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### **ABSTRACT**

The Institute of Medicine (IOM) of the National Academy of Sciences recently completed a critical review of the scientific literature pertaining to the association of indoor dampness and mold contamination with adverse health effects. In this paper, we report the results of quantitative meta-analysis of the studies reviewed in the IOM report. We developed point estimates and confidence intervals (CIs) to summarize the association of several respiratory and asthma-related health outcomes with the presence of dampness and mold in homes. The odds ratios and confidence intervals from the original studies were transformed to the log scale and random effect models were applied to the log odds ratios and their variance. Models were constructed both accounting for the correlation between multiple results *within* the studies analyzed and ignoring such potential correlation. Central estimates of ORs for the health outcomes ranged from 1.32 to 2.10, with most central estimates between 1.3 and 1.8. Confidence intervals (95%) excluded unity except in two of 28 instances, and in most cases the lower bound of the CI exceeded 1.2. In general, the two meta-analysis methods produced similar estimates for ORs and CIs. Based on the results of the meta-analyses, building dampness and mold are associated with approximately 30% to 80% increases in a variety of respiratory and asthma-related health outcomes. The results of these meta-analyses reinforce the IOM's recommendation that actions be taken to prevent and reduce building dampness problems.

### **INTRODUCTION**

The association of adverse health effects with dampness and mold in buildings has been the subject of much research. Most studies on this topic have found an increased risk of one or more adverse health effects in buildings with signs of dampness or visible mold. The Institute of Medicine (IOM) of the National Academy of Sciences recently completed a critical review (IOM 2004) of this scientific literature. The IOM concluded that *excessive indoor dampness is a public health problem*, noted that dampness problems are common, and recommended corrective measures. While the IOM report summarized the main features and results of the reviewed studies, which included a broad range of health outcomes, it provided no quantitative summaries of these studies.

In this paper, we report the results of quantitative meta-analyses of the studies reviewed in the IOM report. A meta-analysis uses statistical methods to combine data from different but comparable research studies, in order to provide a quantitative summary on the size and variability of an association. Studies are generally selected for relevance, quality, and similarity. The contribution of larger, more precise studies to the summary estimate is generally more heavily weighted. Results of meta-analyses presented here are central point estimates and confidence intervals (CIs) of odds ratios (ORs) that summarize the magnitude of increased risk of several health outcomes in buildings with dampness and mold. The central estimates and CIs of ORs, if assumed to reflect causality, can be used to communicate the importance of dampness and mold as health risks, to estimate the economic significance of dampness- and mold-related health effects to society, and to estimate the magnitude of health and economic benefits from programs that reduce dampness and mold.

## **METHODS**

We began with the full list of studies included in Tables 5-1, 5-2, 5-3, 5-6, 5-7, 5-8 of the recent IOM review (IOM 2004). Details on the studies included in the meta-analyses are provided in Appendix 1.

Ideally, meta-analyses would combine estimates only from studies with the same precisely defined health outcome, risk factor, and population/subjects. Because the original studies included many differently defined respiratory health outcomes, risk factors, and populations, this was not possible, and we analyzed groups of studies that were as similar as practicable with respect to these. Table 1 shows the health outcome categories and specific outcomes from the studies included in each category.

### Subject types

We grouped studies by subject type. The reviewed studies included diverse populations: adults, male adults, female adults, children (age < 18), and children (infants). We performed, where possible, separate analyses for: adults (including studies of mixed or single gender), children (including studies of age < 18 or infants), and all ages combined. However, for ever-diagnosed with asthma and asthma development, too few studies were available to support separate meta-analyses for children and adults.

### Risk factors

In general, the risk factors in the reviewed studies included were visible signs of dampness, visible mold, dampness or mold, dampness and mold, and measured concentrations of airborne mold spores or related agents of microbial origin. We included in meta-analyses only the studies with reports of dampness and/or mold as risk factors<sup>1</sup>. A large majority of all studies used these risk factors. We did not distinguish among dampness, mold, dampness or mold, and dampness and mold as risk factors. Our rationale – visible mold is always considered the result of excess dampness, whether or not the dampness is reported, and excess dampness is very often

**Table 1. Health outcomes from reviewed studies, grouped into outcome categories used in meta-analysis**

| <b>Outcome Category for the Meta-Analysis</b> | <b>Outcomes from Individual Studies Used in Each Category</b>  |
|---|--|
| Upper respiratory tract (URT) symptoms        | irritated, stuffy, or runny nose; nasal symptom; nasal congestion; nasal congestion or runny nose; nasal excretion; nose irritation; rhinitis; sinusitis; allergic rhinitis; allergy; hay fever  |
| Cough   | cough; cough with phlegm; cough without phlegm; day or night cough; dry cough; morning cough; long-term cough; night cough with wheeze; persistent cough   |
| Wheeze  | wheeze; persistent wheeze; wheeze apart from cold; wheeze including shortness of breath and asthma; wheeze/shortness of breath   |
| Ever diagnosed with asthma                    | <ul style="list-style-type: none"> <li>• positive response to -- has a doctor ever diagnosed mother (father) to have attacks of shortness of breath (asthma)<sup>2</sup>;</li> <li>• positive response to-- did a doctor ever diagnose your having attacks of shortness of breath or asthma?;</li> <li>• physician-diagnosed asthma;</li> <li>• physician-diagnosed asthma, ever (atopic and non-atopic);</li> <li>• physician diagnosis of asthma since age &gt; 16;</li> <li>• self-reported physician-diagnosed or nurse-diagnosed asthma</li> </ul>  |
| Current asthma                                | <ul style="list-style-type: none"> <li>• current physician-diagnosed asthma, defined as diagnosis plus symptoms in last 12 months;</li> <li>• ever doctor-diagnosed asthma plus asthma symptoms or medication in past 12 months;</li> <li>• current asthma defined as combination of bronchial hyper-responsiveness and at least one of wheeze or breathlessness in last 12 months;</li> <li>• subjective symptoms of asthma plus one or more of the following: doctor diagnosed asthma attack and the disappearance of wheezing; doctor diagnosed asthma attack and &gt; 15% decrease in PEF or FEV1; &gt; 15% decrease in PEF or FEV1 in exercise test; &gt; 20% daily variation in PEF at least 2 days per week in 4 weeks of tracking; &gt; 15% rise in PEF or FEV1 in a bronchodilating test;</li> <li>• asthma - current and diagnosed by physician;</li> <li>• current asthma diagnosed by a doctor -- text implies that current refers to the last 12 months;</li> <li>• asthma currently present and reported to be confirmed by a physician;</li> <li>• occurrence of doctor diagnosed asthma in past year;</li> <li>• positive response to following two questions -- has your doctor ever said your child has asthma? does he or she still have asthma?</li> </ul> |
| Asthma development                            | <ul style="list-style-type: none"> <li>• newly doctor-diagnosed cases of asthma in past 2.5 years;</li> <li>• physician diagnosis of asthma since age &gt; 16;</li> <li>• first time diagnosis of asthma</li> </ul>  |

accompanied by mold, although the mold may not be visible. Thus, it is not possible to make a clean distinction among these risk factors. We excluded from the meta-analyses ORs from

<sup>2</sup> The question's wording reflects the fact that the study assessed the risk of asthma in mothers and fathers of school children as a function of dampness in the home as part of a broader study focusing on children's asthma symptoms

studies with measured concentrations of microbial agents or measured or reported high air humidity (Appendix 2).

Presence of dampness and/or mold were made in each study by either the occupants or the researchers. We did not distinguish between occupant-reported dampness and/or mold and researcher-reported dampness and/or mold. Most studies that have compared occupant reports and researcher reports of dampness and/or mold have found the two types of reports to be fairly well correlated. Also, whether or not researcher-based reports are more accurate is still a subject of debate.

The large majority of studies have assessed the risks of dampness and/or mold in homes. ORs associated with dampness and/or mold in other types of buildings, such as schools or work places, were excluded from our analyses (Appendix 2).

#### Health outcome categories

For the non-asthma outcomes of upper respiratory tract (URT) symptoms, cough, and wheeze (Table 1), we categorized the health outcomes as in the IOM report (IOM 2004). The URT symptom category included the broadest set of health outcomes, but nasal symptoms predominated.

For asthma outcomes, however, based on review of the original papers, we developed different outcome categories than were used in the IOM report (IOM 2004). Our asthma development category included ORs from studies that attempted to assess whether the *development* of asthma, as opposed to *presence* of asthma symptoms, was associated with dampness and mold; however, the associated time period for the asthma diagnosis or development ranged widely and there were few studies in this category.

Several studies were excluded from meta-analyses because of outcomes used (Appendix 2). For the asthma diagnosis and development categories, we excluded ORs from Wever-Hess et al. (2000) and Oie et al. (1999), with outcomes of asthma diagnosis or bronchial obstruction in children with an age less than 2, because it is not clear that asthma can be diagnosed before age 2. We excluded results from a single study performed in rural Kenya (Mohamad et al. 1995) because the living and health care conditions in this study population were distinctively different from those in other studies. The ORs from Pihronen et al (1996) were also excluded because they indicated the odds of having one or more of a diverse set of outcomes (asthma, hay fever, allergic rhinitis, or eczema).

#### Statistical methods

Some of the reviewed studies reported separate estimates for multiple outcomes within the same subjects in the same study. Because these findings within the same study may not be statistically "independent," ignoring this dependence within a meta-analysis might overestimate the number of truly independent inputs to the summary model, and thus overestimate the precision of the summary estimates produced. These meta-analyses use "random effect" models, which assume a single fixed mean effect (i.e., the association between the risk and the outcome in each model) across all studies, plus a random component that varies across studies or sub-studies. Random effect models can estimate any within-study correlations included in the meta-analysis, and

adjust the estimates produced as necessary. Such adjustment makes little difference in point estimates, but may increase the confidence interval for estimates. We used the SAS procedure PROC MIXED, which allows fixing the within-study variances (matrix  $R$  in SAS) while estimating between-study variance (matrix  $G$  in SAS) at a different level.

The odds ratios and 95% confidence intervals reported in each reviewed study were first transformed to the log scale. The transformed results were then combined using a random effect model (DerSimonian & Laird, 1986). Models were constructed both accounting for the correlation between multiple results *within* studies (“dependent sub-studies”), and ignoring such potential correlation (“independent sub-studies”).

The model for independent sub-studies was

$$y_{ij} \sim N(\beta_0 + \beta_{0ij}, \sigma_{ij}^2) \quad (1)$$

The model for dependent sub-studies was

$$y_{ij} \sim N(\beta_0 + \beta_{0i}, \sigma_{ij}^2) \quad (2)$$

where:

- $y_{ij}$  is the  $\ln$  OR in  $j$ th sub-study of  $i$ th study;
- $\beta_0$  is the fixed effect across all studies;
- $\beta_{0ij}$  is the random effect in the  $j$ th sub-study of the  $i$ th study;
- $\beta_{0ij} \sim N(0, \sigma^2)$ ;  $\sigma^2$  is the between-sub-study variance;
- $\beta_{0i}$  is the random effect in the  $i$ th study.  $\beta_{0i} \sim N(0, \sigma^{*2})$ ;
- $\sigma^{*2}$  is the between-study variance; and
- $\sigma_{ij}^2$  is the within-study variance, calculated from log confidence interval.

## RESULTS

Major results of the meta-analyses are summarized in Table 2. (Appendix 3 shows, as an example, ORs and CIs for the association of wheeze with dampness and mold in the original studies, and also from the summary estimates produced in the meta-analysis.) Central estimates of ORs ranged from 1.32 to 2.10, with most central estimates between 1.3 and 1.8. Confidence intervals (95%) excluded unity for 26 of 28 analyses, and in most cases the lower bound of the CI exceeded 1.2. In general, the two meta-analysis methods produced similar estimates for ORs and CIs. ORs for health effects in children were not consistently larger or smaller than corresponding ORs for adults. CIs tended to be smaller for analyses including both adults and children, presumably because of the larger numbers of studies. CIs for asthma development were broad, with lower bounds near unity, presumably because the analyses included data from only three studies.

**Table 2. Key results of the meta-analyses**

| Outcome                          | Subjects   | # of Studies | Odds Ratio<br>Random-Effect Model<br><b>Dependent</b><br>Sub-studies | Odds Ratio<br>Random-Effect Model<br><b>Independent</b><br>Sub-studies |
|----------------------------------|------------|--------------|--|--|
| Upper respiratory tract symptoms | <b>All</b> | <b>10</b>    | <b>1.53 (1.26-1.87)</b>  | <b>1.54 (1.33-1.78)</b>  |
|                                  | Adults     | 6            | 1.39 (1.12-1.71)   | 1.37 (1.17-1.59)   |
|                                  | Children   | 4            | 1.92 (1.08-3.41)   | 2.04 (1.41-2.96)   |
| Cough                            | <b>All</b> | <b>19</b>    | <b>1.77 (1.47-2.12)</b>  | <b>1.79 (1.57-2.03)</b>  |
|                                  | Adults     | 5            | 2.10 (1.27-3.47)   | 2.04 (1.55-2.68)   |
|                                  | Children   | 14           | 1.62 (1.35-1.94)   | 1.65 (1.44-1.88)   |
| Wheeze                           | <b>All</b> | <b>16</b>    | <b>1.81 (1.45-2.26)</b>  | <b>1.65 (1.48-1.83)</b>  |
|                                  | Adults     | 3            | 1.68 (1.14-2.49)   | 1.66 (1.42-1.95)   |
|                                  | Children   | 13           | 1.91 (1.42-2.57)   | 1.65 (1.43-1.90)   |
| Current asthma                   | <b>All</b> | <b>10</b>    | <b>1.51 (1.40-1.62)</b>  | <b>1.51 (1.41-1.61)</b>  |
|                                  | Adults     | 3            | 1.82 (1.28-2.59)   | 1.82 (1.52-2.19)   |
|                                  | Children   | 7            | 1.45 (1.33-1.58)   | 1.45 (1.34-1.57)   |
| Ever diagnosed asthma            | <b>All</b> | <b>8</b>     | <b>1.59 (1.26-2.00)</b>  | <b>1.70 (1.42-2.04)</b>  |
| Asthma development               | <b>All</b> | <b>3</b>     | <b>1.39 (0.69-2.80)</b>  | <b>1.32 (.98-1.77)</b>   |

## DISCUSSION

### Importance of building dampness

Based on the meta-analyses described in this report, building dampness and mold are associated with 30% to 80% increases<sup>3</sup> in a variety of health outcomes in a variety of populations. These associations are statistically significant – with 95% CIs excluding unity -- in almost all cases. The similar results obtained from two analysis methods suggest little problem with correlation of health outcomes within studies. Statistical associations do not prove that dampness and mold are causally related to the health outcomes. Building dampness itself is very unlikely to directly cause adverse health effects. However, the consistent and relatively strong associations of dampness with adverse health effects strongly suggest causation by dampness-related exposures. Building dampness may cause the building to become contaminated with microorganisms such

<sup>3</sup> The 30% to 80% increase in symptoms is an approximate estimate based on the central estimates of the ORs for the various health outcomes in Table 2. When the health outcome prevalence is below approximately 15%, which is typically the case for wheeze and asthma-related outcomes, the percentage increase in the outcome among the population experiencing the risk factor (e.g., dampness) is well estimated by 100%(1-OR). The central estimates of ORs for these health outcomes ranges from 1.32 to 1.91, implying a 33% to 91% increase in health outcome prevalence. However, when the prevalence of the outcome is substantially higher than 15%, as is often the case for URT symptoms and cough, this simple calculation overestimates the percentage increase in the outcome in the population with the risk factor. For example, assuming an outcome prevalence of 0.3 for URT symptoms and cough in the population with dampness, the OR in Table 2 of 1.79 for cough indicates a 53% increase in cough among the exposed population and the OR of 1.54 in Table 2 for URT symptoms indicates a 38% increase in URT symptoms among the exposed population.

as mold or bacteria, which might in-turn cause adverse health effects (IOM 2004). Building dampness could also cause increased emissions of some chemical pollutants from materials and surfaces (IOM 2004). Research has not yet determined the causal agent(s) (IOM 2004).

Implication of building dampness as a public health problem requires that the presence of building dampness increase health risks, and also that a substantial proportion of the population is exposed to dampness. Most available data indicate that at least 20% of homes have dampness problems or visible mold (IOM 2004). In addition, the adverse consequences of building dampness go beyond health effects and the related personal and economic costs. Dampness causes structural damage to buildings that is expensive to repair. Also, mold contamination resulting from building dampness often precipitates very expensive remediation efforts (Levin 2005).

Despite the current lack of proof that dampness or mold actually causes these health effects, available knowledge suggests that it is prudent to prevent building dampness and mold and to take corrective actions where such conditions occur (IOM 2004). Many of the preventive and corrective actions are straightforward. Examples include better training of those in the construction industry about the means of reducing dampness risks and instituting ongoing preventive maintenance programs to identify and quickly remedy roof and plumbing leaks or other causes of moisture accumulation or mold growth.

#### Limitations in this analysis

These meta-analyses used data only from studies referenced in the IOM's recent critical review (IOM 2004), and, thus, omitted more recently published studies. However, as research on dampness and mold has occurred for over two decades, it is unlikely that studies published in the last few years (i.e., since 2003) would substantially affect the outcomes of our meta-analyses.

Because our meta-analyses used only studies cited in the IOM's review, we have effectively relied on the IOM to select studies of suitable quality. All original studies were published in refereed archival journals, which is one indicator of study quality. The IOM did not precisely describe other study selection criteria, but in general their reviews consider only studies without significant evident methodological flaws, with control for major known confounding factors via the study design or method of data analysis, and with a statistical analysis of study data. Remaining errors from any confounding and bias in the reviewed studies may be reflected in results of the meta-analyses, although some of these, due to the combination of different studies, may cancel out and have a modest impact on results of the meta-analyses.

One potential source of bias pertains to the methods used to determine whether a building had dampness or mold. Most studies have relied on the occupants to report whether dampness or mold is present in their home. It is possible that homeowners with respiratory health problems would be more aware of, and thus, more likely to report dampness and mold than homeowners without such health problems. If true, this reporting bias would lead to overestimated ORs in the original studies and corresponding overestimated ORs from our meta-analyses. On the other hand, as homeowners within each study would report dampness or mold in a relatively unstandardized way, the resulting random error in assessment could result in what is called "nondifferential exposure misclassification," leading to underestimated ORs in those studies.

Alternately, some studies have relied on trained surveyors who inspected buildings for signs of dampness and mold. Surveyors would have used standardized methods of assessment for dampness or mold within each study, thus reducing that source of inaccuracy. Surveyors, however, are likely to have missed indicators of dampness and mold that were not present or evident during their brief survey, leading to random errors in exposure assessment and consequent underestimates of any true risk. In general, both types of studies have found increased risks of respiratory health effects among occupants of homes with dampness and molds. Unfortunately, we do not have a sufficient number of studies with surveyor-assessed dampness and mold to enable separate meta-analyses.

Reviews and meta-analyses are also subject to publication bias – the overestimation of summary estimates of association that can occur because studies with positive findings are published more often (IOM 2004, pg 20) and more quickly than studies that failed to find significant associations. Publication bias would bias the results of our meta-analyses upward; i.e., estimated ORs based on all published studies would exceed true central estimates based on all performed studies. While there are statistical tools available that enable one to check for evidence of publication bias, it remains difficult to quantify the extent of publication bias or to make corrections in the resulting central estimates of ORs.

It is important to note that the confidence intervals associated with our central estimates of ORs reflect only the probabilistic or chance uncertainties. The full uncertainties in the magnitudes of increased health risks are likely to be larger because they would also include the potential uncontrolled confounding and bias noted above.

#### Asthma development -- comparison to findings of IOM

The IOM Committee found limited or suggestive evidence of an association between building dampness and asthma development, and inadequate or insufficient evidence to determine whether an association exists between mold and asthma development. These statements are consistent with the results of our meta-analysis. We calculated ORs of 1.32 and 1.39 for asthma development if the home had dampness or mold; however, neither CI excluded unity. Also, our meta analysis for asthma development was based on only three studies and the definitions for asthma development used in these three studies were variable.

## **CONCLUSIONS**

Based on our meta-analyses, building dampness and mold are associated with 30% to 80% increases in a variety of respiratory and asthma-related health outcomes and the associations are statistically significant in nearly all cases. Given what is known today, it would be prudent to avoid building dampness and mold problems and to take corrective actions where such problems occur.

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## Appendix 1. Description of studies included in the meta-analyses.

**Table A1.1 Studies with upper respiratory tract symptoms**

| Subjects       | Author      | Year                | Risk Factor                                     | Symptomx                         |
|----------------|-------------|---------------------|---|----------------------------------|
| adults         | Engvall     | 2002                | moldy odor & water leakage in preceding 5 years | nasal                            |
|                | Koskinen    | 1999                | surveyor assessed moisture                      | rhinitis                         |
|                |             |                     | mold  | sinusitis                        |
|                | Wan         | 1999                | flood   | rhinitis                         |
|                |             |                     | mold  | sinusitis                        |
| Wieslander     | 1999        | damp concrete floor | nasal congestion or runny nose                  |                                  |
| men            | Brunekreef  | 1992                | damp stains or mold growth in last 2 years      | irritated, stuffy, or runny nose |
| women          |             |                     |   |                                  |
| children       | Brunekreef  | 1989                | damp ever                                       | allergy                          |
|                |             |                     | mold ever                                       |                                  |
|                | Jaakkola    | 1993                | mold odor in past year                          | hay fever                        |
|                |             |                     | water damage >1 year ago                        | nasal congestion                 |
|                | Koskinen    | 1999                | surveyor assessed moisture                      | nasal excretion                  |
|                |             |                     |   | rhinitis                         |
| Zacharasiewicz | 2000        | damp                | nasal congestion                                |                                  |
| Kilpeläinen    | 2001        | visible mold        | nasal excretion                                 |                                  |
| students       | Kilpeläinen | 2001                | visible mold or damp stains or water damage     | allergic rhinitis                |

**Table A1.2 Studies with cough as an outcome**

| Subjects  | Author  | Year     | Risk                                  | Health outcome                          |                  |
|---|---|----------|---------------------------------------|---|------------------|
| adults  | Engvall   | 2001     | moldy odor & major water leakage      | cough                                   |                  |
|   | Engvall   | 2001     | moldy odor & signs of hi humidity     | cough                                   |                  |
|   | Gunnbjörnsdottir                                | 2003     | water damage or mold                  | long-term cough                         |                  |
|   | Koskinen  | 1999     | moisture                              | cough w/ phlegm                         |                  |
|   | Koskinen  | 1999     | moisture                              | cough w/o phlegm                        |                  |
|   | Koskinen  | 1999     | moisture                              | night cough                             |                  |
|   | Koskinen  | 1999     | mold                                  | cough w/ phlegm                         |                  |
|   | Koskinen  | 1999     | mold                                  | cough w/o phlegm                        |                  |
|   | Koskinen  | 1999     | mold                                  | night cough                             |                  |
| men   | Pirhonen  | 1996     | mold or damp                          | cough                                   |                  |
| men   | Brunekreef                                      | 1992     | damp stains or mold growth last 2 yrs | cough                                   |                  |
| women   | Waegemaekers                                    | 1989     | damp                                  | cough                                   |                  |
| women   | Brunekreef                                      | 1992     | damp stains or mold growth last 2 yrs | cough                                   |                  |
|   | Waegemaekers                                    | 1989     | damp                                  | cough                                   |                  |
| children  | Andriessen                                      | 1998     | moisture stains                       | cough                                   |                  |
|   | Andriessen                                      | 1998     | mold                                  | cough                                   |                  |
|   | Austin  | 1997     | damp                                  | cough                                   |                  |
|   | Austin  | 1997     | mold                                  | cough                                   |                  |
|   | Brunekreef                                      | 1989     | damp ever                             | cough                                   |                  |
|   | Brunekreef                                      | 1989     | mold ever                             | cough                                   |                  |
|   | Dales   | 1991     | flood                                 | cough                                   |                  |
|   | Dales   | 1991     | moisture                              | cough                                   |                  |
|   | Dales   | 1991     | Mold site                             | cough                                   |                  |
|   | Dales   | 1991     | Mold sites                            | cough                                   |                  |
|   | Dales   | 1991     | mold or damp                          | cough                                   |                  |
|   | Dales   | 1999     | mold or mildew                        | night cough or wheeze                   |                  |
|   | Dijkstra  | 1990     | mold & damp                           | cough                                   |                  |
|   | Dijkstra  | 1990     | mold or damp                          | cough                                   |                  |
|   | Jaakkola  | 1993     | mold odor past yr                     | persistent cough                        |                  |
|   | Jaakkola  | 1993     | water damage >1 yr ago                | persistent cough                        |                  |
|   | Jedrychowski                                    | 1998     | mold or damp                          | cough                                   |                  |
|   | Koskinen  | 1999     | moisture                              | cough w/ phlegm                         |                  |
|   | Koskinen  | 1999     | moisture                              | cough w/o phlegm                        |                  |
|   | Koskinen  | 1999b    | moisture                              | night cough                             |                  |
|   | Verhoeff  | 1995     | damp                                  | cough                                   |                  |
|   | Verhoeff  | 1995     | mold                                  | cough                                   |                  |
|   | Waegemaekers                                    | 1989     | damp                                  | day or night cough                      |                  |
|   | Waegemaekers                                    | 1989     | damp                                  | morning cough                           |                  |
|   | infants w/ asthmatic sibling                    | Gent     | 2002                                  | water leaks                             | cough            |
|   | infants w/ asthmatic sibling + asthmatic mother | Belanger | 2003                                  | persistent mold or mildew previous year | persistent cough |
| infants w/ asthmatic sibling + non-asthmatic mother |   |          |                                       |   |                  |
| adolescents   | Nicolai   | 1998     | past or present damp                  | cough                                   |                  |

**Table A1.3 Studies with wheeze as an outcome.**

| Subjects  | Author           | Year         | Risk  | Outcome           |
|---|------------------|--------------|---|-------------------|
| adults  | Gunnbjörnsdottir | 2003         | water damage or mold                                      | wheeze            |
|   | Norbäck          | 1999         | >1 signs of dampness                                      | wheeze            |
|   |                  |              | damp floor  |                   |
|   |                  |              | visible mold on indoor surfaces                           |                   |
|   |                  |              | moldy odor  |                   |
| water damage or flood                               |                  |              |   |                   |
| men   | Brunekreef       | 1992         | damp stains or mold growth in last 2 yrs                  | wheeze            |
|   | Waegemaekers     | 1989         | damp  | wheeze            |
| women   | Brunekreef       | 1992         | damp stains or mold growth in last 2 yrs                  | wheeze            |
|   | Waegemaekers     | 1989         | damp  | wheeze            |
| children  | Brunekreef       | 1989         | damp ever   | wheeze            |
|   |                  | 1989         | molds ever  | wheeze            |
|   | Dales            | 1991         | flood   | wheeze            |
|   |                  |              | moisture  |                   |
|   |                  |              | mold site   |                   |
|   |                  |              | mold sites  |                   |
|   | Dijkstra         | 1990         | mold & damp   | wheeze            |
|   |                  |              | mold or damp  |                   |
|   | Jaakkola         | 1993         | mold odor in past year                                    | persistent wheeze |
|   |                  |              | water damage >1 yr ago                                    |                   |
|   | Jedrychowski     | 1998         | mold or damp  | wheeze            |
|   | Maier            | 1997         | basement water  | wheeze            |
|   |                  |              | mold  |                   |
|   |                  |              | mold, water damage, basement water, or water condensation |                   |
|   |                  |              | water condensation  |                   |
| water damage  |                  |              |   |                   |
| Slezak  | 1998             | mold or damp | wheeze  |                   |
| Strachan  | 1990             | mold         | wheeze  |                   |
| Taskinen  | 1999             | damp         | wheeze  |                   |
| Waegemaekers  | 1989             | damp         | wheeze  |                   |
| infants w/ asthmatic sibling                        | Gent             | 2002         | Water leaks   | wheeze            |
| infants w/ asthmatic sibling + asthmatic mother     | Belanger         | 2003         | persistent mold or mildew in previous year                | wheeze            |
| infants w/ asthmatic sibling, + nonasthmatic mother |                  |              |   |                   |
| adolescent  | Nicolai          | 1998         | damp  | wheeze            |
|   |                  |              | damp, adjusted for mite allergen concentration            |                   |

**Table A1.4 Studies with asthma diagnosis as an outcome.**

| Subjects          | Author       | Year | Risk                              | Outcome description*  |
|-------------------|--------------|------|-----------------------------------|---|
| adults            | Hu           | 1997 | indoor damp                       | Dr. dx asthma   |
|                   |              |      | visible mold                      |   |
|                   |              |      | water leaks                       |   |
|                   | Norbäck      | 1999 | >1 damp                           | current asthma defined as combination of bronchial hyper-responsiveness and at least one asthma sx in last year |
|                   |              |      | damp floor                        |   |
|                   |              |      | moldy odor                        |   |
| visible mold      |              |      |                                   |   |
|                   |              |      | water damage or flood             |   |
| men               | Brunekreef   | 1992 | damp or mold                      | Dr. dx. asthma  |
| men               | Waegemaekers | 1989 | damp                              | Dr. dx. asthma or dyspnea   |
| women             | Brunekreef   | 1992 | damp or mold                      | Dr. dx. asthma  |
| women             | Waegemaekers | 1989 | damp                              | Dr. dx asthma or dyspnea  |
| children          | Jedrychowski | 1998 | mold or damp                      | Dr. dx. asthma  |
|                   | Rönmark      | 1999 | damp home                         | Dr. dx atopic asthma  |
|                   |              |      |                                   | Dr. dx atopic or non-atopic asthma  |
|                   |              |      |                                   | Dr. dx non-atopic asthma  |
|                   | Slezak       | 1998 | damp or mold                      | Dr. or nurse dx asthma  |
| Waegemaekers      | 1989         | damp | Dr. dx asthma or dyspnea          |   |
| children & adults | Williamson   | 1997 | damp                              | Dr. dx asthma   |
|                   |              |      | damp or condensation current home |   |
|                   |              |      | damp previous home                |   |
|                   |              |      | mold                              |   |
|                   |              |      | severe damp                       |   |
|                   |              |      | significant mold                  |   |

Abbreviations: sx = symptom; dx = diagnosis

**Table A1.5 Studies with current asthma as an outcome.**

| Subjects             | Author      | Year      | Risk                                      | Outcome description*  |  |
|----------------------|-------------|-----------|---|---|--|
| adults               | Hu          | 1997      | indoor damp                               | Dr. dx asthma + sx or medication in past year   |  |
|                      |             |           | visible mold                              |   |  |
|                      |             |           | water leaks                               |   |  |
|                      | Norbäck     | 1999      | >1 damp                                   | current asthma defined as combination of bronchial hyper-responsiveness and at least one asthma sx in last year |  |
|                      |             |           | damp floor                                |   |  |
| moldy odor           |             |           |   |   |  |
| visible mold         |             |           |   |   |  |
|                      |             |           | water damage or flood                     |   |  |
| children             | Brunekreef  | 1989      | damp ever                                 | Dr. dx asthma in past year  |  |
|                      |             |           | mold                                      |   |  |
|                      | Dales       | 1991      | flood                                     | Current asthma confirmed by Dr.   |  |
|                      |             |           | moisture                                  |   |  |
|                      |             |           | mold                                      |   |  |
|                      |             |           | mold 2                                    |   |  |
|                      |             |           |   | mold or damp  |  |
|                      | Dekker      | 1991      | damp or visible mold                      | Dr. dx asthma + current sx  |  |
|                      | Jaakkola    | 1993      | any damp indicator ever                   | current Dr. dx asthma   |  |
|                      |             |           | moisture > 1yr ago                        |   |  |
| moisture past yr     |             |           |   |   |  |
| mold odor past yr    |             |           |   |   |  |
| visible mold past yr |             |           |   |   |  |
|                      |             |           | water damage >1 yr ago                    |   |  |
| Taskinen             | 1999        | damp home | Dr. dx asthma + sx                        |   |  |
| Yang                 | 1997        | damp home | current Dr. diagnosed asthma              |   |  |
| students             | Kilpeläinen | 2001      | visible mold                              | current Dr. dx asthma   |  |
|                      |             |           | visible mold, damp stains or water damage |   |  |
| adolescent           | Nicolai     | 1998      | past or present damp                      | >5 asthma attacks previous yr   |  |

Abbreviations: sx = symptom; dx = diagnosis

**Table A1.6 , Studies with asthma development as an outcome.**

| Subjects | Author   | Year                         | Risk                         | Outcome description*             |
|----------|----------|------------------------------|------------------------------|----------------------------------|
| adults   | Jaakkola | 2002                         | damp stains or paint peeling | newly Dr. dx asthma in past year |
|          |          |                              | visible mold or odor         |                                  |
|          |          |                              | water damage                 |                                  |
|          | Thorn    | 2001                         | damp                         | Dr. dx asthma since age > 16     |
|          |          |                              | damp or visible mold         |                                  |
|          |          |                              | visible mold                 |                                  |
| Yang     | 1998     | damp or mold or water damage | first-time Dr. dx asthma     |                                  |

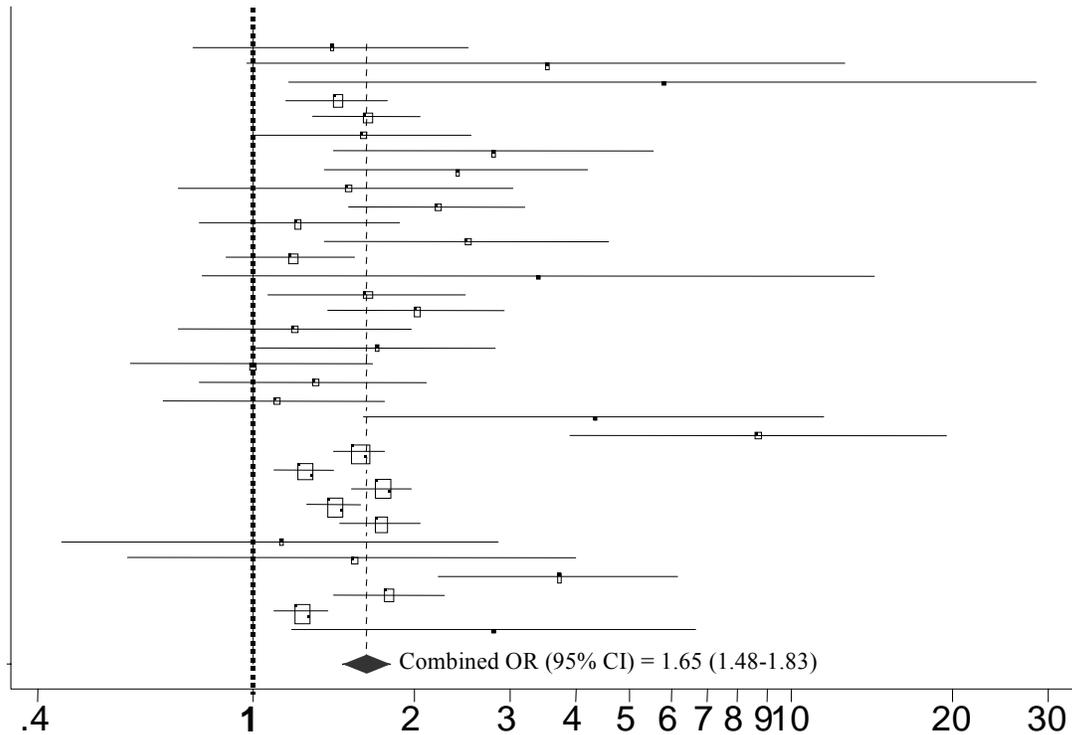
Abbreviations: dx = diagnosis

## Appendix 2. Excluded Studies

| Author         | Year | Excluded from                               | Reason for exclusion*   |
|----------------|------|---|---|
| Belanger       | 2003 | cough, wheeze                               | excluded measured conc of microbial agent   |
| Dales          | 1999 | upper respiratory sx                        | some sx not upper respiratory sx  |
| Dijkstra       | 1990 | asthma sx                                   | no clear diagnosis of asthma  |
| Engvall        | 2002 | upper respiratory sx                        | excluded throat sx  |
| Gent           | 2002 | cough, wheeze                               | excluded measured conc. of microbial agent; or excluded humidifier as risk factor                         |
| Infante-Rivard | 1993 | newly diagnosed                             | excluded humidifier as risk factor  |
| Jaakkola       | 2002 | newly diagnosed asthma                      | Excluded studies of risks at workplaces   |
| Kilpeläinen    | 2001 | common cold>4/yr                            | excluded cold sx  |
| Koskinen       | 1999 | sore throat                                 | excluded throat sx  |
| Mohamed        | 1995 | asthma sx                                   | socio-economic status and housing conditions of the Kenyan subjects was atypical of that in other studies |
| Nafstad        | 1998 | bronchial obstr                             | age < 2 too early for asthma diagnosis  |
| Park           | 2001 | wheeze                                      | excluded measured conc. of microbial agent  |
| Pirhonen       | 1996 | asthma sx                                   | ORs are for atopy and should not be used for asthma sx  |
|                |      | dry or sore throat                          | excluded throat sx  |
| Rylander       | 1998 | cough, wheeze                               | excluded risk factors at school   |
| Rylander       | 2000 | cold, sore throat                           | excluded cold sx  |
|                |      |   | humidity is not used in our study as an indicator of a dampness or mold                                   |
|                |      |   | excluded throat sx  |
| Taskinen       | 1999 | asthma sx, cough, wheeze                    | excluded studies of risks of dampness at school   |
| Thorn          | 1998 | cough, UR                                   | excluded measured conc. of microbial agent  |
| Waegemaekers   | 1989 | wheeze includes shortness of breath, asthma | excluded measured conc. of microbial agent  |
| Wever-Hess     | 2000 | asthma                                      | age < 2 too early for asthma diagnosis  |
| Wieslander     | 1999 | UR  | excluded eye sx   |
| Yazicioglu     | 1998 | asthma sx                                   | excluded self-reported high humidity as risk factor   |
| Zock           | 2002 | wheeze                                      | meta-analysis itself  |
| Øie            | 1999 | bronchial obstruction                       | age < 2 too early for asthma diagnosis  |

Abbreviations: sx= symptom

### Appendix 3. Example of original data and results of a meta- analysis.



### OR for wheeze, random effects model for independent studies

Figure A3-1. Odds ratios and confidence intervals for wheeze from original studies and from a meta-analysis performed using the random effects model and assuming independent sub-studies. The width of the boxes (some so small they appear as points) is proportional to the precision (inverse of variance) of the study and the ends of the horizontal lines represent lower and upper 95% confidence limits. The dark vertical line is located at an odds ratio of unity which corresponds to no increased risk of wheeze, while nearly all the reported odds ratios are greater than unity indicating an increase in risk with dampness and mold. The central estimate from the meta-analysis is indicated by the light dashed vertical line and the left- and right-side points of the diamond at the bottom (labeled combined) of the figure indicate the lower and upper 95% confidence limits from the meta-analysis.