



Bristol Childrens Vaccine Centre



# PCV in developing countries Give 2+1



*Adam Finn*  
*@adamhfinn*



MRF 5<sup>th</sup> Nov 2019, London

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# Is this your ideal perspective?





B V C  
C C

..or do you prefer to take  
the broader view?



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PCVs have important indirect effects







This is not new...



## **Efficacy of pneumococcal conjugate vaccines and their effect on carriage and antimicrobial resistance**



Keith P Klugman

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Lancet Infectious Diseases 2001

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**Table 1. Effect of conjugate pneumococcal vaccines on the nasopharyngeal carriage of pneumococci**

Country	Type of study and type of vaccine and valency	Doses of vaccine	Age at vaccination (months)/carriage measurement (months after primary series)	Carriage of vaccine serotypes [number (%)] in/vaccinees controls	p value or 95% CI of difference	Carriage of non-vaccine serotypes in vaccinees/controls or relative risk (95% CI)	p value or 95% CI of difference
Gambia <sup>7</sup>	CRM 5*	3	2,3,4/20	13/26 (50)/144/160 (90)	<0.001	20/26 (77)/68/160 (43)	0.0023
Finland <sup>16</sup>	CRM 7†	4	2,4,6,12/12	.. (9.5)/ .. (16.2)	33–55%	.. (11.2)/ .. (7.5)	9–103%
USA <sup>10</sup>	CRM 7†	4	2,4,6,12/1,6,12	61/257(24)/83/234 (36)	0.004	RR1.2 (95 CI 1.1–1.3)	0.004
UK <sup>12</sup>	CRM 7*	3	2,3,4/20–44	17/150(11.2)/17/126(13.5)	NS	20/150 (13)/17/126 (13)	NS
South Africa <sup>8</sup>	CRM 9†	3	1.5,2.5,3-5/5-5	43/242 (18)/87/239 (36)	<0.001	87/242 (36)/58/239 (24)	0.007
Israel <sup>10</sup>	CRM 9†	1 or 2	12–35/>1	161/973(17)/264/971(27)	0.001	368/973(38)/274/971(28)	0.001
Israel <sup>9</sup>	OMP 7†	1 or 2	12,15,18/12	17/135 (13)/14/57 (25)	0.065	48/135 (36)/18/57 (32)	NS
Israel <sup>17</sup>	D4 or T4†	3	2,4,6/1,6,7	10/134 (7.5)/19/70 (27)	..	.. (17–47)/ .. (16–22)	NS
Iceland <sup>18</sup>	D8 or T8*	3 or 4	3,4,6,12/>1	.. (26)/ .. (40)	0.0003	Not stated	..
Israel <sup>19</sup>	DT 11*	4	2,4,6,12/12	22/141 (16)/18/57 (32)	0.019	41/141 (29)/16/157 (28)	NS

CRM=CRM<sub>19F</sub>, conjugate, D=diphtheria toxoid conjugate, NS=not significant, T=tetanus toxoid conjugate, OMP=outer membrane protein complex of *Neisseria meningitidis* serogroup B. \*Case-control study, †randomised study.





# Salivary antibody responses

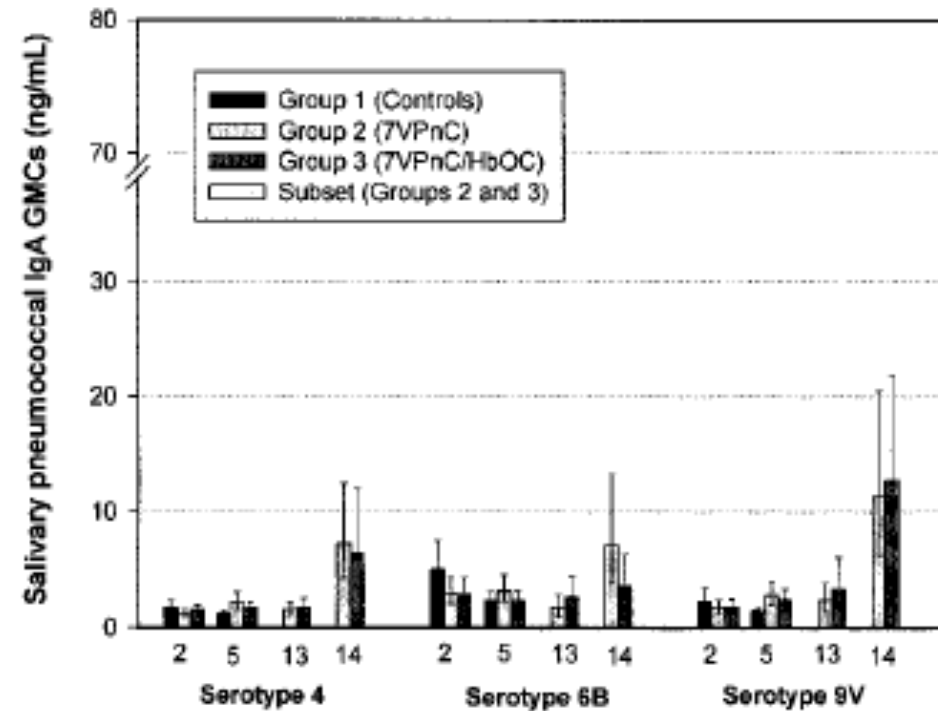
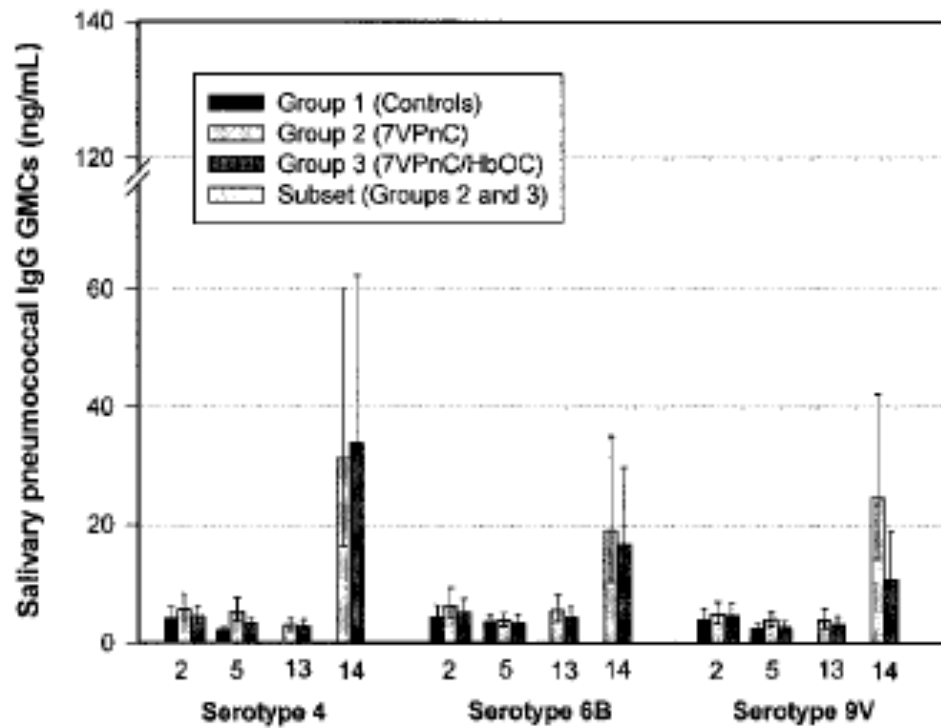


Figure 2. Salivary anticapsular IgG antibody geometri

Figure 1. Salivary anticapsular IgA antibody geometri



Choo et al. JID 2000 182





# Functional antibody after priming wanes..

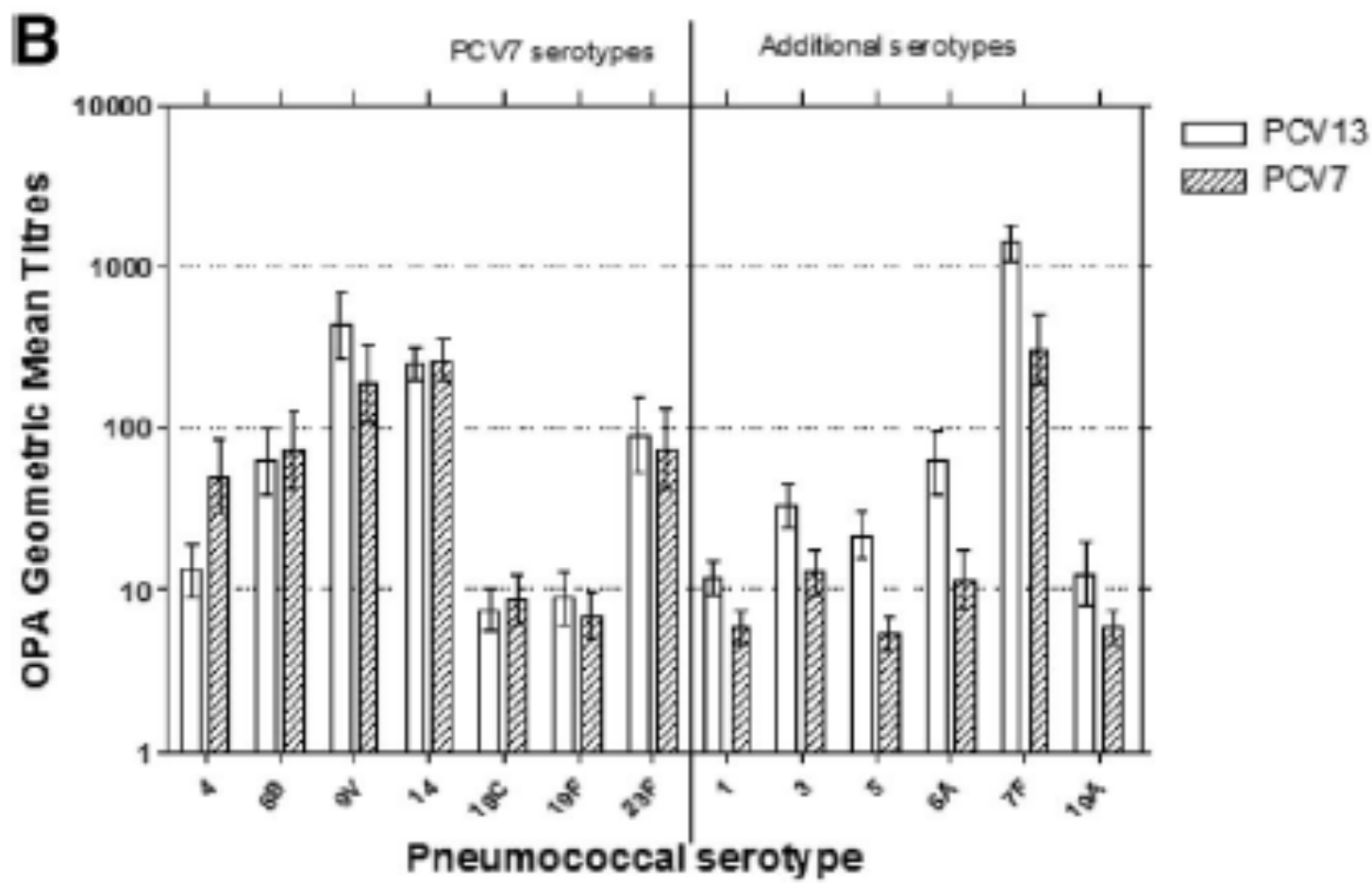
Immunogenicity and Reactogenicity of a 13-Valent-  
pneumococcal Conjugate Vaccine Administered at 2, 4, and 12  
Months of Age

*A Double-blind Randomized Active-controlled Trial*

*Matthew D. Snape, MB BS, MD,\* Chaam L. Klinger, MB BS,\* Elvis D. Daniels, MD, PhD,†  
Tessa M. John, RN,\* Helen Layton, BA,\* Llinos Rollinson, RN,\* Sarah Pestrige, BSc,‡  
Sandra Dymond, RN,§ Eva Galiza, BSc, MB BS,¶ Susan Tansey, MB ChB,† Daniel A. Scott, MD,†  
Sherryl A. Baker, PhD,† Thomas R. Jones, PhD,† Ly-Mee Yu, MSc,|| William C. Gruber, PhD,†  
Emilio A. Emini, PhD,† Saul N. Faust, PhD,‡ Adam Finn, PhD,§ Paul T. Heath, FRACP, FRCPCH,¶  
and Andrew J. Pollard, MB BS, PhD\**



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# Functional antibody after boosting persists..

[PLoS One](#). 2014; 9(3): e91413.

PMCID: PMC3950188

Published online 2014 Mar 11. doi: [10.1371/journal.pone.0091413](https://doi.org/10.1371/journal.pone.0091413)

PMID: [24618837](https://pubmed.ncbi.nlm.nih.gov/24618837/)

## Pneumococcal Serotype-Specific Antibodies Persist through Early Childhood after Infant Immunization: Follow-Up from a Randomized Controlled Trial

[Johannes Trück](#),<sup>1, \*</sup> [Matthew D. Snape](#),<sup>1</sup> [Florescia Tatangeli](#),<sup>1</sup> [Merryn Voysey](#),<sup>2</sup> [Ly-Mee Yu](#),<sup>2</sup>  
[Saul N. Faust](#),<sup>3</sup> [Paul T. Heath](#),<sup>4</sup> [Adam Finn](#),<sup>5</sup> and [Andrew J. Pollard](#)<sup>1</sup>

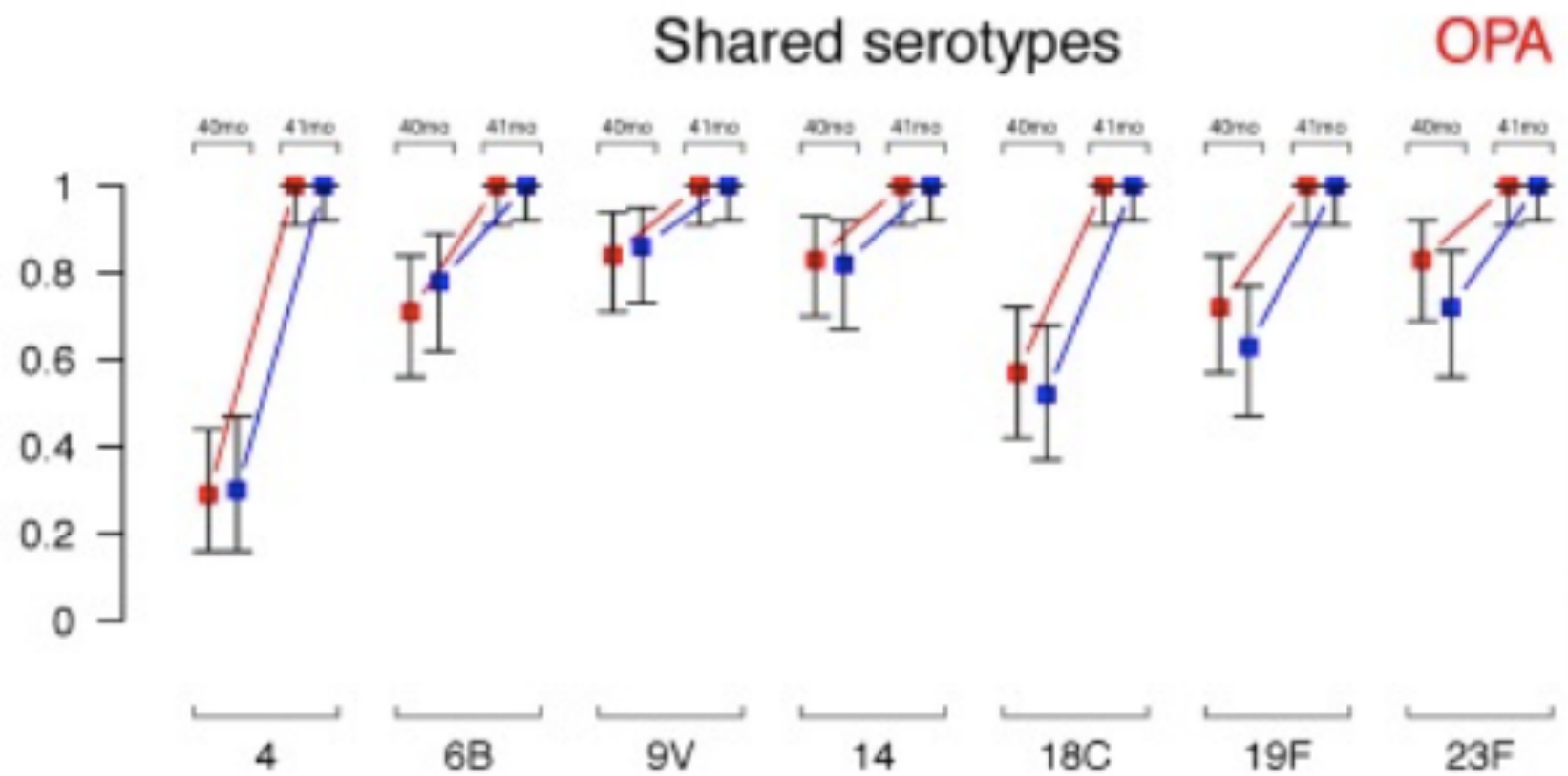




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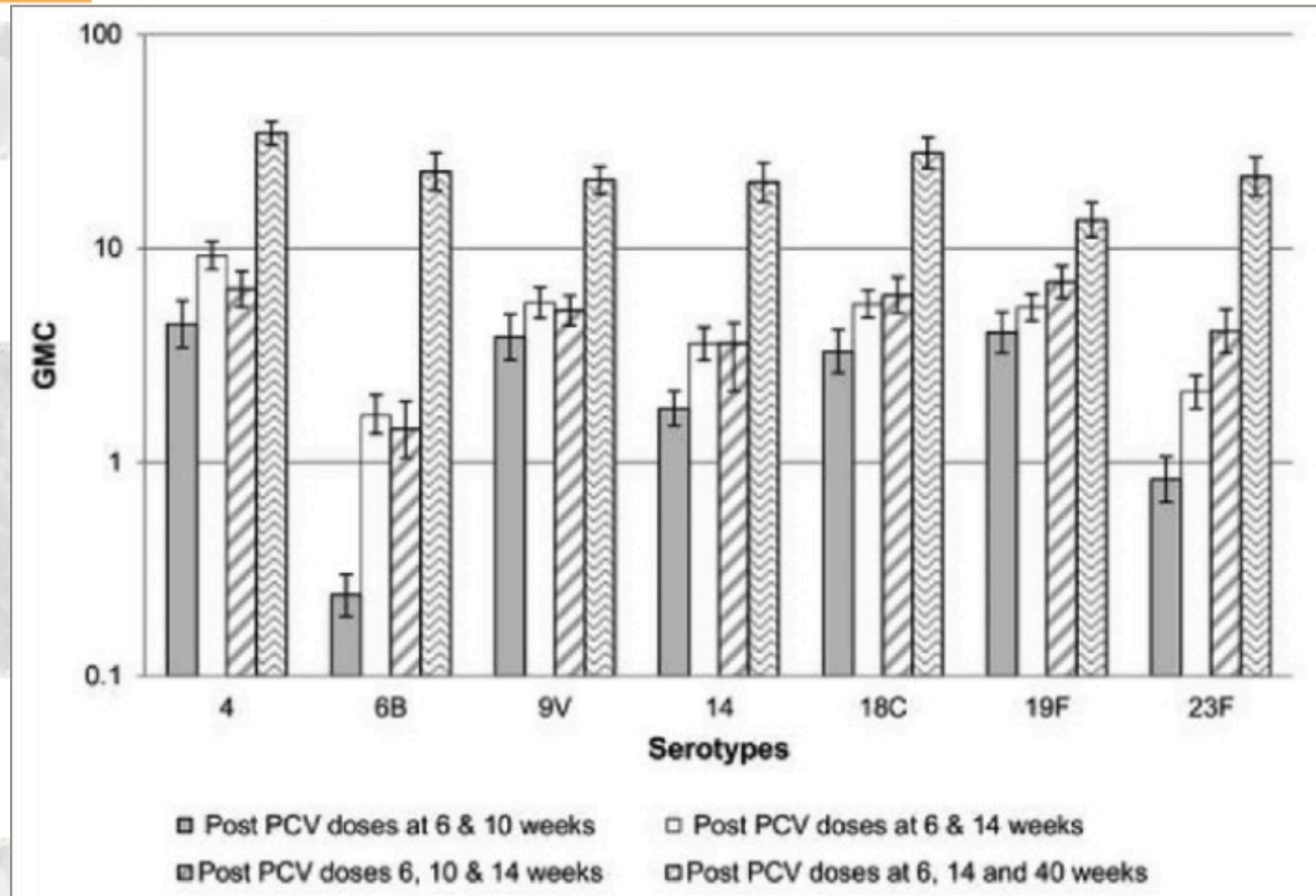


Proportion of participants above threshold



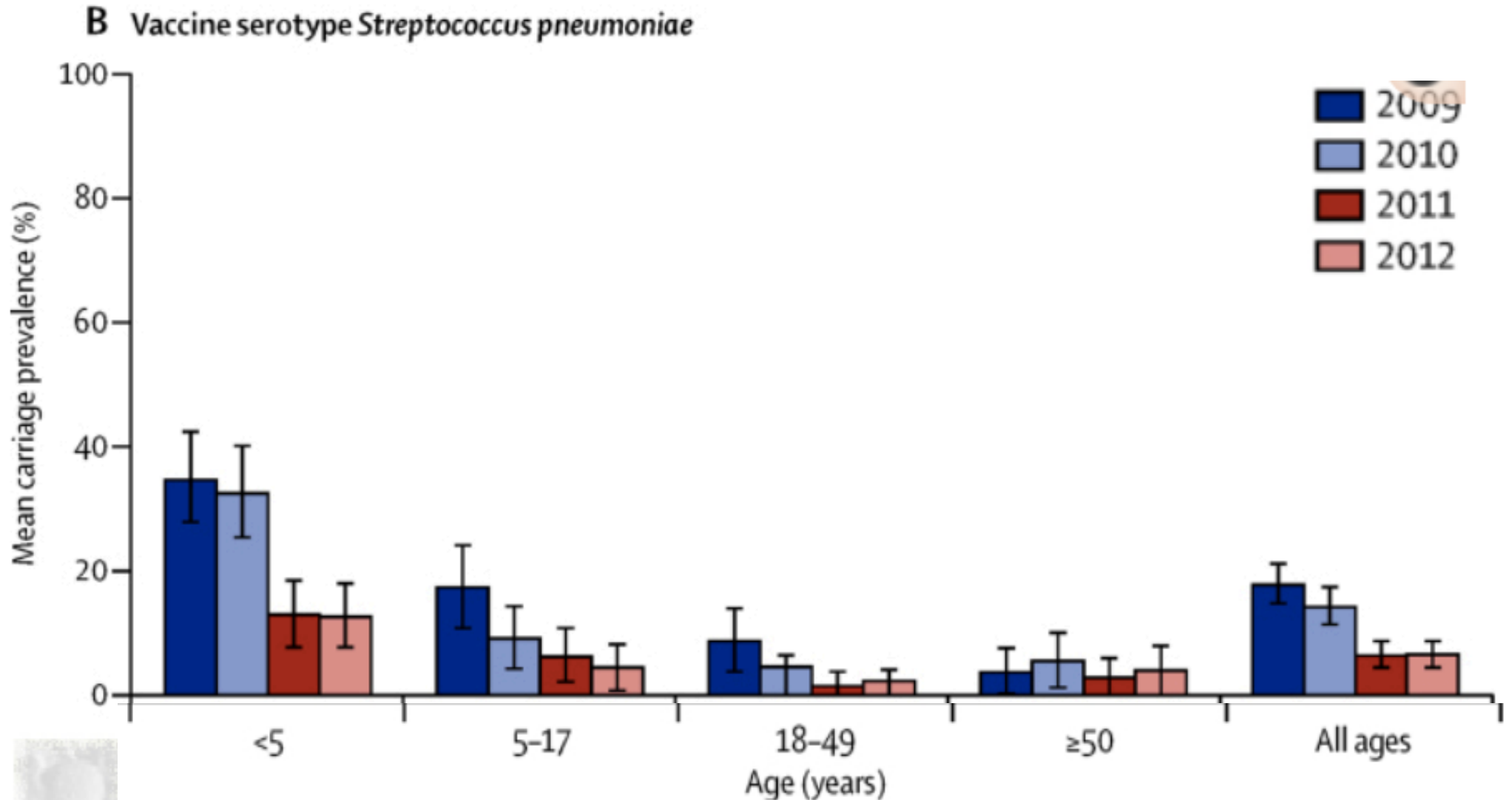


# More antibody..





# VT carriage - Kenya



Hammitt et al [Lancet Glob Health](#). 2014 Jul;2(7):e397-405





..and, of course, it's not just about indirect protection..

## Effectiveness of 7- and 13-Valent Pneumococcal Conjugate Vaccines in a Schedule Without a Booster Dose: A 10-Year Observational Study FREE

Sanjay Jayasinghe ✉, Clayton Chiu, Helen Quinn, Rob Menzies, Robin Gilmour, Peter McIntyre

*Clinical Infectious Diseases*, Volume 67, Issue 3, 1 August 2018, Pages 367–374,

<https://doi.org/10.1093/cid/ciy129>

**Published:** 17 February 2018    **Article history** ▼





Dose	Age Range, Months	Cases N (% Vaccinated)	Case-Control		Indirect Cohort	
			Controls N (% Vaccinated)	Vaccine Effectiveness, % (95% CI, P)	Controls <sup>a</sup> N (% Vaccinated)	Vaccine Effectiveness, % (95% CI, P)
3	Age <12	16 (31.3)	169 (72.8)	92.9 (27.7 to 99.3, 0.025)	101 (84.2)	91.4 (72.0 to 97.4, <0.001)
	Age 12-24	24 (83.3)	265 (95.1)	70.6 (5.2 to 90.9, 0.040)	198 (90.4)	46.9 (-71.5 to 83.6, 0.290)

From 12 months post-dose 3, the odds of VT IPD by 24-36 months increased significantly for PCV7 (5.6, 95% CI, 1.2-25.4) and PCV13 (5.9, 95% CI, 1.0-35.2).



So:

- 3+0 provides direct protection for a limited period - as shown in 2 RCTs.
- For people with blinkers it's a dead cert to do that - and only that
- 2+1 provides both sustained direct and indirect protection across the population
- For people with a broader perspective it's the obvious choice
- More evidence on 2+1 is coming soon