
Jonathan M. Wortham,\(^1\) Elizabeth R. Zell,\(^2\) Tracy Pondo,\(^2\) Lee H. Harrison,\(^3\) William Schaffner,\(^4\) Ruth Lynfield,\(^5\) Ann Thomas,\(^6\) Arthur Reingold,\(^7\) Nancy M. Bennett,\(^8\) Susan Petit,\(^9\) Deborah Aragon,\(^10\) Joseph Bareta,\(^11\) Billie A. Juni,\(^5\) Monica M. Farley,\(^12,13\) Bernard Beall,\(^2\) and Matthew R. Moore\(^2\)

\(^1\)Epidemic Intelligence Service, and \(^2\)National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia; \(^3\)Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland; \(^4\)Department of Preventive Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee; \(^5\)Minnesota Department of Health, St Paul; \(^6\)Oregon Public Health Division and Oregon Emerging Infections Program, Portland; \(^7\)California Emerging Infections Program, Oakland; \(^8\)University of Rochester School of Medicine and Dentistry, New York; \(^9\)Connecticut Department of Public Health, Hartford; \(^10\)Colorado Department of Public Health and Environment, Denver; \(^11\)Emerging Infections Program, New Mexico Department of Health, Santa Fe; and \(^12\)Emory University, and \(^13\)Atlanta Veterans Affairs Medical Center, Georgia

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\textbf{Background.} Before the introduction of 7-valent pneumococcal conjugate vaccine (PCV7), invasive pneumococcal disease (IPD) rates among blacks were twice the rates in whites. We measured the effects of trends in PCV7-type and non-PCV7-type IPD rates on racial disparities in overall IPD and estimated the proportion of IPD caused by serotypes included in the 13-valent pneumococcal conjugate vaccine (PCV13).
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\textbf{Methods.} We analyzed data from the Active Bacterial Core surveillance system, which performs active, laboratory- and population-based surveillance for IPD for 29.2 million people in the United States, for the period 1998–2009. For patients with unknown race, we multiplied imputed race to calculate age-, race-, and serotype-specific IPD incidence rates.
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\textbf{Results.} During 1998–2009, 47 449 IPD cases were identified; race was unknown for 5 419 (11%). After multiple imputation, 31 981 (67%) patients were considered white and 13 750 (29%) black. PCV7-type IPD rates in all ages in both races decreased to <1 case per 100 000, whereas there were no decreases in overall IPD rates after 2002. By 2009, PCV13 serotypes caused 71% of cases among whites aged <5 years compared with 58% among blacks (\(P<.01\)). PCV13 serotypes caused 50% of IPD cases in whites aged \(\geq 5\) years compared with 43% among blacks (\(P<.01\)).
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\textbf{Conclusions.} Despite near elimination of PCV7-type IPD in both races, overall disparities in IPD rates persisted because non-PCV7-type IPD rates are higher among blacks. Whereas PCV13 introduction may reduce racial disparities in IPD, higher valency conjugate vaccines and strategies to directly address underlying causes are needed to eliminate IPD disparities.
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\textbf{Keywords.} pneumococcal vaccines; continental population groups; \textit{Streptococcus pneumoniae}.
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routine PCV7 vaccination for all children aged 2–23 months and for all children aged 24–59 months with certain chronic medical conditions that increase risk for IPD [3, 4]. With hopes of reducing the higher rates of IPD observed among black children and those of American Indian or Alaska Native descent compared with white children, the ACIP prioritized black children aged 24–59 months (2–5 years) for vaccination with PCV7 along with children aged 24–59 months of American Indian or Alaska Native descent in its initial recommendations for PCV7.

After introduction of PCV7, IPD rates declined dramatically among all ages and racial groups, despite these recommendations for only select groups of children <5 years old [1]. Flannery et al reported that, by 2002, PCV7 had substantially reduced racial disparities in rates of IPD with hope that these disparities could be eliminated [1, 5, 6]. However, after the dramatic reductions in IPD rates seen through 2002, increases in rates of IPD caused by non-PCV7 serotypes—particularly serotype 19A—have prevented further reductions in overall IPD rates [7, 8]. Despite the tremendous reductions in IPD rates, >43,000 cases of IPD still occur annually in the United States, resulting in approximately 5000 deaths and >7 billion dollars of direct and indirect annual healthcare expenditures [9]. The effects of higher rates of non-PCV7 serotype IPD on racial disparities in overall IPD have not been examined.

Reducing racial disparities in health outcomes, including pneumococcal disease, was an objective of Healthy People 2010 and remains an objective in Healthy People 2020, the US Department of Health and Human Services’ most recent 10-year national objectives for improving health of Americans [10, 11]. We measured the effects of increasing rates of IPD due to non-PCV7 serotypes on racial disparities in IPD rates using active, population-based surveillance. We also estimated the proportion of IPD in blacks and whites caused by serotypes included in the 13-valent pneumococcal conjugate vaccine (PCV13) (Prevnar-13, Pfizer) in 2009 [12].

**METHODS**

Active, population-based surveillance for IPD was conducted by the US Centers for Disease Control and Prevention (CDC) Active Bacterial Core surveillance (ABCs)/Emerging Infections Program network. ABCs conducts active, laboratory-based surveillance for IPD cases in San Francisco, California; children aged <5 years in Alameda and Contra Costa Counties, California; the 5-county Denver, Colorado, metropolitan area; the 20-county Atlanta, Georgia, metropolitan area; the Baltimore, Maryland, metropolitan area; the 7-county Rochester, New York, metropolitan area; the 8-county Albany, New York, metropolitan area; children aged <5 years in Erie County, New York; the 3-county Portland, Oregon, metropolitan area; 11 counties in Tennessee; and all counties in Connecticut, Minnesota, and New Mexico. According to the 2000 US census, the surveillance population was 78% white, 16% black, and 5% Asian or Pacific Islander compared with 75% white, 12% black, and 3.6% Asian or Pacific Islander in the general US population [13]. The total population under surveillance was approximately 29.2 million persons (9.5% of the US population) in 2009.

All clinical laboratories serving the surveillance population were contacted regularly to ensure complete case ascertainment. Cases of IPD were defined as isolation of *Streptococcus pneumoniae* from a normally sterile body site (eg, blood or cerebrospinal, peritoneal, or pleural fluid) obtained from a resident of the surveillance areas during 1998 through 2009. Clinical and demographic data, including race, were collected from the medical records of case patients and reported to the CDC on a standardized case report form.

IPD annual incidence rates were calculated for 1998 through 2009 using population estimates from the US Census Bureau for each year. Race was defined according to the US Census prior to 2000 [13]. Race-specific incidence rates for 2000–2009 were calculated using bridged census files to maintain consistent single race categories. To calculate race-specific incidence rates, we assigned race to case patients with missing race using a 69-variable regression model, which allowed the inclusion of these cases in race-specific IPD rate calculations. Our model used relationships between race and other variables (eg, state of residence, age, county of residence, hospitalization status, presence of specific underlying conditions) among cases with known race to predict race among cases with unknown race, assuming race was missing at random [14, 15]. To test the appropriateness of the regression model, we removed race data from 10% of cases with known race and used the model to predict race of these cases. The actual number of cases in each race category fell within confidence intervals calculated from the multiply imputed datasets.

Pneumococcal isolates from cases were sent to reference laboratories for serotyping using the Quellung reaction. Serotype information was available for 87.9% of cases among whites and for 88.5% among blacks (P < .01). For cases where serotype was not available, serotype was proportionally assigned based on the distribution of cases with known serotype within each race and age category. Serotypes in PCV7 are 4, 6B, 9V, 14, 18C, 19F, and 23F. Because PCV7 also protects against disease from serotype 6A IPD, we included serotype 6A with PCV7 serotypes [16]. The remaining serotypes in PCV13, but not in PCV7 are 1, 3, 7F, 5, and 19A.

Multiply imputed datasets were created using IVEware software (Institute for Social Research, University of Michigan, Ann Arbor). Variance estimates were calculated using standard combining rules for multiply imputed data [17]. Rate ratios were calculated comparing age- and race-specific incidence rates with a baseline pre-PCV7 rate, defined as the average of 1998

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and 1999 incidence rates to account for variability in annual rates before vaccine introduction, as well as in 2002 and 2009. Confidence intervals for rate ratios and rate differences were calculated using Poisson regression with terms for race, age category (0–4, 5–17, 18–49, 50–64, and ≥65 years) and time period. The analysis was performed using SAS software, version 9.3 (SAS Institute, Cary, North Carolina).

RESULTS

Patient Characteristics

During 1998–2009, 47 449 cases of IPD were detected. Among 42 030 (89%) case patients with known race, 27 504 (65%) were white, 12 862 (31%) were black, 760 (2%) were Asian, 656 (1%) were American Indian or Alaska Native, and 248 (1%) were Native Hawaiian or other Pacific Islander. Because numbers of cases among nonwhite, nonblack persons were small, they were combined into a single race category, “other,” for the purposes of multiple imputation. After imputing race, 31 981 (67%) case patients were considered white, 13 750 (29%) black, and 1718 (4%) other. Because of the heterogeneity in the “other” category and its limited size, we excluded this group from the remainder of the analysis.

Trends by Age, Race, and Serotype

During 1998–1999, black children <5 years had higher rates of IPD compared with white children (Figure 1), and the majority of IPD cases in children aged <5 years of both races were caused by PCV7 serotypes (84% among blacks, 83% among whites, \( P = .42 \)). IPD rates decreased dramatically after PCV7 introduction in 2000. Compared with pre-PCV7 IPD rates, rates in 2002 among black children aged <5 years had decreased by 82% (95% confidence interval [CI], 76%–86%), compared with 71% (95% CI, 65%–76%) among whites (Figure 1). These reductions in overall and PCV7-type IPD rates corresponded with significant reductions in rate ratios and rate differences (Figure 2), indicating a reduction in the racial disparity. After 2002, no further reductions in overall IPD rates, rate ratios, or rate differences occurred through 2009. Two opposing trends were observed during 2002–2009, continued reductions in PCV7-type IPD and gradual increases in non-PCV7-type IPD in both races (Figure 2). Because of the disproportionately large increase in non-PCV7-type IPD rates among black children <5 years, the rate ratio between black and white children actually increased between 2002 and 2009. By 2009, PCV7-type IPD was virtually eliminated from both races, to <1 case per 100 000 population, with only 2 cases of PCV7-type IPD occurring in black persons <5 years and only 5 cases among whites. Overall rates of IPD,

![Figure 1](cid:201458155)
however, remained higher in black children compared with white children because of the disparity in non-PCV7-type IPD (Figure 1). Among black persons <5 years old, the rate of non-PCV7-serotype IPD increased by 98.4% (95% CI, 93.2%–106%), from 18.9 (95% CI, 15.4–22.5) in 2002 to 37.5 (95% CI, 31.7–43.4) in 2009, compared with a 35.5% (95% CI, 35.0%–36.1%) increase in rates among whites from 12.5 (95% CI, 10.9–14.0) in 2002 to 16.8 (95% CI, 14.9–18.9) in 2009. In both of these groups, serotypes 19A and 7F accounted for the vast majority of the increase in non-PCV7-type IPD (data not shown).

IPD rates also declined among older children and adults (Figure 3). Pre-PCV7 IPD rates among persons aged ≥5 years were 37.9 per 100 000 population (95% CI, 36.2–39.5) among blacks and 15.7 (95% CI, 14.2–17.3) among whites. Similar to observed trends in children aged <5 years, the majority of IPD cases in persons aged ≥5 years of both races were caused by PCV7 serotypes. However, PCV7 serotypes caused a lower proportion of IPD cases among persons aged ≥5 years compared with children <5 years. Only 58% of pre-PCV7 cases among blacks ≥5 years old were caused by PCV7 serotypes compared with 54% of cases among whites (P < .01). IPD rates in this age group also decreased dramatically after PCV7 was recommended for children <5 years old in 2000. Compared with pre-PCV7 IPD rates, rates among black persons aged ≥5 years declined 34.2% (95% CI, 33.3%–35.2%) between 1998 and 2002 compared with a decline of 24.8% (95% CI, 24.6%–25.1%) among white persons (Figure 4).

Similar to our observations among young children, there were no statistically significant reductions in overall IPD rates among persons aged ≥5 years of either race during 2002–2009. Whereas rates of IPD due to PCV7 serotypes decreased to <1 case per 100 000 by 2009 among adults and children ≥5 years in both races, disparities persisted in overall IPD, again, because of disparities in non-PCV7-type IPD. Among black persons ≥5 years old, the rate of non-PCV7-serotype IPD increased by 25% (95% CI, 23%–26%), from 14.8 (95% CI, 12.9–16.6) in 2002 to 18.5 (95% CI, 15.9–21.0) in 2009, compared with a 76% (95% CI, 74%–80%) increase in rates among whites from 6.9 (95% CI, 6.3–7.5) in 2002 to 12.2 (95% CI, 11.3–13.1) in 2009. As such, rate ratios and rate differences of non-PCV7-serotype IPD rates between black and white persons ≥5 years old actually decreased from 2002 to 2009, because of the disproportionate increase in non-PCV7-type IPD rates among white persons (Figure 4). By 2009, overall IPD rates were 12.6 (95% CI, 12.2–13.1) among whites aged ≥5 years compared with 19.4 (95% CI, 18.0–20.8) among blacks. Although IPD rates stabilized during 2002–2009 among both

Figure 2. Invasive pneumococcal disease rate differences between black and white children <5 years of age, by serotype—Active Bacterial Core surveillance, 1998–2009. Abbreviations: IPD, invasive pneumococcal disease; PCV7, 7-valent pneumococcal conjugate vaccine; PCV13, 13-valent pneumococcal conjugate vaccine.

Confidence intervals for rate differences were calculated using Poisson regression.
PCV7 includes serotypes 4, 6B, 9V, 14, 18C, 19F, 23F, and 6A.
Serotypes 1, 3, 5, 7F, and 19A are included in PCV13, but not PCV7.
Non-PCV13 includes all serotypes not included in the 13-valent pneumococcal conjugate vaccine.
races, a statistically significant decrease in overall IPD rates was observed in 2009 compared with the pre-PCV7 period.

By 2009, a higher proportion of IPD in whites of all ages was potentially preventable by PCV13. Only 58% of IPD cases among black children aged <5 years were caused by PCV13 serotypes, compared with 71% of cases in white children (P < .01; Figure 5). Together, serotypes 7F and 19A accounted for 92% and 91% of PCV13-type disease occurring among black and white children aged <5 years, respectively, in 2009. Among adults and children ≥5 years old, PCV13 serotypes caused 50% of IPD in whites, compared with only 43% in blacks (P < .01). The proportion of IPD caused by non-PCV13 serotypes increased directly with age (Figure 5). Among adults ≥65 years, the majority of IPD was caused by non-PCV13 serotypes in both races.

The 6 most common non-PCV13 serotypes causing IPD during 2009 among white children aged <5 years were serotypes 8, 10A, 11A, 12F, 22F, and 33F, accounting for 88% of non-PCV13-type IPD in this group. Among black children, the 6 most common non-PCV13 serotypes during 2009 were 10A, 12F, 15B, 17F, 22F, and 33F, accounting for 96% of non-PCV13-type IPD in this group. Among persons aged ≥5 years, the majority of IPD was caused by non-PCV13 serotypes in both races.

The 6 most common non-PCV13 serotypes causing IPD during 2009 among white children aged <5 years were serotypes 8, 10A, 11A, 12F, 22F, and 33F, accounting for 88% of non-PCV13-type IPD in this group. Among black children, the 6 most common non-PCV13 serotypes during 2009 were 10A, 12F, 15B, 17F, 22F, and 33F, accounting for 96% of non-PCV13-type IPD in this group. Among persons aged ≥5 years, the 6 most common non-PCV13 serotypes causing IPD were serotypes 9N, 10A, 11A, 12F, 22F, 33F. These serotypes accounted for 71% of non-PCV13-type IPD among white persons ≥5 years. Among black persons ≥5 years, the 6 most common non-PCV13 serotypes during 2009 were 8, 9N, 11A, 22F, and 33F, accounting for 75% of non-PCV13-type IPD.

**DISCUSSION**

Racial disparities are well-described for noninfectious conditions, such as myocardial infarction, stroke, colorectal cancer, and end-stage renal disease, and infectious conditions, such as human immunodeficiency virus (HIV)/AIDS, tuberculosis, influenza, and pneumococcal disease [10]. One goal of Healthy People 2020 is “to achieve health equality, eliminate disparities, and improve the health of all groups” [10]. PCV7 introduction has resulted in dramatic decreases in overall rates of IPD and the elimination of racial disparities in PCV7-serotype IPD among all age groups, despite recommendations to immunize only young infants and children. However, although racial disparities in PCV7-serotype IPD were eliminated, disparities in overall IPD rates persisted because prevaccine rates of non-PCV7 serotype IPD were higher among black persons of all ages. Several factors may explain the observed higher rates of non-PCV7 IPD among black persons.

A higher prevalence of underlying medical conditions that are independent risk factors for IPD among black persons could account for these persistent racial disparities in
non-PCV7 IPD rates. For example, sickle cell disease, HIV/AIDS, asthma, diabetes, and end-stage renal disease are more prevalent among black persons than whites [18–20]. Despite differences in the prevalence of these underlying medical conditions between races, vaccination of children was a highly effective strategy for eliminating racial disparities in PCV7 serotype disease in all ages. However, vaccination with PCV7 does not protect from IPD caused by non-PCV7 serotypes. Therefore, disparities in the prevalence of underlying medical conditions between blacks and whites may explain some of the racial disparities in IPD.

Lower socioeconomic status, and its associated morbidity, may also explain some of the observed racial disparities in non-PCV7 IPD rates. Low socioeconomic status has been associated with negative health outcomes, including increased incidence of both infectious and noninfectious disease [18]. Poverty rates among black persons in the United States are more than twice the rates in whites [21]. Recent analyses have demonstrated a strong relationship between poverty rates in a census tract and the rate of bacteraemic pneumonia in that tract, including pneumococcal pneumonia [22]. Furthermore, one study found that, although black race was a risk factor for IPD, this increased risk disappeared when the investigators controlled for markers of low socioeconomic status, such as lack of health insurance and low household income [23, 24]. Both behavioral factors, such as cigarette smoking, and environmental factors, such as crowding and air pollution, may also contribute to racial disparities in IPD as these factors have been associated with both IPD risk and low socioeconomic status [25–28].

Differences in vaccine coverage do not explain the higher observed rates of non-PCV7 IPD and overall IPD. Between 2001, 1 year after PCV7 was introduced, and 2009, there were no statistically significant differences in PCV7 coverage between black and white children aged 19–35 months [1, 29]. In fact, the ability of PCV7 to induce herd protection, by reducing colonization with and transmission of PCV7 serotypes, likely is responsible for the observation that racial disparities in PCV7-type IPD were virtually eliminated despite vaccination of only children aged <5 years. Thus, neither differences in PCV7 coverage nor differences in PCV7 vaccine effectiveness at the population level can explain racial disparities in non-PCV7 IPD rates in 2009.

This analysis has limitations. Race data were abstracted from medical chart reviews rather than interviews of patients. As such, the race documented in the medical record may have come from patient self-report or from an observation by a
healthcare worker; the patient’s self-reported race may differ. Importantly, although this analysis showed that increases in rates of non-PCV7 serotype IPD were responsible for persistent racial disparities, we were unable to explain the reasons behind this observation because we did not have data regarding case patients’ other determinants of health, such as socioeconomic status, environmental factors, or behavioral factors. Additionally, we are unable to reliably report on trends in ethnic disparities in IPD with this dataset, as ethnicity data were available for only 55%–60% of patients. Because multiple imputation assumes that missingness occurs at random and because we are not confident that ethnicity data are missing at random in this dataset, we cannot justify multiple imputation of ethnicity to report trends in ethnic disparities.

PCV7 eliminated racial disparities in PCV7-type IPD; however, rates of IPD remain higher among black persons because of higher rates of non-PCV7-type IPD. Introduction of PCV13 immunization has the potential to reduce PCV13-type IPD rates in both races; therefore, vaccination remains the best known strategy for reducing IPD incidence as well as racial disparities in IPD rates.

Because rate differences are a more meaningful measure of racial disparities as IPD rates decrease, this measure should be closely followed as the PCV13 immunization program is implemented. However, because rates of non-PCV13-serotype IPD are higher among black persons of all ages, and non-PCV13 serotypes cause a higher proportion of IPD among black persons of all ages, racial disparities, with smaller but still measurable rate differences, are likely to persist despite introduction of PCV13. Because the majority of IPD cases in persons aged >65 years old are caused by non-PCV13 serotypes, PCV13 introduction may have a smaller effect on IPD rates in this age group. In the future, conjugate vaccines effective against more, or all, pneumococcal serotypes and efforts to define and ultimately address underlying causes of racial disparities, whether they are socioeconomic, behavioral, environmental, or biological are needed to eliminate racial disparities in overall IPD.

Notes

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Figure 5. Proportion of invasive pneumococcal disease cases caused by PCV13 serotypes, by race and age group—Active Bacterial Core surveillance, 2009. Abbreviations: IPD, invasive pneumococcal disease; PCV13, 13-valent pneumococcal conjugate vaccine.

PCV13 includes serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F. Non-PCV13 includes all other serotypes.

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Potential conflicts of interest. W. S. serves as a member of the data safety monitoring board for Merck and is an occasional consultant for Merck, Sanofi, Dynavax, and Pfizer. L. H. has served on scientific advisory boards for Sanofi Pasteur, GSK, Merck, Novartis, and Pfizer. All other authors report no potential conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References