eISSN: 2233-6567

Systemic Review

Fatigue and exposure to mold and/or dampness: A systematic review of the literature from 2011-2018

Ming Dooley 1,* , and Scott W. McMahon 2

- ¹ Holistic Resonance Center, San Diego, California, USA
- ² Whole World Health Care, Roswell, New Mexico, USA
- *Correspondence: ming@holisticresonancecenter.com

Received: March 31, 2025 Accepted: June 17, 2025 Recommended by: Prof. Yoon-Hyeong Choi

Abstract

This review expands upon prior work, which established that 112 out of 114 (98.2%) epidemiological articles published between 2011 and 2018 supported an association between exposure to elevated indoor mold/dampness and various single/multi-system health symptoms. Focusing on fatigue, our review rigorously examined these studies for statistically significant associations with mold and dampness exposure. We analyzed six articles involving a collective cohort from five cross-sectional studies with 40,933 participants, and a case-control study comprising 95 cases and 110 controls. We introduced a six-point ranking scale to assess the evidence, categorizing the studies from very low to very high support based on their methodological rigor and findings. Our evaluation revealed one study with very low support, one with moderate support, three with moderately high support, and one with very high support. Two studies were considered reference only. Our systematic review supports the assertion that fatigue is associated with exposure to indoor mold and dampness, highlighting the need for enhanced awareness and interventions in affected environments.

Keywords: Mold, Fatigue, Chronic Inflammatory Response Syndrome (CIRS), Chronic Fatigue Syndrome, Innate Immune System, Sick Building Syndrome

Introduction

A review of the literature from 2011-2018

Currently, there are more and more claims that mold and dampness can cause adverse human health effects in body systems besides the respiratory system. Nevertheless, many medical professionals and landlords are not aware of this data. The purpose of this review is to look for and evaluate the quality of the evidence in the published literature supporting the association of mold and dampness with fatigue.

Background

Respiratory system adverse health effects

Over the past 50 years, there has been increasing evidence supporting associations between exposure to dampness and microbes with respiratory health. However, the impact on other body systems has been less studied. Whether or not exposure to damp indoor environments is causative of extra-respiratory adverse human health effects is an ongoing area of controversy. Water-damaged buildings (WDB) are defined as those buildings that have incurred water intrusion that was not resolved within 24 to 48 hours. While there are few prospective experimental studies that could confirm risk, there is a robust epidemiologic literature examining the association of a diversity of symptoms acquired following chronic exposure to WDB as reviewed in Dooley and McMahon [1].

There is widespread agreement that damp indoor spaces are associated with an increase in respiratory and allergic health problems since the 2004 publication of the Health Committee of the Institute of Medicine (IOM) [2]. The 2009 World Health Organization's (WHO) report [3] concluded that the level of evidence was almost adequate to establish causality for asthma exacerbation as well as concurring with the 2004 Damp Indoor Spaces report [2] findings that sufficient evidence of an association with upper respiratory tract symptoms, cough and wheeze existed. Between 2009 and 2018, sufficient evidence of an association between qualitative mold exposure and asthma development was established as additional data from meta-analyses and reviews was published investigating the increased risk of asthma or rhinitis associated with exposure to mold. Taking it one step further, Caillaud et al. [4], concluded that in children there were both sufficient

evidence of a causal relationship for asthma development and exacerbation as well as sufficient evidence of an association with allergic rhinitis. This was the first time that a meta-analysis concluded causality.

Adverse health effects associated with other systems

Although the certainty of an association between mold exposure and respiratory symptoms has increased, broader health effects from exposure have less data. Beginning in 2008, the Government Accountability Office of the United States (GAO), citing data derived only from Federal guidance documents, published a table reporting the potential adverse health effects of exposure to indoor mold [5]. While not listed in the table because they were only cited in five or fewer guidance documents, the report also referenced fatigue, fever, dizziness, and gastrointestinal tract problems as adverse health effects resulting from exposure to indoor mold [5]. The GAO report was not intended to be comprehensive as it only reviewed governmental "fact sheets" and 20 mold review articles. In 2010, Shoemaker et al. [6] wrote a more comprehensive review that cited 632 papers.

From 1997 on, Shoemaker noted that chronic exposure to the interior of WDB triggered a syndrome in many patients. Thirty-seven symptoms were identified (thirty-five out of thirty-seven symptoms were statistically significant) as differentiating cases from controls in a retrospective study of one thousand consecutive patients seen at a single medical clinic specializing in diagnosis and treatment of patients made ill by exposure to WDB [7]. The thirty-seven symptoms were fatigue, weakness, aches, cramps, unusual pain (including ice pick pain and lightning bolt pain), joint pain, morning stiffness, headache, skin sensitivity, light sensitivity, red eyes, blurred vision, tearing, sinus problems, cough, shortness of breath, abdominal pain, diarrhea, numbness, tingling, metallic taste, vertigo, memory loss, decreased focus/concentration, confusion, decreased assimilation of new knowledge, decreased word finding ability, disorientation, excessive thirst, frequent urination, static shocks, night sweats, mood swings, temperature regulation and appetite swings [7].

Chronic inflammatory response syndrome - Dysregulation of the innate immune system

The mechanism of illness for this syndrome was declared to be chronic innate immune activation leading to immune system dysregulation [8]. This was deduced as a result of multiple cohorts of patients having abnormalities in no fewer than 5 innate immune and endocrine system markers [9]. The hypothesis that repeated quantified doses of both toxic and nontoxic mold stimuli would cause innate immune activation with concomitant neural effects and cognitive, emotional, and behavioral symptoms was recently tested in a mouse model. It confirmed that innate immune system activation occurred as a direct result of toxigenic and nontoxigenic indoor microbial exposure and documented cognitive and behavioral impairments [10]. Chronic innate immune system activation, as evidenced by elevated cytokine levels (TGF-beta 1, MMP-9 and/or C4a) paired with a Human Leukocyte Antigen (HLA) predisposing risk factor in antigen presentation eventually leads to innate immune system dysregulation evidenced by low levels of α -MSH (melanocyte stimulating hormone) and VIP (vasoactive intestinal polypeptide). The name of Chronic Inflammatory Response Syndrome (CIRS) was given to this multi-symptom multi-system illness in 2010 [11].

Materials and Methods

Identification of articles for this review

In a previous publication, we performed a comprehensive review of the literature and found that 112 of 114 epidemiological articles (98.2%) identified through our search criteria linked chronic exposure to elevated indoor microbial growth/dampness with adverse human health effects [1]. That review searched published data to answer the questions of whether or not there was adequate evidence supporting causation of multi-system illnesses from exposure to the interior of WDB and what organ systems showed associations of adverse effects following exposure(s). Statistically significant results with either Odds Ratio (OR) or Relative Risk (RR) \geq 2 were documented in 79 of these articles [1]. For the present analysis, we conducted a focused subset review targeting studies from our original dataset that specifically reported statistically significant associations with fatigue.

In order to provide more evidence for the association between microbial exposure and chronic fatigue, this review builds upon our previous report. The purpose of this study is to further evaluate the references in the published literature that document statistically significant associations between fatigue and exposure to elevated indoor mold and/or dampness.

Study selection

The previous search yielded 1396 articles based on the following a priori eligibility criteria: the study (i) was an original study, (ii) was a cohort/longitudinal, cross-sectional, case/control, or case series/case history, (iii) reported on the relationship between mold or dampness with any adverse human health effect, without regard to method for quantifying exposure, and (iv) was published in the peer-reviewed literature between 2011 and November of 2018 [1]. One hundred fourteen studies met these search parameters. This included two articles translated using Google Translate [12, 13], as well as one abstract from an article published in Chinese [14], as the abstract provided detailed data with statistically significant

Page2 / 11 http://eaht.org

results [1]. The sequential approach to the literature search is found in Figure 1 and includes the additional step of searching and compiling the results from the previous data extraction worksheet for statistically significant references to fatigue.

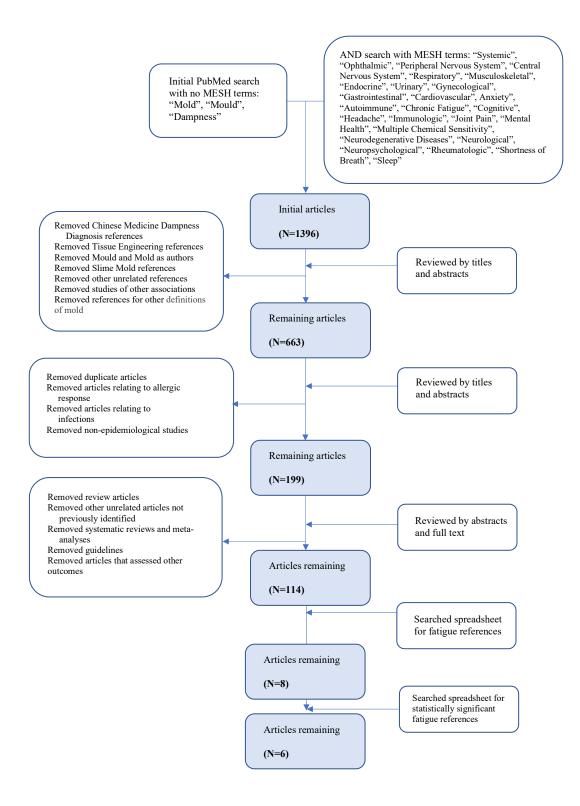


Figure 1. Sequential approach to literature search

Of the 114 articles that met search criteria, six articles (5%) met the criteria for statistically significant results associated with fatigue. Two additional studies, Tuuminen and Rinne [15], and Brewer et al. [16], did not document statistically significant associations with fatigue; however, both studies reference chronic fatigue syndrome as associated with exposure to microbial growth, for a total of eight articles. That literature review evaluated these eight scholarly journal articles published between 2011-2018 to determine the level of support in the published literature for associations between fatigue and chronic exposure to mold and/or dampness. Studies are reviewed according to support rankings, excluding the two studies which did not document statistically significant associations and were considered Reference Only.

Overview of articles documented statistical significance

Articles were classified based on study design, that is, the level of evidence on the evidence pyramid [17] as described by the evidence hierarchy in Table 1.

Table 1. Levels of evidence.

Level on the Evidence Pyramid	Study Design
Level I	Systematic review or meta-analysis of randomized controlled trials (RCT)
Level II	A well-designed RCT
Level III	Controlled trial without randomization
Level IV	Single nonexperimental study
Level V	Systematic review of descriptive and qualitative studies
Level VI	Single descriptive or qualitative study
Level VII	Opinion of authorities and/or reports of expert committees

Of the six articles that documented statistical significance, five studies were cross-sectional, and one, Thomas et al. [18], was a case-control study; therefore, all else being equal, they rank at Level IV on the evidence pyramid. All articles included calculations with statistically significant results with p<0.05 and a 95% confidence level. The combined number of participants in the cross-sectional studies was 40,933, and the case-control study included 95 cases and 110 controls. Three of the studies were from Europe, two from China, and one from the United States, supporting similar findings across the globe. The characteristics of the studies are listed in Table 2, and the relevant data for these six studies are listed in Table 3.

Method for study ranking by level of support

To ensure a rigorous evaluation of the studies, we developed a transparent, replicable six-point scoring system grounded in core epidemiologic principles. While standardized quality assessment tools such as the Newcastle-Ottawa Scale (NOS) and GRADE were reviewed, they were found unsuitable for the context of environmental exposure and symptom-level outcomes like fatigue. Our custom framework emphasizes objective exposure measurement, physician-documented outcomes, statistical strength, and sample size, and was applied to assess the relevance and strength of each study's support for an association between mold exposure and fatigue.

This approach is conceptually aligned with weight-of-evidence (WOE) frameworks developed in environmental health literature, such as Chapman et al. [19], which proposed a scoring and logic-based matrix to evaluate sediment quality and ecological risk using multiple lines of evidence. Like their model, our framework integrates quantitative strength-of-association metrics with qualitative indicators of exposure validity and outcome assessment to provide a structured, transparent synthesis across heterogeneous study designs.

Criteria and point assignment

Physician Assessment (2 points): Recognized as a high-quality measure due to the reliability of professional medical diagnosis, studies with physician-documented assessments of participants were allocated two points.

Environmental Testing (2 points): Given the importance of objective measurement in establishing exposure levels, studies conducting laboratory testing of the environment received two points.

Statistical Significance (1 point): Studies presenting statistically significant results with direct associations to fatigue were given one point to acknowledge the importance of robust statistical analysis.

High Odds Ratio (OR \geq 1.5) (1 point): Reflecting a strong association, studies reporting an OR \geq 1.5 were awarded one point. Odds ratios were rounded to the nearest whole tenth.

Multiple Significant References to Fatigue (1 point): To appreciate replication within the literature, studies with more than one statistically significant reference to fatigue received one point.

Large Sample Size (>1000 participants) (1 point): Larger sample size is more supportive for the generalizability of findings; thus, studies with more than 1000 participants were assigned one point.

Page4 / 11 http://eaht.org

Table 2. Characteristics of 6 articles referencing fatigue.

Author/Date/Country	Title	Type of Study	# of Participants ^a	# of Cases	# of Controls	OR /RR ≥1.5	# of associations
Thomas et al., 2012, USA [18]	Comparison of work-related symptoms and visual contrast sensitivity between employees at a severely water-damaged school and a school without significant water damage	Case/Control	•	95	110	Yes	1
Zhang et al., 2018, China [22]	Dampness and mold in homes across China: Associations with rhinitis, ocular, throat and dermal symptoms, headache and fatigue among adults	Cross- sectional	36,541			Yes	13
Lu et al. 2018, Romania [20]	Evidence from SINPHONIE project: Impact of home environmental exposures on respiratory health among school-age children in Romania	Cross- sectional	280			Yes	2 ^b
Roussel et al., 2012, France [24]	Microbiological evaluation of ten French archives and link to occupational symptoms	Cross- sectional	144			Yes	1
Lu et al., 2016, China [23]	Outdoor air pollution, meteorological conditions and indoor factors in dwellings in relation to sick building syndrome (SBS) among adults in China	Cross- sectional	3,485			Yes	4
Karvala et al., 2011, Finland [21]	Prolonged exposure to damp and moldy workplaces and new-onset asthma	Cross- sectional	483				
Total			40,933	95	110	5	

^a Excludes number of cases and controls; ^b These statistically significant associations include fatigue with a constellation of other symptoms.

Table 3. Assessment methods and statistically significant associations.

Study and Country	Method for Environmental Assessment	Method for Health Assessment	Statistically Significant Associations	OR	Statistical Analysis Type
Thomas et al., 2012, USA [18]	Observation and assessment with spore trap, bulk, swab and Environmental Relative Moldiness Index (ERMI)	Self-reported by participant, Visual Contrast Sensitivity (VCS) Testing by Physician Interviews with Physician	Unusual tiredness or fatigue	1.78	Chi square or Fisher's exact tests were used to compare the prevalence of symptoms,
Zhang et al., 2018, China [22]	Self-reported	Self-reported	Fatigue associated with: Mold spots Damp stains Damp bed clothing Water Damage in past years	1.63 1.66 1.41 1.55	Multilevel logistic regression

Karvala et al., 2011, Finland [21]	analysis/technical reports		the unexposed patients (p <0.0004)	OR	
	80% with verifying microbial	Self-reported	Symptom scores for fatigue was lower for	No.	
			Having 2 mold variables Having >2 mold variables	1.6 2.15	
Lu et al., 2016, China [23]			Mold/floor or ceiling damp	1.6	
L 1 2016 Chi [22]			condensation	1.6	regression models
	Self-reported	Self-reported	Fatigue associated with: windowpane	1.73	Multiple logistic
Roussel et al., 2012, France [24]	Air samples and Electrostatic Dust Samples, Quantitative real-time PCR	Self-reported	Handling moldy documents was associated with fatigue	2.9	Logistic regression models
	Air comples and Electrostatic Duct	Salf rapartad	bedroom and Flu-like Symptoms	2.9	Logistic regression
24 et al. 2010, Romana [20]			Dampness/visible mold in children's	4.72	
Lu et al. 2018, Romania [20]			months and Flu-like Symptoms		logistic regression,
	Self-reported	Self-reported	Visible mold/water leakage in past 12	2.09	Firth's corrected
			Dampness/mold index ≥2	2.15	
			Dampness/mold index 2	1.69	
			Dampness/mold index 1	1.41	
			Perception of humid air weekly	3.14	
			Perception of humid air sometimes	1.32	
			Mold odor - weekly	2.27	
			Mold odor -sometimes	1.56	
			Windowpane condensation in winter	1.45	
			Water damage in last 12 months	1.63	

p < 0.05 with a 95% confidence interval

Table 4. Ranking points assigned.

Author/Date/Country	Statistically significant results for Direct Associations with Fatigue Title	Statistically Significant OR ≥ 1.5	>1 Statistically Significant Reference for Fatigue	Physician Assessment of Participants	Environmental Assessment by Testing	Number of Participants >1000	Total
Thomas et al., 2012, USA [18]	1	1		2	2		6
Zhang et al., 2018, China [22]	1	1	1			1	4
Lu et al. 2018, Romania [20]			1				1
Roussel et al., 2012, France [24]	1	1			2		4
Lu et al., 2016, China [23]	1	1	1			1	4
Karvala et al., 2011, Finland [21]	1			2			3

Page6 / 11

A meta-analysis was not conducted due to significant heterogeneity in study design, exposure assessment methods, and outcome definitions across the included studies, which precluded quantitative synthesis.

Total points and support levels

The sum of the points determined the study's level of support for the association between mold exposure and fatigue:

Very Low Support (1 point)

Low Support (2 points)

Moderate Support (3 points)

Moderately High Support (4 points)

High Support (5 points)

Very High Support (6 or more points)

Each study could receive a maximum of 8 points. The rankings reflect a cumulative measure of quality, with higher total points indicating stronger and more reliable evidence.

Ranking examples for clarification

To illustrate, consider two hypothetical studies:

Study A conducted both physician assessment and environmental testing, reported statistically significant results with an $OR \ge 1.5$ for the association with fatigue, and involved over 1000 participants. This study would score 6 points, categorizing it as providing Very High Support

Study B only included a physician assessment, with statistically significant results but with an OR < 1.5, and a sample size of fewer than 1000 participants. This study would score 3 points, falling into the Moderate Support category.

This ranking system ensured that the studies contributing to our understanding of the relationship between mold exposure and fatigue are evaluated on a consistent and reliable basis, reflecting their overall quality and relevance to the research question.

Results

Individual rankings and totals are shown in Table 4 (the front page).

The number of the studies for each of the rankings are shown in Table 5:

Table 5. Support rankings.

Support Ranking	Number of Studies
Reference Only	2
Very Low Support	1
Low Support	0
Moderate Support	1
Moderately High Support	3
Very High Support	1

Discussion

Reference Only Studies

Both Reference Only studies presented case reports. Tuuminen and Rinne [15] presented two cohorts. The first cohort described nine people who moved into a new house infested with pathogenic mold, while the second assessed thirty teachers and fifty students in a mold-infested school. References to fatigue as an associated symptom were present in this publication. Of note, if one calculated an odds ratio based on the disease outcomes reported, the results are statistically significant, with an OR for hypothyroidism of 3 and an OR for cancer of 6 based on the incidence in this cohort compared with the incidence in the population [15]. Brewer et al. [16] documented three case histories with multi-system/multi-symptom illness and made a case for production of mycotoxins by fungi in the nasal and sinus cavities, as well as correlations with urinary mycotoxins and fungi in nasal washings with exposures to water-damaged buildings. This paper described chronic fatigue syndrome in this population with a reference to a previous publication by the author [16].

Very Low Support

One study, Lu et al. [20], documented very low support. This study reported two statistically significant associations with fatigue included in a constellation of flu-like symptoms. On a more detailed review, the appendix listing the details of the self-reported outcomes listed only one individual with a report of fatigue; therefore, it provided a Very

Low Support level for the research question as it documented statistically significant results, but not directly associated with fatigue. However, given the common occurrence of fatigue with the other flu-like symptoms described and given that this was not the primary outcome of their research, further investigation of their data collection methods might provide better support for the association of fatigue.

Moderate Support

One study, Karvala et al. [21], documented moderate-level support. This article found a high prevalence of general symptoms, including fatigue, reported in both the population that went on to develop asthma (79.0%) and the population that did not go on to develop asthma (84.3%) [21]. This study did not calculate OR as the article was documenting the onset of work-related asthma but referenced a statistically significant result for the increased fatigue in exposed as compared to unexposed patients [20]. Review of the data for this calculation could provide additional support for the association. This study earned the ranking of Moderate Support primarily based on the physician assessment of patients, although this was focused on the asthma diagnosis and symptom reporting.

Moderately High Support

Three studies documented moderately high support. Zhang et al. [22] created a dampness/mold index on a 0-6 scale from answers to questions about the four variables of mold spots, damp stains, water damage, and mold odor [22]. Statistically significant results for odds ratios were found between dampness and mold and fatigue for mold spots; damp stains; damp bed clothing; water damage in past years; water damage in the last twelve months; window pane condensation in winter; mold odor, sometimes; mold odor, weekly; perception of humid air, sometimes; and perception of humid air, weekly. Statistically significant results for increasing odds ratios for fatigue with increasing levels of the dampness/mold index were also found [22]. Despite the fact that the collected data was completely self-reported, this study achieves the ranking of Moderately High Support by the weight of the 36,541 participants and the thirteen statistically significant associations reported.

The second study in this category, Lu et al. [23], created a dampness score based on how frequently individuals experienced symptoms. Variables rated included mold/damp stains on floor/ceiling; moldy odor; dampness on bed/clothing; window pane condensation in winter; and water damage. Statistically significant odds ratios were found between mold/dampness and fatigue for the following variables: mold/damp stains on floor/ceiling; moldy odor; dampness on bed/clothing; window pane condensation in winter; and, although not directly related to the research question, home redecoration. Statistically significant results for increasing odds ratios as the dampness score increased were also found [23]. This is similar to the increase in statistical significance as the dampness/mold index increased in the results found by Zhang et al. [22]. This study, with the same ranking point distribution as Zhang et al. and also based on self-reported data, received its Moderately High Support rating from the number of participants and the number of statistically significant associations, although neither of these were as numerous as those reported by Zhang et al. [23].

The third and final study in this category, Roussel et al. [24], documented that statistically significant results for odds ratios were found for associations with headache, fatigue, eye irritation, throat irritation, coughing, and rhinorrhea. Of note, the authors specifically observed these associations were with handling moldy documents. Archives with the documented mold or moldy documents had the most contaminated air quality measurements. The Moderately High Support rating is derived from the use of environmental testing in this study [24].

Very High Support

One study, Thomas et al. [18], documented Very High Support. This study was conducted by The National Institute for Occupational Safety and Health (NIOSH), a division of the Centers for Disease Control and Prevention (CDC), and provided both physician-documented assessment of subjects and environmental evaluation by visual inspection and multiple sample types [spore trap, bulk, swab, and Environmental Relative Moldiness Index (ERMI)]. This case-control study compared adverse health effects between 95 employees at an extensively water-damaged school located in New Orleans with 110 employees at a comparable school in Cincinnati that was minimally water-damaged [18].

In addition to the statistically significant results found for fatigue, the researchers found statistically significant increases with ORs that were ≥1.5 in 18 of the 22 symptoms. These symptoms were located in every system they evaluated: neurobehavioral, upper and lower respiratory, dermatologic, and constitutional systems [18]. This is the only study that provided detailed symptom reporting similar to that used by Shoemaker, as well as objective patient data using Visual Contrast Sensitivity results [7]; thus, it reproduced and validated the multi-system illness that is a hallmark of CIRS. As CIRS research is in its infancy, it is not surprising that there is not more published research assessing microbial exposure to the level of detail observed and documented by Shoemaker.

This study is the only one that achieves the ranking of Very High Support because it provided both physiciandocumented assessment for the participants and laboratory testing for the environment of these locations, as well as

Page8 / 11 http://eaht.org

documenting a statistically significant $OR \ge 1.5$ directly associated with fatigue. As above, the parameters of physician-documented assessment for the participants and laboratory testing for the environment are considered higher-quality metrics in epidemiological studies of this nature.

The discussion in our review reveals a nuanced spectrum of evidence regarding mold exposure and its association with fatigue, graded from reference-only cases to studies providing Very High Support. Notably, reference-only studies, while not statistically significant, do contribute qualitative case data supporting this association. Studies with Very Low to Moderate Support typically utilized self-reported measures, potentially underrepresenting the true association due to methodological constraints. Conversely, the studies yielding Moderately High to Very High Support not only featured larger sample sizes but also included objective environmental testing, reinforcing the reliability of the reported associations. Among them, the case-control study by Thomas et al. stands out with Very High Support, as it combines physician assessments and comprehensive environmental testing, marking it as particularly robust.

Limitations

While our review has illuminated a potential link between mold exposure and fatigue, it is important to recognize its limitations. The review was not exhaustive in evaluating all literature for fatigue outcomes and was limited to studies published between 2011 and 2018. As such, more recent research — including studies reflecting post-2019 indoor environmental changes influenced by the COVID-19 pandemic — was not included. These shifts may reflect different characteristics of exposure and occupant behavior, which could affect health outcomes. Alternatively, it would be difficult to discern the etiology of patients developing chronic fatigue who both developed long COVID and had mold exposure. Additionally, a larger cohort of studies may have yielded different results. Recognizing these limitations is essential for a balanced interpretation of our findings and highlights the need for updated, comprehensive reviews. We plan to conduct a follow-up systematic review covering studies published between 2019 and 2024 to address these emerging trends.

Conclusions

The comprehensive review critically evaluated the literature from 2011 to 2018 on the association between fatigue and exposure to indoor mold and/or dampness. Our findings indicated that there was a consistent pattern across the eight studies that either referenced fatigue or demonstrated some level of support for its association with mold exposure, with four studies (50%) providing moderately high to very high levels of evidence. These studies are geographically diverse and collectively involved a cohort from five cross-sectional studies with 40,933 participants and a case-control study comprising 95 cases and 110 controls, lending credence to the global relevance and the potential impact of mold exposure on health beyond the respiratory system.

Peer-reviewed publications document that approximately 25% of the population has a genetic susceptibility for developing CIRS [24], an estimated 50% of the buildings in the U.S. are water-damaged [3], and the prevalence of CIRS is conservatively calculated at \geq 7.01% in children and likely higher in adults due to the progressive nature of CIRS [25]. CIRS remains underrecognized, and individuals suffering from exposure to mold and dampness frequently do not receive the diagnosis and treatment they require. The genetic predisposition found in approximately 25% of the population further complicates this public health challenge.

The review's findings signal an imperative for change in both clinical practice and public health policy. Clinically, it is paramount that healthcare providers recognize the array of symptoms linked to mold exposure and adopt improved guidelines and training to enable prompt diagnosis and treatment, thereby potentially enhancing patient outcomes. At the policy level, there is a call to action for strategies that reduce mold and dampness exposure through the enforcement of stricter building regulations, education of landlords, prompt water damage remediation protocols, addition of explicit language guaranteeing freedom from dampness and mold in the warranty of habitability, and public education initiatives to increase awareness of mold-related health risks. Together, these changes are essential in addressing the underdiagnosed health burden of mold exposure, ensuring early intervention, and fostering healthier living environments.

In conclusion, while the existing literature provides evidence of the association between mold exposure and fatigue, substantial gaps remain. There is a critical need for further well-designed epidemiological studies to clarify the causal relationships between exposure to elevated levels of indoor mold and non-respiratory symptoms and to explore the underlying mechanisms. Such research would not only validate and potentially expand upon the findings of this review but could also inform the development of effective strategies to combat the health issues associated with exposure to mold and dampness.

Acknowledgement

Authors thank James Ryan, Ph.D. for his review of the initial manuscript.

Conflict of interest

Ming Dooley has no conflicts of interest to report. Ming Dooley and Scott McMahon provide expert witness testimony in chronic inflammatory response syndrome cases for both plaintiffs and defense. Scott McMahon is an equity owner in CIRSx and MoldCo.

CRediT author statement

MD: Conceptualization, Methodology, Formal analysis, Investigation, Writing- Original draft preparation, Project administration. SWM: Validation, Writing- Reviewing and Editing.

ORCID

Ming Dooley: 0009-0009-3680-8005

References

- [1] Dooley M, McMahon SW. A comprehensive review of mold literature from 2011-2018. Internal medicine review 2020;6(1):1-39. http://doi.org/10.18103/imr.v6i1.836
- [2] Institute of Medicine (US), Committee on Damp Indoor Spaces and Health. Damp indoor spaces and health. National Academies Press; 2004.
- [3] World Health Organization (WHO). WHO guidelines for indoor air quality: dampness and mould. [cited Mar 31, 2025]. Available from: https://www.who.int/publications/i/item/9789289041683
- [4] Caillaud D, Leynaert B, Keirsbulck M, Nadif R, mould ANSES working group. Indoor mould exposure, asthma and rhinitis: findings from systematic reviews and recent longitudinal studies. Eur Respir Rev 2018;27(148):170137. https://doi.org/10.1183/16000617.0137-2017
- [5] U.S. Government Accountability Office (GAO). Indoor mold. [cited Mar 31, 2025]. Available from: https://www.gao.gov/assets/gao-08-980-highlights.pdf
- [6] Shoemaker RC, Mark L, McMahon S, Thrasher JD, Grimes C. Research committee report on diagnosis and treatment of chronic inflammatory response syndrome caused by exposure to the interior environment of water-damaged buildings. [cited Mar 31, 2025]. Available from: https://www.survivingmold.com/docs/POA MOLD 7 27 10 final.pdf
- [7] Shoemaker RC, Rash JM, Simon EW. Sick building syndrome in water-damaged buildings: Generalization of the chronic biotoxin-associated illness paradigm to indoor toxigenic fungi. In: Johanning E, editor. Bioaerosols, fungi bacteria, mycotoxins and human health. Fungal Research Group Foundation; 2005. 52-63.
- [8] Janeway Jr. CA. Approaching the asymptote? Evolution and revolution in immunology. Cold Spring Harb Symp Quant Biol 1989;54(Pt 1):1-13. https://doi.org/10.1101/sqb.1989.054.01.003
- [9] Shoemaker RC, House D, Ryan JC. Vasoactive intestinal polypeptide (VIP) corrects chronic inflammatory response syndrome (CIRS) acquired following exposure to water-damaged buildings. Health. 2013;5(3):396-401. https://doi.org/10.4236/health.2013.53053
- [10] Harding CF, Pytte CL, Page KG, Ryberg KJ, Normand E, Remigio GJ, et al. Mold inhalation causes innate immune activation, neural, cognitive and emotional dysfunction. Brain Behav Immun 2020;87:218-228. https://doi.org/10.1016/j.bbi.2019.11.006
- [11] Shoemaker RC, Johnson K, Jim L, Berry Y, Dooley M, Ryan J, et al. Diagnostic process for chronic inflammatory response syndrome (CIRS): A consensus statement report of the consensus committee of surviving mold. [cited Mar 31, 2025]. Available from: https://www.survivingmold.com/Publications/CIRS diagnostic protocol final 5 1 2018.pdf
- [12] Sahin ON, Yaprak P, Gülen F, Perçin AK. Mold hypersensitivity in children with frequent respiratory tract infection and prolonged cough attacks. Kulak Burun Bogaz Ihtisas Derg 2014;24(4):195-199. https://doi.org/10.5606/kbbihtisas.2014.63644 [Turkish]
- [13] Pegas PN, Alves CA, Scotto MG, Evtyugina MG, Pio CA, Freitas MC. Risk factors and prevalence of asthma and rhinitis among primary school children in Lisbon. Rev Port Pneumol 2011;17(3):109-116. https://doi.org/10.1016/j.rppneu.2011.01.004 [Portuguese]

Page10 / 11 http://eaht.org

- [14] Zhu CH, Liu JX, Zhao XH. Risk factors of asthma among children aged 0-14 in Suzhou city. Zhonghua Yu Fang Yi Xue Za Zhi 2012;46(5):456-459. [Chinese]
- [15] Tuuminen T, Rinne KS. Severe sequelae to mold-related illness as demonstrated in two Finnish cohorts. Front Immunol 2017;8:382. https://doi.org/10.3389/fimmu.2017.00382
- [16] Brewer JH, Thrasher JD, Hooper D. Chronic illness associated with mold and mycotoxins: Is naso-sinus fungal biofilm the culprit? Toxins (Basel) 2013;6(1):66-80. https://doi.org/10.3390/toxins6010066
- [17] Lobiondo-Wood G, Haber J, Titler MG. Evidence-based practice for nursing and healthcare quality improvement. Elsevier; 2019.
- [18] Thomas G, Burton NC, Mueller C, Page E, Vesper S. Comparison of work-related symptoms and visual contrast sensitivity between employees at a severely water-damaged school and a school without significant water damage. Am J Ind Med 2012;55(9):844-854. https://doi.org/10.1002/ajim.22059
- [19] Chapman PM, McDonald BG, Lawrence GS. Weight-of-evidence issues and frameworks for sediment quality (and other) assessments. Human and Ecological Risk Assessment 2022;8(7):1489-1515. https://doi.org/10.1080/20028091057457
- [20] Lu Y, Lin S, Lawrence WR, Lin Z, Gurzau E, Csobod E, et al. Evidence from SINPHONIE project: Impact of home environmental exposures on respiratory health among school-age children in Romania. Sci Total Environ 2018;621:75-84. https://doi.org/10.1016/j.scitotenv.2017.11.157
- [21] Karvala K, Toskala E, Luukkonen R, Uitti J, Lappalainen S, Nordman H. Prolonged exposure to damp and moldy workplaces and new-onset asthma. Int Arch Occup Environ Health 2011;84(7):713-721. https://doi.org/10.1007/s00420-011-0677-9
- [22] Zhang X, Norbäck D, Fan Q, Bai X, Li T, Zhang Y, et al. Dampness and mold in homes across China: Associations with rhinitis, ocular, throat and dermal symptoms, headache and fatigue among adults. Indoor Air 2019;29(1):30-42. https://doi.org/10.1111/ina.12517
- [23] Lu C, Deng Q, Li Y, Sundell J, Norbäck D. Outdoor air pollution, meteorological conditions and indoor factors in dwellings in relation to sick building syndrome (SBS) among adults in China. Sci Total Environ 2016;560-561:186-196. https://doi.org/10.1016/j.scitotenv.2016.04.033
- [24] Roussel S, Reboux G, Millon L, Parchas MD, Boudih S, Skana F, et al. Microbiological evaluation of ten French archives and link to occupational symptoms. Indoor Air 2012;22(6):514-522. https://doi.org/10.1111/j.1600-0668.2012.00781.x
- [25] Shoemaker RC. Linkage disequilibrium in alleles of HLA DR: Differential association with susceptibility to chronic illness following exposure to biologically produced neurotoxins. [cited Mar 31, 2025]. Available from: https://www.survivingmold.com/docs/Linkage_disequilibrium_in_alleles_of_HLA_DR.PDF
- [26] McMahon SW. An evaluation of alternate means to diagnose chronic inflammatory response syndrome and determine prevalence. [cited Mar 31, 2025]. Available from: https://esmed.org/MRA/mra/article/view/1125