al., 1992; Jaakkola et al., 1991) for each. Also, one positive study (Nagda et al., 1991) used a design which could not separate effects of time and repeated measures from effects of ventilation, and was thus likely to have exaggerated the effects found. On the other hand, all negative studies used relatively less accurate methods for measuring ventilation rate (compared with tracer gas methods); this, along with the inability of current measurement techniques to assess *variation* in outdoor air ventilation delivery throughout a building, might have obscured effects. Comparison of ventilation effects across buildings while ignoring possible differences in contaminant loads may distort findings, as ventilation rates can only modify exposures from existing sources. And lastly, this review considered only the statistical significance of the study findings, rather than the actual magnitude of effects reported at different ventilation levels.

Some other inconsistencies in reported findings may also have plausible explanations. For instance, regarding humidification (see Table 1): both experimental studies which used newly installed humidification systems to increase humidity found *reductions* in symptom prevalence (Reinikainen et al., 1992; Wyon, 1992). Yet all cross-sectional studies of buildings selected without regard to worker complaints found the presence of humidification systems to be associated with *higher* prevalence of some symptoms (Hedge et al., 1989; Reinikainen et al., 1991; Zweers et al., 1992; Finnegan and Pickering, 1987a). It is reasonable to hypothesize that: a) *short-term* (e.g., experimental) humidification will simply reduce symptoms where normal indoor humidity is low, by eliminating the negative health effects of excessively low humidity; b) *long-term* humidification may reduce some symptoms by increasing humidity (Reinikainen et al., 1991), but may more substantially increase the risk of symptoms from microbiologic contamination (in the humidifier or elsewhere). The inconsistent findings for direct measurements of relative humidity may be partly due to such opposing effects of humidification systems, as well as to the health effects resulting from either very high or very low humidities. Long-term comparison studies (or the identification of specific etiologic microbiologic exposures) will be necessary to resolve this question.

For ionization, one study of strong design found that symptom prevalence decreased after the use of ionization and a very large increase in ion concentrations (Wyon, 1992), although findings from other studies were mixed (Finnegan et al., 1987; Hawkins and Morris, 1984). Another well-designed study found no effect, but was not included in Table 1 because its intended ionization intervention produced *no* changes in airborne ion concentrations (Daniell et al., 1991), and thus provided no information on effects of changed ion concentrations. If the beneficial effects of ionization persuasively demonstrated by Wyon (1992) occurred not from changed concentrations of ions, but from reductions of microbiologic or other airborne particulate matter, then ionization would reduce only particle-related symptoms.

The scope of this review limited the consideration of many important details. For instance, both consistency and strength of study designs were summarized without regard for differences in study size, quality of measurements (e.g., objective vs. subjective, current vs. retrospective, type of instrument, etc.), or strength of *findings* (e.g., magnitude of effect), which can substantially affect persuasiveness of studies. Also, lumping of all symptoms together limits inference about disease mechanisms.

Nevertheless, the overall literature confirms both the importance and the usefulness of continued research into the causes of unexplained office worker symptoms. Symptom prevalence data from "normal" buildings shows that for office workers to experience various symptoms which improve away from their buildings is a relatively common phenomenon. The correlation of subjective symptom reports with objective health measurements (Wyon, 1992; Franck et al., 1991) and of both with blind environmental manipulations (Wyon, 1992) lend credibility to symptom reports and suggest that some represent preventable physiologic effects of environmental exposures or conditions in office buildings.

This review also corroborates that this is a multifactorial problem. Currently, one *must* invoke microbiologic, chemical, physical, and psychological mechanisms to logically explain all the associations with increased symptoms reported, either consistently or from studies of strong design. As this syndrome may thus represent overlapping sets of symptoms involving multiple causes and physiologic pathways, effective intervention strategies may include changes in the physical as well as the psychosocial environments. For psychosocial factors particularly, however, the associations found with subjective symptom reporting in cross-sectional studies have not established direction of causality: symptoms could have induced stress or vice versa.

Future research should make full use of our current knowledge, not only of *risk factors implicated* and related *biologically plausible causes*, but also about *good study designs*. Where feasible, experimental (or quasi-experimental) designs will be stronger than observational. Good models of experimental design are already available (Menzies et al., 1993; Wyon, 1992; Leinster et al., 1990; Reinikainen et al., 1992; Raw et al., 1991; Jaakkola et al., 1991), although modifications will be needed for some assessments, such as of long-term effects of humidification. An inherent limitation of field experiments, however, is the impracticality of randomizing *individuals* to exposure groups. A crossover strategy, which sequentially applies both active and placebo treatments to each individual and performs within-subject comparisons, can help protect against prior differences between study groups (Jaakkola et al., 1990; Reinikainen et al., 1992; Daniell et al., 1991), especially with some designs (Menzies et al., 1993); however, a crossover design is usable only when residual treatment effects do not occur.

For the many questions for which experimental designs are not feasible, observational studies will be necessary. Broader use of certain approaches would improve the quality of future observational studies. These include techniques to control for multivariate confounding; blinding of subjects and technicians (even in observational studies) to study hypotheses and data; improved symptom assessment, including use of current symptom intensity (Hodgson et al., 1991, 1992; Wyon, 1992) symptom diaries (Jaakkola et al., 1990; Reinikainen et al., 1992), or simultaneous environment/health measurements (Hodgson et al., 1991, 1992; Wyon, 1992; Menzies et al., 1992); objective health measurements (Wyon 1992; Franck and Skov, 1991; Koenig, 1988; Menzies et al., 1992); person-specific environmental measurements (Hodgson et al., 1991, 1992; Menzies et al., 1992); data analyses based on hypothesized effect levels; and more efficient case-control designs (Sundell et al., 1992; Menzies et al., 1992). Building-level case-control designs (Skov and Valbjørn, 1990a; Burge et al., 1990) will have very low power unless they contain many buildings or include person-level case-control comparisons as well.

Meanwhile, maximum effectiveness of these studies awaits the development of measurement and interpretation approaches which capture the relevant exposures or conditions with appropriate specificity of time, place, and exposure, based on hypothesized mechanisms. Promising targets for such new approaches include temperature and humidity (Berglund and Cain, 1989), VOC (Mølhave, 1991), and particularly microbiologic materials (Miller, 1992; Platt et al., 1989; Rylander et al., 1992; Brundage et al., 1988; Jaakkola et al., 1990a). Until we can identify these specific causes, appropriate mitigation and prevention of building-related symptoms may need to be at the level of prudent design, operation, and maintenance practices, focused on factors which reduce the *likelihood* of problem indoor exposures or conditions.

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