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Impact of 13-Valent Pneumococcal Conjugate Vaccine on Invasive Pneumococcal Disease Among Adults with HIV — United States, 2008–2018

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Introduction

Despite the introduction of highly active antiretroviral therapy (HAART), people with HIV (PWH) continue to be at increased risk of invasive pneumococcal disease (IPD)[1–3]. PWH

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have a slow and incomplete therapy-associated recovery of protective immune functions, and impaired immunity persists even in individuals who maintain CD4 T cell levels of ≥500 cells/μl [4–6].

Two pneumococcal vaccines are currently recommended for use for PWH in the United States: the 23-valent pneumococcal polysaccharide vaccine (PPSV23), and the 13-valent pneumococcal conjugate vaccine (PCV13). PPSV23 is recommended for individuals aged ≥2 years with certain underlying conditions, including PWH, and for all adults aged ≥65 years, and has been available since the 1980s [7, 8]. PCV13 was recommended in 2010 for routine use among children aged <5 years and replaced the 7-valent pneumococcal conjugate vaccine (PCV7)[9]. PCV use in U.S. children dramatically reduced IPD incidence not only in children but also in unvaccinated adults[10–13] due to indirect effects from vaccination of children. Our previous analyses of 1998–2007 data showed that IPD incidence among people with AIDS (used in place of PWH since the number of PWH could not be obtained for the entire study period) decreased, suggesting that PWH also benefited from indirect effects[2, 3]; however, IPD incidence among PWH aged 18–64 years was still 40 times higher than in those without HIV infection.

Pneumococcal conjugate vaccine use in U.S. adults was first recommended in 2012 when the Advisory Committee on Immunization Practices recommended routine use of PCV13 for adults aged ≥19 years with immunocompromising conditions, including HIV, functional or anatomic asplenia, cerebrospinal fluid leaks, or cochlear implants, in series with PPSV23.[14] In 2014, all adults aged ≥65 years were recommended to receive PCV13 in series with PPSV23, which was changed to a recommendation based on shared clinical decision-making in 2019 in adults without immunocompromising conditions, functional or anatomic asplenia, cerebrospinal fluid leaks, or cochlear implants[15, 16]. We evaluated the population-level impact of current U.S. PCV13 policy on IPD incidence among PWH aged ≥19 years compared to those not diagnosed with HIV (non-PWH).

Methods

Surveillance methods

IPD cases were identified through the Active Bacterial Core surveillance (ABCs), an active, laboratory- and population-based surveillance platform for invasive bacterial diseases in select counties of 10 states across the United States[17]. Medical records were abstracted to collect demographic and clinical information on each case, including HIV infection status.[18, 19] Pneumococcal isolates from ABCs cases were serotyped at the Minnesota Department of Health or the CDC *Streptococcus* Laboratory by Quellung, polymerase chain reaction, or whole genome sequencing (2015–2018). For this study, we included cases reported during 2008–2018 among adults aged ≥19 years old residing in ABCs catchment areas in 9 states (California, Connecticut, Colorado, Georgia, Maryland, Minnesota, New Mexico, Oregon, or Tennessee) (Supplemental Digital Content).

Definitions

An IPD case was defined as isolation of *Streptococcus pneumoniae* from a normally sterile site (e.g., blood, cerebrospinal fluid) from a surveillance area resident. We grouped pneumococcal serotypes for analysis of disease trends into the following categories: 1) PCV13-types defined as the 13 serotypes contained in PCV13 (serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) and serotype 6C due to cross-protection from the serotype 6A antigen;[20] 2) PPSV23 unique types defined as the 11 serotypes contained in PPSV23 but not in PCV13 (serotypes 2, 8, 9N, 10A, 11A, 12F, 15B/C, 17F, 20, 22F, and 33F); and non-vaccine types (NVT), which included all other serotypes. Given the recent licensure of the 15- and 20-valent pneumococcal conjugate vaccines (PCV15 and PCV20) for adults[21, 22], we evaluated contribution of additional serotypes included in PCV15 but not PCV13 (PCV15-unique types: 22F and 33F) and PCV20 but not PCV15 (PCV20-unique types: 8, 10A, 11A, 12F, and 15B/C) to IPD in this population. AIDS was defined as ever having a diagnosis of AIDS or CD4 count of <200 cells/mm^3.

Statistical methods

Characteristics of IPD cases were summarized by HIV status and by study period: baseline prior to PCV13 introduction in the pediatric immunization program (2008–2009), and before (2011–2012) and after (2017–2018) PCV13 recommendation in immunocompromised adults. To estimate IPD incidence per 100,000 adults among PWH and non-PWH, we used two data sources for population denominators. For PWH, we used the number of adults aged ≥19 years with known HIV infection in the ABCs catchment area[17] (Supplemental Digital Content). For non-PWH, we used the U.S. Census estimates for ABCs catchment area, less the number of PWH in the same ABCs catchment area. Overall and serotype-group specific IPD incidence for PWH and non-PWH was stratified by age group (19–64 years, ≥65 years) and race and ethnicity (non-Hispanic black, non-Hispanic white, and Hispanic). For IPD incidence calculation, simple proportions were used to impute missing serotype and race/ethnicity data (Supplemental Digital Content).

Incidence at the baseline period (2008–2009) was compared with incidence before (2011–2012) and after (2017–2018) PCV13 introduction in immunocompromised adults, both after PCV13 introduction for children. Percent changes of incidence rates were calculated as 1-(IPD incidence post-PCV13)/(IPD incidence at baseline). Incidence rate ratio (IRR) was calculated to compare incidence rate of PWH to that of non-PWH. Variance of IPD incidence was calculated using the assumption that IPD cases followed a Poisson distribution. We drew 10,000 values from the distribution of IPD cases and reported the 95% confidence interval (CI) of the estimates based on the upper and lower 2.5^{th} percentile of the 10,000 calculated percent changes and IRR.

We compared the distribution of PCV13-types, serotypes unique to PPSV23, and the most common NVTs, between 2008–2009 and 2017–2018 for both PWH and non-PWH using Chi-Square test. To account for multiple comparisons (n=30), we used a Bonferroni correction, where a P value of <0.002 (0.05/30) was considered statistically significant. Analyses were performed using SAS version 9.4 (SAS Institute Inc.).

Results

Description of IPD cases pre- and post-PCV13 introduction by HIV status

During 2008–2009, a total of 29,668 IPD cases were reported, including 2,440 (8.2%) among PWH. Characteristics of IPD cases in 2008–2009 (n=6,548), 2011–2012 (n=5,226), and 2017–2018 (n=5,169) are shown in Table 1. Of IPD cases among PWH in 2008–2009, 49.8% (275/552) ever had an AIDS diagnosis, compared to 55.8% (232/416) in 2017–2018. For all study periods, the proportions of adults aged 19–64 years (95–97% in PWH vs. 56–60% in non-PWH), males (60–67% in PWH vs. 51–53% in non-PWH), and non-Hispanic blacks (63–73% in PWH vs. 17–19% in non-PWH) were higher in IPD cases in PWH compared to non-PWH (Table 1). The proportion with ≥1 chronic medical conditions or people who smoke was similar between the two groups (63–67% in PWH vs. 64–69% in non-PWH) (Table 1). The proportion with ≥1 immunocompromising conditions other than HIV (i.e., sickle cell disease, asplenia, congenital or acquired immunodeficiency, organ transplantation, dialysis, and malignancy) was higher in IPD cases in non-PWH compared to PWH, and increased steadily for both groups through 2017–2018 (PWH 25% vs. non-PWH 34%) compared to baseline years (PWH 16% vs. non-PWH 26%).

Pneumonia with bacteremia was the most common syndrome, associated with 77–80% of IPD cases among PWH, and 73–76% of those in non-PWH. Case fatality ratio (CFR) in adults aged ≥65 years (0–21%) was generally higher compared with adults aged 19–64 years (4–11%) in both PWH and non-PWH, though IPD cases in PWH aged ≥65 years was small.

Changes in IPD incidence

At baseline (2008–2009), IPD incidence among PWH was 306.7 per 100,000 (Table 2) and was higher among those aged 19–64 years (308.6 per 100,000) compared to those aged ≥65 years (248.5 per 100,000). Overall IPD incidence declined by 40.3% to 183.0 per 100,000 in 2017–2018 compared to baseline (Table 2). In non-PWH, overall IPD incidence was 15.2 per 100,000 persons at baseline, and was 3.6 times higher in those aged ≥65 years compared to those aged 19–64 years (39.2 and 10.8 per 100,000, respectively). Overall IPD incidence declined by 28.2% from baseline to 10.9 per 100,000 in 2017–2018.

PCV13-type IPD incidence in PWH declined by 72.5% (from 143.9 to 39.6 per 100,000) from baseline to 2017–2018 (Figure1, Table 2), although incidence was stable during 2014–2018 (Figure 1). Reduction in PCV13-type IPD incidence was greater (-84.7%; from 177.5 to 27.2 per 100,000) in those aged ≥65 years, compared to those aged 19–64 years (-71.7%; from 142.3 to 40.4 per 100,000); moreover, PCV13-type IPD incidence in those aged 19–64 years remained higher compared to those aged ≥65 years. In non-PWH, PCV13-type IPD incidence declined by 62.2% (from 8.3 to 3.1 per 100,000) from baseline to 2017–2018, and the percent reduction was similar between age groups.

In PWH, a 28.0% (from 91.1 to 65.1 per 100,000) reduction in NVT-IPD incidence was observed, with year-by-year variation in incidence (Figure 1) and the reduction was significant only among adults aged 19–64 years. Changes in PPSV23-unique IPD incidence was not significant. In non-PWH, NVT-IPD incidence (from 3.0 to 3.4 per 100,000) and

PPSV23-unique IPD incidence (from 3.9 to 4.4 per 100,000) increased, although trends varied by age group (Table 2).

Given that serotype distribution may differ by HIV status and by race/ethnicity, we compared the serotype distribution by HIV status and race/ethnicity before and after imputing missing values, and the serotype distributions were similar (Supplementary Table 1). Therefore, IPD incidence calculation by race/ethnicity used imputed data. In PWH, overall IPD incidence at baseline was highest among non-Hispanic blacks (517.8 per 100,000), and lowest among non-Hispanic whites (142.9 per 200,000) (Supplementary Table 2). The largest reduction in PCV13-type IPD incidence was observed in non-Hispanic blacks (from 231.4 to 42.4 per 100,000; 81.7% reduction); at baseline, PCV13-type incidence in non-Hispanic blacks was 2.8 times higher than that of non-Hispanic whites, but in 2017–2018, PCV13-type IPD incidence between non-Hispanic blacks and non-Hispanic whites was similar. However, overall IPD incidence in non-Hispanic blacks remained nearly twice as high in 2017–2018 as that in non-Hispanic whites (249.9 vs. 131.4 per 100,000). In non-PWH, non-Hispanic blacks also had the highest IPD incidence at baseline and in 2017–2018 (20.2 and 13.8 per 100,000, respectively). PCV13-IPD incidence declined in all race/ethnicity groups (non-Hispanic Blacks, non-Hispanic Whites, and Hispanics), and PCV13-IPD incidence rates were similar across groups in 2017–2018.

Comparing incidence between adults with and without HIV

At baseline, IRR of overall IPD between PWH and non-PWH was 20.2 (95% CI: 18.4–22.0) and declined to 16.8 (95% CI: 15.1–18.5) in 2017–2018 (Table 3). IRRs were lower in 2017–2018 compared to baseline in both age groups, but remained higher among adults 19–64 years (2008–2009: 28.6, 2017–2018: 25.4) compared to adults aged ≥65 years (2008–2009: 6.3, 2017–2018: 4.0). PCV13-type IRR declined, most notably after 2011–2012 (17.3 in 2008–2009, 16.7 in 2011–2012, and 12.6 in 2017–2018). Similar trends were noted in adults aged 19–64 years. NVT IRR also declined (30.0 to 19.6) due to decline in adults aged 19–64 years (53.7 to 36.9).

Serotype distribution pre- and post-PCV13 introduction

From the three periods (2008–2009, 2011–2012, 2017–2018), 89.6% of isolates had serotype information available. In PWH, PCV13-types contributed to 46.9% (228/486) of all IPD in 2008–2009, and declined to 21.5% (81/376) in 2017–2018 (Supplementary Table 3). Serotype 19A, a PCV13-type, was the most common serotype causing IPD among PWH in 2008–2009 (103/486, 21.2% of all IPD), but accounted for 4.5% (17/376) of IPD in 2017–2018 (P<.002) (Figure 2a, Supplementary Table 3). In 2017–2018, serotypes 9N (32/396, 8.5%) and 22F (28/376, 7.4%) were the most common serotypes overall, and serotype 4 (23/376, 6.1%) was the most common PCV13-type IPD. Both the proportion (Figure 2a) and the incidence (Supplementary Table 5) of serotype 4 increased from baseline to 2017–2018, although the percent increase in incidence was not statistically significant (95.2%; 95% CI: -2.6, 394.8). Of the 23 serotype 4 cases in 2017–2018, 91.3% were in adults aged 19–64 years, 91.3% occurred in California or Colorado, and 60.9% were in persons experiencing homelessness (Supplementary Table 6).

In non-PWH, serotypes 7F (973/5,292, 8.4%) and 19A (769/5,292, 14.6%) were the most common serotypes in 2008–2009; in 2017–2018, they accounted for 1.5% (63/4,242) and 2.9% (121/4,242) of all IPD, respectively, (P<.002). In 2017–2018, serotype 3 was the most common serotype (15.3%; 650/4,242) causing IPD in non-PWH adults (Figure 2b, and Supplementary Table 4). From baseline to 2017–2018, serotype 3 IPD incidence increased by 15.5% (95% CI: 3.6 to 28.9). Serotype 4 incidence also increased, though much smaller compared to that observed in PWH (Supplementary Table 5).

In PWH, PCV15-unique types and PCV20-unique types comprised 11.2% (42/376) and 17.0% (64/376) of IPD, respectively, in 2017–2018 (Supplementary Table 3). These proportions were similar to those in non-PWH adults (PCV15-unique types: 584/4,242, 13.8%; PCV20-unique types: 715/4,242, 16.9%) (Supplementary Table 4).

Discussion

Dramatic reductions in IPD incidence were observed in both PWH and non-PWH in the United States following PCV13 introduction for children in 2010, primarily driven by the decline in PCV13-type IPD incidence. Despite these large declines, in 2017–2018, overall and PCV13-type IPD incidence among PWH was still approximately 17 and 13 times the incidence among non-PWH adults, respectively, with the highest overall IPD rates observed among PWH of non-Hispanic blacks both before and after PCV13 introduction. Among PWH and non-PWH, PCV13-type IPD incidence within each group was similar across race/ethnicity in 2017–2018 (Supplementary Table 2), and the remaining difference in IPD incidence was primarily due to non-PCV13-type IPD.

Significant reductions in PCV13-type IPD incidence that occurred from 2008–2007 to 2011–2012 were due to indirect effects from PCV13 vaccination in children[23], and reductions observed from 2011–2012 to 2017–2018 reflect a combination of indirect PCV13 effects and potential effects from PCV13 use among adults with immunocompromising conditions including PWH, or PCV13 use among adults aged ≥65 years. The decline of IRR of PCV13-type IPD in 2017–2018 compared to 2011–2012 in adults aged 19–64 years who currently do not have an age-based PCV13 recommendation may indicate that PWH benefited directly from PCV13 vaccination; however, the degree of impact of direct PCV13 vaccination is unclear. Data on PCV13 coverage among PWH are limited. Analysis of medical claims data estimated that PCV13 coverage for PWH aged 18–64 years was 6.6% in October 2013 and had reached only 31.3% in December 2016 (IQVIA, anonymized patient-level data, December 2017; and Pfizer Inc, internal sales data for PCV13 2017, unpublished data). National Health Interview Survey reported 20–25% coverage of any pneumococcal vaccine in adults aged 19–64 years with indications for vaccination[24]. In older adults for whom PPSV23 has been recommended since the 1980s, PPSV23 coverage among U.S. Medicare beneficiaries aged ≥65 years with immunocompromising conditions has been around 50% in the past 10 years, whereas PCV13 coverage did not increase until 2015 after the age-based recommendation for PCV13 was introduced (CDC unpublished data). Given these estimates showing low pneumococcal vaccine coverage in this population, direct effects from vaccinating PWH was likely limited during our observation period.

While the incidence of PCV13-type IPD among PWH declined for most serotypes, the exception was serotype 4, which increased. We previously reported that during 2010–2018, increase in serotype 4 IPD were observed within 3 of the 10 ABCs sites (California, Colorado, and New Mexico), most notable among persons experiencing homelessness[25]. This is consistent with the serotype 4 cases observed in PWH in our study. Since serotype 4 is rarely detected in young children, the transmission reservoir is thought to exist in adults[26]. In non-PWH, the incidence of both serotype 3 and serotype 4 increased, and serotype 3 was the most common IPD serotype in 2017–2018. Post-licensure data have shown varying estimates of PCV13 effectiveness against serotype 3 disease[27, 28], and minimal population-level impact of PCV13 against serotype 3 disease was observed in the United States in adults aged ≥65 years[29] for whom routine PCV13 use was recommended, or in the UK where routine PCV13 is not recommended routinely for adults[30]. Therefore, improving vaccine coverage in high-risk populations such as persons experiencing homelessness may help reduce transmission of vaccine-type serotypes circulating among adults such as serotype 4; however, improved coverage by itself is unlikely to eliminate the remaining vaccine-preventable disease burden such as serotype 3 disease, which may require a more effective vaccine.

We observed reductions in NVT IPD incidence in PWH, which were not apparent among adults with other underlying conditions that are indications for PCV13 use[23]. Factors other than PCV13 direct and indirect effects, such as improved access to HIV care[31] could have contributed to the decline in IPD incidence in PWH, as HAART has been associated with reduced risk of IPD.[1, 32] However, given that the reductions were not observed for PPSV23 unique serotypes and given the year-to-year variability in NVT incidence (Figure 1), the decline in NVT incidence that we observed should be interpreted with caution, as natural trends in individual serotypes and arbitrary selection of baseline against which NVT incidence changes are measured could overestimate or underestimate the measured effects[10].

In the general population, IPD incidence increases with age, with highest incidence observed among older adults.[23, 33] In our analysis, IPD incidence among PWH aged 19–64 years was higher than those aged ≥65 years. Additionally, non-Hispanic blacks had higher IPD rates compared to those of other race/ethnicity groups in both PWH and non-PWH. Younger adults and Blacks with HIV infection are less likely to have sustained viral suppression compared to other age or race/ethnicity groups[34], and this may be contributing to the increased IPD rates in these groups. Increased IPD incidence in Blacks compared to non-Blacks has previously been reported, regardless of HIV status;[35–37] lower social economic status[38] and higher proportion of underlying conditions among Blacks that increase the risk of IPD[37, 39] are thought to be contributing factors. Introduction of PCV7 in children reduced racial disparities in all age groups due to the dramatic reduction of PCV7-type IPD[37]. Our analysis demonstrates that disparities in PCV13-type IPD between non-Hispanic blacks and non-Hispanic whites with HIV were eliminated by 2017–2018, and most of the remaining differences in IPD incidence were due to non-PCV13 types.

Limitations

Our study is subject to several limitations. First, CDC's HIV surveillance data, which we used as denominators for IPD incidence in PWH, only captures diagnosed HIV cases. In 2008 and 2018, approximately 20% and 14% of people with HIV infection were estimated to not have had been diagnosed, respectively.[40, 41] Therefore, we could have overestimated IPD incidence in PWH, if patients with IPD (the numerator) were more likely to know their HIV status. Second, IPD cases with missing information on race/ethnicity were reclassified based on the distribution in cases with known race/ethnicity regardless of HIV status. Given the smaller proportion of non-Hispanic blacks among non-PWH, we could have underestimated incidence among non-Hispanic blacks with HIV, although the impact was likely small since <5% were missing race/ethnicity information in PWH. A larger proportion (12–50%) of cases had missing data on ethnicity, and we likely underestimated IPD incidence among Hispanics in both PWH and non-PWH, since the proportion of Hispanics among IPD cases in our study (6 –10%) was much smaller than the 18.5% that is estimated for the general US population[42] or >20% among PWH[43]. Third, we could not estimate IPD incidence for people with AIDS over time, since ABCs data captured AIDS diagnosis at any point, whereas the HIV surveillance data captured persons with AIDS during a specified year, by residence at diagnosis. Fourth, ABCs does not capture vaccine coverage (for both PWH and non-PWH) or detailed information on HIV status, such as CD4 count at the time of illness, or antiretroviral treatment history, which are known to impact IPD risk[44]. Therefore, we were unable to assess the contribution of these factors to changes in IPD incidence over time or by age or race/ethnicity groups. Fifth, since our analysis is based on IPD data from 9 ABCs sites that are mostly urban[17], the findings may not be nationally representative. Lastly, we were underpowered to assess changes in incidence rates among older adults and Hispanics with HIV.

Our study showed that introduction of PCV13 in the United States led to reduction in PCV13-type disease burden in both PWH and non-PWH, and eliminated the disparity of PCV13-type IPD across race/ethnicity groups among PWH. However, PWH continue to be at increased risk of IPD, including PCV13-type IPD, compared to non-PWH. While the 2012 recommendation may have had impact in reducing PCV13-type disease burden in PWH, the impact could have been limited, in part, due to low vaccine coverage among PWH. Higher-valency pneumococcal conjugate vaccines that were recently licensed for adults may help further reduce the disease burden among PWH and decrease racial disparities, along with efforts to ensure improved vaccine coverage in PWH to maximize vaccine benefits.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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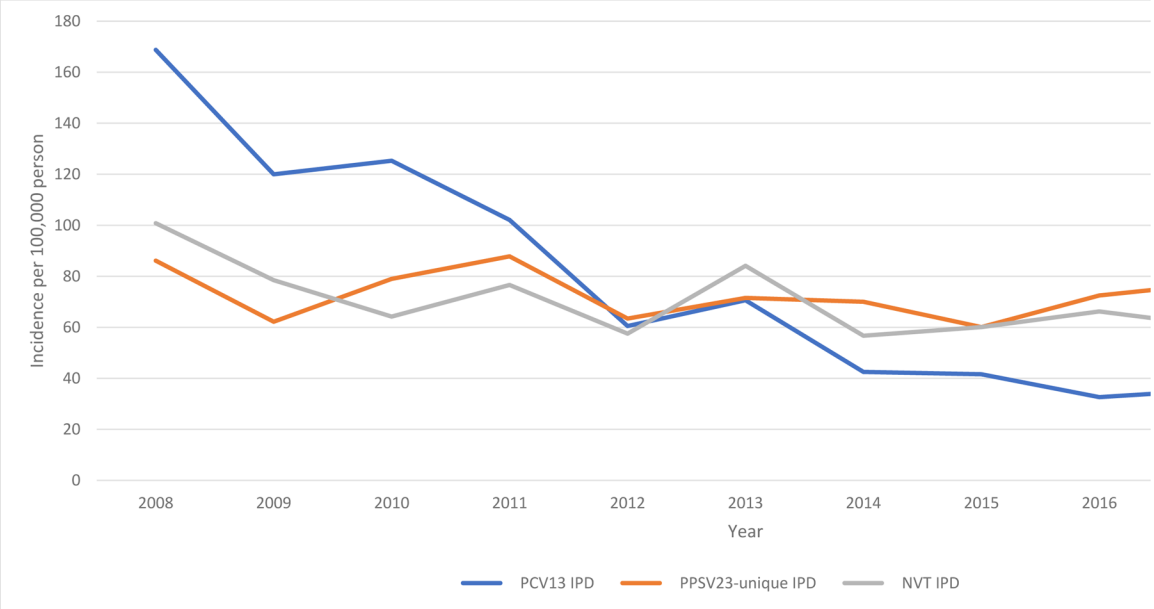

Figure 1. Annual Invasive Pneumococcal Disease Incidence by Serotype Group among Adults Aged ≥19 Years Old with HIV infection, 2008–2018

IPD, invasive pneumococcal disease; NVT, non-vaccine type; PCV13, 13-valent pneumococcal conjugate vaccine; PPSV23, 23-valent pneumococcal polysaccharide vaccine

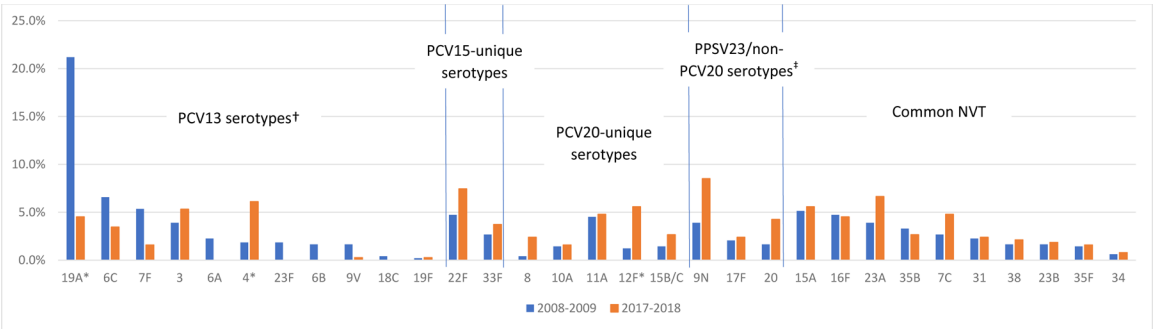

Figure 2a. Distribution of Invasive Pneumococcal Disease Serotypes in Adults Aged ≥19 Years with known HIV infection, 2008–2009 vs. 2017–2018

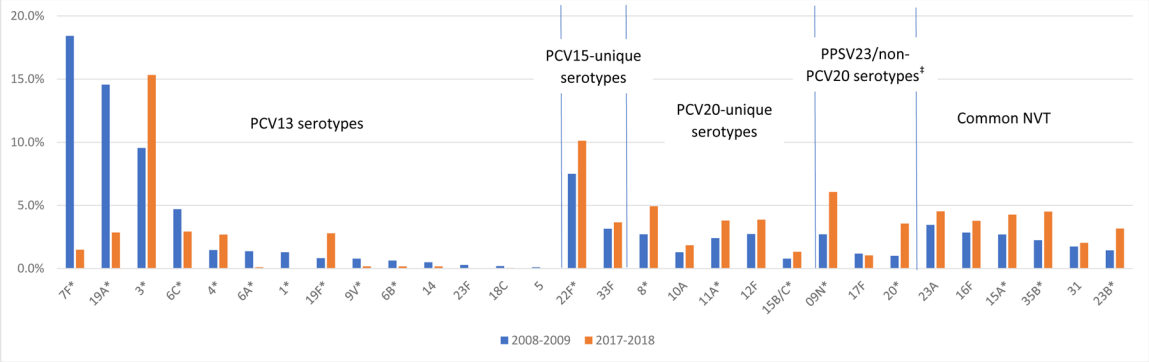

Figure 2b.

Distribution of Invasive Pneumococcal Disease Serotypes in Adults Aged ≥19 Years without known HIV infection, 2008–2009 vs. 2017–2018

Abbreviations: PCV13, 13-valent pneumococcal disease; PCV15, 15-valent pneumococcal disease; PCV20, 20-valent pneumococcal disease; NVT, non-vaccine type

*P<.002

†Invasive pneumococcal disease cases due to serotypes 1, 5, 14 were not detected

‡Invasive pneumococcal disease cases due to serotype 2 were not detected

Table 1.

Characteristics of adults with and without known HIV infection by study period, ABCs 2008–2018

	Pre-PCV13 in both children and adults 2008–2009 (N=6,548)		Post-PCV13 in children, Pre-PCV13 in adults 2011–2012 (N=5,226)		Post-PCV13 2017–2018 (N=5,169)	
	PWH	Non-PWH	PWH	Non-PWH	PWH	Non-PWH
Number of patients	552	5996	443	4783	416	4753
Median age in years (range)	46 (20–76)	60 (19–104)	48 (19–81)	62 (19–100)	51 (20–74)	63 (19–105)
Age group						
19–64 year old, n(%)	538 (97)	3602 (60)	430 (97)	2703 (57)	394 (95)	2661 (56)
>=65 year old, n(%)	14 (3)	2394 (40)	13 (3)	2080 (43)	22 (5)	2092 (44)
Sex						
Male, n(%)	331 (60)	3037 (51)	271 (61)	2448 (51)	286 (69)	2520 (53)
Female, n(%)	221 (40)	2955 (49)	172 (39)	2334 (49)	130 (31)	2232 (47)
Unknown, n(%)	0	4 (<1)	0	1 (<1)	0	1 (<1)
Race and Ethnicity **						
Hispanic, n(%)	35 (6)	414 (7)	25 (6)	352 (7)	41 (10)	429 (9)
White, non-Hispanic, n(%)	91 (16)	3609 (60)	85 (19)	3125 (65)	97 (23)	2905 (61)
Black, non-Hispanic, n(%)	403 (73)	1014 (17)	315 (71)	799 (17)	260 (63)	912 (19)
Other †, n(%)	8 (1)	264 (4)	6 (1)	215 (4)	10 (2)	289 (6)
Unknown, n(%)	15 (3)	695 (12)	12 (3)	292 (6)	8 (2)	218 (5)
Ethnicity						
Hispanic, n(%)	35 (6)	414 (7)	25 (6)	352 (7)	41 (10)	429 (9)
Non-Hispanic, n(%)	284 (51)	2604 (43)	276 (62)	2856 (60)	324 (78)	3599 (76)
Unknown, n(%)	233 (42)	2978 (50)	142 (32)	1575 (33)	51 (12)	725 (15)
Ever diagnosed with AIDS *	275 (49.8)	NA	178 (40.2)	NA	232 (55.8)	NA
Pneumonia with bacteremia, n(%)‡	444 (80)	4517 (75)	342 (77)	3621 (76)	334 (80)	3457 (73)
Meningitis, n(%)‡	29 (5)	312 (5)	30 (7)	288 (6)	15 (4)	315 (7)
Bacteremia w/o focus, n(%)	69 (13)	907 (15)	51 (12)	604 (13)	46 (11)	663 (14)
Deaths, n(%)						
19–64 year old, n(%)	37/538 (7)	336/3602 (9)	2¼30 (5)	247/2703 (9)	14/394 (4)	29½661 (11)
>=65 year old, n(%)	3/14 (21)	397/2394 (17)	2/13 (15)	322/2080 (15)	0/22 (0)	296/2092 (14)
Other chronic medical conditions§, n(%)	360 (65)	3830 (64)	298 (67)	3297 (69)	264 (63)	3205 (67)
Other immunosuppressive condition‖, n(%)	88 (16)	1558 (26)	82 (19)	1486 (31)	102 (25)	1623 (34)

PWH, people with HIV

*AIDS defined as ever having a diagnosis of AIDS or CD4 count <200

[**] Race and ethnicity groups were assigned by first identifying those with Hispanic ethnicity. Those who were not Hispanic (including those with unknown or missing ethnicity) were categorized by their race

[†] Other includes American Indian, Alaska Native, Asian, Pacific Islander, other races not otherwise specified, and multiple races recorded

[‡] Not mutually exclusive. Diagnosis based on clinical diagnosis and detection of S. pneumoniae rom a normally sterile site.

[§] Defined as chronic medical conditions (chronic heart, lung, and liver disease, diabetes mellitus, cerebrospinal fluid leaks, cochlear implants, alcoholism, cigarette smoking) for which 23-valent pneumococcal polysaccharide vaccine (PPSV23) alone is recommended

[‖] Defined as other immunosuppressive conditions besides HIV (sickle cell disease, asplenia, congenital or acquired immunodeficiency including HIV, organ transplantation, dialysis, and malignancy) for which PCV13 is recommended in series with PPSV23

Table 2.

Invasive pneumococcal disease (IPD) incidence among adults ≥19 years with or without HIV diagnosis by age and serotype group, 2008–2018

	Incidence among adults diagnosed with HIV Cases/100,000 persons						Incidence among adults diagnosed without HIV Cases/100,000 persons					
	2008–2009 (a)	2011–2012 (b)	% change (95%CI) (b) – (a)		2017–2018 (c)	% change (95%CI) (c) – (a)	2008–2009 (a)	2011–2012 (b)	% change (95%CI) (b) – (a)		2017–2018 (c)	% change (95%CI) (c) – (a)
≥19 year olds(All)												
All IPD	306.7	222.8	−27.4%	(−36.0, −17.7)	183.0	−40.3%	(−47.7, −32.3)	15.2	11.8	−22.6%	(−25.5, −19.6)	10.9	−28.2%	(−30.9, −25.5)
PCV13 * IPD	143.9	80.0	−44.4%	(−54.6, −32.5)	39.6	−72.5%	(−78.8, −65.6)	8.3	4.8	−42.2%	(−45.4, −38.9)	3.1	−62.2%	(−64.5, −59.8)
PPSV23-unique † IPD	73.9	75.4	2.6%	(−19.2, 29.6)	79.2	7.5%	(−14.6, 35.2)	4.0	4.2	5.3%	(−1.7, 12.7)	4.5	12.6%	(5.2, 20.0)
PCV15-unique ‡	22.8	20.3	−10.8%	(−43.9, 38.2)	20.3	−10.8%	(−42.0, 35.9)	1.6	1.7	8.1%	(−3.1, 20.4)	1.5	−6.9%	(−16.6, 3.7)
PCV20-unique §	27.8	34.6	24.5%	(−13.6, 81.0)	31.2	12.4	(−20.8, 62.6)	1.6	1.7	3.5%	(−7.2, 15.3)	1.8	11.7%	(0.7, 23.7)
NVT IPD	90.0	66.9	−24.9%	(−41.1, −6.4)	64.2	−28.0%	(−43.3, −10.5)	2.9	2.8	−5.0%	(−12.6, 3.1)	3.3	12.1%	(4.0, 21.3)
19–64 year olds														
All IPD	308.6	226.6	−26.6%	(−35.4, −16.7)	191.9	−37.8%	(−45.6, −29.2)	10.8	8.0	−26.4%	(−30.0, −22.7)	7.6	−30.1%	(−33.5, −26.5)
PCV13 IPD	142.3	81.7	−42.5%	(−53.2, −30.0)	40.4	−71.7%	(−78.3, −64.1)	6.1	3.3	−45.8%	(−49.6, −41.6)	2.3	−62.2%	(−65.3, −59.1)
PPSV23-unique IPD	74.6	76.4	2.4%	(−19.3, 30.7)	84.3	13.0%	(−10.2, 43.0)	3.0	3.1	3.1%	(−5.5, 12.5)	3.4	15.1%	(5.8, 25.1)
NVT IPD	91.8	68.5	−25.4%	(−41.0, −5.7)	67.2	−26.8%	(−42.2, −7.7)	1.7	1.6	−8.3%	(−15.5, 6.9)	1.8	6.6%	(−4.7, 19.2)
≥65 year olds														
All IPD	248.5	144.0	−42.0%	(−75.0, 31.1)	99.9	−59.8%	(−79.3, −15.2)	39.2	31.3	−20.2%	(−24.8, −15.4)	25.1	−36.0%	(−39.6, −32.2)
PCV13 IPD	177.5	44.3	−75.0%	(−95.8, −25.1)	27.2	−84.7%	(−96.1, −57.4)	20.1	12.3	−38.9%	(−44.1, −33.2)	6.6	−67.1%	(−70.3, −63.7)
PPSV23-unique IPD	53.2	55.4	4.0%	(−82.2, 337.0)	36.3	−31.8%	(−80.8, 181.4)	9.7	10.1	4.8%	(−6.3, 17.2)	9.1	−5.5%	(−15.0, 5.3)

	Incidence among adults diagnosed with HIV Cases/100,000 persons						Incidence among adults diagnosed without HIV Cases/100,000 persons					
	2008–2009 (a)	2011–2012 (b)	% change (95%CI) (b) – (a)		2017–2018 (c)	% change (95%CI) (c) – (a)	2008–2009 (a)	2011–2012 (b)	% change (95%CI) (b) – (a)		2017–2018 (c)	% change (95%CI) (c) – (a)
NVT IPD	17.7	33.2	87.3%	(−100.0, 274.5)	36.3	104.7% (−61.2, 232.6)	9.5	8.9	−6.0%	(−16.3, 5.6)	9.4	−1.1% (−11.0, 10.2)

IPD, invasive pneumococcal disease; NVT, non-vaccine types; PCV13, 13-valent pneumococcal conjugate vaccine; PCV15, 15-valent pneumococcal conjugate vaccine; PCV20, 20-valent pneumococcal conjugate vaccine; PPSV23, 23-valent pneumococcal polysaccharide vaccine

*Serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, and 6C

†Serotypes 2, 8, 9N, 10A, 11A, 12F, 15B/C, 17F, 20, 22F, and 33F

‡Serotypes 22F, 33F

§Serotypes 8, 10A, 11A, 12F, and 15B/C

Table 3.

Incidence rate ratio (IRR) comparing incidence among adults ≥19 years old diagnosed with HIV to those without HIV by age and vaccine-serotype group, 2008–2018

	IRR among adults with and without a diagnosis of HIV					
	2008–2009 IRR (95% CI)		2011–2012 IRR (95% CI)		2017–2018 IRR (95% CI)	
≥19 year olds (All)						
All IPD	20.2	(18.4, 22.0)	18.9	(17.1, 20.8)	16.8	(15.1, 18.5)
PCV13[*] IPD	17.4	(15.1, 19.6)	16.7	(14.1, 19.4)	12.6	(9.9, 15.3)
PPSV23-unique[†] IPD	18.4	(15.1, 21.8)	17.9	(15.0, 20.9)	17.6	(14.9, 20.3)
NVT IPD	30.9	(25.8, 36.1)	24.2	(20.0, 28.7)	19.6	(16.3, 23.0)
19–64 year olds						
All IPD	28.6	(25.9, 31.2)	28.5	(25.7, 31.5)	25.4	(22.7, 28.1)
PCV13[*] IPD	23.3	(20.3, 26.4)	24.7	(20.7, 28.9)	17.5	(13.7, 21.5)
PPSV23-unique[†] IPD	25.1	(20.5, 29.8)	24.9	(20.8, 29.4)	24.6	(20.8, 28.7)
NVT IPD	53.7	(44.4, 63.7)	43.7	(34.5, 50.6)	36.9	(30.3, 43.7)
≥65 year olds						
All IPD	6.3	(3.2, 9.9)	4.6	(2.1, 7.3)	4.0	(2.4, 5.7)
PCV13[*] IPD	8.8	(3.6, 14.7)	3.6	(0.9, 7.5)	4.1	(1.3, 7.7)
PPSV23-unique[†] IPD	5.5	(1.8, 12.9)	5.5	(1.1, 10.8)	4.0	(1.5, 6.9)
NVT IPD	1.9	(1.8, 7.3)	3.7	(0.0, 8.5)	3.9	(1.4, 6.8)

IRR, incidence rate ratio; IPD, invasive pneumococcal disease; NVT, non-vaccine types; PCV13, 13-valent pneumococcal conjugate vaccine; PCV15, 15-valent pneumococcal conjugate vaccine; PCV20, 20-valent pneumococcal conjugate vaccine; PPSV23, 23-valent pneumococcal polysaccharide vaccine

[*] Serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, and 6C

[†] Serotypes 2, 8, 9N, 10A, 11A, 12F, 15B/C, 17F, 20, 22F, and 33F