Int Arch Occup Environ Health (2008) 81:769–776
DOI 10.1007/s00420-007-0244-6

SHORT COMMUNICATION

Structural equation analysis of the causal relationship between health and perceived indoor environment

Charlotte Brauer · Esben Budtz-Jørgensen · Sigurd Mikkelsen

Received: 29 December 2006 / Accepted: 17 August 2007 / Published online: 5 October 2007

Abstract

Objectives To explore the temporal relationship and reversed effects between health and perception of the indoor environment using structural equation models.

Methods The study was a two-phase prospective questionnaire study with a cross-lagged design. Altogether 1,740 adults participated on both occasions.

Results The perceived indoor environment had only weak effects on health at follow-up. However, the results strongly indicated a reversed effect that health problems may lead to increased complaints about the indoor environment.

Conclusions Structural equation models are powerful analytical tools for disentangling the effects of a specific variable on another in high dimensional data with complex patterns of associations. The analyses confirmed the results of our previous logistic regression analysis about the strong reversed effect. Hence, it is probable that a reversed effect between health and complaints about the indoor environment exists.

Keywords Sick building syndrome · Statistical models · Epidemiological studies · Cohort studies

C. Brauer · S. Mikkelsen
Department of Occupational Medicine,
Copenhagen University Hospital, Glostrup, Denmark

E. Budtz-Jørgensen
Department of Biostatistics, University of Copenhagen,
Copenhagen, Denmark

C. Brauer (✉)
Arbejdsmedicinsk Klinik, Glostrup Hospital,
Nordre Ringvej 57, 2600 Glostrup, Denmark
e-mail: chabra01@glo.regionh.dk

Introduction

For more than 25 years extensive research has tried to assess the relationship between the indoor environment and different symptoms that occur among persons while staying in a building. The studies are predominantly cross-sectional and therefore they do no permit conclusions about causal relations. Nevertheless, previous research is based on the assumption that exposures in the indoor environment lead to adverse health effects, not vice versa. However, many of the associations reported in previous research may also be explained by reversed causal relationships: that health may influence the perception of the indoor environment. For example, a person with irritated eyes may perceive more glare and reflections, and likewise a person who often has a headache may be more susceptible to noise. Hence a true causal relationship may exist in the reverse. Alternative explanations for a reversed relationship are reporting bias and bias due to concern about potential hazards in the environment (Lees-Haley and Brown 1992; Moffatt et al. 2000; Roht et al. 1985; Spurgeon et al. 1996). This may especially be true in cross sectional studies, if self-reported measures of both exposures and health are used. In a longitudinal design the exposure and outcome are measured on different points in time, which will reduce but not eliminate reporting bias in self-reports.

In a recent longitudinal study we studied whether perceived exposures in the indoor environment at time 1 predicted symptoms at time 2 as well as the reversed direction assessing whether symptoms at time 1 predicted complaints about the indoor environment at time 2. We found significant associations in both directions (Brauer et al. 2006a, b). We used multiple logistic regression analysis, which is a standard statistical technique for observational studies in epidemiology. However, this technique may be too simple for these complex longitudinal data. Therefore we have re-analysed the data using a more sophisticated set of models known as structural equation models. This type of analysis combines path analysis with confirmatory factor analysis and allows variables to be both dependent and independent variables (Streiner 2005). Thus, in a structural equation analysis observed variables are typically viewed as manifestations of a limited number of latent (unobserved) variables, which are interrelated using a set of regression equations. Compared to standard regression methods, the structural equation analysis is more powerful because information from multiple exposure and outcome variables may be utilised simultaneously in the same model. In addition, the effects of main interest can often be modelled as relationships between a few latent variables and therefore the multiple testing problems associated with the standard analysis is avoided (Budtz-Jorgensen et al. 2002). Finally, the models also allow for measurement error in predictor variables (Budtz-Jorgensen et al. 2002). This is important when analyzing cross lagged longitudinal data, as response at time 1 is often included as a predictor of response at time 2. If measurement error in the response level at time 1 is ignored, then bias may be induced in regression coefficients of all predictor variables. In particular this may invalidate results about the effect of baseline exposure. We present results using structural equation analysis to explore the relationship between health and the perception of the indoor environment over time.

Methods

The study is a two-phase prospective questionnaire study on indoor environment aspects, psychosocial work environment and health among a random sample of adults from the Danish population. Altogether 1,740 adults participated at baseline as well as at follow-up [See (Brauer et al. 2006a) for more information]. Fifty-two percent of the participants were women and the mean age was 41 years (range 18–59 years). The participants completed a self-administered questionnaire twice with a time lag of exactly 1 year. Identical questions on symptoms and potential risk factors were used on both occasions. The recall period was 4 weeks. The response rates were 68% at baseline and 80% at follow-up.

Eight questions about symptoms were used. They were grouped into two symptom groups with five mucous membrane symptoms (eye irritation, nose irritation, nasal congestion, throat irritation, and hoarseness) and three general symptoms (fatigue, headache, and concentration difficulty), respectively. Each question had four response options: “No”, “yes, sometimes”, “yes, several times a week”, and “yes, daily”. In this paper, the structural equation analysis will be illustrated with the mucous membrane symptoms only.

Perceptions of the indoor environment were grouped into nine indices: (1) a draught index (draught, too low temperature and draught along the floor), (2) a temperature index (too high temperature and temperature variations), (3) a stuffy air index (stuffy air and unpleasant odour), (4) a dry air index (dry air and static electricity), (5) a noise index (noise in the room, noise from other rooms and noise from outside), (6) a light index (illumination problems and reflective surfaces), (7) a space/dust index (cramped for space and poor cleaning), (8) environmental tobacco smoke, and (9) patches of damp or mildew. The same four response options were used as for the questions on symptoms.

The questionnaire also included questions about sex, age, marital status, socioeconomic status, smoking habits, hypersensitivity, job demands and job decision latitude in addition to a checklist of 15 symptoms that are not usually connected with problems in the indoor environment, for example, heart palpitations, muscle tension and stomach ache. These symptoms were considered to represent a general tendency to complain and will be referred to as “dummy symptoms” in the following (Brauer et al. 2006b). The study was carried out in accordance with the requirements of the national and regional ethics committees in Denmark.

Statistical analysis

The temporal relationship between variables on perceived indoor environment and health was analysed in structural equation models (Bollen 1989; Muthen 1984). A detailed description of the structural equation model used is given in the Appendix.

Structural equation models generally consist of two parts: a measurement model and a structural model. In the measurement model observed variables are considered reflections of a limited number of unobserved latent variables and in the structural model causal relationships among the latent variables and a set of covariates are described. Figure 1 illustrates the measurement model. Here the five observed variables for the mucous membrane symptoms were linked to a common latent health variable at baseline as well as follow-up.

The associations between health and perceived indoor environment were analysed in three steps. Firstly, we considered each of the indoor environment indices separately and explored its relationship with the latent health variable for the mucous membrane symptoms using the structural model illustrated in Fig. 2. This model allows the

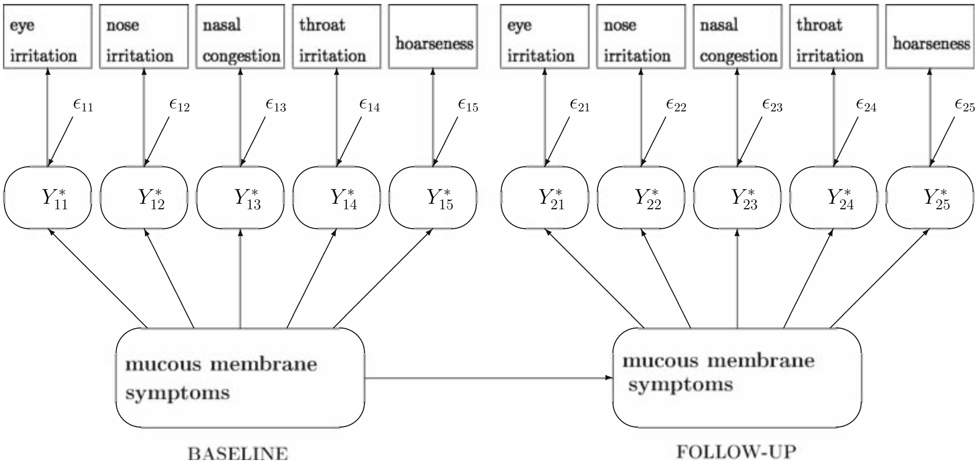

Fig. 1 The measurement model using the mucous membrane symptoms as an example. The model assumes that the five observed health outcomes (eye irritation, nose irritation, nasal congestion, throat irritation, and hoarseness) have arisen from one underlying latent variable, here called mucous membrane symptoms. This latent variable has a linear effect on five continuous variables (Y*), which are also affected by a measurement error (ε). The observed ordinal values are assumed to be coarsened versions of these underlying continuous outcomes (Muthen 1984). To allow for temporal dependence in health status, the latent mucous membrane symptom level at follow-up was allowed to depend on the corresponding baseline level. This structure will induce temporal correlation also between observed outcomes. In addition, measurement errors were allowed to be correlated with errors of the same variable recorded at a different time (Farrell 1994), but these associations were omitted from the figure for clarity

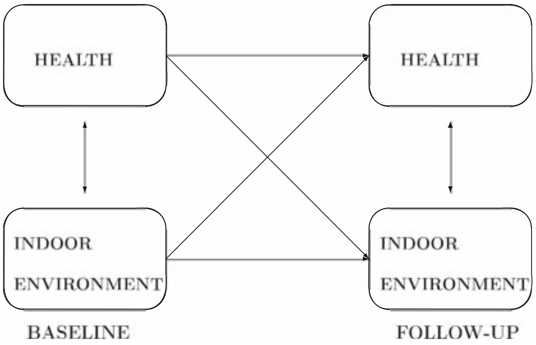

Fig. 2 Path diagram illustrating the structural model with the relationships between perceived indoor environment and health at baseline and follow-up. Here *single headed arrows* indicate the direction of linear effects while *doubled headed arrows* indicate non-directional associations. Thus, perceived environment and health at follow-up may depend on both variables at baseline. Environment may affect health, but health may also affect environment (reversed effect). In addition a variable at follow up may depend on its level at baseline (autoregressive effect). Variables collected at the same time may be associated but no assumptions are made about the direction of the relationship

perceived indoor environment and health at follow-up to depend on the corresponding variables at baseline. Thus, health was allowed to depend on the indoor environment, but the model also included a possible effect of health on assessment of the indoor environment. In the following the effect of health on the indoor environment will be referred to as “reversed effect”. Note that the model also accounts for effects of a variable at time 1 on the same variable at time 2. This means, for instance, that we adjusted for the effect of baseline health when we assessed the effect of the indoor environment at baseline on health at follow-up. Thus, we were inferring whether baseline exposure predicted a change in health.

In the second step of the analysis, all variables on the indoor environment were included simultaneously in the model. In this model, health and the perception of the indoor environment at follow-up were allowed to depend on all the nine indoor environment indices and the latent health variable at baseline. In addition to providing adjusted effect estimates, this model also allowed calculation of joint tests of no effects from indoor environment on health as well as no reversed effects. The model was then reduced using the backward elimination procedure ($P = 0.10$) to exclude indoor environment variables, which had a statistically insignificant effect on health.

In the third and final step, we additionally included information on “dummy symptoms” at baseline and at follow-up. These variables entered the model in a similar fashion as the variables on indoor environment. Thus, the dummy symptom level at baseline was allowed to affect both the indoor environment and health at follow-up. The aim of this additional analysis was to decide whether relationships between the indoor environment and health also existed after adjusting for the overall level of complaining.

In all models a set of covariates were included as potential confounders. This set included sex, age, hypersensitivity, marital status, smoking, socioeconomic status, job demands and job decision latitude. The covariates were collected at baseline and each of these was allowed to affect the other variables both at baseline and at follow-up.

Effect parameters are given as standardised regression coefficients indicating the change in standard deviations of the response upon a one standard deviation increase in the predictor. Calculations were done using the software package Mplus version 3 (Muthen and Muthen 2004).

Results

Effects of indoor environment on health

Table 1 shows the effects of the nine indices of perceived indoor environment at baseline on mucous membrane symptoms at follow-up. We first considered the effect of each of the indoor environment indices separately adjusting for the health status and potential confounders at baseline (model 1). All effects on mucous membrane symptoms were positive indicating that poorer perception of the indoor environment led to poorer health at follow-up. However, only the space/dust index and draught index were statistically significant at the 0.05 level with standardised effects of about 10%. Including all indoor environment variables in the model (model 2), none of the indoor environment indices were significantly associated with mucous membrane symptoms (Table 1). However, in the joint test the hypothesis of no effects of the indoor environment on mucous membrane symptoms was rejected with $P = 0.015$. Hence, the observed positive relation between indoor environment and health cannot be explained by chance. A backward elimination procedure showed that only the space/dust index had a significant effect (effect: 0.124, 95% CI: 0.037; 0.211, $P = 0.003$). To test whether the observed effect was an artefact caused by a general tendency in some people to complain, we adjusted for the dummy symptom level (model 3). The dummy symptom level at baseline had a strong effect on reporting mucous membrane symptoms at follow-up (effect: 0.175, 95% CI: 0.087; 0.263, $P = 0.0001$). After correction for this effect, the hypothesis of no effect of the indoor environment was accepted in the joint test ($P = 0.12$). However, when the adjustment was performed in the reduced model including only the space/dust index, the effect of the space/dust index remained statistically significant although the coefficient was slightly smaller (effect: 0.100, 95% CI: 0.012; 0.188, $P = 0.013$).

Effects of health on perception of indoor environment (reversed effect)

Table 2 shows the reversed effect indicating that symptoms may lead to poorer perception of the indoor environment. A higher level of mucous membrane symptoms at baseline was associated with poorer perception of indoor environment at follow-up no matter which of the indoor environment variables was considered. When analysing the different indoor environment indices separately (model 1) this effect was statistically significant for all of the variables except for environmental tobacco smoke and patches of damp/mildew. Especially the effects of the light index,

Table 1 Effects of different aspects of perception of the indoor environment at baseline on mucous membrane symptoms at follow-up

Risk factor	Mucous membrane symptoms[a]								
	Model 1[b]			Model 2[c]			Model 3[d]		
	Effect	(95% CI)	*P* value	Effect	(95% CI)	*P* value	Effect	(95% CI)	*P* value
Draught index	0.082	(0.006; 0.158)	0.03	0.018	(–0.103; 0.139)	0.77	0.001	(–0.077; 0.079)	0.98
Temperature index	0.031	(–0.046; 0.108)	0.43	–0.046	(–0.158; 0.066)	0.42	–0.038	(–0.151; 0.075)	0.51
Stuffy air index	0.069	(–0.010; 0.148)	0.09	0.03	(–0.100; 0.160)	0.65	0.004	(–0.100; 0.108)	0.94
Environmental tobacco smoke	0.063	(–0.016; 0.142)	0.12	0.022	(–0.086; 0.130)	0.69	0.017	(–0.092; 0.126)	0.76
Dry air index	0.038	(–0.043; 0.119)	0.36	–0.006	(–0.110; 0.098)	0.91	0.006	(–0.098; 0.110)	0.91
Noise index	0.069	(0.000; 0.138)	0.05	0.024	(–0.071; 0.119)	0.62	0.027	(–0.069; 0.123)	0.58
Light index	0.077	(–0.007; 0.161)	0.07	0.021	(–0.098; 0.140)	0.73	0.016	(–0.108; 0.140)	0.80
Space/dust index	0.099	(0.027; 0.171)	0.01	0.069	(–0.039; 0.177)	0.21	0.073	(–0.034; 0.180)	0.18
Patches of damp/mildew	0.036	(–0.082; 0.154)	0.55	0.006	(–0.128; 0.140)	0.93	0.004	(–0.152; 0.160)	0.96

Results from structural equation modelling. Effect parameters are given as standardised regression coefficients, $N = 1{,}740$

[a] Mucous membrane symptoms: eye irritation, nose irritation, nasal congestion, throat irritation, and hoarseness

[b] Model 1: Each of the indoor environment indices analysed separately

[c] Model 2: A joint analysis including all the indoor environment indices simultaneously in the model

[d] Model 3: As model 2, but in addition adjusted for "dummy" symptoms, see text

All models are adjusted for sex, age, smoking, hypersensitivity, marital status, socioeconomic status, job demands and job decision latitude

Table 2 Reversed effect. Effects of mucous membrane symptoms at baseline on different aspects of perception of the indoor environment at follow-up. Results from structural equation modelling

Risk factor	Perception of the indoor environment																	
	Draught index		Temperature index		Stuffy air index		Environmental tobacco smoke		Dry air index		Noise index		Light index		Space/dust index		Patches of damp	
	Effect	*P* value	Effect	*P* value	Effect	*P* value	Effect	*P* value	Effect	*P* value	Effect	*P* value	Effect	*P* value	Effect	*P* value	Effect	*P* value
Mucous membrane symptoms[a]																		
Model 1[b]	0.120	0.006	0.157	<0.001	0.125	0.015	0.064	0.140	0.149	<0.001	0.091	0.011	0.169	0.001	0.081	0.035	0.079	0.330
Model 2[c]	0.162	0.004	0.160	0.004	0.120	0.047	0.087	0.140	0.166	0.001	0.102	0.031	0.186	0.003	0.062	0.210	0.065	0.490
Model 3[d]	0.155	0.016	0.167	0.007	0.112	0.110	0.069	0.290	0.176	0.003	0.094	0.080	0.184	0.008	0.052	0.370	0.136	0.220

Effect parameters are given as standardised regression coefficients, $N = 1,740$

[a] Mucous membrane symptoms: eye irritation, nose irritation, nasal congestion, throat irritation, and hoarseness

[b] Model 1: Each of the indoor environment indices analysed separately

[c] Model 2: A joint analysis including all the indoor environment indices simultaneously in the model

[d] Model 3: As model 2, but in addition adjusted for "dummy" symptoms, see text

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the dry air index and the temperature index were strong with standardised effects of about 0.15. Adjusting for the effect of all indoor environment variables at baseline (model 2), did not lead to important changes in the effect estimates. In the joint test, the hypothesis of no effects of health on indoor environment aspects was clearly rejected with $P < 0.0001$, strongly indicating the existence of a reversed relationship. Furthermore, this effect remained almost unchanged even after adjustment for the dummy symptom level ($P = 0.0005$) (model 3).

Other effects

In the cross-sectional analyses we found strong positive effects of the indoor environment on health at baseline as well as follow-up ($P < 0.0001$). The only exception was environmental tobacco smoke, which may be due to adjustment by being a smoker (data not shown).

In addition, each variable had a strong effect on itself over time. The standardised effect of the mucous membrane symptoms at baseline on mucous membrane symptoms at follow-up was 0.680 ($P < 0.0001$). For the nine indoor environment indices the standardised regression coefficients between the variable at baseline and the same variable at follow-up ranged between 0.410 and 0.698 (all *P*-values <0.0001).

As regards the covariates, women and persons with hypersensitivity, high job demands, and low job decision latitude were more likely to report mucous membrane symptoms. However, these associations disappeared in the analysis of follow-up data where we adjusted for the level of the health variable at baseline—except for hypersensitivity that led to worse mucous membrane symptoms (data not shown). Likewise high job demands and low job decision latitude was associated with poorer perception of the indoor environment and with higher dummy symptom level at baseline, but the associations generally disappeared in the analysis of follow-up data where we adjusted for the level of the respective variable at baseline.

Discussion

The focus of the present study was to determine the direction in relationship between perceived indoor environment and health using structural equation models. Originally data were analysed using multiple logistic regression (Brauer et al. 2006a, b), but subsequently we were recommended to re-analyse data using structural equation modelling because of the complex nature of our data. The present results only weakly suggested that complaints about the indoor environment may lead to adverse health effects. However, the results strongly indicated a reversed effect: that having mucous membrane symptoms may lead to increased complaints about the indoor environment even when adjusting for the overall level of complaining. For the general symptoms there was an indication of a reversed relationship too, but it was somewhat weaker (data not shown, but the authors will send the results on request).

We found strong cross-sectional associations both at baseline and at follow-up. However, these associations do not hold information about the direction of the causal relationship. This can only be obtained by exploiting the longitudinal aspect of the data. Our statistical models were based on the principle that causes take time to exert their effects, and therefore no causal relationships were assumed between variables recorded at the same time. Instead the relationships were explored in a model allowing baseline variables to affect variables at follow-up. In order to determine whether, for instance, indoor environment affects health, we estimated the effect of baseline environment on health at follow-up after adjustment for the baseline health level. In this approach it is not enough for environment at time 1 to predict health at time 2. In case of a reversed effect, environment at time 1 would be correlated to health at time 2, partly because both variables would be affected by health status in an earlier time. This (spurious) effect was removed by controlling for the effect of health at time 1, when evaluating the relationship between environment at time 1 and health at time 2. Similar approaches to causal analysis were advocated by Farrell (1994) and have been used to in research on psychosocial work characteristics (de Jonge et al. 2001), personality traits (Kivimaki et al. 2002), and behaviour (Sieving et al. 2000). To our knowledge this approach based on structural equation has not previously been used in research on indoor environment problems.

The present results agree with our previous results from the logistic regression analysis that the effect of indoor environment on health was weaker than the reversed effect. However, the two methods found different effects of the indoor environment on health. Using structural equation modelling and backward elimination the space/dust index was identified as the only important predictor for an increase in health problems, while draught, dry air and noise were identified as predictors for incident symptoms in our previous logistic regression analysis (Brauer et al. 2006a). This difference cannot be explained as a result of weaker power in the logistic regression. Here it must be noted that because different types of outcome variables are considered (latent continuous versus dichotomous), the two methods consider different types of effects and therefore results cannot be expected to fully agree. Nevertheless, results may also differ because the logistic regression analysis does not take measurement error in predictor variables into account. Structural equation models allow for measurement error because effects are modelled between latent variables. In analysis of cross lagged exposure-response data this is important as baseline variables are assumed to affect variables at follow-up. Failure to account for imprecision in, for instance, the response variable will lead to bias in both the main effect parameters, i.e. the effect of time 1 response on time 2 exposure and the effect of time 1 exposure on time 2 response (Carroll 1998).

The reversed effects were generally more statistically significant in the structural equation models than in the logistic regression analysis. This tendency was to be expected as the structural equation analysis is a generally stronger method. In the structural equation model information from different health outcomes may be pooled into a joint analysis thereby gaining power and reducing the multiple testing problems associated with a separate regression analysis for each outcome. Furthermore, ad hoc methods for development of scales (simple sums) are replaced by a firm mathematical framework where observed variables are weighed optimally into latent variables. So although information from multiple variables can be utilised also in other methods, the structural equation model uses more sophisticated weights and in the analysis these models will allow for the statistical uncertainty in the pooled information.

A further advantage of the structural equation models it that all information provided by ordinal outcomes it utilised and the analysis do not involve dichotomisations of study variables. In our previous logistic regression analysis outcomes were dichotomised. If the dichotomisation of the outcome is based on appropriate biological knowledge, then the logistic regression approach may be more appropriate. As regards health problems related to indoor environment a well-defined cut-off point that is able to distinguish sick from healthy does not exist. Hence, the present analysis where we examined a change in the continuous measure of health may be more suitable for these data.

A limitation in our study is that our findings were based on self-reports. There is no ideal method to assess the occurrence of common daily health problems from which everybody may suffer once in a while, but it may be supplemented with more objective outcome measures as for instance information from the general practitioners about the participants' health. Objective measurements of the indoor environment are also preferable to self-reports but very time consuming and expensive. There is a time lag of one year between the two rounds of questionnaires. During this period the indoor environment may have changed because of redecorations on the workplace. In addition, some persons may have changed job because of symptoms they have attributed to the indoor environment at work. The analyses are made on all persons who participated on both occasions irrespective of redecorations or job change during the follow-up period. We have no information about redecorations at the workplace, but we have re-analysed data omitting persons who had changed job, and the results were the same (data not shown). The strengths of our study are the large cohort and the prospective design with information about perceived exposure and health on both occasions. The cross-lagged longitudinal data structure offered rich possibilities for explorations of the reversed effects.

The main contribution of our study is that it proposes the use of structural equation models when assessing longitudinal data that are interrelated in a complex manner as, for instance, the relationship between complaints about the indoor environment and health. We found the structural equation models to be very useful in disentangling the relationships in a data set of high dimension. This more advanced method confirmed the results of our previous logistic regression analysis about the strong reversed effect. Hence, it is probable that a reversed effect between health and complaints about the indoor environment exists. We suggest further studies of reversed causality in the research into indoor environment problems.

Acknowledgments This study received financial support from The Danish Working Environment Council and the Danish Medical Research Council.

Appendix: Technical details on the structural equation analysis

The model for mucous membrane symptoms is described in detail to illustrate the structural equation analysis. Thus, let Y_{jkl} denote the value at the *j*th examination ($j = 1, 2$) of the *k*th ($k = 1, ..., 5$) ordinal health variable for the *l*th subject ($l = 1, ..., n$). Similarly, let X_{jml} denote value on the *m*th (m = 1, ..., 9) indoor environment variable and let Z_{1l}, ..., Z_{ql}, denote values of q covariates measured at baseline. First, each ordinal health outcome Y_{jkl} was linked to a latent continuous variable Y^*_{jkl} using a threshold model. Thus, the value of the ordinal variable is v ($v = 1, ..., 4$), if the underlying continuous variable falls in the vth interval, i.e., if $\tau_{jk(v-1)} \leq y^*_{jkl} \leq \tau_{jkv}$, where the thresholds ($\tau$) are unknown parameters to be estimated in the analysis (Muthen 1984). Then the continuous outcomes (Y^*_{jkl}) were assumed to depend on common latent variables η_{1l} and η_{2l} representing the latent mucous membrane symptoms at baseline and follow-up respectively, i.e., $Y^*_{jkl} = \nu_{jk} + \lambda_{jk}\eta_{jl} + \epsilon_{jkl}$. Thus, outcomes at baseline were all assumed to depend on η_{1l}, while outcomes at follow-up were all assumed to depend on η_{2l} (Fig. 1). In addition, all outcomes were assumed to be affected by a normally distributed random error (ϵ_{jkl}). These error terms are often assumed to be independent (Bollen 1989), but here we allowed for correlation in error terms in the same variable at two different occasions, i.e., $\mathrm{cov}(\epsilon_{1kl}, \epsilon_{2kl}) \neq 0$.

The relationship between the *m*th indoor environment variable and the health outcomes illustrated in Fig. 2 were modeled using four equations:

$$\eta_{2l} = \alpha_4 + \sum_{g=1}^{q} \gamma_{4g} Z_{gl} + \beta_1 X^*_{1ml} + \beta_2 \eta_{1l} + \varsigma_{4l} \tag{1}$$

$$X^*_{2ml} = \alpha_3 + \sum_{g=1}^{q} \gamma_{3g} Z_{gl} + \beta_3 X^*_{1ml} + \beta_4 \eta_{1l} + \varsigma_{3l} \tag{2}$$

$$\eta_{1l} = \alpha_2 + \sum_{g=1}^{q} \gamma_{2g} Z_{gl} + \varsigma_{2l} \tag{3}$$

$$X^*_{1ml} = \alpha_1 + \sum_{g=1}^{q} \gamma_{1g} Z_{gl} + \varsigma_{1l} \tag{4}$$

where X^*_{1ml} and X^*_{2ml} are underlying continuous versions of the observed ordinal environment variables. Thus, perceived environment and mucous membrane symptoms at follow-up were assumed to depend linearly on the variables measured at baseline. The strength of these effects are reflected by the values of the parameters β_1, ..., β_4 each corresponding to a single headed arrow in Fig. 2. Standardized effects were obtained by multiplying β with the standard deviation in the predictor and deviding by the standard deviation in the outcome. The covariates were allowed to affect all four variables. Residual variation was modeled using ζ-variables, which were assumed to follow a normal distribution with mean zero. Residual variation in variables collected at the same time-point were allowed to be correlated as indicated by the double headed arrows in Fig. 2. In the joint analysis including all nine indoor environment indices, Eqs. (2) and (4) were repeated for each index. Furthermore, Eqs. (1) and (2) were modified so that they allowed for linear effects of each of the indoor environment variables measured at baseline.

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