Chapter 1. Introduction

This chapter describes the background, scope, purpose, target populations, practice settings, audience, and limitations of the evidence report. It also identifies the key research questions addressed, provides an overview of the epidemiology and disease biology of allergic rhinitis, and describes the burden of illness associated with this condition.

Background

Allergic rhinitis, also known as hay fever, is one of the most common allergic diseases in the United States. The National Institute of Allergy and Infectious Diseases currently estimates that allergic rhinitis affects as many as 35 million Americans and accounts for 16.7 million office visits to healthcare providers each year (National Institute of Allergy and Infectious Diseases, 2002; National Institutes of Health, 2002). A recent report from the American Academy of Allergy, Asthma & Immunology estimates that about 19 million employed adults suffer from allergic rhinitis, and that approximately $4.5 billion in direct costs and 3.8 million lost work and school days are attributable to this disease annually (American Academy of Allergy, Asthma & Immunology, 2000).

Allergic rhinitis usually begins in childhood, adolescence, or early adulthood, and often wanes, but may persist, with increasing age. Rhinitis is defined as inflammation of the membranes lining the nose. The symptoms of allergic rhinitis usually include sneezing, rhinorrhea, itching and watery eyes, nasal congestion, and, in severe cases, facial pressure or pain. These symptoms may be associated with headache, irritability, poor concentration, loss of sleep, and fatigue. The functional impact of allergic rhinitis ranges from mild to seriously debilitating effects on social, physical, and emotional functioning, which may interfere with cognitive tasks, impair work performance, and cause work absences.

Because allergic rhinitis is so common and allergens are ubiquitous, allergic rhinitis creates a significant burden in the workplace in terms of work performance and healthcare costs. Although exposures to airborne allergies present in the workplace can cause occupational rhinitis, non-occupational rhinitis represents a vastly greater burden in workplace settings overall.

An evidence report on the topic of allergies and their effect on working-age populations was proposed to the Agency for Healthcare Research and Quality (AHRQ) by the American Association of Health Plans (AAHP), who became the Duke Evidence-based Practice Center's partner in developing this report. The specific research questions were refined in consultation with AHRQ, AAHP, and an advisory panel of eight experts convened especially for this study. The key research questions addressed in this report are:

1) How do currently clinically available treatments for allergic rhinitis affect costs and work performance?

2) What is the relationship between symptom outcomes or disease-specific quality-of-life measures and work performance among adults with allergic rhinitis? Can data on symptomatic outcome or quality of life be reliably translated into work performance measures?

3) How effective are (a) environmental measures, (b) immunotherapy, and (c) combined treatments, such as with antihistamines and nasal steroids or antihistamines and oral decongestants, for relief of symptoms in adults with allergic rhinitis?

4) How do different types of healthcare providers (generalists, allergy specialists, and otolaryngologists) treat adults with allergic rhinitis, and how do treatment outcomes vary by provider?

5) In adult patients with symptoms of allergic rhinitis, does the prevalence, treatment patterns, or response to treatment vary according to a patient's race or ethnicity?

Scope and Purpose

The purpose of this evidence report is to review the published evidence on strategies for managing the treatment of patients with allergic rhinitis, particularly those of employment age (18 to 64 years old). The report covers both seasonal and perennial allergic rhinitis. Seasonal allergic rhinitis is associated with sensitization to fungal, tree, grass, and weed pollens, and with symptoms that vary seasonally. Perennial allergic rhinitis is associated with sensitization to indoor allergens such as fungi, cockroaches, dust mites, and animal proteins (e.g., cat dander), and with year-round symptoms, with or without seasonal exacerbations.

Treatment options considered in this report are environmental measures (allergen avoidance), immunotherapy, and combination therapies employing antihistamines and nasal steroids or antihistamines and oral decongestants.

Also considered in the present report are the unique issues raised by the emphasis on working-age populations, including the relationship between symptoms or functional status and work performance, and the effects of allergic rhinitis and its treatment on costs and work performance. In addition, the report reviews the evidence on variability in management approaches and patient outcomes by type of clinician (generalist physician vs. allergy specialist vs. otolaryngologist), as well as by patient race and ethnicity.

Our goals were primarily to identify, review, and evaluate the published literature on these topics and, secondarily, where relevant evidence could not be identified or had important limitations, to describe the type of data that would be needed to more fully address the research questions. Ultimately, we hope to provide clinicians, policymakers, and patients with the evidence they need to decide for themselves on the best treatment and management options from among those considered here.

Epidemiology of Allergic Rhinitis

Allergic rhinitis affects 20 to 40 million people in the United States annually, including 10 to 30 percent of adults and up to 40 percent of children (Joint Task Force on Practice Parameters in Allergy, Asthma and Immunology, 1998). Approximately one-third to one-half of these patients suffer from seasonal allergic rhinitis, with the remainder experiencing perennial disease or both seasonal and perennial forms of the disease (Joint Task Force on Practice Parameters in Allergy, Asthma and Immunology, 1998). Other atopic conditions, such as atopic eczema, allergic conjunctivitis, and asthma, often co-occur with allergic rhinitis.

Allergic rhinitis may begin at any age, with most individuals developing symptoms as children or young adults. Risk factors include a family history of atopy, higher socioeconomic class, and exposure to indoor allergens such as animals and dust mites (Joint Task Force on Practice Parameters in Allergy, Asthma and Immunology, 1998). The risk of allergic rhinitis is 30 percent if one parent is atopic, at least 50 percent if both parents are atopic, and greater than 70 percent if both parents have the same allergic disease (Nimmagadda and Evans, 1999).

The Centers for Disease Control and Prevention (CDC) report an overall population prevalence rate of 89.8/1,000 persons, representing 23,721,000 Americans, in 1996, the latest year for which data are available (Centers for Disease Control and Prevention, 1999). Table 1 shows US prevalence rates and numbers by age, sex, race, and family income. Generally, prevalence is higher in females and in the white population. In the working-age population, 18- to 44-year-olds represent approximately one-half of all persons with allergic rhinitis, and 45- to 64-year-olds represent approximately one-fourth of allergic rhinitis cases. In families with incomes of $10,000 or higher, the prevalence rate generally increases with increasing income; however, the lowest income families (< $10,000) have a prevalence rate approaching those found in families at higher income levels.

By geographic location, the CDC reports that persons in the Western part of the US have the highest prevalence of allergic rhinitis (36 percent of total US prevalence), while residents of the Northeast have the lowest (18 percent of total US prevalence); by place of residence, four times as many persons in Metropolitan Statistical Areas (MSAs) have allergic rhinitis than persons living in non-MSAs (Table 2) (Centers for Disease Control and Prevention, 1999).

Overview of Disease Biology

The symptoms of allergic rhinitis result from exposure to particulate allergens that are large enough to be filtered by the nose. In susceptible adults, allergen-specific T cell sensitization leads to B cell production of allergen-specific immunoglobulin E (IgE) antibodies after an initial allergen exposure (e.g., pollen) (American Academy of Allergy, Asthma & Immunology, 2000). Allergen-specific IgE then binds to the surface of mast cells in the nasal mucosa or to circulating basophils. With subsequent exposure, the allergen is recognized by its specific antibody, resulting in the activation of IgE-primed mast cells and basophils, with release of a variety of potent inflammatory mediators. These include granule-associated mediators (e.g., histamine), membrane-derived lipid mediators (e.g., leukotriene), as well as cytokines and chemokines that attract inflammatory cells from the peripheral circulation to the site of degranulation. These mediators cause immediate mucosal edema and vasodilation and the clinical features of allergic rhinitis. “Early-phase” symptoms occur within minutes of the allergen exposure and are due to release of preformed mediators; “late-phase” symptoms occur 4 to 12 hours after exposure and involve synthesis of newly formed mediators and infiltration of inflammatory white blood cells from the circulation (Bellanti and Wallerstedt, 2000; Parikh and Scadding, 1997; Skoner, 2001). The late phase has been observed with large exposure allergen challenges, but the clinical importance of this observation is uncertain. Symptoms affect about 30 to 40 percent of individuals during the “late-phase” time period. Nasal itching is prominent during the early phase. Sneezing, nasal congestion, and rhinorrhea are common to early and late phases, and nasal congestion dominates during the late-phase reaction.

Burden of Illness

The symptoms of allergic rhinitis, such as sneezing, rhinorrhea, and nasal congestion, may interfere with one's ability to carry out daily activities. Rhinitis symptoms may be associated with headache, irritability, poor concentration, loss of sleep, and resulting fatigue. The functional impact of these symptoms ranges from mild to seriously debilitating effects on social, physical, and emotional functioning (Blaiss, 1999; Thompson, Juniper, and Meltzer, 2000). In a study comparing 116 healthy subjects to 111 patients with moderate to severe perennial allergic rhinitis, patients with allergic rhinitis had significantly decreased functioning in eight domains; negative effects were particularly prominent for physical and emotional role limitations, social functioning, and general health perceptions (Bousquet, Bullinger, Fayol, et al., 1994). Allergic rhinitis may interfere with cognitive tasks, may impair work performance, and may cause work absences. In a pooled analysis of 1,948 patients with moderate to severe allergic rhinitis, over 90 percent reported that their classroom or work performance was affected negatively (Tanner, Reilly, Meltzer, et al., 1999).

In addition to direct symptom effects, allergic rhinitis may be related to the development of asthma, sinusitis, or otitis media (Bousquet, van Cauwenberge, Khaltaev, et al., 2001; Spector, 1997). Asthma symptoms occur in 17 to 19 percent of patients with allergic rhinitis, a prevalence that is significantly higher than the five percent prevalence observed in the general population (Blair, 1977; Moller, Dreborg, Ferdousi, et al., 2002; Pedersen and Weeke, 1983; Settipane, 1986). In a cohort of 7,225 children followed from birth to age 23, children with allergic rhinitis were 2.0 to 2.9 times more likely to develop asthma during followup (Anderson, Pottier, and Strachan, 1992). A similar cohort study of college students found that those with allergic rhinitis were three times more likely to develop asthma than non-atopic controls during the 23-year followup (Settipane, Hagy, and Settipane, 1994). In cross-sectional studies, allergic rhinitis is associated with acute and chronic bacterial sinusitis (Long, McFadden, DeVine, et al., 2002).

Adverse effects from therapies are an additional burden associated with this illness, since they may impact more significantly on functional status than the disease itself, especially for patients with very mild disease. For adults, the only life-threatening effect from commonly used treatments is anaphylaxis associated with immunotherapy, which occurs at a rate of about one fatality per two million doses (Cook and Farias, 1998). Non-fatal systemic reactions are more common; estimates of their frequency vary widely, from 0.3 percent to more than 30 percent (Cook and Farias, 1998). Minor adverse effects of somnolence, dry mouth, dizziness, and headache may occur in up to 50 percent of patients taking sedating antihistamines (Long, McFadden, DeVine, et al., 2002). Published experimental work suggests that adverse effects associated with some treatments, particularly sedating antihistamines, which cause somnolence and psychomotor impairment, have an adverse impact on driving performance and reaction time (Adelsberg, 1997; Weiler, Bloomfield, Woodworth, et al., 2000); these effects may also interfere with work productivity and increase on-the-job accidents. The most frequently reported adverse effects associated with nasal corticosteroids are epistaxis, headache, and pharyngitis; with cromolyn, nasal irritation and headache are the most commonly reported adverse effects.

Management Strategies and Treatment Options

Allergen avoidance, immunotherapy, and an array of pharmacotherapies are commonly used to treat allergic rhinitis. For clinicians, management begins with accurate diagnosis, distinguishing between allergic and non-allergic etiologies. The clinical evaluation may include radioallergosorbent testing (RAST) or allergy skin testing to confirm allergy sensitization. For patients with allergic rhinitis, relevant treatment issues are: the efficacy of individual treatments; monotherapy versus combinations of treatments; the most cost-effective sequencing of treatments; and the effectiveness of generalist versus specialist care. In working populations, relevant treatment outcomes are: symptom control; effects on health-related quality of life; cost-effectiveness; and effects on work performance.

The specific therapies covered in this evidence report are environmental measures, or allergen avoidance; immunotherapy; and combination therapies such as antihistamines and nasal steroids or antihistamines and oral decongestants. Given the variety of treatment options, the variability in acceptability and cost of treatments, and the lack of a previous focus on work-related outcomes, a systematic review that addresses these issues is timely.

Environmental Measures

Given the known biology of allergic rhinitis, environmental measures (allergen avoidance) represent a conceptually appealing treatment option. Such measures are recommended in the rhinitis clinical guidelines developed by the Joint Task Force on Practice Parameters in Allergy, Asthma, and Immunology (1998), and by the American Academy of Otolaryngic Allergy (Fornadley, Corey, Osguthorpe, et al., 1996); they have also been recognized by the American Academy of Allergy, Asthma & Immunology in its recent report (2000). Allergen avoidance measures range from relatively inexpensive measures, such as removing feather pillows and down comforters, to more intensive measures, such as high-flow air filtration units like a high efficiency particulate air (HEPA) cleaner, elimination of carpeting in favor of tile or hardwood floors, and acaricides or dust-proof covers for mattresses and bedding to control house dust mites. Allergen avoidance may be more difficult in the case of outdoor allergens and may have important life implications for individuals working outdoors or who experience occupational rhinitis.

Immunotherapy

Immunotherapy (allergen desensitization) is most often used by specialists for patients with more severe allergic rhinitis or for patients who do not tolerate or respond well to multiple medications. A program of immunotherapy requires once- or twice-weekly injections of escalating doses of allergen extracts over a period of months. This is followed by once- or twice-monthly maintenance injections, typically for a period of at least 2 to 3 years. Immunotherapy is costly and inconvenient to patients, but has the potential for continued efficacy after the treatment is discontinued (Durham, Walker, Varga, et al., 1999; Mosbech and Osterballe, 1988). Given the potential for long-term effectiveness, immunotherapy may be cost-effective compared to continuous treatment with medications for patients with more severe disease. In addition, immunotherapy has the potential to prevent the development of asthma (Ragusa, Passalacqua, Gambardella, et al., 1997).

Pharmacologic Therapy

Symptoms of allergic rhinitis may be treated with any of several different types of medication, including antihistamines, intranasal corticosteroids, decongestants, cromolyn sodium, and ipratropium. Each of these medications has a different mechanism of action and a different pattern of symptom relief. Clinically, these drugs are often used concurrently for improved symptom relief or for relief of multiple symptoms.

Antihistamines are the most commonly used medications for allergic rhinitis and are usually administered on an intermittent basis for patients with mild or seasonal symptoms. Oral antihistamines act in part by competitively inhibiting the binding of histamine to H1 receptors. Second generation oral antihistamines such as cetirizine, fexofenadine, loratadine, and desloratadine are more pharmacologically selective and less sedating than earlier antihistamines. A unique topical antihistamine, azelastine, is non-selective, but may be associated with less sedation and fewer other systemic adverse effects than oral non-selective antihistamines. Sedating and non-sedating antihistamines appear roughly equivalent for controlling symptoms of seasonal and perennial allergic rhinitis (Long, McFadden, DeVine, et al., 2002).

Intranasal corticosteroids are anti-inflammatory medications that require days to weeks for maximal symptom relief. Nasal steroids inhibit multiple steps in the inflammatory cascade of allergic rhinitis and provide excellent relief for numerous symptoms, including itching, sneezing, rhinorrhea, and nasal congestion. Multiple preparations are available: beclomethasone dipropionate (Beconase® and Vancenase®), budesonide (Rhinocort®), flunisolide (Nasarel® and Nasalide®), fluticasone propionate (Flonase®), mometasone (Nasonex®), and triamcinolone acetonide (Nasacort®). In head-to-head comparisons, nasal corticosteroids relieve allergic rhinitis symptoms more effectively than sedating or non-sedating antihistamines (Long, McFadden, DeVine, et al., 2002).

Nasal decongestants reduce nasal congestion through vasoconstriction. They are available in topical (phenylephrine, oxymetazoline) and oral (phenylephrine, pseudoephedrine) formulations. Oral agents are less likely to cause rebound vasodilation, accompanied by increased nasal congestion, than topical decongestants. Two studies have shown some benefit for nasal congestion but not for the other symptoms of allergic rhinitis (Long, McFadden, DeVine, et al., 2002).

Cromolyn sodium is postulated to prevent mast cell degranulation and is thus best used prophylactically. It requires four-times-per-day dosing and may require up to 2 weeks of continuous use for maximal benefit. In 32 randomized trials of cromolyn, all but two showed significant improvements in symptoms of allergic rhinitis. Cromolyn appeared to have higher efficacy for seasonal than perennial rhinitis. Dosing studies showed greater effect at higher doses (Long, McFadden, DeVine, et al., 2002). The anticholinergic ipratropium (Atrovent® nasal) decreases rhinorrhea for non-allergic rhinitis and has the potential for similar benefits in allergic rhinitis (Long, McFadden, DeVine, et al., 2002).

Although drug treatments for allergic rhinitis are often used clinically in regimens that combine more than one drug from different classes, most clinical trials have focused on proving individual drugs superior to placebo (Long, McFadden, DeVine, et al., 2002). Combined drug treatments, compared with single-agent treatments, may work synergistically to provide greater efficacy, may complement one another to relieve a broader array of symptoms, and may allow lower dosing and, hence, reduce adverse effects.

Costs and Work Performance

The American Academy of Allergy, Asthma & Immunology estimates that approximately 19 million employed adults are affected by allergic rhinitis, resulting in several million lost work days each year and annual direct healthcare costs of $4.5 billion (American Academy of Allergy, Asthma & Immunology, 2000). An evaluation of the evidence on costs and on work performance and symptoms requires the review of several types of literature. Determining the overall economic impact of allergic rhinitis requires a review of burden-of-illness studies. The effects of allergic rhinitis on work performance can be measured by studying employees' subjective estimates of their work performance and/or through the use of objective measurements of employee productivity. The impact of specific treatments can also be assessed by cost-effectiveness analysis, which estimates the costs associated with observed improvements in symptoms or quality of life, and by cost-benefit analysis, which considers the benefit of treatment in monetary terms, such as improvements in work productivity, balanced against the cost of treatment. There are few studies that directly associate allergic rhinitis symptoms and work performance, but studies of the treatment effects of various pharmacologic therapies, such as comparisons of sedating and non-sedating antihistamines, may be informative.

Treatment Outcomes by Clinician Specialty

The research question for this topic focuses on two issues: (a) whether different types of clinicians treat allergic rhinitis patients differently; and (b) whether treatment outcomes vary by type of clinician. Primary care clinicians are likely to be the first medical contact for someone with allergic rhinitis, and they have been shown to effectively treat a significant proportion of allergic rhinitis sufferers. On the other hand, allergy specialists and otolaryngologists tend to treat patients with more severe cases of allergic rhinitis (often referred by a primary care clinician), have more precise diagnostic tools available (e.g., nasal endoscopy), and are skilled in administering more specific and complex treatments (e.g., immunotherapy). Also at issue is whether there are variations in treatment and patient outcomes between specialists, i.e., between medically trained allergists and surgically trained otolaryngologists.

Prevalence and Patient Outcomes by Race and Ethnicity

There are some indications that susceptibility to allergic diseases may vary for reasons such as genetic predisposition and exposure to environmental factors. Prevalence of allergic rhinitis has been shown to vary by race, with whites having an overall higher prevalence rate than blacks. In the under-45 age group, the rates are 92.0/1,000 persons versus 66.2/1,000. The difference holds in the 45 to 64 age group, 110.0/1000 persons versus 64.6/1000 (Table 1). There have been few empirical research studies on variations in types of treatment or treatment outcomes by patient race or ethnicity.

Target Populations

We focused on patients with either seasonal or perennial allergic rhinitis. Given our focus on working populations, we prioritized studies in adults. Due to sparse data, we broadened the target population to include school-age children for questions with little relevant data in adults. Our rationale was that the clinical syndrome and underlying biology are similar in children and adults, and that effects on school performance may serve as a rough proxy for work productivity.

Subclinical or clinical asthma frequently co-exists with allergic rhinitis, and patients with co-occurring asthma were included in our review. Because data were extremely limited on the effects of environmental measures in adults with allergic rhinitis, we expanded our scope to patients with asthma. This decision is supported by the "unified airway" theory, according to which treatments for allergic rhinitis may affect asthma and, conversely, treatments for asthma may affect allergic rhinitis (Bousquet, van Cauwenberge, Khaltaev, et al., 2001).

We did not specifically target patients with occupational rhinitis. By definition a work-related illness, occupational rhinitis has allergic and non-allergic mediators, but its prevalence is far lower than non-occupational allergic rhinitis.

Target Practice Settings

Because of the broad scope of this report, multiple practice settings were relevant. We were interested in primary care and specialty settings, where pharmacological and immunotherapy treatments are often initiated. Environmental control measures are usually prescribed in medical settings, but are typically carried out in the home. In addition, interventions aimed at increasing worker productivity may be designed for, or delivered in, the work setting.

Target Audience

Our principal audience is groups developing guidelines or educational documents on allergic rhinitis for healthcare professionals. In addition, we expect healthcare professionals who provide care to patients with allergic rhinitis will have a particular interest in the report. These include family physicians, internal medicine physicians, allergy specialists, otolaryngologists, occupational medicine physicians, nurse practitioners, and physician assistants. Secondary target audiences include employers, policymakers involved in payment decisions, agencies involved in funding research, media involved in dissemination and education about health issues, and patients interested in state-of-the-art medical literature.

Limitations of the Report

This report reviews published evidence relevant to the five key research questions listed above. It does not cover topics addressed in the evidence report on "Management of Allergic and Nonallergic Rhinitis" recently completed by the Evidence-based Practice Center at the New England Medical Center (Long, McFadden, DeVine, et al., 2002). The latter report includes comprehensive assessments of the literature on diagnosis of allergic and non-allergic rhinitis, efficacy of single-agent treatments for both conditions, and co-morbidity with asthma and acute rhinosinusitis.

Occupational rhinitis is much less common than non-occupational rhinitis, and includes both allergic and non-allergic causes. Because of its relatively high prevalence, non-occupational allergic rhinitis creates a greater burden in the workplace in terms of work performance and healthcare costs than does occupational rhinitis. Although occupational allergic rhinitis falls within the scope of this report, few data on this condition focus on the key questions addressed here, and thus nearly all the data reviewed concern allergic rhinitis associated with the most common allergens rather than workplace-specific exposures.

Finally, several agents are currently being evaluated in clinical trials, but are not yet in common use, and are thus not reviewed in this report. These agents include leukotriene inhibitors, anti-immunoglobulin E (anti-IgE) therapy, and cytokine antagonists.

Table 1. 1996 US prevalence rates and numbers for hay fever/allergic rhinitis without asthma by age, sex, race, and family income

Prevalence rates	Age 18-44 (unless otherwise noted)	Age 45-64	Total population
Per 1,000 persons	109.4	104.8	89.8
By sex	Male, under 45: 86.3 Female, under 45: 92.1	Male: 85.6 Female: 122.8	Not available (NA)
By race	White, under 45: 92.0 Black, under 45: 66.2	White: 111.0 Black: 64.6	NA
By family income	< $10,000, under 45: 82.7 $10,000-19,999, under 45: 69.1 $20,000-34,999, under 45: 75.1 $35,000 or more, under 45: 108.9	< $10,000: 106.9 $10,000-19,999: 111.8 $20,000-34,999: 105.0 $35,000 or more: 109.2	NA

Prevalence numbers, in thousands	Age 18-44 (unless otherwise noted)	Age 45-64	Total population
Number	11,809	5,572	23,721
By sex	Male, under 45: 7,751 Female, under 45: 8,248	Male: 2,198 Female: 3,374	NA
By race	White, under 45: 13,404 Black, under 45: 1,665	White: 5,077 Black: 350	NA
By family income	< $10,000, under 45: 1,128 $10,000-19,999, under 45: 1,673 $20,000-34,999, under 45: 2,797 $35,000 or more, under 45: 8,406	< $10,000: 290 $10,000-19,999: 621 $20,000-34,999: 983 $35,000 or more: 2,866	NA

Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Current estimates from the National Health Interview Survey, 1996. Vital and Health Statistics, Series 10, No. 200. DHHS Publication No. (PHS) 99-1528. Hyattsville, MD: US Department of Health and Human Services. October 1999.

Table 2. 1996 US prevalence rates and numbers for hay fever/allergic rhinitis without asthma, by geographic location and place of residence

Geographic location	Prevalence rates per 1,000 persons	Prevalence numbers, in thousands
US	89.8	23,721
Northeast	78.3	4,220
Midwest	85.5	5,424
South	94.9	8,593
West	97.3	5,484

Place of residence	Prevalence rates per 1,000 persons	Prevalence numbers, in thousands
All Metropolitan Statistical Areas (MSA)	90.6	18,887
Central city	86.3	6,742
Not central city	93.3	12,145
Not MSA	86.5	4,834

Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Current estimates from the National Health Interview Survey, 1996. Vital and Health Statistics, Series 10, No. 200. DHHS Publication No. (PHS) 99-1528. Hyattsville, MD: US Department of Health and Human Services. October 1999.