Ruth Bishop Address 2022

Australian Government

INDO-PACIFIC CENTRE FOR HEALTH SECURITY

In memoriam
Professor Ruth Bishop AC

Speakers

- Professor Graeme Barnes AO
- Professor Julie Bines

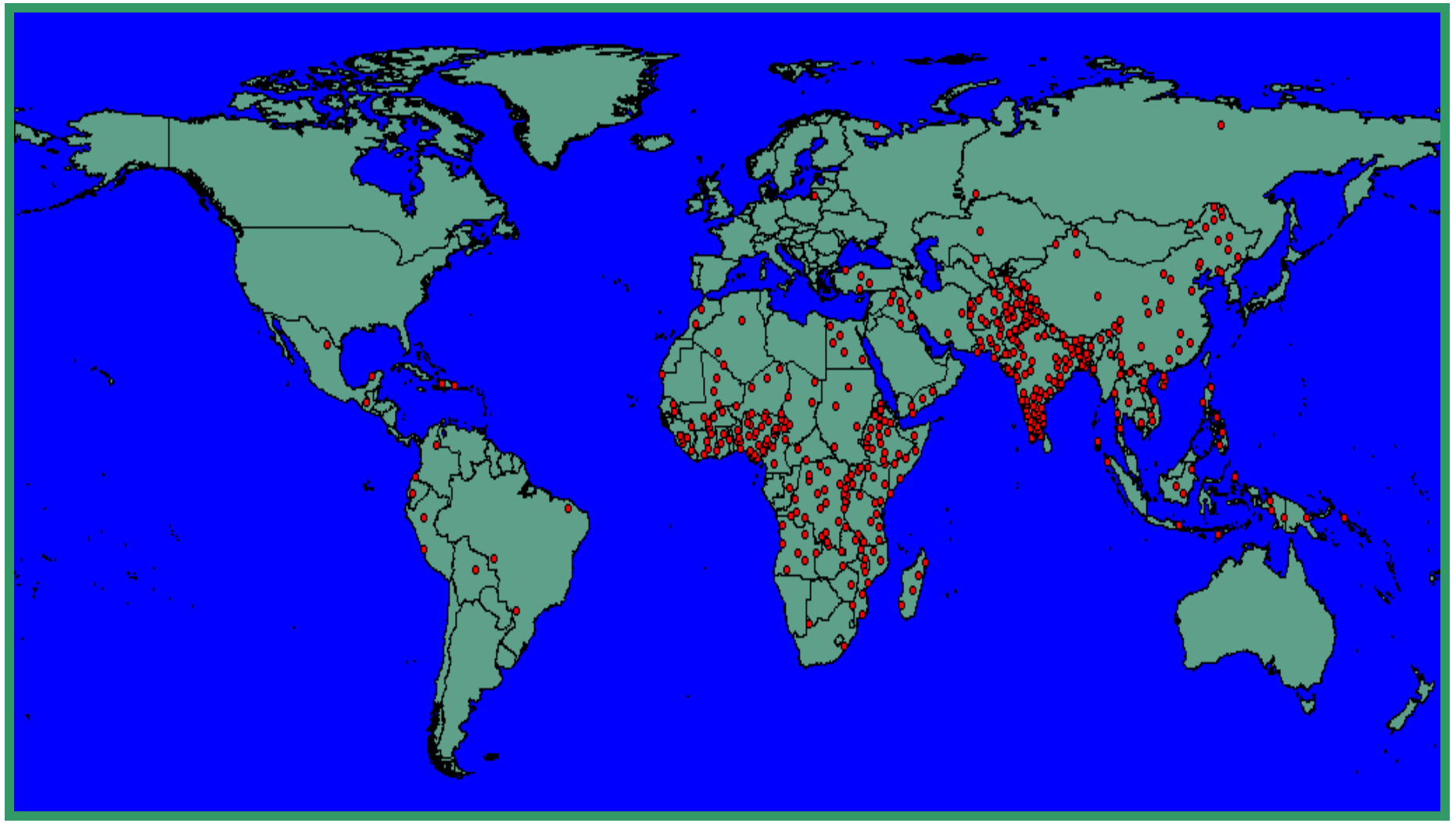
Melbourne Children's
A world leader in child and adolescent health

The Royal Children's Hospital Melbourne

murdoch children's research institute

THE UNIVERSITY OF MELBOURNE

600,000 annual rotavirus deaths



1 dot = 1000 deaths

CHARLOTTE ANDERSON

MD, MSc, FRACP, FRCP

HEAD,
GASTROENTEROLOGY

RESEARCH UNIT, RCH

1962 - 1968

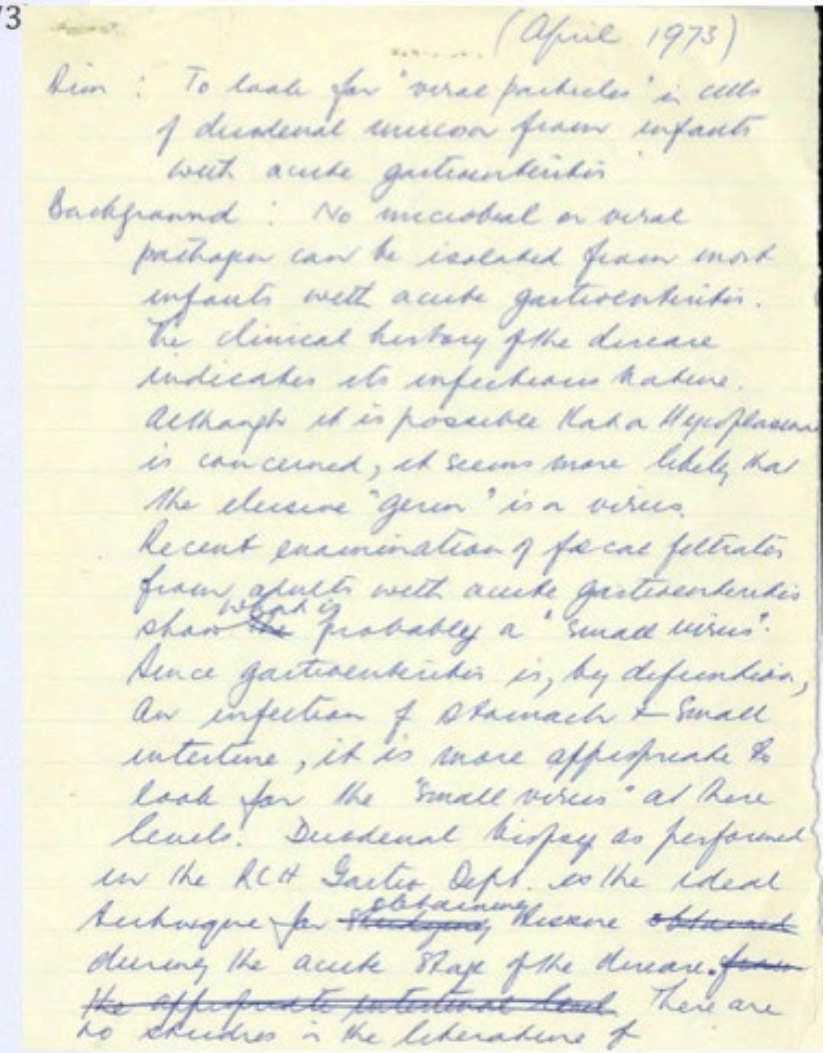
Portrait by Lillaine Gedye


Children's Vaccine Initiative Award

(April 1973)

Aim: To look for "viral particles" in cells of duodenal mucosa from patients with acute gastroenteritis

Background: no microbial or viral pathogen can be isolated from most infants with acute gastroenteritis. The clinical history of the disease indicates its infectious nature. Although it is possible that a Mycoplasma is concerned, it seems more likely that the elusive "germ" is a virus. Recent examination of faecal filtrates from adults with acute gastroenteritis show what is probably a "small virus". Since gastroenteritis is, by definition, an infection of stomach + small intestine, it is more appropriate to look for the "small virus" at these levels. Duodenal biopsy as performed in the RCH Gastro Dept. is the ideal technique for obtaining tissue during the acute stage of the disease. There are no studies in the literature of



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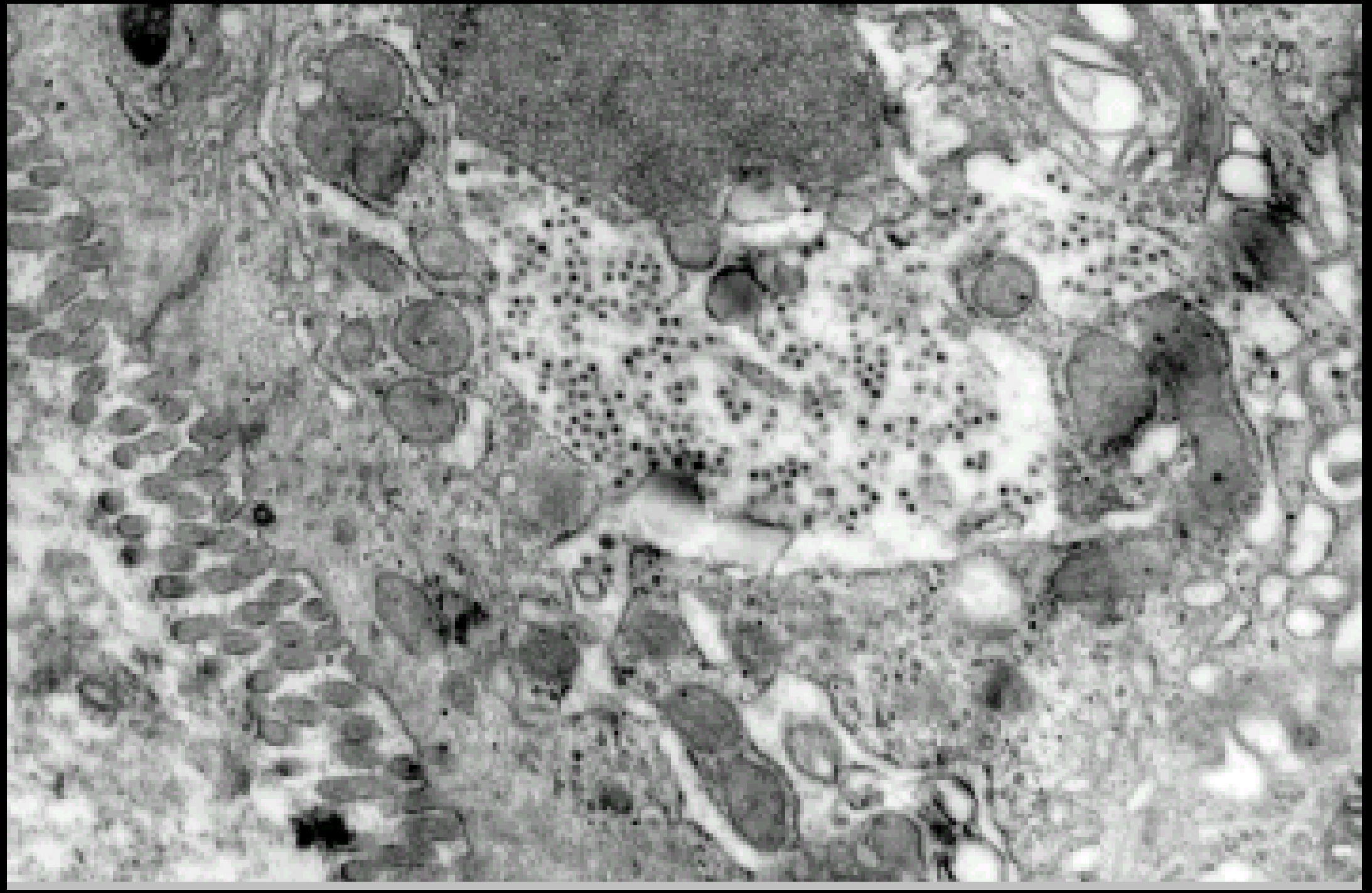


Brian Ruck Max Murray Ian Holmes Geoff Davidson

Rudge Townley Ruth Bishop Anneke Veenstra

VIRUS PARTICLES IN EPITHELIAL CELLS OF DUODENAL MUCOSA FROM CHILDREN WITH ACUTE NON-BACTERIAL GASTROENTERITIS

RUTH F. BISHOP G. P. DAVIDSON

Department of Gastroenterology, Royal Children's Hospital, Melbourne, Australia

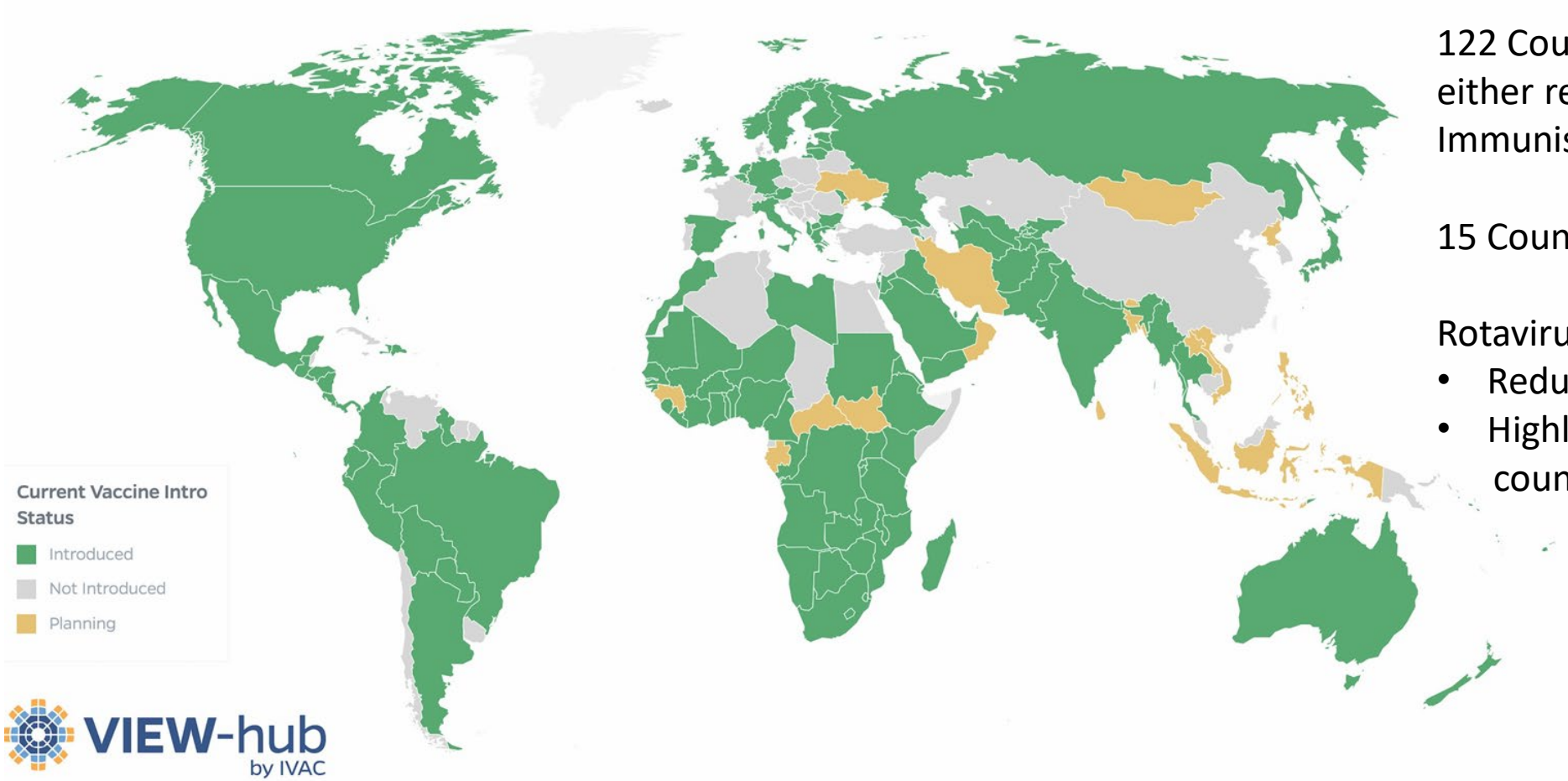
I. H. HOLMES B. J. RUCK

Department of Microbiology, University of Melbourne, Australia

Summary Electron microscopy of duodenal mucosa from nine children with acute non-bacterial gastroenteritis revealed virus particles in epithelial cells from six patients. The morphology of the virus particles was identical in each of the six children. The virus belonged to the orbivirus group. No virus particles were observed in duodenal mucosa obtained from three of these children after clinical recovery. This orbivirus is believed to have been an important cause of sporadic gastroenteritis in children in Melbourne during the 3 months of the survey.

Current Status of Rotavirus Vaccine Introduction

In 2009 WHO Global recommendation all infants should receive rotavirus vaccines



122 Countries have introduced either regional or national Immunisation Programs

15 Countries planning

Rotavirus Vaccine observed to:

- Reduce rotavirus hospitalisations
- Highly cost effective in ALL countries where analysed

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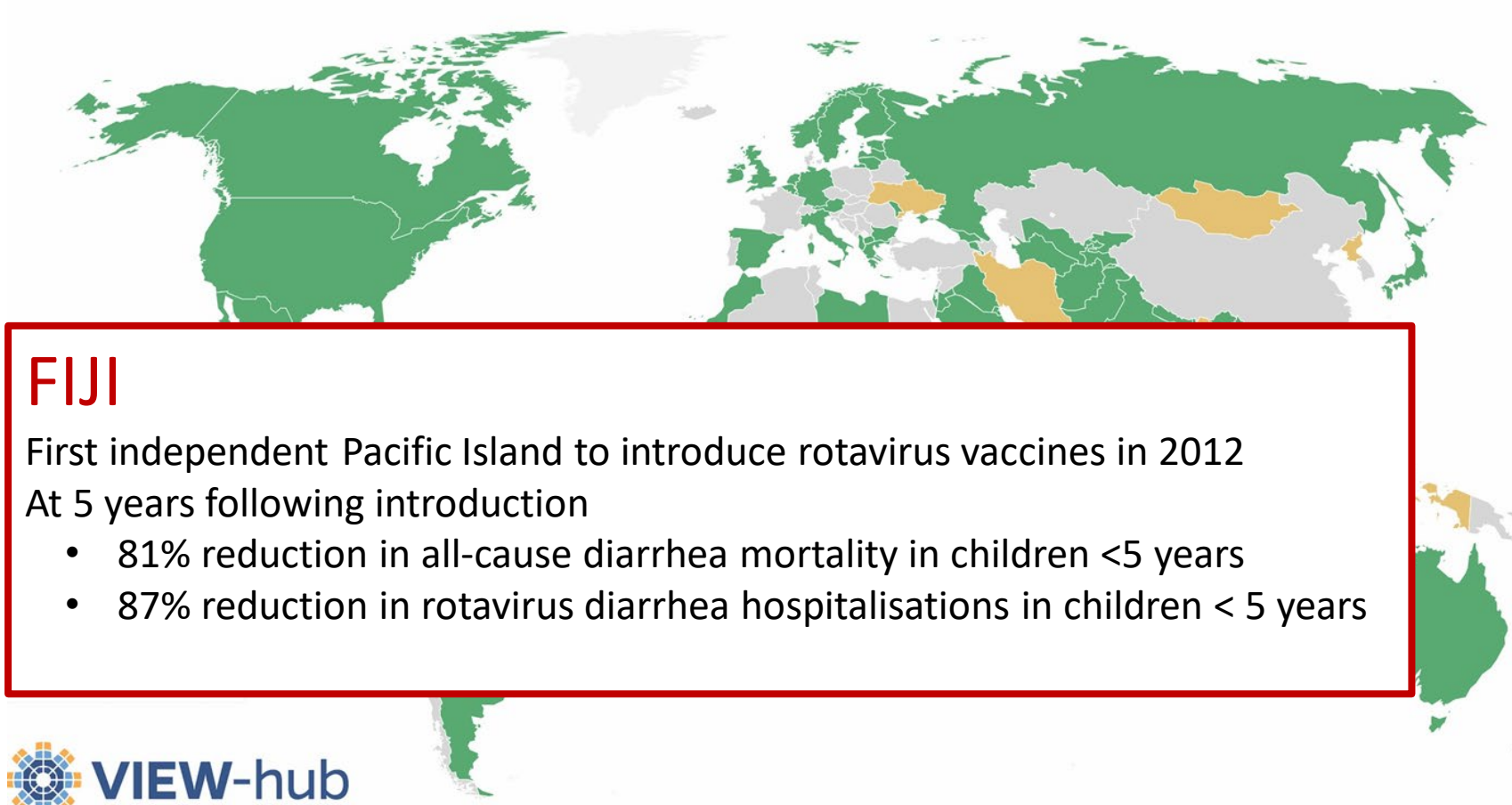

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FIJI

First independent Pacific Island to introduce rotavirus vaccines in 2012

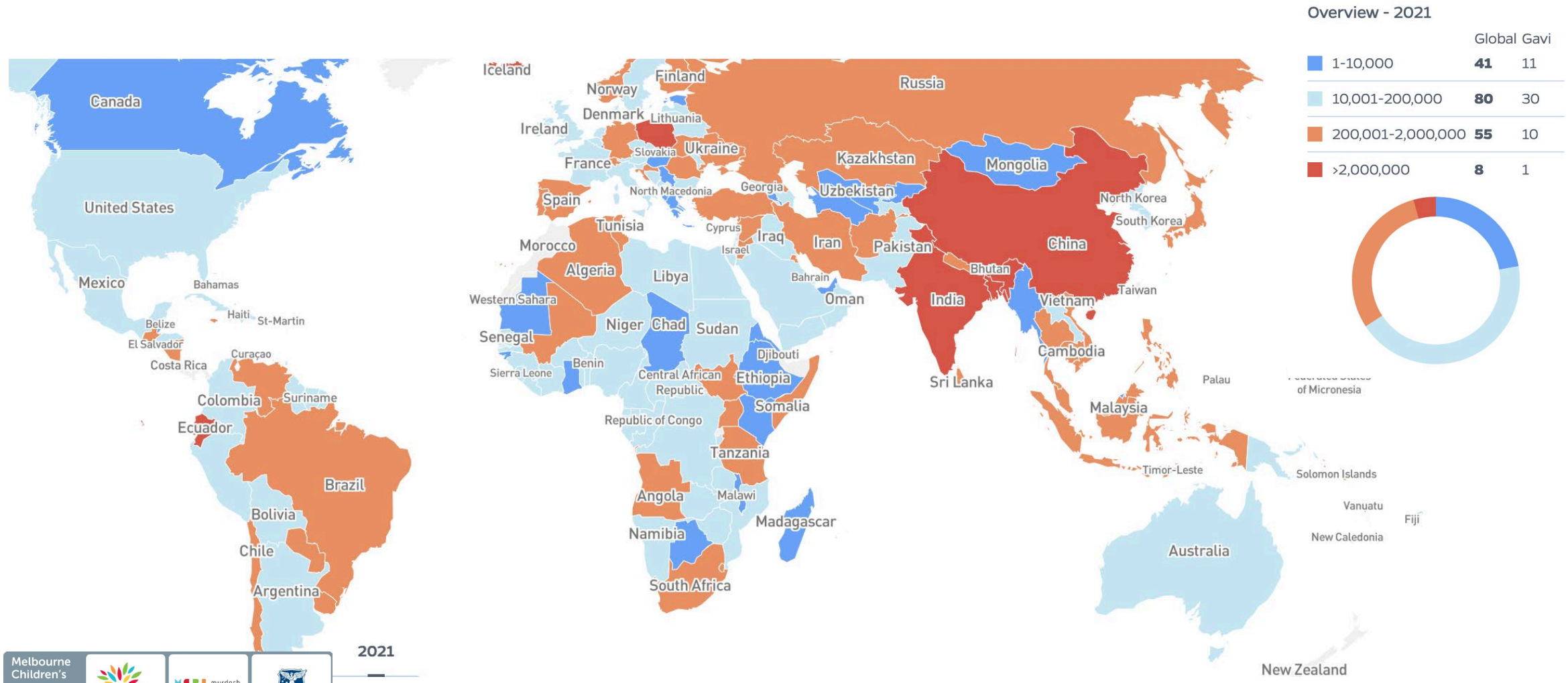
At 5 years following introduction

- 81% reduction in all-cause diarrhea mortality in children <5 years
- 87% reduction in rotavirus diarrhea hospitalisations in children < 5 years

VIEW-hub by IVAC

Worldwide, 58.6 million or 40% children lack access to rotavirus vaccines

Indo-Pacific region lagging with ~30 million children still unvaccinated



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Challenges to current rotavirus vaccines

- Rotavirus vaccines have lower coverage compared with other vaccines
- Less effective in high child mortality regions in Asia and Africa

  Median Vaccine Effectiveness estimated <12mo of age

  - Low mortality 86% (95%CI: 81-90)
  - Medium mortality 77% (95%CI: 66, 85),
  - **High mortality 63% (95%CI: 54, 70)**

- Reduced duration of protection in high mortality regions

RV3-BB Rotavirus Vaccine

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RV3-BB Rotavirus Vaccine

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RV3-BB Rotavirus Vaccine

Human neonatal rotavirus vaccine to target protection from birth

Novel Vaccine

- Based on unique neonatal strain (RV3) identified in Melbourne newborn nurseries in 1980s
- Associated with asymptomatic infection
- Developed at MCRI to high titre in WHO prequalified vero cell line suitable for vaccines
- Oral 1ml, 3 dose course, co-administered with EPI vaccines

Novel Administration Schedule

- First dose at Birth or from 6 weeks

Novel Approach to Development

- Developed in collaboration with partners at Universitas Gadja Mada and BioFarma Indonesia
- Licensed to other emerging country vaccine manufacturers in Indo-Pacific region

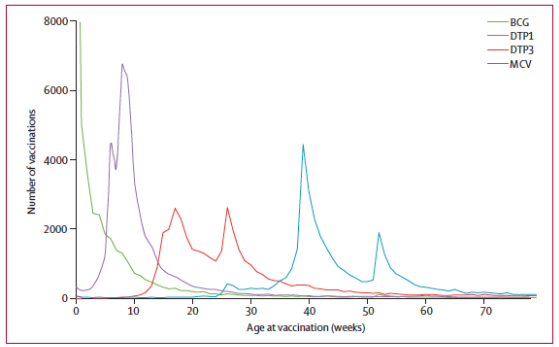


Figure 2: **Age distributions for administration of BCG, DTP1, DTP3, and MCV1 vaccines, based on card dates only in children aged 18–35·9 months**
BCG=bacille Calmette-Guérin. DTP=diphtheria, tetanus, and pertussis. MCV=measles-containing vaccine.

Birth dose schedule

Address gap in protection in very young

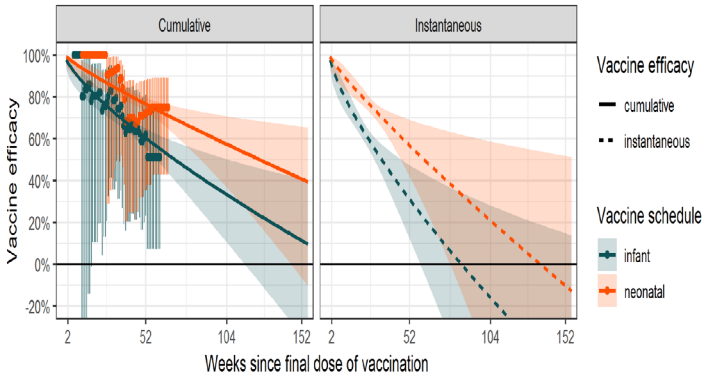
Improve coverage

Overcome barriers to vaccine take

Increase duration of protection

Potential to improve benefit-risk

Gastric pH
Complex gut microbiome
Enteric enteropathy



Efficacy of live oral rotavirus vaccines by duration of follow-up: a meta-regression of randomized controlled clinical trials
A Clark, K Van Zandvoort, S Flache, C Sanderson, J Bines, J Tate, U Parashar, M Jit
Lancet Infectious Diseases 2019 19(7): 717-727

"Neonatal schedules that involve giving the first two doses as early as possible (ie, with BCG and DTP1) had the fewest excess intussusception deaths and favourable benefit–risk ratios compared with other schedules"

Mortality reduction benefits and intussusception risks of rotavirus vaccination in 135 low-income and middle-income countries: a modelling analysis of current and alternative schedules
Andrew Clark, Jacqueline Tate, Umesh Parashar, Mark Jit, Mateusz Hasso-Agopsowicz, Nicholas Henschke, Benjamin Lopman, Kevin Van Zandvoort, Clint Pecenka, Paul Fine, Colin Sanderson

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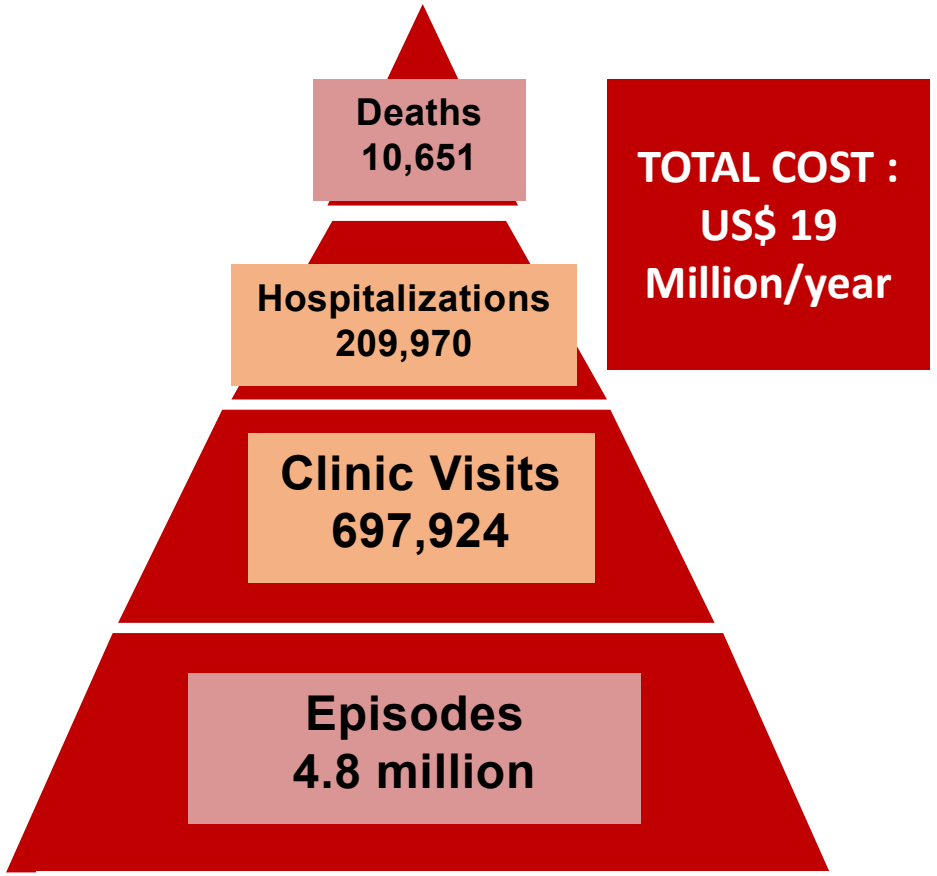
Indonesia and the need for a rotavirus vaccine

High rotavirus disease burden

- ~4.77 million babies born annually
- High child mortality region
  - Infant mortality is 20 per 1,000 live births
  - child mortality is 24 per 1,000 live births
- Diarrhea was causes:
  - ~12% deaths in <12months of age
  - ~10% of deaths at ages 1-4 years
- ~45-60% diarrhea-related hospitalisations in children <5 years due to rotavirus



Soenarto et al. JID 2009:200 (Suppl 1): S188-194;
Wilopo et al. Vaccine 275 (2009)

Indonesia and the need for a rotavirus vaccine

Vaccine manufacturing capability

Bio Farma

- State owned vaccine manufacturer
- Supplies Indonesian National Immunisation Program
- Supplies UNICEF and >100 countries

Bio Farma has partnered with MCRI >15 years in development of the RV3-BB rotavirus vaccine

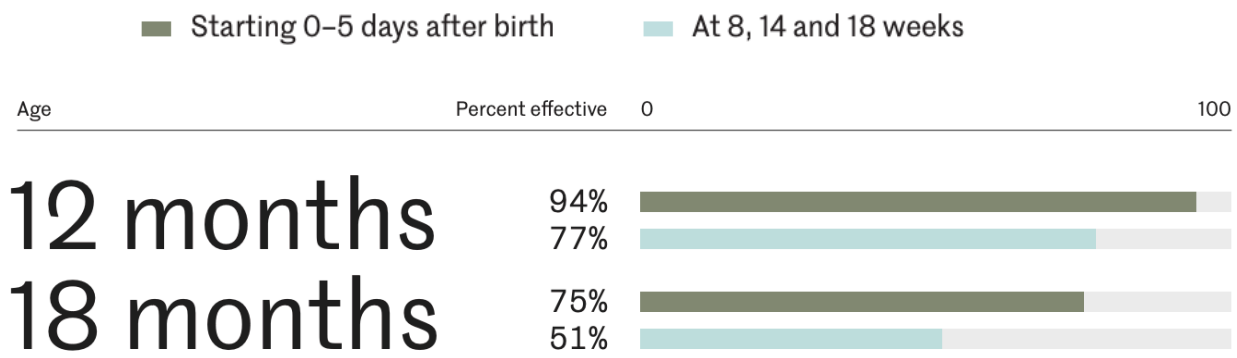
Advantages of Bio Farma's RV3 vaccine for Indonesia

- Self-sufficiency of vaccine production & security
- Low cost, affordable
- Porcine free manufacture to meet Halal requirements
- Economic development

RV3-BB rotavirus vaccine protects against rotavirus disease in Indonesian children

Double blind randomized clinical trial
Yogyakarta and Central Java
>1600 infants
>500 researchers, primary health centre staff and midwives
Supported by grants from NHMRC & Bill and Melinda Gates Foundation

Vaccine Efficacy against severe rotavirus gastroenteritis



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Human Neonatal Rotavirus Vaccine (RV3-BB) to Target Rotavirus from Birth

J.E. Bines, J. At Thobari, C.D. Satria, A. Handley, E. Watts, D. Cowley, H. Nirwati, J. Ackland, J. Standish, F. Justice, G. Byars, K.J. Lee, G.L. Barnes, N.S. Bachtiar, A. Viska Icanervilia, K. Boniface, N. Bogdanovic-Sakran, D. Pavlic, R.F. Bishop, C.D. Kirkwood, J.P. Buttery, and Y. Soenarto

New England Journal of Medicine 22 February 2018

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bioforma

Update on RV3-BB vaccine development in Indonesia

Support development of BioFarma RV3 vaccine

Technology transfer: vaccine growth, assays etc

Large scale process development, formulation development
(Batavia BioSciences, University of Kansas; funding BMGF)

Clinical development: Phase 3 to be completed in Q1 2023

Cost-effectiveness Study of introduction into the NIP

Highly cost-effective <<1GDP/per capita

Modelled impact of RV3-BB vaccine on rotavirus disease

95% reduction of infection & disease when vaccine coverage is 85%

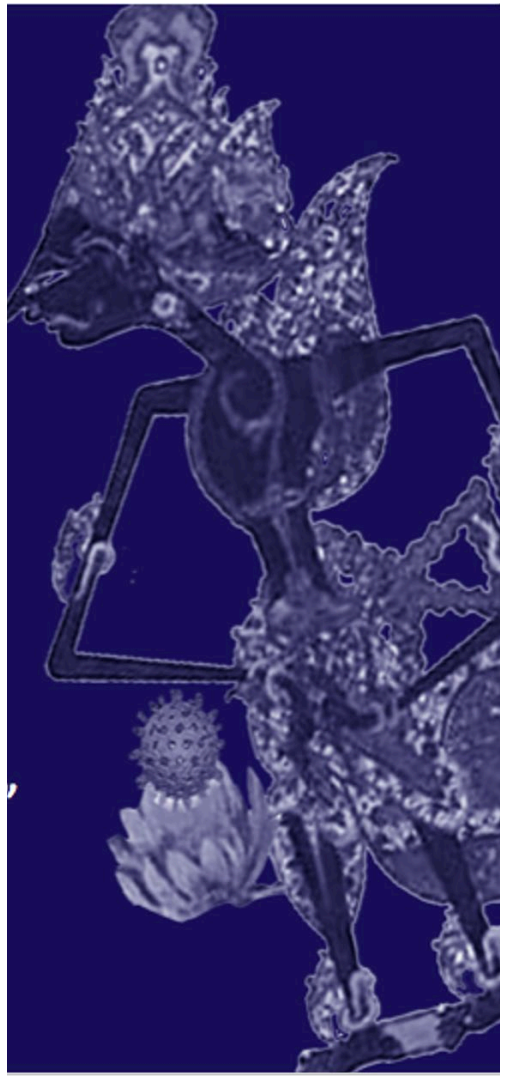
84% reduction even if coverage is 55%

RV3-BB vaccine immunogenicity not impacted by:

Co-administration with Oral Polio Vaccine

Genetic differences in histoblood group antigens

Breast milk antibodies or maternal antibodies



Indonesia plans to introduce the Bio Farma manufactured RV3 vaccine into the National Immunisation Program from 2023

Broad range of Enteric Disease research
- Gut microbiome & virome
- Changes in genetic diversity of rotavirus
- Rotavirus vaccine "Escape"

Global Paediatric Diarrhea Surveillance Program
Global multi-enteric pathogen diagnostic platform

Development of Enteric Vaccines
- Novel vaccine candidates
- Novel vaccine schedules
- Clinical vaccine trials
- Cost-effective analysis
- Support commercial
- Antimicrobial Resistance

Wastewater Surveillance Indonesia
- COVID-19
- Typhoid

COVID-19
- COVID and the gut
- Long-term impact of COVID in Indonesian children
- Probiotics in modifying disease in Indonesian children

World Health Organization

Collaborating Centre for Child Health
WPRO Rotavirus Regional Reference Laboratory

PhD & Masters UOM students from the IP region

PRIME Health partnership sponsored by Indonesian Gov
(Universitas Indonesia, Gadja Mada Uni, Uni Airlangga, Uni Melb)

Laboratory training – surveillance, research, commercial partners

Teaching & training in Global Health & Vaccinology

Supporting and mentoring future leaders

WGH
WOMEN IN GLOBAL HEALTH AUSTRALASIA

Support between colleagues during during crisis:
- COVID-19 pandemic
- Acute Kidney Injury

Thank you for attending the Ruth Bishop Address 2022

Please leave your reflections as a chat message now.

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