CHEST

Pulmonary Hypertension Surveillance
United States, 2001 to 2010

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Pulmonary hypertension (PH) is an uncommon but progressive condition, and much of what we know about it comes from specialized disease registries. With expanding research into the diagnosis and treatment of PH, it is important to provide updated surveillance on the impact of this disease on hospitalizations and mortality. This study, which builds on previous PH surveillance of mortality and hospitalization, analyzed mortality data from the National Vital Statistics System and data from the National Hospital Discharge Survey between 2001 and 2010. PH deaths were identified using *International Classification of Diseases, Tenth Revision* codes I27.0, I27.2, I27.8, or I27.9 as any contributing cause of death on the death certificate. Hospital discharges associated with PH were identified using *International Classification of Diseases, Ninth Revision, Clinical Modification* codes 416.0, 416.8, or 416.9 as one of up to seven listed medical diagnoses. The decline in death rates associated with PH among men from 1980 to 2005 has reversed and now shows a significant increasing trend. Similarly, the death rates for women with PH have continued to increase significantly during the past decade. PH-associated mortality rates for those aged 85 years and older have accelerated compared with rates for younger age groups. There have been significant declines in PH-associated mortality rates for those with pulmonary embolism and emphysema. Rates of hospitalization for PH have increased significantly for both men and women during the past decade; for those aged 85 years and older, hospitalization rates have nearly doubled. Continued surveillance helps us understand and address the evolving trends in hospitalization and mortality associated with PH and PH-associated conditions, especially regarding sex, age, and race/ethnicity disparities.

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ABBREVIATIONS: AAPC = average annual percent change; AI/AN = American Indian/Alaska native; APC = annual percent change; ICD-9-CM = *International Classification of Diseases, Ninth Revision, Clinical Modification*; ICD-10 = *International Classification of Diseases, 10th Revision*; NH = non-Hispanic; NHDS = National Hospital Discharge Survey; NIH = National Institutes of Health; PAH = pulmonary arterial hypertension; PH = pulmonary hypertension; REVEAL Registry = Registry to Evaluate Early and Long-term PAH Disease Management; UCOD = underlying cause of death

Pulmonary hypertension (PH) is an uncommon but progressive condition. In the past, it has been called an orphan disease because it affects small numbers of individuals, is associated with many diseases, and is often overlooked by doctors.[1] Previous surveillance from the Centers for Disease Control and Prevention[2] from 1980

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to 2002 identified decreasing mortality rates associated with PH among men, but increasing mortality rates among women, along with stable rates among whites but increasing rates among blacks. Increasing rates of hospitalization associated with PH were identified as well. The symptoms of PH during the initial stage of the disease are common to many other medical conditions (eg, difficulty breathing, fatigue), often resulting in a delayed diagnosis until more severe symptoms arise (eg, dizziness, chest pain, ankle swelling, palpitations).[3,4]

PH is characterized by increased pressure in the pulmonary arteries (resting mean pulmonary artery pressure $\geq$25 mm Hg) and increased pulmonary arterial resistance but it is associated with many underlying conditions.[5] The World Health Organization classification of PH, known as the Dana Point classification, was last updated in 2008[6] (Table 1), after the most recent PH surveillance summary from the Centers for Disease Control and Prevention.[2] Some common underlying causes include pulmonary arterial hypertension (PAH) from congenital heart disease, connective tissue disease, or persistent PH of the newborn; PH due to left-sided heart disease; chronic lung diseases and hypoxemia; and chronic thromboembolic pulmonary disease. Genetics also plays a role in PH, and although PH occurs at all ages, the incidence increases with age. Registries from France and the United Kingdom report an incidence rate of 1.1 to 2.4 cases per million population per year, a prevalence of 6.6 to 15.0 cases per million population per year for PAH, and a 5-year mortality of approximately 40%.[7]

Much of what we know about PH comes from specialized disease registries.[8-10] With expanding research into the diagnosis and treatment of PH, it is important to provide updated surveillance on the impact of this disease on hospitalizations and mortality. The surveillance report by Hyduk et al[2] described trends in mortality and hospitalization rates associated with PH among adults aged 45 years and older from 1980 through 2002 by demographic characteristics. This study builds on previous PH surveillance of mortality and hospitalization using data from the National Vital Statistics System and the National Hospital Discharge Survey (NHDS).[11] The purpose of our report is to describe trends in diagnosed PH-related mortality and hospitalizations during the period 2001 to 2010. Because PH is frequently reported as a secondary diagnosis, our report presents data for PH as any contributing cause of death or as any listed hospital diagnosis.

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Materials and Methods

Mortality

Mortality data from the National Vital Statistics System for the period 2001 to 2010 were analyzed. Bridged-race July 1 population estimates produced by the US Census Bureau in collaboration with the National Center for Health Statistics were compiled using intercensal estimates for the period 2001 to 2009 and postcensal estimates for 2010. For this report, all diseases and conditions reported on death certificates were classified according to codes from the *International Classification of Diseases, 10th Revision* (ICD-10). For this analysis, PH deaths are defined as those with decedents having ICD-10 codes I27.0, I27.2, I27.8, or I27.9 reported as any contributing cause of death (ie, any of the possible 20 conditions, including underlying cause) on the death certificate. An ICD coding change for mortality occurred in 2003 with the addition of ICD-10 code I27.2 for secondary PH. This resulted in a shift from coding most cases of death related to PH from primary PH (ICD-10 I27.0) to other secondary PH (Fig 1,[12] Table 2). These changes require careful interpretation of PH surveillance data over time when relying on individual ICD-10 codes.[13]

Rates are expressed per 100,000 population and were directly age standardized to the 2000 US standard population and eight age groups (0-12 months followed by those aged 1 to 34 years, 35 to 44 years, 45 to 54 years, 55 to 64 years, 65 to 74 years, 75 to 84 years, and $\geq$85 years). Age-standardized death rates and 95% CIs were calculated by sex, race/ethnicity (ie, non-Hispanic [NH] white, NH black, NH American Indian or Alaska native (AI/AN), NH Asian/Pacific Islander, Hispanic), and the decedent's state of residence at time of death. Age-specific death rates were calculated. It should be noted that race and ethnicity may not be captured accurately on the death certificate, especially for Hispanics and races other than black or white.[14] This may affect the observed death rates for Hispanics and other nonwhite/nonblack individuals, especially AI/AN decedents.

Trend analyses and comparability tests for age-standardized or age-specific death rates plotted over time by year were conducted using Joinpoint software, developed by the National Cancer Institute. (Joinpoint version 4.0.3; National Cancer Institute). The number of trend segments is based on a segmented line regression analysis of best fit with the smallest number of "joinpoints" or points (0 or 1) at which the direction of the trend line changes. Annual percent change (APC) was calculated for each of the trend segments. Average annual percent change (AAPC) was calculated for the time period 2001 to 2010 to quantify the average trend over this time period. To determine whether the trend lines were parallel or coincident, tests were conducted to assess pairwise differences between race/ethnicity, with NH white as the referent; age-specific differences, with 0 to 12 months as the referent; and sex differences, with men as the referent. Tests determined whether (1) two joinpoint regression functions were identical (test of coincidence) or (2) two regression mean functions were parallel (test of parallelism) at $P < .05$.

The distribution of selected disease categories reported as the underlying cause of death (UCOD) among decedents with reported PH was examined for 2001 through 2010 by race/ethnicity and sex. Rates and trends for these distributions were calculated over that time period.

Hospitalizations

The NHDS, conducted annually from 1965 to 2010 by the Centers for Disease Control and Prevention's National Center for Health