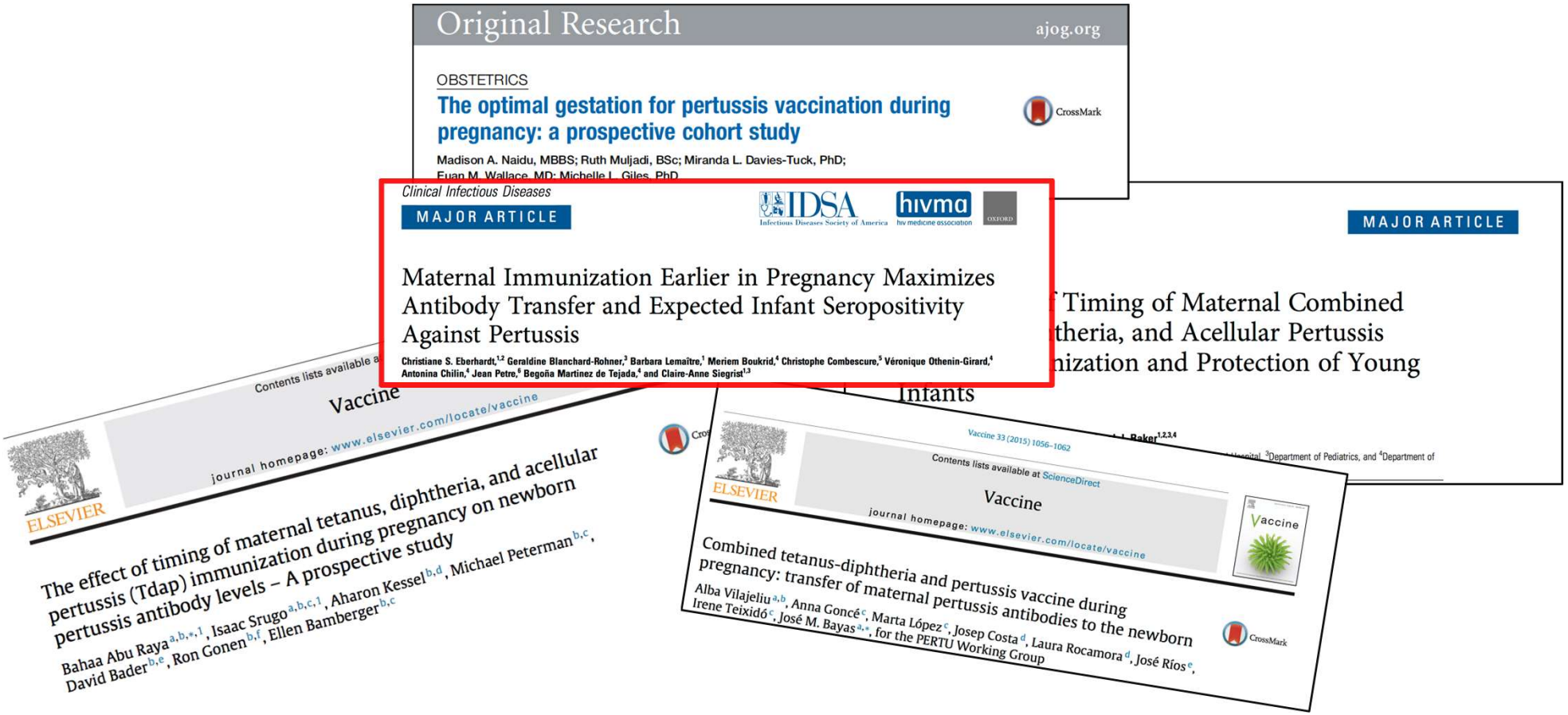
St George's
University of London

Anna Calvert

NISEC meeting

12th January 2024

A question of timing



OpTIMUM: A study of several parts

RCT: Primary and secondary objectives

Functional work: SBA

Attitudes work: Questionnaire

Breast milk work

Optimising the timing of whooping cough immunisation in mums (OpTIMUM) through investigating pertussis vaccination in pregnancy: an open-label, equivalence, randomised controlled trial

*Anna Calvert, Gayatri Amirthalingam, Nick Andrews, Sneha Basude, Matthew Coleman, Hannah Cuthbertson, Anna England, Vanessa Greening, Bassam Hallis, Edward Johnstone, Christine E Jones, Konstantinos Karampatsas, Asma Khalil, Kirsty Le Doare, Mary Matheson, Elisabeth Peregrine, Matthew D Snape, Manu Vatish, Paul T Heath, on behalf of the OpTIMUM Study Group**

Primary objective

To determine if pertussis vaccination at different time points in pregnancy results in equivalent concentrations of pertussis specific antibodies in the term infant at birth

Secondary objectives

- To describe the kinetics of the antibody response to pertussis vaccination during pregnancy
- To explore the impact of repeated vaccination on the antibody response in women who have received a pertussis vaccination in a previous pregnancy
- To determine if pertussis vaccination at different time points in pregnancy results in equivalent concentrations of pertussis specific antibodies in the preterm infant at birth
- To describe the placental transfer of antibody following administration of vaccine at three discrete time points
- To investigate the rate of fever and local reactions in women receiving the vaccine in pregnancy comparing those who are receiving the vaccine for the first time and those who have previously received the vaccine in pregnancy
- To evaluate the impact of timing of pertussis vaccination in pregnancy on antibody concentration in the infants following their primary immunisation schedule

Study visits

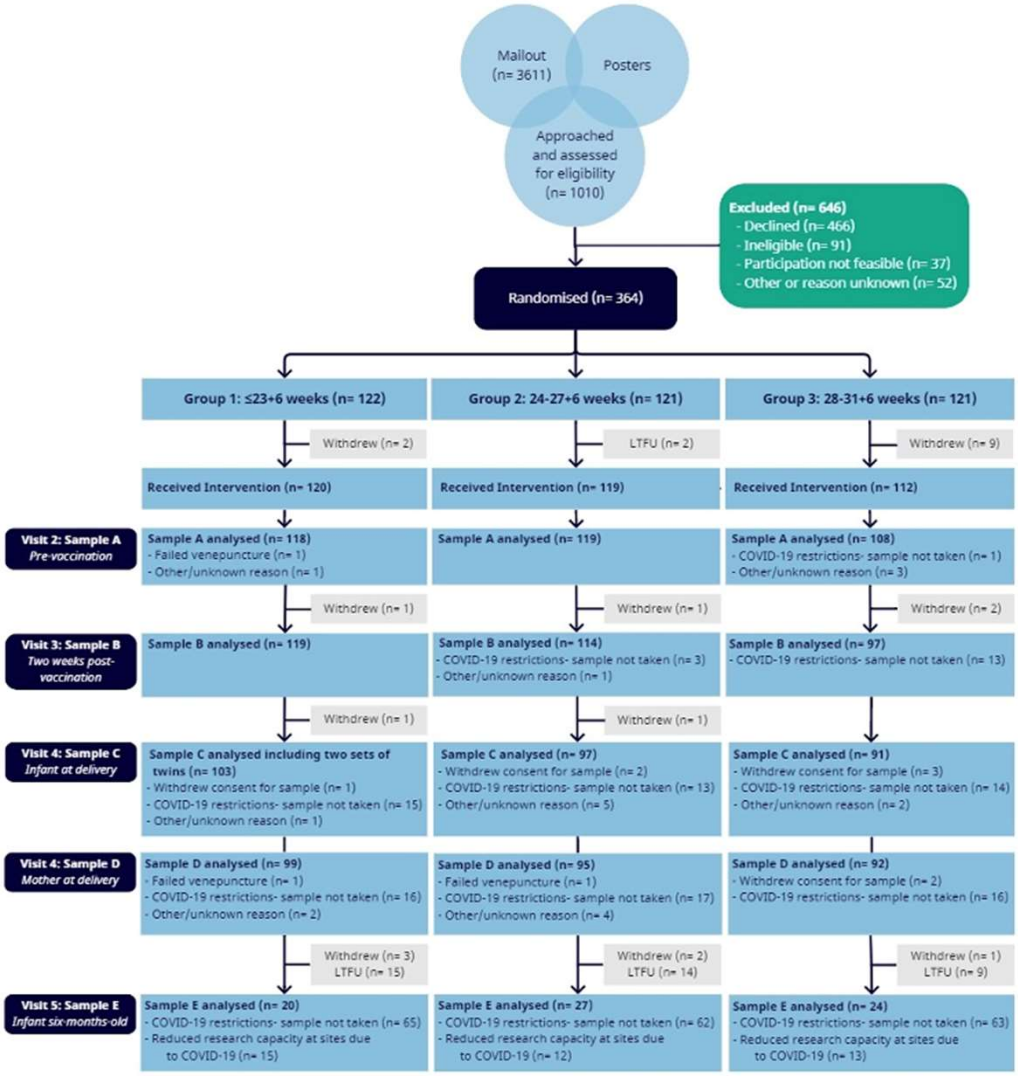
Visit Number	Screening visit	Vaccination visit	Follow up visit	Delivery visit	Infant visit
Timing	At or before 23+6 weeks	According to study allocation	V+14 (+/- 2)	Delivery	28-70 days following third pertussis vaccination
Activity	Screening & enrolment	Maternal blood sampling and vaccination. Diary card provided. Questionnaire.	Maternal blood sampling. Diary card collected.	Maternal blood and cord blood sampling	Infant blood sampling

Group 1 <=23+6 weeks Group 2= 24-28 weeks Group 3= 28-32 weeks

Recruitment

Recruitment took place from May 2019 until February 2020.

363 women were randomised and 351 of these received the intervention and are considered to be participants in the study.



Primary objective: To determine if pertussis vaccination at different time points in pregnancy results in equivalent concentrations of pertussis specific antibodies in the term infant at birth

GMCs for FHA, PRN and PT in cord blood of term infants

	FHA (n=278)			PRN (n=279)			PT (n=276)		
	GMC IU/ml (95% CI)	Ratio to grp 3 (28-31+6w)	P value	GMC IU/ml (95% CI)	Ratio to grp 3 (28-31+6w)	P value	GMC IU/ml (95% CI)	Ratio to grp 3 (28-31+6w)	P value
1	189.1 (163.2-219.1)	0.59 (0.48-0.72)	**<0.001**	268.9 (205.6-351.8)	0.87 (0.58-1.30)	0.49	51.2 (43.7-60.1)	0.76 (0.61-0.95)	**0.02**
2	232.4 (202.2-267.2)	0.72 (0.58-0.89)	**0.003**	271.4 (200.7-367.0)	0.88 (0.58-1.32)	0.53	61.8 (53.1-72.0)	0.92 (0.73-1.15)	0.47
3	322.3 (272.8-380.6)			309.9 (229.3-418.8)			67.3 (56.7-79.8)		

Equivalence criteria were met for **PT** and **PRN**

Equivalence criteria for **FHA** was not reached

Equivalence criteria

95% CI contained within the equivalence margin (upper end 1.8, lower end 0.55)

Secondary objective 1: To describe the kinetics of the antibody response to pertussis vaccination during pregnancy

		FHA			PRN			PT		
	Study group	GMC IU/ml (95% CI)	Ratio to grp 3 (95% CI)	P value	GMC IU/ml (95% CI)	Ratio to grp 3 (95% CI)	P value	GMC IU/ml (95% CI)	Ratio to grp 3 (95% CI)	P value
Pre-vaccination	1	26.5 (22.4-31.4)	0.89 (0.69-1.16)	0.39	19.9 (14.4-27.5)	0.94 (0.59-1.49)	0.78	10.4 (8.5-12.6)	1.08 (0.82-1.42)	0.59
	2	27.2 (22.7-32.4)	0.91 (0.70-1.18)	0.50	16.4 (12.1-22.1)	0.77 (0.49-1.22)	0.27	10.7 (9.0-12.7)	1.11 (0.84-1.46)	0.46
	3	29.8 (24.1-36.8)			21.2 (14.9-30.2)			9.6 (7.8-11.9)		
2 weeks following vaccination	1	156.0 (134.8-180.5)	0.70 (0.57-0.86)	**0.001**	208.7 (167.4-260.1)	0.87 (0.62-1.22)	0.42	46.7 (40.2-54.3)	0.85 (0.68-1.06)	0.15
	2	183.2 (162.6-206.4)	0.82 (0.67-1.01)	0.06	195.7 (153.9-248.8)	0.81 (0.58-1.15)	0.24	55.0 (47.5-63.6)	1.00 (0.80-1.25)	1.0
	3	222.6 (189.8-261.2)			240.5 (184.2-314.1)			55.0 (46.3-65.4)		
At delivery	1	100.9 (87.3-116.7)	0.57 (0.46-0.70)	**<0.001**	148.2 (114.0-192.6)	0.81 (0.54-1.20)	0.291	28.9 (24.6-34.0)	0.74 (0.59-0.93)	**0.008**
	2	125.3 (109.1-143.9)	0.71 (0.58-0.87)	**0.001**	142.7 (107.7-189.1)	0.78 (0.52-1.16)	0.218	32.9 (28.1-38.6)	0.84 (0.68-1.06)	0.138
	3	176.6 (150.4-207.4)			183.5 (134.6-250.0)			39.0 (33.4-45.5)		

For FHA higher GMCs in group 3 two weeks following vaccination, but significant only for FHA when comparing groups 1 and 3

Secondary objective 1: To describe the kinetics of the antibody response to pertussis vaccination during pregnancy

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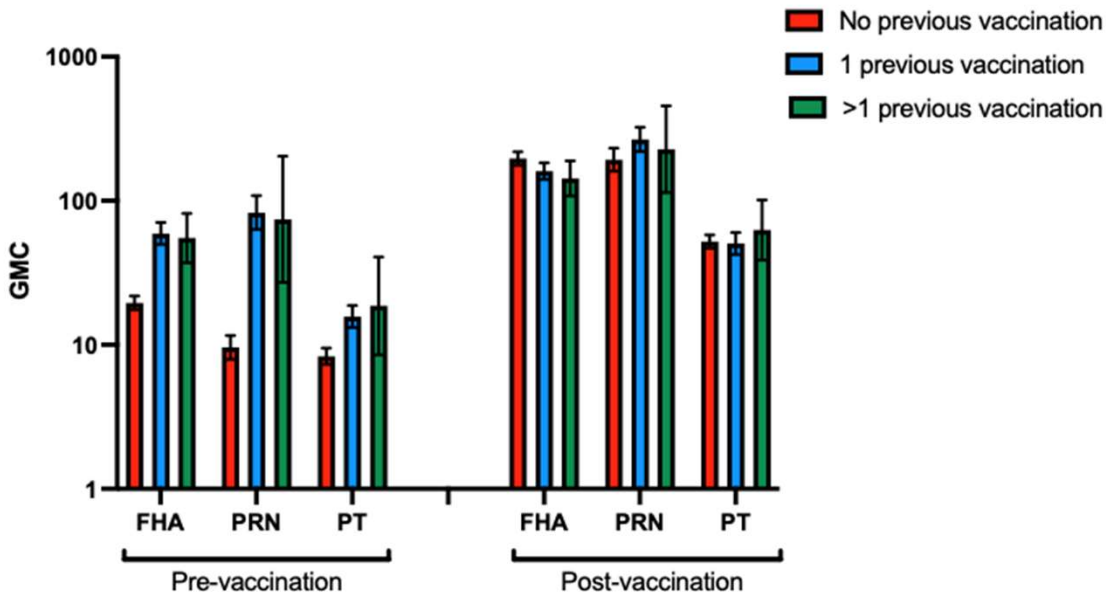
At delivery GMCs have waned- most evident in groups 1 and 2 in which the time since vaccination was greatest

At delivery GMCs were higher in group 3 compared to group 1 and 2 for FHA and compared to group 1 for PT

Secondary objective 2: To explore the impact of repeated vaccination on the antibody response in women who have received a pertussis vaccination in a previous pregnancy

- **Prior to vaccination-** significant difference for all antigens between those who had not received recent vaccination and those who had received one or more prior vaccinations
- **Following vaccination-** no difference between those who had received recent vaccination and those who had not



Findings

Pertussis vaccination at three different time intervals in pregnancy resulted in equivalent concentrations of IgG antibodies in term infants against 2 of the 3 pertussis antigens assessed.

Insufficient numbers to draw conclusions about preterm infants

Results in context

JOURNAL ARTICLE ACCEPTED MANUSCRIPT

Optimisation of timing of Maternal Pertussis Immunisation from 6 years of post-implementation surveillance data in England Get access >

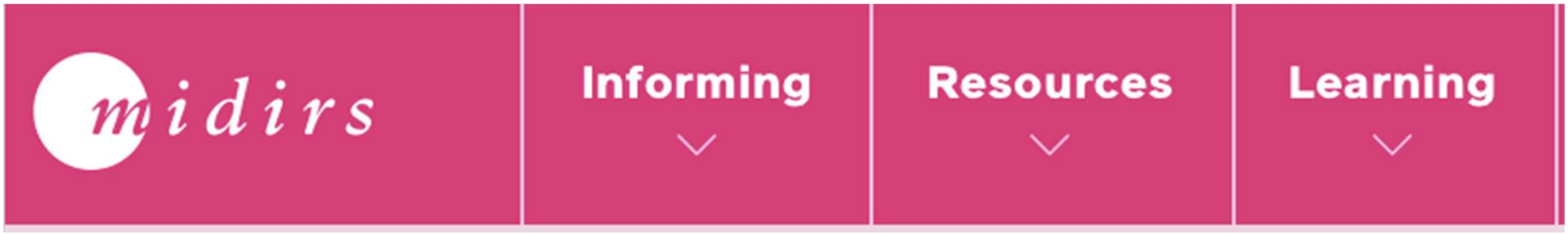
Gayatri Amirthalingam, MFPH, Helen Campbell, PhD ✉, Sonia Ribeiro, BA, Julia Stowe, PhD, Elise Tessier, MSc, David Litt, PhD, Norman K Fry, PhD, Nick Andrews, PhD

Clinical Infectious Diseases, ciac651, https://doi.org/10.1093/cid/ciac651
Published: 17 August 2022 **Article history** ▾

Vaccine effectiveness equivalent in infants born to mothers vaccinated at different gestational ages

Extending the window for vaccination improved coverage

Attitudes work



Acknowledgements

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Questions