# Effects of routine infant vaccination with the 7-valent pneumococcal conjugate vaccine on nasopharygeal colonization with streptococcus pneumoniae in children and parents in the Netherlands.

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The aim of the present study is to determine the impact of national PCV-7 implementation on NP pneumococcal carriage in children of 11 and 24 months of age and to evaluate NP colonization of one parent of a 24-month-old child.

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|---|---|
| **Ethische beoordeling** | Positief advies |
| **Status** | Werving gestopt |
| **Type aandoening** | - |
| **Onderzoekstype** | Interventie onderzoek |

## Samenvatting

### ID

NL-OMON23549

**Bron**
NTR

**Verkorte titel**
OKIDOKI-1

**Aandoening**

Prevenar vaccination, Immune system, pneumococcal carriage.

### Ondersteuning

**Primaire sponsor:** Nederlands Vaccin Instituut (NVI)
**Overige ondersteuning:** Nederlands Vaccin Instituut (NVI)

### Onderzoeksproduct en/of interventie

## Uitkomstmaten

### Primaire uitkomstmaten

The percentage of the (the seven) vaccine and non-vaccines pneumococcal serotypes found in the NP swabs from children at 11 and 24 months of age and parents of the 24-month-old children.

# Toelichting onderzoek

### Achtergrond van het onderzoek

Two years ago, in June 2006, the 7-valent pneumococcal conjugate vaccine (PCV-7) was introduced in the Dutch National Infant vaccination Program (NIP) for protection against disease with the vaccine-serotypes 4, 6B, 9V, 14, 18C, 19F and 23F.

Streptococcus pneumoniae (pneumococcus) is the leading cause of invasive pneumococcal disease (IPD) like meningitis and sepsis as well as of respiratory infections like community acquired pneumonia and otitis media, all with the highest disease incidence below two years of age. At present >95% of all two-years old Dutch children have been fully vaccinated against the 7 serotypes included in the current vaccine.

All disease caused by Streptococcus pneumoniae is preceded by asymptomatic nasopharyngeal (NP) colonization. The peak age for colonization and person to person transmission is in the first years of life, which coincides with the peak age for disease. Apart from protection against IPD, the pneumococcal conjugate vaccine also reduces asymptomatic NP colonisation by vaccine-serotype pneumococci. This may account for the large reductions in vaccine-serotype IPD that have been observed in the US also in unvaccinated children and adults following the introduction of PCV-7 in 2000 and suggesting an indirect (herd) effect. The indirect protection by herd effects is presumed to result from decreased transmission rate by vaccinated children and consequently diminished circulation of vaccine-serotypes in the community.

In pre-licensure clinical studies with PCV-vaccinated infants and toddlers, NP colonization of vaccine-serotypes was found decreased compared with unvaccinated controls, but no or only marginal decreases of overall pneumococcal colonization rates were observed due increased colonization of non-vaccine serotypes. In surveys of NP pneumococcal colonization following routine infant PCV-7 vaccinations in the US or Canada in subgroups of healthy or acutely ill children, vaccine-serotypes were found to be reduced but NP colonization of non-vaccine serotypes increased and vaccine-related serogroups persisted or even increased. With regard to IPD monitoring, indeed an increase of non-vaccine serotype IPD has occurred, particularly in adults and in some subpopulations with high susceptibility to IPD, like HIV-positive adults or Alaskan Natives. In Alaskan native adults, following introduction of PCV-7 for children, overall IPD even increased despite a decrease of vaccine-serotype IPD,.This was in line with

the increase of pneumococcal NP colonization by non-vaccine serotypes in adults living with PCV-7 vaccinated children. Next to IPD monitoring in countries where PCV-7 has been introduced, surveys of NP carriage in vaccine recipients and non-vaccinated contacts for indirect effects are considered relevant for monitoring of changes in circulating pneumococcal serotypes and predicting herd effects or future replacement disease by non-vaccine serotypes.

In the Netherlands, PCV-7 was implemented in the NIP at 2, 3, 4 and 11 months of age for all newborns, born after March 31, 2006 and the first vaccinations started in June 2006. The aim of the present study is to determine the impact of national PCV-7 implementation on NP pneumococcal carriage in children of 11 and 24 months of age and to evaluate NP colonization of one parent of a 24-month-old child. The 11 months time point, before the booster PCV-7 vaccination at 11 months of age, is chosen since the incidence of pneumococcal acquisition and IPD is the highest in the period of 4-11 months of age and changes in vaccine- and nonvaccine-serotype proportions at 11 months will result from both direct vaccine effects after the 3 primary PCV-7 doses and potentially also herd effects in the third year after the introduction of routine PCV-7. The time point of 24 months of age will reflect effects of PCV-7 vaccinations one year after the booster vaccination, as well as effects of the child’s maturing immunity and may be influenced by herd effects, all of which may contribute to herd effects in the community. To monitor changes in close adult contacts, NP pneumococcal colonisation of one parent of the 24-month-old children will also be evaluated. Data from the present survey will be compared with unvaccinated control children aged 12 and 24 months and parents from 24-month-old unvaccinated children that were part of a previous study (MINOES) that started in June 2005 before the implementation of PCV-7 in the Dutch NIP (ISRCNTN25571720). Data from 12-month-old children were collected between April - December 2006 and from 24-month-old children and parents between April - December 2007. No herd immunity effects were observed in these periods and these data are considered representative for the pre-PCV-7 era. Next to pneumococcal NP colonization, effects on other common bacterial NP colonisers that are potential disease pathogens will be evaluated (S. aureus, H. influenzae, M. catarrhalis).
This study will provide insight in the impact of PCV-7 in the Dutch NIP with respect to NP colonisation in children and close adult contacts.

## Doel van het onderzoek

The aim of the present study is to determine the impact of national PCV-7 implementation on NP pneumococcal carriage in children of 11 and 24 months of age and to evaluate NP colonization of one parent of a 24-month-old child.

## Onderzoeksopzet

Inclusion 6 months (1-7-2009).

Evaluation 3 months (1-10-2009).

## Onderzoeksproduct en/of interventie

2 groups of children, in both groups a transnasal nasopharyngeal swab will be collected of the children and transnasal and transoral swabs will be taken of the parents.

# Contactpersonen

## Publiek

RIVM
Alienke Wijmenga-Monsuur
Bilthoven 3720 BA
The Netherlands
NA

## Wetenschappelijk

RIVM
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NA

# Deelname eisen

## Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. The children have to be of normal health (same health criteria apply as used in well-baby clinics when a child receives a vaccination, e.g. also children with small increases in temperature or cold are seen as children with normal health);

2. They have to be willing and able to participate in the trial according to procedure;

3. Presence of a signed informed consent (the parents/legally representatives have given written informed consent after receiving oral and written information);

4. The children have received the Prevenar® vaccinations according to the 3+1 schedule of the Dutch NIP;

5. Parents are included when their children fulfil inclusion criteria.

## Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Previous vaccinations with Prevenar® using a schedule that differs from the Dutch 3+1 schedule;

2. Previous vaccinations with other pneumoccocal vaccines;

3. Previous vaccinations of older brother(s) and/or sister(s) and/or parents with a pneumococcal conjugate vaccine (e.g. brother(s) and/or sister(s) that participated in the MINOES trial);

4. Chromosomal abnormalities or craniofacial abnormalities (like Trisomy 21 or schisis), known or suspected immunodeficiency disease or other medical conditions that will severely affect immunological responses to vaccinations or nasopharyngeal carriage rates;

5. Coagulation disorder/anticoagulant medication;

Parents are excluded:

when they have a bleeding disorder/ anticoagulant medication (because of the transnasal swab).

# Onderzoeksopzet

## Opzet

| | |
|---|---|
| Type: | Interventie onderzoek |
| Onderzoeksmodel: | Anders |
| Toewijzing: | Niet-gerandomiseerd |

**Controle:** N.v.t. / onbekend

## Deelname

Nederland

| | |
|---|---|
| Status: | Werving gestopt |
| (Verwachte) startdatum: | 15-12-2008 |
| Aantal proefpersonen: | 660 |

| | |
|---|---|
| Type: | Werkelijke startdatum |

### Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

**Wordt de data na het onderzoek gedeeld:** Nog niet bepaald

## Ethische beoordeling

Positief advies

| | |
|---|---|
| Datum: | 04-12-2008 |
| Soort: | Eerste indiening |

## Registraties

### Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

### Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

### In overige registers

| Register | ID |
|---|---|
| NTR-new | NL1507 |
| NTR-old | NTR1577 |
| Ander register | CCMO08.2611 : NVI-249 |
| ISRCTN | ISRCTN wordt niet meer aangevraagd |

## Resultaten

**Samenvatting resultaten**
N/A