Global Pneumococcal Disease and Policies for Control

Oral Poster Abstracts

ISPPD-0508
Global Pneumococcal Disease and Policies for Control

GLOBAL SEROTYPE DISTRIBUTION OF INVASIVE PNEUMOCOCCAL DISEASE (IPD) IN OLDER CHILDREN AND ADULTS: THE AGEDD STUDY

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Background and Aims: Global serotype distribution of IPD in children ≥5 years old and adults pre-pneumococcal conjugate vaccine (PCV) introduction has not been described. We aimed to estimate the proportion due to top serotypes by geographic region.
Methods: A systematic literature review identified studies reporting ≥20 IPD cases with serotype/serogroup information. We estimated the proportion of IPD due to 20 serotypes: PCV13-type, 22F, 32F, and any others in the top 13 of each geographic region (8, 9N, 10A, 12F, 16F, 20D). All other serotypes were grouped. Random-effects meta-analysis was used to estimate the average serotype proportion, normalizing to 100 percent.
Results: Analyses included 72,954 isolates (>3500 in each region) from children ≥5 years and adults from 77 studies in 53 countries. 70% of disease was accounted for by 9 serotypes in Africa, 12 in North America, 12 in Europe, 13 in Oceania, 14 in Latin America and Caribbean and 16 in Asia. Serotype 1 or 14 was the most common in all regions. Six serotypes (3, 6B, 7F, 14, 19F, 23F) were among the top 13 in all regions. Eleven serotypes (1, 3, 4, 5, 6B, 8, 9V, 14, 19A, 19F, 23F) covered the top 5 in all regions. Vaccine serotypes accounted for >50% of IPD: regional PCV10 plus 6A coverage range=52-62%, PCV13=60-75%, PCV15=64-77%, and 19/23 serotypes in polysaccharide vaccine (PPV23)=72-87%.
Conclusion: A limited set of serotypes are common in older children and adults in all regions. Serotypes in existing vaccines included >50% of IPD. PCV13 and PPV23 add approximately 10% and 24%, respectively.

No conflict of interest

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Global Pneumococcal Disease and Policies for Control

MENINGOENCEPHALITIS: STREPTOCOCCUS PNEUMONIAE IS AMONG THE MAJOR CAUSES IN ADULTS IN RURAL KENYA

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Background and Aims: We aimed to identify the aetiology of meningoencephalitis in adult patients at Kilifi District Hospital (KDH) and to describe their clinical presentations and outcomes.
Methods: Adult patients admitted to KDH, January 2007 - October 2012, with any two of: temperature >37.5°C, meningism, altered mental status; were suspected meningoencephalitis cases, eligible for a lumbar puncture (LP). Patients with cerebrospinal fluid (CSF) collected and stored during this period were included. Real-time multiplex PCR (Fast-Track Diagnostics, Luxembourg) targeting 21 pathogens and a cryptococcal antigen lateral-flow assay (Immuno-Mycologics, USA) were performed retrospectively and analyzed with microscopy, culture, antigen tests and clinical data from admission.
Results: Adults admitted to the wards were 18,527; 665 (3.6%) met the LP criteria, performed in 554 (83%) patients. CSF samples for 357 (64%) clinical episodes were sufficient for storage. Of 268 (75%) episodes tested, 11 from 2007 and 257 from 2010 to 2012, 161 (60%) were abnormal and consistent with suspected meningoencephalitis. A pathogen was identified in 50 (31%) abnormal episodes; 22/159 (14%) with *Cryptococcus neoformans*, 11/160 (7%) with *Streptococcus pneumoniae*. HIV prevalence recorded in cryptococcal or pneumococcal meningitis patients was 20/21 (95%) and 5/10 (50%) respectively and overall at 71% (104/147). Death in hospital occurred in 76/159 (48%) episodes, 7 (64%) with pneumococcal meningitis, 10 (45%) with cryptococcal meningitis.
Conclusion: *S. pneumoniae* is a major cause of morbidity and mortality in adult meningoencephalitis in Kenya, after *C. neoformans*. Pneumococcal conjugate vaccine was introduced in Kenya in 2011 and CSF PCR may enhance the evaluation of impact.

No conflict of interest

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IMPACT OF THIRTEEN-VALENT PNEUMOCOCCAL CONJUGATE VACCINE ON PNEUMOCOCCAL CARRIAGE IN DIFFERENT COUNTRIES - MATHEMATICAL MODELLING STUDY

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Background and Aims: Many developed countries have introduced various pneumococcal conjugate vaccines (PCV) and almost eliminated PCV serotypes from their populations. Many other countries, inspired by this impact, are now considering introduction of PCV into their National Immunisation Programmes. As the carriage prevalence and serotype distributions can vary widely between countries, a different impact of the PCV programme is possible. PCV13's protection against development of invasive disease is high, but protection against carriage is weaker; the degree of protection against acquisition of carriage is little more than 50%, and the duration of this protection is thought to be short. This raises the question of whether such a vaccine will be able to eliminate PCV subtypes from high prevalence populations. This question is addressed using mathematical models.
Materials and Methods: A simple age-structured compartmental model was developed to describe the transmission dynamics of pneumococci in the Gambia, and in England & Wales (E&W). Local pre-PCV carriage data were used to estimate transmission parameters in the model. A simulation model assessed the long-term impact of the PCV13 programmes in these two countries.
Results: Simulation results suggest that all E&W vaccination scenarios have the potential to eliminate PCV13 serotypes from circulation. Conversely, model simulations for the Gambia scenarios produced a reduction in the level of PCV13 serotype carriage prevalence but failed to eliminate PCV13 serotypes.
Conclusion: In developed countries, where carriage is concentrated among young children, PCV13, despite its limited protection against carriage, can eliminate PCV13 serotypes from the population. However, in developing countries with a high carriage prevalence among adults, PCV13 may not be able to eliminate PCV13 serotypes.

No conflict of interest

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UNDERSTANDING THE IMPACT OF PNEUMOCOCCAL CONJUGATE VACCINE IN INDIA: A SYSTEMATIC COMPARISON OF IMPACT ESTIMATES FOR PCV, HIB AND ROTAVIRUS VACCINES

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Background & Aims: The Indian National Technical Advisory Group on Immunization (NTAGI) recommended pneumococcal conjugate vaccine (PCV) introduction in >1 state in 2008, but the recommendation has not yet been implemented. Some stakeholders argued there were insufficient health and economic impact data to support use of PCV in India. Multiple estimates are now available, creating a challenge for advocacy and communication efforts.
Methods: We conducted a review of all published and unpublished national-level modeled estimates of pneumococcus, Haemophilus influenzae type b (Hib), and rotavirus morbidity and mortality, and health and economic impact estimates of these preventive vaccines.
Results: Four national pneumococcal mortality estimates are available–two published estimates for year 2000 (all syndromes) and 2010-2011 (pneumococcal pneumonia only) and two unpublished estimates (2005, 2008—all syndrome). 142,361 pneumococcal deaths were estimated in 2000; 136,100 in 2005; and 79,450 in 2008; but models and assumptions are not consistent across estimates. State-level pneumococcal mortality estimates(year 2005) are available but not yet published. National health or economic impact estimates for PCV in India exist but are unpublished. Impact estimates for Hib (n = 1) and rotavirus vaccines (n = 7) are available but assumptions, disease burden and economic inputs are not consistent with PCV impact models.
Conclusion: Pneumococcal disease burden estimates in India are available for various years; inferences about changes in disease burden over time are not recommended because modeling strategies are not consistent. Generating robust health and economic impact estimates for PCV –at the state and national level using methods that are comparable to other vaccine impact estimates– will support evidence-based decisions for PCV introduction in India.

No conflict of interest

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METHODOLOGICAL ISSUES IN THE ANALYSIS OF 'BEFORE AND AFTER' VACCINE STUDIES

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Background and Aims: Evaluation of vaccine impact using 'before and after' data is complicated by temporal changes in factors which may confound or bias results. We addressed these issues in a study of the impact of pneumococcal conjugate vaccine in The Gambia.
Methods: We analysed incidence of primary end-points in pre- and post-intervention periods and performed a cohort analysis. For the pre- and post- analysis, we defined the start of the intervention period as the date when coverage of ≥2 doses across an age range approached its maximum. Individuals may contribute time in both 'before' and 'after' periods (accounted for by a random effect for subject) to reduce loss of information. We defined potential confounders (e.g. season, malaria) and adjusted for changes in the comparison periods. We identified potential biases, such as changes in case ascertainment or the prevalence of serotypes known to vary markedly over time, and included these variables in stratified and multivariable modelling. End-points unrelated to vaccination (e.g. Gram-negative bacteraemia) were used to indicate potential confounding or bias. We estimated variance using robust methods. Children eligible for vaccination were included in the cohort analysis which may be interpreted as vaccine effectiveness at the individual level. To facilitate control of confounding we used a time-to-event approach specifying vaccination status and age as time-varying covariates. Results are presented in plenary session 6.
Conclusion: Analytic techniques are available to improve the evaluation of new vaccines using 'before and after' data while taking into account potential confounding and bias.

No conflict of interest

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INVASIVE SEROTYPES AND PNEUMOCOCCAL MENINGITIS FATALITY IN BURKINA FASO AND TOGO, 2002-2013

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Background and Aims: Many pneumococcal (Sp) meningitis cases in the African meningitis belt result from the invasive serotype 1, which data from other areas indicate should present with relatively low mortality.
Methods: We evaluated all age acute bacterial meningitis mortality data from healthcare structure based surveillance systems in northern Togo and western Burkina Faso. All patients had received care based on standard algorithms. Etiologic determination was performed via culture, antigen detection, or polymerase chain reaction (PCR) while serotype/group was determined by PCR or Quellung.
Results: Among 4838 patients, the case fatality ratio (CFR) was 34% (275/808) for Sp, and 9% (56/639), 11% (26/229), and 15% (17/111) for serogroups A, W135, and X meningococcus, respectively. Sp CFR varied only modestly by study year (23% [2005] to 46% [2010]) and age group (31% [5-14 years] to 43% [50+ years]) with no particular trend; 56% of Sp deaths occurred from age 5-49 years. Of 355 (43%) evaluated Sp cases, 51% were serotype 1 and 66% were invasive (serotype/groups 1, 4, 5, 7, 14, 18). CFR was 42% for serotype 1 versus other serotypes and for invasive versus non-invasive serotypes. Serotype 1 and invasive serotypes were not associated with lower CFR when stratified by country, age group, or study year. Antibiotic resistance did not predict death.
Conclusion: In the African meningitis belt Sp meningitis mortality is higher than other etiologies, affects all age groups, shows no evidence of decreasing, and is not lower for serotype 1 or the broader category of invasive serotypes.

Conflict of interest

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RELATIVE RATES OF PNEUMOCOCCAL DISEASE ARE DISPROPORTIONATELY HIGH IN ADULTS WITH MULTIPLE CHRONIC MEDICAL CONDITIONS

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Background: The high risk of pneumococcal infection among adults with immunocompromising conditions is well recognized; however, the risk among immunocompetent adults with chronic medical conditions, especially those with multiple conditions, is less well established.
Methods: A retrospective cohort design using US healthcare claims data (2007-2010) from >35M persons annually was employed. Study population included persons aged ≥18 years, and was stratified by age and risk profile (high-risk [immunocompromised], at-risk [immunocompetent with ≥1 chronic condition], healthy); at-risk individuals were further stratified by number of conditions. At-risk and high-risk conditions, and episodes of pneumococcal disease (PD)—invasive (IPD), pneumococcal pneumonia (PP), all-cause pneumonia (PNE)—were identified via diagnosis, procedure, and drug codes.
Results: Persons with ≥2 at-risk conditions accounted for 9-32% of all at-risk adults, depending on age. PD rates increased markedly with number of conditions, and for those with ≥2 conditions, were similar to those in the high-risk group (Table). Among adults 18-34 years, 66-71% of PD occurred in healthy individuals and 4-7% among those with ≥2 at-risk conditions; among adults ≥65 years, corresponding figures were 20-21% and 26-29%.

Table. Rates of IPD, PP, and PNE

		IPD		PP		PNE	
	No. of Person-Years	Rate per 100K PY	Rate Ratios* (95% CI)	Rate per 100K PY	Rate Ratios* (95% CI)	Rate per 100K PY	Rate Ratios* (95% CI)
Age 18-34 Years							
Healthy	18,980,832	1.2	–	11	–	281	–
At-Risk	1,712,531	3.9	3.3 (2.5-4.3)	37	3.4 (3.1-3.7)	935	3.3 (3.3-3.4)
1 Condition	1,559,181	3.4	2.9 (2.1-3.9)	28	2.6 (2.3-2.8)	766	2.7 (2.7-2.8)
2 Conditions	135,037	7.4	6.3 (3.3-11.8)	101	9.2 (7.7-10.9)	2,224	7.9 (7.6-8.2)
≥3 Conditions	18,362	16.3	13.8 (4.4-43.2)	332	30.2 (23.4-39.0)	5,805	20.6 (19.4-21.9)
High-Risk	275,065	18.2	15.4 (11.3-20.9)	109	9.9 (8.8-11.2)	2,057	7.3 (7.1-7.5)
Age 35-49 Years							
Healthy	23,491,681	2.4	–	17	–	428	–
At-Risk	3,960,157	6.3	2.7 (2.3-3.1)	47	2.8 (2.7-3.0)	1,238	2.9 (2.9-2.9)
1 Condition	3,916,661	5.0	2.1 (1.8-2.5)	37	2.2 (2.1-2.4)	969	2.3 (2.2-2.3)
2 Conditions	464,846	10.8	4.5 (3.4-6.1)	85	5.1 (4.6-5.6)	2,267	5.3 (5.2-5.4)
≥3 Conditions	98,650	29.4	12.4 (8.6-18.0)	216	12.9 (11.2-14.8)	5,641	13.2 (12.8-13.5)
High-Risk	836,208	18.7	7.9 (6.6-9.4)	101	6.0 (5.6-6.5)	2,253	5.3 (5.2-5.3)
Age 50-64 Years							
Healthy	20,972,935	4.5	–	25	–	651	–
At-Risk	7,696,247	12.0	2.7 (2.5-2.9)	80	3.2 (3.0-3.3)	2,024	3.1 (3.1-3.1)
1 Condition	5,569,514	8.5	1.9 (1.7-2.1)	54	2.1 (2.1-2.2)	1,412	2.2 (2.2-2.2)
2 Conditions	1,337,596	17.0	3.8 (3.3-4.4)	127	5.0 (4.7-5.3)	3,187	4.9 (4.8-5.0)
≥3 Conditions	369,137	50.4	11.3 (9.7-13.2)	326	12.8 (12.0-13.6)	7,738	11.9 (11.7-12.0)
High-Risk	1,951,128	30.8	6.9 (6.2-7.6)	140	5.5 (5.4-6.1)	3,601	5.5 (5.5-5.6)
Age >=65 Years							
Healthy	5,389,930	8.5	–	67	–	1,874	–
At-Risk	4,579,505	23.0	2.8 (2.5-3.1)	210	3.1 (3.0-3.2)	5,662	3.0 (3.0-3.0)
1 Condition	3,120,576	16.1	1.9 (1.7-2.2)	138	2.1 (2.0-2.1)	3,843	2.1 (2.0-2.1)
2 Conditions	1,109,472	29.9	3.5 (3.1-4.1)	286	4.2 (4.0-4.5)	7,754	4.1 (4.1-4.2)
≥3 Conditions	349,456	63.0	7.6 (6.4-8.9)	618	9.2 (8.7-9.7)	15,255	8.1 (8.1-8.2)
High-Risk	1,774,181	36.7	4.4 (3.9-5.0)	290	4.3 (4.1-4.5)	7,594	4.1 (4.0-4.1)

PY: person-years; *Excess rate versus age-matched healthy counterparts

Conclusion: Notwithstanding widespread childhood pneumococcal vaccination and an overall decline in PD among adults, disease risk remains disproportionately high in those with at-risk and high-risk conditions. PD rates are notably high among adults with multiple at-risk conditions; comparable to those among adults with high-risk conditions.

Conflict of interest

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Global Pneumococcal Disease and Policies for Control

PNEUMOCOCCAL POLYSACCHARIDE VACCINE AT 9 MONTHS OF AGE IS NOT ASSOCIATED WITH IMPAIRED B-CELL MEMORY OR HYPO-RESPONSIVENESS IN CHILDREN IN PNG

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Introduction: 23-valent pneumococcal polysaccharide vaccine (PPV) following pneumococcal conjugate vaccines (PCV) should increase protection however concerns exist regarding hypo-responsiveness and B-cell memory impairment after PPV. We evaluated the persistence of antibody and B-cell memory following PPV at 9 months of age in 3-5 year old children in Papua New Guinea.
Methods: 150 children who had received PPV at age 9 mo (after PCV7 at 0-1-2 or 1-2-3 months or no PCV7) and 130 age-matched unvaccinated controls received a 0.1 mL PPV challenge dose at age 3-5 years and blood was collected pre- and 1 month post-challenge. Serotype-specific IgG for serotypes in PCV7 (VT), 2, 5 & 7F was measured by ELISA. B-cell memory for serotypes 1, 2, 7F, 14, 19A, 19F & 23 was measured at age 10 and 18 months (prior-PPV groups) and pre-challenge by polyclonal B-cell stimulation and detection of antibody forming cells on polysaccharide-coated plates by ELISpot.
Results: Post-PPV, memory B-cells numbers increased from age 10 months to 3-5 years for 8/9 serotypes (not 23F) and did not differ to PPV naïve controls. Pre-challenge, IgG levels were high, with no significant differences between groups in GMCs or proportions ≥1 µg/mL (range 58-95%). IgG increases after PPV-challenge were modest (1.2 to 2.8-fold) with no significant differences in GMCs, fold-rises or % ≥1 µg/mL between groups. Increased pre-challenge antibody concentrations were associated with a decreased IgG response to challenge.
Conclusion: We found no evidence of hypo-responsiveness or impairment of memory B-cells in PNG children at 3-4 years of age after PPV at age 9 months.

Conflict of interest

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OTITIS MEDIA AND ITS SEQUELAE IN KENYAN SCHOOL CHILDREN

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Background and Aims: Chronic suppurative otitis media (CSOM), a sequel of acute otitis media (AOM) is a major cause of preventable hearing loss in children in developing countries. In Africa there are few recent studies on the prevalence of AOM and its sequelae. Obtaining representative Kenyan data on the point prevalence of AOM and its sequelae, otitis media with effusion (OME), CSOM and hearing impairment was the goal.
Methods: Study subjects were children aged 2 to 15 years enrolled from randomly selected preprimary and primary schools. With parental/guardian consent, subjects had a questionnaire administered, otoscopy and tympanometry done, and audiometry performed on those with ear problems detected on these examinations.
Results: Of the 13,109 children examined, 75% were from rural schools. The prevalence's of CSOM and OME were 15/1000 children and AOM was 7/1000. Apart from retraction of the tympanic membrane (urban 0.3%, rural 0.1%, $p < 0.001$), there was no statistically significant difference between the prevalence of other middle ear disorders in rural and urban school children. However in rural children, those from the Rift Valley had a significantly higher rate of CSOM 24/1000 than other regions 12/1000; $p < 0.0001$. The age of onset of ear discharge was before 3.5 years in 50% of children and before 6 years in 75%.
Conclusion: Since a significant burden of AOM sequelae occur in Kenyan preschool and school children with the onset mostly, in the first 4 years of life, we question: would pneumococcal vaccines that prevent early recurrent AOM, prevent these nonreversible sequelae?

No conflict of interest

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Global Pneumococcal Disease and Policies for Control

EPIDEMIOLOGY OF INVASIVE PNEUMOCOCCAL DISEASE IN HIV EXPOSED-UNINFECTED CHILDREN <1 YEAR OF AGE IN SOUTH AFRICA, 2009 THROUGH 2012

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Background: The prevention of mother-to-child transmission (PMTCT) programme has been rapidly scaled-up in South Africa with a reported decrease in HIV transmission rates from 3.5% (2010) to 2.7% (2011). There are no published data quantifying specific increased risk or mortality of IPD in HIV-exposed uninfected (HEU) children.
Methods: We conducted a cohort surveillance study in children <1 year of age with invasive pneumococcal disease (IPD), using data obtained from a national, laboratory-based, surveillance programme. HIV and outcome data were obtained at sentinel sites. Incidences in HIV-infected, HIV-uninfected, HEU and HIV-unexposed uninfected (HUU) children were calculated assuming similar annual HIV prevalence in tested and untested children.
Results: We identified 1805 IPD cases in children <1 year of age from 2009 through 2012 from all sites. In children from sentinel sites (n=863), 89% (768/863) had known HIV status. The highest incidence of IPD was in HIV-infected (608/100,000 population) compared with HIV-uninfected children (31/100,000; crude relative risk 19.61 [95% CI 13.67-29.12]). In addition, HEU children had higher incidence of IPD (61/100,000 population) than HUU children (22/100,000; crude relative risk 2.77 [95% CI 1.68-4.74]).
Overall case-fatality ratio was high (27%, 234/863), differed between HIV-infected (32%, 75/231) and HIV-uninfected children (24%, 129/537, p=0.008); as well as between HEU (27%, 59/220) and HUU children (21%, 57/266, p=0.08).
Discussion: The numbers of HIV-exposed children infected annually continue to drop due to improvements in PMTCT; however we have now shown that these exposed but uninfected children are at increased risk of IPD and mortality compared with HIV-unexposed children.

No conflict of interest

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Global Pneumococcal Disease and Policies for Control

SEROTYPE DISTRIBUTION OF STREPTOCOCCUS PNEUMONIAE ASSOCIATED WITH INVASIVE PNEUMOCOCCAL DISEASE IN CHINA

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Background and Aims: Invasive pneumococcal disease (IPD) is a serious public health problem in China, yet epidemiology data are limited, especially in adults. The study aimed to examine the serotype distribution of *Streptococcus pneumoniae* isolated from Chinese patients with IPD.
Methods: The multicenter study collected *S. pneumoniae* positive IPD isolates from normally sterile sites in both pediatric (<18 years) and adult (≥18 years) patients in China between 2009 and 2013. Serotypes were analyzed by Chinese Center for Disease Control and Prevention using Capsule-quellung test.
Results: A total of 110 isolates from 60 pediatric and 50 adult IPD cases were collected from 16 hospitals in 13 provinces in China. Overall, the most common serotypes in all ages were 19A, 19F, 23F, 3 and 14. The most frequent serotypes were 19A, 19F, 23F, 1, 5, 14, 6B and 6C in pediatric patients and 3, 19F, 19A, 23F, 14, 20 and 6A in adults. Interestingly, serotype 19A appeared significantly more frequent in infants (<2 years) than other age groups, whereas serotype 3 was the most common type in the elderly (>65 years). The common serotypes for main IPD diagnoses (invasive pneumonia, meningitis and sepsis) were 19A, 19F and 23F in invasive pneumonia and meningitis, and 19F, 19A, 5, 1 and 23F in sepsis.
Conclusion: Serotypes 19A and 3 were the most prominent serotypes in pediatric and adult patients with IPD, respectively. Findings demonstrate the different serotype distribution among various age groups in Chinese population with IPD.

Conflict of interest

Poster Abstracts

ISPPD-0195
Global Pneumococcal Disease and Policies for Control

ASSESING THE ECONOMICS OF INVASIVE PNEUMOCOCCAL DISEASE IN OLDER CHILDREN AND ADULTS IN THE LATIN AMERICA AND CARIBBEAN REGION

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Background: The economic burden of invasive pneumococcal disease (IPD) is substantial in the Latin American and Caribbean region.
Objectives: To estimate the economic burden of IPD in the region from the healthcare system perspective and its impact on the gross domestic product (GDP) per capita.
Methods: We contacted experts in five selected countries (Argentina, Brazil, Chile, Colombia and Uruguay) and asked them specific questions about the diagnosis and treatment of bacteremic pneumonia and meningitis in three age groups: 5-17 year olds, 18-64 year olds and 65+ year olds. Estimates of disease burden and costs were based on extensive literature review and public databases. Diseases considered included: pneumococcal pneumonia (inpatient/outpatient), and pneumococcal meningitis.
Results: A total of 153 physicians responded to targeted questions. The total direct medical cost per treatment of pneumonia ranged from US$993 to US$3,132 in older children, US$1,274 to US$3,247 in adults and US$1,746 to U$3,535 in elderly, respectively. Overall, the costs of hospital stay accounted for 45% of the total treatment costs in these countries. Across the region, health care costs of IPD per country ranged from US$8.2 million to US$14.1 million, with higher costs incurred by the elderly due to higher level of resources used for treating the elderly. Healthcare spending for IPD in older children and adults as a percentage of GDP was estimated at 0.1%, compared to the reported 8-10% of GDP spent on healthcare overall.
Conclusion: IPD poses a sizable economic burden among persons > 5 years in the LAC.

No conflict of interest

ISPPD-0196
Global Pneumococcal Disease and Policies for Control

ECONOMICS OF INVASIVE PNEUMOCOCCAL DISEASE AMONG OLDER CHILDREN AND ADULTS IN LATIN AMERICA: RESULTS FROM A REVIEW OF THE LITERATURE

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Background: To review the economic evidence of hospitalized invasive pneumococcal disease (IPD) among age groups ≥5 years in the Latin American and Caribbean (LAC) region.
Methods: We systematically searched 5 databases of published and unpublished literature to identify studies from 1980–2012 presenting economic data for IPD cases among persons ≥5 in the LAC region. We summarized data from studies we found by study characteristics (e.g. study location, age groups), methodology (e.g. time horizon, perspective), and economic outcome data (e.g. cost per case, life years gained). Authors of unpublished studies were contacted for additional information on study methods and outcomes.
Results: A total of 15 studies presenting economic data on IPD from 8 LAC countries were identified. Studies were exclusively among older adults (69% among ≥50 years old; 44% among ≥60 years old). Most studies were from the health system or third party payer perspective and included only direct medical and non-medical costs. Nine studies assessed the costs and benefits of pneumococcal vaccination and 6 assessed the total cost and cost per case of pneumococcal disease. The cost per single case of meningitis was found to be greater than for pneumonia (average, US$17,114 versus US$4,817). The cost of meningitis sequelae was found to be substantial (19-75% of acute management costs in two studies).
Conclusion: Economic data on IPD among ≥ 5 year olds and hospitalized IPD among this population are limited. Available studies indicate that IPD incurs significant costs to society.

No conflict of interest

ISPPD-0363
Global Pneumococcal Disease and Policies for Control

BUDGET OPTIMIZATION MODEL FOR PNEUMOCOCCAL VACCINATION IN INFANTS AND ELDERLY: THE CASE OF SPAIN AND THE NETHERLANDS

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Background and Aims: Recommending bodies today may have to consider routine immunization with pneumococcal conjugate vaccines (PCV) in two groups (infants and elderly). This analysis aimed to identify an optimal PCV strategy within a constrained budget from the health-care payer perspective. Two countries, Spain and The Netherlands with different baseline PCV uptake, pediatric schedules and age indication in elderly are considered in this analysis.
Methods: We developed an optimization model that is linked to a prevalence-based disease management sub-model. This program allows to find an optimal solution given an objective function (minimize cases; minimize quality-adjusted life-years lost; minimize life-years lost) under budget constraints. In case of budget increase, the model calculates an optimal vaccine uptake in both groups. The vaccine efficacy against overall community-acquired pneumonia (VE-CAP) in elderly needed to justify a switch from infant to elderly vaccination is also estimated. Herd protection resulting from infant vaccination is included and varies with VE and uptake.
Results: In Spain, though pneumonia disease burden is high in the elderly, the model estimates that additional budget should be first allocated to increase uptake amongst infants, irrespective of VE-CAP in elderly. In The Netherlands, the VE-CAP in the elderly would have to be at least 3-fold higher than that of infants to prioritize elderly vaccination.
Conclusion: VE-CAP in the elderly would have to be very high to prioritize elderly vaccination. Infant immunization with PCV is identified as the optimal strategy to reduce the impact on invasive and non-invasive pneumococcal disease in both countries.

Conflict of interest

ISPPD-0503
Global Pneumococcal Disease and Policies for Control

METHODS AND DATA AVAILABILITY TO ESTIMATE PNEUMOCOCCAL MENINGITIS BURDEN IN PERSONS >5 YEARS BY GEOGRAPHIC REGION: THE AGEDD STUDY

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Background: Few have assessed the global pneumococcal disease burden in persons ≥5 years. We assessed available data to estimate one component, pneumococcal meningitis, by geographic region pre-pneumococcal conjugate vaccine (PCV) introduction.
Methods: We systematically searched literature and national surveillance databases from 1980-2010 for age-stratified (5-19, 20-64, ≥65 years) pneumococcal meningitis incidence and inputs for two indirect estimation approaches: invasive pneumococcal disease (IPD) incidence multiplied by proportion of IPD that is meningitis and all-cause bacterial (AB) meningitis incidence multiplied by proportion of AB meningitis due to pneumococcus for persons >5 years.
Results: Of 21,331 studies, 21 had pneumococcal meningitis incidence data. Data were sparse in Africa, Asia, and LAC (Table). For Asia, none of the approaches had data in every age strata.

Table: Number of studies (countries) with relevant data for estimating meningitis incidence

Region	Pneumococcal Meningitis Incidence	IPD Incidence	% of IPD that is Meningitis	AB Meningitis Incidence	% of AB Meningitis due to Pneumococcus
Africa	**6(5)**	1(1)	0(0)	2(2)	15(11)
Asia	0(0)	**2(2)**	2(2)	2(2)	**7(5)**
Europe	**8(7)**	**8(7)**	**5(5)**	**5(2)**	**7(4)**
LAC	**4(2)**	**4(2)**	**16(14)**	**4(2)**	3(2)
North America*	**2(2)**	**2(2)**	**1(1)**	**1(1)**	**1(1)**
Oceania*	**1(1)**	**3(2)**	**1(1)**	0(0)	**1(1)**

* Detailed, multi-year surveillance data. **Bold**=data for all age-strata available.

Conclusion: Data to estimate pneumococcal meningitis incidence in persons ≥5 years were limited from Africa, Asia, and LAC, especially from adults ≥20 years. At least one approach is possible in all regions. For Asia, it requires extrapolating from the age distribution pattern from other regions.

No conflict of interest

ISPPD-0506
Global Pneumococcal Disease and Policies for Control

METHODS AND DATA AVAILABILITY TO ESTIMATE PNEUMOCOCCAL PNEUMONIA BURDEN IN PERSONS >5 YEARS BY GEOGRAPHIC REGION: THE AGEDD STUDY

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Background: Few have assessed the global pneumococcal disease burden in persons ≥5 years. We assessed data available to estimate one component, pneumococcal pneumonia, by geographic region pre-pneumococcal conjugate vaccine (PCV) introduction.
Methods: We systematically searched studies conducted 1980-2010 for data to estimate regional pneumococcal community-acquired pneumonia (PCAP) incidence in persons >5 years. PCAP can be estimated directly, or indirectly by summing pneumococcal bacteremic pneumonia (PBP) and non-bacteremic pneumonia (non-PBP) incidence. The ratio PBP:non-PBP (previously estimated) can be applied to PBP incidence to estimate CAP incidence. Inputs to estimate PCAP indirectly are listed in the Table. Models using multiple inputs require age-stratified (5-19, 20-64, ≥65 years) data.
Results: PCAP incidence data was only available for North America and Oceania. For other regions, no single study had data from all age-strata, and no indirect approach had data for all age-strata.

Table: Number of studies (countries) with relevant data for each inputs.

Region	PBP Incidence	IPD Incidence	%IPD that is PBP	Spn Meningitis Incidence	PBP:Spn Meningitis	PCAP:Spn Meningitis
Africa	1(1)	1(1)	0(0)	**6(5)**	0(0)	0(0)
Asia	0(0)	**2(2)**	2(2)	0(0)	2(2)	1(1)
Europe	1(1)	**8(7)**	1(1)	**8(7)**	1(1)	0(0)
LAC	1(1)	**4(2)**	1(1)	**4(2)**	1(1)	**21(20)**
North America*	**1(1)**	**2(2)**	**1(1)**	**2(2)**	**1(1)**	**1(1)**
Oceania*	**1(1)**	**3(2)**	**1(1)**	**1(1)**	**1(1)**	0(0)

*Detailed, multi-year surveillance data. **Bold**=data for all age-strata available. IPD=invasive pneumococcal disease, Spn=pneumococcal.

Conclusion: Data to estimate pneumococcal pneumonia incidence globally were lacking in adults. No single method was possible for all regions, but each region has data for ≥1 method.

No conflict of interest

ISPPD-0511
Global Pneumococcal Disease and Policies for Control

PNEUMOCOCCAL MENINGITIS INCIDENCE AND CASES IN CHILDREN >5 YEARS AND ADULTS BY GEOGRAPHIC REGION: THE AGEDD STUDY

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Background and Aims: Global pneumococcal disease burden in persons ≥5 years has not been described. We aimed to estimate one component, pneumococcal meningitis, by geographic region pre-pneumococcal conjugate vaccine (PCV) introduction.
Methods: A systematic review of 17 literature databases and national surveillance reports identified studies conducted 1980-2010 reporting pneumococcal meningitis incidence in persons ≥5 years pre-PCV introduction.

Regional meta-estimates of age-stratified (5-19, 20-64, ≥65 years) incidence were obtained for studies reporting standard errors. Year 2013 UN Region age-specific population sizes were used to weight these and estimate incidence and cases ≥5 years.
Results: All regions had ≥1 study representing all age strata except Africa (but all age-groups were represented) and Asia (no data). Adults ≥65 years had highest incidence in all regions. Cases were CSF culture-positive or latex agglutination-positive (occasionally blood culture-positive); PCR testing was rare.

Table: Estimated regional pneumococcal meningitis incidence per 100,000 population age ≥5 years

Region	N studies (with SE)	Incidence	95% CI	Cases	Upper-Lower Bound
Africa	6 (5)	4.02	2.9-9.8	45,000	26,900-91,400
Europe	8 (6)	0.88	0.51-2.0	6,500	3,600-13,700
LAC	4 (3)*	0.65	0.50-0.89	3,900	2,700-4,900
North America	2 (2)*	0.72	0.56-1.1	2,500	1,800-3,500
Oceania	1 (1)*	0.16	0.14-0.23	59	46-78
Asia	0	Not available			

*detailed, multi-year, surveillance databases

Conclusion: Pneumococcal meningitis incidence measures in persons ≥5 years were scarce from most regions but suggest disease burden in Africa, Europe and LAC exceeds that in North America (Asia is unknown) despite different age distributions. Values are likely underestimated due to imperfect lab sensitivity and case detection.

No conflict of interest

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Global Pneumococcal Disease and Policies for Control

HIGH CASE FATALITY RATE OF ACUTE RESPIRATORY INFECTIONS AND WIDE RANGE OF PNEUMOCOCCAL SEROTYPE DISTRIBUTION IN AFGHANISTAN

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Background and Aims: Afghanistan is said to have high case fatality rate of acute respiratory infections (ARI) among under-5 year old children, however no data have been published. Serotype distribution of pneumococcus is unknown. We aimed to determine case fatality rate, risk factors for death, and prevalence of pneumococcus with its serotype distribution in Afghanistan.
Methods: A prospective study was conducted in the Paediatric Ward of Mazar-e-Sharif Regional Hospital, Afghanistan from December 2012 to March 2013. Under-5 year old children admitted with clinical pneumonia (WHO) were recruited. Nasopharyngeal samples were tested for *Streptococcus pneumoniae* (pneumococcus), *Haemophilus influenzae* and *Moraxella catarrhalis* by multiplex PCR. Molecular serotyping and quantification of pneumococcus was done by nanofluidic real time PCR.
Results: Total recruited children were 639 and 326 samples were collected. Case fatality rate of pneumonia was 12.1% (75/639). Risk factors associated with death were: age less than 1 month, unable to breastfeed, chest indrawing, cyanosis, altered consciousness, hypothermia, hypoxemia and acute malnutrition. *S. pneumoniae*, *H. influenzae* and *M. catarrhalis* were detected in 41.1%, 31.2%, and 22.7% respectively. Twenty-two pneumococcal serotypes/serogroups were identified. PCV13 covered 38.1% of prevalent serotypes. Multiple serotypes were present in 15.9% (21/132) of pneumococcus colonized children, and their prevalence was higher, 36.3% (4/11) in death cases than 12.7% (15/118) in survived cases (p = 0.057). Pneumococcal load was also higher in death cases (4.6 log10/mL) than survived cases (3.1 log10/mL) (p = 0.07).
Conclusion: High case fatality rate of ARI should be addressed. Wide range of pneumococcal serotype distribution and low serotype coverage of PCV13 warrant further studies.

No conflict of interest

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Global Pneumococcal Disease and Policies for Control

ECONOMIC EVALUATION OF 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE FOR PRIMARY IMMUNISATION OF NEW ZEALAND INFANTS BASED ON A 3+1 DOSING SCHEDULE

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Background: Pneumococcal conjugate vaccines (PCV) available in New Zealand (NZ) and listed on National Immunisation Schedule for the prevention of pneumococcal disease (PD) are (i) 10-valent PCV (PCV10) for all infants and children, and (ii) 13-valent PCV (PCV13) for high risk children <5 years and those aged <16 years pre- or post-splenectomy or with functional asplenia. The objective of this economic analysis was to assess the cost-effectiveness of PCV13 replacing PCV10 in NZ based on 3+1 dosing for all infants and children.
Methods: A 1-year cross-sectional, steady-state, population model was developed from a payer's perspective to estimate PD cases avoided (bacteraemia, meningitis, inpatient and outpatient pneumonia, simple and complex otitis media). Recent disease incidence, serotype coverage, and population data obtained from the NZ Ministry of Health (MoH). Utilities sourced from published literature. Medical costs derived from the MoH and literature. Price parity per dose was assumed. Vaccine direct effectiveness derived from 7-valent PCV, and observed effectiveness of PCV10 and PCV13. The base analysis also included PCV13 indirect effects.
Results: PCV13 for primary immunisation reduces the number of PD cases (n = 4,026) relative to PCV10. It also leads to an increase in the number of life-years (n = 352) and quality-adjusted life-years saved (n=387). Annual direct medical costs (including vaccination) were estimated to decrease by more than $5.7 million when vaccinating with PCV13. Thus, PCV13 dominated. Sensitivity analyses supported this in all scenarios.
Conclusion: Sole supply of PCV13 for primary immunisation against PD in NZ is a cost-saving programme compared with PCV10.

Conflict of interest

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Global Pneumococcal Disease and Policies for Control

CRITERIA FOR EVALUATING THE PUBLIC HEALTH IMPACT AND COST-EFFECTIVENESS OF HIGHER-VALENT PNEUMOCOCCAL CONJUGATE VACCINES USING AVAILABLE AND APPROPRIATE EFFECTIVENESS DATA

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Introduction: Cost-effectiveness analyses (CEAs) of 10-valent and 13-valent pneumococcal conjugate vaccines (PCV10, PCV13) have been based on extrapolation of efficacy and effectiveness data from the 7-valent vaccine (PCV7). PCV10/PCV13 efficacy and effectiveness data are now public, therefore we assessed application of this data into CEAs.
Methods: Publicly available PCV10 and PCV13 efficacy and effectiveness data through October 2013 were analyzed. Model inputs recommendations for both vaccines were based on assessment of competent and reliable scientific evidence, statistical significance, and across-study comparability. Results: No head to head vaccine efficacy or effectiveness data are available. Data demonstrate higher-valent vaccines reduced IPD, pneumonia, and otitis media in vaccinated individuals, supporting direct protection. Otitis media and pneumonia endpoints differ across studies, limiting ability to directly compare impact across vaccines. PCV13 consistently exhibited rapid and robust indirect effects across age groups, while one PCV10 study showed reduction in unvaccinated children <5 years. PCV13 consistently demonstrated significant 19A protection, while PCV10 has not. Neither PCV10, nor PCV13's 6 additional serotypes have yet demonstrated significant evidence of effect on disease or carriage caused by non-vaccine specific serotypes, non-typeable *Haemophilus influenzae*, or other pathogens (Table).

Table 1: Available Efficacy and Effectiveness Data to Support Appropriate Cost-effectiveness Models Inputs and Recommendations

Disease Category	Relevant Data: PCV10	Relevant Data: PCV13	Model Input Recommendations
Direct protection			
Vaccine type IPD	Finland, Latin America, Brazil, Kenya, New Zealand	US, UK, Spain, Israel, Canada, Italy, Ireland, South Africa, Australia, Denmark, France, Germany	Both vaccines effective, assume similar effectiveness against serotypes contained in the vaccine
Hospitalized Pneumonia (All-cause)	Finland, Latin America	US, Spain, France, Uruguay, Argentina, Nicaragua, Israel	Early results consistent with PCV7. Assume effect equal to PCV7 for covered serotypes; extrapolate based on serotype coverage in the higher-valent vaccines
Non Hospitalized Pneumonia (all-cause)	Finland	France	Early results consistent with PCV7. Assume effect equal to PCV7 for covered serotypes; extrapolate based on serotype coverage in the higher-valent vaccines
Acute otitis media (All-cause)	Finland, Latin America	Israel	Early results consistent with PCV7. Assume effect equal to PCV7 for covered serotypes; extrapolate based on serotype coverage in the higher-valent vaccines
Indirect Protection			
Vaccine type IPD	Finland, Brazil: limited impact in 18 mos to 4 year olds. No statistically significant effect in older ages.	Spain, US, UK	Include PCV13 indirect effects across all age groups Include PCV10 indirect effects for children 18 mos to 4 years, exploratory sensitivity analysis for other age groups
Hospitalized Pneumonia (All-cause)	No significant effects	US	Include PCV13 indirect effects Do not include PCV10 indirect effects
Ambulatory Pneumonia (All-cause)	No significant effects		Assume no vaccine impact. Monitor for significant changes in adult disease post-licensure.
Acute otitis media (All-cause)	No significant effects	No significant effects for the 6 additional serotypes in PCV13	Assume no vaccine impact. Monitor for significant changes to disease in excess of direct effects
Cross Protection (Protection against serotypes not contained in the vaccine)	No significant effects	No significant effects for the 6 additional serotypes in PCV13	Assume no vaccine impact until significant changes reported
Other organisms (e.g., NTHi)	Data support no impact versus NTHi	No significant effects	Assume no vaccine impact until significant changes reported

Conclusion: Data informing higher-valent PCV CEAs continue to evolve. Model estimations of direct protection from pneumococcal diseases should be based on a common value, adjusted to reflect local coverage of serotypes included in the vaccines. PCV13 indirect effects should be included; PCV10 indirect effects should be limited to sensitivity analyses until proven.

Conflict of interest

ISPPD-0279
Global Pneumococcal Disease and Policies for Control

PUBLIC HEALTH AND ECONOMIC BENEFITS OF 13 VALENT PNEUMOCOCCAL CONJUGATED VACCINATION PROGRAMS IN PARAGUAY

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Background: Routine vaccination against *Streptococcus pneumoniae* needs government investment. Policy makers need information about the projected health benefits, costs and cost-effectiveness of vaccination.
Objective: The main objective was to assess the cost-effectiveness of 13 valent pneumococcal conjugated vaccines (PCV13) for infants and children aged <5 years in Paraguay.
Methods: We developed a Markov model simulating the lifetime evolution of a local birth cohort without vaccination as a base case. Different scenarios were considered for comparison, according to the evidence of effectiveness, efficacy and herd effect of PCV. We established a universal 3 (2+1) dose vaccination schedules and we modeled the burden of diseases from local and regional data and paraguayan cost. The results were expressed as incremental cost in 2013 US dollars per life years gained (LYG)
Results: The incremental cost per LYG for PCV13 (2+1) according to PCV-13 pneumonia hospitalization effectiveness regional data with and without herd immunity was 618, 96 USD and1.095 USD, respectively. The incremental cost per LYG for PCV13 (2+1) according to non-inferiority PCV-7 efficacy and herd effect, was 813, 17 USD. The incremental cost per LYG for PCV10 (2+1) according to efficacy/effectiveness data was 1.219, 74 USD. The model was sensitive to variation with regards to assumptions around pneumonia incidence and mortality rate.
Conclusion: All scenarios are cost effective and lower than Paraguay gross domestic product. Evidence of herd effect associated with PCV13 improves pneumococcal vaccines and is cost saving in Paraguay.

No conflict of interest

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Global Pneumococcal Disease and Policies for Control

SEROTYPE PREVALENCE AND ANTIBIOTIC RESISTANCE IN STREPTOCOCCUS PNEUMONIAE CLINICAL ISOLATES IN SFAX,SOUTH OF TUNISIA

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Background and Aims: *Streptococcus pneumoniae* causes a wide range of infections that could be deliterious. Prevention through vaccination is a valuable tool to decrease the burden of disease. Nevertheless, none of the marketed internationally vaccines, PCV 7, PCV 10 and PCV 13 is currently part of the national program of immunization in Tunisia. We undertook this study to determine the serotype distribution and to analyze the antimicrobial resistance of *S. pneumoniae* isolates .
Methods: All pneumococcal strains isolated in the microbiology laboratory of the University Hospital, Sfax, Tunisia, from January 2012 to August 2013 were included. *S. pneumoniae* was identified by Gram straining, optochin susceptibility and bile solubility. Antimicrobial susceptibility was determined by the disk diffusion and E test methods. Serotyping was performed by multiplex PCR. Statistical analysis was done using SPSS 2O.
Results: Among 125 collected pneumococcal isolates, 39 were invasive isolates (31%). The mean age of patients was 29.7 years. Seventy four percent of the strains were penicillin non-susceptible (PNSP). Forty four percent had decreased susceptibility to amoxicillin and 23.2% to cefotaxim. The PNSP were more frequently resistant to other antibiotics. Serotype 14 was the most frequently isolated (21.4%) followed by serotypes 19F (20.4%), 6A/6B (10.2%), 23F (9%) and 3(8.2%). Serotype 19F was associated with higher level of PNSP (p = 0.03). The potential coverage by the 7, 10 and 13 valent pneumococcal conjugate vaccines were 65.3%, 65.3% and 77.6% respectively.
Conclusion: A high rate of *S. pneumoniae* antibiotic resistance is observed in Tunisia. Conjugate vaccines and particularly PCV 13 provide good coverage for pneumococcal isolates .

No conflict of interest

ISPPD-0332
Global Pneumococcal Disease and Policies for Control

OTITIS MEDIA IN INDONESIAN URBAN AND RURAL SCHOOL CHILDREN

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Background: While the epidemiology of otitis media is well known in industrialized countries, the burden of otitis media in developing Asian countries especially in south East Asia is not well studied.
Methods: To define the burden of otitis media and its sequelae in children 6 - 15 years of age we enrolled elementary and junior high school children in 6 areas in rural and urban Indonesia. Randomly selected schools and classrooms were selected. All children were screened with a questionnaires, ear examination and pneumatic otoscopy. Children with any abnormality on examination or with a relevant history underwent diagnostic audiometry and tympanometry.
Results: Of the 7005 children studied, 116 had chronic suppurative otitis media (CSOM), 30 had acute otitis media and 26 had otitis media with effusion. 2.7% of rural children had CSOM compared to 0.7% of urban children (p < 0.0001). The rates /1000 of CSOM in rural Bali and Bandung were significantly higher (75 and 25 respectively) than the rest of Indonesia (15) (p < 0.05). In rural Bali the rates/1000 children of inactive CSOM was 63 in 6-9 year olds, compared to 37 in children aged 13-15 years. Concomitantly the rates of tympanosclerosis were 7 and 26/1000 respectively in these age groups.
Conclusion: In Indonesia the prevalence of CSOM is relatively high with most disease occurring in rural areas. The high rates in rural Bali with early progression to tympanosclerosis suggest a significant burden of potentially vaccine preventable illness.

Conflict of interest

ISPPD-0416
Global Pneumococcal Disease and Policies for Control

VARIATIONS IN PNEUMOCOCCAL SEROTYPES AND ANTIBIOTIC RESISTANCE: IMPLICATIONS FOR VACCINE POLICY IN INDIA AND ITS NEIGHBORING COUNTRIES

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Background and Aim: Asia is a continent extremely impacted by pneumococcal infections and only limited children in this region have access to life saving serotype-based vaccines, mainly because the true burden of disease and serotype distribution in this region remains unclear and becomes an issue in introducing the vaccines for routine use. The 13 serotypes included in available vaccines are most common in developed countries and will not reflect the serotype distribution across the world. This study aims to analyze the variations of pneumococcal epidemiology in India, Sri Lanka and Nepal, over a period of six years and emphasize the need of country specific serotype data to strengthen current vaccines.
Materials and Methods: 430 Invasive *Streptococcus pneumoniae* isolates from children <5 years were included in this study. Serotyping for the isolates were performed with co-agglutination technique and reconfirmed by PCR. Antibiotic susceptibility profile for the isolates were determined by vitek 2.
Results: The most common serotypes in India are 14, 19F, 5, 6A and 6B. In Sri Lanka the most common serotypes are 14, 19F, 6B, 23F and 3. Nepal had 1, 5, 2, 14 and 12A as most common serotypes. Penicillin non-susceptibility in India and Nepal is 5%, while Sri Lanka showed 60% penicillin non-susceptibility.
Conclusion: PCV7 vaccine can provide only 14.3% expected coverage against IPD in Nepal. In India PCV-7 can provide 48% coverage, while Sri Lanka can benefit most with 65% coverage against IPD. Country level data is indispensable for efficient vaccine formulation.

Conflict of interest

ISPPD-0377
Global Pneumococcal Disease and Policies for Control

PERSISTENCE OF IMMUNITY AFTER A RANDOMISED OPEN-LABEL IMMUNOGENICITY STUDY OF A 10 VALENT PNEUMOCOCCAL VACCINE (PCV10) IN THE KATHMANDU VALLEY, NEPAL

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Background: The imminent introduction of a PCV into the routine immunisation schedule of Nepal creates logistical and immunological challenges. This study aimed to assess the persistence of immunity in childhood to PCV10 serotypes in children who had received a standard three dose priming schedule (3+0) compared with a two dose schedule with a booster at 9 months of age (2+1) and a group ofchildren who received two late infant doses (0+2) compared with unvaccinatedcontrols.
Methods: We conducted a follow-on study in children aged 2-4 years who were originally recruited as infants in an open-label randomised trial of PCV10 in the Kathmandu Valley, Nepal and an additional group of unvaccinated controls. A single blood sample was collected from enrolled participants and analysed for PCV10 serotype-specific IgG.
Results: 269 children were enrolled into the study: 68, 75, 76, and 50 participants in the 2+1, 3+0, 0+2 and control groups respectively. Significantly higher proportions of children had serum antibody concentrations ≥0.2 µg/min the 2+1 versus 3+0 group for serotypes 1, 5, 6B and 18C. Geometric mean ratios were significantly higher for the 2+1 compared to the 3+0 group forserotypes 1, 7F and 18C. Significantly higher proportions of children in the 0+2 versus 2+1 group had antibody responses above the 0.2 µg/ml threshold for serotype 4.
Conclusion: This is the first study of persistence of immunity after a 2+1 schedule of PCV in South Asia and strongly supports the use of this schedule to maintain individual protection through early childhood and to drive herd immunity.

Conflict of interest

ISPPD-0015
Global Pneumococcal Disease and Policies for Control

SPECIFIC ANTIBODY RESPONSE TO TWO PNEUMOCOCCAL VACCINES IN CROHN'S DISEASE PATIENTS TREATED WITH IMMUNOSUPPRESSIVE DRUGS

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Background and Aims: Crohn's disease (CD) is a relapsing transmural inflammatory bowel disease of the gastrointestinal mucosa. CD is caused by an imbalance in the immune system. Therefore, the main purpose of the medical treatment is to moderate the immune response and thereby lower the symptoms and activity of the disease. Immunosuppressive drugs such as azathioprine and tumor necrosis factor (TNF)-α inhibitors are used in the treatment of CD. These drugs inhibit the immune system and thereby, unfortunately, put patients at increased risk of opportunistic infections, such as *Streptococcus pneumoniae*. *S. pneumoniae* infections can be prevented by vaccination. Currently, the two pneumococcal vaccines Pneumovax and Prevnar13 are licensed for use in adults in Denmark. However, there seems to be no valid data on the efficacy of these vaccines in CD patients. The primary goal of this project is to investigate the specific antibody response to pneumococcal vaccination in CD patients, secondary as a function of their medical immunosuppressive treatment.
Methods: 150 CD patients will be stratified in three groups according to the immunosuppressive treatment: 1) Patients treated with azathioprine. 2) Patients treated with azathioprine and TNF-α inhibitors. 3) Patients not treated with any immunosuppressant drugs. Patients will be randomised to receive either Pneumovax or PCV13. Blood samples from patients are collected prevaccination, 4 weeks, and one year after vaccination. Twelve specific anti-pneumococcal IgG antibodies will be measured and used for comparison of vaccine response from the two vaccines.
Results: At present 29 out of 150 patients are included in this study. We aim at presenting preliminary data on 4 weeks post vaccination antibody levels.

Conflict of interest

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PNEUMOCOCCAL IMMUNIZATIONS IN CHILDREN IN PRIMARY HEALTH CARE SETTING IN POLAND

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Introduction: Pneumococcal infections are vaccine-preventable diseases. Immunization against pneumococci is recommended in Poland but not reimbursed. The aim was to assess the coverage of the vaccination.
Material and Methods: A retrospective chart analysis of 1356 children in a large primary health care centre. The type of the vaccine, the number of doses, compliance with the dosing regimen and age of first doses were analyzed.
Results: Pneumococcal conjugate vaccine was administered in 499 children (36.8%), in majority of them (230/499; 46.1%) the immunization started in the first 6 months of life, in 63/499 patients (12.6%) at age 7-11 months, in 63/499 children (12.6%) at age 12-23 months and in 143 patients (28.7%) at age over 24 months. The schedule was correct only in 16/230 children immunized in first 6 months of life, 4/63 children at age 7-11 months and 54/143 children immunized at age 12-23 month.
Conclusion: Pneumococcal immunizations are used ineffectively in Polish children. Introduction of reimbursed, universal immunization would improve the coverage and adherence to recommended schedule.

No conflict of interest

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PNEUMOCOCCAL SEROTYPE EPIDEMIOLOGY BASED ON A SINGLE-CENTER STUDY IN MALAYSIA

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Background: Pneumococcal-conjugate vaccines (PCVs) represent the most promising pneumococcal immunization approach for the younger children. The herd immunity and overall beneficial protections will only be pronounced if this vaccine is to be implemented into the national childhood immunization scheme. Thus, the pneumococcal serotype distribution data is important for countries like Malaysia at which none of the PCV has been widely in-use to evaluate the potential coverage of PCVs.
Methods: A total of 208 pneumococcal isolates from various sites stored at the microbiology laboratory of University of Malaya Medical Centre, Kuala Lumpur from 1997 – 2012 were subjected to multiplex PCR serotyping. Minimum inhibitory concentration (MIC) was determined using agar dilution method or broth microdilution method. Statistical analysis was performed using chi-squared or fisher's exact tests whenever appropriate. **Results:** The predominant serotype was 19F (33%), followed by 23F (9%), 6A/B (6%), 1 (6%), and 14 (5%). Penicillin non-

susceptible strain (PNSP) constituted 51% of all isolates. Statistical testing found serotype 19F to be associated with penicillin resistance (62%). Moreover, 19F was associated with noninvasive site (44%) while serotype 19A was associated with invasive site (11%). Notably, the invasive isolates were associated with penicillin susceptible strains while the noninvasive isolates were likely to be PNSP.
Conclusion: The PCVs (PCV7, PCV10, and PCV13) are expected to cover substantial portions of 56%, 63%, and 71% of Malaysian serotypes, respectively. Hence, the use of PCVs would benefit the local population. Furthermore, continuous surveillance to monitor the temporal fluctuation in the local serotypes is highly desired.

No conflict of interest

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DISTRIBUTION OF PNEUMOCOCCAL SEROTYPES POST PCV13 INTRODUCTION IN ALBERTA, CANADA

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Background: Pneumococcal serotyping in Alberta is centralized at the Public Health Laboratory located in Edmonton, Alberta. PCV7 was introduced in Alberta in 2002 and PCV13 in 2012. We report the serotype distribution for cases of invasive pneumococcal disease from January 2003 to August 2014.
Methods: Invasive pneumococcal disease (IPD) is a notifiable disease reportable to Provincial Health Authorities. This results in IPD isolates in Alberta (population 3.5 million) forwarded from diagnostic microbiology laboratories to the Public Health Laboratory for serotyping. This serotyping data from January 2003 to August 2013 was collated for this analysis.
Results: From 2003 to August 2013, the top ten serotypes in Alberta in order were serotype 5 (527 isolates – 10.9%), 8 (363-7.5%), 22F (354-7.3%), 4 (340-7%), 3 (321-6.6%), 19A (317-6.5%), 7F (241-5.0%), 14 (205-4.2%), 19F (135-2.8%) and 12F (134-2.8%). This large collection of serotype 5 isolates was the result of a previously documented outbreak that occurred from 2005 to 2008. In 2012, the last full calendar year collected, the top ten serotypes in order were 22F (42-11.1%), 19A (40-10.6%), 7F (34-9.0%), 20 (31-8.2%), 8 (29-7.7%), 4 (26-6.9%), 3 (24-6.3%), 23B (15-4.0%), 33F (13-3.4%), and 15A (13-3.4%). The only PCV7 serotype remaining in the top ten serotypes is serotype 4. All other PCV7 serotypes have declined to levels of less than 1%.
Conclusion: The serotype distribution of pneumococcal isolates from cases of IPD in Alberta, Canada has fluctuated over the 12 years. Of particular concern is the increase in nonPCV13 serotypes, 22F, 20 and 8.

Conflict of interest

ISPPD-0524
Global Pneumococcal Disease and Policies for Control

INTRODUCTION OF 10-VALENT AND 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINES IN PERUVIAN NATIONAL IMMUNIZATION PROGRAM: A COST-EFFECTIVENESS ANALYSIS

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Background: Pneumococcal diseases (PD) prevention through pneumococcal conjugate vaccines (PCV) is a public health priority. The aim of this study is to evaluate the cost-effectiveness of the introduction of the 10-valent PCV (PCV10) or 13-valent PCV (PCV13) to the National Immunization Program to prevent PD in children under five years in Peru.
Methods: We carried out a cost-effectiveness analysis using the TRIVAC model. We evaluated 20 successive cohorts of children. Clinical outcomes were pneumococcal pneumonia (PP), pneumococcal meningitis (PM), pneumococcal sepsis (PS) and acute otitis media from any cause (AOM). We measured the prevention of cases, deaths, neurological sequelae (NS), auditory sequelae (AS) and disability-adjusted life years (DALY). We also performed a sensitivity analysis.
Results: For the 20 cohorts, net cost with PCV10 and PCV13 were US$369.57 millions and US$416.32 millions, respectively. PCV10 prevented 482,543 AOM; 67,640 PN; 1,876 PM; 2,383 NS; 384 AS and 6,284 deaths. PCV13 prevented 355,164 AOM; 95,032 PN; 2,636 PM; 2,383 NS; 550 AS and 8,689 deaths. The DALYs avoided were 189,405 with PCV10 and 261,987 with PCV13. Treatment costs saved were US$31,08 millions (PCV10) and US$ 39,18 millions (PCV13). For PVC10 and PCV13, costs per DALY avoided, death avoided and prevented hospitalization were: US$1,951 vs US$1,984; US$58,808 vs US$47,914 and US$1,589 vs US$1,615; respectively. Sensitivity analysis showed similar differences.
Conclusion: Both vaccines are cost effective in the Peruvian context. Although the net cost of vaccination with PCV10 is lower; PCV13 prevented more deaths, PN, PM, PS, NS and AS. Moreover, cost by each prevented DALY, death, hospitalization and sequelae were lower with PCV13.

No conflict of interest

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A RETROSPECTIVE STUDY OF INVASIVE STREPTOCOCCUS PNEUMONIAE INFECTIONS AMONG CHILDREN IN CAMBODIA, JANUARY 2007 - JULY 2012

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Background and Aims: *Streptococcus pneumoniae* is a major international public health problem and is the leading cause of death in children <5 years in developing countries where detection is also problematic. In many countries, pneumococcal conjugate vaccines (PCV) active against 7/10/13 serotypes of *S. pneumoniae* are routinely given to young children and protect against vaccine serotypes causing invasive pneumococcal disease (IPD). We aimed to retrospectively examine the characteristics of IPD in Cambodian children admitted to the Angkor Hospital for Children (AHC), given little data is currently available from Cambodia.
M**ethods:** We retrospectively examined the isolates, clinical features, predisposing factors and outcomes of paediatric patients admitted to AHC between January 2007-July 2012 with confirmed IPD (blood, cerebrospinal fluid [CSF] or other sterile site).
Results: During the study 98 pneumococcal strains were isolated from 92 patients (78 blood cultures, 4 CSF, 10 sterile fluid). Forty-seven percent of patients with IPD were female, the median age of patients was 2.3 years (range 0-14 years, inter quartile range (IQR) 0.1-6.3); 9.2% of patients died (7/76 with outcome data). Isolates were available for 53 patients: seventeen serotypes were detected (the most common were 1, 23F, 14 and 5). Vaccine coverage was 43% (PCV7), 74% (PCV10) and 89% (PCV13). Resistance was: 28% to erythromycin, 30% to chloramphenicol, 60% to co-trimoxazole, 2% to penicillin (MICs, non-meningitis breakpoints), and 0% to ceftriaxone (by CLSI guidelines).
Conclusion: More examination of IPD is needed in Cambodia. Our analysis suggests that PCV13 would be appropriate in this setting.

No conflict of interest

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Global Pneumococcal Disease and Policies for Control

EVALUATING SERIOUS ADVERSE EVENTS FOLLOWING IMMUNIZATION WITH THE 10-VALENT PNEUMOCOCCAL CONJUGATE VACCINE: THE VACCINE ADVERSE EVENTS IN KENYA (VAEIK) STUDY

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Background and Aims: Ten-valent pneumococcal conjugate vaccine (PCV10) was introduced in Kenya in 2011 as a two-dose vial, without preservative. The second dose carried a risk of contamination. We assessed the risk of shock and death following immunization at four sites.
Methods: Subjects were study-site residents aged <1 year who received ≥1 dose of PCV10. Vaccinations were observed at vaccine clinics. Morbidity and mortality data were collected through household and hospital-based surveillance. Shock was defined as ≥2 of lethargy, unconsciousness, convulsions or heart rate >180; impaired perfusion was ≥1 of capillary refill time ≥3 seconds, lower-limb gradient, weak radial-pulse volume or heart rate >180. Deaths were investigated by verbal autopsy. We calculated age-adjusted rate-ratios for a 2-day time lag following vaccination compared to the rest of infancy for 2011-2013 (PCV10) and for 2010 (pentavalent vaccine). We also compared event rates following the first or second vial-aliquot of PCV10.
Results: No admissions with shock occurred within the 2-day lag at any site. In Kilifi, admissions with impaired perfusion were elevated in the two days following PCV10 (age-adjusted rate ratio, aRR, 5.73; 95% CI 3.08-10.6) and following pentavalent vaccine (aRR 7.27; 95% CIs 2.84-18.60). There was no difference between aliquots (aRR 0.62; 95% CI 0.11-3.36). None of eight deaths recorded within 7-days of PCV10 were vaccine-related.
Conclusion: The elevated rate of admission with impaired perfusion is probably attributable to health-provider contact and not specific to vaccination. There was no evidence that introduction of PCV10 increased the risk of shock or death following immunization.

No conflict of interest

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COST-EFFECTIVENESS OF 10- VERSUS 13-VALENT PEDIATRIC PNEUMOCOCCAL CONJUGATE VACCINATION IN THE NETHERLANDS

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Background and Aims: The introduction of a seven-valent pneumococcal conjugate vaccine (PCV7) had profound public health impacts across the globe. PCV7 vaccination in a national immunization program (NIP) is generally considered cost-effective and potentially cost-saving. Two new PCVs have been launched, a ten-valent vaccine (PCV10) and a thirteen-valent vaccine (PCV13). This paper examines the public health and economic impacts of pediatric NIPs of PCV10 and PCV13 in the Netherlands.
Methods: A decision-analytic model was used to estimate the impact of PCV10 and PCV13 on reducing cases of invasive pneumococcal disease (IPD), pneumonia (PNE), and acute otitis media (AOM), using recent country-specific incidence, serotype coverage, disease sequelae, mortality, vaccine effectiveness, indirect effects, costs, and utilities. Direct effects for PCV13- and PCV10-covered serotypes were assumed similar to PCV7. PCV13 was assumed to confer an indirect effect, similar to PCV7, while PCV10 was not. Assumptions were tested in various scenario analyses.
Results: Compared to PCV10, PCV13 is predicted to prevent more disease (IPD, PNE, and AOM cases avoided) and deaths, and increase Life Years Gained and Quality Adjusted Life Years gained. When assuming similar vaccine prices PCV13 is also expected to have substantial cost-savings compared to PCV10.
Conclusion: In this analysis, a NIP with PCV13 was found to save costs compared with PCV10 while preventing additional cases of disease among children and non-vaccinated individuals, in the Netherlands.

Conflict of interest

ISPPD-0190
Global Pneumococcal Disease and Policies for Control

COVERAGE, COMPLIANCE AND ASSOCIATED RISK FACTORS OF PNEUMOCOCCAL CONJUGATE VACCINE SHORTLY AFTER ITS INTRODUCTION IN A BRAZILIAN DEVELOPED MUNICIPALITY

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Objectives: 10-valent pneumococcal conjugate vaccine (PCV10) was introduced into the immunization routine program of Brazil in 2010, with three schedules: 3+1, 2+1, and single dose (≥12 mo). This study aimed to investigate coverage and compliance six to eight months after the introduction of PCV10 into childhood vaccination at Goiania (~1,300,000 inhabs), a municipality where both routine immunization and vaccination campaign have been used.
Methods: A household survey was conducted from December 2010 through February 2011. A systematic sampling was used to enroll 1,237 children aged 7-11 months (*n* = 647), and 15-18 months (*n* = 590). Vaccination status was retrieved from immunization cards. A questionnaire on socioeconomic characteristics was applied to assess variables associated with vaccination coverage (number of children who received all recommended doses) and compliance (number of children who received all doses without any delay).
Results: Vaccination coverage was 53.4% (95%CI 50.7–56.2%), ranging from 88.3% (≥12 mo) to 39.3% (7-11 mo). Compliance with the recommended schedule was 16.6% (95%CI 14.6–18.7%), with variations of 18.8% (≤6 mo), 6.0% (7-11 mo), and 35.6% (≥12 mo). Variables independently associated with not being completely vaccinated (coverage) were mother's lower schooling (odds Ratio/OR=1.68; 95%CI 1.08–2.61), and ≥3 household children (OR=2.06; 95%CI 1.09–3.91). Variables independently associated with noncompliance were mother's lower schooling (OR=1.67; 95%CI 1.12–2.50), and not having private health insurance (OR=1.46; 95%CI 1.03–2.07).
Conclusion: Immunization program must focus on initiatives that might increase 'complete and on time' vaccination rates, especially for children in catch-up schedules and those in the lowest socioeconomic strata.
Financial support: CNPq, IATS, FUNAPE-GO.

No conflict of interest

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REDUCTION IN ALL-CAUSE OTITIS-RELATED OUTPATIENT VISITS IN CHILDREN AFTER PCV10 INTRODUCTION IN BRAZIL

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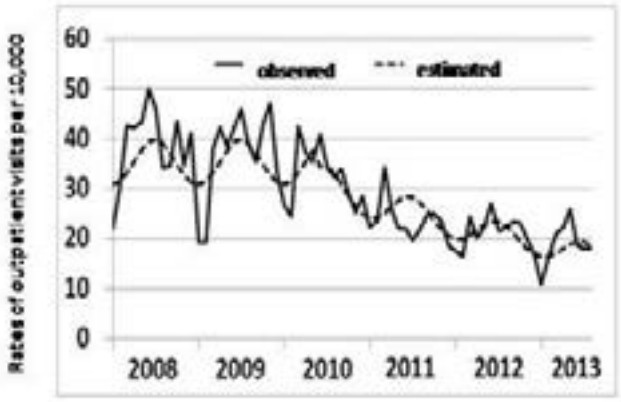
Background and Aims: Acute otitis media (AOM) is the most common cause of pediatric outpatient visits. *Streptococcus pneumoniae* is one of the leading bacterial pathogens causing AOM. We assessed the impact of PCV10 in outpatient visits for all-cause otitis in children.
Methods: We used individual-level secondary data from outpatient Electronic Medical Records of patients covered by the Public healthcare system in Goiania, Brazil, which covers 63% of all pediatric visits. Study period was January 2008-August 2013. All children aged 2-23 months with diagnosis of all-cause otitis (ICD-10 codes: H65-H67) were identified. Rates of overall and all-cause otitis outpatient visits per 10,000 children were calculated, considering monthly population estimates from 2000 and 2010 census. PCV10 was introduced in June 2010, being the intervention evaluated. Rates of outpatient visits due to other causes, except respiratory, ear and mastoid diseases, were the comparator. A time-series analysis was conducted fitting a Prais-Winsten autoregressive model, adjusted for monthly, random and seasonal variations.
Results: During the study period 456,153 outpatient visits among children aged 2-23mo were identified, of which 6,177 (1.4%) were due to all-cause otitis, and 241,379 (52.9%) to other causes. Time-series analysis indicated a monthly average rate reduction for all-cause otitis of 1.58% (95%CI: 0.41%-2.73%; p=0.009) after vaccination (Figure 1), whereas the monthly rate of outpatient visits due to other causes increased by 0.51% (95%CI: 0.06%-0.95%; p=0.026).
Conclusion: Three years after the introduction of PCV10 in Goiania, a significant reduction in rates of outpatient visits due to all-cause otitis was observed in children aged 2-23 months.

Figure 1 – Observed and estimated monthly rates of outpatient visits for all-cause otitis (ICD-10 codes: H65-H67) among children aged 2-23 months by time-series analysis, Goiania, Brazil, January 2008-August 2013.



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Conflict of interest

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OTITIS MEDIA RELATED HEARING IMPAIRMENT IN INDONESIAN SCHOOL CHILDREN

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Background and Aim: We investigated the impact of otitis media (OM) and its sequelae on hearing impairment in Indonesian school children.
Methods: This was a prospective epidemiological survey in a sample of 7005 public school children (6-15 years) from urban and rural subdistricts, in 6 locations on 5 islands in Indonesia. Children had otoscopic and hearing screening tests. Those with abnormalities on either, had diagnostic audiometry and tympanometry performed.
Results: The overall rate of hearing impairment (HI) in the school children was 167/10,000. OM was detected in 172 children (2.5%), consisting of acute otitis media (AOM) (17%), otitis media with effusion (OME) (15%) and chronic suppurative otitis media (CSOM) (67%). Among children with ear disease, 41% had mild and moderate conductive HI, mostly bilateral. OME resulted mostly in mild HI(9/11; 81%), while CSOM resulted mostly moderate HI(26/41;63%), a significant difference (P= 0.01). HI was disabling in 31/56 children, mostly (26/31) due to CSOM. Of the better ear hearing there was a significantly higher rate of OM related HI in rural (113.3/10,000), than in urban areas (48/10,000), p = 0.002. In rural areas this was mostly due to CSOM 96/10,000 whereas in urban areas AOM and OME contributed to about ½ of the HI.
Conclusion: Otitis media or its sequelae contributed to the cause of almost two thirds of all HI in Indonesian school children. CSOM was associated with about 50% of the HI in urban children and 85% in rural school children. Prevention of CSOM could potentially prevent a significant burden of HI in Indonesian school children.

No conflict of interest

ISPPD-0500
Global Pneumococcal Disease and Policies for Control

OTITIS MEDIA RELATED HEARING IMPAIRMENT IN KENYAN CHILDREN

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Background: We investigated the impact of otitis media (OM) and its sequelae on hearing impairment in Kenyan children.
Methods: This was a prospective study of 13,109 school and preschool children aged 2-15 years in 9 regions in Kenya. All children had a history, otoscopic examination and a hearing screen test. Children with otoscopic abnormalities or who failed the hearing screen underwent diagnostic audiometry and tympanometry.
Results: The prevalence of hearing impairment (HI) was 1032/10,000, with no difference between rural and urban areas. OM was detected in 487 children (3.7%), acute otitis media (AOM) (80, 16%), otitis media with effusion (OME) (189, 39%), Retractions (15, 3%), and chronic suppurative otitis media (CSOM) (203, 42%). Among children with OM, 61% had mild and moderate conductive HI, mostly bilateral. OME accounted for most of the mild HI, while CSOM accounted for most of the moderate HI, = 0.0024. In 51 cases (0.4%), the HI was disabling, 69% due to CSOM. Of the worse ear hearing levels, the rates/10,000 urban and rural children for HI due to AOM were 24 and 36; OME were 116 and 101; and for CSOM were 161 and 133 respectively. The rate of disabling HI associated with CSOM in urban and rural children were 113/10,000 and 84/10,000 respectively. There was an increasing incidence of disabling HI in those with CSOM from 35% in those <6 to 65% in those 14 years of age (p = 0.028).
Conclusion: CSOM results in a significant burden of hearing impairment in Kenyan school children, and its early prevention might mitigate some of this burden.

No conflict of interest

ISPPD-0561
Global Pneumococcal Disease and Policies for Control

HIGH COST IS THE PRIMARY BARRIER REPORTED BY PEDIATRICIANS WHO PRESCRIBE PNEUMOCOCCAL VACCINE IN INDIA

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Background: Pneumococcal conjugate vaccine (PCV) is not included in India's Universal Immunization Program (UIP) but is available on the private market and is recommended by the Indian Academy of Pediatrics (IAP).
Methods: A random selection of IAP member pediatricians was surveyed regarding their practices for administering PCV. Half were assigned to complete the survey over the telephone with a study coordinator and half were emailed the survey to complete at their discretion. Sample size was calculated to give proportions with ±5% confidence intervals, assuming a 50% response rate.
Results: Response rates differed significantly, with 59/382 (15%) completing the survey by email and 275/382 (72%) by telephone, for an overall response rate of 44%. 73% of pediatricians administer PCV to some patients, but only 7% administer to all patients. The most common reason for not prescribing PCV was that it is too expensive (94%). Other reasons included: unsure of vaccine efficacy (10%), unsure risk of disease warrants it (5%), unsure of vaccine safety (2%), concerns about serotype coverage (1%). Results differed by type of practice. Pediatricians at government health centers were the least likely to administer PCV. 88% of pediatricians have their own children vaccinated or recommend PCV to close friends, and 83% would like to see it included in the UIP.
Conclusion: There is support for the use of PCV by IAP member pediatricians, with a majority already prescribing the vaccine to some patients. High cost is the most commonly reported barrier to universal access.

No conflict of interest

ISPPD-0471
Global Pneumococcal Disease and Policies for Control

THE COSTS ASSOCIATED WITH PNEUMOCOCCAL DISEASES IN THE GAMBIA

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Background: The Gambia introduced the pneumococcal conjugate vaccine (PCV) into EPI in 2009. The introduction is expected to lower the significant economic burden of pneumococcal disease.
Aim: To estimate the costs associated with pneumococcal diseases in the Gambia.
Method: We recruited children under 5 years with pneumococcal meningitis, sepsis and pneumonia at outpatient (OP) and inpatient (IP) facilities from rural and urban Gambia.
For each diagnostic category we estimated the societal costs to the health system (patient specific costs and bed day costs) and out-of-pocket costs (OOP) before, during, and one week after discharge from hospital/OP visit.
Results: A total of 340 children were enrolled; 29 meningitis, 36 sepsis, 175 inpatient and 100 outpatient pneumonia (21, 32, 94 and 50 respectively from rural Gambia). Mean provider costs per case for treating OP, IP, pneumococcal sepsis and meningitis were US$8, US$64, US$87 and US$124 respectively. The average family's OOP per case for OP, IP, sepsis, and meningitis in the rural area were US$2, US$20, US$44 and US$31 respectively, and US$10, US$44 US$41 and US$60 in the urban setting. The economic burden of inpatient pneumonia, pneumococcal sepsis and meningitis increased to US$722, US$407 and US$688 respectively when time loss from work by family was taken into account.
Conclusion: The economic burden of pneumococcal disease in The Gambia is substantial, with high disease annual incidence before PCV introduction of 500/100,000 in infants and 200/100,000 in children under 5 years. Prevention by PCV promises to be cost-effective and potentially cost-saving.

Conflict of interest

ISPPD-0433
Global Pneumococcal Disease and Policies for Control

SEROTYPE DISTRIBUTION, ANTIMICROBIAL RESISTANCE AND EXPECTED VACCINE COVERAGE FOR INVASIVE PNEUMOCOCCAL DISEASE IN INDIAN ADULTS

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Background and Aim: *Streptococcus pneumoniae* infections in adults are associated with substantial morbidity, mortality, and costs. Pneumococcal infections in adults for the most part underestimated especially in low and middle income countries. Pneumococcal polysaccharide vaccines (PPV-23) are available to prevent penumococcal infections. Despite its controversies it is in routine use for adults in most developed countries. Developing countries will need pneumococcal disease burden and serotype prevalence data in adults for implementing PPV-23 for routine

use. Here we present the pneumococcal serotype data for adults generated over a period of two decades and aim to estimate the expected protective coverage of available vaccines
Materials and Methods: Invasive *S. pneumoniae* isolates from more than six years of age group was included in this study. Isolates were serotyped with co-agglutination technique. Antibiotic susceptibility profile for the isolates were determined by vitek system 2
Results: The most common serogroup/types in India causing invasive bacterial infections in adults are 1, 19, 6, 3 and 5. 93% of the isolates were non-susceptible to co-trimoxazole, and 20% of the isolates were non-susceptible to erythromycin. 8% of the isolates were non-susceptible to penicillin and only 4% of the isolates were non-susceptible to cefotaxime
Conclusion: PCV-13 vaccine can protect 62% of the isolates causing invasive pneumococcal infections. PPV-23 can provide better coverage with 72% coverage for IPD in Indian adults. Routine use of PPV-23 can reduce a substantial limit of pneumococcal diseases in Indian adults

No conflict of interest

ISPPD-0518
Global Pneumococcal Disease and Policies for Control

ARGENTINAS EXPERIENCE 2 YEARS AFTER UNIVERSAL PCV 13 INTRODUCTION: THE IMPORTANCE OF A NATIONAL EPIDEMIOLOGICAL SURVEILLANCE SYSTEM TO MONITORING A VACCINATION STRATEGY

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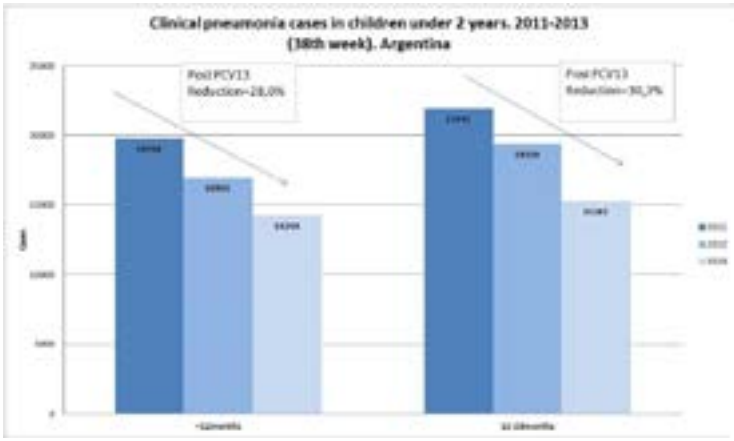
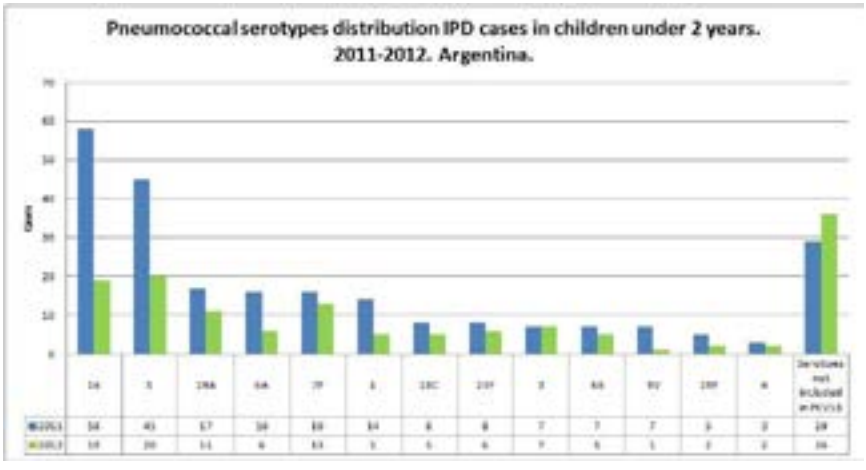
Introduction: Argentina introduced routine immunization with PCV13 in January 2012 for children <1 year (2+1 schedule) and catch-up between 12-24 months. National Epidemiological Surveillance System was used to monitor the evolution of the strategy.
Objectives: Describe evolution of clinical pneumonia, pneumococcal pneumonia/meningitis and identify pneumococcal serotypes of invasive pneumococcal disease (IPD) in children under 2 years old pre and post PCV13 introduction.
Methods: Prospective epidemiological surveillance data of clinical pneumonia were used to compare 2011, 2012, 2013 (1-38th week). We compared pneumoccocal serotype distribution from 2011 and 2012.
Results: Clinical pneumonia was reduced 28.06% (95%IC 26.49-29.59%; $p < 0.001$) in children <12months and 30.34% (95CI% 28.88-31.76%; $p < 0.001$) in children 13-23 months. Cases of pneumococcal pneumonia declined 47% (2011:102;2012:55) and meningitis 39% (2011:61;2012:37). IPD cases declined 42% (2011:162;2012:92). 33 serotypes were identified from IPD. PCV13 serotypes declined from 87.9% to 73.9% ($p < 0.001$). Serotype 14 reduced from 24.1% to 13.7% ($p = 0.01$) and not PCV13 serotypes increased from 12.1% to 26.1% ($p < 0.001$).





Conclusion: We observed a decline in clinical pneumonia, pneumococcal pneumonia and meningitis in children under 24 months, pneumonia showed greater reduction. PCV13 serotypes were reduced (mainly serotype 14) and not PCV13 serotypes which increased. These preliminary data is from National Epidemiological Surveillance and should strengthen the need to monitor the strategy.

No conflict of interest

ISPPD-0517
Global Pneumococcal Disease and Policies for Control

UNIVERSAL VACCINATION WITH PCV13 IN ARGENTINA: TIME SERIES ANALYSIS 2008-2013 OF BACTERIAL PNEUMONIA ADMISSIONS IN CHILDREN UNDER 5 YEARS OLD

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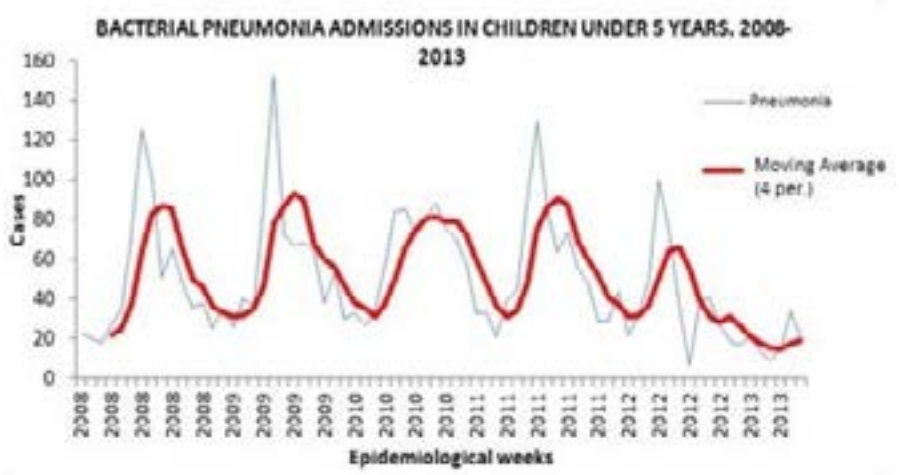
Introduction: Argentina introduced PCV13 into National Immunization Programme in 2012 for healthy children <1 year with 2 + 1 schedule and catch-up between 12-24 months. Sentinel pneumococcal surveillance units (SU) started in the same year in 7 hospitals to assess the impact of this strategy.
Objectives: Describe the evolution of bacterial pneumonia hospitalizations pre and post PCV13 introduction and describe confirmed cases of *Streptococcus pneumoniae* isolated after vaccine introduction.
Methods: Retrospective (2008-2011) and prospective (2012-2013) data of probably bacterial pneumonia under 5 years according to clinical and XRay were analyzed in 2 of 7 SU. Time-series were performed calculating moving averages (range= 4). Invasive pneumococcal disease (IPD) prospective data (2012-2013) were analyzed in 3 SU.
Results: There was a 41.3% reduction (95% CI 15.7-66.9%, p <0.001) of monthly admissions for pneumonia.



Sentinel surveillance between Jul/2012-Jun/2013 confirmed 32 IPD cases. 19 pneumonia with effusion; 9 pneumonia: 2 meningitis and 2 bacteriemia. Lethality: 3.3%(1/32). 11 patients had history of PCV 13 immunization; 4 isolations included in PCV13.

Serotype	History of immunization with PCV13			Total
	1 dose	2 doses	3 doses	
In Study	1	1	1	3
Non-typeable	-	1	1	2
11A	-	1	-	1
16-36-37	1	-	-	1
19A	-	-	1	1
3	1	-	-	1
7F	-	-	1	1
9V	-	1	-	1
Total	3	4	4	11

Conclusion: There was a significant reduction in hospitalizations for pneumonia. To assess impact of the vaccine, it is necessary to continue with epidemiological and laboratory surveillance in children.

No conflict of interest

ISPPD-0438
Global Pneumococcal Disease and Policies for Control

PNEUMOCOCCAL VACCINATION COVERAGE IN MEDICAID-ENROLLED ADULTS WITH HIGH-RISK CONDITIONS IN THE UNITED STATES

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Background and Aims: Pneumococcal vaccination is recommended for adults younger than 65 with high-risk conditions (HRCs) in the U.S. and many other countries. However, there are limited pneumococcal vaccination coverage data in these high-risk adults, especially those enrolled in Medicaid, the insurance program for low-income and disabled people. This study aimed to examine pneumococcal vaccination coverage and associated factors in the U.S. Medicaid population with HRCs.
Methods: This retrospective observational cohort study included adults aged 19-64 years with newly diagnosed HRCs from 2007-2010, and with continuous enrollment ≥3 years in the U.S. Medicaid database. Descriptive and regression analyses were applied to examine pneumococcal vaccination coverage and time to pneumococcal vaccination from initial diagnosis to the end of enrollment or 2011.
Results: Overall pneumococcal vaccination coverage was 6.2% among 57,089 Medicaid-enrollees with HRCs. Coverage was highest in patients with HIV/AIDS (25.0%), followed by chronic renal disease (7.6%), chronic lung disease (6.8%), diabetes (6.5%), chronic heart disease (5.7%), asplenia (5.4%), chronic liver disease (5.3%), cochlear implant (5.2%), cancer (4.2%), transplant (3.7%), and alcoholism (3.4%). Average time to vaccination was 524 days, ranging from 295 days for HIV/AIDS to 582 days for chronic heart disease. Multivariable logistic regression showed that older age, more healthcare encounters, more chronic medical conditions, influenza vaccination, chronic renal disease, chronic lung disease, diabetes, and HIV were significant predictors of receiving pneumococcal vaccination (all $p<0.001$).
Conclusion: Pneumococcal vaccination coverage remains low among Medicaid-enrolled adults with HRCs. Findings highlight the unmet medical need of pneumococcal vaccination in this vulnerable population.

Conflict of interest

ISPPD-0440
Global Pneumococcal Disease and Policies for Control

PNEUMOCOCCAL VACCINATION COVERAGE IN THE ELDERLY IN THE UNITED STATES

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Background and Aims: The U.S. Advisory Committee on Immunization Practices recommends all adults 65 years and older should receive pneumococcal vaccination. Yet there are limited real-world data on the timing of when older adults receive pneumococcal vaccination. This study aimed to examine pneumococcal vaccination coverage and factors associated with receiving pneumococcal vaccination in a large U.S. managed care elderly population.
Methods: This retrospective observational cohort study included adults who turned 65 years old in 2007 and with continuous enrollment from 2007-2012 in a large administrative claims database. Applying descriptive and regression analyses, the study population were followed from age 65 to 70 to examine their pneumococcal vaccination coverage.
Results: Among 56,983 adults who turned 65 years old in 2007, 16.5% received pneumococcal vaccination between ages 65-70. Of those vaccinated, pneumococcal vaccination coverage was highest when patients were 65 years old (23.7%), followed by 66 (19.2%), 70 (16.3%), 69 (14.7%), 67 (14.1%), 68 (12.1%) years of age. The majority were vaccinated in the physician's office (92.4%). There were no significant sociodemographic and health status differences between vaccinated and non-vaccinated adults. Multivariable logistic regression analysis showed that increased number of healthcare encounters and types of health plans were significant predictors of receiving pneumococcal vaccination (all $p<0.01$).
Conclusion: Findings suggest sub-optimal pneumococcal vaccination coverage in older adults between 65 and 70 years of age in the U.S.. Better interventions to improve pneumococcal vaccination as the elderly enter the recommended age range for vaccination are warranted.

Conflict of interest