

## **CHAPTER IV.3 COST OF ACUTE RESPIRATORY DISEASES: HYPERSENSITIVITY PNEUMONITIS, HUMIDIFIER FEVER, AND LEGIONNAIRES' DISEASE**

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## CHAPTER IV.3 COST OF ACUTE RESPIRATORY DISEASES: HYPERSENSITIVITY PNEUMONITIS, HUMIDIFIER FEVER, AND LEGIONNAIRES' DISEASE

### IV.3.A Background

Indoor air contamination in non-industrial buildings has received increased attention in recent years due to improved understanding of the potential impact of indoor air quality on the health of residents and workers. Air pollutants that are known to cause irritation, allergic responses, and infection are numerous, and vary widely in their potency and in the responses they elicit. Groups of illnesses that result from exposure to contaminants in indoor air have been categorized as “sick or tight building syndrome,” or with other designations that encompass a variety of diseases and symptoms. Some groups of illnesses have highly specific target organs. For example, hypersensitivity pneumonitis, which includes over 30 specific diseases, is characterized by specific pathology in the lung.

This chapter addresses illnesses with a rapid onset that are associated with indoor air pollutants. At this time, three diseases of this type have been evaluated for direct medical costs:

- Legionnaires' disease (Legionellosis),
- hypersensitivity pneumonitis, and
- humidifier fever.

Humidifier fever is included because it is considered by some to be a type of hypersensitivity pneumonitis, even though the most obvious symptoms are not respiratory.<sup>1</sup>

Humidifier fever, hypersensitivity pneumonitis, and Legionellosis are all illnesses that have been associated with exposure to allergenic or pathogenic materials in indoor air. The first two are similar in both cause and resolution. A variety of allergens can trigger these illnesses, which are mediated by the immune system, and elimination of exposure can eliminate the illness. Legionellosis results from exposure to the bacteria of the genus *Legionella*. Antibiotics are effective in eliminating the illness.

Hypersensitivity pneumonitis and humidifier fever share the characteristic that removal of the patient from the contaminated environment, or removal

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<sup>1</sup>Patients with this disease typically have reduced lung function, although this symptom is often not evaluated.

of the contaminant from the patient's environment, is the primary and only fully effective method of treatment. Symptomatic treatments exist (e.g., fever-reducing medications for humidifier fever), but do not provide long-term solutions.

Cost estimates for the three diseases were developed to address specific requirements of the Indoor Environments Division, which was evaluating impacts of various indoor air pollutants<sup>2</sup>. The Agency wanted cost estimates for these diseases developed on a quick-response basis, in the absence of other complicating factors or diseases. Consequently, the methods used to estimate costs were relatively simple and direct. The usual format of chapters in the Handbook, with considerable detail on medical definition, causality, susceptibility, prognosis, etc., was not considered appropriate under the circumstances.

This chapter contains a discussion of incremental direct medical costs incurred by individuals in whom these diseases occur in response to poor indoor air quality. The symptoms associated with these diseases could also result from other causes, but the cost may be different, depending on the circumstances (indicating differences in underlying pathology)<sup>3</sup>. The costs are for a single occurrence of the disease, which can last from one day to a few months, depending on the disease.

Regulation of ambient air pollutants may result in a reduced number of individuals with air-related symptoms. Programs to reduce indoor air pollutants are also crucial in reducing adverse health effects. The benefits of such activities can be estimated in part by evaluating the direct medical costs avoided as a result. Some elements of total benefit, such as the avoided indirect medical costs, willingness to pay to avoid pain and suffering, the value of lost time of unpaid caregivers, the value of lost productivity of patients, etc., are not included here. These costs may be substantial. The direct medical costs presented in this chapter may be useful in providing a lower-bound measure of total benefit. The reader is referred to Chapter I.1 for a discussion of direct cost estimation methods and cost elements that are relevant to all benefits estimates.

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<sup>2</sup>This work was done in conjunction with the work on Chapter V.1, Costs of Symptoms, and shares a common methodology.

<sup>3</sup>For example, hypersensitivity pneumonitis associated with agricultural activities may occur with other, more serious pathological conditions.

The costs presented in this chapter were current in the year the chapter was written. They can be updated using inflation factors accessible by clicking on the sidebar at left.

*[Link to Chapters I.1 and IV.1](#)*

*[Link to inflation factors](#)*

## **IV.3.B Cost Estimation**

### **IV.3.B.1 Sources**

Medical costs were estimated for this chapter by:

- 1) describing the anticipated diagnosis and treatment services using national guidelines and the medical literature, and
- 2) assigning costs to those services, based on current (1999) Medicare reimbursement values.

The primary sources consulted to identify medical services were clinical practice guidelines (AHCPR, 1999; CDC, 1999), medical texts (e.g., Bennett and Plum, 1996), and the Medicare reimbursement *Federal Register* notices regarding costs (numerous; discussed Chapter IV.2). EPA also reviewed numerous journal article abstracts, but used these primarily as supporting information (to confirm other sources). The abstracts are cited when used as the only source. EPA obtained most information on medical services from the National Guidelines Clearinghouse ([www.guidelines.gov](http://www.guidelines.gov)) developed by clinicians and researchers, which provides clinical practice guidelines for specific diseases.

*[Link to Chapter IV.2](#)*

EPA estimated costs of medical services using current (1999) Medicare reimbursements. The rationale for using this source of cost information is that it is a national system for medical services reimbursement that approximates the average cost of medical services in the United States. For a more detailed discussion of the use of Medicare information, see Section B in Chapter IV.2, Medical Costs of Asthma. Supporting information for medical services came from the medical and economics literature.

*[Link to Chapter IV.2, Section B.](#)*

EPA estimated medication costs for common, over-the-counter medications (i.e., those available at both drug and other types of stores such as groceries and discount stores) using the lowest cost for a generic

product, based on prices obtained from a relatively low-cost national pharmacy chain store on October 27, 1999. EPA preferred prices taken directly from consumer goods over those taken from an industry source (e.g., the Red Book) because these are over-the-counter medications and their consumer prices were readily available directly from the marketplace.

Since the medications considered are very common (e.g., aspirin) and there is a high demand for these products, market pressures have made their prices fairly uniform. Most patients are not expected to pay substantially higher prices than those used in this analysis. For prescription medications, the Health Care Financing Authority (HCFA) prices were used.

### **IV.3.B.2 Humidifier Fever**

Humidifier fever, which may be a type of hypersensitivity pneumonitis, is a hypersensitivity disease that occurs in response to exposure to a variety of airborne organisms and materials, often organic (EPA, 1999; Mamolen, et al., 1993). Responses will vary considerably from individual to individual because it is an immune system-mediated disease. The disease will affect some but not all individuals who are exposed. Humidifier fever has a delayed onset of a few hours from the time of exposure and usually is self-limiting. Fever, myalgia, and other symptoms last up to 24 hours. Humidifier fever may also cause transient changes in lung function and white blood cell count, although these changes are not the focus of clinical evaluation for a single event of a short-term fever. Numerous studies confirm the short-term nature of the illness and the lack of long-term effects (Teake et al., 1999; Baur et al., 1988; McSharry et al., 1987; Edwards, 1980; Philipp, 1983; Belin, et al., 1979; Anderson et al., 1989; Mamelon et al., 1993; Cockcroft et al., 1981).

Due to the short-term and mild nature of its effects, individuals with humidifier fever would not be expected to see a physician when allergic response first occurs. According to EPA's Indoor Environments Division webpage, "It [humidifier fever] normally subsides within 24 hours without residual effects, and a physician is rarely consulted" (EPA, 1999). The likely course would be to take one of the following over-the-counter medications for a maximum of one day: aspirin, ibuprofen, or acetaminophen. These medications lower fever and lessen pain (e.g., those associated with myalgia), and are the most commonly used fever-reducing medications.

If the illness recurs repeatedly, an individual might visit a physician. The length of the office visit would depend on the patient and physician, and no estimate is made here of the level of visit that would occur. This report presents all five levels of both new and established patient visit costs. The analyst can choose the level determined to be most appropriate.

If a cluster of individuals experienced this illness at the same time (as reported in the literature), a local or state health department would likely investigate the cause. The costs of this type of effort are not estimated in this analysis, but could be substantial as a public sector expense.

Table IV.3-1 provides cost estimates for medications. A 12-hour average duration of illness was assumed because it is one half, or the midpoint, of the total potential duration of 24 hours. Table IV.3-1 also lists costs for the five potential levels of office visits. Using the values in this table, the costs could range from \$0.03 (three cents) for a patient who takes two doses of aspirin only and does not visit a physician, to \$139.02 for a patient who has an extended new patient visit to a physician's office (level 5) and takes acetaminophen for fever and pain. *It is not possible to accurately estimate the average cost*, but the literature suggests that most patients would not see a physician. This assumption would indicate a cost of less than one dollar for most patients. Patients can incur other costs if they visit a physician who in turn performs some tests. This alternative appears very unlikely for a 24-hour fever.

<b>Table IV.3-1. Cost components for humidifier fever</b>		
<b>Goods or Service</b>	<b>Medicare Code</b>	<b>Cost (1999\$)</b>
aspirin: 2 doses	not applicable	0.03
acetaminophen: 2 doses	not applicable	0.09
ibuprofen: 2 doses	not applicable	0.08
office visit: new patient level 1	99201	34.73
level 2	99202	53.53
level 3	99203	76.06
level 4	99204	111.14
level 5	99205	138.93
office visit: established patient level 1	99211	16.32
level 2	99212	30.22
level 3	99213	41.68
level 4	99214	63.56
level 5	99215	97.94

If the episodes of humidifier fever are frequent, and humidifier fever is not diagnosed on the first visit, further investigation by a physician might include blood tests for white cell counts, tests of delayed hypersensitivity allergic response, and respiratory function tests. The costs of these tests

are not listed above because they are not anticipated. These costs are described in the next section of this chapter on hypersensitivity pneumonitis and in Chapter IV.2, submitted on October 22, 1999. Additional office visits may also occur in response to these symptoms.

*Link to Chapter IV.2*

Humidifier lung appears to be a more advanced form of this disease, wherein the response is also seen prominently in the respiratory system (Bauer et al., 1988).

### **IV.3.B.3 Hypersensitivity Pneumonitis**

This group of similar illnesses encompasses a very large number of different diseases (Pitcher, 1990), with 30 or more specific diseases defined (Ando and Suga, 1997). This type of pneumonitis is characterized by diffuse, predominantly mononuclear inflammation of the lung parenchyma, particularly the terminal bronchioles and alveoli. Hypersensitivity pneumonitis may progress to fibrosis under extreme conditions. This illness is suspected when repeated bouts of influenza-like pneumonitis, or active interstitial lung disease occur. No single clinical feature or laboratory test is diagnostic of the disease. In addition to symptoms and physical findings, X-rays, pulmonary function tests, and immunological tests are used to diagnose the disease. Numerous immunological tests may be considered because a large group of potential antigens can cause the disease. IgG immunoglobulins occur as serum precipitins in the presence of the causative antigens (CDC, 1996; Pitcher, 1990).

Hypersensitivity pneumonitis is treated through removal of either 1) the allergen(s) from the patient's environment, or 2) the patient from the contaminated environment (all sources consulted). Treatment may also involve the use of steroids, such as prednisone (at 40 mg/day in doses of 10 mg for 10 days) to reduce lung inflammation (Pitcher, 1990). Steroid use is not a long-term solution and is not recommended for the majority of patients. Only 10 percent of patients are assumed to receive this medication because routine use of steroids is discouraged (Pitcher, 1990). Hypersensitivity pneumonitis is not a bacterial disease, and therefore requires no antibiotics (unless an infection secondary to hypersensitivity pneumonitis occurs).

Table IV.3-2 lists the direct medical costs of diagnosis and treatment. The patient is assumed to have an initial office visit of average duration (level 3), during which a chest X-ray, lung function test, and allergen test for 20 allergens are administered. The patient is assumed to be established,

because the nature of IgG allergic responses would likely lead most people to have seen a physician in the past. Costs are available for new patients visits and for all level of office visits in Table IV.3-1 above.

*Link to Table IV.3-1*

Although the diagnosis procedures are fairly well-defined, the average period of illness prior to disease diagnosis is not described and will vary, depending on the patient and physician. When not diagnosed and treated, this disease can cause fever, chills, malaise, dry cough, dyspnea, tiredness, weight loss, and other effects. If diagnosis is delayed, these effects can lead to lost work time and the use of over-the-counter medications.

<b>Table IV.3-2. Cost components for hypersensitivity pneumonitis</b>		
<b>Goods and Services</b>	<b>Medicare Code</b>	<b>Cost (1999\$)</b>
office visit: established patient , level 3	99213	41.68
chest X-ray in physician's office	71020	34.74
allergen tests, delayed type: 20 allergens	95028	8.68 x 20 = 173.60
lung function test	94010	30.56
prednisone (HCFA price) x 10% of patients	not applicable	1.80 x 0.1 = 0.18 *
<b>Total</b>		<b>280.76</b>

\* The cost of this medication is very low and is assumed to be provided to only 10 percent of patients (as discussed in the text). The listed cost represents the cost for the full course of treatment.

Patients may be hospitalized if the disease becomes severe. Although no statistics were located on its probability, hospitalization is unlikely, based on qualitative information provided in the sources reviewed for this analysis. Hypersensitivity pneumonitis, aggregated with other types of interstitial lung diseases as a diagnostically related group (DRG) category (93), is often not treated as a specific disease in hospitalization information. The National Hospital Discharge Database does not make distinctions among different categories within DRG 93. Additional information may be obtainable on hospitalization probabilities, but extensive searching and consulting was not performed due to the quick-turnaround nature of this task

If the Agency plans to include hospitalization costs, then the Medicare hospitalization cost for interstitial lung disease without complications (DRG 93) can be used. This category maps to the International Classification of Diseases Code (ICD-9) for hypersensitivity pneumonitis (495.9). The Medicare reimbursement values for adult hospitalizations are \$3450.58 for urban areas and \$3262.43 for rural areas.

#### IV.3.B.4 Legionnaires' Disease (Legionellosis)

Legionnaires' disease is a respiratory disease caused by the pathogen *Legionella*. Patients with this disease may have numerous symptoms, with fever and pneumonia predominating. The pneumonia is not clinically distinguishable from the most common type of pneumonia (pneumococcal), and some cases of Legionnaires' disease are indistinguishable from other causes of pneumonia. One to five percent of all pneumonias are estimated to be due to Legionnaires disease (Edelstein, 1996); many cases of Legionnaires' disease may not be diagnosed as such.

Although a variety of clinical test results may be abnormal, the definitive diagnosis is made through a positive test for the pathogen *Legionella* (Edelstein, 1996; CDC, 1994; CDC, 1997).

As with hypersensitivity pneumonitis described in this chapter, the period prior to diagnosis may vary widely, depending on the physician(s) consulted and patient characteristics. When not diagnosed and treated, the disease may cause numerous symptoms and lead to lost work time and the use of over-the-counter medications. The costs associated with delayed diagnosis are not considered in this analysis.

Diagnostic tools specifically used for Legionnaires' disease include chest X-ray and sputum culture for *Legionella*. Serological testing is primarily useful for epidemiologists rather than for clinicians, and is not considered in this analysis. The first choice for therapy is erythromycin, which may be administered orally, or, when the patient is hospitalized with a serious case, intravenously. Oral dosage is 500 mg, four times per day for 14 to 21 days (the average of 18 days was used) (Edelstein, 1996)<sup>4</sup>. Most patients respond within one to two days of specific antimicrobial therapy. Fever may persist for a week, and weeks to months are required to resolve pulmonary infiltrates. Patients with respiratory failure due to Legionnaires' disease have a relatively poor prognosis and a much slower recovery (CDC, 1994). Other antibiotics and therapy regimens may be used to treat this disease and are likely to incur different costs than those reported in this chapter.

Table IV.3-3 summarizes the direct medical costs of goods and services and hospitalization for Legionnaires' disease. For patients who do not require hospitalization, costs for a chest X-ray, sputum culture, and erythromycin are listed with an office visit (level 3, established patient) in Table IV.3-3 below.

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<sup>4</sup> Doxycycline, which is somewhat less expensive, was cited as the drug of choice in one paper (Klein and Cunha, 1998). The authors note, however, that erythromycin is the most commonly used. Erythromycin is therefore used in this analysis.

Table IV.3-3 also lists hospitalization costs for the more seriously affected patients. An office diagnosis may be made prior to hospitalization. Given the relatively low cost of office visit diagnoses and treatment compared with hospitalization, the addition of the office visit costs will have a minimal impact on the overall cost estimate.

Hospitalization costs should not always be added to the other costs because they are relevant to a different patient subset. To obtain hospitalization costs from Medicare reimbursement data, the ICD-9 code for Legionella (482.4) was mapped to DRG codes 80 and 81 for hospitalization of adults and children, respectively. Hospitalization costs vary considerably between adults and children.

No data were located on the percentage of patients with Legionnaire's disease who are hospitalized. Analysts may use the costs in Table IV.3-3 with a proportionate allocation of patients to hospital and non-hospital treatment, based on their best judgement. The likelihood of hospitalization varies with many factors, including health status of the patient (i.e., other respiratory diseases), age, and promptness of diagnosis and treatment.

<b>Table IV.3-3. Cost components for Legionellosis</b>		
<b>Goods and Services</b>	<b>Medicare Code</b>	<b>Cost (1999\$)</b>
office visit: established patient level 3	99213	41.68
chest X-ray, physician's office	71020	34.74
sputum culture for Legionella (least expensive culture option)	87278	16.58
erythromycin (HCFA price)	not applicable	25.82
<b>Total outpatient care</b>		<b>118.82</b>
<b>Hospitalization</b>	<b>DRG Code</b>	<b>Cost (1999\$)</b>
hospitalization: urban, adult	80	4,093.17
hospitalization urban, child 0 - 17 years	81	6,756.17
hospitalization rural, adult	80	3,869.99
hospitalization: rural, child 0 - 17 years	81	6,387.78