

Effectiveness versus efficacy of conjugated pneumococcal vaccine:

A systematic review of randomized controlled trials with meta-analysis examining absolute risk reduction and relative risk

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Plain English Summary

Numbers Needed to Treat (NNT) is a measure of the effectiveness.

How many children need to be vaccinated so that one life is saved?

How much does it cost to vaccinate one child?

With these one can calculate the cost per life saved.

We did a meta analysis of Pneumococcal vaccine data.

The vaccine has very poor efficacy that the NNT to save one life could not be calculated.

We calculated the NNT to prevent one case of clinical pneumonia (a condition that is usually easily treated with very inexpensive medicines).

There was a small but statistically significant benefit of vaccination on clinical pneumonia (OR=0.927, 95%CI 0.885-0.971, NNT=200), radiological pneumonia (OR=0.749; 95%CI 0.682-0.822, NNT=143) and invasive disease caused by vaccine serotypes (OR=0.215, 95%CI 0.149-0.311, NNT=500).

The small benefit in terms of reduction of clinical pneumonia is also partly offset by an increase in Asthma (0.001, 95% CI 0.000 to 0.002, p=0.007, NNT=1000)

Objectives

- Previous systematic reviews have examined vaccine efficacy in terms of odds ratio and relative risk. However, effectiveness of PCV in reducing childhood morbidity and mortality (in terms of absolute risk reduction (ARR) and numbers needed to treat (NNT)) has not been published.
- At the threshold of introducing the PCV13, such an assessment of the old vaccine is useful for comparison.
- The objective here was to evaluate the effectiveness of PCV through a systematic review of literature.

Methods

Systematic literature search for randomized controlled trials.

Data were analysed to calculate odds ratio, relative risk and absolute risk reduction (ARR); and pooled through meta-analysis. Number needed to treat (vaccinate) was calculated for effectiveness.

Results

There were five methodologically good trials presenting data through 11 publications

Meta-analysis showing efficacy and safety data of Pneumococcal conjugate vaccine

Outcome	RCT	Vaccinated (n)	Control (n)	OR (95% CI), I ²	RR (95% CI), I ²	RD (95% CI), I ²	NNT (95% CI)
Clinical Pneumonia	3	43335	43284	0.927 (0.885, 0.971), 0%	0.940 (0.905, 0.977), 0%	-0.005 (-0.010, 0.001), 41.1%	200 (100, 1000)
Radiological Pneumonia	3	43335	43284	0.749 (0.682, 0.822), 64.7%	0.744 (0.636, 0.870), 64.4%	-0.007 (-0.012, 0.002), 84.9%	143 (83, 500)
IPD (vaccine serotypes)	5	46998	45886	0.215 (0.149, 0.311), 0%	0.158 (0.075, 0.333), 24.0%	-0.002 (-0.004, -0.000), 90.6%	500 (250, -)
IPD (all serotypes)	5	46998	45886	0.395 (0.297, 0.526), 57.7%	0.341 (0.180, 0.645), 62.2%	-0.002 (-0.004, -0.000), 85.7%	500 (250, -)
IPD (Vaccine related serotype)	4	45407	45092	0.838 (0.376, 1.866), 35.8%	0.931 (0.286, 3.027), 25.8%	-0.000 (-0.001, 0.001), 59.1%	**
IPD (Vaccine unrelated serotype)	5	46998	45886	1.199 (0.667, 2.155), 10.3%	1.151 (0.599, 2.210), 5.2%	0.000 (-0.000, +0.000), 100.0%	**
Meningitis	0						
All cause mortality	3	27411	28065	0.88 (0.78-0.99), 0%	0.88 (0.78-0.99), 0%	0.00 (-0.00, 0.00)	**
Pneumococcal disease specific mortality	0						
Adverse Events							
Mortality	4	28753	27618	1.02 (0.53, 1.96), 28.5%	1.02 (0.53, 1.96), 28.4%	0.00 (-0.002, 0.002), 14.8%	
Hospitalization	3	27162	26824	0.910 (0.857, 0.965), 72.3%	0.925 (0.831, 1.031), 77.8%	-0.008 (-0.020, 0.005), 76.2%	125 (50, 200)
Serious adverse events as defined by authors	4	31745	30632	0.987 (0.785, 1.242), 69.9%	1.500 (0.748, 3.006), 67.8%	0.000 (-0.002, 0.003), 73.6%	***
Seizures	2	33810	33804	1.095 (0.721, 1.664), 88.7%	0.957 (0.255, 3.598), 88.2%	0.000 (-0.002, 0.002), 89.2%	***

** NNT cannot be calculated
*** NNT result suggests that vaccination could benefit as well as harm

Conclusions

- PCV has limited effectiveness against pneumonia; but is not effective in reducing all-cause mortality.
- There is significant reduction in invasive Pneumococcal disease caused by vaccine serotypes.
- There is no data to draw conclusions for other clinical problems of public health significance such as meningitis, and Pneumococcal disease specific mortality.
- Thus this systematic review shows that although currently available PCV have fair efficacy, they have limited effectiveness, for clinically relevant outcomes of importance.
- Examination of multiple adverse events did not show a difference in risk compared to control, except for a small but statistically significant increase in risk of asthma.