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INDIRECT EFFECTS OF 10-VALENT PNEUMOCOCCAL CONJUGATE VACCINE AGAINST ADULT PNEUMOCOCCAL PNEUMONIA IN RURAL WESTERN KENYA

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Abstract

Background: Data on pneumococcal conjugate vaccine (PCV) indirect effects in low-income countries with high HIV burden are limited. We examined adult pneumococcal pneumonia incidence before and after 10-valent PCV introduction in Kenya in 2011.

Methods: From 1/1/2008 to 12/31/2016, we conducted surveillance for acute respiratory infection (ARI) among ~12,000 adults (≥18 years) in western Kenya, where HIV prevalence ~17%. ARI cases (cough or difficulty breathing or chest pain, plus temperature ≥38.0°C or oxygen saturation <90%) presenting to a clinic underwent blood culture and pneumococcal urine antigen testing (UAT). We calculated ARI incidence and adjusted for healthcare seeking using data from household visits. The proportion of ARI cases with pneumococcus detected among those with complete testing (blood culture and UAT) was multiplied by adjusted ARI incidence to estimate pneumococcal pneumonia incidence.

Results: Pre-PCV (2008–2010), crude and adjusted ARI incidence were 3.14 and 5.30/100 person-years-observation (pyo), respectively. Among ARI cases, 39.0% (340/872) had both blood culture and UAT; 21.2% (72/340) had pneumococcus detected, yielding baseline pneumococcal pneumonia incidence of 1.12/100 pyo (95% confidence interval [CI] 1.0–1.3). In each post-PCV year (2012–2016), pneumococcal pneumonia incidence was significantly lower than baseline; with incidence rate ratios (IRR) of 0.53 (95%CI 0.31–0.61) in 2012 and 0.13 (95%CI 0.09–0.17) in 2016. Similar declines were observed in HIV-infected (IRR 0.13, 95%CI 0.08–0.22), and HIV-uninfected (IRR 0.10, 95%CI 0.05–0.20).

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Conclusions: Adult pneumococcal pneumonia declined in western Kenya following 10-valent PCV introduction, likely reflecting vaccine indirect effects. Evidence of herd protection is critical for guiding PCV policy decisions in resource-constrained areas.

Summary of article's main point:

Data on pneumococcal conjugate vaccine (PCV) indirect effects on adult pneumococcal pneumonia in Africa are very limited. In rural western Kenya, following PCV introduction, the incidence of adult pneumococcal decreased by 47–94%.

Keywords

Pneumococcal vaccines; herd immunity; adult; pneumonia; Kenya

Introduction

Streptococcus pneumoniae is a leading vaccine-preventable bacterial etiology of pneumonia, which causes significant morbidity and mortality in children, the elderly and immuno-compromised individuals [1, 2]. However in resource-poor settings, pneumococcal pneumonia is difficult to measure because of poor diagnostics and sub-optimal surveillance methods. A systematic review and meta-analysis of pneumococcal pneumonia burden among adults estimated that 27.3% of community-acquired pneumonia episodes are caused by *S. pneumoniae*; yet that study included data primarily from hospitalized patients in high-income countries [3]. In sub-Saharan Africa, the burden of invasive pneumococcal disease (IPD) among adults is high and is compounded by high prevalence of human immune-deficiency virus (HIV) [4–7]. Data on the incidence of bacteremic and non-bacteremic adult pneumococcal pneumonia are limited.

Pneumococcal conjugate vaccines (PCV) are highly effective in reducing the burden of pneumococcal disease among vaccinated children [8–10], and, importantly, protect against nasopharyngeal colonization with serotypes included in the vaccine [11, 12]. The resulting decrease in transmission of vaccine serotypes has led to robust indirect (or herd) effects in high-income settings, with reductions in pneumococcal disease among non-vaccinated adults [13]. However, several factors may affect the development of herd effects in low-/middle-income countries, including higher baseline prevalence of pneumococcal carriage, crowding, suboptimal immune response among malnourished or HIV-infected vaccinated children, and different dosing schedules. Recent data from resource-poor countries provide evidence of PCV indirect protection against vaccine-type nasopharyngeal carriage [14] and vaccine-type IPD [15, 16]. Yet data on indirect effects against pneumococcal pneumonia – the cause of most pneumococcal deaths – are limited.

With support of the GAVI Alliance, Kenya introduced 10-valent pneumococcal conjugate vaccine (PCV10) in January 2011, using a 3-dose schedule (6, 10, 14 weeks, no booster). A catch-up campaign was implemented in select areas. We examined the indirect effects of PCV10 on adult pneumococcal pneumonia in an area in rural western Kenya with a catch-up program.

Methods

Study site

Since 2006, the Kenya Medical Research Institute (KEMRI) in collaboration with the United States Centers for Disease Control and Prevention (CDC) has implemented Population Based Infectious Disease Surveillance (PBIDS) among ~25,000 people (~12,000 aged ≥18 years) in Asembo, in rural western Kenya. The study site and population have been described previously [17, 18]. The site is nested within a larger Health and Demographic Surveillance System (HDSS) [19] whose population is enumerated though routine census conducted 2–3 times per year. The area is malaria endemic, with HIV prevalence ~17% among persons ≥18 years in 2008 [20]. A PCV10 catch-up campaign (2 doses for children aged 12–59 months) was conducted in Asembo from April to July 2011.

Household surveillance

From January 2008 to April 2015, PBIDS participants were interviewed every two weeks in their homes by study staff about recent illness and health-care seeking [18]. From May 2015, the frequency of home interviews was reduced to monthly in 10 of 33 villages [21] and biannually in the other 23; data collection tools and methods remained unchanged. Temperature was measured for participants reporting symptoms of illness. For adults, acute respiratory infection (ARI) at home was defined as report of cough or difficulty breathing or chest pain plus subjective or documented fever in the past 14 days. Vaccination data for children <5 years were obtained from cards or verbal reports during HDSS census rounds and/or PBIDS household interviews.

Facility-based surveillance

PBIDS participants received free care for acute illnesses at St. Elizabeth Lwak Mission Hospital (LMH), a centrally located facility with a large outpatient clinic and a small in-patient ward [4, 18]. Patients arriving at LMH were screened by trained study staff (initially medical clerks, and starting in July 2009 by nurses), and examined by clinical officers. For adult PBIDS participants, ARI was defined as cough or difficulty breathing or chest pain, plus a temperature ≥38.°C or oxygen saturation <90%. Specimens obtained from ARI cases included: blood for culture (7–10 mls for adults, inoculated into commercially available bottles [BACTEC™, Beckton Dickinson, Belgium]), nasopharyngeal and oropharyngeal (NP/OP) swabs for influenza testing, and urine for pneumococcal antigen testing (UAT). Blood for malaria testing was also collected from febrile patients.

Laboratory testing

Specimens were transported twice daily to KEMRI laboratories ~1 hour away from LMH. Blood culture bottles were placed in an automated incubator for up to five days; alarm-positive samples were sub-cultured on plates for 18–24 hours. Pneumococcus was identified by colony morphology, opthochin susceptibility and bile solubility tests [4]. Serotyping of isolates was done primarily at the CDC Streptococcal Laboratory in Atlanta, by Quellung reaction with serotype-specific antiserum [22] or sequential multiplex polymerase chain reaction (PCR) [23]; since 2016, isolates have been serotyped at KEMRI using multiplex

PCR. Pneumococcal UAT was performed using BinaxNOW® Kit (Inverness Medical, Scarborough, Maine, USA) according to manufacturer's instructions. NP/OP swabs were tested for influenza virus using reverse-transcriptase PCR [17]. Malaria diagnosis was done in the LMH laboratory by microscopy of Giemsa-stained blood slides.

HIV status data

In 2008–2009, all PBIDS participants ≥13 years were offered home-based HIV counseling and testing; 78% of eligible adults agreed to be tested [20, 24]. Subsequently, HIV testing targeted new adult enrollees and previously HIV-uninfected residents who requested testing. At LMH, HIV testing was offered to patients based on clinicians' assessment and national HIV testing guidelines [25].

Data analysis

We used data from participants aged ≥18 years, who presented to LMH from January 1, 2008 to December 31, 2016. Pneumococcal pneumonia cases were defined as ARI cases for whom a blood culture and/or UAT was performed and *S. pneumoniae* detected in either sample. We calculated annual crude ARI incidence rates using all ARI cases seen at LMH (outpatient and inpatient) and person-time denominator from the HDSS [19]. We adjusted annual rates to account for healthcare seeking by dividing by the proportion of all medically attended ARI cases reported through the household surveillance that sought care at facilities other than LMH for each year. We then estimated the proportion of ARI cases with pneumococcal etiology for each study year based on the subset of ARI cases with complete testing (both blood culture and UAT), and multiplied that by the adjusted ARI incidence to estimate pneumococcal pneumonia incidence [17].

We compared pneumococcal pneumonia incidence in each of the post-PCV10 introduction years (2012–2016) to the baseline period (2008–2010) using incidence rate ratios (IRR) with 95% confidence intervals (CI) calculated using exact Fisher's method. The year of vaccine introduction (2011) was considered a transition year and was not included in incidence comparisons.

Additionally, we stratified incidence and IRRs by HIV status. Participants with only one HIV test result during the study period were assumed to have that status throughout the study period. This assumption is supported by the low estimated annual HIV incidence in the study area [26]. Those with an initial negative result who later tested positive were assumed to be HIV-uninfected until the date of the last negative result, and HIV-infected from that date on. Those with no HIV test results were excluded from the HIV-stratified analysis.

We calculated annual PCV10 coverage (≥1 dose) among PBIDS participants aged 6 weeks to 59 months based on age and vaccination status as of December 31 of each year.

Ethical considerations

The protocol was approved by the institutional review boards of KEMRI and CDC. For household surveillance, compound heads provided written consent for the participation of

their compound members. At LMH, individual participants provided consent for sample collection.

Results

Among 53,229 sick visits seen at LMH, 1,995 (3.7%) met ARI criteria. Blood or urine specimens were obtained from 1,322 (66.3%) ARI case-patients, of whom 172 (13.0%) had pneumococcal pneumonia (Figure 1). The median age of adults with pneumococcal pneumonia was 36 years and 39.5% were male (Table 1). *S. pneumoniae* was isolated from the blood of 57 (33.1%) cases; among 52 (92.1%) with serotype data, 28 (53.8%) were PCV10 serotypes. Among those with known HIV status, 75/138 (54.3%) were HIV-infected; among those with known HIV status and pneumococcus isolated from blood, 30/35 (85.7%) were HIV-infected. Hospitalization was required for 40.1% of pneumococcal pneumonia case-patients, and 5 (2.9%) died from any cause within 30 days of the diagnosis.

ARI cases with incomplete pneumococcal testing (i.e. blood only, or urine only, or no specimen collected) were more frequently admitted than those with complete testing (26.9% [284/1056] vs. 19.0% [178/939], p-value <0.001) and had higher mortality within 30 days of diagnosis (5.3% [56/1056] vs. 1.9% [18/939], p-value <0.001). Overall, 7.7% (153/1995) of ARI case-patients reported having taken an antibiotic for the current illness before visiting LMH, including 8.0% (69/939) of those with incomplete testing and 7.3% (84/1056) of those complete testing.

From 2008 to 2010, 872 ARI cases were identified at LMH, yielding a baseline crude ARI incidence of 3.14 (95% CI 2.93–3.35) and adjusted incidence of 5.30 (95% CI 5.03–5.58) per 100 person-years-observation (pyo) (Table 2). Among 340 (39.0%) ARI cases with complete testing, 72 (21.2%) had pneumococci detected. Multiplying this percentage by the adjusted ARI incidence, the estimated baseline pneumococcal pneumonia incidence was 1.12 (95% CI 1.00–1.25)/100 pyo.

By 2012, pneumococcal pneumonia incidence had fallen to 0.60/100 pyo (IRR 0.53, 95% CI 0.31–0.61), and further declined to 0.07 in 2014 (IRR 0.06, 95% CI 0.02–0.10) (Table 2). The incidence increased in 2015 (0.33/100 pyo), then decreased in 2016 (0.14/100 pyo). Throughout the post-PCV period, the annual incidence was significantly lower than baseline.

Among HIV-infected persons, baseline incidence of pneumococcal pneumonia was 2.82/100 pyo, declining to 0.41/100 pyo in 2014, and declining further to 0.37/100 pyo in 2016 (IRR 0.13, 95% CI 0.08–0.22) (Table 2). Among HIV-uninfected persons, baseline incidence was 0.59/100 pyo, which fell to zero cases in 2014. In 2015, the incidence among HIV-uninfected increased to 0.26/100 pyo, and declined to 0.06/100 pyo in 2016 (IRR 0.10, 95% CI 0.05–0.20). PCV10 coverage (≥1 dose) among children increased from 64% in 2011 to 93% in 2016, as incidence of pneumococcal pneumonia among HIV-infected and –uninfected declined (Figure 2). Among cases with pneumococcus isolated from blood, the proportion with a PCV10 serotype in the baseline period ranged from 50–64% (Figure 3 and Table 3); there was no clear trend in that proportion post-introduction due to diminished case counts of both PCV10 and non-PCV10 serotypes.

Both ARI incidence and the detection of pneumococcal etiology declined over time from the baseline period. The frequency of prior antibiotic use among all ARI cases presenting to LMH was not significantly different between baseline (61/869, 7.0%) and the post-PCV10 period (64/849, 7.5%, p=0.711). Detection of influenza A virus also did not change significantly (70/354, 19.8% baseline; 115/472, 24.4% post-PCV; p=0.129)

Discussion

The incidence of adult pneumococcal pneumonia declined substantially within a year following PCV10 introduction for children in a rural area of Kenya with a high HIV prevalence. While there was year-to-year variability in pre-PCV10 incidence, every post-PCV10 year had a significantly lower burden compared with pre-vaccine baseline. We observed a decrease in both the incidence of medically attended ARI among adults and in the proportion of ARI attributable to *S. pneumoniae* among those tested, resulting in a reduction of 47 to 94% in adult pneumococcal pneumonia during the study period. Although this decline is greater in magnitude than what might be expected, these data contribute to a growing evidence base of the indirect effects of PCV in low-/middle-income countries, and suggest a substantial impact on pneumococcal pneumonia in adults in a high-burden setting.

The incidence of pneumococcal pneumonia fell in both HIV-infected and –uninfected adults following PCV10 introduction. Some of the decline among HIV-infected persons was likely attributable to improvements in HIV care in the area over time. The reduction in non-PCV10 serotypes among bacteremic cases, who were disproportionately HIV-infected, is probably a reflection of better HIV management. Following rapid scale-up of antiretroviral therapy in Malawi, there was a decline in IPD in both adults and children [27]. In South Africa, reductions of 51% in pneumococcal bacteremia were observed in children <18 years after five years of initiation of highly active antiretroviral therapy [28]. In our study area, access to HIV care and treatment has expanded. Previously, antiretroviral initiation was recommended for persons with CD4 counts <250 cells/mm^3; in 2010, the cut-off was revised to <350 cells/mm^3, expanding the numbers of HIV-infected people eligible for treatment [29]. Furthermore, the proportion of HIV-infected adults eligible for antiretroviral treatment who received it increased from 37% in 2008 to 64% in 2014 [25, 29]. Although improved access to HIV care likely contributed to declines in adult pneumococcal pneumonia in Asembo, we observed a dramatic drop among HIV-uninfected adults as well, with no cases identified in 2014 and a 90% reduction in 2016 compared to baseline. Thus, expanded HIV treatment alone cannot fully explain the fall in adult pneumococcal pneumonia. Both HIV treatment scale up and PCV introduction in routine infant immunization programs are important interventions for preventing pneumococcal pneumonia in HIV-infected adults, who suffer a disproportionate burden of pneumococcal disease.

The PCV10 catch-up campaign targeting children aged 1 to 4 years residing in Asembo may have accelerated the decline in adult pneumococcal pneumonia. During the catch-up, 81% of 7,087 children aged 1 to 4 years in Asembo received ≥1dose of PCV10 (KEMRI, unpublished data). High vaccine uptake may have contributed to the rapid establishment of herd protection in unvaccinated persons. In Kilifi County, another Kenyan site where PCV10 catch-up was implemented for children <5 years (coverage 69% with ≥1 dose),

nasopharyngeal carriage of PCV10 serotypes in older children and adults declined by 66% within 2 years [14]. Subsequent modeling work based on the Kilifi data has estimated that catch-up campaigns for children <1, <2, and <5 years accelerate both direct and indirect protection against pneumococcal disease and are a more efficient use of PCV doses in terms of cases averted over a 10 year period [30]. Low-/middle-income countries infrequently use catch-up campaigns for PCV introduction, representing an important missed opportunity to prevent both pediatric and adult pneumococcal disease.

The indirect protection conferred to adults by vaccinating infants with PCV greatly improves cost-effectiveness estimates of the vaccine [31]. A cost-effectiveness analysis using population-based surveillance data from the U.S. after 7-valent PCV introduction found that incorporating herd protection into the model reduced the vaccine cost per life saved from $110,000 USD to $7,000 USD [32]. Given the high burden of adult pneumococcal disease in sub-Saharan African countries, particularly those with a high HIV prevalence, it is likely that consideration of herd effects would favorably affect PCV cost-effectiveness estimates. PCV is the most expensive of routine infant immunizations, requiring a substantial investment to introduce and sustain its use. The Kenyan government introduced PCV10 with support from the GAVI Alliance. In coming years, as Kenya and other countries graduate from GAVI support [33], cost-effectiveness of vaccines will become increasingly important. Decisions about sustained PCV use in Kenya and other similar settings should consider indirect effects on adult pneumococcal pneumonia.

The decline observed in adult pneumococcal pneumonia was more rapid and larger than might be expected for PCV indirect effects. A meta-analysis of PCV indirect effects reported a mean time of 2–3 years for achieving a 50% reduction in vaccine-type IPD in adults, and 8–9 years to reach a 90% reduction [34]. Yet we found a similar decrease in a non-serotype specific outcome in a shorter time period. A review of PCV indirect protection noted that the magnitude of decline varied greatly, with larger effects in settings with high baseline disease rates and high PCV coverage [13]. Thus, in our study setting, where the burden of pneumococcal disease was high [4] and vaccine coverage increased rapidly, the indirect effects could be quite robust. Nonetheless, we must consider additional factors beyond PCV10 which might have contributed to the reduction in pneumococcal pneumonia and ARI. As noted above, improved HIV care likely played an important role. Other changes, such as improvements in healthcare access, socioeconomic or nutritional status, and greater availability of antibiotics in the community might have led to some reduction in disease over time. A change in surveillance methods in mid-2009, having nurses conduct initial screening of patients rather than clerks, may have led to a stricter application of the case definition, thus resulting in an apparent decline in ARI starting during the baseline period. However, the case definition required objective criteria (measured fever or hypoxemia), therefore any impact of this change would likely have been small.

Our study had additional limitations. We had only three years of pre-PCV10 data. Within that baseline period, the incidence of adult pneumococcal pneumonia was variable, reflecting the tendency of pneumococcal disease incidence and respiratory infections in general to vary over time and illustrating the challenge of measuring PCV impact using observational data from a single site with a relatively small population. We also lacked

etiologic testing results for ARI case-patients seeking care at non-surveillance facilities. We adjusted ARI incidence estimates to account for those cases, but the results may have been biased if ARI case-patients going to other facilities had a different likelihood of having a pneumococcal etiology. The ARI case definition we used is not a standard pneumonia definition, and may include persons with less severe illness. Nonetheless, adult ARI cases with pneumococcus detected by blood culture or UAT are likely true pneumococcal pneumonia cases [35], therefore our estimates of pneumococcal pneumonia incidence (based on proportion of ARI cases testing positive for pneumococcus) are unlikely to be biased by an overly sensitive ARI case definition. Lastly, we assumed that HIV status remained unchanged for individuals with a single documented test, which may have resulted in some misclassification of HIV status in our analysis.

Despite these limitations, our study provides data that may be used to inform vaccine policy. The findings suggest that adult pneumococcal pneumonia in a high-burden setting can be dramatically reduced through routine use of PCV10 in infants. These results complement data from other African countries demonstrating PCV indirect effects on pneumococcal carriage and IPD in adults. Ongoing surveillance and data from other settings are needed to better understand the sustained impact of infant PCV use on adult pneumococcal pneumonia. Decisions about PCV introduction and sustained use in low-/middle-income countries should consider indirect effects.

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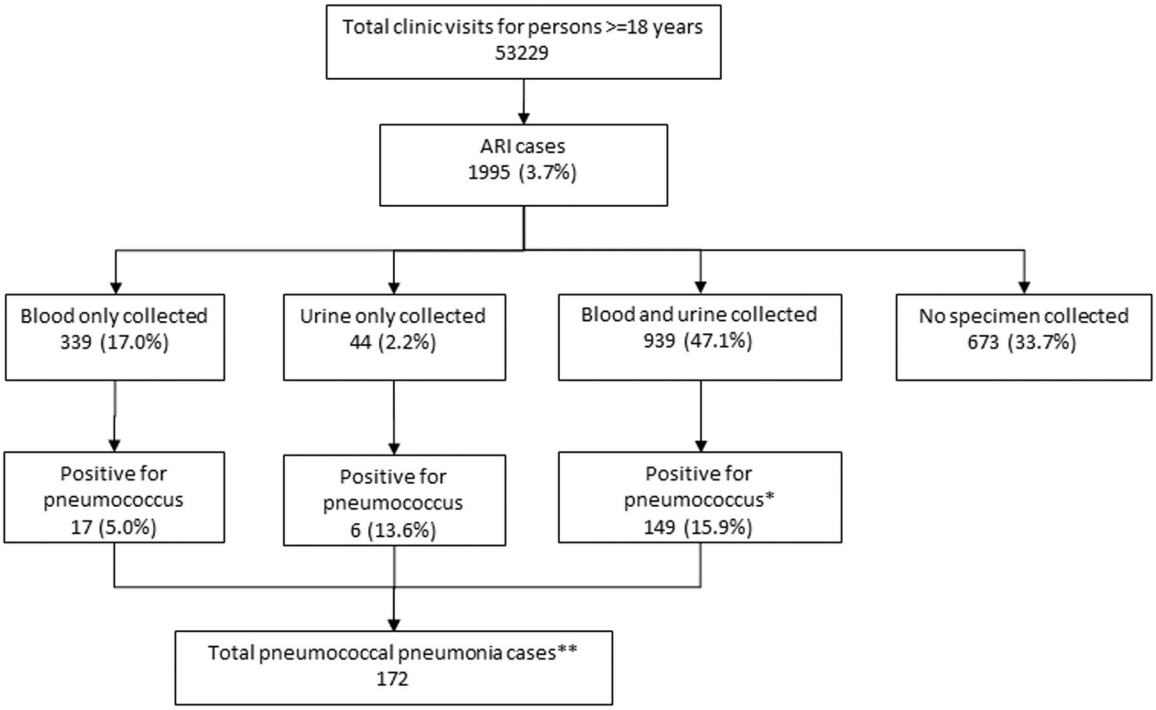

Figure 1.

Flow diagram for sample collection and pneumococcal pneumonia cases among patients with acute respiratory illness visiting Lwak Mission Hospital in rural western Kenya, 2008 – 2016 *Percent positive among ARI cases with both blood and urine tested used for incidence calculations. In this group, 21 (14.1%) had pneumococcus detected in both blood and urine, 19 (12.8%) detected in blood only, and 109 (73.1%) in urine only.

**In this group 57(33.1%) cases had pneumococcus isolated from blood.

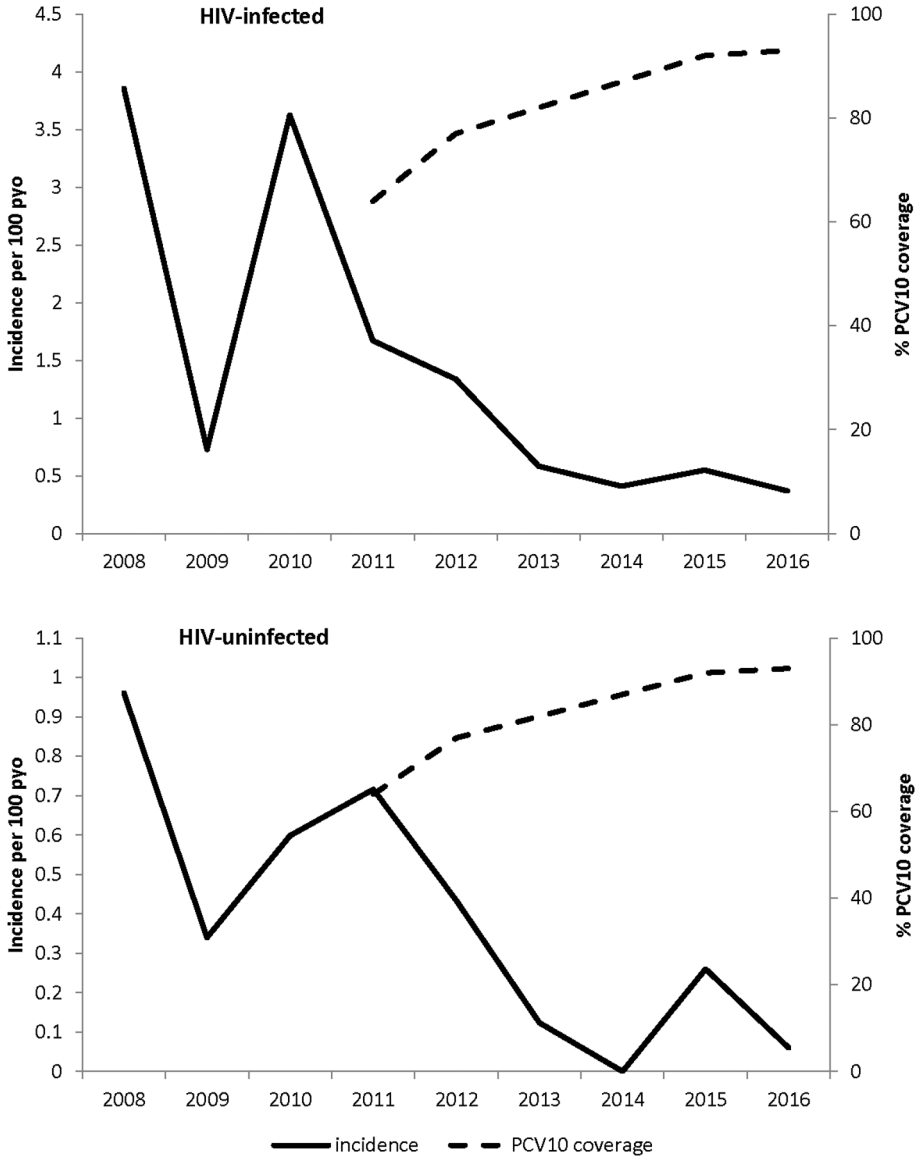

Figure 2.

Trends in pneumococcal pneumonia incidence in HIV-infected and –uninfected adults in Asembo, Kenya, 2008 – 2016, and coverage of at least 1 PCV10 dose among children aged 6 weeks to 59 months, 2011 – 2016

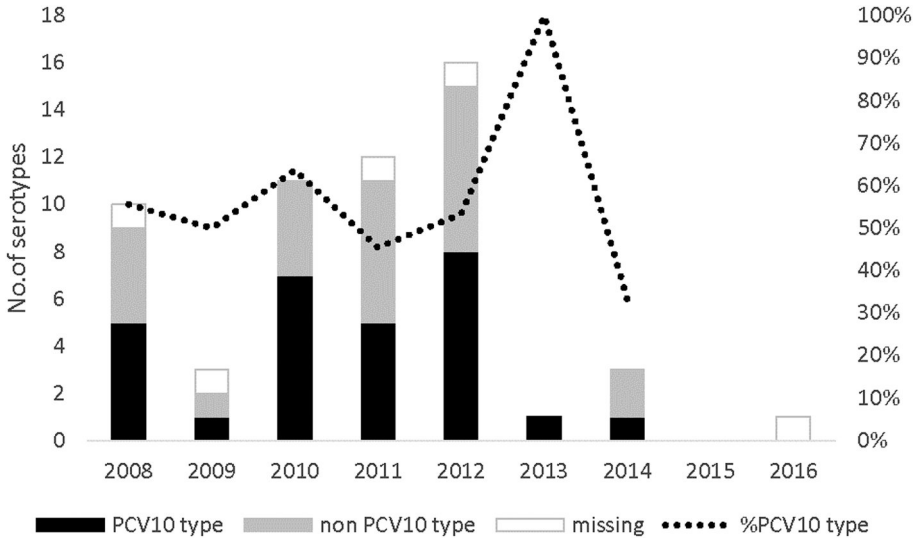

Figure 3.

Trends in PCV10 and non-PCV10 serotypes from blood culture isolates from pneumococcal pneumonia cases (n=57) in Asembo, Kenya, 2008 – 2016

Table 1:

Characteristics of patients with ARI with pneumococcus visiting Lwak Mission Hospital, 2008 – 2016

Patient characteristic	N=172 n (%)
Median age, years	36
Interquartile range, years	29 – 49
Gender	
Males	68 (39.5)
Pneumococcus isolated from blood	57 (33.1)
PCV10 serotype[a]	28/52 (53.8)
HIV status	
Known	138 (80.2)
HIV-infected	75/138 (54.3)
HIV-infected among cases with pneumococcus isolated from blood	30/35 (85.7)
Prior care-seeking[b]	75/141 (53.2)
Signs and symptoms	
Fever	
History	166 (96.5)
Documented ≥38.0	157 (91.3)
Cough	155 (90.1)
Chills	102 (59.3)
Chest pain	99 (57.6)
Difficult breathing	60 (34.9)
Crackles	46 (26.4)
O2 saturation <90%	25 (14.5)
Wheezing	17 (9.9)
Lethargic	10 (5.8)
Hospitalized	69 (40.1)
Died while hospitalized	1 (1.4)
Mortality within 30 days of diagnosis	5 (2.9)
Co-infected with	
Influenza virus[c]	38/153 (24.8)
Malaria[d]	12/154 (7.8)

[a] Serotype not available for 5 isolates.

[b] Care-seeking data not available for January 2008 – June 2009.

[c] Denominator is pneumococcal pneumonia cases with nasopharyngeal and oropharyngeal swab collected and tested.

[d] Denominator is pneumococcal pneumonia cases with malaria test result.

Table 2:

Population based Incidence of pneumococcal pneumonia in HIV-infected and -uninfected adults in Lwak in rural western Kenya, 2008 – 2014

Year	ARI cases	Person years	Crude ARI Incidence (per 100 pyo)	Adjusted ARI Incidence (per 100 pyo)	ARI cases with both blood and urine tested N(%)	N(%) positive for *S. pneumoniae* among tested cases	Pneumococcal pneumonia incidence (per 100 pyo)	Incidence rate ratio (95% CI)
Overall								
Baseline[a]	872	27814.7	3.14 (2.93 – 3.35)	5.30 (5.03 – 5.58)	340 (39.0)	72 (21.2)	1.12 (1.00 – 1.25)	Ref.
2012	304	11349.6	2.68 (2.39 – 3.00)	4.05 (3.69 – 4.44)	170 (55.9)	25 (14.7)	0.60 (0.47 – 0.76)	**0.53 (0.31 – 0.61)**
2013	175	12068.9	1.45 (1.24 – 1.68)	2.69 (2.41 – 3.00)	81 (46.3)	6 (7.4)	0.20 (0.13 – 0.30)	**0.20 (0.08 – 0.23)**
2014	135	12411.1	1.09 (0.91 – 1.29)	2.01 (1.76 – 2.27)	91 (67.4)	3 (3.3)	0.07 (0.03 – 0.13)	**0.06 (0.02 – 0.10)**
2015	122	12772.12	0.96 (0.79 – 1.14)	1.95 (1.71 – 2.21)	66 (54.1)	11 (16.7)	0.33 (0.24 – 0.44)	**0.29 (0.23 – 0.37)**
2016	111	13483.51	0.82 (0.68 – 0.99)	1.57 (1.37 – 1.80)	58 (52.3)	5 (8.6)	0.14 (0.08 – 0.22)	**0.13 (0.09 – 0.17)**
HIV-infected								
Baseline[a]	297	4237.3	7.01 (6.23 – 7.85)	10.16 (9.23 – 11.18)	115 (38.7)	32 (27.8)	2.82 (2.33 – 3.36)	Ref.
2012	84	1558.8	5.39 (4.30 – 6.67)	7.28 (5.97 – 8.72)	49 (58.3)	9 (18.4)	1.34 (0.83 – 2.06)	**0.48 (0.24 – 0.76)**
2013	67	1567.5	4.27 (3.31 – 5.43)	6.42 (5.25 – 7.83)	33 (49.3)	3 (9.1)	0.59 (0.26 – 1.09)	**0.21 (0.07 – 0.39)**
2014	55	1557.0	3.53 (2.66 – 4.60)	5.18 (4.13 – 6.47)	38 (69.1)	3 (7.9)	0.41 (0.14 – 0.84)	**0.15 (0.05 – 0.32)**
2015	28	1558.42	1.80 (1.19 – 2.60)	2.95 (2.16 – 3.94)	16 (57.1)	3 (18.8)	0.55 (0.26 – 1.10)	**0.20 (0.13 – 0.30)**
2016	26	1573.31	1.65 (1.08 – 2.42)	2.01 (1.39 – 2.87)	11 (42.3)	2 (18.2)	0.37 (0.14 – 0.83)	**0.13 (0.08 – 0.22)**
HIV-uninfected								
Baseline[a]	304	14802.3	2.05 (1.83 – 2.30)	3.51 (3.22 – 3.83)	119 (39.1)	20 (16.8)	0.59 (0.47 – 0.72)	Ref.
2012	136	5958.5	2.28 (1.91 – 2.70)	3.51 (3.05 – 4.02)	73 (53.7)	9 (12.3)	0.43 (0.29 – 0.64)	0.73 (0.33 – 1.09)
2013	70	6243.5	1.12 (0.87 – 1.42)	2.16 (1.81 – 2.56)	35 (50.0)	2 (5.7)	0.12 (0.05 – 0.23)	**0.20 (0.06 – 0.40)**
2014	47	6460.6	0.73 (0.53 – 0.97)	1.43 (1.15 – 1.75)	33 (70.2)	0 (0.0)	0	**0**
2015	58	6724.35	0.86 (0.65 – 1.12)	1.87 (1.56 – 2.23)	29 (50.0)	4 (13.8)	0.26 (0.15 – 0.40)	**0.44 (0.30 – 0.64)**
2016	47	7103.89	0.66 (0.49 – 0.88)	1.41 (1.15 – 1.71)	22 (46.8)	1 (4.5)	0.06 (0.02 – 0.14)	**0.10 (0.05 – 0.20)**

[a]Baseline period was 2008 – 2010. 2011 was vaccine introduction year

Table 3:

Serotypes by year from blood culture isolates from pneumococcal pneumonia cases (n=57) in Asembo, Kenya, 2008 – 2016

	Year									
	2008	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**Total**
PCV10 serotypes										
001	0	0	1	1	5	0	0	0	0	7
004	4	0	2	1	0	0	0	0	0	7
014	0	0	1	2	2	1	0	0	0	6
06B	1	0	1	0	0	0	0	0	0	2
19F	0	0	1	0	0	0	1	0	0	2
23F	0	1	1	0	0	0	0	0	0	2
005	0	0	0	1	0	0	0	0	0	1
07F	0	0	0	0	1	0	0	0	0	1
Total	5	1	7	5	8	1	1	0	0	28
nonPCV10 serotypes										
003	0	0	3	1	0	0	0	0	0	4
15A	3	1	0	0	0	0	0	0	0	4
35B	0	0	0	0	2	0	1	0	0	3
09L	0	0	0	0	0	0	1	0	0	1
013	1	0	0	1	0	0	0	0	0	2
038	0	0	0	1	1	0	0	0	0	2
12A	0	0	0	0	2	0	0	0	0	2
12F	0	0	0	1	1	0	0	0	0	2
034	0	0	0	1	0	0	0	0	0	1
10A	0	0	1	0	0	0	0	0	0	1
22F	0	0	0	0	1	0	0	0	0	1
33C	0	0	0	1	0	0	0	0	0	1
Total	4	1	4	6	7	0	2	0	0	24
Missing	1	1	0	1	1	0	0	0	1	5