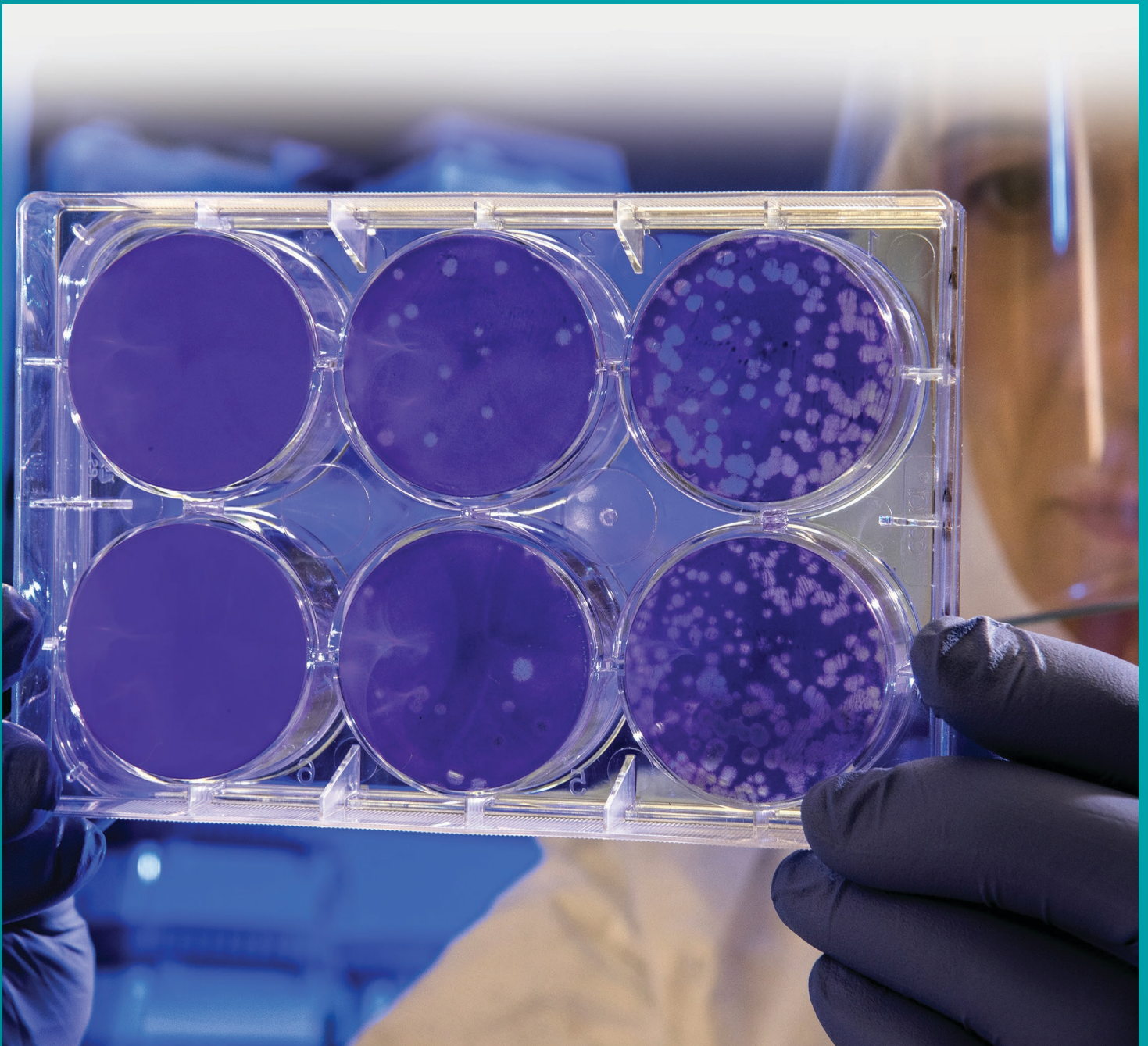




Biotoxins (indoor damp and mould) Clinical Pathway

November 2023



August 2023

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Biotoxins (indoor damp and mould) Clinical Pathway

(Note: Patients may be on multiple parts of the pathway simultaneously. This pathway is for patients assessed to be **clinically stable**.)

Target population: Patients of all ages presenting at primary care with new onset or unresolved debilitating symptoms, + history of exposure to indoor damp or mould.

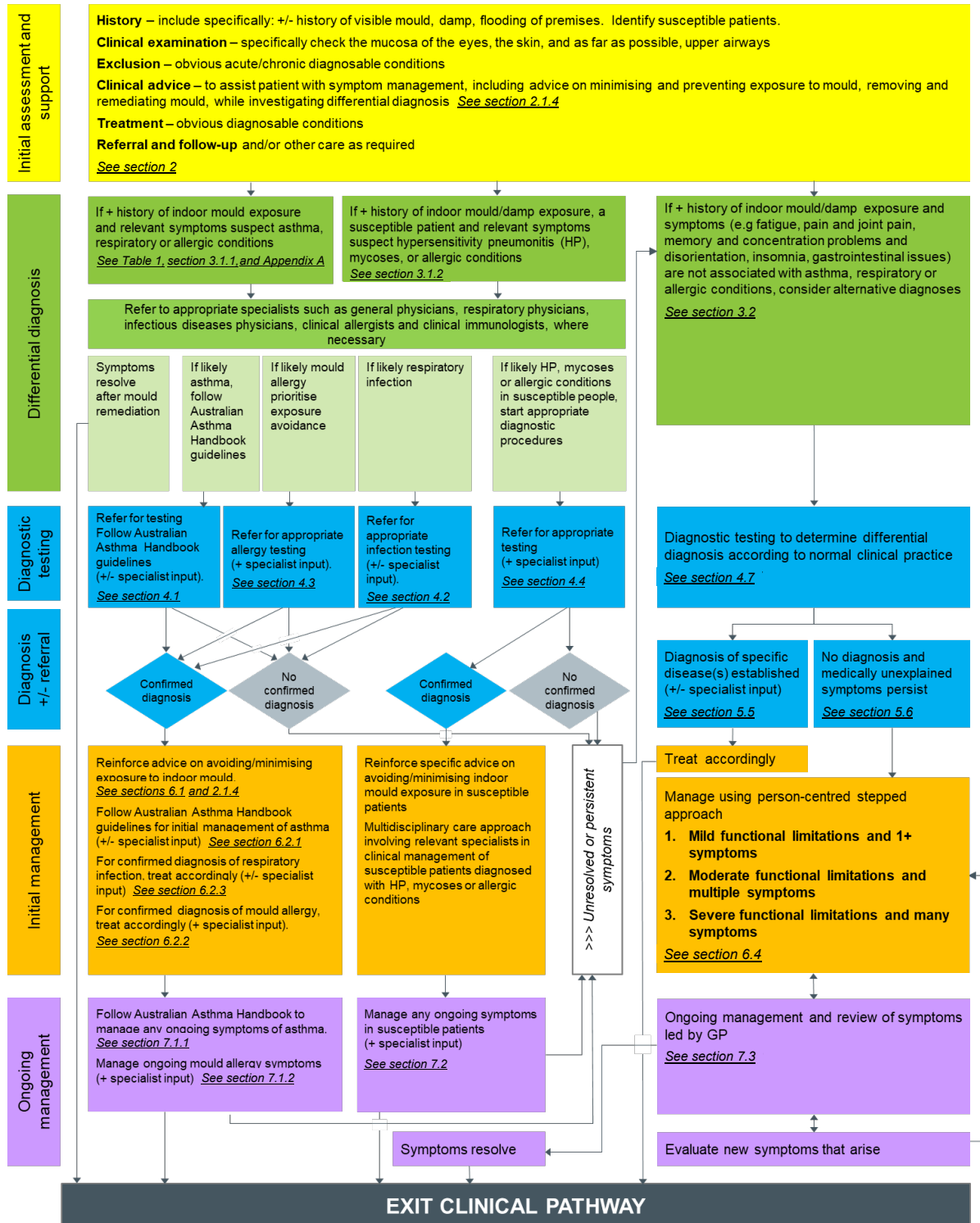


Table 1: Likely, less likely, and unlikely differential diagnoses or symptoms in patients with a history of exposure to indoor damp and mould

Likely differential diagnoses or symptoms	Less likely differential diagnoses or symptoms	Unlikely differential diagnoses or symptoms
<p>Health effects for which there is sufficient evidence of association with exposure to indoor damp and mould:</p> <ul style="list-style-type: none"> • asthma (development, current, exacerbation) • allergic rhinitis • dyspnoea • wheeze • cough • respiratory infection • bronchitis • eczema • upper respiratory tract symptoms • hypersensitivity pneumonitis (HP), mycoses and allergic effects in susceptible people. <p>See section 1.3.1, section 3.1.2 and Appendix A for further details.</p>	<p>Health effects for which there is limited or suggested evidenced of association with exposure to indoor damp and mould:</p> <ul style="list-style-type: none"> • common cold • allergy/atopy • mucous membrane irritation. <p>See section 1.3.2 and Appendix B for further details.</p>	<p>Health effects for which there is inadequate or insufficient evidence of an association with indoor damp and mould:</p> <ul style="list-style-type: none"> • acute idiopathic pulmonary haemorrhage (acute idiopathic pulmonary hemosiderosis) in infants • altered lung function/airway obstruction • COPD (development of COPD) • rheumatic disorders and autoimmune disease • cancer • reproductive effects • gastrointestinal effects • renal effects • teratogenicity • sarcoidosis • skin problems • neuropsychological and neurotoxic effects • sleep issues • fatigue • mood disorders and non-specific symptoms • mycotoxicosis • sick building syndrome (SBS) and toxic mold syndrome (TMS) • Chronic Inflammatory Response Syndrome (CIRS) <p>See section 1.3.3 and Appendix C, Appendix E and Appendix F for further details.</p>

Summary information

The Biotoxins (indoor damp and/or mould) Clinical Pathway has been developed to support decision-making on differential diagnosis, treatment and referral pathways for patients who report debilitating symptoms with a history of exposure to indoor damp or mould, and that cannot be attributed to another condition. The Biotoxins (indoor damp and mould) Clinical Pathway is not instructive; rather a tool/pathway to help structure assessments and management of patients with a wide variety of symptoms and severity of disability, including new onset or unresolved symptoms. This pathway is for patients assessed to be clinically stable.

Initial assessment

- Follow usual clinical assessment practice in the case of suspected health effects or symptoms due to indoor damp and mould including:
 - a history of recent or long-term exposure to damp and/or visible mould, and/or mouldy odour in indoor environments, at both home and work, and during leisure time (such as holiday homes where exposure can be forgotten, and may be severe) (e.g., leaking roofs and walls, faulty plumbing, condensation), and
 - whether symptoms get worse when in such environments (see [section 2.1](#) and [section 2.1.1](#) for further details).
- Breathing in mould spores and fragments can trigger nasal congestion, sneezing, coughing or wheezing and respiratory infections. It can also exacerbate asthma and allergic conditions. Contact with mould can also irritate eyes and skin.
- Response to exposure to mould varies between individuals and is influenced by personal susceptibility: age, health status, immune status, concurrent exposures, previous sensitisations, socioeconomic status, and genetic factors (see [section 1.2.3](#) for further details).
- A causal relationship to any health effect from exposure to indoor damp or mould in the general population is yet to be established. For individuals it is not possible to prove unambiguous causality between mould exposure and particular health complaints or disease (see [section 1.2.1](#), [section 1.2.5](#), [section 1.2.6](#), and [section 2.1.6](#) for further details).
- Patients with pre-existing health conditions are more likely to experience symptoms associated with exposure to indoor damp or mould or poor indoor air quality. The medical history should identify the most vulnerable and sensitive persons, such as immunocompromised individuals, allergic (atopic) persons and individuals with pre-existing pulmonary diseases like asthma, chronic obstructive pulmonary disease (COPD), and cystic fibrosis (CF). These people are also more susceptible to other serious health effects, such as aspergillosis ('Farmer's lung') (see [section 1.2.4](#) and [section 2.1.2](#) for further details).
- People living in vulnerable circumstances may be more susceptible to exposure to indoor damp and mould and potential health effects from exposure. International evidence indicates dampness and mould may be particularly prevalent in poorly maintained housing in low-income communities. Furthermore, the prevalence of indoor damp in low-income communities can be higher, as dampness is more likely to occur in houses that are overcrowded and lack appropriate heating, ventilation and insulation (see [section 1.2.4](#) for further details).

- A thorough subjective and objective clinical assessment will assist in forming a differential diagnosis. Adopt a multidisciplinary approach to patient care, involving general practitioners (GP), and where necessary, non-GP specialists such as general physicians, respiratory physicians, infectious diseases (ID) physicians, clinical allergists, clinical immunologists, occupational and environmental physicians, and psychiatrists. The multidisciplinary approach to patient care also involves allied health and non-medical health professionals, including occupational health nurses. A number of potential causes of these debilitating symptoms may be relevant and, as a result, each patient should undergo a thorough clinical assessment that considers the patient's complete history (see [section 2.2](#) for further details).
- In the case of suspected health effects or symptoms due to mould, the target organs noted in the medical history should take priority in the physical examination. Particular attention should be paid to the mucosa of the eyes, the skin, and the upper airways as the non-specific symptoms that patients often complain relate to these organs (see [section 2.1.3](#) for further details).
- Infants aged zero to 12 months with clinically significant wheezing should be referred to a paediatric respiratory physician or paediatrician as per the Australian Asthma Handbook guideline <https://www.astmahandbook.org.au/diagnosis/children> (see [section 4.1.4](#) for further details).
- Make appropriate referral for diagnostic investigations as part of a multidisciplinary approach to care. Refer to other specialists, for investigations on sensitivity to mould and fungus, (such as clinical immunologists, or allergy specialists). These specialists then in turn can undertake tests or refer to a pathologist for “*in vitro* laboratory-based testing”. If respiratory symptoms are present, patients can be referred to a respiratory physician for management and/or further investigations.
- Provide advice on avoiding or minimising exposure to indoor mould and damp, even in the absence of a health effect. Also provide advice on prevention and remediation of indoor damp and mould when it is present, as per the Environmental Health Standing Committee (enHealth) of the Australian Health Protection Principal Committee factsheet (enHealth factsheet) on potential health effects of mould in the environment. The enHealth factsheet is available at <https://www.health.gov.au/resources/publications/enhealth-guidance-potential-health-effects-of-mould-in-the-environment> (see [section 2.1.4](#) for further details).
- Provide patients with a hard copy of the enHealth factsheet on mould ([Appendix D](#)). The enHealth factsheet also provides advice about various professional and consumer bodies that people can go to for more information or advice, including on remediation (see [Appendix D](#) for the enHealth factsheet on Potential health effects of mould in the environment).
- Chronic Inflammatory Response Syndrome (CIRS) was the subject of a House of Representatives Standing Committee on Health, Aged Care and Sport Inquiry in 2018 into Biotoxin-related illnesses. CIRS is not a recognised disease in Australia, with no scientifically validated or approved diagnostic criteria, and it is not a notifiable disease. The most commonly described symptoms reported by patients experiencing CIRS include fatigue, pain, memory and concentration problems, disorientation, insomnia, gastrointestinal issues, sinus issues, fever, headaches, and respiratory issues. These symptoms can have multiple different causes, depending on the particular symptoms, cluster, and timeframe of symptoms.
- None of the international guidelines, or advice from international authorities or medical professional association evidence reviews include CIRS or Chronic Inflammatory Response Syndrome – Water-Damaged Buildings (CIRS-WDB) as a possible health effect from exposure to indoor damp or mould. As such, CIRS or CIRS-WDB has been categorised in this Clinical Pathway as a syndrome or health effect for which there is insufficient or inadequate evidence of an association with exposure to indoor damp or mould (see [Appendix E](#), [Appendix F](#), section on ‘SBS and TMS’ in Appendix C, [section 2.1.5](#), and [section 2.1.7](#) for further details).

Likely differential diagnoses or symptoms: health effects for which there is sufficient evidence of an association with exposure to indoor damp or mould

- In patients presenting with a history of exposure to indoor damp and/or mould and with relevant symptoms, likely differential diagnoses (based on epidemiological evidence) are:
 - asthma (development, current, exacerbation)
 - allergic rhinitis
 - dyspnoea
 - wheeze
 - cough
 - respiratory infection
 - bronchitis
 - eczema
 - upper respiratory tract symptoms
 - hypersensitivity pneumonitis (HP), mycoses and allergic effects in susceptible people.

(See [Appendix A](#) for an overview of the epidemiologic evidence on exposure to indoor damp and mould, and asthma, allergic rhinitis, dyspnoea, wheeze, cough, respiratory infection, bronchitis, and eczema.)

- Exposure to indoor dampness and mould is associated with asthma, particularly in children. Sufficient evidence for an association between moisture/mould damage and the manifestations, progression and exacerbation of asthma has been established. Particularly in children, this link can be considered undisputed.
- In 2015, the Institute of Medicine updated its conclusions for dampness and dampness-related agents to be:
 - in children, there was sufficient evidence of a causal association between dampness and dampness-related agents and exacerbation of asthma
 - in adults there was sufficient evidence of an association.
- Young children appear to be at higher risk of developing bronchial asthma where moisture damage or mould exposure occurs in the bedroom or living room.
- While there is sufficient evidence of a causal association between asthma (exacerbation) in children, and exposure to dampness and dampness related agents, there is not sufficient evidence of causation (i.e. there is no evidence for a direct cause and effect relationship). For other indoor exposures, there is sufficient evidence for causation for asthma exacerbation from exposure to house dust mite allergens, cat allergens and cockroach allergens (in individuals sensitised to these allergens).
- The sensitising potential of mould is considered significantly lower compared with other environmental allergens such as fur-bearing pets, grass and tree pollen, house dust mites, or cockroaches. The sensitising prevalence of mould is comparatively low at 3–10%.
- The risk of respiratory infection from common indoor mould species is low in healthy individuals. In developed countries, fungal infections such as mucormycosis occurs primarily in severely immunocompromised patients (e.g., those with haematological malignancies, organ transplantation, neutropenia, autoimmune disorders, or other impairments in immunity). Only 6–10% of cases occur in people with no underlying disease

- In susceptible individuals presenting with a history of exposure to indoor damp and/or mould, there is sufficient clinical evidence of an association between mould and other dampness-associated microbiological agents and diseases such as HP, allergic alveolitis and mould infections, as well as humidifier fever and inhalation fevers (see [section 3.1.2.1](#), [section 3.1.2.2](#), [section 3.1.2.3](#), and [section 3.1.2.4](#) for further details).
- HP (extrinsic allergic alveolitis) is an interstitial granulomatous, cell-mediated lung inflammation caused by repeated inhalation of antigens from microorganisms or other sources in susceptible people. Many different fungi, bacteria, animal proteins, plants, and chemicals are known causes of HP. The most frequent causal antigens are bird proteins and bacteria such as thermophilic actinomycetes. In addition, fungi have also been implicated in both occupational and non-occupational outbreaks. Damp in office buildings or homes or air conditioning and humidification systems has been acknowledged to have a role in the development of HP. HP is frequently misdiagnosed as a pneumonia of infectious aetiology.
- Immuno-compromise or immunosuppression has been linked with increased mould infection in susceptible patients. Infection with *Aspergillus* and other fungi such as *Fusarium* spp. is a well-known complication in the treatment of immuno-compromised patients (for example, cancer treatment or infection with human immunodeficiency virus. Invasive *Aspergillus* infections are an important cause of morbidity and mortality in immunodeficient patients and are associated with high mortality rates of between 30–95% in the more than 200,000 annual cases of life-threatening *Aspergillus* infection globally. Increased fungal infections are linked with high incidence in haemato-oncological patients with long phases of neutropenia, as well as in recipients of allogeneic stem cell transplantation. Other forms of immunosuppression, such as prolonged corticosteroid use and interstitial lung disease (including residual cavitation, e.g., following tuberculosis) as well as a combination of these factors, especially in COPD, have also been linked to increased mould infection rates.
- Follow the Australian Asthma Handbook guidelines <https://www.asthmahandbook.org.au/> in diagnosing and managing asthma in adults, adolescents and children. Provide referral to respiratory physicians or paediatricians, where appropriate.
- Where appropriate, provide referral to other specialists such as clinical immunologists, or allergy specialists for investigations on sensitivity to mould and fungus. These specialists then in turn can undertake tests or refer to a pathologist for “*in vitro* laboratory-based testing”. If respiratory symptoms are present, patients can be referred to a respiratory physician for management and/or further investigations.

Diagnostic testing

- Follow the Australian national guidelines in the Australian Asthma Handbook for diagnostic testing and clinical considerations for diagnosing asthma in adults, adolescents and children (see [section 4.1](#), [section 4.1.1](#), [section 4.1.2](#), [section 4.1.3](#), and [section 4.1.4](#) for further details).
- Core elements of the diagnostic work-up for mould infection include microbiological, immunological, molecular biological, and radiological testing. Lung or airways infection by endemic fungi or *Aspergillus* can be diagnosed with respiratory sample culture or serum IgG testing. Sputum, induced sputum, or bronchial specimens are suitable specimens for detecting fungi. Microscopy, fungal culture, galactomannan antigen, and *Aspergillus* polymerised chain reaction (PCR) are also useful tests (see [section 4.2](#) for further details).
- Allergic disorders due to mould allergens can essentially manifest as conjunctivitis, rhinitis, rhinosinusitis, allergic bronchial asthma, urticaria, HP and allergic bronchopulmonary aspergillosis (ABPA). As such, the differential diagnosis based on the medical history and clinical laboratory *in vitro/in vivo* testing is of central importance for managing patients. In individual cases, the allergic reaction needs to be confirmed and the allergy trigger identified.

- In principle, the same guidelines and recommendations apply to the diagnostics of mould allergy as to other allergen sources that cause immediate-type allergies (see [section 4.3](#), [section 4.3.1](#) and [section 4.3.2](#) for further details).
- The core element of allergy diagnostics include:
 - medical history
 - skin prick testing
 - *in vitro* serological examination of specific IgE antibodies in type I sensitisation, or specific IgG antibodies in HP only (noted as being extremely rare in non-occupational indoor exposure)
 - provocation testing (nasal, conjunctival, bronchial, as indicated).
- Mould-specific IgG antibody determination is recommended only in the case of suspected ABPA (type I and III allergy) or HP (type III and intravenous (IV) allergy). It can make a helpful contribution to diagnosis of ABPA and HP as both of these conditions show significant increase in overall IgE and specific IgEs and IgGs against *A. fumigatus*.
- The determination of specific IgG antibodies in the diagnostic work-up for immediate-type IgE mould allergy (type 1 allergy) is of no diagnostic relevance and is not recommended. This is because people develop IgGs to foreign proteins when exposed to them; however, IgGs do not measure allergies. IgG testing is highly costly to patients and there is no clinical benefit to performing these tests.
- The analysis of immune complexes is confined to particular disorders of type III allergic reactions such as HP. Beyond this, it has no value in the diagnostics of mould exposure.
- HP is diagnosed with various clinical and paraclinical tests, including pathological examination and imaging of the lungs (see [section 4.4](#) for further details).
- Diagnostic testing in Australia should only be undertaken in a pathology laboratory accredited by National Association of Testing Authorities, Australia (NATA), and the Royal College of Pathologists of Australasia (RCPA). NATA accreditation is highly regarded both nationally and internationally as a reliable indicator of technical competence.
- Lymphocyte transformation test, mycotoxins in serum, cytokines and eosinophil cationic protein (ECP), and toxicological diagnostics are not recommended as diagnostic tests by international mainstream medical guidance (see [section 4.6](#) and [Appendix C](#) for further details).

Diagnosis

- Follow the Australian Asthma Handbook guidelines <https://www.astmahandbook.org.au/> and recommendations on making a diagnosis of asthma in adults, and in children aged one year and over (see [section 5.1](#) for further details).
- The 2015 National Allergy Strategy advises accurate diagnosis of allergy is essential and requires appropriate specialist care.
- The following five conditions need to be met for a mould allergy diagnosis:
 - A pathogenic mould antigen is present in the environment
 - There is an unequivocal temporal relationship between allergic symptoms and exposure to the mould allergen
 - Atopic predisposition is present
 - There is evidence of specific IgE formation to mould antigens
 - Measures to avoid mould allergens exhibit clear clinical effects (see [section 5.2](#) for further details).

- Mould-allergic patients and patients with a weak immune system should be provided with specialist patient information about the hazards of indoor mould exposure and preventative steps they can take to minimise exposure.
- Diagnosis of mould infection is based on positive diagnostic findings for microbiological, immunological, molecular biological, and radiological tests (see [section 5.3](#) for further details).
- Diagnosis of HP will be made by a specialist, based on relevant diagnostic tests (see [section 5.4](#) for further details).

Initial patient management

- Reinforce advice to patients regarding minimising/avoiding, preventing and remediating exposure to indoor damp and mould. Provide patients with a hard copy handout of the enHealth factsheet on mould ([Appendix D](#)). It is available at <https://www.health.gov.au/resources/publications/enhealth-guidance-potential-health-effects-of-mould-in-the-environment> (see [section 6.1](#) for further details).
- Follow usual clinical practice for patients diagnosed with mould allergy or mould-related infection. For information refer to Therapeutic Guidelines (<https://www.tg.org.au/>) Australian Medicines Handbook, NPS MedicineWise, Australian Prescriber or the TGA (see [section 6.2](#) for further details).
- Follow the Australian Asthma Handbook (<https://www.astmahandbook.org.au/>) for management of asthma in adults, adolescents and young adults, and children (see [section 6.2.1](#) for further details) (National Asthma Council Australia, 2022).
- While exposure avoidance (allergen avoidance) takes priority, as with all allergic diseases, prompt medication is required in order that a symptom-free period is not followed by full-blown allergic disease. It is of paramount importance to eliminate the causes of the dampness creating a basis for indoor mould growth.
- In principle, topical and/or systemic treatment is indicated in mould allergy depending on the organ-specific manifestation of the allergic disorder (see [section 6.2.2](#) for further details).
- Antifungal treatment is indicated in almost all patients with chronic cavitary pulmonary infections, chronic invasive and granulomatous rhinosinusitis, and aspergillosis bronchitis (see [section 6.2.3](#) and [section 6.2.3.1](#) for further details).

Management of patients who have persistent symptoms or remain undiagnosed

This section on 'Management of patients who have persistent symptoms or remain undiagnosed' is aligned with the Australian Government Department of Health and Aged Care's Debilitating Symptom Complexes Attributed to Ticks (DSCATT) Clinical Pathway.

- This section applies for patients who have medically unexplained symptoms i.e. patients with a history of exposure to indoor damp and mould, whose symptoms have been investigated through this clinical pathway but no diagnosis of a specific disease(s) is established.
- If the symptoms are medically unexplained, GPs and other medical professionals should treat and manage symptoms according to common best-practice and provide person-centred, stepped care. Stepped care includes:
 - developing an individualised, time contingent, care plan

- actively managing symptoms to improve the functioning of the patient in accordance with evidence-based guidelines
 - offering a variety of support/care options for people with different levels and types of need, from low intensity to high intensity
 - providing clear pathways between these care options as individuals' needs change
 - intensifying stepped care as required by referring to relevant specialists
 - providing regular follow-up and exploring symptoms if recovery stagnates
 - reviewing new symptoms for information that may lead to diagnosis, or for indications of a new disease process.
- Where symptoms are medically unexplained, good communication and empathy are important. Take each patient's concerns seriously and acknowledge and alleviate their symptoms.
 - Patients with medically unexplained symptoms (MUS) may need support to manage distressing symptoms and any disability that accompanies the symptoms. Acknowledging the difficulty of chronic symptoms and supporting the important mental health strategies is vital to person-centred care in chronic disease.
 - Practice harm minimisation by avoiding fragmented care from multiple different practitioners; repeated diagnostic testing; use of non-accredited laboratories for diagnostic testing and use of unconventional diagnostic techniques; unnecessary referrals and interventions; and treatments with known harm and/or no benefit.
 - The management plan for patients who have persistent symptoms or remain undiagnosed would be led by the patient's general practitioner (GP), in consultation with the patient so the patient can achieve their goals. However, management of ongoing symptoms should involve a multidisciplinary approach, incorporating the teamwork of all medical specialties and skills relevant to the individual patient's care. The management of patients must be a collaborative approach between GPs and specialists. Telehealth can also be used where appropriate.
 - Consider referring patients who have MUS to appropriate specialists based on best clinical practice and relevant evidence (see [section 6.4](#) and [section 7.3](#) for further details).

Ongoing management

- Follow the Australian Asthma Handbook (<https://www.astmahandbook.org.au/>) for managing asthma in adults, adolescents, and children (see [section 7.1.1](#) for further details) (National Asthma Council Australia, 2022).
- In patients with mould allergy, ongoing monitoring would be led by a Clinical Allergist or Immunologist.
- If symptoms have resolved, the patient exits the Clinical Pathway.
- If symptoms persist, consider alternative diagnoses (see [section 3.2](#) and [section 3.2.1](#) for further details).

Advice for avoiding and minimising exposure to mould, preventing exposure, and remediation

- While a quantitative and/or causal relationship between the occurrence of individual mould species and health problems has yet to be established, indoor mould growth is a potential health risk.
- The enHealth advise dampness and mould related problems should be prevented. When they occur, they should be rectified- remove mould where present, find it when you smell it, repair and control sources of excessive moisture – this is the best approach for controlling potential health risks. The enHealth factsheet is available at

<https://www.health.gov.au/resources/publications/enhealth-guidance-potential-health-effects-of-mould-in-the-environment>.

- There is no exposure limit or health guideline value for exposure to mould. Where possible, exposure to mould should be minimised – this is particularly recommended for people who are more sensitive to mould exposure.
- Mould-allergic patients and patients with a weakened immune system should be provided with specialist patient information about the hazards of indoor mould exposure and preventative steps they can take to minimise exposure.
- Although mould naturally occurs in the environment and can be found almost anywhere, it requires damp surfaces and moisture to grow. People can reduce their exposure through simple measures, however there is no practical way to eliminate all exposure to mould.
- In indoors, people should prevent moisture and dampness and ensure adequate ventilation. This will minimise mould growth; fix leaky plumbing, roofs and other building faults; clear and maintain gutters; and reduce and remove condensation (e.g., use exhaust fans and wipe up excess water).
- Buildings and homes with inadequate ventilation resulting from poor design, modifications or lack of maintenance may be more prone to developing mould. The cheapest and easiest way of reducing indoor moisture and humidity is by ventilating a room by opening a door or window.
- During periods of extended high outdoor humidity, another practical method of reducing interior humidity levels is using a dehumidifier suitably sized for the indoor areas affected.
- Air purifiers can be used as a way of reducing fungal particle exposure and improving indoor air quality.
- enHealth factsheet advises that occupational hygienists can provide consultancy services at a fee to remove mould, locate mould by inspections (if it can be smelled but not seen), or to find a solution. A list of Australian occupational hygienists can be found at <https://www.aioh.org.au/resources/consultants/>.
- While this Clinical Pathway is focused on exposure to indoor damp and mould, it is acknowledged that people can be exposed to mould in other environments.
 - The enHealth advises that mould occurs naturally in the environment and can be found almost anywhere, including in garden composts and on decaying or damp organic material, and food. Mould spores and fragments exist naturally in the air people breathe. The amount that people are exposed to depends on various factors including the season, surrounding land, wind, and people's activities/actions both indoors and outdoors.
 - Indoors, mould grows best in damp and poorly ventilated areas, typically on wood, plasterboard, tile grout and furnishings.
 - Outdoors, use appropriate personal protective equipment such as gloves and a P1 or P2 face mask when handling garden composts, mulch, straw or hay, and mouldy and decaying organic materials.
- Additionally, it is also acknowledged that people can be exposed to other potential indoor air pollutants. A 2020 evidence review by the National Institute for Health and Care Excellence (NICE) aimed to identify clinical signs and symptoms that should prompt healthcare professionals to consider exposure to poor indoor air quality at home in people presenting to health services. NICE considered exposure to indoor mould and damp, along with multiple other exposures. NICE did not make a specific conclusion about the health effects associated with exposure to indoor dampness and mould, rather that, 'For the outcomes that matter most', stating:
 - "The committee noted the pollutants such as NO₂ [nitrous dioxide], volatile organic compounds (VOCs), particulate matter (PM) from open solid-fuel fires, polycyclic aromatic hydrocarbons (PAHs) and biological agents such as mould and pet dander are sometimes associated with many symptoms including those affecting the respiratory,

cardiovascular and neurological systems”.

Periodic review of the Clinical Pathway

- This Biotoxins (indoor damp and mould) Clinical Pathway is informed by the current peer-reviewed evidence base and Australian and international authority guidance.
- There is a research project currently in place to further understand the origin and pathophysiology of the biotoxin-related illnesses and associated symptom complexes (so called CIRS-like symptoms) to improve the diagnosis, treatment and management.
- There is potential for this Clinical Pathway to be reviewed in future should the evidence base change significantly.

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1. Introduction

1.1. Purpose of the Clinical Pathway

The purpose of the Biotoxins (indoor damp and mould) Clinical Pathway is to support decision-making for general practitioners (GPs) and other medical professionals for the diagnosis, treatment and management of patients with biotoxin-related illnesses and symptoms that cannot be attributed to another diagnosable condition. This Clinical Pathway has been developed in consultation with the Biotoxins-related Illness Advisory Committee (BIAC) which comprises of members from a broad range of allied health and specialist medical fields, as well as consumer representatives.

This evidence based Biotoxins (indoor damp and mould) Clinical Pathway has been developed to support decision-making on differential diagnosis and referral pathways for patients presenting with either new onset or unresolved debilitating symptoms with a history of exposure to indoor damp or mould and that cannot be attributed to another condition (acute or chronic). The Clinical Pathway is not instructive; rather it is a tool/pathway to help structure assessments and management of patients with a wide variety of symptoms and severity of disability. It has also been designed specifically for use in the Australian context.

This Biotoxins (indoor damp and mould) Clinical Pathway is focused on health effects for which the evidence is sufficient for an association with exposure to indoor damp and mould. The Clinical Pathway is also designed for the management of patients for whom a diagnosis cannot be established and who have persistent symptoms. It is informed by an evidence evaluation of the current peer-reviewed evidence and is consistent with international advice. It has been developed using guidance from international and national authorities and medical professional associations. The information and recommendations on the diagnosis of health effects associated with exposure to indoor damp and mould in this Clinical Pathway include three international authority guidelines:

- The 2009 World Health Organization (WHO) guideline on Indoor air quality was developed by international leading air quality medical, scientific and research organisations and professionals (World Health Organization, 2009). It remains the most current guideline from the WHO on indoor mould or damp.
- An abridged version of the Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (Association of the Scientific Medical Societies, Germany) (AWMF) guideline for the medical clinical diagnostics of indoor mould exposure published in 2017 (Wiesmüller et al., 2017). It is described as a European consensus based (S2k) Guideline of the German Society of Hygiene, Environmental Medicine and Preventive Medicine (GHUP) in collaboration with multiple scientific medical societies, German and Austrian societies medical associations and experts were involved in producing the guideline.
- The UK National Institute for Health Care and Excellence (NICE) guideline on indoor air quality at home (National Institute for Health Care and Excellence, 2020a) and the associated evidence review for exposure to pollutants and health outcomes (National Institute for Health and Care Excellence, 2020b).

Other guidance from multiple international authorities and medical professional associations also underpins this Clinical Pathway. Key examples are provided below:

- The section 'Health effects associated with dampness and mould' in the 2009 WHO guideline (World Health Organization, 2009) was authored by Mendell et al. and updated the conclusions of a prior review by the Institute of Medicine (IOM) (2004).
- The 2011 review by Mendell et al. (Mendell et al., 2011) is widely cited as seminal evidence on exposure to indoor damp or mould and respiratory and allergic health effects.
- Mendell was also an author of the 2015 Indoor environmental exposures and exacerbation of asthma: Update to the 2000 Review by the IOM (Kanchongkittiphon et al., 2015).
- A clinical guidance paper that was identified as the companion review of the evidence that underpinned the AWMF guidelines (Hurraß et al., 2017).
- A clinical commentary review (Larenas-Linnemann et al., 2016) on the clinical evaluation and management of patients with suspected fungus sensitivity on behalf of the Environmental Allergens Workgroup, with Category 1 Continuing Medical Education (CME) accreditation from the American Academy of Allergy, Asthma and Immunology (AAAAI).

This Biotoxins (indoor damp and mould) Clinical Pathway is aligned with the Australian Government Department of Health and Aged Care's existing Debilitating Symptom Complexes Attributed to Ticks (DSCATT) Clinical Pathway, regarding referral pathways and guidance on management of patients with persistent symptoms or who remain undiagnosed, including management of patients with MUS. The DSCATT Clinical Pathway, published on the Department of Health and Aged Care (the Department)¹ website in 2020, provides current Australian guidance for investigating and managing new onset or unresolved debilitating symptoms. The DSCATT Clinical Pathway recommends the use of a Stepped Care model, including an individualised care plan. The Australian guidance on MUS and Stepped Care model used in the DSCATT Clinical Pathway are applicable to patients with unresolved debilitating symptoms with a history of exposure to indoor damp or mould.

The National Health and Medical Research Council (NHMRC) is currently funding a research project to improve broader understanding of the origin and pathophysiology of biotoxin-related illnesses, including so called CIRS-like symptoms. The outcomes of the research may provide further insights into biotoxin-related illnesses in Australia and help improve the support available for patients experiencing these illnesses.

There is potential for the Biotoxins (indoor damp and mould) Clinical Pathway to be reviewed in future should the evidence base change significantly.

¹ References to the Department in this document refer to the Australian Government Department of Health and Aged Care, and its predecessor the Australian Government Department of Health. The Department of Health and Aged Care name took effect from 23 June 2022.

1.1.1. Context to the development of the Clinical Pathway

In 2018, the House of Representatives Standing Committee on Health, Aged Care and Sport issued its Inquiry Report into Biotoxin-related Illnesses² in Australia (House of Representatives Standing Committee on Health, Aged Care and Sport, 2018). The House of Representatives Inquiry (the Inquiry) noted that spores produced by mould have the potential to cause health issues if inhaled by susceptible individuals. While the prevalence of a condition referred to as CIRS has been described in Australia and internationally as a biotoxin-related illness, the Inquiry Committee reported that biotoxin-related illnesses and CIRS are not widely recognised medical conditions among the Australian medical profession. Additionally, advice from the Australian Government Department of Health and Aged Care (the Department) to the Inquiry noted that biotoxin-related illnesses are not captured within the National Notifiable Diseases Surveillance System, data is not retained on their frequency or distribution, and that there are no clinical guidelines for the diagnosis and treatment of CIRS (House of Representatives Standing Committee on Health, Aged Care and Sport, 2018).

In March 2020, the Australian Government responded to the Inquiry (Australian Government, 2020). Specifically, the Australian Government acknowledged that it sympathises with, and is concerned for patients who are suffering with debilitating symptoms that the patients believe to be associated with exposure to mould and/or biotoxins. The Australian Government advised that further research was required into the link between such symptoms and exposure to mould. Additionally, the Australian Government noted an opportunity to take a broad multidisciplinary approach given the similarities between such symptom complexes and others, such as those attributed to ticks or chronic fatigue-like symptoms. This approach would include working with patients, health groups and practitioners to investigate how to provide better care to all patients with complex symptom groups that are not yet medically explained (Australian Government, 2020).

The Australian Government agreed to implement Recommendation 5 and Recommendation 7 of the Inquiry. Recommendation 5 relates to conduct an evaluation of the evidence into the treatment of patients presenting with complex illnesses that are difficult to diagnose, such as those with CIRS-like symptoms. This piece of work informs Recommendation 7, which is to develop clinical guidelines for general practitioners (GPs) for the diagnosis, treatment and management of CIRS-like conditions, in consultation with patient groups, medical practitioners, and health bodies (Australian Government, 2020).

² The Inquiry report did not define 'biotoxin'. A number of submitters provided information to answer the Inquiry's question 'What is a biotoxin-related illness? The Royal Australasian College of Physicians (RACP) advised the Inquiry "biotoxins" is an umbrella term for substances of biological origin, some of which can produce toxic effects in humans".

1.2. Important context to inform clinical decision making and advice to patients reporting exposure to indoor damp and mould

1.2.1. A causal relationship between mould damage and different health effects is yet to be established

The international consensus in the medical literature, including guidelines, evidence reviews from international authorities and medical professional associations is that the level of evidence is still not sufficient to establish a causal relationship to any health effect for exposure to indoor damp and mould in the general population.

The WHO (2009) concluded that the epidemiological evidence is not sufficient to conclude causal relationships between indoor dampness or mould or any specific human health effect. Although it was also highlighted that the findings of one strong epidemiological intervention study, in conjunction with other available studies suggest that dampness and mould exacerbates asthma in children (World Health Organization, 2009).

Since the WHO guideline, other high-quality guidelines and literature have made similar conclusions or statements about the levels of confidence in an association i.e. the level of evidence is insufficient to establish a causal relationship between exposure to indoor damp and mould and health effects in humans. These reviews include:

- the abridged AWMF guideline in collaboration with multiple scientific medical societies, German and Austrian societies, medical association and experts (Wiesmüller et al., 2017), and its associated evidence review (Hurraß et al., 2017)
- evidence reviews by international authorities such as the US Institutes of Medicine (IOM) (Kanchongkittiphon et al., 2015; Mendell et al., 2011)
- evidence review of the National Collaborating Centre for Environmental Health (NCCEH) (Palaty & Shum, 2012)
- a review on behalf of the Environmental Allergens Workgroup (Baxi et al., 2016).

The 2017 AWMF guideline (Wiesmüller et al., 2017) for the medical clinical diagnostics of indoor mould exposure and the associated evidence review (Hurraß et al., 2017), included a wider range of health effects than covered by Mendell et al. in their 2011 review (Mendell et al., 2011). They also concluded that there was no, or insufficient, evidence to establish a causal relationship between indoor mould exposure or dampness and disorders/diseases (without mould mycoses) (Hurraß et al., 2017; Wiesmüller et al., 2017). Additional advice included that while there are known evidence levels for associations between mould damage and the different health effects, for individuals, it is not possible to prove unambiguous causality between mould exposure and particular health complaints or diseases (Hurraß et al., 2017).

1.2.2. Exposure to mould should be minimised even though causality has not been established

Australian and international advice is consistent in that exposure to indoor mould should be minimised or avoided, and dampness and mould-related problems should be prevented, even in the absence of health effects/symptoms (Denning & Chakrabarti, 2017; Environmental Health Standing Committee (enHealth) of the Australian Health Protection Principal Committee, 2021; Hurraß et al., 2017; Larenas-Linnemann et al., 2016; Wiesmüller et al., 2017).

The AWMF guideline cautioned that indoor mould growth is a potential health risk, even if a quantitative and/or causal relationship between the occurrence of individual mould species and health problems is yet to be established. The core messaging in this guideline include:

- indoor mould infestation should not be tolerated.
- cause identification and appropriate remediation are the most important measures (see [section 2.1.4](#) for further details) (Wiesmüller et al., 2017).

1.2.3. Response to exposure to mould varies between individuals

Whether moulds pose a health risk largely depends on the disposition of the exposed individuals (Hurraß et al., 2017; Palaty & Shum, 2012; Park & Cox-Ganser, 2011; Wiesmüller et al., 2017) and there is wide variability in how people are affected by airborne mould exposure (American Industrial Hygiene Association Indoor Environment Quality Committee, 2020; Baxi et al., 2016). A person's response to mould is influenced by personal susceptibility related to their age, health status, immune status, concurrent exposures, previous sensitisations, socioeconomic status, and genetic factors (Palaty & Shum, 2012). Further, many fungal allergens are broadly cross-reactive, and in sensitised individuals, exposure to related species can cause symptoms due to shared epitopes (Baxi et al., 2016).

1.2.4. Individuals and patients at risk of health effects due to indoor damp or mould or other factors associated with indoor air quality

The risk of infection from common indoor mould species is low in healthy individuals and the sensitising potential of moulds is considered significantly lower compared with other environmental allergens. For example, fur-bearing pets, grass and tree pollen or house dust mites. Recent studies have shown a comparatively low sensitising prevalence of 3–10% to moulds in the general population across Europe (Wiesmüller et al., 2017).

The National Collaborating Centre for Environmental Health (Canada) noted that in healthy individuals, most case reports of adverse health reactions from mould (e.g., mucus membrane irritation syndrome, organic dust toxic syndrome (ODTS), interstitial lung disease, and inhalation fevers) have been associated with mould exposures in agricultural or industrial environments but not in residential environments (Palaty & Shum, 2012). ODTS is an acute, systemic flu-like disease caused by the inhalation of high concentrations of bioaerosols found almost exclusively in work places, and is significantly more common than HP, or Farmer's

lung from which it is sometimes difficult to distinguish diagnostically (Wiesmüller et al., 2017). Both conditions are more frequently seen in agricultural workplaces.

HP may affect from 1–5% or more of a specialised population exposed to appropriate antigens, examples being farmers and Farmer’s lung, and pigeon breeders and pigeon breeder’s disease (American Lung Association et al., 2014). The prevalence of HP in the general population is unknown (American Lung Association et al., 2014), but is noted by the CDC to be rare (Park & Cox-Ganser, 2011).

People with pre-existing health conditions may be vulnerable to ill-health as a result of exposure to indoor damp or mould or poor indoor air quality, including mould. A review of an individual’s medical history should identify the most vulnerable and sensitive persons, such as immunocompromised individuals, allergic (atopic) persons and individuals with pre-existing pulmonary diseases like asthma, COPD, and CF.

The abridged AWMF guideline advised that at-risk groups may need particular protection. Mould-allergic patients and patients with a weakened immune system should be provided with specialist patient information about the hazards of indoor mould exposure and preventative steps they can take to minimise exposure (see [section 2.1.2](#) for further details) (Wiesmüller et al., 2017).

The WHO estimated the prevalence of indoor dampness may affect between 10%–50% of indoor environments in Australia, with the same prevalence estimates of indoor dampness provided for Europe, North America, India and Japan (World Health Organization, 2009)

International guidelines and guidance acknowledge that people who live in vulnerable circumstances, such as in poor quality housing may be more susceptible to exposure to indoor damp and mould and potential health effects from exposure. NICE advised people who live in poor quality housing, people who live in poverty and people exposed to tobacco smoke in their home are at risk of ill health due to indoor air quality (including mould) (National Institute for Health Care and Excellence, 2020a). The WHO advised that dampness and mould may be particularly prevalent in poorly maintained housing for low-income people. Furthermore, the prevalence of indoor damp in low-income communities can be substantially higher than the national average, as dampness is more likely to occur in houses that are overcrowded and lack appropriate heating, ventilation and insulation (Institute of Medicine 2004 in World Health Organization, 2009).

1.2.5. Mechanisms to explain various health effects from exposure to indoor damp or mould are largely unknown

The mechanisms by which non-infectious microbial exposures contribute to adverse health effects associated with indoor air dampness and mould are largely unknown (World Health Organization, 2009). It is difficult to determine conclusively the exact mechanism by which mould in the indoor environment contributes to health effects (Palaty & Shum, 2012). No single mechanism or factor is able to explain the various health effects related to moisture damage and/or mould exposure (Mendell et al., 2011; Wiesmüller et al., 2017; World Health Organization, 2009).

Atopic and allergic individuals are particularly susceptible to biological and chemical agents in damp indoor environments (World Health Organization, 2009). As both atopic and non-atopic individuals are susceptible to adverse effects of dampness or mould (Mendell et al., 2011; Wiesmüller et al., 2017; World Health Organization, 2009), the epidemiologic evidence suggests involvement of both allergological (allergic) and non-immunoglobulin E (IgE) mediated immunological (non-allergic) mechanisms (Mendell et al., 2011; Wiesmüller et al., 2017), and toxic, immunomodulatory mechanisms (Wiesmüller et al., 2017).

The mechanisms of adverse health effects from fungal exposure were described by Larenas-Linnemann et al. in a CME accredited clinical commentary review as follows:

- the patient could be allergic to the fungus
- the patient could be experiencing an irritant effect from exposure
- the patient could be infected by the fungus
- the patient could be allergic to other allergens, and co-exposure to fungi acts as an adjuvant stimulating a Th2 response via non-specific routes of the innate immune system
- there could be other mechanisms that are unknown (Larenas-Linnemann et al., 2016).

1.2.6. Limitations and issues about the human evidence base highlighted in key international guidelines, reports, and reviews

The key (inter)national authority and medical professional body reports, guidelines, evidence reviews, along with systematic reviews and literature reviews that informed this evidence-based Clinical Pathway raised many issues with the evidence base on exposure to indoor damp and mould and human health effects. The main themes identified throughout the body of literature evaluated are listed below:

- Study designs make it difficult to establish causality between exposure to indoor damp or mould and health effects.
- Measuring mould and dampness is problematic with the vast majority of epidemiological studies reporting qualitative exposure to mould with very limited data on quantitative exposure to mould.
- Response to exposure to mould varies between individuals and is influenced by personal susceptibility: age, health status, immune status, concurrent exposures, previous sensitisations, socioeconomic status, and genetic factors.
- The complex microbiome that exists in water damaged buildings (WDB) or damp indoor environments inhabited by humans, makes it virtually impossible to attribute causality to one organism, including mould/fungi.
- No dose-response relationship has yet been established. Further focused research (including studies that can characterise dose–response relationship) is required to determine safe levels and identify age-or dose-related protective effects.

1.3. Consideration of health effects from exposure to indoor damp and mould in the differential diagnosis, and management of patients with persistent symptoms or who remain undiagnosed, including management of patients with MUS

Acknowledging the House of Representatives Inquiry was focused on biotoxin-related illnesses from exposure to indoor damp and mould, this Clinical Pathway includes the consideration of differential diagnoses or symptoms based on currently established levels of association, (from epidemiological or clinical evidence), with indoor damp and mould.

1.3.1. Differential diagnoses or symptoms for which there is sufficient evidence of an association with exposure to indoor damp or mould include several respiratory and allergic health effects, and HP, mycoses, and allergic effects in susceptible people

There was strong consensus in the international literature and epidemiological evidence underpinning this Clinical Pathway that exposure to indoor damp or mould is positively associated (i.e. linked but not a direct cause and effect relationship) with several respiratory or allergic health effects (American Industrial Hygiene Association Indoor Environment Quality Committee, 2020; Baxi et al., 2016; Cheong, 2013; Hurraß et al., 2017; Mendell et al., 2011; Palaty & Shum, 2012; Park & Cox-Ganser, 2011; Wiesmüller et al., 2017; World Health Organization, 2009). These health effects include asthma (development and exacerbation), respiratory infections, rhinitis, wheeze, cough, dyspnoea, bronchitis, upper respiratory tract symptoms, eczema, and HP, mycoses and allergic effects in susceptible people.

The WHO concluded in their 2009 guideline that there was sufficient epidemiological evidence of associations between exposure to indoor dampness or mould and asthma (development, current and exacerbation), respiratory infections (except otitis media), upper respiratory symptoms, cough, wheeze and dyspnoea. Indoor dampness also appeared to be associated with bronchitis and allergic rhinitis, but the evidence is either mixed (allergic rhinitis) or based on relatively few studies (bronchitis).

A review by Mendell et al. on respiratory and allergic health effects of dampness mould and dampness related agents for the US IOM published in 2011 and the aforementioned 2017 abridged AWMF guideline from Germany continued to confirm the conclusions of the WHO. Both the 2009 WHO guideline, and the 2011 Mendell et al. review were widely cited throughout the literature that informs this Clinical Pathway.

The body of evidence (ranging from international guidelines, advice from international authorities and medical professional bodies, systematic reviews, reviews, and studies) acknowledges that exposure to indoor dampness and mould is associated with asthma,

particularly in children. However, associations shown between indoor dampness and mould and a variety of respiratory and allergic health effects, including asthma, have been limited to observation-based, qualitative indicators of damp or mould. These indicators include visible mould, mouldy or musty odour, water-damaged materials or (observed) moisture of materials. Additionally, an update of the 2000 review by the US IOM on indoor environmental exposures and exacerbation of asthma advised on the issue. The US IOM review advised that while the evidence indicates that in children there is sufficient evidence of a causal association between dampness and dampness-related agents and exacerbation of asthma, there is not sufficient evidence for causation. For other indoor exposures, sufficient evidence for causation was found between exposure to dust mite allergen and exacerbation of asthma in children sensitised to dust mites, between cat allergen exposure and exacerbation of asthma in individuals specifically sensitised to cats, and between cockroach allergen exposure and exacerbation of asthma in individuals specifically sensitised to cockroaches, especially adults.

The specific advice on respiratory infections is included in the 2017 abridged AWMF guideline. It advised that while there is evidence of a consistent association between water damage or indoor mould exposure and the development of medically diagnosed respiratory tract diseases, the risk of infection from common indoor mould species is low in healthy individuals.

Regarding susceptible people, the WHO concluded in their 2009 guideline that 'there was sufficient clinical evidence of associations between mould and other dampness-associated microbiological agents and HP, allergic alveolitis and mould infections in susceptible individuals, and humidifier fever and inhalation fevers'. The WHO stressed this was the only conclusion that is based primarily on clinical evidence and also the only conclusion that refers explicitly to microbial agents, as opposed to dampness-related factors. This 2009 guideline remains the current guideline from the WHO on indoor damp or mould.

For susceptible individuals, there was consensus in the literature that there is sufficient clinical evidence of associations between mould and other dampness-associated microbiological agents and HP and mould infections, as well as humidifier fever and inhalation fevers. HP, also called extrinsic allergic alveolitis, is an interstitial granulomatous, cell-mediated lung inflammation caused by repeated inhalation of antigens from microorganisms or other sources in susceptible people. The most frequent causal antigens are bird proteins and bacteria such as thermophilic actinomycetes. However, fungi have also been implicated in both occupational and non-occupational outbreaks. Several international authority reports and an evidence review acknowledged the role of damp in office buildings or homes or air conditioning and humidification systems and the development of HP. HP is frequently misdiagnosed as a pneumonia of infectious aetiology.

See [section 3.1](#) for further details on 'Differential diagnoses or symptoms for which a sufficient level of evidence exists for an association with exposure to indoor damp and mould'. An overview of the epidemiological evidence for health effects from exposure to indoor damp and mould such as asthma, respiratory infections, other respiratory symptoms (rhinitis, wheeze, cough, dyspnoea, bronchitis, upper respiratory tract symptoms) and eczema is provided in [Appendix A](#). See [section 3.1.2](#) for further clinical epidemiological information on HP, mould-related infections and allergic health effects in susceptible people.

1.3.2. Health effects for which there is limited or suggested evidence of an association with indoor damp or mould

Overall, in the body of literature, there was only limited or suggested evidence of an association between exposure to indoor damp or mould and the common cold, allergy/atopy, and mucous membrane irritation (MMI). See [Appendix B](#) for an overview of the epidemiological evidence on these health effects.

1.3.3. Health effects for which there is inadequate or insufficient evidence of an association with indoor damp or mould

While there was some disagreement within the body of literature evaluated, overall there was a fairly strong consensus in the body of literature (in particular, evidence reviews and reports from the international guidelines, international authority and medical professional associations) about the differential diagnoses or symptoms for which there was inadequate or insufficient evidence for an association between exposure to indoor damp or mould. These differential diagnoses or symptoms with insufficient evidence for an association between exposure to indoor damp or mould include, acute idiopathic pulmonary haemorrhage (AIPH) in infants; altered lung function/airway obstruction; COPD; rheumatic disorders and autoimmune disease; cancer; reproductive effects; gastrointestinal effects; renal effects; teratogenicity; sarcoidosis; neuropsychological and neurotoxic effects; sleep issues, fatigue, mood disorders and non-specific symptoms; mycotoxicosis, SBS and TMS, and CIRS.

See [Appendix C](#) for an overview of the epidemiologic evidence on these health effects.

See [Appendix E](#) for further information on CIRS. Appendix E also includes:

- information on CIRS from the House of Representatives Inquiry
- diagnostic tests used in the diagnosis CIRS (note these tests not recommended due to limited evidence)
- treatments for patients that are diagnosed by CIRS practitioners (note there are significant side effects with many of the medications used in the treatment of CIRS).

See also [Appendix F](#) for further details on the 'Potential side effects of pharmaceuticals used in the treatment of CIRS'.

1.3.4. Management of patients with persistent symptoms or who remain undiagnosed

This section is aligned with the Australian Government Department of Health DSCATT Clinical Pathway, published in October 2020. The guidance can be applied to the management of patients who have unresolved debilitating symptoms that cannot be attributed to tick-borne disease, exposure to indoor damp or mould or another diagnosable condition.

The Clinical Pathway acknowledges that because of the imprecise nature of the symptom complexes, some patients may remain undiagnosed. Therefore, evidence-based ways to manage ongoing symptoms through a comprehensive patient-centred care plan has been included for patients for whom there is no diagnosis and who are considered to have MUS or 'undifferentiated illness'.

In such patients, it is especially important to ensure that patient or person-centred care is provided to validate, address and manage their symptoms as much as possible. Good communication and empathy are important. Take patients concerns seriously and acknowledge and alleviate their symptoms. Provide support to manage distressing symptoms and any disability that arises from them.

The management plan for patients who have persistent symptoms or remain undiagnosed should be led by the patient's GP, in consultation with the patient so the patient can achieve their goals.

Management of ongoing symptoms should involve a multidisciplinary approach, incorporating the teamwork of all medical professionals relevant to the individual patient's care. The management of patients must be a collaborative approach between GPs and specialists. Telehealth can also be used where appropriate.

Consider referring patients who have MUS to appropriate specialists based on best clinical practice and relevant evidence.

For more details, see [section 6.4](#) on 'Management of patients with persistent symptoms and who remain undiagnosed', [section 6.4.1](#) on 'MUS', [section 6.4.2](#) on 'Practice Harm Minimisation', and [section 6.4.3](#) on 'The Stepped Care Model'.

2. Initial assessment and support

The initial assessment and support for a patient who presents at primary care with new onset of respiratory or allergic symptoms or persistent debilitating symptoms (with a history of exposure to indoor damp or mould) should follow usual clinical practice. The Clinical Pathway is to assist GPs and medical professionals with the diagnosis and management of patients who are assessed to be clinically stable.

2.1. Follow usual clinical assessment practice including a history of exposure to indoor damp or mould

Initial assessment and support should include the following steps:

- In the clinical examination of an acute case, specifically check the mucosa of the eyes, upper airways (as far as possible) as well as the skin. Patients who report being exposed to indoor damp and mould often complain about non-specific symptoms that relate to these organs.
- From the history and examination, exclude obvious acute illnesses or chronic diagnosable conditions.
- Treat obvious diagnosable conditions.
- Provide clinical advice to assist patient with symptom management, including avoiding/minimising exposure to indoor damp and mould, while investigating any differential diagnoses or symptoms.
- Arrange referral and follow-up and/or other care as required.

If a person presents with symptoms that suggest the possibility of health effects that have been shown to be associated with exposure to indoor damp and mould, explore how long the person has had the symptoms and their history of possible exposure to indoor damp or mould.

2.1.1. Clinical advice for medical professionals to identify an association between fungus exposure and increased symptoms

In general, patients seek medical advice from exposure to mould for several reasons indicated below:

- They experience health problems, the circumstances of which suggest an environmental-related link to moisture damage and/or mould exposure (Larenas-Linnemann et al., 2016; Wiesmüller et al., 2017).
- They seek care for medical conditions that subsequently turn out to be triggered, at least in part, by fungi (Larenas-Linnemann et al., 2016).
- They have mood disorders and non-specific symptoms for which there is a clear temporal relationship to certain environmental or ambient conditions or activities (Wiesmüller et al., 2017).

- They are concerned about possible exposure to mould [and damp] and health effects from exposure to mould [and damp] that they have observed in their house (Larenas-Linnemann et al., 2016; Wiesmüller et al., 2017).
- Measurements are already available (Wiesmüller et al., 2017).
- Medical support is sought in rental and construction disputes (Wiesmüller et al., 2017).

Medical history and physical examination are the basic elements of any diagnostic work-up. Association of fungal exposure with increased symptoms of allergic rhinitis, asthma and atopic dermatitis is well established (Larenas-Linnemann et al., 2016). Noting this, Larenas-Linnemann et al. advised the clinical evaluation of a patient with any one of these conditions is the same regardless of the patient's fungus sensitivity, beginning with eliciting a history consistent with increased symptoms that are triggered by exposure to the suspected allergen (Larenas-Linnemann et al., 2016).

The AWMF guideline advises taking the medical history should involve a holistic approach, including the psychosocial dimension as well as environmental exposure and aspects of physical disease. The guideline notes giving equal priority to the psychological and social aspects rarely produces difficulties in the consultation setting once the approach has been explained to the patient (Wiesmüller et al., 2017).

In addition to the general and differential diagnostic history, the following elements should be considered while taking the medical history in the case of suspected health conditions due to mould:

- history of exposure in the home, in the workplace and during leisure time
- history of infections, including predisposing factors
- history of allergies, including predisposing factors
- history about irritant toxic effects
- history about mould odours
- history about mood disorders (Wiesmüller et al., 2017).

Indoor environments that have high fungal exposure usually also have increased moisture content such as in a basement or other damp environment (Larenas-Linnemann et al., 2016). Additionally, old buildings were noted as often experiencing moisture problems that may result in fungal growth. As such Larenas-Linneman et al. advises 'it is helpful to ask if symptoms increase in the presence of dampness, visible mould in the home, and a mouldy odour'. They mentioned this question is necessarily non-specific, noting old buildings often have multiple air quality issues such as rodent and cockroach infestations, lack of ventilation and increased particle counts due to decaying organic material that can trigger symptoms (Larenas-Linnemann et al., 2016). Questions about whether there is visible mould and whether there is a mouldy smell have been shown to correspond to health effects from fungi (Larenas-Linnemann et al., 2016).

2.1.2. Identify susceptible people

People with a pre-existing health condition may be vulnerable to ill-health as a result of exposure to indoor damp or mould or poor indoor air quality, including mould (American Industrial Hygiene Association Indoor Environment Quality Committee, 2020; Environmental Health Standing Committee (enHealth) of the Australian Health Protection Principal

Committee, 2021; Hurraß et al., 2017; National Institute for Health Care and Excellence, 2020a; Wiesmüller et al., 2017).

enHealth advises people with weakened immune systems, allergies, severe asthma or lung diseases are more likely to experience symptoms triggered by breathing in mould spores and fragments, as well as being more susceptible to other serious health effects, such as the lung condition aspergillosis ('Farmer's lung') (Environmental Health Standing Committee (enHealth) of the Australian Health Protection Principal Committee, 2021).

The AWMF guideline advised at risk groups warranting particular protection include individuals on immunosuppression, individuals with CF, and individuals with bronchial asthma (Wiesmüller et al., 2017). The evidence review underpinning the AWMF guideline notes the medical history should identify the most vulnerable and sensitive persons like immunocompromised individuals, allergic (atopic) persons and individuals with pre-existing pulmonary diseases like asthma, COPD, and CF (Hurraß et al., 2017). Mould-allergic patients and patients with a weakened immune system should be provided with specialist patient information about the hazards of indoor mould exposure and preventative steps they can take to minimise exposure (see also [section 1.2.4](#) for further details on 'Individuals and patients at risk of health effects due to indoor damp and mould or other factors associated with indoor air quality') (Wiesmüller et al., 2017).

2.1.3. Clinical examination

The target organs noted in the medical history should be prioritised in the physical examination, with particular attention paid to the mucosa of the eyes, and, as far as possible, upper airways, as well as to the skin (Wiesmüller et al., 2017). This is because the non-specific symptoms that patients often complain relate to these organs in particular (Wiesmüller et al., 2017). The physical examination should follow usual clinical practice, including being performed in a structured and standardised manner and be well-documented (Wiesmüller et al., 2017).

2.1.4. Provide advice on avoiding or minimising exposure to indoor damp or mould, while investigating any differential diagnosis

Australian and international advice is consistent in that exposure to indoor mould should be minimised or avoided, and dampness and mould-related problems should be prevented and, when present, remediated, even in the absence of health effects/symptoms (Denning & Chakrabarti, 2017; Environmental Health Standing Committee (enHealth) of the Australian Health Protection Principal Committee, 2021; Hurraß et al., 2017; Larenas-Linnemann et al., 2016; Wiesmüller et al., 2017).

2.1.4.1. Official Australian advice (enHealth)

Provide patients with a hard copy handout of the enHealth factsheet on potential health effects of mould in the environment. The enHealth factsheet (Environmental Health Standing Committee (enHealth) of the Australian Health Protection Principal Committee, 2021) is provided at [Appendix D](#). It is available on the Department's website at

<https://www.health.gov.au/resources/publications/enhealth-guidance-potential-health-effects-of-mould-in-the-environment>.

enHealth factsheet includes the following advice:

- Dampness and mould related problems should be prevented. When they occur, they should be rectified – remove mould where present, find it when you smell it, repair and control sources of excessive moisture – this is the best approach for controlling potential health risks.
- There is no exposure limit or health guideline value for exposure to mould³. Where possible, exposure to mould should be minimised – this is particularly recommended for people who are more sensitive to mould exposure.
- Although mould naturally occurs in the environment and can be found almost anywhere, it requires damp surfaces and moisture to grow. People can reduce their exposure through simple measures, however there is no practical way to eliminate all exposure to mould.
- Indoors, people should: prevent moisture and dampness and ensure adequate ventilation – this will minimise current and future mould growth; fix leaky plumbing, roofs and other building faults; clear and maintain gutters; and reduce and remove condensation (e.g., use exhaust fans and wipe up excess water).
- Homes with inadequate ventilation resulting from poor design, modifications or lack of maintenance may be more prone to developing mould. The cheapest and easiest way of reducing indoor moisture and humidity is by ventilating a room by opening a door or window.

2.1.4.2. enHealth advice on how to remove mould from a home

enHealth advice is that if a person can see or smell mould (often a dirty or earthy smell), they need to clean it up as mould can damage surfaces it grows on and affect their health. If the person decides to remove the mould themselves, make sure there is good ventilation and wear protective clothing. For example, wear a shower cap and use gloves, eye protection, overalls, suitable footwear, and a P1 or P2⁴ face mask (Environmental Health Standing Committee (enHealth) of the Australian Health Protection Principal Committee, 2021).

Household detergent or white vinegar is usually sufficient to clean the mould. Use a microfibre cloth and rinse the dirty cloth regularly in a separate container of clean water to prevent spreading the mould. DO NOT dry brush the mould area, as the brush can flick spores into the air where they may be breathed in. Contaminated soft furnishings may be difficult to clean and may need to be thrown away.

If there are large areas of mould or mould regrowth, people should consult a remediation professional. Some mould may not be visible as it might be in a roof space, behind a wall or under floor coverings, so people may need to consult a professional if they can smell but can't see it (Environmental Health Standing Committee (enHealth) of the Australian Health

³ Mould assessment typically contrasts ambient outdoor spore concentrations with indoor concentrations when investigating potential issues.

⁴ P2 face mask is recommended for people who have a pre-existing health condition as they may be vulnerable to ill-health as a result of exposure to indoor damp or mould or poor indoor air quality, including mould.

Protection Principal Committee, 2021). enHealth advises people that occupational hygienists provide consultancy services at a fee to remove mould, locate mould by inspections (if it can be smelled but not seen), or to find a solution. Australian occupational hygienists can be found at <https://www.aioh.org.au/resources/consultants/>.

Separately to this Clinical Pathway, the Australian Government (Australian Government, 2020) is addressing issues of the prevalence of dampness and mould in the built environment; and testing and remediation of buildings affected by water damage and/or mould as part of other key recommendations from the Report (House of Representatives Standing Committee on Health, Aged Care and Sport, 2018).

2.1.4.3. **International advice**

Evidence from key international literature advocates for a remediation of premises as a preventive or therapeutic measure regardless of the suspected health effects, even in the absence of health effects (Denning & Chakrabarti, 2017; Hurraß et al., 2017; Wiesmüller et al., 2017). Specifically, several of these key pieces of international literature recommend minimisation or avoidance of exposure for those with asthma, allergy, other fungal sensitivities or immunocompromised individuals (Denning & Chakrabarti, 2017; Hurraß et al., 2017; Larenas-Linnemann et al., 2016; Wiesmüller et al., 2017).

The abridged AWMF guidelines (Wiesmüller et al., 2017) recommend remediation of buildings for all suspected symptoms and illness from exposure to indoor damp or mould:

Even if no causal link can be established between symptoms/findings/disorders and the occurrence of indoor mould/dampness, the first “therapeutic” measure to be undertaken from a preventive and hygienic perspective in the case of dampness/mould damage is prompt appropriate and professional remediation; moreover, in the case of severe clinical pictures associated with high risk (immune suppression, cystic fibrosis, asthma) immediate minimization of exposure needs to be achieved. (Wiesmüller et al., 2017, p. 185)

As with all allergic diseases, exposure avoidance (allergen avoidance) takes priority. Nevertheless, prompt medication is required in order that a symptom-free period is not followed by full-blown allergic disease. It is of paramount importance to eliminate the causes of the dampness creating a basis for indoor mould growth. (Wiesmüller et al., 2017, p. 185)

The review by Hurraß et al. associated with the AWMF guideline reported it important to address water damage even if no health problems were present:

From a health care point of view, moisture damage and/or mold growth indoors are always a hygienic problem that – even without present health disorders – must not be tolerated and therefore must be precautionary minimized or terminated if possible. The most important preventive measure for indoor mold exposure is to identify the cause of the moisture/water damage and the proper remediation (Hurraß et al., 2017, p. 307).

2.1.5. **Mould testing and mould testing reports**

International and Australian guidance concurs that where mould is visible it is not generally necessary to test for it in the home (Environmental Health Standing Committee (enHealth) of the Australian Health Protection Principal Committee, 2021; Wiesmüller et al., 2017).

EnHealth advises, that generally, testing for mould is not recommended at all because there

are no health guideline values for which to compare test results to, meaning that test results cannot be used to determine if a health risk exists. “Mould is everywhere, so if you go testing for it, you will find it” (Environmental Health Standing Committee (enHealth) of the Australian Health Protection Principal Committee, 2021). In certain circumstances, enHealth recommends consulting an occupational hygienist to evaluate whether a property has a potential indoor damp or mould problem (e.g., identification of hidden mould). These professionals may utilise mould sampling methods consistent with international best practice^{5,6}.

The AWMF guideline advises that, as a rule, there is no medical indication to determine mould indoors, in building materials or fixtures. For visible mould infestation, increased moisture levels in materials or structural abnormalities (moisture or water damage), the identification of indoor mould is not indicated from a diagnostic or therapeutic perspective (Wiesmüller et al., 2017). From a medical perspective, a visual inspection of mould infestation is sufficient to initiate medically justified measures. The greatest relevance is attributed to site visits, which are ideally performed by a physician or experts with structural expertise (Wiesmüller et al., 2017).

The US Centers for Disease Control and Prevention (CDC) does not recommend environmental testing for moulds or evaluation of patients for mycotoxin-related disease, even in those who live or work in WDBs, in part because of lack of clinical relevance to these tests (Chang & Gershwin, 2019).

Of note, an indoor air quality testing procedure exists in Australia called the ‘Environmental Relative Moldiness Index (ERMI)’. This test was developed by the US Environmental Protection Agency (EPA). However, the EPA issued updated information in 2021, confirming that ERMI is not suitable for use in diagnosing mould in premises, and the EPA does not recommend the routine public use of ERMI in homes, schools, or other buildings⁷. The submissions to the House of Representatives Inquiry also reported that numerous issues exist in relation to ERMI being used as a reliable, validated diagnostic test for mould outside a research environment.

2.1.6. Precautionary advice about linking mould to allergic diseases

Penicillium sensitisation has been linked to indoor allergen exposure, particularly in humid mouldy environments and after floods, while data related to *Aspergillus* and *Candida* suggests these species have a possible role as allergens (Larenas-Linnemann et al., 2016). While convincing data are lacking for other allergy-causing fungi other than *Alternaria*, *Cladosporium*, *Penicillium*, *Aspergillus*, and *Candida*, it does not mean that they do not exist (Larenas-Linnemann et al., 2016).

It is easy for mould to be blamed when a patient sees grey, brown or black stains on sheetrock or plasterboard and they develop symptoms consistent with allergic disease such

⁵ Green Book - Recognition Evaluation and Control of Indoor Mold 2nd edition

⁶ ASTM-D7338-Assessment-Of-Fungal-Growth-in-Buildings

⁷ United States Environmental Protection Agency. (2021). ERMI factsheet. <https://www.epa.gov/air-research/environmental-relative-moldiness-index-ermi>

as allergic rhinitis or asthma (Chang & Gershwin, 2019). However, with a few exceptions there has been no evidence that visible mould correlates with fungal spores in the air. Additionally, many of the symptoms do not match the disease (Chang & Gershwin, 2019).

Chang and Gershwin provide the following example of a differential diagnosis.

If someone presents with headache, it is unlikely to be allergic in nature, as headache is simply not a symptom of allergy (Chang & Gershwin, 2019). If the patient is truly suffering from allergic rhinitis, the differential diagnosis includes chronic rhinitis, non-allergic rhinitis with eosinophilia (NARES), anatomical issues, cholinergic or gustatory rhinitis, and many other conditions. If the patient is complaining of headache and vague symptomology, for example loss of concentration or memory loss, then “allergic diseases should not even be in the differential diagnosis” (Chang & Gershwin, 2019, p. 450).

Chang and Gershwin (Chang & Gershwin, 2019) added more context and explanation to this issue, with the concepts also highlighted by the AWMF guideline (Wiesmüller et al., 2017). Even if there is visible mould this does not mean that the mould is what is causing the disease and to assume a patient is mould allergic or suffers from any type of mould-allergic disease just because there is mould in the home “is profoundly unscientific” (Chang & Gershwin, 2019, p. 450).

Larenas-Linnemann et al. in the CME Category 1 clinical commentary review advised that patients who have observed mould/fungi in their home and consequently believe that they have symptoms caused by mould/fungus exposure will, in many cases, display confirmatory bias in their history (Larenas-Linnemann et al., 2016). As such, they advised it is important to determine whether the patient had symptoms first and then concluded that fungi in the home must be causing them or whether the patient first observed the fungi and then looked for symptoms that have occurred as a result. The temporal ordering can provide an insight into the role of psychological bias in the development of clinical symptoms (Larenas-Linnemann et al., 2016). Larenas-Linnemann et al. further advised that it may be helpful to ask such patients why they believe that fungi are causing the symptoms and how they came to their belief. In the initial stages of evaluation it is important to accept patients’ statements and not to contradict their beliefs until a more trusting relationship has been established (Larenas-Linnemann et al., 2016).

It is recommended that medical practitioners keep an open mind when patients speak of symptoms associated with indoor damp or mould. While the patient may have other underlying medical issues brought to light at the time of the exposure, a considered investigation of the whole clinical history is indicated.

2.1.7. Advice on managing discussions about SBS or TMS in presenting patients

Larenas-Linnemann et al. advise patients who present with concerns about fungi may refer to an illness caused by “toxic mould” or “black mould” or that they or their family may have been harmed by exposure to mycotoxins.

These patients should be evaluated in the same way as any other patient who has symptoms (Larenas-Linnemann et al., 2016). Following this evaluation and provided no cause of the symptoms has been identified, they advise it may help to have a frank discussion about the evidence (or lack thereof) for TMS. In their experience, patients who are honestly seeking

information about their illness will usually respond favourably to this approach. However, patients who hold a pre-existing belief that exposure to mould has caused harm pose additional challenges. Patients with this belief are often unwilling to accept any conclusion other than which they already have, and in some cases are seeking confirmation or validation of their beliefs (Larenas-Linnemann et al., 2016). In such cases, the best approach is to provide the best information that is available about what is and what is not known about the health effects of exposure to fungi and avoid causing harm by doing unnecessary tests or treatment. The advice further notes that “by engaging in this type of discussion, it is possible that reason will prevail” (Larenas-Linnemann et al., 2016).

2.2. Consult with and refer to appropriate experts in relevant medical specialty to provide multi-disciplinary care

On the basis of medical history and physical examination further special investigations are performed within the relevant medical speciality, depending on the diagnostic question and differential diagnosis (Wiesmüller et al., 2017).

Adopt a multidisciplinary approach to patient care, involving general practitioners (GP), and where necessary, non-GP specialists such as general physicians, respiratory physicians, infectious diseases (ID) physicians, clinical allergists, clinical immunologists, occupational and environmental physicians, and psychiatrists. The multidisciplinary approach to patient care also involves allied health and non-medical health professionals, including occupational health nurses.

Follow the Australian Asthma Handbook, available at <https://www.astmahandbook.org.au/> (National Asthma Council Australia, 2022) for the diagnosis and management of patients with suspected asthma. The reported symptomology of so called CIRS in relation to WDBs includes respiratory symptoms, and thus overlaps with the symptomology of asthma.

The action plan of the 2015 National Allergy Strategy (Australian Society of Clinical Immunology and Allergy & Allergy & Anaphylaxis Australia, 2015) advises that accurate diagnosis is essential, and requires appropriate specialist care, and that a shared care model for allergy management is considered optimal:

There is increasing evidence that multidisciplinary team-based healthcare contributes to improved health outcomes. This evidence also indicates that a multidisciplinary approach improves the consumer experience of care and reduces the need for hospital and emergency care which is expensive and avoidable. (Australian Society of Clinical Immunology and Allergy & Allergy & Anaphylaxis Australia, 2015, p. 35)

Methods for the diagnosis and management of fungus-allergic patients should follow the same clinical pathways used for patients with allergic conditions in general (Larenas-Linnemann et al., 2016).

3. Differential diagnosis

The AWMF guideline advises the differential diagnosis always takes priority when assessing the health effects of exposure to mould (Wiesmüller et al., 2017). As the effect of mould is influenced by personal susceptibility, any delay in taking steps (for example, delay caused through mould determination efforts), may increase risk for persons requiring particular protection from mould. Risk groups warranting particular attention include immunosuppressed individuals and individuals with CF (mucoviscidosis) or bronchial asthma (Wiesmüller et al., 2017).

3.1. Differential diagnoses or symptoms for which a sufficient level of evidence exists for an association with exposure to indoor damp and mould

3.1.1 Asthma, respiratory infections, rhinitis, wheeze, cough, dyspnoea, bronchitis, upper respiratory tract symptoms, and eczema

As mentioned in [section 1.3.1](#) there are health effects for which a sufficient level of evidence exists for an association with exposure to indoor damp and mould. These health effects include asthma (development, current, exacerbation), respiratory infections, rhinitis, wheeze, cough, dyspnoea, bronchitis, upper respiratory tract symptoms, eczema, and HP, mycoses and allergic effects in susceptible people. An overview of the epidemiological evidence on exposure to indoor damp and mould, and these health effects or symptoms for which a sufficient level of evidence exists, is provided in [Appendix A](#).

Further advice on diagnosis of asthma is provided later in this document:

- For advice on diagnostic testing for asthma, see [section 4.1](#) and sections [4.1.1](#) to [4.1.4](#).
- For advice on the diagnosis of asthma, see [section 5.1](#) and sections [5.1.1](#) to [5.1.5](#).
- For advice on the initial management of asthma, see [section 6.2.1](#).
- For advice on the ongoing management of asthma, see [section 7.1.1](#).

3.1.2. Hypersensitivity pneumonitis (HP), mould-related infections and allergic health effects in susceptible people

As mentioned earlier, there is sufficient evidence for an association between HP, mycoses and allergic effects in susceptible people and exposure to indoor damp and mould. The sections below on HP, mould-related infections and allergic health effects in susceptible people contain both clinical and epidemiological information. The information is included to assist GPs and other medical practitioners when considering these health effects as differential diagnoses in susceptible people who report being exposed to indoor damp and/or mould.

3.1.2.1. HP

HP, also called 'extrinsic allergic alveolitis', is an interstitial granulomatous, cell-mediated lung inflammation. HP is caused by repeated inhalation of antigens from microorganisms or other sources in susceptible people (American Lung Association et al., 2014; Borchers et al., 2017; Mendell et al., 2011; Park & Cox-Ganser, 2011). Many different fungi, bacteria, animal proteins, plants, and chemicals are known causes of HP (National Institute for Occupational Safety and Health et al., 2012). The antigens that can cause HP are found in dust and aerosols mixed with possible microbially contaminated sources (for example, microbes from birds, feathers, hay, wood dust, air humidifiers, air conditioning systems, indoor fountains, aquariums and steam irons). Most commonly, these antigens come from birds, mould and Actinomycetes (Wiesmüller et al., 2017). The most frequent causal antigens for HP are bird proteins and bacteria such as thermophilic actinomycetes. However, fungi have also been implicated in both occupational and non-occupational outbreaks (Baxi et al., 2016).

Characteristics of the antigens, individual susceptibility, and gene-environment interactions are all important factors working together in HP. Genetic susceptibility is also an important factor for HP (Park & Cox-Ganser, 2011). HP may affect from 1–5% or more of a specialised population (for example, farmers and pigeon breeders because it can cause farmer's lung and pigeon breeder's disease) exposed to appropriate antigens (American Lung Association et al., 2014). The prevalence of HP in the general population is unknown (American Lung Association et al., 2014), but is noted by the CDC to be rare (Park & Cox-Ganser, 2011).

Two guidelines (Wiesmüller et al., 2017; World Health Organization, 2009) and three evidence reviews (Hurraß et al., 2017; Palaty & Shum, 2012; Park & Cox-Ganser, 2011), advised that, in susceptible people, sufficient evidence exists for an association between indoor damp or mould and HP. The association is based on clinical, not epidemiological evidence (Mendell et al., 2011; Wiesmüller et al., 2017; World Health Organization, 2009). Current knowledge is based on outbreak investigations and limited epidemiology, mostly in industrial and agricultural settings, but also in office buildings (Mendell et al., 2011).

Several international authority reports and an evidence review acknowledged the role of damp in office buildings, homes or air conditioning and humidification systems and the development of HP (American Industrial Hygiene Association Indoor Environment Quality Committee, 2018; American Lung Association et al., 2014; Borchers et al., 2017; National Institute for Occupational Safety and Health et al., 2012; Park & Cox-Ganser, 2011). There is also advice on air conditioning and humidification systems contaminated with bacteria and moulds. Regarding this the CDC noted HP has been recognised for decades among occupants of residential and office buildings with contaminated heated-water reservoirs, humidifiers, cool-mist vaporisers, wooden water buckets, water flume slides, and water-damaged carpets (Park & Cox-Ganser, 2011). Borchers et al. also noted an increasing number of reports linking other types of household or office mould exposure to the development of HP, including humidifier lung from humidifiers, dehumidifiers, or contaminated air conditioners (Borchers et al., 2017). The American Lung Association, American Medical Association, EPA, and the Consumer Product Safety Commission noted outbreaks of HP in office buildings have been traced to air conditioning and humidification systems contaminated with bacteria and moulds (American Lung Association et al., 2014). Within the home environment, HP has been often caused by contaminated humidifiers or by pigeon or pet bird antigens (American Lung Association et al., 2014).

3.1.2.2. Clinical presentation of HP and potential for misdiagnosis

While the presentation of HP is traditionally subdivided into acute, sub-acute and chronic, considerable overlap in these forms of presentation has been increasingly recognised; a computed tomography (CT) scan can be used to identify these forms (Borchers et al., 2017). The clinical course of the disease is variable and its diagnosis is difficult since no specific test or biomarker provides a consistent diagnosis (Baxi et al., 2016). When fungi are involved, HP is characterised by the presence of precipitating immunoglobulin G (IgG) antibodies directed at the fungus (Baxi et al., 2016).

The clinical presentations and characteristics of HP include the following:

- HP can mimic a respiratory infection (National Institute for Occupational Safety and Health et al., 2012)
- There are two symptom patterns in HP:
 - Some individuals experience acute disease symptoms of episodic shortness of breath and flu-like symptoms, including cough, muscle aches, fever, chills, sweating, and fatigue, that start within four to six hours of exposure (American Lung Association et al., 2014; National Institute for Occupational Safety and Health et al., 2012). These symptoms may last for one to three days if there is no further exposure (National Institute for Occupational Safety and Health et al., 2012). It is very important to recognise this disease in its earliest stages, when antigen removal is often sufficient for recovery (Borchers et al., 2017). Acute HP may show pulmonary oedema on a CT scan (Borchers et al., 2017). Individuals with HP may be at risk for progression to more severe disease if the relationship between illness and exposure to the damp building is not recognised and exposures continue (National Institute for Occupational Safety and Health et al., 2012).
 - Other individuals develop gradual and progressive shortness of breath and cough, often accompanied by weight loss (National Institute for Occupational Safety and Health et al., 2012). Where antigen exposure continues, chronic HP with irreversible pulmonary fibrosis can develop. Chronic HP usually demonstrates bronchiectasis or signs of pulmonary fibrosis such as reticulation on CT scan (Borchers et al., 2017).
- The first signs that the illness is due to exposures in a damp building may be: 'improvement in symptoms and medical tests during a period of time away from the building and worsening on return' (National Institute for Occupational Safety and Health et al., 2012).

HP is frequently misdiagnosed as a pneumonia of infectious aetiology (American Lung Association et al., 2014). The sub-acute and acute forms of the disease may imitate any interstitial lung disease. The sub-acute form may be misdiagnosed as sarcoidosis, tuberculosis, or histoplasmosis, and the chronic form may be misdiagnosed as idiopathic pulmonary fibrosis (Park & Cox-Ganser, 2011). Relationships of duration and intensity of exposure to different clinical forms of HP are currently not understood (Park & Cox-Ganser, 2011).

Organic dust toxic syndrome is an acute, systemic flu-like disease caused by the inhalation of high concentrations of bioaerosols found almost exclusively in workplaces. Organic dust toxic syndrome is significantly more common than HP from which it is sometimes difficult to distinguish diagnostically (Wiesmüller et al., 2017).

Further advice on diagnosis of HP is provided later in this document:

- See [section 4.4](#) on 'HP diagnostics' and [section 4.3.1.3](#) on 'Mould-specific IgG determination is only recommended for suspected allergic bronchopulmonary aspergillosis (ABPA) or HP'.
- See [section 4.3.1.4](#) on 'Diagnostic tests for specific disorders' and [section 5.4](#) on diagnosis of 'HP'.
- See [section 7.2](#) on ongoing management of patients with 'HP, mould-related infections and allergic conditions in susceptible people'.

3.1.2.3. Allergic bronchopulmonary aspergillosis (ABPA) and allergic fungal sinusitis or rhinosinusitis (AFRS) in susceptible people

ABPA is a rare immunological lung disease involving hypersensitivity to *Aspergillus fumigatus* antigens (Borchers et al., 2017; Hurraß et al., 2017; Wiesmüller et al., 2017). While rare, it is one of the most severe fungus-induced allergic diseases and occurs in patients with asthma, CF, or COPD (Borchers et al., 2017). It is caused by the inhalation of *Aspergillus* spores that then trigger an immunological reaction (Wiesmüller et al., 2017). There is no evidence that indoor dampness or exposure to mould is associated with ABPA (Borchers et al., 2017; Hurraß et al., 2017). However, it is probable that mould exposures may induce symptoms or possibly modify prognosis for ABPA patients (Hurraß et al., 2017).

A clinical entity similar to ABPA, called 'allergic bronchopulmonary mycosis (ABPM)' is caused by several other fungi (not *Aspergillus*) and appears to be associated with asthma much less frequently than ABPA (Borchers et al., 2017).

The clinical presentation of ABPA includes cough, worsening asthma, haemoptysis and tenacious mucous leading to mucous plugging. ABPA should be considered if more than two of the following criteria are met: CF; bronchial asthma; eosinophilia of unknown aetiology; volatile antibiotic-resistant infiltrates; acquired central bronchiectasis; *Aspergillus* detection in sputum; expectoration of brownish mucous plugs; or delayed cutaneous reaction to *Aspergillus* (Wiesmüller et al., 2017).

Moulds can trigger chronic inflammation of the nasal and paranasal sinus mucosa via a number of mechanisms. AFRS is a localised hypersensitivity reaction similar to that seen in patients with ABPA. AFRS occurs when fungi colonise the sinuses of patients that have underlying allergic disease and impaired tissue drainage (Borchers et al., 2017). *A. fumigatus* is the most frequently isolated mould species associated with AFRS, however other fungal species can cause AFRS (Borchers et al., 2017).

There are five forms of rhinosinusitis triggered by fungi. These are:

- acute invasive (including rhinocerebral mucormycosis)
- chronic invasive
- granulomatous invasive
- non-invasive AFRS without spherical mycetoma formation
- non-invasive AFRS with spherical mycetoma formation (Hurraß et al., 2017; Wiesmüller et al., 2017).

Invasive forms of rhinosinusitis are more prevalent in severely immunocompromised patients (e.g., patients with AIDS, diabetes, patients on chemotherapy) and can cause death within a matter of weeks in acute cases (Hurraß et al., 2017; Wiesmüller et al., 2017). In contrast, the chronic invasive form follows a protracted course with immunocompromised patients predominantly affected (Hurraß et al., 2017; Wiesmüller et al., 2017).

Fungal colonisation of the lungs is common in patients with asthma, CF, or COPD. Fungal colonisation in the sinuses is seen in the vast majority of healthy people (Borchers et al., 2017; Wiesmüller et al., 2017). However, only some of these people develop ABPA or AFRS (Borchers et al., 2017). Currently the reasons for this are unclear and genetic or other predisposing factors are likely to play a major role (Borchers et al., 2017).

A. fumigatus is a common outdoor mould even though it has been associated with building moisture in some studies. Most of the moulds implicated in ABPM and AFRS are found primarily outdoors or detected with near equal frequency in outdoor and indoor environments. As such, there is no evidence to conclusively link indoor mould exposure to the development of ABPA, ABPM, or AFRS (Borchers et al., 2017).

Further advice on diagnostics and management of mould-related allergic conditions is provided later in this document:

- See [section 4.3](#) on 'Mould allergy diagnostics' and [section 5.2](#) on the diagnosis of 'Mould allergy'.
- See [section 6.2.2](#) on the initial management of 'Mould allergy'.
- See [section 7.2](#) on the ongoing management of patients with 'HP, mould-related infections and allergic conditions in susceptible people'.

3.1.2.4. Mycoses (mould-related infections) in susceptible people

The WHO advised there is sufficient evidence of an association with mould infections in susceptible people [and humidifier fever and inhalation fevers]. This association was based primarily on clinical evidence, not epidemiological evidence, and was the only conclusion that referred explicitly to microbial agents, not dampness and mould (World Health Organization, 2009).

Mould-related mycoses (infections caused by environmental fungi) in susceptible patients are usually acquired via the airways. The most common primary site of infection is the lung, with the paranasal sinuses, ear or injured skin more rarely being primary sites (Wiesmüller et al., 2017).

Aspergillus appears to be the most aggressive of these fungi, giving rise to infections also in patients with less severe airway disease, such as CF, asthma and COPD (World Health Organization, 2009). People who are atopic can on occasion contract a severe infection in which aspergillosis causes an allergic reaction with the infection, giving the person wheeze, pulmonary infiltrates and eventually fibrosis (Kauffman 2003 in World Health Organization, 2009). This syndrome can also be found with an aspergilloma (i.e., a tumour in a lung cavity consisting of *Aspergillus* hyphae) (Tanaka 2004 in World Health Organization, 2009). Chronic pulmonary aspergillosis can occur in people with an intact immune system and also in patients who have pre-existing lung disease, such as tuberculosis, non-tuberculous mycobacterial disease, COPD, pneumothorax, asthma, or sarcoidosis (Borchers et al., 2017). Aspergilloma (mycetoma or fungus ball), is a localised form of aspergillosis that

generally develops in preformed cavities such as the paranasal sinuses or lungs. This can occur due to a build-up of mould mycelia, with predisposing factors including caverns secondary to tuberculosis, bronchiectasis and malignant disease (Hurraß et al., 2017; Wiesmüller et al., 2017).

Invasive *Aspergillus* infections are an important cause of morbidity and mortality in immunodeficient patients (Hurraß et al., 2017; Wiesmüller et al., 2017). It is associated with high mortality rates of between 30–95% in more than 200,000 annual cases of life-threatening *Aspergillus* infection globally (Wiesmüller et al., 2017). In developed countries, fungal infections such as mucormycosis occurs primarily in severely immunocompromised patients (e.g., those with haematological malignancies, organ transplantation, neutropenia, autoimmune disorders, or other impairments in immunity). Only 6–10% of cases occur in people with no underlying disease (Reid et al., 2020).

Infection with *Aspergillus* and other fungi such as *Fusarium* spp. was a well-known complication in the treatment of patients who are immune compromised (for example, due to cancer treatment or infection with human immunodeficiency virus) (Iwen et al. 1994, 1998; Geisler & Corey 2002; Lednicky & Rayner 2006 in World Health Organization, 2009). Fungal infections have increased in recent years and high incidence rates are seen particularly in haemato-oncological patients with long phases of neutropenia, as well as in recipients of allogeneic stem cell transplantation. Other forms of immunosuppression, such as prolonged corticosteroid use and interstitial lung disease (including residual cavitation, e.g., following tuberculosis) as well as a combination of these factors, especially in COPD, have also been linked to increased mould infection rates (Wiesmüller et al., 2017).

However, the WHO advises that some of these patients contract mould infection after exposure indoors. This does not occur because of water damage in the facilities (where they are being treated) but because an opportunistic, ubiquitous mould finds a suitable host (World Health Organization, 2009). At the time, the WHO noted that no studies have been conducted to link such infections to mould in the indoor environment. Additionally, the type of disease appears to determine the type of infection and the infecting agents are not those typically encountered in damp houses (World Health Organization, 2009).

People with atopy have been reported to sometimes develop sinus disease as a consequence of *Aspergillus* infection (Dufour et al. 2006 in World Health Organization, 2009). Exposure to mould has been proposed as the cause of chronic sinusitis. These patients are reported to show exaggerated humoral and cellular responses (both type 1 T helper (TH-1) and type 2 T helper (TH-2)) to common airborne fungi, particularly *Alternaria* (Shin et al. 2004 in World Health Organization, 2009).

As such, at risk patients require individualised medical advice regarding risk of infection upon exposure to indoor mould and preventive measures (Wiesmüller et al., 2017).

Further information on diagnosis and management of mould-related infections is provided later in this document:

- See [section 5.3](#) on the diagnosis of 'Mould-related infection'.
- See [section 6.2.3](#) on the initial management of 'Mould-related infection'.
- See [section 7.2](#) on the ongoing management of patients with 'HP, mould-related infections and allergic conditions in susceptible people'.

3.2. Patients presenting with persistent debilitating symptoms and no diagnosis

This section and its subsection are aligned with the Australian Government Department of Health DSCATT Clinical Pathway, published in October 2020. The guidance can be applied when considering an alternative diagnosis for patients with unresolved debilitating symptoms with a history of exposure to indoor damp or mould, and where symptoms are not associated with asthma, respiratory or allergic conditions.

3.2.1. If a health effect associated with exposure to indoor damp or mould is not suspected, consider alternative diagnoses

Take care to identify any potentially treatable illness.

The identification of MUS, including in patients with unresolved debilitating symptoms with a history of exposure to indoor damp or mould and that cannot be attributed to another diagnosable condition, is one of exclusion. These patients require ongoing review as new symptoms arise or treatments are trialled. A full history and examination are critical.

A clue to the underlying cause may be found in the particular symptom cluster, time course of symptoms, family history, social history, medications, travel or occupation.

Develop a differential diagnosis with consideration of the following causes:

- infectious – including blood-borne or sexually transmitted infections, vector-borne diseases, travel related, food and water-borne
- autoimmune – including inflammatory arthritis, motor neurone disease, multiple sclerosis
- neoplastic
- psychological – including depression, anxiety and reactions to traumatic events
- inflammatory
- vascular
- neurological
- cardio-respiratory
- lifestyle related – including diet, exercise, sleep and stress.

4. Diagnostic testing

4.1. Asthma

Follow the Australian national guidelines in the Australian Asthma Handbook (National Asthma Council Australia, 2022) for diagnostic testing and clinical considerations for diagnosing asthma in adults, adolescents and children.

4.1.1. Adults

In adults, asthma is defined clinically as the combination of variable respiratory symptoms (e.g., wheeze, shortness of breath, cough and chest tightness) and excessive variation in lung function.

Refer to Clinical processes and considerations for diagnosing asthma in adults and adolescents at:

- <https://www.astmahandbook.org.au/diagnosis/adults>
- <https://www.astmahandbook.org.au/diagnosis/adults/initial-investigations>.

4.1.2. Adolescents

Refer to Special considerations for asthma diagnosis and management in adolescents and young adults at: <https://www.astmahandbook.org.au/diagnosis/adolescents>.

For appropriate investigations, follow the recommendations at:

<https://www.astmahandbook.org.au/diagnosis/adolescents/investigations>.

4.1.3. Children aged 1+ year

Follow the Australian Asthma Handbook (National Asthma Council Australia, 2022) for clinical processes and considerations for investigating wheezing and diagnosing asthma in children; <https://www.astmahandbook.org.au/diagnosis/children>.

There is no single reliable test ('gold standard') and there are no standardised diagnostic criteria for asthma.

4.1.4. Infants aged zero to 12 months

The Australian Asthma Handbook (<https://www.astmahandbook.org.au/diagnosis/children>) advises the following for infants aged zero to 12 months:

- Asthma should not be diagnosed in infants aged less than 12 months old.
- Wheezing at this age group is most commonly due to acute viral bronchiolitis or to small and/or floppy airways.
- Infants with clinically significant wheezing should be referred to a paediatric respiratory physician or paediatrician (National Asthma Council Australia, 2022).

4.2. Mould infection diagnostics

The AWMF guideline advises the core elements of the diagnostic work-up for mould infection include microbiological, immunological, molecular biological, and radiological testing (Wiesmüller et al., 2017).

Denning & Chakrabarti⁸ advise that lung or airways infection by endemic fungi or *Aspergillus* can be diagnosed with respiratory sample culture or serum IgG testing (Denning & Chakrabarti, 2017). Sputum, induced sputum, or bronchial specimens are all suitable specimens for detecting fungi. Microscopy, fungal culture, galactomannan antigen, and *Aspergillus* polymerised chain reaction (PCR) are useful tests (Denning & Chakrabarti, 2017). The detection of galactomannan for diagnostic purposes is only indicated in invasive aspergillosis (Wiesmüller et al., 2017).

The detection of β -1,3-D-glucan in serum, while technically challenging could be helpful in the diagnostic workup on invasive mycosis. However, its application is not indicated in conjunction with indoor mould (Wiesmüller et al., 2017).

4.3. Mould allergy diagnostics

The AWMF guideline advises that allergic disorders due to mould allergens can essentially manifest as conjunctivitis, rhinitis, rhinosinusitis, allergic bronchial asthma, urticaria, HP and ABPA. As such, the differential diagnosis based on the medical history and clinical laboratory *in vitro/in vivo* testing is of central importance. In individual cases, the allergic reaction needs to be confirmed and the allergy trigger should be identified.

While there is a wide variety of *in vitro* tests to measure parameters of the cellular and humoral allergic reaction on different levels, the repertoire of commercially available mould allergen extracts is limited and primarily covers typical species found in outdoor air (not indoor air) (Wiesmüller et al., 2017).

4.3.1. Recommended diagnostic tests

In principle, the same guidelines and recommendations apply to the diagnostics of mould allergy as to other allergen sources that cause immediate-type allergies (Wiesmüller et al., 2017).

The core element of allergy diagnostics in the AWMF guideline include:

- medical history: holistic approach; taking the psychosocial dimension into account equally as for environmental exposure and physical disease
- skin prick testing
- *in vitro* serological examination of specific IgE antibodies in type I sensitisation, or specific IgG antibodies in HP only (this is noted as being **extremely rare** in non-occupationally related indoor exposure)

⁸ The 2017 review by Denning & Chakrabati was published in the Lancet-Infectious Diseases (IF: 25.071). The lead author is an expert in the field of Aspergillosis and medical mycology including being involved with the North American and European production of Aspergillosis guidelines and medical mycology standards of care.

- provocation testing (nasal, conjunctival, bronchial, as indicated):
 - Identification of a specific IgE means that a specific sensitisation is present, but this should not be conflated with clinically relevant allergy any more than a positive skin test reaction
 - Negative *in vitro* and *in vivo* tests do not exclude sensitisation or mould allergy.

The following five conditions need to be met for a mould allergy diagnosis:

1. A pathogenic mould antigen is present in the environment.
2. There is an unequivocal temporal relationship between allergic symptoms and exposure to the mould allergen.
3. Atopic predisposition is present.
4. There is evidence of specific IgE formation to mould antigens.
5. Measures to avoid mould allergens exhibit clear clinical effects (Wiesmüller et al., 2017).

4.3.1.1. Serological investigations

Serological *in vitro* tests include specific IgE antibody determination in the case of IgE-mediated disease, or specific IgG antibody determination in the case of HP. While the identification of elevated specific antibodies provides a clear indication of sensitisation, the AWMF advises this does not equate to clinical relevance; although the predictive value for clinical relevance increases according to the degree of sensitisation (van Kampen et al. 2008 in Wiesmüller et al., 2017).

4.3.1.2. Identification of mould-specific IgE antibodies

The AWMF guideline advises that the identification of allergen-specific IgE indicates specific sensitisation, but not necessarily disease. Results can only be correctly interpreted in conjunction with medical history, clinical picture and the results of organ-specific provocation tests. Positive reactions caused by cross-sensitivity are only of partial relevance (Wiesmüller et al., 2017).

4.3.1.3. Mould-specific IgG determination is only recommended for suspected allergic bronchopulmonary aspergillosis (ABPA) or HP

Mould-specific IgG antibody determination **is recommended** only in the case of **suspected ABPA** (type I and III allergy) or **HP** (type III and intravenous (IV) allergy), as it can make a helpful contribution to diagnosis (Wiesmüller et al., 2017). In ABPA, a significant increase is not only seen in total IgE and specific IgE against *A. fumigatus*, but also in specific IgG against *A. fumigatus*. The specific IgG against *A. fumigatus* is markedly elevated compared with patients allergically sensitised to *A. fumigatus*, with the AWMF guideline advising it is therefore recommended in the differential diagnosis of ABPA (Wiesmüller et al., 2017).

The determination of specific IgG antibodies in the diagnostic work-up for **immediate-type IgE mould allergy (type 1 allergy)** is of no diagnostic relevance and **is not recommended** (Chang & Gershwin, 2019; Wiesmüller et al., 2017). People develop IgGs to foreign proteins when exposed to them. However, IgGs do not measure allergies (Chang & Gershwin, 2019). IgG testing is highly costly to patients and there is no clinical benefit to performing these tests (Chang & Gershwin, 2019).

4.3.1.4. Diagnostic tests for specific disorders

The analysis of immune complexes is confined to particular disorders of type III allergic reactions such as HP. Beyond this, it has no place in the diagnostics of mould exposure (Wiesmüller et al., 2017).

4.3.1.5. Provocation tests

Where medical history, physical examination and serology fail to unequivocally establish the diagnosis of mould allergy, the AWMF guideline advises provocation testing may be indicated if this will significantly impact treatment, prevention, and/or compensation. Organ specific provocation testing (skin testing, or nasal, conjunctival or bronchial provocation testing) is aimed at confirming the clinical relevance of existing sensitisations or supposedly observed symptoms (Wiesmüller et al., 2017).

4.3.2. Provide advice to patients about the tests for allergy to mould

Even if there is visible mould and if a patient has a negative skin prick or specific IgE blood testing to mould it is likely that their symptoms are not due to mould, but to another allergen, this most probably being dust mites (Chang & Gershwin, 2019). If the patient has a positive skin test or specific IgE test for mould and has allergy symptoms this does not mean the patient has an allergy to mould as both *in vivo* and *in vitro* tests only test for sensitisation, not clinical allergy (Chang & Gershwin, 2019). Pet dander and dust mites, that often co-exist in homes where there is mould, are much more potent than mould spores as allergic proteins and are much more relevant than mould spores on patients with allergic rhinoconjunctivitis or asthma (Chang & Gershwin, 2019).

The AWMF guideline reinforces this, noting the sensitisation potential of moulds is considered significantly lower compared with other strong allergens (for example, fur-bearing pets and house dust mites indoors, and grass and tree pollen outdoors) (Wiesmüller et al., 2017). The updated IOM conclusions on exacerbation of asthma found sufficient evidence of a causal relationship between exacerbation of asthma and exposure to house dust mite allergens, cat allergens, and cockroach allergens (in individuals sensitised to these allergens), but not for people exposed to indoor dampness and dampness related agents (Kanchongkittiphon et al., 2015). As a general rule, sensitisation, including to moulds, is not equivalent to a clinically relevant allergy (Wiesmüller et al., 2017).

However, if a patient is truly sensitised to mould and reports suffering from nasal symptoms such as rhinorrhoea, congestion or sneezing, then the mould spores can be a cause of their allergies. The pathophysiology of allergic rhinitis is through cross-linking of antigen-specific IgE on the surface of mast cells with consequent release of mediators such as histamine and other inflammatory substances.

4.4. HP diagnostics

Allergic alveolitis is diagnosed with various clinical and paraclinical tests, including pathological examination and imaging of the lungs (Wild, Lopez et al. 2001 in World Health Organization, 2009).

While the presentation of HP is traditionally subdivided into acute, subacute and chronic, considerable overlap in these forms of presentation has been increasingly recognised; a CT scan can be used to identify these forms (Borchers et al., 2017). The clinical course of the disease is variable and its diagnosis is difficult since no specific test or biomarker provides a consistent diagnosis (Baxi et al., 2016). When fungi are involved, HP is characterised by the presence of precipitating IgG antibodies directed at the fungus (Baxi et al., 2016).

4.5. Refer for laboratory testing in a NATA/RCPA accredited laboratory

4.5.1. NATA/RCPA Accreditation and Accredited Laboratories

It is essential to use NATA/RCPA-accredited, internationally recognised laboratories for diagnostic testing. NATA accreditation provides a means of determining, formally recognising and promoting that an organisation is competent to perform testing, inspection, calibration, and other related activities. Accreditation delivers confidence and underpins the quality of results. NATA's accreditation is based on a peer-review process and is based on international standards. Since NATA accreditation is highly regarded both nationally and internationally as a reliable indicator of technical competence, use of the NATA logo and use of a NATA endorsement on reports tells prospective and current clients that the facility has been assessed against best international practice (National Association of Testing Authority, Australia, n.d.).⁹

Additionally, RCPA notes Australia leads the world in laboratory accreditation and advises all pathology laboratories in Australia receiving funding via Medicare must be accredited by the NATA/RCPA Laboratory Accreditation Program. The Standards are set by the NPAAC. The quality management aspects of the NPAAC requirements are based on the international standard ISO 15189 Standard for Medical Laboratories (Royal College of Pathologists of Australasia, n.d.).

4.6. Diagnostic tests that are not recommended by international mainstream medical guidance

4.6.1. Lymphocyte transformation test

Lymphocyte transformation testing (LTT) for mould is not indicated as a diagnostic method. This is because mould allergens do not cause type IV sensitisation (Wiesmüller et al., 2017).

⁹ A database of NATA accredited facilities is available here: <https://www.nata.com.au/accredited-facility>.

4.6.2. Mycotoxins in serum

Testing for antibodies to mycotoxins has not been validated and has no clinical utility (Chang & Gershwin, 2019; Wiesmüller et al., 2017). Current analytical possibilities do not permit reliable determination or evaluation of indoor mycotoxin exposure. The determination of mycotoxins in blood, serum or urine is of no relevance in practical medicine, and for the time being, must remain confined to scientific investigations (Wiesmüller et al., 2017).

See [Appendix C](#) for more information on 'Concerns about unvalidated tests and testing to detect mycotoxins in humans'.

4.6.3. Cytokines and eosinophil cationic protein (ECP)

No special indication occurs for these nonspecific markers of eosinophil activation and recruitment in the identification of mould allergy (Wiesmüller et al., 2017).

4.6.4. Toxicological diagnostics

Currently, there are no practicable and validated toxicological test methods that could be applied in clinical diagnostic practice for indoor mould exposure (Wiesmüller et al., 2017).

4.7. Patient presenting with persistent debilitating symptoms and no diagnosis

This section is aligned with the Australian Government Department of Health DSCATT Clinical Pathway, published in October 2020. The guidance can be applied when considering diagnostic testing for patients with unresolved debilitating symptoms with a history of exposure to indoor damp or mould, and where symptoms are not associated with asthma, respiratory or allergic conditions.

Investigations should be underpinned by clinical evidence. International evidence indicates patients with MUS are at risk of potentially harmful additional testing and are often subjected to repeated diagnostic investigations, and unnecessary and costly referrals and interventions. Unnecessary investigations that do not show anything are often not reassuring. They can make someone worry that there is something still to be found and more tests are needed.

For fatigue, diagnostic testing is determined by the differential diagnosis as per normal clinical practice (Murtagh, 2003).

5. Diagnosis

5.1. Asthma

5.1.1. Confirmed diagnosis of asthma in adults

Follow the Australian Asthma Handbook guidelines (National Asthma Council Australia, 2022) and recommendations on making a diagnosis of asthma in adults;

<https://www.astmahandbook.org.au/diagnosis/adults/making-a-diagnosis>

Make a diagnosis of asthma if all of the following apply:

- The person has a history of variable symptoms (especially cough, chest tightness, wheeze and shortness of breath).
- Expiratory airflow limitation has been demonstrated (FEV₁/VC less than lower limit of normal for age).
- Expiratory airflow limitation has been shown to be variable.
- There are no signs that suggest an alternative diagnosis.

5.1.2. No confirmed diagnosis of asthma in adults- consider alternative diagnoses

If no confirmed diagnosis of asthma, consider alternative diagnoses for respiratory symptoms; <https://www.astmahandbook.org.au/diagnosis/adults/alternative-diagnoses>. The Australian Asthma Handbook (National Asthma Council Australia, 2022) advises that alternative diagnoses for respiratory symptoms in adults include:

- poor cardiopulmonary fitness
- other respiratory conditions (e.g., bronchiectasis, COPD, hyperventilation/dysfunctional breathing, inhaled foreign body, large airway stenosis, pleural effusion, pulmonary fibrosis, rhinitis/rhinosinusitis, upper airway dysfunction)
- cardiovascular disease (e.g., chronic heart failure, pulmonary hypertension)
- comorbid conditions (e.g., obesity, gastro-oesophageal reflux)
- lung cancer
- rare disorders (e.g., alpha-1 antitrypsin deficiency).

5.1.3. Confirmed diagnosis of asthma in children aged one year and over

Follow the guidelines and recommendations of the Australian Asthma Handbook (National Asthma Council Australia, 2022) to confirm a diagnosis of asthma in children. A clinical definition of asthma in children (<https://www.astmahandbook.org.au/diagnosis/children>) is:

Asthma is defined clinically as the combination of variable respiratory symptoms (e.g., wheeze, shortness of breath, cough and chest tightness) and excessive variation in lung function, i.e., variation in expiratory airflow that is greater than that seen in healthy children ('variable airflow limitation').

The diagnosis of asthma is based on:

- history
- physical examination
- considering other diagnoses
- clinical response to a treatment trial with an inhaled short-acting beta2 agonist reliever or preventer.

Refer to the Australian Asthma Handbook (National Asthma Council Australia, 2022) for guideline recommendations for the diagnosis of asthma in children aged one to five years, and in children aged six years and over.

As referred to in diagnostic testing for asthma in [section 4.1.4](#) (on 'Infants aged zero to 12 months'), infants aged zero to 12 months should not be diagnosed with asthma as wheezing in this age group is most commonly due to acute viral bronchiolitis or to small and/or floppy airways (National Asthma Council Australia, 2022).

5.1.4. No confirmed diagnosis of asthma and symptoms resolve

Explain to the patient that no treatment is required. Reinforce enHealth advice about avoiding/minimising exposure to mould, and preventing and remediating mould and damp (Environmental Health Standing Committee (enHealth) of the Australian Health Protection Principal Committee, 2021).

5.1.5. No confirmed diagnosis of asthma and symptoms persist

Follow guidance in the Australian Asthma Handbook (National Asthma Council Australia, 2022). Refer to relevant specialists in respiratory medicine if not already referred. Consider alternative diagnoses including both infectious and non-IDs. See [section 3.2](#) for further details on 'Patients presenting with persistent debilitating symptoms and no diagnosis'.

5.2. Mould allergy

5.2.1. Confirmed diagnosis of mould allergy

The action plan of the 2015 National Allergy Strategy advises accurate diagnosis of allergy is essential, and requires appropriate specialist care (Australian Society of Clinical Immunology and Allergy & Allergy & Anaphylaxis Australia, 2015).

The AWMF guideline states that the following five conditions need to be met for a mould allergy diagnosis:

- A pathogenic mould antigen is present in the environment
- There is an unequivocal temporal relationship between allergic symptoms and exposure to the mould allergen
- Atopic predisposition is present
- There is evidence of specific IgE formation to mould antigens

- Measures to avoid mould allergens exhibit clear clinical effects (Wiesmüller et al., 2017).

Mould-allergic patients and patients with a weakened immune system should be provided with specialist patient information about the hazards of indoor mould exposure and preventative steps they can take to minimise exposure (Wiesmüller et al., 2017).

5.2.2. No confirmed diagnosis of mould allergy and symptoms resolve

Explain to the patient that no treatment is required. Reinforce enHealth advice about avoiding/minimising exposure to mould, and preventing and remediating mould and damp (Environmental Health Standing Committee (enHealth) of the Australian Health Protection Principal Committee, 2021). See [section 2.1.4](#), for further details on providing advice on avoiding or minimising exposure to indoor damp or mould, while investigating any differential diagnosis.

5.2.3. No confirmed diagnosis of mould allergy and symptoms persist

Consider alternative diagnoses including both infectious and non-IDs (see [section 3.2](#) for further details on 'Patients presenting with persistent debilitating symptoms and no diagnosis').

5.3. Mould-related infection

5.3.1. Confirmed diagnosis of mould-related infection

Diagnosis of mould infection is based on positive diagnostic findings for microbiological, immunological, molecular biological, and radiological tests (Wiesmüller et al., 2017).

5.3.2. No confirmed diagnosis of mould-related infection and symptoms resolve

Explain to the patient that no treatment is required. Reinforce enHealth advice about avoiding/minimising exposure to mould, and preventing and remediating mould and damp (Environmental Health Standing Committee (enHealth) of the Australian Health Protection Principal Committee, 2021). See [section 2.1.4](#) for further details on providing advice on avoiding or minimising exposure to indoor damp or mould, while investigating any differential diagnosis.

5.3.3. No confirmed diagnosis of mould-related infection and symptoms persist

Consider alternative diagnoses including both infectious and non-IDs (see [section 3.2](#) for further details on 'Patients presenting with persistent debilitating symptoms and no diagnosis').

5.4. HP

5.4.1. Confirmed diagnosis of HP

Diagnosis of HP will be made by a specialist based on relevant diagnostic tests.

5.4.2. No confirmed diagnosis of HP and symptoms resolve

Explain to the patient that no treatment is required. Reinforce enHealth advice about avoiding/minimising exposure to mould, and preventing and remediating mould and damp (Environmental Health Standing Committee (enHealth) of the Australian Health Protection Principal Committee, 2021). See [section 2.1.4](#) for further details on providing advice on avoiding or minimising exposure to indoor damp or mould, while investigating any differential diagnosis.

Mould-allergic patients and patients with a weakened immune system should be provided with specialist patient information about the hazards of indoor mould exposure and preventative steps they can take to minimise exposure (Wiesmüller et al., 2017).

5.4.3. No confirmed diagnosis of HP and symptoms persist

Consider alternative diagnoses including both infectious and non-IDs (see [section 3.2](#) for further details on 'Patients presenting with persistent debilitating symptoms and no diagnosis').

Reinforce enHealth advice about avoiding/minimising exposure to mould, and preventing and remediating mould and damp (Environmental Health Standing Committee (enHealth) of the Australian Health Protection Principal Committee, 2021) (see [section 2.1.4](#) for further details on providing advice on avoiding or minimising exposure to indoor damp or mould, while investigating any differential diagnosis').

Mould-allergic patients and patients with a weakened immune system should be provided with specialist patient information about the hazards of indoor mould exposure and preventative steps they can take to minimise exposure (Wiesmüller et al., 2017).

5.5. Patient presenting with persistent debilitating symptoms – diagnosis of specific disease(s) is established

Where a specific disease or diseases are diagnosed, with or without specialist input, treat accordingly, as per usual clinical practice. When symptoms resolve, the patient exits this Biotoxins (indoor damp and mould) Clinical Pathway.

5.6. Patient presenting with persistent debilitating symptoms – no diagnosis is established, and MUS persist

This section is aligned to the Australian Government Department of Health DSCATT Clinical Pathway, published in October 2020. The guidance is relevant to patients with unresolved debilitating symptoms with a history of exposure to indoor damp and mould and that cannot be attributed to another diagnosable condition.

If no diagnosis of a specific disease(s) is established through this phase of the pathway and symptoms persist, move to the next phase, the stepped care approach.

People with MUS may obtain a diagnosis over time as symptoms develop and guide to the origin of the illness. Others may find that symptoms resolve over time without ever identifying a cause (see [section 6.4](#) for further details on 'Management of patients with persistent symptoms and who remain undiagnosed', including the stepped care approach).

6. Initial management

6.1. Reinforce minimising/avoiding exposure to indoor damp and mould, preventing and remediation

Reinforce advice to patients regarding minimising/avoiding, preventing and remediating exposure to indoor damp and mould. See [section 2.1.4](#) for further details on 'Provide advice on avoiding or minimising exposure to indoor damp or mould, while investigating any differential diagnosis'.

Provide patients with a hard copy handout of the enHealth factsheet on potential health effects of mould in the environment. See [Appendix D](#) for the enHealth factsheet on mould. It is also available at <https://www.health.gov.au/resources/publications/enhealth-guidance-potential-health-effects-of-mould-in-the-environment>.

Australian and international advice is consistent in that exposure to indoor mould should be minimised or avoided. Dampness and mould-related problems should be prevented, and remediated when present, even in the absence of health effects/symptoms (Denning & Chakrabarti, 2017; Environmental Health Standing Committee (enHealth) of the Australian Health Protection Principal Committee, 2021; Hurraß et al., 2017; Larenas-Linnemann et al., 2016; Wiesmüller et al., 2017).

6.2. General medication treatment

Follow usual clinical practice for patients diagnosed with mould allergy or mould-related infection. For information refer to Therapeutic Guidelines <https://www.tg.org.au/>, Australian Medicines Handbook, NPS MedicineWise, Australian Prescriber or the TGA.

Note that to minimise antibiotic resistance, Australian guidelines (Choosing Wisely Australia, n.d.) recommend that an antibiotic should only be prescribed:

- when benefits to the patient are likely to be substantial
- with the narrowest spectrum to treat the likely pathogen
- at the appropriate dose and for the appropriate duration.

6.2.1. Asthma

Follow the Australian Asthma Handbook (National Asthma Council Australia, 2022) for management of asthma in:

- adults; <https://www.astmahandbook.org.au/management/adults>
- adolescents and young adults;
<https://www.astmahandbook.org.au/management/adolescents>
- children; <https://www.astmahandbook.org.au/management/children>.

Most patients with fungal asthma benefit from antifungal therapy (Denning & Chakrabarti, 2017).

6.2.2. Mould allergy

The AWMF guideline advises while exposure avoidance (allergen avoidance) takes priority, as with all allergic diseases, prompt medication is required in order that a symptom-free period is not followed by full-blown allergic disease. It is of paramount importance to eliminate the causes of the dampness creating a basis for indoor mould growth (Wiesmüller et al., 2017).

In principle, topical and/or systemic treatment is indicated in mould allergy depending on the organ-specific manifestation of the allergic disorder (Wiesmüller et al., 2017).

6.2.2.1. Specific immunotherapy (SIT) using mould extracts

Advice from the AWMF guideline on SIT using mould extracts includes:

- relevant mould allergens need to be unequivocally confirmed at diagnosis as the trigger of allergic symptoms
- SIT using mould extracts should be applied as early in the disease course as possible, particularly if drug treatment and avoidance have previously failed to stabilise symptoms
- evidence of clinically relevant allergen-specific IgE sensitisation is the prerequisite for SIT. The combination of different test methods, together with medical history, provides an adequate basis for SIT
- hyposensitisation presupposes a confirmed diagnosis
- there is currently insufficient scientific evidence to support the efficacy of sublingual immunotherapy (SLIT) in terms of hyposensitisation to indoor relevant moulds (Wiesmüller et al., 2017).

6.2.3. Mould-related infection

Antifungal treatment is indicated in almost all patients with chronic cavitary pulmonary infections, chronic invasive and granulomatous rhinosinusitis, and aspergillosis bronchitis (Denning & Chakrabarti, 2017).

6.2.3.1. Australian consensus guidelines for treatment of invasive mould infections in patients with haematological malignancy and haemopoietic stem cell transplantation

The 2014 consensus treatment guidelines for the treatment of invasive mould infections in patients with haematological malignancy and haemopoietic stem cell transplant note that the increasing prevalence of cancer and advances in cancer have led to a growing population at risk of invasive mould disease (Blyth et al., 2014). The guidelines present evidence-based recommendations for the antifungal management of common, rare and emerging mould infections in adults and paediatric patients.

The guidelines are available at

<https://www.wslhd.health.nsw.gov.au/ArticleDocuments/2739/Australia%20and%20New%20Zealand%20Mycoses%20Interest%20Group%20Guidelines%20for%20Treatment%20of%20Mould%20Infections%202014.pdf.aspx>.

6.3. Awareness that symptoms may persist even after building remediation

A randomised controlled trial (RCT) (Vuokko et al., 2015) included in the evidence evaluation that underpins this Clinical Pathway highlighted the challenges in managing patient's reactions to specific building-related diseases and non-specific symptoms related to indoor air environments. Symptoms attributed to the indoor environment may persist over time and even after remediation.

Vuokko et al. noted the symptomology among the participants in their study had been present for years. The authors claimed that their present findings of long-lasting and persistent multiple symptoms in participants with reduced work ability were in accordance with previous observations of environmental sensitivity features in building-associated symptoms with asthma (Vuokko et al., 2015, p. 66).

In their RCT, in nearly all of the patients, previous arrangements to solve environment-related problems in the workplace had been done without recovery of the symptomology, suggesting the nature of the symptoms is non-specific (Vuokko et al., 2015). The authors claimed their findings were corroborated by several earlier studies that reported symptoms may persist despite building remediation (Al-Ahmad et al. 2010, Edvardsson et al. 2008, and Sauni et al. 2015 in Vuokko et al., 2015), and even in cases where the remediation was considered substantial or technically successful (Haverinen-Shaughnessy et al. 2008, and Iossifova et al. 2011 in Vuokko et al., 2015). As such, clinicians and patients face problems when symptoms persist despite improvements in indoor air quality (Vuokko et al., 2015)¹⁰.

6.3.1. Building-related respiratory illness and asthma attributed to the indoor environment shared features with MUS

Vuokko et al. hypothesised that respiratory symptoms and asthma attributed to the indoor environment share features with SBS. In their study, Vuokko et al. discussed that the patients suspected of workplace indoor air-related respiratory occupational disease with reduced self-rated work ability and sick leave showed prevalent asthma as well as abundant environmental attributed non-specific symptoms. The majority of those with asthma were reported having normal lung function tests but reporting several respiratory symptoms. In only four patients, asthma fulfilled the criteria of occupational asthma induced by indoor moulds, with Vuokko et al. noting this suggested that indoor environment attributed asthma and symptomology is multifactorial (Vuokko et al., 2015). In their cohort of patients, Vuokko et al. noted that it seemed likely that the respiratory symptoms of the asthma patients were not fully explained by their asthma, as lung function tests were normal in most of the cases (Vuokko et al., 2015). Environmental sensitivities can enhance illness behaviour (Baliatsas et

¹⁰ The NICE committee noted in their indoor air quality at home evidence review for exposure to pollutants and health outcomes that pollutants such as NO₂ [nitrous dioxide], volatile organic compounds (VOCs), particulate matter (PM) from open solid-fuel fires, polycyclic aromatic hydrocarbons (PAHs) and biological agents such as mould and pet dander are sometimes associated with many symptoms including those affecting the respiratory, cardiovascular and neurological systems. (National Institute for Health and Care Excellence, 2020b, p. 66).

al. 2014 in Vuokko et al., 2015), which Vuokko et al. noted was a plausible explanation for disproportional asthma symptoms (Vuokko et al., 2015). Regarding asthma, Vuokko et al. noted that stress-related exacerbation and other cognitive affective states affect the severity of asthma (Eisner et al. 2005, and Lehrer et al. 2002 in Vuokko et al., 2015) and perception of respiratory symptoms (Bogaerts et al. 2005 in Vuokko et al., 2015).

Vuokko et al. note the care of these conditions requires a multifactorial approach. In management of asthma, psychosocial interventions have been shown to be effective, including cognitive and educational techniques (illness beliefs reattribution, skills involved in the symptom perception, stress reduction techniques, psychoeducation on the nature of asthma (Smith et al. 2005, and Yorke et al. 2007 in Vuokko et al., 2015). Vuokko et al. noted “these treatments aim to increase patients’ awareness of symptom perception and attribution accuracy, support self-management and modify interpretations about illness (i.e., all or nothing attributions and catastrophising) to more objective interpretations” (Vuokko et al., 2015, p. 60).

6.4. Management of patients with persistent symptoms and who remain undiagnosed

This part of the Biotoxins (indoor damp and mould) Clinical Pathway is aligned with the Australian Government Department of Health DSCATT Clinical Pathway and pertains to management of patients who have unresolved debilitating symptoms that cannot be attributed to tick-borne disease, exposure to indoor mould and damp or another diagnosable condition.

The guidance in this section ‘Management of patients with persistent symptoms and who remain undiagnosed’ and its subsections is the same as the DSCATT Clinical Pathway. The DSCATT Clinical Pathway recommends a Stepped Care Model which has an individualised care plan at its core. The evidence evaluation that underpins this Clinical Pathway identified that internationally there are effective clinical practice guidelines and other guidance for some syndromes similar to “so-called” CIRS. From the US, the Veterans Association in conjunction with the Department of Defence developed a clinical practice guideline for chronic multi-symptom illness (CMI) (The Management of Chronic Multisymptom Illness Work Group, 2021). CMI symptoms overlap considerably with the symptoms attributed to “so-called” CIRS, including the point that symptoms are distributed across more than one bodily system. Like the DSCATT Clinical Pathway, the CMI guideline advocates for individualised, patient-centred care with shared decision making, and the use of a multi-disciplinary team which can also address any comorbidities.

Where there is no diagnosis and the patient is experiencing symptoms that are medically unexplained, it is especially important to ensure that person-centred care is provided that validates, addresses and manages their symptoms as well as possible.

The Australian Commission on Safety and Quality in Health Care advises that “Person centred-care” involves:

- seeking out and understanding what is important to the patient
- fostering trust
- establishing mutual respect

- working together to share decisions and plan care (Australian Commission on Safety and Quality in Health Care, 2018).

Key dimensions include respect, emotional support, physical comfort, information and communication, continuity and transition, care coordination, access to care, and partnerships with patients, carers and family in the design and delivery of care (Australian Commission on Safety and Quality in Health Care, n.d.).

Patients should be treated symptomatically and are also encouraged to consider the potential for harm with complementary medicines for which there is no evidence in those with comorbidities. All people with MUS, (including those identifying as experiencing the symptoms associated with DSCATT and unresolved debilitating symptoms with a history of exposure to indoor damp or mould and that cannot be attributed to another diagnosable condition) can be assisted to have an improved quality of life with good care in a partnership between patient and the health care team.

International and Australian guidelines provide evidence-based, practical and consistent recommendations. These guidelines can be applied to patients with the symptom complex described as DSCATT and to patients with unresolved debilitating symptoms with a history of exposure to indoor damp or mould and that cannot be attributed to another diagnosable condition. Good communication and empathy are important. Patients' concerns need to be taken seriously and their symptoms acknowledged and alleviated.

The most common unexplained symptoms reported by patients experiencing DSCATT include fatigue, disordered thinking, sensory disturbance, arthralgia, and headache (Brown, 2018). These symptoms can have multiple different causes, depending on the particular symptoms, cluster, and timeframe of symptom(s). For patients with MUS, and equally for patients identifying as experiencing symptoms associated with DSCATT, it is also important to provide support to assist them to manage distressing symptoms and any disability that accompanies them (Stone, 2015). A similar approach can be applied to patients with unresolved debilitating symptoms with a history of exposure to indoor damp or mould and that cannot be attributed to another diagnosable condition.

It is important to help patients understand that the mind and body are interconnected in complex ways, and that holistic care is often essential to improve health. It may be useful for the patient to encourage psychological care to address the impact of the illness and underlying issues that may exacerbate symptoms (Stone, 2015).

For children for whom no diagnosis can be established and who have unresolved symptoms, referral to a paediatrician should be considered.

6.4.1. MUS

MUS are defined as physical symptoms persisting for more than several weeks and for which adequate medical examination has not revealed a condition that adequately explains the symptoms (Olde Hartman et al., 2017). Patients with MUS may be very unwell and require complex care. People experiencing debilitating symptoms attributed to ticks (or people experiencing unresolved debilitating symptoms with a history of exposure to indoor damp or mould), without any definitive diagnosis could be considered to fall within the definition of MUS. A recent review of MUS guidelines in Europe (Olde Hartman et al., 2017) estimates that between 3–11% of patients visiting general practice repeatedly consult their GP for

MUS. However, this finding might not be entirely applicable to Australia. MUS exist along a continuum ranging from self-limiting symptoms to recurrent and persistent symptoms through to symptom disorders.

Advice from the Royal Australian College of General Practitioners (RACGP) (Stone, 2015) and the review of the international MUS guidelines (Olde Hartman et al., 2017) summarising guidelines from the Netherlands, Denmark, UK and Germany (two of which provide evidence graded recommendations) is consistent. Patients with MUS often feel stigmatised and not taken seriously. To manage these concerns, all guidelines recommend:

- The importance of paying attention to the doctor-patient relationship.
- An individualised approach that recognises the patient's illness and taking the patient's symptoms seriously.
- Empathy with consultations aiming to validate the patient's distress.
- Providing an explanation in the patient's language about the possible causes of their symptoms (Patients benefit from an explanation that makes sense, removes blame from the patient, generates ideas on how to manage the symptoms. The 2011 UK guidance published by the Royal College of General Practitioners in the UK (Chitnis et al., 2011), advises that GPs should be explicit about their thoughts, uncertainties and expectations of referrals to specialist care).
- Caution that "patients with persistent [MUS] suffer from their symptoms, are functionally impaired, and are at risk of potentially harmful additional testing and treatment" (Olde Hartman et al., 2017).

A qualitative study into the experiences of patients identifying with 'chronic Lyme disease' reported on the importance of actively engaged and sympathetic clinical encounters. They showed that where patient concerns are fully acknowledged and addressed, they experience greater satisfaction with their healthcare (Ali et al., 2014).

Having any chronic medical condition of any cause increases the likelihood of mental health conditions, which in turn can lead to poorer outcomes. An article on managing medically unexplained illness in general practice published by RACGP, notes that acknowledging the difficulty of chronic symptoms and supporting the important mental health strategies is vital to person centred care in chronic disease (Stone, 2015). Additionally, all patients with MUS need support to manage distressing symptoms and the disability that accompanies them (Stone, 2015). Helping patients understand that the mind and body are interconnected in complex ways and that holistic care is often essential to improve health is important. Reattribution, the technique of shifting the focus away from only physical symptoms and biomedical diagnoses to a more holistic understanding of illness, was noted as a useful technique in primary care (Stone, 2015).

6.4.2. Practice Harm Minimisation

International evidence indicates patients with MUS are at risk of potentially harmful additional testing (Olde Hartman et al., 2017). In addition, these patients are often subjected to repeated diagnostic investigations, and unnecessary and costly referrals and interventions (Royal College of Psychiatrists, 2017). An analysis of the Senate submissions (in relation to DSCATT) noted that patients identifying as having DSCATT, experience social and financial

harms and are at risk of nosocomial harms and may also have sought alternative and potentially non-evidence-based diagnoses and treatments (Brown, 2018).

A key challenge for GPs to manage MUS in general practice is to balance the iatrogenic risk of investigation with the therapeutic risk of missing something important (Stone, 2015).

[Table 2](#) overleaf provides recommendations for managing MUS.

Table 2: Recommendations for managing MUS

Avoid

Avoid:

- Repeated diagnostic testing.
 - Harms include worry that there is still something to be found that hasn't been tested for yet, repeated investigations and treatment, multiple primary care practitioners increased likelihood of false positives, and the finding of minor, non-significant abnormalities in test results that increase anxiety
- Use of non-accredited laboratories for diagnostic testing and use of unconventional diagnostic techniques (e.g., kinesiology).
 - Harms include false positives and wrong diagnosis
- Unnecessary referrals and interventions.
 - Harms include repeating and extending unnecessary testing and iatrogenic harm as well as financial costs
- Treatments with known harm and no benefit (e.g., long-term antibiotics, extreme diets, miracle mineral solution, hyperbaric oxygen treatments).
 - Harms include toxicity, hypersensitivity reactions, predisposition to *Clostridium difficile* infection, development of antibiotic resistance, line sepsis, severe and persistent vomiting and diarrhoea, and large financial cost without benefit.

Encourage

Encourage:

- Discussion of intended “natural” or alternative therapies for evaluation of individualized harms versus benefits.
 - An awareness of the evidence base and side effects to be aware of can assist patients in choosing alternative therapies wisely and avoiding unnecessary out of pocket costs and unintended harms.
 - Periodic re-evaluation of symptoms and new symptoms to determine an identifiable cause and efficacy of treatment.
 - Small changes over time may not be noticed by patients. Review allows encouragement regarding improvements, detection of deterioration, and evaluation of new symptoms arising.
 - Discussion of possible causes of and treatments for symptoms that have been found on the internet or recommended by friends.
 - Not having a diagnosis is difficult for patients in many ways and leads to a vulnerability to looking for a cause of their symptoms. The internet, social media and social contacts can be spreaders of both good and poor information. Remaining open to a patient discussing what they have found allows for education, exploration of misinformation, identification of reliable sources and identification of potential treatments to trial.
 - Enlistment of other members of a multidisciplinary team.
 - Consideration of mental health strategies.
-

6.4.2.1. *MUS and complementary therapies*

National Prescribing Service (NPS) MedicineWise reports that a poll conducted in 2018 shows almost seven million Australians take some form of complementary medicine every day (National Prescribing Service MedicineWise, 2019). Without a full understanding of patients' health practices, including their use of complementary therapies, it is difficult for clinicians to provide safe and patient-centred health care.

Refer to the National Health and Medical Research Council (NHMRC) and Therapeutic Goods Administration (TGA) for information on complementary and alternative medicines in Australia.

A useful resource, *Talking with your patients about Complementary Medicines* (National Health and Medical Research Council, 2014), published by the NHMRC has found that many Australians report that they use complementary medicine but do not disclose this information to their clinicians (Williamson et al., 2008). One of the most common reasons patients have not discussed their use of complementary medicines is that their clinician has not asked them about it (Xue et al., 2007). The RACGP advises that it is important for GPs to ask patients about their use of complementary therapies and to be aware of the evidence basis, or lack thereof. GPs should also have the knowledge to provide patients with balanced information about potential benefits and risks in order to enable informed decision making (Royal Australian College of General Practitioners, 2016).

The NHMRC resource recommends that (National Health and Medical Research Council, 2014):

- clinicians should be sensitive to the variety of other reasons for patients not disclosing complementary medicines use. These reasons include:
 - a belief that complementary medicines products and therapies are 'natural' and 'safer' than conventional medicine
 - a feeling of dissatisfaction with conventional medicine
 - a lack of awareness of the risk of unintended drug interactions
 - awareness of the clinician's attitude to or knowledge of complementary medicines
 - discomfort in raising the topic
 - fear of the practitioner's response.
- when clinicians initiate discussions about complementary medicines with their patients, it is important to use an approach that increases collaboration and trust.
- clinicians should encourage patients to make treatment decisions based on evidence and can ask their patients if they would like help identifying and interpreting evidence of effectiveness for the complementary therapies they use.
- clinicians should explain to their patients that all health and treatment decisions involve weighing up potential benefits and potential risks and that this process can help patients to decide whether a treatment is appropriate for them.

Many consumers are not aware of the side effects of some complementary medicine products and their potential interactions with conventional medicines, which may put some users at unnecessary risk of harm. Clinicians may need to consider and explain to their patients the risk of adverse reactions (including unintended medicine interactions).

Encourage patients to ask questions about the efficacy, risks, contraindications and costs of the complementary therapies and the qualifications of the practitioner (Cancer Council Australia, 2015).

If considered clinically necessary, GPs may refer their patient to a pharmacist for a Medicare-supported Home Medicines Review to prevent medication-related problems.

Further information about complementary therapies

For further information on complementary and alternative medicines in Australia and around the world, refer to:

- the NPS MedicineWise; <https://www.nps.org.au/consumers/complementary-medicines-explained>
- the Therapeutic Research Center – a US website that has an interaction checker, effectiveness checker and a database of natural therapies; <https://naturalmedicines.therapeuticresearch.com>
- the Memorial Sloan Kettering Cancer Centre has information about herbs, botanicals and a number of complementary therapies; <https://www.mskcc.org/cancer-care/diagnosis-treatment/symptom-management/integrative-medicine/herbs>
- the Cochrane Complementary Medicine; <https://cam.cochrane.org/cochrane-reviews-related-complementary-medicine> accessed 9 August 2020
- the Victorian State Government Better Health Channel; <https://www.betterhealth.vic.gov.au/health/ConditionsAndTreatments/complementary-therapies>

6.4.3. The Stepped Care Model

The challenge for the GP involves managing individual symptoms, but also creating a framework for the chronic care of patients with significant ongoing illness (Stone, 2015).

The stepped care model of care is internationally recognised and familiar to and widely used by GPs in Australia in all aspects of patient care. The model is recommended for use in patients with MUS by international and Australian guidelines.

Stepped care is an evidence-based, staged system comprising a hierarchy of interventions, from the least to the most intensive, matched to the individual's needs. Within a stepped care approach an individual will be supported to transition up to higher intensity services or transition down to lower intensity services as their needs change (General Practice Mental Health Standards Collaboration, 2019).

As background, international guidelines on MUS recommend a stepped care approach to address three levels of severity of symptoms, which lack clear cut-off points. They also advise that it is important that one care provider, preferably the GP, keeps control and coordinates the care process.

In addition to being recommended as an approach for managing care for people with MUS, the stepped care service model has been shown in RCTs to be effective for the management of chronic pain (US Department of Veterans Affairs, 2009), and for the management of depression and anxiety (Australian Government Department of Health, 2019) and in the assessment and management of anxiety and depression in adult cancer patients (Butow et

al., 2015). Stepped care models are widely used in England, Scotland, USA, New Zealand and Australia.

GPs make assessments to determine the best management approach to guide their patients in accessing services appropriate to their level of need, and thus ensure that more intensive and often costly services are directed to patients best able to benefit from them (General Practice Mental Health Standards Collaboration, 2019). While referrals are made to other relevant health practitioners as appropriate, it is important that one care provider, preferably the GP, coordinates care.

Stepped care models aim to:

- offer a variety of support options for people with different levels and types of need, from low intensity to high intensity
- provide clear pathways between these care options as individuals' needs change, and
- improve collaboration and integration between services (General Practice Mental Health Standards Collaboration, 2019).

Central to the stepped approach is the development of an individualised care plan, developed in discussion with the patient.

International guidelines concur that doctor-patient communication is key. They emphasise the importance of exploring patient's ideas, concerns and expectations, providing acceptable explanations, providing practical and constructive advice that is applicable to their daily lives is important and offering advice on symptom management. Considering the patient's ethical-cultural background in all steps is also recommended (Olde Hartman et al., 2013). [Table 3](#) overleaf provides of the Stepped Care approach for managing MUS.

Table 3: Overview of Stepped Care approach to managing MUS (Olde Hartman et al., 2013)

Step 1: For patients with mild functional limitations and who experience one or several symptoms

For patients with mild functional limitations and who experience one or several symptoms:

- Explore symptoms, conduct physical examination and or additional investigations. List the symptoms.
- Summarise findings discussing clearly what was found and explicitly mentioning what was not found.
- Try to reach a shared definition of the problem. It is important to recognise the symptoms and the fact the patient is troubled by them. Explore and address anxieties and misconceptions. It is very important that the patient's concerns are treated seriously and in a sensitive manner.
- Provide the patient with targeted and tangible information about ways to manage symptoms and an individualised care plan.

Step 2: For patients with moderate functional limitations with several symptoms, cluster symptoms or a symptom duration longer than expected

For patients with moderate functional limitations with several symptoms, cluster symptoms or a symptom duration longer than expected:

- Continue GP led care as in Step 1 and if the patient is unable to expand his/her level of activity to an acceptable standard, refer to either primary or secondary care practitioners (e.g., physiotherapy, nurse practitioners, specialist GPs, psychotherapy/CBT).
- Refer to secondary specialist services as required. Telehealth can be used where appropriate.
- Make regular follow-up appointments if functional limitation persists (e.g., every four to six weeks).

Step 3: For patients with severe functional limitations and a large number of symptoms and duration of three months or more

For patients with severe functional limitations and a large number of symptoms and duration of three months or more:

- Refer to secondary, tertiary care providers and or multi-disciplinary teams or treatment centres.
- Continue to stimulate the expansion of the patient's functioning and monitor for deterioration in function.
- It is important that one care provider, ideally a GP, coordinates the care provided.
- Limit long term treatments and investigations that are not useful and may even be harmful.
- Make regular follow-up appointments during treatment (e.g., four to six weeks).

7. Ongoing management

7.1. Asthma, respiratory and allergic conditions

7.1.1. Asthma

Follow the Australian Asthma Handbook (National Asthma Council Australia, 2022) for managing asthma in:

- adults, including ongoing management and management of flare ups; <https://www.astmahandbook.org.au/management/adults>
- adolescents; <https://www.astmahandbook.org.au/management/adolescents>
- children; <https://www.astmahandbook.org.au/management/children>.

General principles of asthma treatment in children as per the Australian Asthma Handbook are:

- Aim for good control of asthma symptoms.
- Try to identify what triggers asthma symptoms (e.g., allergens).
- Manage comorbid conditions that affect asthma (e.g., allergic rhinitis).
- Show parents and children (if old enough) when and how to take reliever medicine.
- Monitor regularly and adjust the treatment regimen to maintain good control of symptoms and prevent flare-ups, while minimising the dose of inhaled corticosteroids (if needed).

Provide parents/carers and children with information and skills to manage their asthma, including:

- a written asthma action plan to follow when symptoms worsen
- information about reducing exposure to triggers, where appropriate (e.g., all tobacco smoke, but allergens only when likely to be helpful and cost-effective)
- training in correct use of medicines, including inhaler technique
- information and support to maximise adherence.
- advice about avoidance of tobacco smoke, healthy eating, physical activity, healthy weight and immunisation.

If symptoms have stabilised/resolved, the patient exits the Biotoxins (indoor damp and mould) Clinical Pathway.

If symptoms persist, consider alternative diagnoses (see [section 3.4](#) for further details on 'Patients presenting with persistent debilitating symptoms and no diagnosis').

7.1.2. Mould allergy

In patients with mould allergy, ongoing monitoring would be led by a Clinical Allergist or Immunologist.

If symptoms have stabilised/resolved, the patient exits the Clinical Pathway.

If symptoms persist, consider alternative diagnoses (see [section 3.2](#) for further details on 'Patients presenting with persistent debilitating symptoms and no diagnosis').

7.2. HP, mould-related infections and allergic conditions in susceptible people

If symptoms have resolved, the patient exits the Clinical Pathway.

If symptoms persist, consider alternative diagnoses (see [section 3.2](#) for further details on 'Patients presenting with persistent debilitating symptoms and no diagnosis').

7.3. Management of patients with persistent symptoms and who remain undiagnosed

This section is aligned with the Australian Government Department of Health DSCATT Clinical Pathway, published in October 2020. The guidance can be applied to the ongoing management of patients who have unresolved debilitating symptoms that cannot be attributed to exposure to indoor mould and damp or another diagnosable condition.

The GP will lead the ongoing review of symptoms and management plan, in consultation with the patient, with regular review of progress in achieving their goals. In the event of persistent dysfunction, evaluate the situation regularly and offer any new treatment options. The review and evaluation of new symptoms may require a change of level in stepped care for the patient.

Management of ongoing symptoms should involve a multidisciplinary approach, incorporating the teamwork of all medical specialties relevant to the individual patient's care. Diagnosis is challenging, and it is important for GPs to seek opinions of experts in indoor damp and mould including clinical immunologists, allergy specialists, or specialist microbiologists with diagnostic experience. The management of patients must be a collaborative approach between GPs and specialists. Telehealth can also be used where appropriate.

Consider referring patients who have MUS to appropriate specialists based on best clinical practice and relevant evidence.

If symptoms have resolved the patient exits the Clinical Pathway.

8. Appendices

This section includes:

- [Appendix A](#): Likely differential diagnoses or symptoms: Health effects for which there is sufficient evidence of association with exposure to indoor damp and mould
- [Appendix B](#): Less likely differential diagnoses or symptoms: Health effects for which there is limited or suggested evidenced of association with exposure to indoor damp and mould
- [Appendix C](#): Unlikely differential diagnoses or symptoms: Health effects for which there is inadequate or insufficient evidence of an association with indoor damp and mould
- [Appendix D](#): enHealth factsheet on Potential health effects of mould in the environment
- [Appendix E](#): Chronic Inflammatory Response Syndrome (CIRS)
- [Appendix F](#): Potential side effects of the pharmaceuticals used in the treatment of CIRS
- [Appendix G](#): Bibliography.

Appendix A: Likely differential diagnoses or symptoms: Health effects for which there is sufficient evidence of association with exposure to indoor damp and mould

The sections below provide an overview of the findings for asthma, respiratory infections, wheeze, cough, dyspnoea, bronchitis, rhinitis, upper respiratory tract symptoms, and eczema. See [section 3.1.2](#) for further details on hypersensitivity pneumonitis (HP), mould-related infections and allergic health effects in susceptible people.

Asthma

The body of evidence from international guidelines, international authorities and medical professional bodies, systematic reviews, reviews, and studies acknowledges that exposure to indoor dampness and mould is associated with asthma, particularly in children. However, consistent associations is shown between indoor dampness and mould and a variety of respiratory and allergic health effects, including asthma. These associations have been limited to observation-based, qualitative indicators of damp or mould, such as visible mould, mouldy or musty odour, water-damaged materials or (observed) moisture of materials (Mendell et al., 2011, 2018; World Health Organization, 2009).

Additionally, while more recent reviews of the evidence indicates that in children there is sufficient evidence of a causal association between asthma (exacerbation) and exposure to indoor dampness and dampness-related agents, there is not sufficient evidence for causation. For other indoor exposures, there is sufficient evidence for causation of asthma (exacerbation) from exposure to house dust mite allergens, cat allergens, and cockroach allergens (in individuals sensitised to these allergens) (Kanchongkittiphon et al., 2015).

In 2009, the WHO concluded that while the epidemiological evidence is not sufficient to determine causal relationships between indoor dampness or mould and any specific human health effect, the findings of one strong epidemiological intervention study, in conjunction with other available studies, suggest that dampness or mould exacerbates asthma in children. The WHO also concluded there is sufficient epidemiological evidence of an association between indoor dampness-related factors and asthma (development, current, exacerbation) (World Health Organization, 2009).

Eight years later, the 2017 AWMF guideline also determined that sufficient evidence for an association between moisture/mould damage and the manifestations, progression and exacerbation of asthma has been established (Wiesmüller et al., 2017). Furthermore, the link between indoor damp and mould and the development of asthma, particularly in children, can be considered undisputed (Wiesmüller et al., 2017). The AWMF guideline reported young children appear to be at higher risk of developing bronchial asthma where moisture damage or mould exposure occurs in the bedroom or living room (Karvonen et al. 2015 in Wiesmüller et al., 2017).

Two reviews by the US IOM detailed their findings and conclusions specific to asthma. A 2011 review, cited widely in the literature, reported that current asthma (defined as either

asthma diagnosis in prior 12 months, asthma diagnosis ever plus asthmatic symptoms in prior 12 months, or recent prescription of asthma medication), was consistently associated in available studies with dampness or mould (Mendell et al., 2011). Among cross-sectional studies of adults, children, or both, almost all odds ratios (ORs) (94%) exceeded 1.0 (ranging from 0.3 to 13.0), and in the systematic review by Fisk et al. (2007) as a summary effect estimate, an OR of 1.6 (1.3–1.9, 95% CI) for current asthma and qualitative dampness factors was reported (Mendell et al., 2011). Ever-diagnosis with asthma was associated consistently with dampness or mould (91% of ORs; range, 0.6–2.6) in both adults and children (Mendell et al., 2011).

A 2015 update to the 2000 Review by the IOM on indoor environmental exposures and exacerbation of asthma, that included studies from 2000 to 2013, reported major updated conclusions on dampness and dampness related agents (Kanchongkittiphon et al., 2015). In the 2015, the IOM updated its conclusions for dampness and dampness-related agents:

- in children, there was sufficient evidence of a causal association between dampness and dampness-related agents and exacerbation of asthma
- in adults there was sufficient evidence of an association (Kanchongkittiphon et al., 2015).

These updated conclusions for dampness and dampness-related agents were reported under 'Sufficient evidence for association', not 'Sufficient evidence for causation'. Of note, and of relevance to the wider subject of indoor air quality, the updated IOM conclusions found sufficient evidence of a causal relationship between exacerbation of asthma and exposure to house dust mite allergens, cat allergens, and cockroach allergens (in individuals sensitised to these allergens) (Kanchongkittiphon et al., 2015).

For exposure to fungi (quantified) and asthma, the updated 2015 IOM conclusions included the following (Kanchongkittiphon et al., 2015):

- there is limited or suggestive evidence of an association between indoor culturable *Penicillium* exposure and exacerbation in asthmatic children with specific sensitisation, any fungal sensitisation, or unspecified sensitisation
- there is limited or suggestive evidence of an association between indoor total culturable fungal exposure and exacerbation of asthma in children with any fungal sensitisation.

As in allergic rhinitis, allergic asthma due to moulds is mostly a seasonal disease and is predominantly induced by seasonal outdoor moulds like *Alternaria* or in rarer cases *Cladosporium*, *Epicoccum*, *Fusarium* (Hurraß et al., 2017). Indoor moulds such as *Aspergillus* sp. Or *Penicillium* sp. may rarely cause perennial asthma (Reponen et al. 2012 in Hurraß et al., 2017). Patients with allergic asthma to moulds were additionally sensitised to other environmental allergens in 95% of cases, but mono-sensitisations to moulds may occur only in rare cases, with the latter especially true for indoor moulds (Inersen & Dahl 1995 in Hurraß et al., 2017; Inersen & Dahl 1995 in Wiesmüller et al., 2017). Furthermore, sensitisation to moulds mostly occurs in patients with a high potential for being sensitised to common inhalation allergens. Sensitisation to moulds is not related to damp dwellings, as it is believed that moulds have a low sensitising potential and genetic factors are of higher importance than exposure (Inersen & Dahl 1995 in Hurraß et al., 2017; Inersen & Dahl 1995 in Wiesmüller et al., 2017).

For advice on diagnostic testing for asthma, see [Section 4.1](#) and Sections [4.1.1](#) to [4.1.4](#). For advice on the diagnosis of asthma, see [Section 5.1](#) and Sections [5.1.1](#) to [5.1.5](#).

For advice on the initial management of asthma, see [Section 6.2.1](#), and for advice on the ongoing management of asthma, see [Section 7.1.1](#).

The Australian situation and Australian studies

The House of Representatives Inquiry Report noted that the WHO estimated the prevalence of indoor dampness may affect between 10–50% of indoor environments in Australia, particularly in settings such as river valleys and coastal areas (House of Representatives Standing Committee on Health, Aged Care and Sport, 2018). To put this into perspective, the WHO provided the same prevalence estimates of indoor dampness for Europe, North America, India and Japan (World Health Organization, 2009). However, the Inquiry Report also noted advice from the Australasian Society of Building Biologists (ASBB) was that while an estimate provided by Dr. Tim Law to the Inquiry indicated that one third of new buildings in Australia may be affected by condensation problems, the true prevalence and geographic distribution of dampness in Australian buildings is yet to be quantified (House of Representatives Standing Committee on Health, Aged Care and Sport, 2018, p. 16).

Three Australian studies have reported on exposure to indoor damp or mould and asthma outcomes. A study by Knibbs et al. (2018) sought to determine the proportion of the national childhood asthma burden associated with exposure to dampness and gas stoves in Australian homes. The study found exposure of Australian children to damp housing and gas stove emissions is common, and is associated with 7.9% and 12.3% respectively of the total asthma burden in children aged 14 years or under:

- For dampness problems, the authors reported 26.1% of Australian homes to be affected. The population attributable fractions (PAFs) for childhood asthma attributable to damp housing was 7.9% (95% CI: 3.2–12.6%), causing 1,760 disability-adjusted life years (DALYs) (DALYs; 95% CI: 416–3,104 DALYs), or 42 DALYs/100,000 children
- For gas stoves, 38.2% of homes were estimated to have natural gas as the main energy source for cooktop stoves. The PAFs associated with gas stoves was 12.3% (95% CI: 8.9–15.8%), corresponding to 2,756 DALYs (95% CI: 1,271–4,242), or 67 DALYs/100,000 children (Knibbs et al., 2018).

While noting the risks at the level of the individual are relatively small, the authors pointed out that the proportion of the population is relatively large so that the contribution to the population asthma burden is considerable (Knibbs et al., 2018). As such, advice was that if all homes with gas stoves were fitted with high efficiency rangehoods to vent gas combustion products outdoors, the PAFs and burden estimates were reduced to 3.4% (95% CI: 2.2–4.6%) and 761 DALYs (95% CI: 322–1,199) (Knibbs et al., 2018).

A hospital-based case–control study, nested within the Melbourne Air Pollen Children and Adolescent Health (MAPCAH) study that sought to understand the influences on indoor environmental and lifestyle characteristics on asthma hospital readmission found factors in the child’s bedroom play an important role in increasing the risk of asthma hospital readmissions (Vicendese et al., 2015). Regarding indoor fungal exposure, the authors found that for every doubling of the concentration of colony forming units (CFU) of airborne *Cladosporium* (per 28 L of air) in the bedroom, there was over a 60% increase in the odds of

readmission, adjusted odds ratio (OR) 1.68, 95% confidence interval (CI) (1.04–2.72), $p = .03$. Similarly, for every doubling of the concentration of CFU of airborne yeast in the bedroom, there was over a 50% increase in the odds of readmission OR 1.52, 95% CI: 0.99–2.34, $p = .05$. Overall, higher levels of airborne *Cladosporium* and yeast in a child's bedroom increased the risk of readmission for asthma (OR 1.68; 95% CI: 1.04–2.72). Of the other environmental or lifestyle factors investigated in this study the authors also found a much higher OR for asthma readmissions for carpeted floors in the bedroom (OR 4.07; 95% CI: 1.03–16.06), synthetic doonas (OR 14.6; 95% CI: 1.26–169.4) and frequent vacuuming using bagged cleaners (OR 15.7; 95% CI: 2.82–87.2). The authors noted the findings have major clinical implications as the identified potential risk factors may be modifiable but that further epidemiological studies with larger sample sizes are required to evaluate the associations further (Vicendese et al., 2015).

A study by Mészáros that investigated the effect of indoor air pollutants on atopic and non-atopic asthma and asthma-related respiratory symptoms in middle age found that exposure to mould was an independent risk factor for current asthma and asthma-related symptoms, and for current non-atopic asthma in males (Mészáros et al., 2014). The authors analysed older survey questionnaire data on respiratory and home environment factors completed by participants in the Tasmanian Longitudinal Health Study in 2004. The study found over a third of the cohort reported mould on any surface in the last 12 months. Mould 'ever' in the house in the last 12 months was associated with current and doctor-diagnosed asthma (OR 1.26; 95% CI: 1.06–1.50). This study found recent mould exposure in the home was associated with a near four-fold increase in the odds of current non-atopic asthma in males, but no other phenotype. Additionally, from modelling, a dose-response effect was suggested where the greater the number of rooms affected by mould, the greater the odds of current asthma and related respiratory symptoms (Mészáros et al., 2014). The authors noted having more than one room affected by mould is likely to increase the airborne spore concentration, creating a more allergenic environment (Mészáros et al., 2014).

Respiratory infections

Two guidelines and two international authority evidence reviews, and the evidence review that underpinned the AWMF guideline reported there was sufficient evidence for an association between exposure to indoor mould or damp and respiratory infections (Hurraß et al., 2017; Mendell et al., 2011; Palaty & Shum, 2012; Wiesmüller et al., 2017; World Health Organization, 2009). The AWMF guideline advised there is evidence of a consistent association between water damage or indoor mould exposure and the development of medically diagnosed respiratory tract diseases (common cold, bronchitis, infections) (Mendell et al. 2011 in Wiesmüller et al., 2017), however, the risk of infection from common indoor mould species is low in healthy individuals (Wiesmüller et al., 2017). The AWMF also noted that an estimated 8–20% of respiratory tract infections in the US are associated with mould or indoor dampness, that the link continues to exist after controlling for independent variables, and *Penicillium* sp., *Cladosporium* sp., *Zygomycetes* and *Alternaria* sp. proved to be the most closely linked to the development of these diseases (Fisk et al. 2010 in Wiesmüller et al., 2017).

For more information, see [section 4.2](#), (on 'Mould infection diagnostics'), [section 5.3](#), (on the diagnosis of 'Mould-related infection'), and [section 6.2.3](#) (on the initial management of 'Mould-related infection').

Wheeze

Two guidelines, two international authority evidence reviews, three systematic reviews, a review associated with the AWMF guideline and an Australian study concluded or advised there was sufficient evidence for an association between exposure to indoor damp and/or mould and wheeze (Fakunle et al., 2021; Fisk et al., 2019; Hurraß et al., 2017; Mendell et al., 2011; Mészáros et al., 2014; Palaty & Shum, 2012; Tischer et al., 2011; Wiesmüller et al., 2017; World Health Organization, 2009).

Mendell et al. reported that for qualitative dampness and mould studies and wheeze, most studies found positive associations with dampness or mould, with 100% of retrospective ORs exceeding 1.0 (range, 1.5–2.8), and 95% of cross-sectional ORs exceeding 1.0 (range, 0.4–5.8) in adults. For children 95% of prospective or retrospective ORs exceeded 1.0 (range, 0.7–6.2) and 92% of cross-sectional ORs exceeded 1.0 (range, 0.5–8.7) (Mendell et al., 2011).

Cough

Two guidelines, two international authority reviews and two reviews concluded or advised there was sufficient evidence for an association between exposure to indoor damp and/or mould and cough (Hurraß et al., 2017; Mendell et al., 2011; Palaty & Shum, 2012; Wiesmüller et al., 2017; World Health Organization, 2009). A meta-analysis of studies on mould and dampness in schools found positive associations for cough among adults and children (Fisk et al., 2019).

Mendell et al. reported that many new studies, some of strong design, including statistically significant elevation of risk identified in a quantitative meta-analysis by Fisk et al. (2007), led them to conclude there was sufficient evidence for an association between indoor dampness and dampness-related agents and cough (Mendell et al., 2011). Most qualitative studies on dampness or mould and cough found positive associations, with 94% of ORs in cross-sectional studies in adults exceeding 1.0 (range, 0.8–4.0). For children, 85% of ORs of prospective or retrospective studies exceeded 1.0 (range, 0.5–2.1) and 94% of cross-sectional studies exceeded 1.0 (range, 0.2–5.7) (Mendell et al., 2011).

The NICE committee found high quality evidence from a large prospective cohort study in Germany that damp condition was associated with cough (Du Prel et al. 2006 in National Institute for Health and Care Excellence, 2020b) and high quality evidence from a prospective cohort study in infants that found mould was associated with cough (Belanger et al. 2003 in National Institute for Health and Care Excellence, 2020b).

Dyspnoea

One guideline and two international authority evidence reviews concluded or advised there was sufficient evidence for an association between indoor damp or mould and dyspnoea (Mendell et al., 2011; Palaty & Shum, 2012; World Health Organization, 2009). Mendell et al. noted that since the 2004 IOM report, the number of available studies for adults and children

had increased and that measures of association with dampness or mould with dyspnoea were predominantly (84%) >1.0 with ORs ranging from 0.7 to 9.4 in adults and from 0.4 to 2.3 in children (Mendell et al., 2011).

Bronchitis

Two guidelines, two international authority evidence reviews and a review that underpinned the AWMF guideline concluded or advised there is sufficient evidence of an association between bronchitis and exposure to indoor mould and/or dampness (Hurraß et al., 2017; Mendell et al., 2011; Palaty & Shum, 2012; Wiesmüller et al., 2017). In 2009, the WHO was a little more circumspect. The WHO had concluded in 2009 that exposure to indoor damp or mould appears to be associated with bronchitis but the evidence is based on relatively few studies (World Health Organization, 2009).

NICE, in their 2020 evidence review reported high quality evidence was found in a German prospective cohort study of 26,888 children showing that damp conditions were associated with bronchitis (ever diagnosed) aOR 1.25 (95% CI: 1.13–1.37) for homes in East Germany, and bronchitis (ever diagnosed) aOR 1.30 (95% CI: 1.03–1.65) for homes in West Germany (Du Prel et al. 2006 in National Institute for Health and Care Excellence, 2020b).

Rhinitis

Two guidelines, two international authority evidence reviews, a systematic review and two reviews provided advice or conclusions about an association between exposure to indoor mould or dampness and allergic rhinitis, most of which indicating that the evidence was sufficient for an association (Caillaud et al., 2018; Hurraß et al., 2017; Mendell et al., 2011; Palaty & Shum, 2012; Tischer et al., 2011; Wiesmüller et al., 2017; World Health Organization, 2009).

The AWMF guideline and associated evidence review noted an association of indoor dampness and moulds with rhinitis risk as the evidence that epidemiological studies on indoor dampness and mould are consistently associated with allergic rhinitis (Mendell et al. 2011 and Jaakola et al 2013 in Hurraß et al., 2017; Mendell et al. 2011 and Jaakola et al 2013 in Wiesmüller et al., 2017).

Mendell et al. only included rhinitis outcomes defined as medically diagnosed allergic rhinitis or the combination of rhinitis symptoms with documented atopy. Dampness and mould were consistently associated with allergic rhinitis in 92% of the findings (all in children) with ORs ranging from 0.7 to 3.5 (Mendell et al., 2011).

Upper respiratory tract symptoms

Two guidelines, two international authority evidence reviews and the review that is associated with the AWMF guideline concluded or advised the evidence was sufficient for an association between upper respiratory tract symptoms and exposure to indoor damp or mould (Hurraß et al., 2017; Mendell et al., 2011; Palaty & Shum, 2012; Wiesmüller et al., 2017). Of the evidence for upper respiratory tract symptoms, Mendell et al. reported most studies found positive associations with dampness or mould (Mendell et al., 2011). Among children 88% of ORs in prospective or retrospective studies reviewed exceeded 1.0 (range, 1.0–1.8), and 95% of ORs in cross-sectional studies exceeded 1.0 (range, 0.4–5.9).

Among adults, 81% of ORs in cross sectional studies exceeded 1.0 (range, 0.4–4.4) (Mendell et al., 2011).

Eczema

The WHO did not make any conclusions about the level of association between exposure to indoor damp or mould and eczema (World Health Organization, 2009). The literature that examined eczema and exposure to indoor damp and mould came to somewhat different conclusions. Two evidence reviews by international authorities concluded or advised there was sufficient evidence for an association between exposure to indoor mould or dampness and eczema (Mendell et al., 2011; Palaty & Shum, 2012), whereas the AWMF guideline and its associated evidence review (Hurraß et al., 2017; Wiesmüller et al., 2017) concluded there was limited or suspected evidence of an association with atopic eczema (manifestation, progression, exacerbation).

Mendell et al.'s update review to the WHO guideline reported dampness or mould was associated consistently with eczema, in the studies they reviewed, with 89% of ORs > 1.0 (range, 0.2–2.9). The strongest study included in the review was a prospective study in children, that found consistently increased ORs up to 2.9 for prenatal mould exposure to infants with no parental atopic history (Mendell et al., 2011). Palaty & Shum's conclusion as to level of association was based on Mendell et al.'s evidence review (Palaty & Shum, 2012).

NICE in their evidence review of indoor air pollutants and health effects reported one prospective cohort study from Germany that provided high quality evidence of a positive association between damp condition and eczema in children, but only in East Germany, not West Germany (Du Prel et al. 2006 in National Institute for Health and Care Excellence, 2020b). NICE did not find any high-quality evidence on exposure to mould and eczema.

Appendix B: Less likely differential diagnoses or symptoms: Health effects for which there is limited or suggested evidenced of association with exposure to indoor damp and mould

The sections below provide an overview of the findings for each health effect.

Common cold

Mendell et al. and the NCCEH both reported there was limited or suggestive evidence for an association between the common cold and exposure to indoor damp or mould, with the NCCEH citing the review by Mendell et al. as their evidence (Mendell et al., 2011; Mendell et al 2011 in Palaty & Shum, 2012). The common cold was positively associated with dampness or mould in 71% of reported findings, but, the methodologically strongest single study, a prospective study in children, found only four of nine estimates elevated, with ORs ranging from 0.6 to 1.8. As such, Mendell et al. considered the association only suggestive (Mendell et al., 2011).

Allergy/atopy (excluding rhinitis and eczema)

Two international authority evidence reviews reported the evidence for an association between the allergy/atopy and exposure to indoor damp or mould as limited or suggestive (Mendell et al., 2011; Mendell et al. 2011 in Palaty & Shum, 2012). Mendell et al. reported that increase in allergy/atopy (excluding rhinitis and eczema) in association with dampness or mould, was found in 77% of reported assessments in the available studies, with ORs ranging from 0.6 to 2.4 (Mendell et al., 2011). Of the evidence overall linking allergy/atopy and dampness or mould, Mendell et al. noted it was inconsistent, and as such, considered the evidence only (strongly) suggestive (Mendell et al., 2011).

Irritant effects (mucous membrane irritation)

Two guidelines and two evidence reviews reported on irritant effects or MMI (Hurraß et al., 2017; Palaty & Shum, 2012; Wiesmüller et al., 2017; World Health Organization, 2009), (Hurraß et al., 2017; Palaty & Shum, 2012), with slightly different conclusions as to level of evidence for an association with indoor damp or mould.

The WHO advised that in epidemiological studies the prevalence of respiratory and irritative symptoms has been associated with perceived mould odour, possibly indicating the presence of volatile organic compounds, and suggestive evidence that they exist in damp buildings at sufficient levels to cause symptoms of irritation in exposed people (World Health Organization, 2009).

The AWMF guideline and associated evidence review categorised the level of evidence between indoor mould exposure or dampness and MMI as limited or suspected evidence for an association (Hurraß et al., 2017; Wiesmüller et al., 2017). The prevalence of mucosal

irritation among individuals occupationally or environmentally exposed to bioaerosols is put at approximately 20–30%, although there is no reliable data as yet, on the prevalence of these non-allergic, irritant, inflammatory effects in general or specifically for indoor mould exposure (Wiesmüller et al., 2017). Possible irritant symptoms in MMI include non-specific irritation of the mucous membrane of the nose (e.g., sneezing, secretion and obstruction of the nasal cavity), the eye (e.g., burning, watering, itching), and the throat (e.g., feeling of dryness, clearing of the throat) (Wiesmüller et al., 2017). Irritant inflammatory processes in the deeper airways (e.g., cough) may manifest as chronic bronchitis.

The AWMF guideline noted that symptoms seen during exposure, such as coughing, burning, itching of the eyes and nose and skin irritation resolve rapidly once exposure ceases. As such, from a differential diagnosis perspective it is important to distinguish between allergic symptoms, that unlike irritant reactions, generally increase upon repeated and long-term exposure due to sensitisation (Wiesmüller et al., 2017). Typical symptoms of MMI are burning or itching eyes, lacrimation, sneezing, runny nose, nasal obstruction, dryness of the throat, frequent clearing of the throat, or cough. Typically, symptoms resolve quickly after exposure cessation.

It is believed that MMI is caused by products of mould metabolism or constituents of the cell walls or a combination of these substances. There are, however, no valid data about indoor mould exposures and MMI (Wiesmüller et al., 2017).

Appendix C: Unlikely differential diagnoses or symptoms: Health effects for which there is inadequate or insufficient evidence of an association with indoor damp and mould

The sections below provide an overview of the findings for each health effect.

Acute idiopathic pulmonary haemorrhage in infants

'Acute idiopathic pulmonary haemorrhage' (AIPH) is also referred to as 'acute idiopathic pulmonary hemosiderosis'. AIPH is a rare disease of unknown origin (Hurraß et al., 2017).

Six pieces of literature concluded or advised there was inadequate or insufficient evidence for an association between AIPH in infants and exposure to indoor damp or mould (Borchers et al., 2017; Hurraß et al., 2017; Palaty & Shum, 2012; Park & Cox-Ganser, 2011; Wiesmüller et al., 2017; World Health Organization, 2009):

- The WHO noted the US IOM (2004) concluded that "available case-report information, taken together, constitutes inadequate or insufficient information to determine whether an association exists between acute idiopathic pulmonary haemorrhage and the presence of *S. chartarum* [*Stachybotrys chartarum*]" (World Health Organization, 2009, p. 81)
- The AWMF guideline advised that while there is no rationale at present to assume a causal link between pulmonary haemorrhage and the presence of indoor mould, nevertheless, a degree of association cannot be ruled out (Wiesmüller et al., 2017)
- Borchers et al. also in 2017, noted that although the early reports in the early 1990s appeared to suggest a link between the unusual cluster of cases of pulmonary haemorrhage in infants and inhalation of mycotoxins, particularly satratoxins, produced by *S. chartarum*, later epidemiological studies failed to confirm any causal relationship (Borchers et al., 2017). As such "a causal relationship between cases of infant pulmonary haemorrhage and exposure to "black mould" has never been proven" (Borchers et al., 2017, p. 305).

Altered lung function/airway obstruction

Mendell et al. listed altered lung function as a health effect for which there was inadequate or insufficient evidence to determine whether an association exists between indoor dampness and dampness-related agents, reporting that the evidence associating altered lung function with dampness or mould was considered too inconsistent to draw conclusions (Mendell et al., 2011).

The NCCHEH listed airflow obstruction in otherwise healthy persons as a health effect for which there was inadequate or insufficient evidence for an association with mould exposure to dampness in indoor environments (Palaty & Shum, 2012).

Cancer

Two guidelines, the review that is associated with the AWMF guideline and one international authority evidence review concluded or advised there was no evidence or suggestion of evidence that exposure to indoor moisture damage or mould is associated with cancer (Hurraß et al., 2017; Palaty & Shum, 2012; Wiesmüller et al., 2017; World Health Organization, 2009).

The WHO advised that heavy occupational exposure by inhalation to mycotoxins in mouldy grain may be linked to an increased risk of cancer but there is no epidemiological evidence for an association between exposure in damp buildings and cancer (World Health Organization, 2009). Some of the microbial toxins produced by fungi and bacteria are known to be genotoxic and carcinogenic but the relevance of these findings to exposure by inhalation in damp buildings is unknown (World Health Organization, 2009).

The AWMF guideline and Hurraß et al. review concluded there was inadequate or insufficient evidence for an association with cancer (Hurraß et al., 2017; Wiesmüller et al., 2017). The Hurraß et al. review advised that in single cases, hypotheses about relationships between fungi and many other different diseases are postulated, with the consequence of frightened patients who “inform” themselves via internet. The review went on to note that additionally, mould is incorrectly equated with “intestinal fungi” (commensal colonisation by *Candida albicans*), and that currently, no systematic examinations or case reports are available that show or suggest an association with moisture damage or mould indoors and [gastrointestinal or renal disease, reproductive disorders, teratogenicity] or cancers (Palaty & Shum, 2012 and Mazur & Kim, 2006 in Hurraß et al., 2017).

It is a medical task, to provide objective information for concerned patients in such cases (Hurraß et al., 2017).

COPD (development of COPD)

The AWMF guideline and associated review (Hurraß et al., 2017; Wiesmüller et al., 2017) and the evidence review by the NCCEH (Palaty & Shum, 2012) concluded or advised there was inadequate or insufficient evidence of an association between indoor damp or mould and COPD. The AWMF guideline and the Hurraß et al. review based their evidence for association on several pieces of evidence (Fisk et al. 2007, 2010; Mendell et al. 2011; Palaty & Shum, 2012; WHO, 2009b in Hurraß et al., 2017).

Note: The evidence reviewed in [section 2.1.2](#) on susceptible patients concerned patients who already had COPD.

Rheumatic disorders and autoimmune diseases/autoimmunity

Two guidelines and four evidence reviews concluded or advised that for rheumatological disorders and other autoimmune diseases there was no or inadequate or insufficient evidence for an association with exposure to indoor damp or mould (Borchers et al., 2017; Chang & Gershwin, 2019; Hurraß et al., 2017; Palaty & Shum, 2012; Wiesmüller et al., 2017; World Health Organization, 2009). The WHO noted in 2009 that cases of autoimmune diseases and related symptoms have been reported among occupants of damp buildings,

however, there were no toxicological data on autoimmune responses caused by microorganisms found in damp buildings or microbial substances (World Health Organization, 2009). Microbial fragments can, however, cause autoimmune reactions by molecular mimicry (World Health Organization, 2009).

The AWMF guideline and the associated review concluded there was inadequate or insufficient evidence for an association with rheumatic disorders, rheumatism or arthritis (Hurraß et al., 2017; Wiesmüller et al., 2017). While an association between inflammatory rheumatic diseases and infections had been hypothesized for many years and there are also reports about dampness and rheumatic complaints, these observations were noted to have been made by one group of researchers and further evidence is not available (Hurraß et al., 2017). Until studies from other centres and countries are available the AWMF guideline authors advised it cannot be assumed the current evidence is sufficiently robust (Wiesmüller et al., 2017), and extending diagnostic measures beyond standard procedures cannot be recommended (Hurraß et al., 2017; Wiesmüller et al., 2017).

Reproductive effects, gastrointestinal effects, renal effects, and teratogenicity

Two guidelines, the review that is associated with the AWMF guideline and one international authority evidence review concluded reproductive effects as health effects for which there is inadequate or insufficient evidence for an association with exposure to indoor dampness or mould (Hurraß et al., 2017; Palaty & Shum, 2012; Wiesmüller et al., 2017; World Health Organization, 2009). The WHO advised no studies were found on the effects of exposure to microbes in damp buildings on reproductive responses, but noted that phthalates (one group of indoor air contaminants) are potential reproductive and developmental toxicants (World Health Organization, 2009).

The AWMF guideline and the associated review both covered a wider number of health effects, advising that no systematic examinations or case reports are available that show or suggest an association with moisture damage or mould indoors and gastrointestinal or renal disease, reproductive disorders, teratogenicity [or cancers] (Palaty & Shum, 2012 and Mazur & Kim, 2006 in Hurraß et al., 2017; Wiesmüller et al., 2017).

Regarding exposure to other potential indoor air pollutants (as mentioned by the WHO above) and reproductive effects, in the evidence review by NICE that considered exposure to indoor mould and damp, along with multiple other exposures, reproductive effects were not specifically mentioned in the section 'For the outcomes that matter most'. Of the range of indoor air pollutants investigated in the evidence review, the NICE committee stated:

The committee noted the pollutants such as NO₂ [nitrous dioxide], volatile organic compounds (VOCs), particulate matter (PM) from open solid-fuel fires, polycyclic aromatic hydrocarbons (PAHs) and biological agents such as mould and pet dander are sometimes associated with many symptoms including those affecting the respiratory, cardiovascular and neurological systems. (National Institute for Health and Care Excellence, 2020b, p. 66)

Sarcoidosis

Sarcoidosis is a granulomatous disease of unknown cause involving multiple organs, including the lung, with the lung being the most commonly affected organ (Hurraß et al., 2017; National Institute for Occupational Safety and Health et al., 2012; Park & Cox-Ganser, 2011). As granulomatous disease is generally linked with infection or reactions to foreign bodies, it has been discussed in the literature that sarcoidosis may represent a microbial-induced disease (Hurraß et al., 2017). The National Institute for Occupational Safety and Health (NIOSH) at the CDC (NIOSH/CDC) noted the occupational causes of sarcoidosis had indicated there to be increasing evidence that sarcoidosis has multiple causes, including exposure to mould, especially in the presence of triggers of inflammation (Newman and Newman, 2012 in National Institute for Occupational Safety and Health et al., 2012).

The most recent guidance comes from the 2017 AWMF guideline and the associated review, both of which advised there was inadequate or insufficient evidence for an association between sarcoidosis and moisture/mould damage (Hurraß et al., 2017; Wiesmüller et al., 2017). This suggested only unreliable evidence that different forms of microbial inhalation exposure, including water damage, can increase the risk of developing sarcoidosis (Wiesmüller et al., 2017). As such, there is currently insufficient data to assume a causal link between the development or exacerbation of sarcoidosis and water damage or mould exposure (Wiesmüller et al., 2017).

Given there is insufficient data to assume a causal link between the development and exacerbation of sarcoidosis and water-damage or mould exposure, the AWMF guideline advised no specific mould-related diagnostic work-up is indicated in sarcoidosis above and beyond the usual procedure (Wiesmüller et al., 2017).

Skin problems

The NCCEH listed skin symptoms as a health effect for which there was inadequate or insufficient evidence for an association with mould exposure or dampness in indoor environments (Palaty & Shum, 2012). The WHO excluded effects related to skin on the basis that limited research had been reported (World Health Organization, 2009). NICE's evidence review reported evidence statements for facial skin symptoms; the committee found one low quality retrospective cohort study that had very serious risk of bias (RoB) (Engvall et al. 2001 in National Institute for Health and Care Excellence, 2020b).

Neuropsychological, neuropsychiatric and neurotoxic effects

The House of Representatives Inquiry Report on biotoxin-related illnesses stated that Australian patients who identified as having CIRS commonly described experiencing memory and concentration problems and disorientation (House of Representatives Standing Committee on Health, Aged Care and Sport, 2018). Other symptoms experienced by patients with CIRS put forward by ACIIDS that are relevant to this section on nervous system effects include light sensitivity, confusion, numbness, tingling, tremors, temperature regulation or dysregulation problems, difficulty with focus/concentration, sweats (especially night sweats),

and decreased assimilation of new knowledge (Australian Chronic Infectious & Inflammatory Disease Society, 2018).

Two guidelines, two international authority evidence reviews/reports and the review that is associated with the AWMF guideline concluded or advised that the level of evidence is inadequate or insufficient for an association between indoor mould or damp and neuropsychological, neuropsychiatric or neurotoxic effects (Hurraß et al., 2017; National Institute for Occupational Safety and Health et al., 2012; Palaty & Shum, 2012; Wiesmüller et al., 2017; World Health Organization, 2009).

The WHO advised that while health effects such as fatigue, headache and difficulties concentrating indicate that microbes or other agents present in damp buildings have neurological effects, no study has shown that people living in damp buildings who complain of nervous system symptoms are exposed to effective levels of mycotoxins (World Health Organization, 2009). The AWMF guideline notes the specialist literature does not point to a consistent causal relationship between indoor toxin levels and neurotoxic effects; as such, evidence of a link is insufficient (Wiesmüller et al., 2017). Additionally, the AWMF guideline advised:

- only moulds that are potentially able to form toxins can be triggers of toxic reactions. Environmental and growth factors, above all the substrate, determine whether or not toxin formation occurs in individual cases
- mould exposure can generally lead to MMI, odour effects and mood disorders. With indoor moisture/mould damage, all people can be affected by odour effects and or mood disorders; however, this is not a health hazard. (Wiesmüller et al., 2017). More on odour effects is outlined in the section on '[Odour effects](#)'.

The evidence review that accompanies the AWMF guideline advised that “there are no systematic reviews on this controversial topic available” (Hurraß et al., 2017, p. 313). On various occasions, exposure to toxin producing moulds (“toxic mould”) indoors has been associated with neurotoxic effects, and cognitive or emotional problems have been causally related to mycotoxins (“black TMS”) (Baldo et al. 2002; Crago et al. 2003; Gordon et al. 1999; Gordon et al. 2004; and Singer 2011 in Hurraß et al., 2017) and toxin detoxifying therapies have been propagated (Hurraß et al., 2017). However, Hurraß et al. advised these works were criticized because of methodological weaknesses (McCaffrey & Yantz 2005 in Hurraß et al., 2017). As such, and consistent with the WHO guideline information above, Hurraß et al. advised that no consistent proof can be deduced from the literature that the toxin concentrations occurring indoors can cause neurotoxic effects (Bush et al. 2006; Chapman et al. 2003; Gordon et al. 2004; Gordon et al. 2006; Khalili et al. 2005; Lees-Haley 2003; and Terr 2009 in Hurraß et al., 2017).

The NCCEH listed neuropsychiatric symptoms as a health effect for which there is inadequate or insufficient evidence of an association with mould exposure or dampness in indoor environments, (Palaty & Shum, 2012). The NIOSH/CDC also noted the evidence is limited for the possible health effects of mycotoxins in indoor environments, including neurological outcomes (National Institute for Occupational Safety and Health et al., 2012).

Sleep issues

The WHO guideline excluded insomnia as a health outcome of exposure to indoor dampness and mould based on the limited reported research (World Health Organization, 2009). NICE made evidence statements regarding sleep issues and exposure to visible damp or mould in the indoor environment from one prospective cohort study in 10-year-old children in Germany (Tiesler et al. 2015 in National Institute for Health and Care Excellence, 2020b). The study was appraised as low quality by NICE. The reported outcomes from this study do not show a consistent positive association between exposure to visible damp or mould and sleep issues.

A study by Wang et al. analysed questionnaires at baseline and 10 years later from a cohort study of 11,318 adults enrolled in the Respiratory Health in Northern Europe (RHINE) study. The study concluded that dampness and mould at home and work can increase the development of insomnia symptoms, snoring and excessive daytime sleepiness, especially with the combined exposure for both dampness and mould at home and at work (Wang et al., 2020). The authors did note limitations including that the study was performed in a limited geographic area (Northern Europe), characterised by cold climate and lack of daylight in winter due to short days (Wang et al., 2020). Therefore, this study may not be generalisable to the Australian setting.

Fatigue

The WHO excluded fatigue in its guideline based on limited research having been reported (World Health Organization, 2009). The NCCEH included fatigue as a health effect for which there was inadequate or insufficient evidence (Palaty & Shum, 2012).

Mood disorders, non-specific symptoms, impairment of well-being, and odour effects

Many studies refer to mould odour as one of the exposures of interest when investigating health impacts from exposure to indoor mould or damp.

Odour effects

Environmental odours can affect health and wellbeing in various ways (Wiesmüller et al., 2017). Mould metabolites can cause relevant odours to be perceived (Wiesmüller et al., 2017) and the sensation of unpleasant odours can cause stress responses and non-specific somatic symptoms such as headache and nausea (World Health Organization, 2009), as well as fatigue, lack of concentration and insomnia (Wiesmüller et al., 2017). Regarding indoor moisture/mould damage, the AWMF guidelines advises, “everyone can be affected by odour effects and/or mood disorders[...] However, this is not a health hazard” (Wiesmüller et al., 2017, pp. 168–169). Predisposing factors for odour effects can include context and adaptation effects, genetic and hormonal influences, and imprinting, whereas, predisposing factors for mood disorders may include anxiety, environmental concerns, condition and attribution, along with various diseases (Wiesmüller et al., 2017).

The perception and cognitive appraisal of – and thus also sensitivity to – odours are subject to considerable inter-individual variability, with genetic and hormonal factors, as well as character, context and adaptation effects, playing a role (Wiesmüller et al., 2017).

The AWMF guideline noted the following points about odours:

- It has not yet been elucidated whether biological signalling effects come from microbial volatile organic compounds (MVOCs) at the low $\mu\text{g}/\text{m}^3$ -range levels found indoors
- Olfactory–psychological coupling reactions with non-specific symptoms are possible in the case of cacosmia-related abnormalities; toxic reactions, on the other hand, are unlikely
- There are other sources of microbial volatile organic compound (MVOC) besides microbial sources (e.g., tobacco smoke, cooking, baking, roasting, pot plant soil, compost bin, etc.)
- A distinction needs to be made between direct physiological effects; odour perception; odour pollution as an effect of the odour on an emotional level; and indirect physiological effects due to odour pollution and the resulting chronic stress.

In the reality of environmental health analysis, it is not always possible to distinguish between the health effects caused by odours via the above-mentioned mechanisms (Wiesmüller et al., 2017).

Impairments of well-being play a major role in environment-associated disorders in general and in indoor-associated health disorders in particular, and that complaints are presented as impairment of mental, physical and social well-being and feeling of subjective impaired productivity ((Wiesmüller et al. 2003 in Hurraß et al., 2017). As an emotional experience, they can be described as annoyance reactions that include cognitive evaluation of specific environmental stimuli (Wiesmüller et al. 2003 in Hurraß et al., 2017).

Although mood disorders as a health effect are possible, the AWMF guideline advised these are not mediated via toxicological mechanisms, but rather via conditioning, attribution (of links), or stress. Mood disorders can be understood as precursors to somatic dysfunction (Wiesmüller et al., 2017).

Non-specific building related syndrome (NBRS-formally called SBS) and chemical intolerance

NBRS and chemical intolerance can, in severe cases lead to significant disability, poor quality of life, suffering of individuals and costly loss of productivity to society (Nordin, 2020). Nordin noted NBRS and chemical intolerance are regarded as functional somatic syndromes and idiopathic environmental intolerances and that typical cases cannot be explained by toxic exposure. Furthermore, the multi-faceted similarities between NBRS and CI strongly favour the notion that the two conditions at large share underlying mechanisms. As such, preventive measures and appropriate treatment call for understanding of the mechanisms underlying NBRS and CI (Nordin, 2020).

Nordin addressed the question about toxicity as an explanation of NBRS and chemical intolerance, noting, typical cases cannot be explained by toxicity since such criteria are not fulfilled, and only a subset of people from the general population or any given chemically exposed group develop these conditions (Nordin, 2020). He noted, as the WHO had done, that no study has shown that people living in damp buildings with nervous system symptoms are exposed to effective levels of *Stachybotrys* or other mycotoxin-producing moulds.

As the mechanisms underlying NBRS and CI are not attributable to toxicity, Nordin takes a biopsychosocial perspective through a 'state-of-the-art' review of neurogenic inflammation, neural sensitisation, classical conditioning, symptom misattribution and somatosensory amplification, and nocebo with regard to these environmental intolerances. Nordin noted these mechanisms also underlie various other types of functional somatic symptoms (Nordin, 2020).

Mycotoxicosis

Mycotoxicosis describes the systemic effects (poisoning) caused by mycotoxins produced by moulds and have been well-documented and occur in humans and animals upon oral ingestion of contaminated foods (Borchers et al., 2017; Hurraß et al., 2017; Wiesmüller et al., 2017). In 2009, the WHO advised that while mycotoxins can induce a wide range of adverse health effects in both animals and human beings, the evidence that they play a role in health problems related to indoor air is "extremely weak" (World Health Organization, 2009, p. 81).

Of mycotoxicosis, the 2017 AWMF guideline stated:

There is no reliable knowledge to date of indoor airborne mycotoxin poisoning. It also remains to be established whether mycotoxin levels in indoor air are relevant in terms of a systemic toxicological risk. According to the findings available to date, this does not appear to be the case. (Wiesmüller et al., 2017, p. 178)

Of mycotoxins, the AWMF guideline advised that numerous mould genera, (e.g., *Penicillium*, *Aspergillus*, *Alternaria*, *Fusarium*, *Stachybotrys*) produce mycotoxins, with mycotoxin production depending on the species, and environmental factors, such as moisture levels, substrate composition, potential for hydrogen (pH) value, nutrient competition and light wavelength (Fischer et al. 2006 in Wiesmüller et al., 2017). Mycotoxins are not volatile and are found in the air bound to spores, cell fragments and other particles and are generally only found at levels relevant to health in foods and animal feed that have been colonised by moulds (Wiesmüller et al., 2017). The available data indicate the level of most airborne mycotoxins found indoors do not exhibit an acute toxic effect (Wiesmüller et al., 2017). The AWMF advises evidence indicates that as a general rule, mycotoxins produced by indoor-relevant moulds can be detected in extremely low concentrations (parts per trillion) in house dust (Bloom et al. 2009 in Wiesmüller et al., 2017), bioaerosols and building materials.

Concerns about unvalidated tests and testing to detect mycotoxins in humans

Several authors highlighted the issue of unvalidated tests and testing being used in humans to detect mycotoxins (Chang & Gershwin, 2019; Larenas-Linnemann et al., 2016; Rudert & Portnoy, 2017). Outside of occupational settings almost all reports of fungal toxins in buildings have been based on methods that have not been validated for this purpose and tests that claim to measure trichothecenes in human sera or urine have not been proven to be analytically reliable (Larenas-Linnemann et al., 2016; Rudert & Portnoy, 2017). Chang and Gershwin further explained that recently a number of laboratories they described as 'disreputable' have been adapting the methodology for testing mycotoxins in pig urine to human patients in an attempt to link mycotoxins in the urine with a variety of diseases, such as autoimmune diseases or to explain vague symptoms reported by patients (Chang & Gershwin, 2019).

There are no FDA-approved urine tests for mycotoxins and low levels of so-called “mycotoxins” that are normally found in foods (Chang & Gershwin, 2019).

For more information, see [section 4.6](#) (on ‘Diagnostic tests that are not recommended by international mainstream medical guidance’), and [section 4.6.2](#), (on ‘Mycotoxins in serum’).

SBS and TMS

SBS and TMS are noted as controversial topics in the literature. ‘Toxic mold syndrome’ or ‘toxic mold’ are terms that are now frequently used as being synonymous with SBS (Borchers et al., 2017). This topic is particularly relevant to CIRS as TMSA also reported to the Inquiry that CIRS-WDB was previously referred to as SBS (Toxic Mould Support Australia, 2018).

The WHO excluded SBS in its review of health effects on the basis that limited research had been reported (World Health Organization, 2009). Several pieces of literature covered SBS or TMS, with four recent reviews concluding or advising there to be no scientific evidence to support claims, (or the claims are unproven), that these syndromes associated with vague and subjective symptoms are caused by exposure to mycotoxins or visible black mould in buildings (Borchers et al., 2017; Chang & Gershwin, 2019; Larenas-Linnemann et al., 2016; Rudert & Portnoy, 2017). Furthermore, these reviews note the media coverage, “media hype”, “mass hysteria” and litigation that sits around SBS. One of these reviews was a clinical commentary review by Larenas-Linnemann et al. (2016) on behalf of the Environmental Allergens Group of the AAAAI, published in the *Journal of Allergy and Clinical Immunology: In Practice* (impact factor (IF): 14.110). Additionally, the clinical commentary review has a Category 1 CME credit.

Borchers et al. noted the long list of poorly defined health effects that some have complained are secondary to mould exposure, but asserted these observations are flawed, they lack controls, and are non-specific and lack medical plausibility (Borchers et al., 2017). The presence of *S. chartarum* in indoor air samples generally means that a building has or had significant moisture problems (Larenas-Linnemann et al., 2016). The primary species blamed for the release of mycotoxins in SBS was *S. chartarum*. However only 30–40% of its strains produce mycotoxins which include macrolytic trichothecenes, satratoxins G and H (Borchers et al., 2017; Chang & Gershwin, 2019). When these chemicals are detected in air, the amounts have been found to be widely variable, although typically in the range of 0.25 to 0.43 ng/m³, and in dust sampled for mycotoxins, the amount is less than one to 43 pg/mg of dust (Chang & Gershwin, 2019). As such, at these concentrations, studies have shown that an individual breathing normally in such an environment for eight hours would inhale only 0.72 and 1.2 ng of satratoxins G and H respectively which is far less than the amount humans are exposed to in their normal daily activities (Chang & Gershwin, 2019).

CIRS

None of the international guidelines, or numerous international authority or medical professional association evidence reviews included in the evidence evaluation that underpins this Clinical Pathway mentioned CIRS or Chronic Inflammatory Response Syndrome – Water-Damaged Buildings (CIRS-WDB) as a possible health effect from exposure to indoor damp or mould. As such, CIRS or CIRS-WDB has been categorised in this Clinical Pathway

as a syndrome or health effect for which there is insufficient or inadequate evidence of an association with exposure to indoor damp or mould.

See [Appendix E](#), (on 'Chronic Inflammatory Response Syndrome (CIRS)'), and [Appendix F](#) (on 'Potential side effects of pharmaceuticals used in the treatment of CIRS), for further relevant information.

Appendix D: enHealth factsheet on Potential health effects of mould in the environment



What is mould?

Mould is a type of fungus that grows in moist or humid places. It occurs naturally in the environment and can be found almost anywhere, including in garden composts and on decaying or damp organic material, and food. Indoors, mould grows best in damp and poorly ventilated areas, typically on wood, plasterboard, tile grout and furnishings. Common causes of mould growth indoors include:

- leaking roofs and walls,
- faulty plumbing, and
- condensation.

To reproduce, mould produces tiny particles called spores. These spores travel easily through the air and may begin to grow and spread when they land on damp surfaces.

Mould is not always easy to recognise. It often looks like ‘fuzz’ or may appear to be a stain, smudge or discoloration. The most common moulds are black, green or white. However, mould can be many other colours, ranging from grey to orange to brown and can also change colour depending on its age or life-stage.

How am I exposed to mould?

Mould spores and fragments exist naturally in the air we breathe. The amount that people are exposed to depends on various factors including the season, surrounding land, wind, and people’s activities / actions both indoors and outdoors.

Mould primarily enters your body through breathing and swallowing.

Some moulds produce toxins (mycotoxins). People are mostly exposed to mycotoxins through eating contaminated food. Australia minimises exposure to mycotoxins in the community by maintaining a hygienic food supply chain.

How can mould affect my health?

Breathing in mould spores and fragments can trigger nasal congestion, sneezing, coughing or wheezing, and respiratory infections. It can also worsen asthma and allergic conditions. Contact with mould can also irritate eyes and skin.

People who are more likely to experience these symptoms include those with weakened immune systems, allergies, severe asthma or lung diseases. These people are also more susceptible to other serious health effects, such as the lung condition aspergillosis ('Farmer's lung').

There is no exposure limit or health guideline value for exposure to mould. Where possible, exposure to mould should be minimised – this is particularly recommended for people who are more sensitive to mould exposure.

If you are concerned about any symptoms you are experiencing, seek medical advice. In the case of a life-threatening emergency, phone 000.

How do I minimise my exposure to mould?

Although mould naturally occurs in the environment and can be found almost anywhere, it needs damp surfaces and moisture to grow. You can reduce your exposure through simple measures, however there is no practical way to eliminate all exposure to mould. These measures include:

Indoors

- Prevent moisture and dampness and ensure adequate ventilation. This will minimise current and future mould growth.
- Fix leaky plumbing, roofs or other building faults.
- Clear and maintain gutters.
- Reduce and remove condensation (e.g. use exhaust fans and wipe up excess water).

Homes with inadequate ventilation resulting from poor design, modifications or lack of maintenance may be more prone to developing mould. The cheapest and easiest way of reducing indoor moisture and humidity is by ventilating a room by opening a door or window.

Food

- Throw away foods that have become visibly mouldy.
- Adequately clean the surface area on which the mouldy food was stored or consider throwing away the container the food was stored in.

Outdoors

- Use appropriate personal protective equipment such as gloves and a P1 or P2 face mask when handling garden composts, mulch, straw or hay, and mouldy and decaying organic materials.

How do I remove mould from my home?

Generally, if you can see or smell mould (often a dirty or earthy smell), you need to clean it up as mould can damage surfaces it grows on and affect your health. You should also try to find and control the source of the mould and/or dampness so that it won't recur after cleaning.

If you have decided to remove mould yourself, make sure there is good ventilation and wear protective clothing. For example, wear a shower cap and use gloves, eye protection, overalls, suitable footwear, and a P1 or P2 face mask.

Household detergent or white vinegar is usually sufficient to clean the mould. Use a microfibre cloth and rinse the dirty cloth regularly in a separate container of clean water to prevent spreading the mould. Do not dry brush the mouldy area, as the brush can flick spores into the air where they may be breathed in. Contaminated soft furnishings are difficult to clean and may need to be thrown away.

If there are large areas of mould or mould regrowth, consult a mould remediation professional. Some mould is not visible as it might be in a roof space, behind a wall or under floor coverings, so you may need to consult a professional if you can smell but can't see it.

Should I test for mould in my home?

Where mould is visible, it is generally not considered necessary to test for it in the home. In general, we do not recommend testing for mould at all because there are no health guideline values for which to compare test results to. This means that test results cannot be used to determine if a health risk exists. Mould is everywhere, so if you go testing for it, you will find it.

In summary, dampness and mould related problems should be prevented. When they occur, they should be rectified – remove mould where present, find it when you smell it, repair and control sources of excessive moisture – this is the best approach to controlling potential health risks.

Where do I go for more information or advice?

- **Your local doctor or Nurse on Call** in your state – if you feel unwell
- **Your local Council or State Health Department** (Environmental Health Section) – for ways to prevent/reduce mould growth and advice on its removal
- **Occupational Hygienist** – for consultancy services at a fee to remove mould, locate the mould by inspection (if you can smell, but can't see it), or to find a solution.
- **Your insurance company** – after a flood
- **The relevant Tenants Union** in your state – for rental properties
- **The relevant Consumer Affairs Authority** in your state
- **The relevant Domestic building complaints / dispute resolution service** in your state

Appendix E: Chronic Inflammatory Response Syndrome (CIRS)

The evidence base on CIRS and exposure to mould is very limited. CIRS is not a recognised disease in Australia, with no scientifically validated or approved diagnostic criteria, and it is not a notifiable disease.

CIRS has been the subject of a House of Representatives Inquiry that notes that biotoxin-related illnesses and CIRS are not widely recognised medical conditions among the Australian medical profession. The Inquiry also noted that a small number of medical practitioners in Australia provide treatment to patients who they diagnosed or provisionally diagnosed as having CIRS, including access to the treatment protocol and the side effects of the medications used.

There is no reliable evidence on the clinical epidemiology of CIRS attributed to exposure to indoor damp or mould in Australia, which can be reliably used to inform an evidence based clinical pathway.

None of the international guidelines, or numerous international authority or medical professional association evidence reviews included in the evidence evaluation that underpins this Clinical Pathway mentioned CIRS or Chronic Inflammatory Response Syndrome – Water-Damaged Buildings (CIRS-WDB) as a possible health effect from exposure to indoor damp or mould. As such, CIRS or CIRS-WDB has been categorised in this Clinical Pathway as a syndrome or health effect for which there is insufficient or inadequate evidence of an association with exposure to indoor damp or mould.

The following sub sections provide more information from the evidence evaluation about the background and context of CIRS in Australia, the symptoms and symptom complexes reported to be associated with CIRS, the limited evidence base on the diagnostic tests and treatments used by CIRS practitioners to diagnose CIRS, and to treat patients diagnosed with CIRS. The potential side effects of the medications used to treat patients diagnosed with CIRS is provided in [Appendix F](#) (on 'Potential side effects of pharmaceuticals used in the treatment of patients with CIRS').

Background and context of CIRS in Australia

In 2018, the House of Representatives Standing Committee on Health, Aged Care and Sport issued its Inquiry Report (the Report) into Biotoxin-related Illnesses in Australia (House of Representatives Standing Committee on Health, Aged Care and Sport, 2018). The House of Representatives Inquiry (the Inquiry) noted that spores produced by mould have the potential to cause health issues if inhaled by susceptible individuals. While the prevalence of a condition referred to as CIRS has been described in Australia and internationally as a biotoxin-related illness, the Inquiry Committee reported that biotoxin-related illnesses and CIRS are not widely recognised medical conditions among the Australian medical profession. Additionally, advice from the Department to the Inquiry noted that biotoxin-related illnesses are not captured within the National Notifiable Diseases Surveillance System, that data is not retained on their frequency or distribution, and there are no clinical guidelines for the diagnosis and treatment of CIRS (House of Representatives Standing Committee on Health, Aged Care and Sport, 2018).

The Australian Government acknowledged it sympathises with, and is concerned for, those patients who are suffering debilitating symptoms they believe to be associated with exposure to mould and/or biotoxins. The Australian Government advised that further research is required into the link between such symptoms and exposure to mould. Additionally, the Australian Government noted that there are many similarities between such symptom complexes and others, such as symptom complexes attributed to ticks or chronic fatigue-like symptoms and therefore there is an opportunity to take a broad multidisciplinary approach. This approach would include working with patients, health groups and practitioners to investigate how to provide better care to all patients with complex symptom groups that are not yet medically explained (Australian Government, 2020).

The Inquiry noted that a small number of medical practitioners in Australia identified as providing treatment to patients who they diagnosed or provisionally diagnosed as having CIRS (Australian Chronic Infectious & Inflammatory Disease Society, 2018; Gupta, 2018; House of Representatives Standing Committee on Health, Aged Care and Sport, 2018). CIRS practitioners and proponents of CIRS claim that there are increasing and clinically significant numbers of cases in Australia, but these claims are not backed up with robust or transparent research.

While a number of submissions by CIRS practitioners and proponents of CIRS reported to the Inquiry that inflammation is central to or at the heart of CIRS (Australian Chronic Infectious & Inflammatory Disease Society, 2018; MouldLab, 2018; Toxic Mould Support Australia, 2018), the WHO concluded the mechanisms by which non-infectious microbial (i.e., not exclusively mould/fungi) exposures contribute to adverse health effects with indoor dampness and mould are largely unknown, but it is clear that no single mechanism can explain the wide variety of effects associated with dampness and mould (World Health Organization, 2009).

Symptoms and symptom complexes associated with CIRS in Australia

The symptoms and symptom complexes associated with CIRS incorporates a wide range of nonspecific symptoms.

There are no clinical studies in the published peer-reviewed literature on the signs and clinical symptoms associated with CIRS, in Australia.

The only relevant information available is self-reported and anecdotal. The information can, however, provide insights for medical professionals when patients present to primary care and question whether they may be experiencing the symptoms associated with CIRS.

Some people may have a diagnosis that has not yet been identified that explains these symptoms while others may have a cluster of MUS that require management.

People with MUS may obtain a diagnosis over time as symptoms develop and guide to the origin of the illness. Others may find that symptoms resolve over time, without ever identifying a cause. All people with MUS, (including those experiencing the symptoms associated with CIRS) can be assisted to have an improved quality of life with good care in a partnership between patient and the health care team.

CIRS was reported to have an extensive symptomology experienced in diverse combinations and with various degrees of severity, across multiple bodily systems

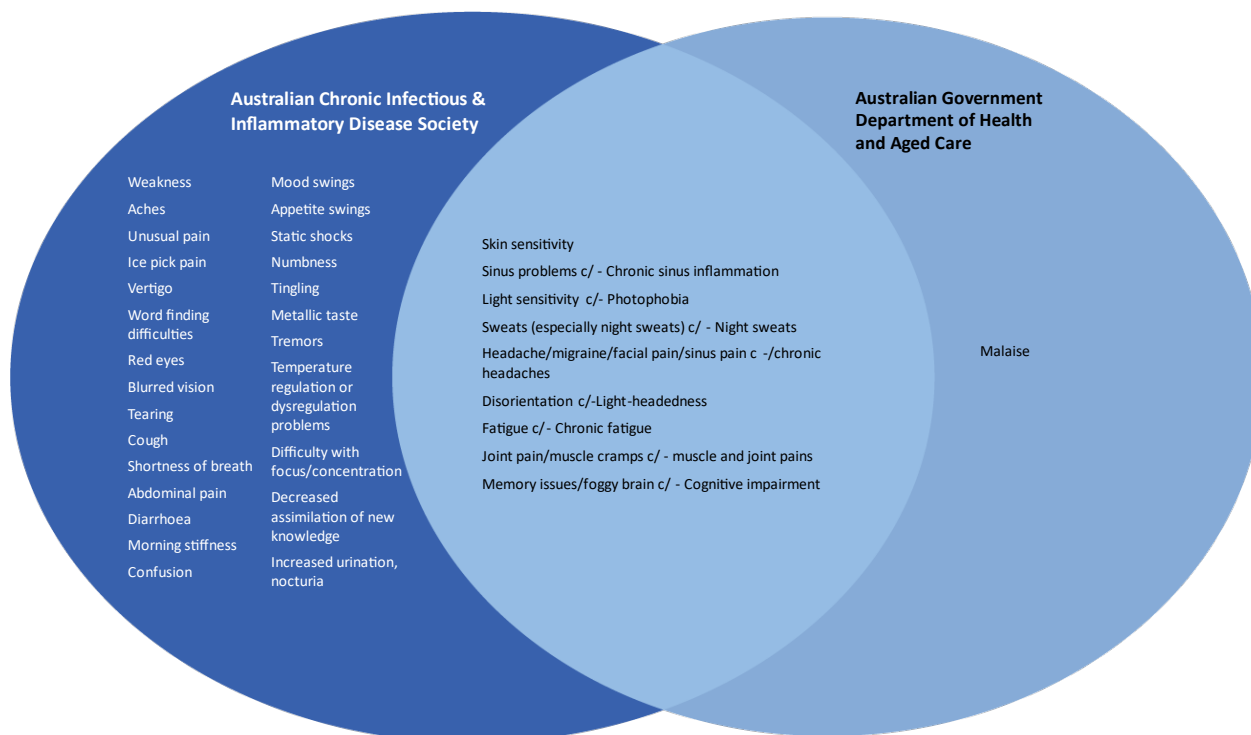
Of the evidence and information provided to the Inquiry into Biotoxin-related illness in Australia, from patients who identified as having biotoxin-related illness or CIRS and their treating doctors (CIRS practitioners), the Report concluded “the illness that has been termed by some as CIRS has been associated with a range of physical and cognitive symptoms, which can affect multiple systems within the body” (House of Representatives Standing Committee on Health, Aged Care and Sport, 2018, p. 60). CIRS was described in submissions as a multi-symptom, multi-system illness or condition (Australasian Integrative Medicine Association & Australasian College of Nutritional and Environmental Medicine, 2018; Australian Chronic Infectious & Inflammatory Disease Society, 2018; Gupta, 2018; House of Representatives Standing Committee on Health, Aged Care and Sport, 2018).

Symptoms reportedly experienced and described by Australian patients who identified as having biotoxin-related illness or CIRS to the House of Representatives Inquiry ranged from mild to severe. The most commonly reported symptoms by submitters to the Inquiry who identified as having CIRS included fatigue, pain and joint pain, memory and concentration problems and disorientation, insomnia, gastrointestinal issues, sinus issues, headaches, and respiratory issues. The reported symptoms are very similar, except for sinus and respiratory issues, to those symptoms reported by people who identified as having DSCATT.

The Department provided a list of symptoms, illustrated in the following figure.

In their submission to the Inquiry, Australian Chronic Infectious and Inflammatory Disease Society (ACIIDS) commented, that “inflammation is at the heart of CIRS,” (Australian Chronic Infectious & Inflammatory Disease Society, 2018, p. not numbered) and also provided a list of presenting symptoms. Neither the Department nor ACIIDS included a citation or other information describing how their respective lists of symptoms have been compiled. As shown in [Figure 1](#) overleaf, the lists of symptoms overlap.

Figure 1: Symptoms attributed to exposure to mould



Diagnostic tests used diagnosing CIRS not recommended due to limited evidence

Anecdotal information indicates patients experiencing biotoxin-related illnesses and CIRS-like symptoms are being diagnosed with CIRS in Australia by a very limited number of medical professionals (CIRS practitioners).

This diagnosis process involves an initial consultation phase consisting of a comprehensive patient assessment which includes a patient history, including environmental history, confirmation of mould at premises with the Environmental Relative Moldiness Index Testing (ERMI) or Health Effects Roster of Type Specific fungal producing-Mycotoxin and Inflammagens (HERSTMI-2) tests commonly recommended, and documentation of symptoms. A range of diagnostic tests are then undertaken to assist with diagnosis, including biomarker testing, visual contrast sensitivity (VCS) testing, Human Leucocyte Antigen (HLA) testing, NeuroQuant®, Multiple Antibiotic Resistant Coagulase Negative Staphylococci (MARCoNS) detection, and transcriptomics.

The limited evidence base is a key issue identified regarding the validity, or reliability of diagnostic processes used for the diagnosis of CIRS.

Treatments provided to Australian patients diagnosed with CIRS; there are significant side effects with many of the medications

There are no published peer-reviewed publications of clinical studies on the treatment and treatment outcomes in Australian patients who identify as having CIRS-like symptoms or, indeed CIRS. The available information on the treatment modalities provided to patients identifying as having CIRS or CIRS-like symptoms in Australia is limited.

Provision of treatment to Australian patients who have been diagnosed with CIRS is by a very few medical practitioners, (primarily GPs) who identify as treating CIRS.

Access to treatment for CIRS, and side effects from the treatment protocol were issues raised to the Inquiry related to the delivery of treatment in Australia. Access to treatment included costs associated with treatment (both the removal of exposure, and patient medications); and the lack of availability of practitioners providing treatment for CIRS. The Inquiry heard that some individuals had pieced-together their own treatment regime or sought medical advice from interstate or overseas doctors who offered an understanding of mould-related disease.

Significant side effects have been identified with many of the medications used in the treatment of patients diagnosed with CIRS including Cholestyramine (CSM), pioglitazone, statins (such as atorvastatin or rosuvastatin) losartan, desmopressin, and vasoactive intestinal polypeptide (VIP) spray. See [Appendix F](#) for further details.

Appendix F: Potential side effects of pharmaceuticals¹¹ used in the treatment of patients diagnosed with CIRS

Drug	Side effects ^	Side effects source	Other recommended sources	Notes
Cholestyramine	<ul style="list-style-type: none"> • Abdominal pain • Flatulence (wind/gas) • Nausea • Vomiting • Heartburn • Diarrhoea • Anorexia (loss of appetite) • Indigestion • Steatorrhoea (the presence of excess fat in the faeces. Stools may be bulky and difficult to flush, have a pale and oily appearance and can be especially foul smelling) • Rash and irritation of the tongue, skin or anal area • Changes in bowel motions • Chest pain • Headache • Anxiety • Dizziness 	MIMS (Monthly Index of Medical Specialities, 2020)	ARTG (CMI)	https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2010-CMI-07313-3 ARTG (CMI) https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2010-PI-07312-3 ARTG (PI)

¹¹ All potential pharmaceuticals, and their side effects, used in the and as described in the ACIIDS submission to the Inquiry to treat Australian patients were included to maximize clinicians' knowledge to enable best practice and duty of care.

Drug	Side effects ^	Side effects source	Other recommended sources	Notes
	<ul style="list-style-type: none"> • Drowsiness • Constipation • Haemorrhoids 			
Pioglitazone	<ul style="list-style-type: none"> • Heart failure, which may show as localised swelling of the ankles, feet and hands (oedema) and/or fluid in the lungs (pulmonary oedema). This has been reported in clinical trials mainly in patients who are taking ACTOS in combination with insulin • Increased risk of bone fracture in women • Macular oedema (an eye disorder that can affect vision) • Altered or impaired liver function • Weight gain • Signs of hypoglycaemia, which may include weakness, trembling or shaking, sweating, light-headedness, headache, dizziness, lack of concentration, tearfulness or crying, irritability, hunger, numbness around the lips and fingers • Eye problems including blurred or double vision • Dark urine or pale stools, yellowing of the skin or eyes, severe cramps of the stomach, nausea or vomiting, loss of weight, tiredness • Shortness of breath when at rest or after minimal physical activity with swelling of legs, feet and hands, rapid increase in weight • Blood in the urine often accompanied by pain and burning, these can be symptoms of bladder cancer 	ARTG (CMI)		<p>https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2015-CMI-02636-1 ARTG (CMI)</p> <p>https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2011-PI-01931-3 ARTG (PI)</p>

<p>Statins Atorvastatin</p>	<ul style="list-style-type: none"> • Yellowing of the skin and eyes and dark coloured urine • Feeling weak and tired, excessively thirsty and passing more urine • Problems with breathing, including shortness of breath, persistent cough and fever. • Symptoms of allergy such as skin rash, itching, swelling of the face, lips, mouth, tongue, throat or neck which may cause difficulty in swallowing or breathing • Chest pain • Unexpected muscle pain, tenderness or weakness not caused by exercise, particularly if you also feel unwell or have a fever • Sudden severe headache, which may be accompanied by nausea, vomiting, loss of sensation, tingling in any part of the body or ringing in the ears • Severe blisters and bleeding of the lips, eyes, mouth, nose or genitals • Muscle and joint pain, muscle weakness, especially in the forearms, thighs, hips, shoulders, neck, and back • Difficulty climbing stairs or standing up from a chair • Difficulty lifting arms over the head • Falling and difficulty getting up from a fall • Constipation, diarrhoea • Stomach or belly pain, nausea (feeling sick) • Heartburn, indigestion or wind • Urine infection • Headache • Stuffy or runny nose • Nose bleeds • Rash 	<p>ARTG (CMI)</p>		<p>https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2017-CMI-02371-1 ARTG (CMI)</p> <p>https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2010-PI-03227-3 ARTG (PI)</p>
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Drug	Side effects ^	Side effects source	Other recommended sources	Notes
Statins Rosuvastatin	<ul style="list-style-type: none"> • Headache • Constipation • Dizziness • Nausea (feeling sick) • Stomach pain • Unusual tiredness • Itchy skin • Memory loss • Stiff or painful joints (arthralgia) • Aching muscles, muscle tenderness or weakness not caused by exercise, particularly if you also have a fever or generally feel unwell • Difficulty breathing, swelling of the face, eyelids or lips • Difficulty breathing, coughing, particularly if you also feel generally unwell (e.g., fatigue, weight loss, fever) 	ARTG (CMI)		https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2021-CMI-01732-1 ARTG (CMI) https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2020-PI-01791-1 ARTG (PI)

Drug	Side effects ^	Side effects source	Other recommended sources	Notes
Losartan	<ul style="list-style-type: none"> • Dizziness • Light-headedness • Tiredness or weakness • Spinning sensation • Generally feeling unwell • Increased sensitivity of the skin to sun • Inability to get or maintain an erection • Skin rash, itchiness • Aching muscles, not caused by exercise • Signs of anaemia, such as tiredness, being short of breath, and looking pale • Bleeding or bruising more easily than normal • Swelling of the face, lips, mouth, tongue or throat which may cause difficulty in swallowing or breathing • Severe and sudden onset of pinkish, itchy swellings on the skin, also called hives or nettlerash 	ARTG (CMI)		<p>https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2010-CMI-04741-3&d=20220714172310101</p> <p>ARTG (CMI)</p> <p>https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2010-PI-03227-3</p> <p>ARTG (PI)</p>

Drug	Side effects ^	Side effects source	Other recommended sources	Notes
Vasoactive intestinal polypeptide	<ul style="list-style-type: none"> Pancreatitis and depression are described as potential side effects from VIP nasal spray 	ACIIDS submission to the Inquiry	ARTG MIMS FDA EMA	Vasoactive intestinal polypeptide (VIP) consumer medical information or product information is not listed on the ARTG. It is not listed on other sources of recommended Australian pharmaceutical information such as MIMS. VIP product information was not identified in the United States Food and Drug Administration (FDA) approved drug porthole nor the European Medicines Agency (EMA) porthole.

^ Side effects as described by ARTG, a trusted, quality, medicine information source for Australian healthcare professionals and consumers as recommended by the Australian Government Department of Health and Aged Care.

Available at: https://tga-search.clients.funnelback.com/s/search.html?collection=tga-artg&profile=record&meta_i=384528

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Glossary

AAAAI	American Academy of Allergy, Asthma and Immunology
ABPA	Allergic bronchopulmonary aspergillosis
ACIIDS	Australian Chronic Infectious and Inflammatory Disease Society
AFRS	Allergic fungal sinusitis or rhinosinusitis
AIPH	Acute idiopathic pulmonary haemorrhage (or acute idiopathic pulmonary hemosiderosis)
AWMF	Association of the Scientific Medical Societies, Germany (or Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften)
BIAC	Biotoxins-related Illnesses Advisory Committee
CBT	Cognitive behavioural therapy
CDC	Centers for Disease Control and Prevention
CF	Cystic fibrosis
CFU	Colony forming units
CI	Confidence interval
CIRS	Chronic Inflammatory Response Syndrome
CIRS-WDB	Chronic Inflammatory Response Syndrome – Water-Damaged Buildings
CME	Continuing medical education
COPD	Chronic obstructive pulmonary disease
DALYs	Disability-adjusted life years
DSCATT	Debilitating Symptom Complexes Attributed to Ticks
enHealth	Environmental Health Standing Committee
ERMI	Environmental Relative Moldiness Index Testing
GHUP	German Society of Hygiene, Environmental Medicine and Preventive Medicine
GP	General practitioner
HERSTMI-2	Health Effects Roster of Type Specific fungal producing-Mycotoxin and Inflammagens
HP	Hypersensitivity pneumonitis
ID	Infectious disease
IgE	Immunoglobulin E
IgG	Immunoglobulin G
IOM	Institute of Medicine, United States
IV	Intravenous
LTT	Lymphocyte transformation testing
MARCoNS	Multiple Antibiotic Resistant Coagulase Negative Staphylococci
MUS	Medically Unexplained Symptoms

NATA	National Association of Testing Authorities
NCCEH	National Collaborating Centre for Environmental Health
NICE	National Institute of Health and Care Excellence, United Kingdom
NIOSH	National Institute for Occupational Safety and Health, United States
NHMRC	National Health and Medical Research Council, Australia
NPAAC	National Pathology Accreditation Advisory Council
NRL	National Serology Reference Laboratory
OR	Odds ratio
PAFs	Population attributable fractions
PCR	Polymerised chain reaction
RACGP	Royal Australian College of General Practitioners
RCPA	Royal College of Pathologists of Australasia
RCT	Randomised controlled trial
RoB	Risk of bias
S2k	European consensus-based guideline
SBS	Sick building syndrome
TGA	Therapeutic Goods Administration
TMS	Toxic mold syndrome
TMSA	Toxic Mould Support Australia
UK	United Kingdom
US	United States
VCS	Visual contrast sensitivity
VIP	Vasoactive intestinal polypeptide
WHO	World Health Organization

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All information in this publication is correct as at 15 December 2022.

