



## RACP Foundation Research Awards

### FINAL REPORT

<b>Project / Program Title</b>	Strategies to reduce the burden of gastroenteritis in Aboriginal children	
<b>Name</b>	Dr Bianca Middleton	
<b>Award Received</b>	2017 RACP P&CHD NHMRC Award for Excellence	
<b>Report Date</b>	31 December 2019	
<b>Chief Investigator / Supervisor</b>	Bianca Middleton/Tom Snelling	
<b>Administering Institution</b>	Menzies School of Health Research	
<b>Funding Period</b>	Start Date:	1 January 2018
	Finish Date:	31 December 2020

#### PROJECT SUMMARY

My PhD thesis 'Strategies to reduce the burden of gastroenteritis amongst Australian Aboriginal children', will explore practical, ethical and implementable strategies to reduce the burden of gastroenteritis amongst Australian Aboriginal children, with particular focus on improving the real world effectiveness of oral rotavirus vaccine

#### PROJECT AIMS / OBJECTIVES

There are three components to this work;

- 1) a systematic review of the literature to evaluate strategies to improve the performance of oral rotavirus vaccine in high rotavirus burden low resource settings; with particular focus on evaluating strategies where an additional/ alternate dose schedule of rotavirus vaccine has been given.
- 2) a case control study to evaluate and compare the current performance of two licensed oral rotavirus vaccine during a recent epidemic amongst Aboriginal children in rural and remote northern Australia.
- 3) evaluation of the immunological results of a NHMRC funded Bayesian adaptive clinical trial which relaxes the upper age limit of oral rotavirus vaccine administration and gives an additional dose of oral rotavirus vaccine to Northern Territory Aboriginal children aged between six and twelve months (ORVAC study – Optimising Rotavirus Vaccine in Aboriginal Children).

## SIGNIFICANCE AND OUTCOMES

Northern Territory Aboriginal children continue to suffer a disproportionate burden of gastroenteritis compared to non-Indigenous children. Epidemics of rotavirus remain common in remote, central and northern Australia and place enormous strains on remote communities and health services. This thesis will explore practical, ethical and implementable strategies to improve the performance of oral rotavirus vaccine and reduce the burden of gastroenteritis amongst the vulnerable population of Australian Aboriginal children.

The retrospective case-control analysis of the G2P[4] rotavirus epidemic in Central Australia and rural/ remote Western Australia, provides a unique and important opportunity to evaluate and compare the performance of two oral rotavirus vaccines ten years after their incorporation into the National Immunisation Program. This will be the first evaluation of the performance of oral Rotarix rotavirus vaccine amongst Northern Territory Aboriginal children since 2009. It will also be the first Australian study to evaluate and compare the performance of both Rotarix and RotaTeq rotavirus vaccine amongst rural and remote Australian Aboriginal children during the same outbreak.

This thesis will also examine the preliminary immunological results of a NHMRC-funded clinical trial, which proposes to reduce the burden of gastroenteritis amongst Northern Territory Aboriginal children by relaxing the upper age limit of Rotarix administration and scheduling a third dose of Rotarix to children aged six to twelve months. This will be the first clinical trial to evaluate both the immunological and clinical effects of administering an additional dose of Rotarix vaccine to children older than six months of age. The pragmatic trial design seeks to evaluate the administration of an additional dose of oral Rotarix rotavirus vaccine under real-life conditions, thus increasing the likelihood of a positive trial outcome being adopted into clinical practice. In addition, it will be the first clinical trial amongst Northern Territory Aboriginal children to take a Bayesian adaptive approach, meaning that no fixed sample size will be set and only as many children as required to determine the study outcome will be enrolled. It is expected that the Bayesian design will prove to be a more flexible and pragmatic trial design, resulting in fewer failed trials, and it is contended that this is both the most ethical and practical way to conduct research amongst the vulnerable population of Northern Territory Aboriginal children

## PUBLICATIONS / PRESENTATIONS

### Publications 2019

Middleton BF, Jones MA, Waddington CS, et al. The ORVAC trial protocol: a phase IV, double-blind, randomised, placebo- controlled clinical trial of a third scheduled dose of Rotarix rotavirus vaccine in Australian Indigenous infants to improve protection against gastroenteritis. *BMJ Open* 2019;0:e032549. doi:10.1136/ bmjopen-2019- 03254

### Proposed Publications for 2020/21

- rotavirus vaccine effectiveness case-control study protocol
- rotavirus vaccine effectiveness case-control study results
- systematic review evaluating the impact of alternate rotavirus vaccine dosing schedules (withholding first dose/additional doses given)
- narrative review regarding the performance of oral rotavirus vaccines amongst children living in rural/ remote northern Australia
- analysis of the immunological outcome of the ORVAC clinical trial

ORVAC Presentation: Northern Territory Centre for Disease Control Conference Partnerships in Public Health, September 2018

Vaccine Symposium Presentation: Australasian Society of Infectious Diseases Annual Scientific Meeting, May 2019

Australian Rotavirus Strain Outbreak Advisory Board Meeting, Sept 2019

ORVAC Clinical Trial Protocol Presentation: Australian Clinical Trials Alliance International Clinical Trials Conference, October 2019

Rotavirus Presentation: Menzies School of Health Research Lunchtime Seminar Series, Oct 2019