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ORIGINAL ARTICLE

Evaluation of individual-based and group-based exposure estimation of microbial agents in health effects associated with a damp building

Sook Ja Cho, Jean M. Cox-Ganser, Kathleen Kreiss and Ju-Hyeong Park

We evaluated attenuation in linear associations between microbial exposure and respiratory symptoms occurring when individual measurements of microbial agents were used for estimating employees' exposure compared with group means. Symptoms, which improved when away from the building (building-related, BR), and measurements of culturable fungi, ergosterol, and endotoxin in floor dust were obtained between 2001 and 2007 from four cross-sectional studies on occupants of a water-damaged building. We compared odds ratios from longitudinal health effect models using individual measurements at employees' workstations with those using floor (group) means. Estimated odds for BR respiratory symptoms in group-based analyses increased by 2 to 5 times compared with those from individual-based analyses for culturable fungi and ergosterol, although they were less precise. For endotoxin, we found substantially increased and significant odds in group-based analyses, while we found no associations in individual-based analyses for various symptoms. Our study suggested that the building floor was useful in constructing exposure groups for microbial agents in this water-damaged building for epidemiologic analysis. Our study showed that group-average exposure estimation provides less attenuated associations between exposures to microbial agents and health in damp indoor environments where measurement error and intrinsic temporal variability are often large.

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INTRODUCTION

Accurate exposure assessment is essential to valid and precise estimates of the relationship between exposure and health in epidemiology. Exposure may be estimated based either on individual measurements or on an average of measurements from randomly selected members in similar exposure groups.[1–3] In an individual-based strategy, cross-sectional or longitudinal exposure measurements are required for all individuals in a given study. In a group-based strategy, exposure groups are constructed based on jobs or other common exposure characteristics shared by workers. Then, an average of randomly selected individuals' measurements from a group is assigned to all the subjects in the same group.[4]

Although exposure estimation based on individual measurements has often been assumed to be a preferred method in exposure assessment, group-based exposures are widely used in occupational epidemiology because of the difficulty in obtaining individual measurements from all subjects. Furthermore, studies have indicated that such group-based exposure assessment can result in a less biased estimate of an association between exposure and disease than the individual-based approach, depending on the sizes of measurement error and temporal variability of exposure.[1,2,4,5] However, the group-based study can result in loss of precision in the point estimate compared with the individual-based study.

Attenuation bias in the regression coefficient of a linear association between exposure and disease is a function of sample size and exposure variability (within- and between-subject or between-group variability).[6–8] Thus, characterization of exposure variability provides valuable information to determine which method, the individual measurement-based or the group average-based exposure estimation, is preferred to minimize attenuation bias in the association.[9] Exposure variability information can be used to refine similar exposure groups rather than solely relying on job characteristics shared by workers, in which variability has been shown to vary by orders of magnitude.[10]

The large intrinsic variability of microbial exposures combined with lack of valid quantitative exposure assessment methods has hampered routine application of quantitative measurements of microbial agents for epidemiological studies.[11,12] Thus, researchers frequently rely on qualitative information obtained by observational assessment or from self-administered questionnaires for exposure assessment of dampness-related agents for epidemiological studies in indoor environments.[11–13] The aim of our study was to evaluate potential attenuation bias in associations between exposure to microbial agents and respiratory symptoms using two exposure estimation methods in longitudinal analyses: individual measurement-based and group average-based exposure estimations. We chose total culturable fungi, ergosterol, and bacterial endotoxin as exposure indices of microbial agents because we found significant associations of such microbial exposures with building-related (BR) lower and upper respiratory symptoms and postoccupancy physician-

Field Studies Branch, Division of Respiratory Disease Studies, National Institute for Occupational Safety and Health, Morgantown, West Virginia, USA. Correspondence to: Dr. Ju-Hyeong Park, Field Studies Branch, Division of Respiratory Disease Studies, National Institute for Occupational Safety and Health, MS 2800, 1095 Willowdale Road, Morgantown, WV 26505, USA.
Tel.: +304 285 5967. Fax: +304 285 5820.
E-mail: gzp8@cdc.gov.
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diagnosed asthma among these building occupants in our previous studies.[3,14]

METHODS

Study Design and Population

We conducted four cross-sectional epidemiological surveys of occupants in a large office building located in the northeastern United States between 2001 and 2007. The building has had a long history of water incursion since being built in 1985. The exterior walls, especially around terraces and windows on the upper floors (17–19), and the roof were the main sources of water leaks. Current tenants first occupied the building in 1994, and, on average, 1240 employees occupied 15 floors. Building occupants had reported respiratory symptoms that they perceived to be BR within a few months after initial occupancy. We conducted the initial health questionnaire and environmental surveys in September 2001 and April 2002, respectively. After completion of major remediation in early 2004, we conducted three subsequent health and environmental surveys in August 2004, 2005, and 2007. Detailed information on respiratory illnesses and environmental changes in relation to remediation of water damage are reported elsewhere.[3,14–17]

Not all health survey participants had individual exposure measurements. On the basis of the results of the four surveys, we identified 513 occupants who participated in one or more health questionnaire surveys and had individual exposure measurements in one or more environmental surveys (Figure 1). We used these occupants to examine the aim of our study in longitudinal epidemiological analyses described later.

Health Questionnaire Surveys

We invited all occupants working in the building to participate in health questionnaire surveys. In the questionnaire, we asked about upper respiratory symptoms (nose, sinus, or throat symptoms) and lower respiratory symptoms (wheeze, chest tightness, attacks of shortness of breath, attacks of cough, or awakened by breathing difficulty) occurring one or more times weekly over the past 4 weeks. We defined BR respiratory symptoms as those that improved when away from the building. We also obtained information on demographics (age, gender, and race/ethnicity), smoking status, and date of building occupancy. The first page of all questionnaires indicated that consent to participate was implied by completing the questionnaire, as approved by the NIOSH Institutional Review Board.

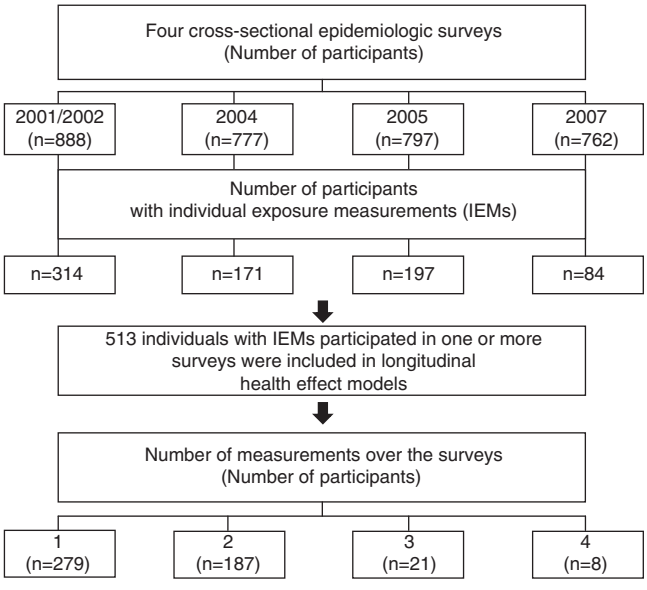

Figure 1. Flow diagram of selection of study population for longitudinal health effect models.

Environmental Sampling

We collected floor dust samples from employees' workstations on 15 occupied floors in conjunction with each of the four surveys. In 2002 and 2004, we collected samples ($n = 338$ and $n = 279$, respectively) from workstations of participants with physician-diagnosed asthma, hypersensitivity pneumonitis, or sarcoidosis, or lower respiratory or systemic symptoms and workstations of asymptomatic participants with no such illnesses, identified from the 2001 initial health questionnaire survey.[15] In 2005, we collected samples from 300 randomly selected employees' workstations stratified by floor, and in 2007, we collected samples from 150 workstations that were randomly selected from the 2005 sampling locations covering all 15 floors. Environmental sampling and analysis for the four surveys have been described in detail elsewhere.[3,14,17] In brief, we vacuumed 2 m^2 of carpeted floor around an employee's chair for 5 min for dust sampling. We analyzed floor dust samples for culturable fungi, ergosterol, and bacterial endotoxin, and used levels of microbial agents per square meter of floor area in our analyses.

Individual Measurement-Based and Group Average-Based Exposure Estimation

For individual exposures, we used measurements of microbial agents in floor dust collected from individual workstations. For group-average exposures, we used a group mean for all employees in the same group.[4]

We created three different grouping schemes based on our understanding of water incursion and building geometry, and we evaluated efficiency of the grouping schemes. The three grouping schemes were as follows: (1) proximity to the building exterior ($\leq$15 feet (4.6 m) and $>$15 feet, number of groups = 2); (2) building floor (number of groups = 15); and (3) a combination of the proximity and the floor (number of groups = 30). The grouping schemes were informed by our previous studies, which showed that water incursion mainly occurred along the building exterior walls, windows, and balconies on upper floors and that the levels of microbial agents significantly differed by floor.[15,17] Most employees' workstations on the 15 floors consisted of cubicles except for some offices along the perimeter of the floor and were located within 45 feet (13.7 m) of the building exterior.

Statistical Analysis

Evaluation of three grouping schemes. As levels of microbial agents in workstation dust for total culturable fungi, ergosterol, and endotoxin from the four environmental surveys were skewed to the right, we used natural log-transformed data to reduce the possible effect of outliers for statistical analyses. We estimated within-workstation and between-workstation variances of microbial agents using general linear mixed-effects models with restricted maximum likelihood estimation and compound symmetry as a covariance structure for repeated measurements within workstations (Proc Mixed in SAS). In these mixed-effects models, we treated survey year and an exposure-grouping variable as fixed effects, and sampled workstation as a random effect.[18,19] As within-workstation variance was not identical across exposure groups using a log-likelihood ratio test,[20] we calculated between-group variance as the difference of sum of within-workstation and between-workstation variances from two nested models: one with and the other without the grouping variable.

We evaluated the efficiency of different grouping schemes on estimating group means using contrast and precision.[6,18] Contrast represents how well a given grouping scheme can categorize workers into similar exposure groups in terms of estimating group

means for epidemiological analyses. Contrast ranges from 0 (a grouping scheme is not useful for health effect models) to 1 (a grouping scheme provides the most distinctive similar exposure groups for health effect models). We estimated contrast for each grouping scheme as between-group exposure variance (σ^2_{bg}) divided by the sum of between-group and between-workstation (σ^2_{bw}) exposure variances. The precision of group means was estimated as the median of $\left[1/\sqrt{(\frac{\sigma^2_{bw}}{k}+\frac{\sigma^2_{ww}}{kn})}\right]$ for all groups given in a particular grouping scheme, where $\sigma^2_{ww}$is within-workstation exposure variance, *k* is group sample size (number of workstations per group), and *kn* is the number of exposure measurements in a group.

Health effect models with individual and group exposure estimation. We analyzed 766 measurements from 513 occupants who participated in one or more health surveys and had individual exposure measurements in one or more environmental surveys. We used generalized linear mixed-effects models with the logit link function, binary distribution, and compound symmetry as a covariance structure to account for correlations of repeated health outcomes within a subject over the four surveys. By comparing sizes of odds in longitudinal health effect models using individual measurements with those using floor averages, we examined which method of exposure estimation resulted in less attenuated associations between microbial exposure and BR respiratory symptoms. These longitudinal models included survey participant as a random effect, estimated microbial exposure as an independent variable of interest, and survey year, age, gender, race/ethnicity, smoking status, and building tenure as covariates.[21] Single environmental exposure models included only one of the three estimated microbial exposures (culturable fungi, ergosterol, or endotoxin in floor dust) and other covariates. Each of the binary BR respiratory symptoms was used as a health outcome in the single environmental exposure models.

Using all health survey participants ($n=1494$) including those who did not have individual exposure measurements, we further evaluated group-based exposure models. The results from these models were compared with individual measurement-based exposure models as described previously to examine whether the benefit of using floor average-based exposure estimates over individual exposure measurements still existed. In these models, floor averages were estimated based on all environmental measurements ($n=1064$).

We examined whether any significant non-linear relationships existed between exposure and health outcomes in the single environmental exposure models using restricted cubic spline functions in generalized estimating equations.[22] We evaluated whether differences in attenuation bias between individual measurement-based and group average-based exposures were consistently observed using two different exposure variables — initial survey exposure by using initial measurements in 2002 (initial survey exposure models) and time-varying exposure allowing exposures to vary over the survey period by using measurements of each survey (time-varying exposure models).

We reported the odds ratio (OR) for BR respiratory symptoms and 95% confidence interval (CI) for a 1-unit increase in the natural log-transformed levels of microbial agents. All analyses were performed in SAS 9.2 (SAS Institute, Cary, NC, USA). We chose a probability value of $P\leq 0.05$ for statistical significance.

Estimation of group sample size. In epidemiological studies using group-based exposure estimation, the sample size of a group with given attenuation bias can be estimated based on information about exposure variability and number of repeated measurements for the same worker as follows:[4] Sample size in an exposure group $(k)=\left(\frac{B^*}{1-B^*}\right)\times\left(\frac{\sigma^2_{ww}}{n\sigma^2_{bg}}\right)-\left(\frac{\sigma^2_{bw}}{\sigma^2_{bg}}\right)$, where B^* is the estimated coefficient divided by the true coefficient of the exposure–response relationship, $1-B^*$ is attenuation bias, σ^2_{ww} is within-workstation exposure variance, σ^2_{bw} is between-workstation exposure variance, σ^2_{bg} is between-group exposure variance, and *n* is the number of repeated measurements per workstation. We estimated required sample size for the floor as an exposure group when 20% or 30% attenuation bias is allowed in the estimated logistic regression coefficient of the health effect model based on information about exposure variances estimated in our study.

RESULTS

Distribution of Levels of Microbial Agents by Grouping Scheme

We collected a total of 1064 dust samples from 689 unique workstations over four surveys (338, 279, 297, and 150 samples, respectively). Sixty percent of 338 sampled workstations in 2002 were resampled in 2004, but only small fractions were resampled in the randomly selected workstations in the 2005 and 2007 surveys (15% and 9%, respectively). Figure 2 shows distributions of unadjusted geometric means of repeated measurements at the same workstations for total culturable fungi, ergosterol, and endotoxin and demonstrates within-group and between-group variability for each grouping scheme. When sampled workstations were classified based on proximity to the building exterior ($\leq$15 feet and $>$15 feet of the building exterior, two groups), group means (open circles in Figure 2) between the two groups were similar. Interquartile ranges (solid box in Figure 2) for the two groups mostly overlapped. For the floor-grouping scheme (15 groups), ranges of group means for the three agents were wider

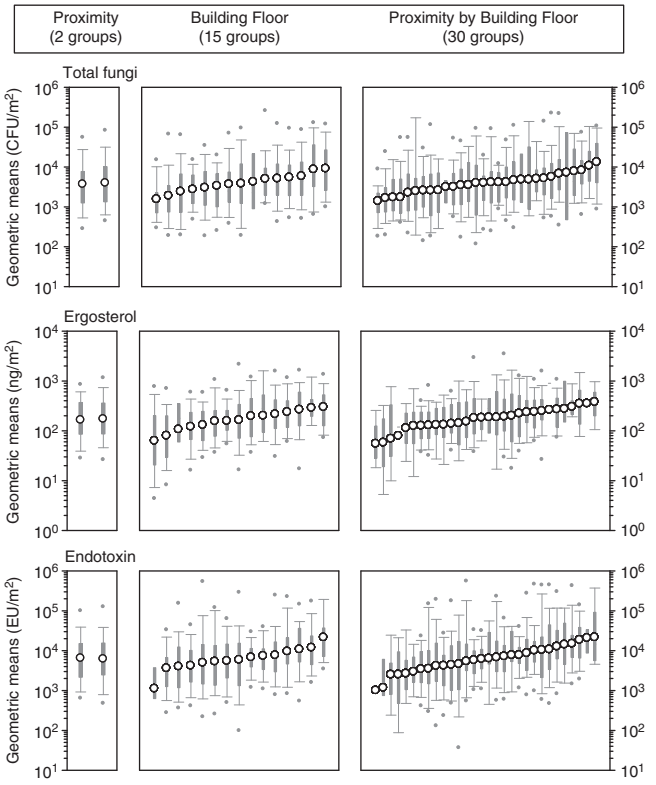

Figure 2. Distribution of means of repeated measurements in each workstation within group by exposure group for each grouping scheme: proximity to the building exterior ($\leq$15 feet and $>$15 feet); building floor (15 floors); and combination of the two (30 groups). Each box (whiskers) plot: an interquartile range (IQR; upper and lower boundaries: 1st/3rd quartile $\pm$1.5 IQR) of geometric means at same workstations across the four surveys within a group. An open circle inside the box plot: a geometric group mean over all measurements across the four surveys within a group.

Table 1. Estimated variance components of microbial agents in floor dust for grouping schemes.

Grouping scheme	*No. of groups*	*Variance components of microbial agents*[a]			*Contrast*[b]	*Precision*[c]
		Within-workstation	*Between-workstation*	*Between-group*		
Total fungi (ln CFU/m^2)						
Proximity	2	2.01	0.40	0.00	0.00	14.16
Floor	15	2.02	0.19	0.19	0.50	5.77
Proximity + floor	30	2.04	0.17	0.20	0.54	3.69
Individual	681	2.01	0.40	NA	NA	NA
Ergosterol (ln ng/m^2)						
Proximity	2	1.05	0.35	0.00	0.00	15.32
Floor	15	1.04	0.21	0.15	0.41	6.23
Proximity + floor	30	1.05	0.21	0.14	0.41	4.05
Individual	517	1.05	0.35	NA	NA	NA
Endotoxin (ln EU/m^2)						
Proximity	2	1.84	0.68	0.01	0.01	13.48
Floor	15	1.82	0.56	0.15	0.21	5.31
Proximity + floor	30	1.84	0.46	0.23	0.33	3.61
Individual	683	1.84	0.69	NA	NA	NA

Abbreviation: NA, not applicable.
Number of dust samples for total fungi and endotoxin across four surveys were 1053 and 1050, respectively. For ergosterol, 723 dust samples across three surveys in 2002, 2004, and 2007 surveys were analyzed.
[a]Within-workstation and between-workstation variance of levels of microbial agents were estimated using general linear mixed-effects models with a random effect of sampled workstation and fixed effects of survey and grouping. Between-group variance was estimated as the difference of sum of within-workstation and between-workstation variances between two models: one without and the other with a grouping variable.
[b]Measure of the difference in mean exposures among groups calculated as between-group variance divided by sum of between-group variance and between-workstation variance.
[c]Measure of precision of a group mean exposure calculated as the median of $\left[1/\sqrt{\left(\frac{\text{Betweenworkstation variance}}{\text{No. of sampled workstations}}+\frac{\text{Withinworkstation variance}}{\text{No. of dust samples in a group}}\right)}\right]$ for all groups in a grouping scheme.

than those for the proximity-grouping scheme. When sampled workstations were classified based on a combination of proximity and floor (30 groups), ranges of group means between groups and interquartile ranges within groups were similar to those for the floor-grouping scheme.

Evaluation of Grouping Schemes

For all three microbial agents, within-workstation variance was much larger (3 to 5 times) than between-workstation variance, after adjusting for the survey-year effect (Table 1). Grouping sampled workstations based on proximity to the building exterior showed no between-group variability of microbial agents as illustrated in Figure 2. Between-group variance of total culturable fungi increased up to 209-fold when building floor was used for a grouping scheme compared with the grouping scheme based on proximity. For the grouping based on a combination of proximity and building floor compared with the floor-grouping scheme, between-group variance of total fungi and endotoxin increased by 4% and 35%, and contrast increased by 9% and 58%, respectively. For ergosterol, however, there was no change in between-group variance compared with the floor-grouping scheme. On the other hand, precision of group means for the three agents decreased as the number of groups within a grouping scheme increased because number of measurements used to calculate precision in each of the groups decreased. For the grouping scheme based on the combination of proximity and floor, the precision for total fungi, ergosterol, and endotoxin decreased by 36%, 35%, and 32%, respectively, compared with those for the floor-grouping scheme. Therefore, we selected building floor to estimate microbial exposures of building occupants in health effect models. We also examined health effect models for endotoxin based on the combination of proximity and building floor because the combination appeared to provide better contrast.

Application of Microbial Exposure Estimates to Health Effect Models

Sixty-five percent of building occupants, on average, had participated in the four cross-sectional surveys (888, 771, 797, and 762, respectively). Of 1494 occupants participating in at least one survey between 2001 and 2007, 513 health questionnaire respondents had at least one individual measurement of a microbial agent over the four surveys (314, 171, 197, and 84, respectively), and 216 had two or more individual measurements (Figure 1). These 513 employees' workstations are a subset of the 689 unique workstations sampled over the four surveys described in the previous section and were used to evaluate attenuation bias as a result of individual or group-average exposure estimation. Floor means of microbial agents calculated based on individual measurements ($n = 766$) from the 513 employees' workstations in the four surveys were similar to those based on all measurements ($n = 1064$) from the 689 workstations (Supplementary Information).

Overall, floor-based estimates consistently resulted in less attenuated ORs for BR respiratory symptoms than did individual measurements in both initial survey and time-varying exposure models (Figures 3 and 4), although precision was lost as reflected in wider CIs. For total culturable fungi, estimated odds for respiratory symptoms using floor averages increased by 3-fold for ''wheeze'' up to 5-fold for ''chest tightness'' in initial survey exposure models compared with those using individual measurements. Although ergosterol exposure based on individual measurements was also significantly associated with various respiratory symptoms, estimated odds using exposures based on floor averages increased by 2-fold for ''sinus symptoms'' up to 5-fold for ''attacks of cough'' in initial survey exposure models and by 3-fold for ''chest tightness'' up to 7-fold for ''attacks of cough'' in time-varying exposure models. For endotoxin, we did not observe significant associations between exposure and respiratory symptoms in individual measurement-based exposure models; however, estimated odds using exposures based on floor averages substantially increased and became significant for respiratory symptoms in both initial survey and time-varying exposure models.

When we ran the same longitudinal health effect models using all survey participants ($n = 1494$), including those who did not have any individual measurement, we still found the same benefit of using floor averages over individual measurements

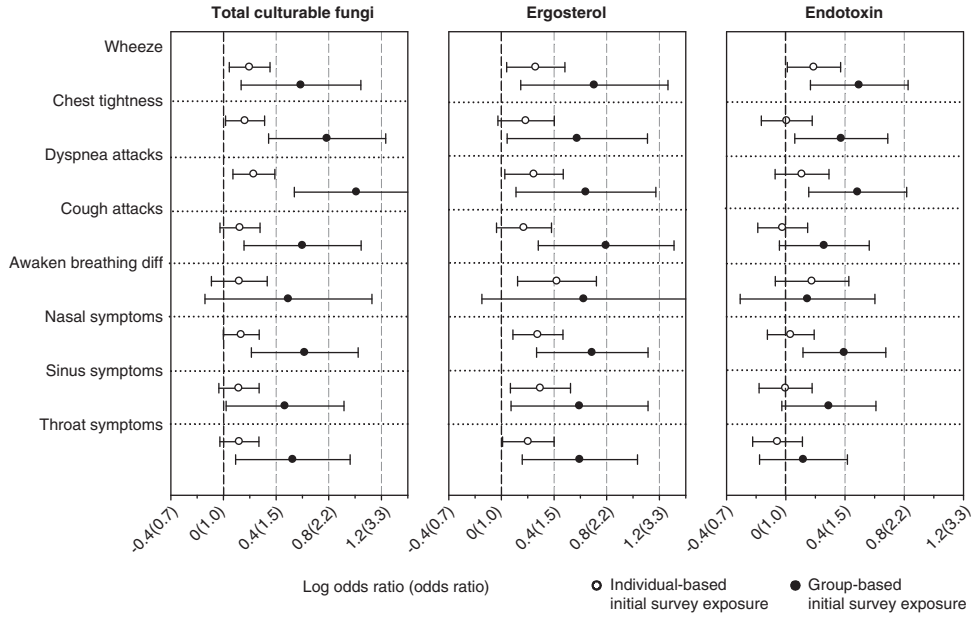

Figure 3. Odds ratios (ORs) and 95% confidence intervals of building-related respiratory symptoms using individual measurement-based and group average-based exposure estimation based on measurement of microbial agents at the initial survey. All models were adjusted for survey, age, gender, race/ethnicity, smoking status, and duration of building occupancy. ORs were based on the 1-unit increase in natural log-transformed levels of microbial agents (total culturable fungi (ln CFU/m^2); ergosterol (ln ng/m^2); endotoxin (ln EU/m^2)).

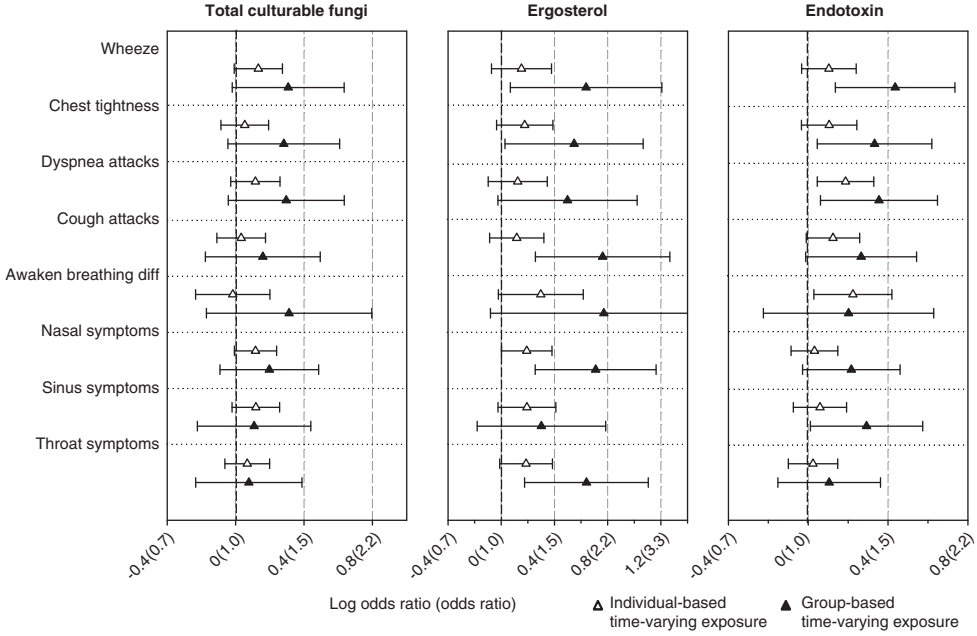

Figure 4. Odds ratios and 95% confidence intervals of building-related respiratory symptoms using individual measurement-based and group average-based exposure estimation based on time-varying exposure over the surveys. All models were adjusted for survey, age, gender, race/ethnicity, smoking status, and duration of building occupancy. ORs were based on the 1-unit increase in natural log-transformed levels of microbial agents (total culturable fungi (ln CFU/m^2); ergosterol (ln ng/m^2); endotoxin (ln EU/m^2)).

(Supplementary Information). Grouping based on a combination of proximity and floor showed better contrast than floor for endotoxin exposure (Table 1), but group means based on the combination of floor and proximity resulted in similar sizes of odds (on average, 2% smaller ORs) for respiratory symptoms compared with those solely based on floor averages in the initial survey exposure models.

In general, linear relationships existed between exposures estimated based on floor averages and BR respiratory symptoms. However, we found a non-linear association with wheeze (P-value = 0.03) for ergosterol exposure in the initial survey exposure model. For endotoxin exposure models, we observed significant non-linear associations of floor average exposures with attacks of cough (P-value = 0.02), awakened by breathing difficulty (P-value = 0.04), sinus symptoms (P-value = 0.04), and throat symptoms (P-value = 0.01) in the initial survey exposure models and with attacks of cough (P-value = 0.03) in the time-varying exposure models.

Estimation of Group Sample Size

On the basis of a theoretical study,[4] we estimated the number of workstations per floor (group sample size) that would be required to allow 20% attenuation bias in the estimated logistic regression coefficient in the health effect model (Figure 5). When only a single measurement is available, which is equivalent to a cross-sectional survey, more than 50 workstations on each floor would be needed for sampling endotoxin to obtain estimates with a bias of 20%, while only 38 workstations and 28 workstations would be needed for culturable fungi and ergosterol, respectively. These numbers decrease by about half when two measurements within-workstation are available. For 30% attenuation bias, 33, 25, and 18 workstations would be needed for endotoxin, culturable fungi, and ergosterol, respectively.

DISCUSSION

Our study of occupants in a damp building demonstrates that floor average-based exposure estimates for microbial agents resulted in less attenuated ORs for respiratory symptoms than did individual measurement-based exposures in the longitudinal health effect models. Overall, we observed the benefit of using group means for all three microbial agents (total culturable fungi, ergosterol, and endotoxin) as well as two types of time course of exposure (initial survey and time-varying). Analyses of variance components showed that within-workstation variability of microbial agents was much larger than between-workstation variability — implying that potentially large attenuation bias may occur if individual measurements are used in health effect models.[4,7,8] Our study also showed that the building floor was a useful grouping method for microbial agents for epidemiological analyses among occupants in this damp building.

Our finding of the advantage of group over individual approaches in exposure estimation for an indoor environment study is consistent with other studies conducted in different occupational settings such as refineries, rubber industry, bakeries, wood manufacture, and electric utility companies[2,5,9] or simulation studies.[1,5] Random measurement error in exposure usually leads to bias in the regression coefficient of the health effect model toward the null when there is a linear exposure–response relationship.[4,23] In studies with individual measurement-based exposure estimation, researchers can decrease the attenuation bias by increasing between-subject variability (achieved by selecting wide exposure ranges of subjects and decreasing the ratio of within-subject to between-subject variability) and by increasing the number of repeated measurements on the same subject.[4] In damp indoor environments where within-subject variability of microbial exposure may be often substantially larger than between-subject variability, a significant amount of attenuation bias would be inevitable without substantially increasing the number of repeated measurements on the same subject in individual-based studies.[11,24,25] Theoretical studies show that the group-based study produces a less biased regression coefficient over the individual-based study due to the modulating effect of the group sample size on within-subject exposure variability when measurement error and within-subject exposure variability are large and within-group exposure variability is small.[1,2,4,5]

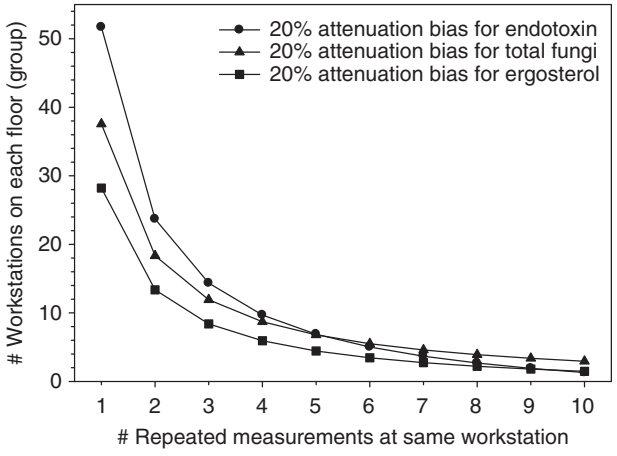

Figure 5. Numbers of workstations on each floor and measurements per workstation that would be required to allow 20% attenuation bias from the true associations (regression coefficient) between microbial exposure and respiratory symptoms in an epidemiological study using group average-based exposure estimation method.

Designing similar exposure groups to maximize differences (contrast) in exposures between groups and to minimize variances within groups (precision) will reduce the attenuation bias in estimating risks for relevant health outcomes in a group-based study.[4,5] We used the same logic as widely applied in occupational settings — grouping based on common characteristics such as job title, plant, and other classification schemes[6] — to construct similar microbial exposure groups among occupants in this water-damaged building. Our previous study showed that the degree of water damage or remediation and microbial exposure varied by floor.[17] In variance analysis of the levels of microbial agents, the floor grouping showed both good contrast and good precision, while a combination of floor and proximity to the building exterior showed the same or better contrast but lower precision compared with floor-based grouping. In health effect models that examined which grouping scheme resulted in stronger associations between exposure and respiratory symptoms, group means based on floors showed similar sizes of odds to those based on the combination of floor and proximity. A floor-specific mean over multiple measurements from different workstations on the same floor (on average, 13 dust measurements per floor in our study), where occupants may dynamically move around within the floor and share contaminated air, appeared to be a good proxy for true microbial exposure, especially for buildings with many open cubicles like our study building.

We found that exposures to fungi and bacterial endotoxin were significantly associated with many of BR respiratory symptoms in longitudinal health effect models, which is consistent with our previous findings based on the 2001 cross-sectional survey.[3,14] Once BR respiratory illness arises, it does not necessarily lessen with lowered exposures after remediation. In this building, the initial survey exposure was the best predictor of BR respiratory symptoms in the later health surveys, which suggests that it seemed as a proxy for exposures during early occupancy. Thus, understanding early occupancy exposure in water-damaged buildings may be important in epidemiological studies on respiratory illnesses due to microbial or other dampness-related exposures among occupants.[26]

We collected floor dust samples from the four surveys with more than a 1-year interval between the consecutive surveys for 6 years, and survey year was an important factor influencing within-workstation variability in our study. Thus, within-workstation variability was estimated with the models that adjusted for survey year as a fixed effect. Therefore, larger within-workstation variability compared with between-workstation variability was less likely due to the long survey period. We found non-linear associations of endotoxin exposures with attacks of cough, awakened by breathing difficulty, sinus symptoms, and throat symptoms in the initial survey exposure models. If exposure–response relationships are not linear, the effects of measurement error on the associations are more complex than simple attenuation.[27]

In conclusion, our study showed that the exposure estimation of microbial agents based on floor means resulted in less attenuation in estimated odds for BR respiratory symptoms among occupants in the water-damaged building than the exposure estimation

based on the individual measurement. This study also showed that the building floor was a useful grouping method of microbial agents in this water-damaged building with cubicle workstations and could be considered in other damp building studies that have similar building geometry.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Supplementary Information accompanies the paper on the Journal of Exposure Science and Environmental Epidemiology website (http://www.nature.com/jes)