



Contents lists available at ScienceDirect

International Journal of Hygiene and Environmental Health

journal homepage: www.elsevier.com/locate/ijheh



Review

The relationship between environmental relative moldiness index values and asthma

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ARTICLE INFO

Article history:

Received 30 October 2015

Received in revised form 26 January 2016

Accepted 27 January 2016

Keywords:

Mold

ERMI

Asthma

Area under the curve

Logistic regression

ABSTRACT

Indoor mold exposures have been qualitatively linked to asthma for more than 25 years. Our goal has been to turn this qualitative link into a quantitative assessment of asthma risk from mold exposures as estimated by the home's environmental relative moldiness index (ERMI) value. The home's ERMI value is derived from the quantitative PCR analysis of 36 molds in a dust sample. Six epidemiological studies of the relationship between ERMI values and asthma, in cities across the U.S., showed that both children and adults with asthma were living in homes with significantly higher ERMI values than the control or comparison homes. Based on these six studies, the accuracy of the ERMI value's link to occupant asthma was analyzed using receiver operating characteristic (ROC) curve and area under the curve (AUC) statistical analysis. The AUC was 0.69 which places the test accuracy in the "fair to good" range for a medical diagnostic test. A logistic regression analysis of the six studies was performed to generate an equation that can be used to predict occupant asthma at specific ERMI values. The ERMI metric may be a useful tool to link the quantification of mold contamination in U.S. homes to some asthma health effects.

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1. Introduction

The prevalence of asthma continues to increase worldwide with about 334 million asthmatics currently (Asher and Pearce, 2014).

In the past 25 years, there have been hundreds of research articles and numerous review articles that have indicated that there was a qualitative link between water-damaged, moldy buildings and asthma (Quansah et al., 2012; Sharpe et al., 2015a). Governmental and international health organizations have also come to the same conclusion in their reviews of the scientific literature (IOM, 2004; WHO, 2009).

In previous studies, the association between mold exposures and asthma was only qualitative because there was no standardized

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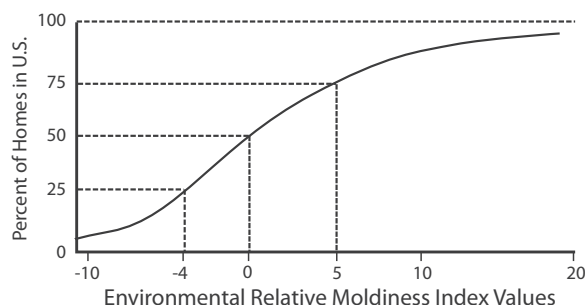


Fig. 1. The environmental relative moldiness scale is the assembled ERMI values (lowest to highest) from the American Health Homes Survey ($n = 1083$). The scale was then divided into quartiles. For example, 25% of homes have ERMI values < -4 and 25% have ERMI values > 5 .

sampling and analytical process for quantifying molds. Often the assessment was limited to a visual inspection or short air samples with many inherent limitations (Vesper, 2011). Our goal has been to turn this qualitative link between mold contamination and asthma into a quantitative assessment that can be acted upon.

To achieve this goal, a DNA-based method of mold identification and quantification called mold specific quantitative PCR (MSQPCR) was created (Haugland and Vesper, 2002). In order to interpret the data from the application of the MSQPCR technology, a standardized approach to sampling and analysis was required. This approach was produced as a result of the use of the MSQPCR technology in the Department of Housing and Urban Development's (HUD, 2010) 2006 American Healthy Homes Survey (AHHS) (Vesper et al., 2007; HUD, 2010). This survey included a national sampling of homes selected to represent the full range of conditions in the U.S. housing stock. The HUD AHHS utilized a living room and bedroom composite, settled-dust sample for the analysis of agents like lead, pesticides, mold, etc. A total of 1083 homes in the U.S. were sampled and EPA researchers obtained a portion of each dust sample for mold analysis.

The MSQPCR technology was used to identify and quantify 82 mold species in each of the AHHS samples. From this panel of 82 molds, 36 molds occurred in the samples at concentrations with a geometric mean of at least one cell per mg dust. From the analysis of these 36 molds in each sample and a mathematical treatment of the data, a relative moldiness scale called the environmental relative moldiness index (ERMI) was created (Fig. 1) (Vesper et al., 2007).

The 36 molds in the ERMI panel are considered "indicators," i.e. indicating water damage/dampness in the home (Table 1). The 26 Group 1 indicator molds were more common in water damaged homes and the ten Group 2 indicator molds were common in homes, even without water damage (Vesper et al., 2009; Vesper, 2011).

The ERMI value for each AHHS home was calculated, as shown in Eq. 1, by taking the sum of the logs of the concentrations of the 26 Group 1 species (s_{1i}) and subtracting the sum of the logs of the concentrations of 10 Group 2 species (s_{2j}) (Vesper et al., 2007). [The Group 2 molds are subtracted from the Group 1 molds to adjust for differences in cleaning habits, use of windows for ventilation, etc. (Vesper, 2011).]

$$\text{ERMI} = \sum_{i=1}^{26} \log_{10}(s_{1i}) - \sum_{j=1}^{10} \log_{10}(s_{2j}) \quad (1)$$

To create the ERMI scale, i.e., the graphic representation of the data, each of the 1083 ERMI values from the AHHS survey were assembled from lowest to highest, as shown in Fig. 1. The resulting ERMI scale is a relative comparison of mold contamination in homes across the continental U.S.

Table 1

Environmental relative moldiness index (ERMI) indicator molds: Group 1 associated with water-damaged homes and Group 2 common in homes, independent of water damage.

Group 1	Group 2
<i>Aspergillus flavus</i>	<i>Acremonium strictum</i>
<i>Aspergillus fumigatus</i>	<i>Alternaria alternata</i>
<i>Aspergillus niger</i>	<i>Aspergillus ustus</i>
<i>Aspergillus ochraceus</i>	<i>Cladosporium cladosporioides</i> 1
<i>Aspergillus penicillioides</i>	<i>Cladosporium cladosporioides</i> 2
<i>Aspergillus restrictus</i>	<i>Cladosporium herbarum</i>
<i>Aspergillus sclerotiorum</i>	<i>Epicoccum nigrum</i>
<i>Aspergillus sydowii</i>	<i>Mucor</i> group
<i>Aspergillus unguis</i>	<i>Penicillium chrysogenum</i>
<i>Aspergillus versicolor</i>	<i>Rhizopus stolonifer</i>
<i>Aureobasidium pullulans</i>	
<i>Chaetomium globosum</i>	
<i>Cladosporium sphaerospermum</i>	
<i>Eurotium amstelodami</i>	
<i>Paecilomyces variotii</i>	
<i>Penicillium brevicompactum</i>	
<i>Penicillium corylophilum</i>	
<i>Penicillium crustosum</i> group	
<i>Penicillium purpurogenum</i>	
<i>Penicillium spinulosum</i>	
<i>Penicillium variabile</i>	
<i>Scopulariopsis brevicaulis</i>	
<i>Scopulariopsis chartarum</i>	
<i>Stachybotrys chartarum</i>	
<i>Trichoderma viride</i>	
<i>Wallemia sebi</i>	

For the sake of convenience, the ERMI scale is divided into quartiles (Fig. 1). For example, 25% of homes in the U.S. have an ERMI value below -4 and are in the lowest relative mold contamination quartile and the 25% of homes, with ERMI values above 5, are in the highest relative mold contamination quartile. Therefore, if the relative mold contamination of any home in the U.S. is sought, the ERMI provides a scale on which that home can be compared to the rest of the U.S. housing stock.

In this review article, six epidemiological studies, in cities across the U.S., will be summarized and the quantitative relationship between ERMI values and asthma described. Based on these six studies, the accuracy of the ERMI value's link to occupant asthma will be analyzed using receiver operating characteristic (ROC) curve and area under the curve (AUC) statistical analysis followed by a logistic regression analysis of the six studies to generate an equation that may be considered for use in predicting occupant asthma at specific ERMI values.

2. Support for the approach to the application of the ERMI metric

There have been many approaches to defining mold contamination. Most often indoor mold contamination is estimated by visual inspection. This approach ignores the fact that mold contamination can be hidden from sight and smell. Also, not everyone performing visual inspections is equally qualified. Therefore, the estimates are subjective and inspector dependent.

Sometimes short air samples (three to five minutes) are used to collect mold cells or spores which are then quantified by microscopic counting or by culturing on specific media. (Longer sampling times can result in too much density on the counting slide or Petri dish.) Short sampling times only provide information about what was in the air at that specific point in time. In addition, most mold spores cannot be identified to the species level and sometimes not even to the genus level, e.g., *Aspergillus* versus *Penicillium*, and vegetative mold cells or fragments cannot be identified at all by microscopic observations.

Table 2

Description of the six home studies of the relationship between environmental relative moldiness index (ERMI) values and asthma. The mean ERMI value and number of homes tested (# homes) in the asthma versus the control groups are enumerated for each study, as well as, the general health end-point utilized in each study.

Location	Occupant	Mean ERMI value Asthma (# homes) vs. Control (# homes)	Health end-point
1. Cincinnati	Infant	6.7 (69) vs. 2.1 (220)	Physician diagnosed
2. Boston	Child	8.7 (76) vs. 5.2 (34)	Physician diagnosed
3. San Diego	Child	8.1 (93) vs. 2.1 (28)	Parental questionnaire
4. Kansas City	Child	9.3 (60) vs. 3.5 (22)	Parental questionnaire
5. Detroit	Child	8.7 (32) vs. 6.2 (83)	Prescribed medication
6. California	Adult	6.0 (139) vs. 2.0 (44)	Physician diagnosed

If culturing is used to evaluate the mold populations, the molds detected are limited to those that will grow on the media selected. All molds do not grow on the same media and some grow faster than others, resulting in “slow-growers” being missed. But the most important problem with traditional methods of mold analysis is that there is no standard, objective method for interpreting the results from either microscopic counting or culturing data (Johnson et al., 2008; Vesper, 2011). On the other hand, the ERMI metric provides an easily understood scale that was the result of a national survey of U.S. homes.

In order to assure the general applicability of the ERMI methodology, several additional issues were investigated related to sampling, reproducibility and ERMI value stability. The standard ERMI sample is a composite of dust from the living room and bedroom obtained at one point in time (Vesper et al., 2007). In a study of homes of asthmatic children, we demonstrated that the separate bedroom and living room samples were highly correlated (Kamal et al., 2014). We also showed that samples collected from one to seven months apart in the same home fell within a 95% confidence interval of each other, indicating a strong likelihood of repeatability of ERMI measurements without any systematic bias in the results (Kamal et al., 2014). Therefore, ERMI values were stable, independent of season and not room specific.

3. Summary of studies that utilized the ERMI metric

There have been six studies that have utilized the ERMI metric in the quantification of mold contamination in U.S. homes and its association with asthma. The most important was a prospective study that followed a cohort of infants until age seven. The other five studies were performed to examine the association between asthma and the ERMI values in homes of either children or adults. The studies took place in the geographically dispersed U.S. States of Massachusetts (MA), Kansas (KS), California (CA), and Michigan (MI). There has been no attempt in this review analysis to adjust for other risk factors, although in some of the specific studies, there were adjustments made.

3.1. Prospective study of the relationship between ERMI values in homes and the development of physician-diagnosed asthma

A prospective study of asthma development was conducted by researchers from the University of Cincinnati's (U.C.) Department of Environmental Health, the U.S. Environmental Protection Agency's Office of Research and Development, the U.C. Medical School and Cincinnati Children's Hospital (Cho et al., 2006). Pregnant women were enrolled in the study. Each home's environment and the child's health were monitored for seven years, until a physician could make a diagnosis of asthma. Settled-dust collected in each infant's home was analyzed for mold, as well as for many other agents, including endotoxin, allergens, etc. Homes were also inspected by making a visual estimate of the mold contamination.

In an initial analysis of 176 children, infants who had lived in homes with a high ERMI value (>5.2) were at more than twice the risk of developing asthma than those in low ERMI value homes (<5.2) (adjusted odds ratio, 2.6; 95% confidence interval [CI], 1.10–6.26) (Reponen et al., 2011). None of the other exposures monitored, including the visible mold contamination estimates, were predictive of the development of asthma.

After the initial evaluation of the 176 homes, an additional 116 homes were analyzed to make a final cohort of 292 homes and infants. In this larger cohort, the average ERMI value in the homes of infants that developed asthma was 6.7 compared to an average of 2.1 for the homes of infants that did not develop asthma (Table 2). In this larger cohort, the multivariate model showed that the risk of asthma at age seven was 1.8 times greater for each 10-unit increase in ERMI values in the infants' homes (Reponen et al., 2012).

3.2. Additional studies of the relationship between home ERMI values and asthma

Four other studies of asthmatic children included cross-sectional studies in the cities of Boston, Detroit, Kansas City, and San Diego. In these cities, asthmatic children were found to be living in homes with average ERMI values significantly greater than the comparison homes (Table 2) (Vesper et al., 2013a). In addition, children in Kansas City with severe asthma were living in homes with an average ERMI value of 12.4 which was significantly greater than those children with only mild to moderate asthma whose homes had an average ERMI value of 7.9 (Vesper et al., 2013a). In a study in Detroit, MI, severely asthmatic children were found to be living in homes with an average ERMI value of 8.7 compared to 6.2 for homes of non-asthmatics (Table 2) (Vesper et al., 2008).

In addition to the study of ERMI values in the homes of asthmatic children, the homes of adult asthmatics were the subject of one study in northern California. The mean ERMI value in homes was 6.0, which was significantly greater than mean ERMI value of 2.0 in the comparison homes (Blanc et al., 2013).

In summary, both asthmatic children and adults were found to be living in homes with high ERMI values. However, because “asthma” was described by many different endpoints in these studies, overlapping in average ERMI values from study to study based on these different endpoints was observed. For example, the fact that infants living in Cincinnati homes with an average ERMI value of 6.7 is associated with disease development but older children living in Detroit homes with an average ERMI of 6.2 did not have asthma was a function of these overlapping endpoints.

4. Statistical evaluation and technical methodology for showing the relationship of ERMI values to asthma

A meta-analysis was considered for the analysis of these six studies but this approach was assessed as premature primarily because of the small number of studies, all of which were connected to one analytical laboratory. In addition, the dust sampling method

used differed in the studies. In the HUD AHHS was a single MiTest™ vacuum sample from the living room plus bedroom of each home (Vesper et al., 2007). Since the MiTest™ sampler is no longer commercially available, dust was collected in the six studies by various methods. The common feature for each study was that settled dust was collected in the bedroom, living room or both.

In addition, the asthma endpoint varied in each of the six studies (Table 2). In the prospective study of asthma development in Cincinnati, the endpoint was physician-diagnosed asthma at age seven. In the Boston MA and the study of adults in CA, asthma was also based on a physician's diagnosis. In the San Diego and Kansas City studies, asthma categorization was based on a parental questionnaire. In the Detroit study, asthma categorization was based on the parent's description of their child's use of prescribed medication for asthma management using the Global Initiative for Asthma (GINA) classification system as non-, intermittent- and persistent asthma (none, occasional and daily, respectively) (GINA, 1995).

The study locations also spanned many of the climactic conditions across the US, from east coast, mid-west and west coast but tropical states, like Florida, were not represented. Therefore a meta-analysis awaits more studies that are conducted more consistently. However, a combined analysis of the six studies was pursued to describe the accuracy and the possible strength of the asthma associations at different ERMI values. Our goal was to provide an easily understood, predictive model like a diagnostic test.

4.1. Receiver operating characteristic (ROC) curve and area under the curve (AUC) analysis

The data from six epidemiological studies of the relationship between ERMI values and asthma were analyzed using receiver operating characteristic (ROC) curve and area under the curve (AUC) statistical methods to determine the accuracy of the ERMI value's link to occupant asthma. ROC curves and their associated AUC are commonly employed for estimating the accuracy of medical diagnostic tests with the goal of achieving high sensitivity and specificity (Mallett et al., 2012). Optimal sensitivity in this case refers to the Youden index which is the maximum difference between the ROC curve and the line of equality between sensitivity and 1-specificity (Youden, 1950). This describes a point which maximizes the discriminatory power of the ERMI and may be a reasonable choice for a cutoff ERMI value given equal weight between sensitivity and specificity.

To create the ROC curve, the diagnostic sensitivity and specificity value for every potential cut-off point was plotted as an empirical histogram for asthmatic and the control/comparison populations. Kernel density estimation with Normal smoothing was used for the distributions of ERMI scores among asthmatic and non-asthmatic populations based on the composite data.

The mean ERMI value in all of the homes associated with asthma ($n=469$) was 7.97 compared to a mean ERMI value of 3.57 for all control/comparison homes ($n=431$) (Table 3). The difference in mean ERMI values between asthma and the controls/comparison group, 4.40, was statistically significant (t -test, $p < 0.001$) (Table 3). Therefore, it appears that the method of collecting the dust (as long as settled dust was collected), where in the home the dust was collected (living room, bedroom or both), the different asthma health endpoints and the specific study city were not limiting for the combined analysis.

The AUC analysis is the most commonly used measure of the overall performance of a diagnostic test (Qin and Hotilovac, 2008). The AUC gives the probability that a randomly selected diseased (e.g., asthmatic) individual will have a higher ERMI value home than a non-diseased individual. A diagnostic test can be characterized for both its sensitivity and specificity. In some cases, sensitivity

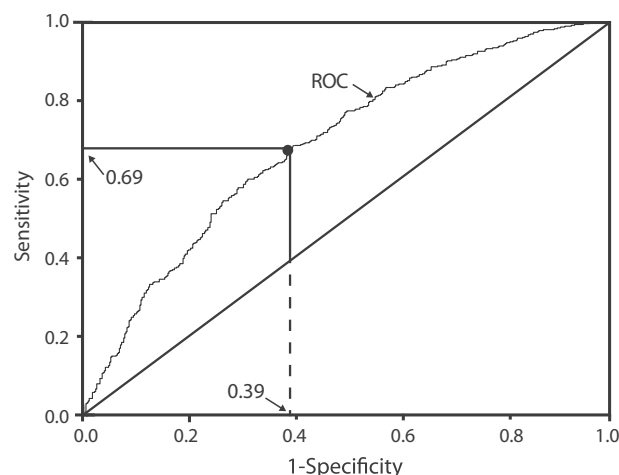


Fig. 2. Receiver operating characteristic (ROC) (jagged curved line) and area under the curve (AUC) which is all of the area under the ROC curve.

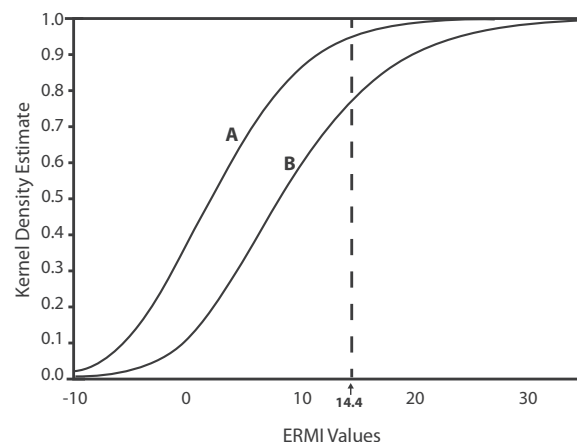


Fig. 3. Example of a smoothed kernel density estimate for the comparison/control homes (A) and the homes associated with asthma (B). An example ERMI cut-point (14.4) is shown when a fixed specificity of 0.95 is selected for the comparison/control homes.

is more important that specificity and in other cases specificity is more important. We have looked at the results both ways.

Diagnostic accuracy for a medical test can be summarized for a single threshold or by combining accuracy across a range of thresholds. In our studies, there is a range of asthma thresholds. For example, the mold exposure that is associated with the development of asthma may be different from exposure that exacerbates asthma. Fig. 2 presents the result for selection for optimal sensitivity. For the combined data, the optimal sensitivity was found to be 0.69 (95% CI, 0.65–0.74) and the corresponding specificity was 0.39 (95% CI 0.35–0.44) (Fig. 2). An AUC value of 0.69 is generally considered to be in the “fair to good” range when evaluating a medical diagnostic test's ability to identify potential cases of illness (Simundić, 2006).

On the other hand, the specificity of the test might be of greater interest. Fig. 3 shows an estimate based on limiting the specificity of the test to 0.95. The result is a sensitivity of 0.77 at an ERMI value of 14.4. The calculated probability of having an occupant with an asthma-related condition in a home with an ERMI value of 14.4 is 31%. Therefore, the probability of finding an occupant with an asthma condition in a home with an ERMI of 14.4 is 3.4 (31%/9%) times more likely than in a home for which the ERMI value is unknown.

Table 3

The means and standard error (SE) for the environmental relative moldiness index (ERMI) values for the six combined studies of asthma in homes, as well as, the 95% confidence intervals about the mean and the statistical difference *p* value based on the Student *t*-test.

Group	Mean	SE	95% Confidence limits		<i>P</i> value
			Lower	Upper	
Asthma	7.97	0.33	7.32	8.62	<0.001
Control	3.57	0.41	2.76	4.39	
Difference	4.40	0.53	3.36	5.44	

Table 4

Asthma predictive result from the logistic regression at an example environmental relative moldiness index (ERMI) value of 10.

ERMI		ASTHMA (9%)	Control/comparison (91%)
10	Asthma positive	$0.09 \times 0.41 = 0.0369$	$0.91 \times 0.13 = 0.1183^a$
10	Asthma negative	$0.09 \times 0.59 = 0.0531$	$0.91 \times 0.87 = 0.7917$

^a $0.0369 + 0.1183 = 0.1552$ and $0.0369/0.1552 = 0.24$ or 24%.

4.2. Logistic regression analysis of the probability of asthma

Logistic regression analysis of the probability of asthma is estimated by

$$P(A|ERMI) = a + b * ERMI \quad (2)$$

In the study data, $P(A|ERMI)$ is added as 1 if the subject has asthma symptoms, 0 otherwise. Given that results from studies such as these, cases and controls are independently sampled, $P(A|ERMI)$ is adjusted so that the adjusted numbers of observed asthma cases and non-asthmatic cases reflect the actual proportion of asthma, $P(A) = 0.09$, in the general population (CDC, 2014).

The logistic equation development from the data set led to the evaluation of asthma's prediction at different ERMI values. For example, if the ERMI value for a home is known to be 10, then the likelihood of the occupant having an asthma condition is 24% (Table 4). At the ERMI value of 10, the probability of asthma for the occupant is increased by 2.7 times (24%/9%) compared to a home in which the ERMI value is unknown. Similar predictions can be generated for other ERMI values.

The successful application of the statistical analyses typically used for estimating and predicting disease suggests that a quantitative assessment of mold contamination, using the ERMI scale, can be applied to assess the relationship between mold exposures and asthma and inform decisions about reducing mold exposure risks. In order to reduce the risk of asthma, the World Health Organization suggested that mold exposures should be "minimized" (WHO, 2009). However, everyone is exposed to mold at some level on a daily basis. To utilize the WHO's advice, a meaningful quantitative estimate of mold exposure is needed. Our results suggest that the ERMI scale might be sufficiently specific and quantitative.

5. Limitations of this review of the application of the ERMI

Although additional epi-studies using the ERMI are being pursued, there has been a general consistency in the results to date. However, there are many limitations to this review analysis of the ERMI. For example, it has been noted that the MSQPCR analysis of molds does not measure viable mold cells; only total cells (Sharpe et al., 2016). However, measuring viable cells, limits one to short air samples and/or the practical limitation of identifying and quantifying large numbers of colonies. Monoclonal antibodies were recently proposed to identify cultured molds (Sharpe et al., 2016). Perhaps a combination of approaches would be useful in enhancing our understanding of the risks from mold exposures.

Another limitation of the ERMI scale is that it was created from results of U.S. housing only. An ERMI-type scale for different

countries should be based on a representative sampling of homes in each country and may require adjusting for conditions in each country (Osborne et al., 2015; Täubel et al., 2015). Homes in tropical environments will certainly require a different ERMI scale, since the homes are generally open to the outside all year (Chen et al., 2015).

Another limitation of this review was that a comprehensive quantification of potential confounding or contributing risk factors was not completed in each study. Since asthma has multiple phenotypes (Chung, 2016), it should not be surprising that multiple exposures contribute to the disease spectrum called asthma (Sharpe et al., 2015b,c, 2016). Mold exposure is certainly only one of many exposures that might contribute to asthma. It is even possible that the ERMI values measured in homes are only coincidental proxies for other relevant exposures.

6. Conclusions

The ERMI studies do not prove that there is a causal relationship between mold exposures for a particular person and the development or exacerbation of asthma. However, at the population level, these studies suggest a quantitative link that is consistent with the many qualitative studies in the scientific literature associating water-damage or dampness in homes/buildings and asthma.

These results would also help to explain why mold exposures, as described by ERMI values, are linked to human asthma and poor lung function, for both children and adults, as measured by spirometry (Vesper et al., 2013b; McSharry et al., 2015). Therefore, the ERMI metric may be a useful tool to link the quantification of mold contamination in U.S. homes to some health effects related to asthma.

Competing financial interest

The U.S. Environmental Protection Agency (EPA) through its Office of Research and Development funded in the research described here. It has been subjected to the Agency's peer review and has been approved for publication. Mention of trade names or commercial products does not constitute endorsement or recommendation by the EPA for use. Since MSQPCR technology is patented by the US EPA, the Agency has a financial interest in its commercial use.

Acknowledgement

We thank Katherine Loizos for preparation of the figures.

References

- Asher, I., Pearce, N., 2014. Global burden of asthma among children. *Int. J. Tuberc. Lung Dis.* 18, 1269–1278.
- Blanc, P.B., Quinlan, P.J., Katz, P.P., Balmes, J.R., Trupin, L., Cisternas, M., Wymer, J., Vesper, S.J., 2013. Higher environmental relative moldiness index values measured in homes of adult asthmatics. *Environ. Res.* 122, 98–101.
- CDC, 2014. Trends in Asthma Prevalence, Health Care Use, and Mortality in the United States, 2001–2010. Online. <http://www.cdc.gov/nchs/data/databriefs/db94.pdf> (accessed 10.12.14).
- Cho, S.H., Reponen, T., Bernstein, D.I., Olds, R., Levin, L., Liu, X., Liu, X., Wilson, K., Lemasters, G., 2006. The effect of home characteristics on dust antigen concentrations and loads in homes. *Sci. Total Environ.* 371, 31–43.
- Chen, C.-H., Chao, H.J., Shen, W.-C., Chen, B.-Y., Lin, K.-T., Guo, Y.L., Vesper, S., 2015. Pilot study of mold in homes of asthmatic children in Taipei, Taiwan using the environmental relative moldiness index. *Aerobiologia* 31, 213–218.
- Chung, K.F., 2016. Asthma phenotyping: a necessity for improved therapeutic precision and new targeted therapies. *J. Intern. Med.* 279, 192–204.
- GINA (Global Initiative for Asthma), 1995. Global Strategy for Asthma Management and Prevention. NHLBI/VVHO Workshop Report. National Institutes of Health, Bethesda, National Heart Lung and Blood Institute publication number 95–3659.
- Haugland, R.A., Vesper, S.J., 2002. Identification and Quantification of Specific Fungi and Bacteria. U.S. Patent and Trademark Office, Patent No. 6,387,652, Granted May 14, 2002.
- HUD, 2010. American Healthy Homes Survey. HUD No. 10–138, Online. <http://portal.hud.gov/>.
- IOM (Institute of Medicine), 2004. *Damp Indoor Spaces and Health*. National Academies Press, Washington, DC.
- Johnson, D., Thompson, D., Clinkenbeard, R., Redus, J., 2008. Professional judgment and the interpretation of viable mold air sampling data. *J. Occup. Environ. Hyg.* 5, 656–663.
- Kamal, A., Burke, J., Vesper, S., Batterman, S., Vette, A., Godwin, C., Chavez-Camarena, M., Norris, G., 2014. Applicability of the environmental relative moldiness index for quantification of residential mold contamination in a study of air pollution and childhood asthma. *J. Environ. Public Health*, 261357, <http://dx.doi.org/10.1155/2014/261357>.
- Mallett, S., Halligan, S., Thompson, M., Collins, G.S., Altman, D.G., 2012. Interpreting diagnostic accuracy studies for patient care. *BMJ* 345, e3999, <http://dx.doi.org/10.1136/bmj.e3999>.
- McSharry, C., Vesper, S., Wymer, L., Howieson, S., Chaudhuri, R., Wright, G.R., Thomson, N.C., 2015. Decreased FEV₁ in asthmatic adults in Scottish homes with high environmental relative moldiness index values. *Clin. Exp. Allergy* 45, 902–907.
- Osborne, N.J., Thornton, C.R., Sharpe, R.A., 2015. Indoor fungal exposure and allergic respiratory disease. *Curr. Allergy Asthma Rep.* 15, 71, <http://dx.doi.org/10.1007/s11882-015-0572-7>.
- Quansah, R., Jaakkola, M.S., Hugg, T.T., Heikkinen, S.A., Jaakkola, J.J., 2012. Residential dampness and molds and the risk of developing asthma: a systematic review and meta-analysis. *PLoS ONE* 7, e47526, <http://dx.doi.org/10.1371/journal.pone.0047526>.
- Qin, G., Hotilovac, L., 2008. Comparison of non-parametric confidence intervals for the area under the ROC curve of a continuous-scale diagnostic test. *Stat. Methods Med. Res.* 17, 207–221.
- Reponen, T., Vesper, S., Levin, L., Johansson, E., Ryan, P., Burkle, J., Grinspun, S.A., Zheng, S., Bernstein, D.I., Lockey, J., Villareal, M., Hershey, G.K.K., LeMasters, G., 2011. High environmental relative moldiness index during infancy as a predictor of age seven asthma. *Ann. Allergy Asthma Immun.* 107, 120–126.
- Reponen, T., Lockey, J., Bernstein, D.I., Vesper, S.J., Levin, L., Zheng, S., Ryan, P., Grinspun, S.A., Villareal, M., Hershey, G.K.K., LeMasters, G., 2012. Infants exposed to specific molds correlated with age seven asthma. *J. Allergy Clin. Immun.* 130, 639–644.
- Sharpe, R.A., Cocq, K.L., Nikolaou, V., Osborne, N.J., Thornton, C.R., 2016. Identifying risk factors for exposure to culturable allergenic moulds in energy efficient homes by using highly specific monoclonal antibodies. *Environ. Res.* 144 (Pt A), 32–42.
- Sharpe, R.A., Bearman, N., Thornton, C.R., Husk, K., Osborne, N.J., 2015a. Indoor fungal diversity and asthma: a meta-analysis and systematic review of risk factors. *J. Allergy Clin. Immunol.* 135, 110–122.
- Sharpe, R.A., Thornton, C.R., Nikolaou, V., Osborne, N.J., 2015b. Higher energy efficient homes are associated with increased risk of doctor diagnosed asthma in a UK subpopulation. *Environ. Int.* 75, 234–244.
- Sharpe, R.A., Thornton, C.R., Tyrrell, J., Nikolaou, V., Osborne, N.J., 2015c. Variable risk of atopic disease due to indoor fungal exposure in NHANES 2005–2006. *Clin. Exp. Allergy* 45, 1566–1578.
- Simundić, A.M., 2006. Diagnostic accuracy. *Acta Med. Croat.* 60 (Suppl 1), 93–111, Translation at: <http://www.ifcc.org/ifccfiles/docs/190404200805.pdf>.
- Täubel, M., Karvonen, A.M., Reponen, T., Hyvärinen, A., Vesper, S., Pekkanen, J., 2015. Application of the environmental relative moldiness index in Finland. *Appl. Environ. Microbiol.* 82, 578–584.
- Vesper, S.J., McKinstry, C., Haugland, R.A., Wymer, L., Ashley, P., Cox, D., DeWalt, G., Friedman, W., 2007. Development of an environmental relative moldiness index for homes in the U.S. *J. Occup. Environ. Med.* 49, 829–833.
- Vesper, S., McKinstry, C., Haugland, R., Neas, L., Hudgens, E., Heidenfelder, B., Gallagher, J., 2008. Higher environmental relative moldiness index (ERMI) values measured in Detroit homes of severely asthmatic children. *Sci. Total Environ.* 94, 192–196.
- Vesper, S., McKinstry, C., Cox, D., Dewalt, G., 2009. Correlation between ERMI values and other moisture and mold assessments of homes in the American Healthy Homes Survey. *J. Urban Health* 86, 850–860.
- Vesper, S., 2011. Traditional mold analysis compared to a DNA-based method of mold analysis. *Crit. Rev. Microbiol.* 37, 15–24.
- Vesper, S., Barnes, C., Ciccio, C.E., Cox, D., Dewalt, G., Jacobs, D.E., Johanns, A., Kennedy, K., Nunez-Alvarez, A., Sandel, M.T., Ashley, P., 2013a. Higher environmental relative moldiness index (ERMI) values measured in homes of asthmatic children in Boston, Kansas City and San Diego. *J. Asthma* 50, 155–161.
- Vesper, S.J., Wymer, L., Kennedy, S., Grimsley, L.F., 2013b. Decreased pulmonary function measured in children exposed to high environmental relative moldiness index homes. *Open Respir. Med. J.* 7, 83–86.
- WHO (World Health Organization), 2009. *WHO Guidelines for Indoor Air Quality: Dampness and Mould*. WHO Regional Office for Europe, Copenhagen, Denmark.
- Youden, W.J., 1950. An index for rating diagnostic tests. *Cancer* 3, 32–35.