The effect of reduced PCV-7 schedules on pneumococcal carriage in infants and adult contacts: a randomized controlled trial

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Introduction

At present, several countries have implemented a reduced dose PCV-7 schedule (2+1-schedule). The effects of reduced dose schedules on pneumococcal nasopharyngeal carriage in infants and adult contacts have not been evaluated in trials before.

Aim

To establish long term effects of a 2-dose and 2+1-dose PCV-7 schedule on pneumococcal carriage in the first two years of life in infants and adult contacts compared to controls.

Methods

Trial design: randomized, controlled trial in 1003 healthy infants in the Netherlands, from July 2005 until February 2008 (ISRCNTN25571720). Children were randomly assigned to receive PCV-7 at 2 and 4 months of age (2-dose group), PCV-7 at 2, 4 and 11 months (2+1-dose group) or none (control group). Nasopharyngeal swabs were collected from infants at the age of 6 weeks and 6, 12, 18 and 24 months. Transnasal and transoral nasopharyngeal swabs were collected from one of the parents at the infant's age of 12 and 24 months. Parents with a positive transnasal and/or transoral nasopharyngeal swab were considered positive. Parents of twins (n=15 pairs) were excluded.

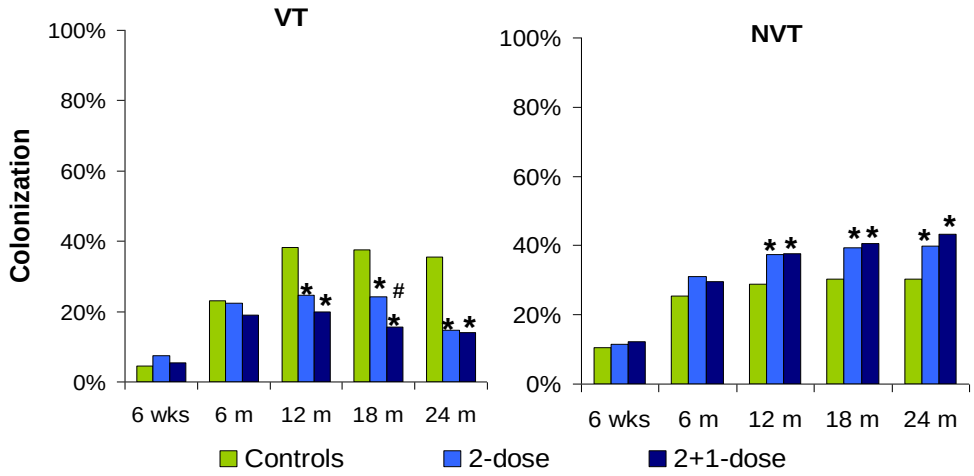
Laboratory methods: nasopharyngeal swabs were cultured for *Streptococcus pneumoniae* (SP) with conventional methods. Serotyping was performed by Quellung reaction.

Statistical methods: The primary endpoint was defined as vaccine type (VT) pneumococcal carriage in infants in the second year of life compared to controls and sample size was calculated hereupon. A Generalized Linear Model taking multiple measurements into account was constructed for the primary outcome. Chi-square or Fisher's exact test were performed where appropriate. All reported p-values are 2-sided.

Results

A total of 4939 swabs were collected in infants (99% of planned) and 3823 in parents (97% of planned). Characteristics did not differ between groups (e.g. sex, age, gestational age, household size, day care attendance).

Figure 1 Decrease of vaccine (VT) and increase of non-vaccine (NVT) serotype pneumococcal carriage in vaccinees compared to controls during follow-up (n=984)



*** p-value < 0.05 versus controls; # p-value < 0.05 versus 2-dose**

Figure 2 Temporarily additional effect of booster dose on reduction of serotype 6B carriage and increase of non-vaccine serotype 19A carriage in PCV-7 vaccinees (n=1003).

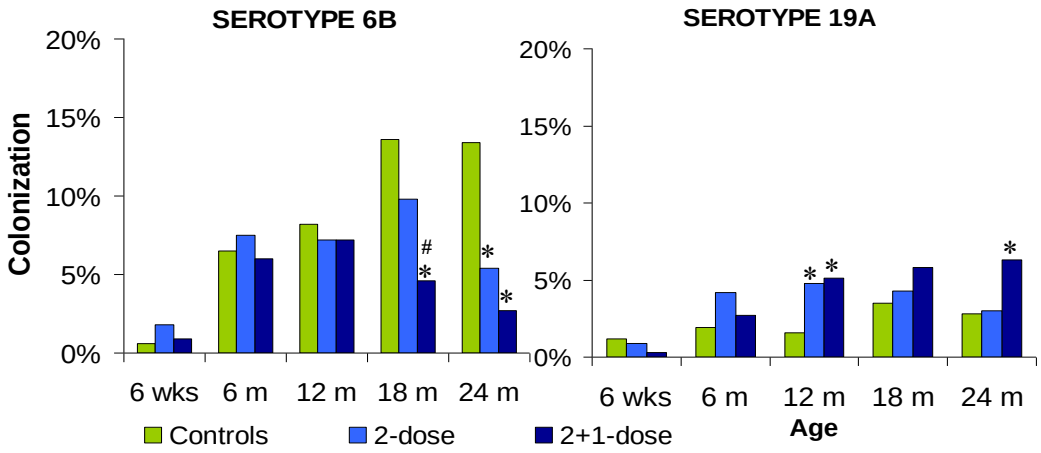
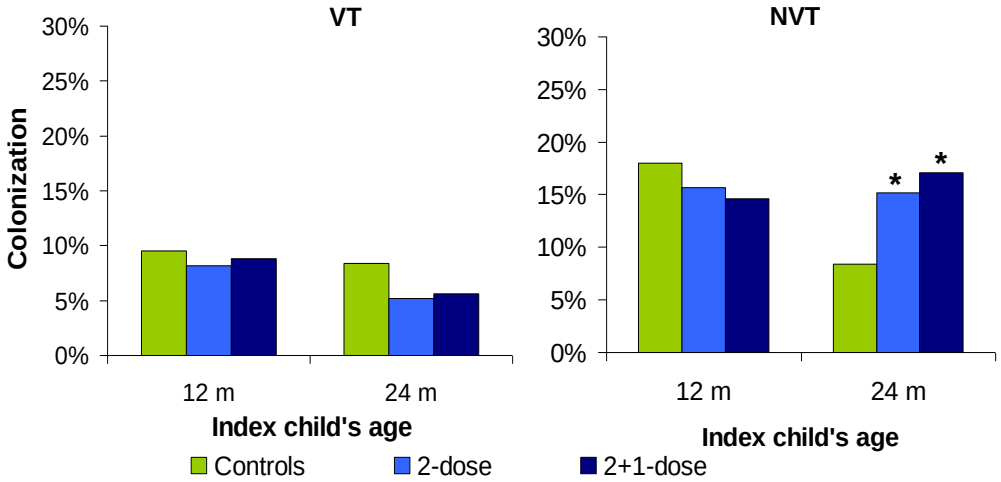


Figure 3 No significant decrease in vaccine serotype (VT) pneumococcal carriage in parents of vaccinees, but a significant increase of non-vaccine (NVT) serotypes compared to controls during follow-up (n=952)



*** p-value < 0.05 versus controls; # p-value < 0.05 versus 2-dose**

Conclusions

Infants

- A 2+1-dose and even a 2-dose PCV-7 schedule significantly reduce VT pneumococcal carriage in infants in the 2nd year of life.
- The booster dose adds to earlier VT carriage reduction in infants, mainly due to earlier reduction of serotype 6B carriage.
- Upon PCV-7 vaccination, a dose-dependent rise in serotype 19A carriage was observed.
- A 2-dose and a 2+1-dose PCV-7 schedule result in significant replacement by non-vaccine serotypes.

Adult contacts

- No significant reduction in VT carriage was observed in parents of vaccinees; this might be due to underpowering.
- Serotype replacement in infants leads to significantly higher NVT-carriage rates in parents of vaccinees.

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