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Review

Dosing regimen of the 23-valent pneumococcal vaccination: A systematic review

Chelsea A. Caya[a], Constantina Boikos[a], Shalini Desai[b], Caroline Quach[a,c,d,e,*]

[a] Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montreal, QC, Canada
[b] Division of Vaccine Preventable Diseases, Public Health Agency of Canada, Ottawa, ON, Canada
[c] Department of Pediatrics, Division of Infectious Diseases, The Montreal Children's Hospital, McGill University, Montreal, QC, Canada
[d] Quebec Institute of Public Health, Montreal, QC, Canada
[e] McGill University Health Centre, Vaccine Study Centre, Research Institute of the MUHC, Montreal, QC, Canada

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ABSTRACT

Background: Currently, one lifetime booster of a 23-valent pneumococcal polysaccharide vaccine (PPV23) is recommended for those at highest risk of invasive pneumococcal disease (IPD) 3–5 years after initial vaccination. Due to a lack of evidence on multiple revaccinations, recommendations on repeat revaccination do not exist. We aimed to determine the optimal dose and timing of PPV23 booster in high-risk groups.
Methods: We searched Google Scholar, Cochrane, EMBASE, Classic EMBASE, and PubMed for articles published in English and French using the MeSH terms pneumococcal infection, invasive pneumococcal disease, pneumonia, pneumo23, pneumovax 23, PPV23, and 23-valent. Articles were included if they examined dosing regimens of PPV23 (i.e., PPV23 priming and boosting) in adult populations, pediatric populations or both. Two authors independently assessed all titles and abstracts. All potentially relevant articles were chosen by consensus and retrieved for full text review. Two authors independently conducted the inclusion assessment.
Results: Database searches resulted in a total of 1233 articles. The review by title and abstracts resulted in the exclusion of 1170 articles, 53 articles were fully reviewed, 2 articles were identified using Google Scholar and 12 articles were finally included. The majority of evidence consistently indicated an increase in antibody response following PPV23 revaccination in both adult and pediatric populations. Evidence on multiple revaccinations was limited and mixed. Revaccination with PPV23 was well tolerated.
Conclusion: The majority of evidence reviewed supports PPV23 revaccination in both adult and pediatric populations. However, data on multiple booster PPV23 vaccinations in these populations is needed.

1. Introduction

Streptococcus pneumoniae (pneumococcus) is responsible for substantial morbidity and mortality worldwide and is a leading cause of vaccine preventable illness in Canada and the U.S. [1,2]. Groups at particularly high risk of invasive pneumococcal diseases (IPD) include young children, the elderly, and those with chronic health conditions that can be subdivided in individuals with immunosuppression – from the disease itself or due to administered treatments – and other chronic conditions, such as hemoglobinopathies (i.e. sickle cell disease), asplenia, chronic kidney or liver disease, chronic cardiac or pulmonary disease, including asthma, chronic cerebrospinal fluid leaks, cochlear implants, chronic neurologic conditions that may impair clearance of oral secretions and diabetes [3,4]. Vaccination with one dose of PPV23 has been recommended in Canada to reduce the burden of IPD in all adults 65 years of age or older and following pneumococcal conjugated vaccine for all children with chronic conditions over two years of age that are at high-risk for IPD and for immunocompromised adults [1,5]. Numerous studies have found, however, that antibody responses and possibly the associated clinical protection conferred by PPV23 decline over time [6–9]. Further,

Abbreviations: ACIP, Advisory Committee on Immunization Practices; CAP, Community-acquired pneumonia; CI, Confidence interval; GMC, geometric mean concentrations; GMT, geometric mean titers; IPD, invasive pneumococcal disease; NACI, National Advisory Committee on Immunization; OPK, opsonophagocytic killing; PPV23, 23-valent-pneumococcal-polysaccharide vaccine; RCT, randomized controlled trial.

* Corresponding author at: The Montreal Children's Hospital, C1242-2300 Tupper Street, Montreal, QC, Canada H3H 1P3. Tel.: +1 514 412 4485; fax: +1 514 412 4494..
E-mail address: caroline.quach@mcgill.ca (C. Quach).

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concerns regarding possible immunological hyporesponsiveness following PPV23 revaccination, as was seen following revaccination with certain meningococcal polysaccharide vaccines [10], have also been raised. Currently in Canada, one lifetime booster of PPV23 is recommended for individuals at highest risk of IPD (i.e., immunosuppressed individuals). Revaccination with PPV23 is recommended 5 years following initial vaccination if, at the time of primary PPV23 vaccination, the individual was 11 years or older. For individuals 10 years or younger at the time of initial PPV23 vaccination, a single revaccination 3 years later is recommended. A recent study showed that when PPV23 was administered in the previous 5 years, it had a vaccine effectiveness of 49% (95%CI 29–84%) in preventing overall pneumococcal community-acquired pneumonia [11]. However, due to a lack of evidence, multiple PPV23 revaccinations are currently not recommended in Canada [1].

Similarly, the American Committee on Immunization Practices (ACIP) does not recommend multiple revaccinations "because of insufficient data regarding clinical benefit, particularly the degree and duration or protection, and safety" [12], for individuals other than those aged 19–64 years with functional or anatomic asplenia and for persons with immunocompromising conditions. The American Academy of Pediatrics recommends an additional dose of PPV23 "no earlier than 3 to 5 years after the initial dose [of PPV23]" [13]. A Belgian Consensus Report on pneumococcal vaccination recommended revaccination with PPV23 after 3–5 years for patients at highest risk, such as those with functional asplenia or splenectomy and after 5 to 7 years for patients with other underlying conditions. It was also recommended to revaccinate elderly patients once after the age of 65 years, 5 to 7 years after the previous dose [14]. Likewise, the WHO suggests one single revaccination 5 years or more after a first vaccination with PPV23 [15].

To date, no review of the dosing regimen of the PPV23 vaccine has been conducted. Furthermore, no review has yet examined whether the time interval between booster doses of PPV23 in young pediatric populations (2–10 years of age) differs relative to older pediatric populations (>10 years of age). Given recent evidence supporting the waning immunity of PPV23 and a lack of evidence on repeat revaccination, we conducted a systematic review of the literature to determine if an optimal dose and timing of a PPV23 booster for high-risk groups can be established.

2. Methods

2.1. Search strategy

In collaboration with a research librarian, we searched the following three electronic databases: Cochrane, EMBASE, and PubMed for articles published in English and French until June 2013. For the PubMed search, we used the following MeSH headings and text words: pneumococcal infection, invasive pneumococcal disease, pneumonia, pneumo23, pneumovax 23, ppv23, and 23-valent. Analogous searches were conducted in the other two databases searched and in Google Scholar. The full search strategy is detailed in Appendix A.

2.2. Inclusion and exclusion criteria

Articles were included if they were published in either French or English and evaluated a dosing regimen of PPV23 in adult populations, pediatric populations, or both. All study types (randomized controlled trials, case-control studies, cohort studies, and surveillance studies), prospective or retrospective, were included. We limited our study population to adults and children 2 years of age and older given the poor immune response of PPV23 in children <2 years of age [1]. Unpublished studies, studies published in a language other than English or French, studies evaluating a dosing regimen of PPV23 in pediatric populations below 2 years of age and studies evaluating the dosing regimen of PPV23 in combination with other vaccines (i.e., studies not evaluating PPV23–PPV23 dosing) were excluded.

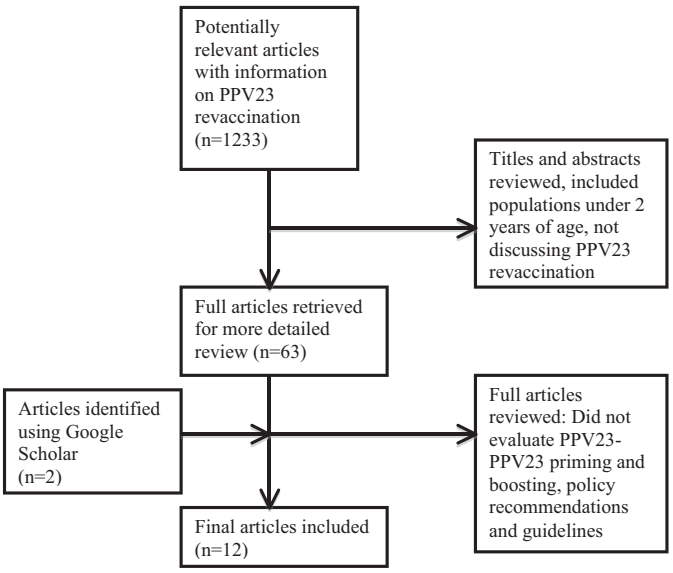

Fig. 1. Description of search and inclusion/exclusion process.

2.3. Assessment of studies

Two authors (CC and CB) independently assessed all titles and abstracts identified by the search strategy described above. All potentially relevant articles were chosen by consensus and were subsequently retrieved as full text and independently assessed for a second time by CC and CB for inclusion. CQ resolved any discrepancies in included articles. All included studies were then independently given a quality ranking by CC and CB based on the ranking system devised by Harris et al. [16] and adapted by the Canadian National Advisory Committee on Immunizations (NACI). The quality ranking system rates the quality of studies across three dimensions labeled as "good", "fair", and "poor" based on the number of methodological flaws present in study design methodology. It was concluded that a meta-analysis of the included studies was not justifiable given that the included studies differed in their primary outcome measures.

3. Results

3.1. Search results

As a result of the combined database searches, a total of 1233 articles were identified (Fig. 1), all of which were reviewed by title and abstract. Following this initial screening, 1170 articles were excluded either because they did not address PPV23–PPV23 regimens exclusively or because they included pediatric populations less than 2 years of age. The remaining 63 articles underwent the full review process by two authors (CC and CB). Fifty-three articles were excluded at the full review stage, as they did not fulfill inclusion criteria previously outlined. Two relevant studies were identified following a literature search of Google Scholar. Twelve articles were included in the final analysis; three are randomized controlled trials (RCT) while the remaining nine are prospective cohort studies (Table 1). One of the 12 studies examined revaccination schedules of PPV23 in asplenic children aged 5 years and older