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Influence of initial vaccination with 13-valent pneumococcal conjugate vaccine or 23-valent pneumococcal polysaccharide vaccine on anti-pneumococcal responses following subsequent pneumococcal vaccination in adults 50 years and older☆

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ABSTRACT

Background: Unlike free polysaccharide vaccines, pneumococcal polysaccharide conjugate vaccines (PCVs) induce a T cell-dependent immune response and have the potential to provide an extended duration of protection with repeated vaccinations.
Methods: This was an extension of a previous study in pneumococcal vaccine-naïve adults aged 50–64 years in which adults 60–64 years of age were given 13-valent PCV (PCV13) or 23-valent pneumococcal polysaccharide vaccine (PPSV23) and adults aged 50–59 were given PCV13. In this follow up study conducted about 4 years later, the 60–64 year olds initially given PCV13 received PCV13 or PPSV23, and those initially given PPSV23 received another PPSV23. All adults aged 50–59 years were re-vaccinated with PCV13. Anti-pneumococcal opsonophagocytic activity (OPA) titers were measured before and 1 month after vaccination.
Results: A second PCV13 given about 4 years after a first vaccination induced OPA titers that were significantly higher than those following the initial vaccination for 7 of 13 serotypes in the older group, and 6 of 13 serotypes in the younger group, and responses to the remaining serotypes were largely non-inferior. In contrast, OPA titers following revaccination with PPSV23 were statistically significantly lower for 9 of the 13 serotypes, and non-inferior for the remaining serotypes, when compared to the responses to the first PPSV23. OPA titers in the older adults who received PPSV23 after initial PCV13 were significantly higher than those following a first PPSV23 for 10 of the 13 serotypes.
Conclusion: In adults 50 to 64 years of age, initial vaccination with PCV13 establishes an immune state that results in recall anti-pneumococcal responses upon subsequent vaccination with either conjugated or free polysaccharide vaccine. In contrast, initial vaccination with PPSV23 results in an immune state in which subsequent PPSV23 administration yields generally lower responses compared with the initial responses.

Abbreviations: ACIP, United States Advisory Committee on Immunization Practices; AE, adverse event; CI, confidence interval; CRM_{197}, cross-reactive material 197; GMR, geometric mean ratio; GMT, geometric mean titer; OPA, opsonophagocytic activity; PCV, pneumococcal polysaccharide conjugate vaccine; PCV13, 13-valent pneumococcal conjugate vaccine; PPSV23, 23-valent polysaccharide vaccine; RCDC, reverse cumulative distribution curve; SAE, serious adverse event.

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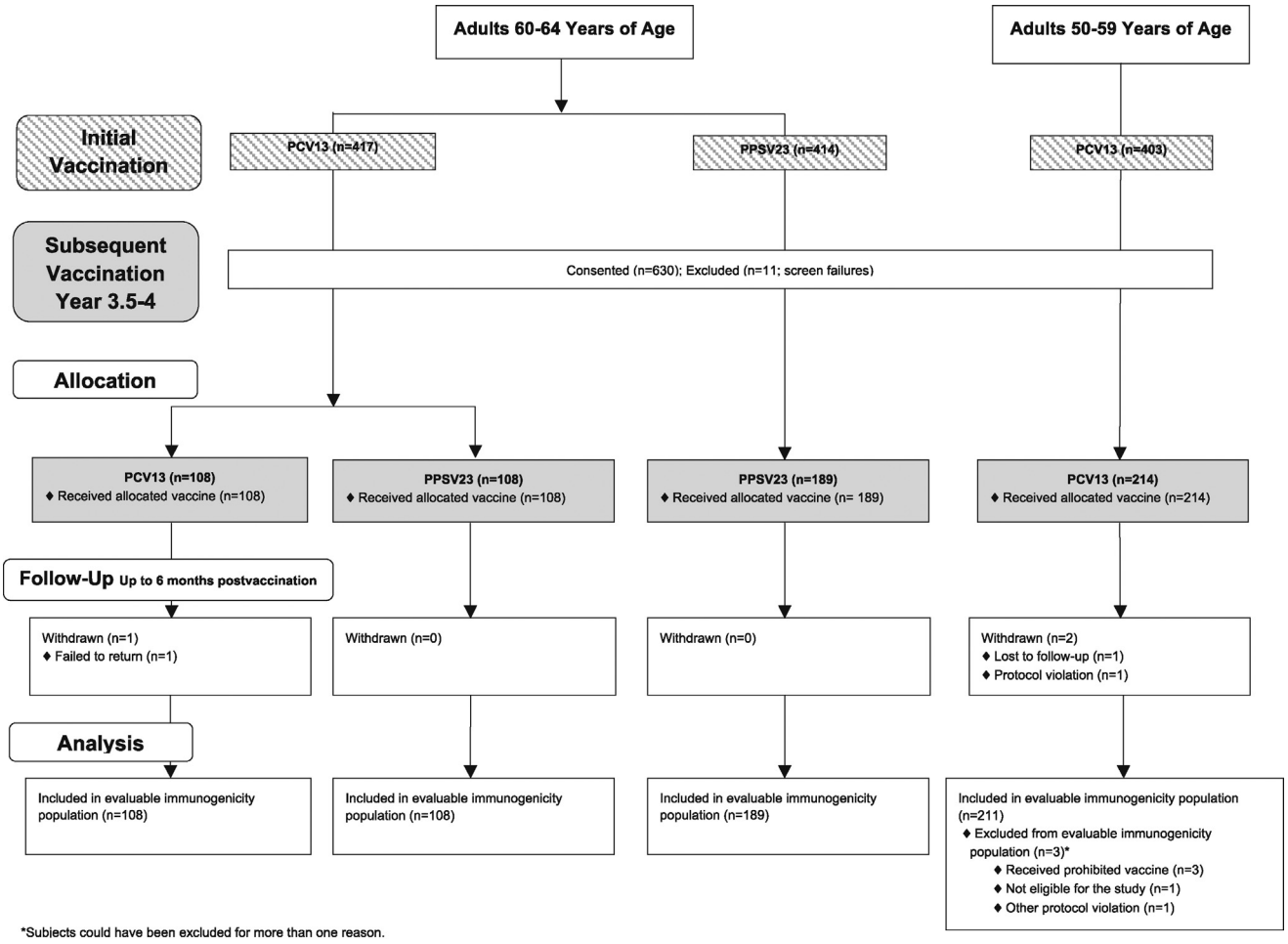

Fig. 1. Study design and disposition of subjects.
Vaccinations received as part of the initial study are shown in the striped boxes [5]. Abbreviations: PCV13, 13-valent pneumococcal conjugate vaccine; PPSV23, 23-valent pneumococcal polysaccharide vaccine.

1. Introduction

The incidence and mortality of pneumococcal disease in adults increase with advancing age [1,2]. A 23-valent pneumococcal vaccine containing free (unconjugated) polysaccharides (PPSV23) has been available for 30 years and a single vaccination is recommended for adults ≥65 years and for younger adults with certain chronic medical conditions or other indications [2]. Revaccination is not routinely indicated in part due to the diminished immune responses that have been observed following revaccination, which may be due to the T cell independent nature of the immune response [2,3]. In contrast to PPSV23, the 13-valent pneumococcal conjugate vaccine (PCV13) was designed to engender T cell-dependent immunity, inducing a recall response on subsequent bacterial exposure or revaccination with the potential to significantly prolong the protection afforded by the vaccine.[4]

A previous clinical study of pneumococcal vaccine-naïve adults 50 through 64 years of age evaluated the functional opsonophagocytic activity (OPA) anti-pneumococcal immune responses elicited by a first vaccination with PCV13 or PPSV23. PCV13 was immunogenic and, in adults 60–64 years of age that were randomized to receive PCV13 or PPSV23, PCV13 elicited significantly higher OPA titers than those elicited by PPSV23 for 9 of 12 serotypes common to both vaccines. Adults 50–59 years of age all received PCV13, and had generally higher OPA titers than observed in adults 60–64 years of age who received PCV13 [5].

This follow-up study was conducted 3.5–4 years after the previous study in order to evaluate the immune responses to a second PCV13 and to a second PPSV23, and to determine the influence of initial PCV13 immunization on the responses to a subsequent PPSV23 vaccination in the adults 60–64 years of age who received PCV13.

2. Methods

2.1. Study design and populations

This was an extension of a previous study in pneumococcal vaccine-naïve adults 50 through 64 years of age, conducted at 23 medical centers in the United States [5]. Both studies were undertaken in accordance with the Declaration of Helsinki and Good Clinical Practice [6,7]. In the initial study, adults 60–64 years of age were randomly assigned with equal probability to receive PCV13 or PPSV23 and those 50–59 years of age received open label PCV13. In this extension study conducted 3.5–4 years after the start of the previous study, informed consent was obtained as for a new study and adults in the 60–64 year old age group who had initially received PCV13 were randomized 1:1 to receive PCV13 or PPSV23, and those who had received PPSV23 received another PPSV23 vaccination. Adults in the 50–59 year old age group received a second PCV13 (Fig. 1).