

# Rotavirus Vaccines

Rationale for Use

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# Conflict of interest

In the past I have received support for vaccine work, clinical trials, presentation of papers and conference attendance from

NZ Ministry of Health, US Government, Foundation Merieux, International Vaccine Institute, CSL, GSK, MSD, Novartis and Pfizer.

# Vaccine Schedule

- Reason not included is Fiscal
- The case for including rotavirus vaccine in childhood schedule is strong
- Rotavirus vaccine has potential to improve on time coverage
- But first dose has to be given by 12 or 14 weeks (ideally 6 weeks). How do you achieve this?

# Disease and Epidemiology

# Rotavirus

- Causes vomiting and diarrhoea of varying severity from relatively mild to fatal
- Most common cause of severe D&V world wide
- Treatment is supportive - rehydration
- The incidence is approximately the same in developed and developing countries
- Only prevention is vaccination

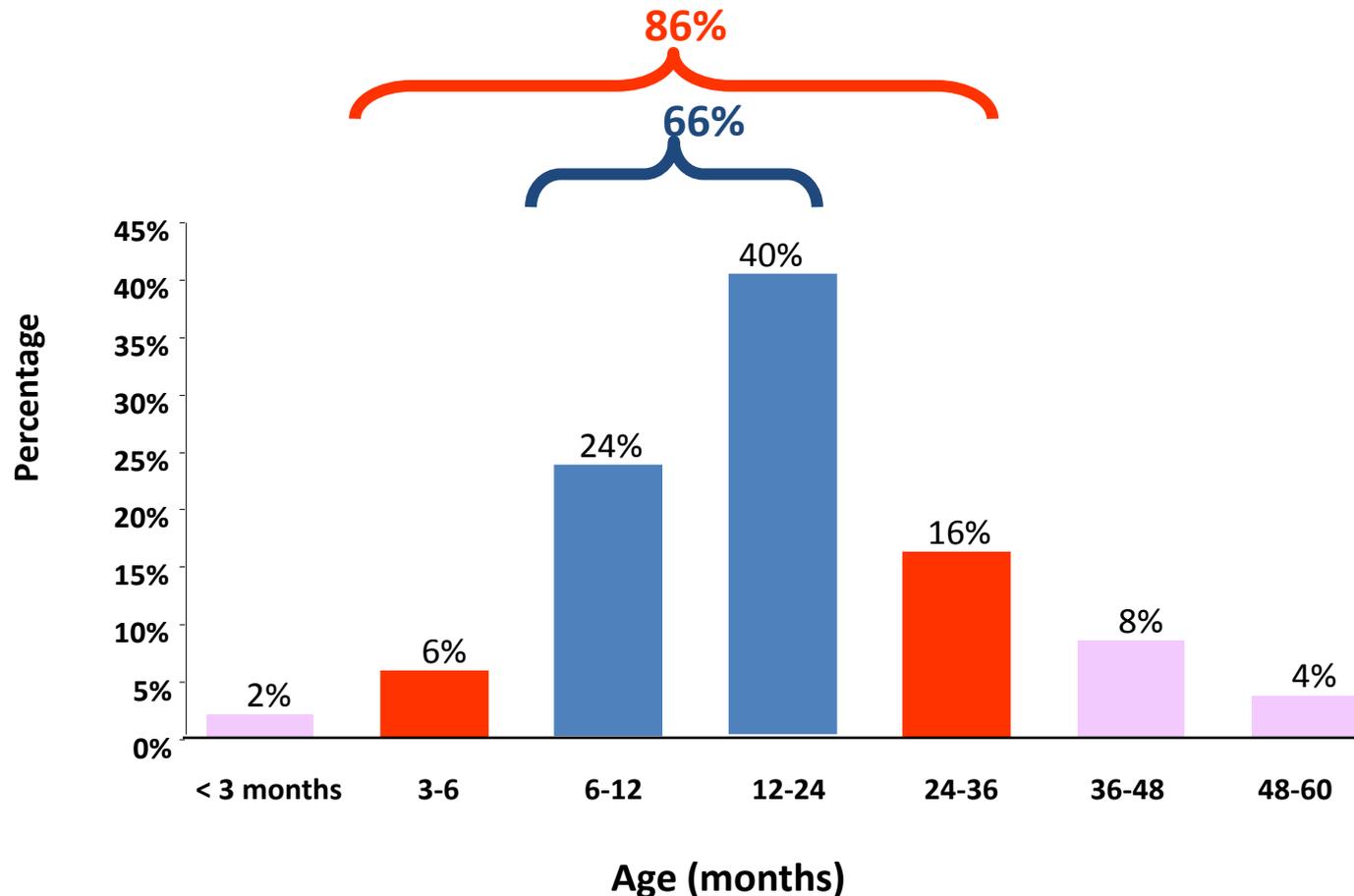
# Rotavirus is a physically robust virus

- RV can survive on human hands for several hours<sup>1,2</sup> and on non-porous inanimate surfaces for several days<sup>1,3</sup>
  - Survives longest on non-porous surfaces in low-temperature, high-humidity environments<sup>3</sup>
- Relatively resistant to chemical disinfectants<sup>1,4,5</sup>
  - Inactivated by relatively high concentrations of alcohol, chlorine or iodine<sup>6,7</sup>

**Standard sanitary measures are relatively ineffective in controlling rotavirus<sup>10</sup>**

# Nearly 90% of rotavirus gastroenteritis cases occur between 3 months and 3 years of age

*Distribution of RVGE cases by age in all settings in Europe (2004-2005)*

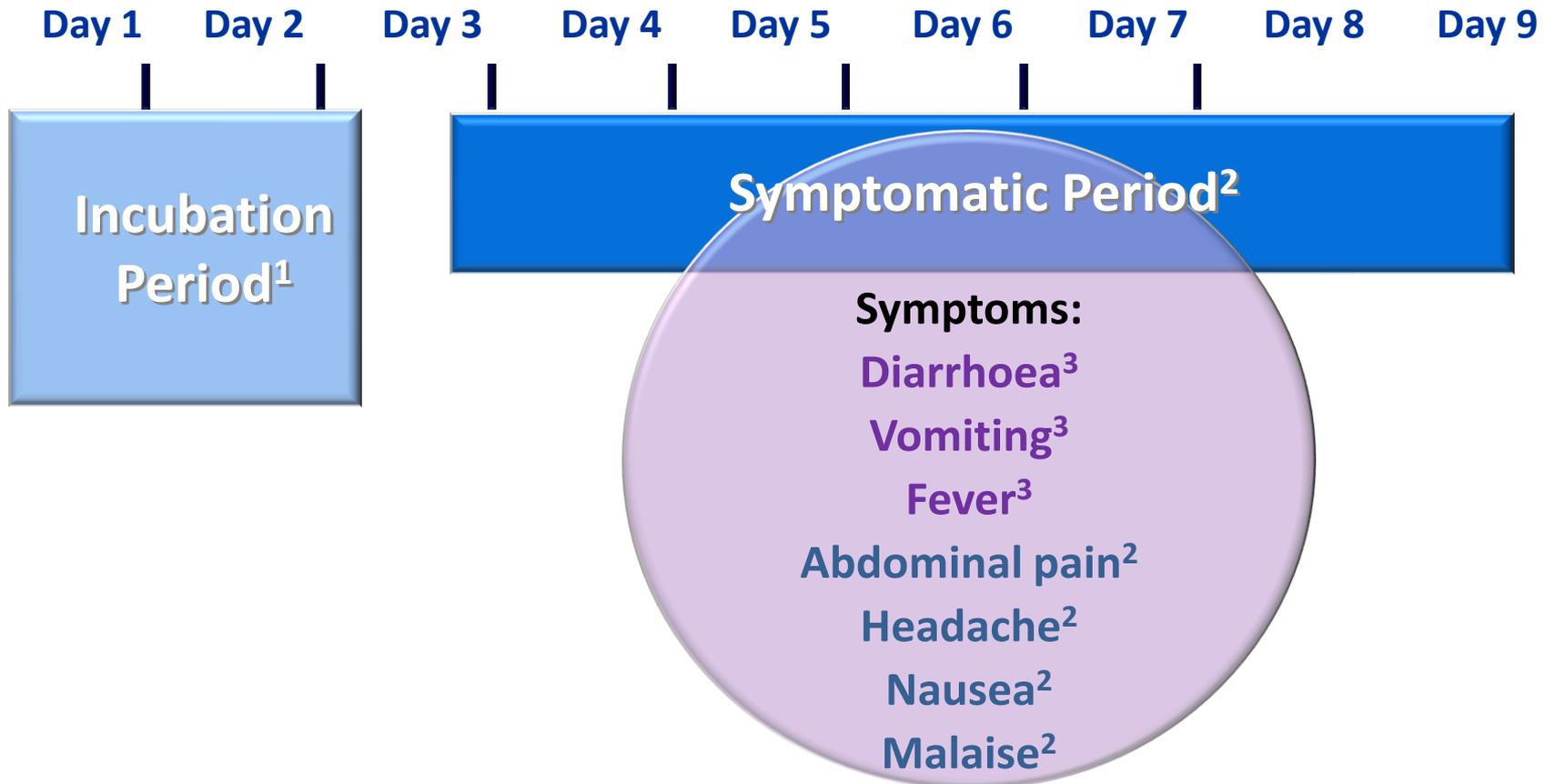


From REVEAL study<sup>1</sup>: prospective, observational study of AGE in 2846 children <5 years of age seeking health care, in 2004–2005, in selected areas of 7 countries  
Total AGE cases: 2 841

1. Van Damme P et al. J Infect Dis 2007;195(suppl 1):S4-S16.

2. REVEAL global report July 2007;SPMSD data on file.

# Typical duration of rotavirus infection

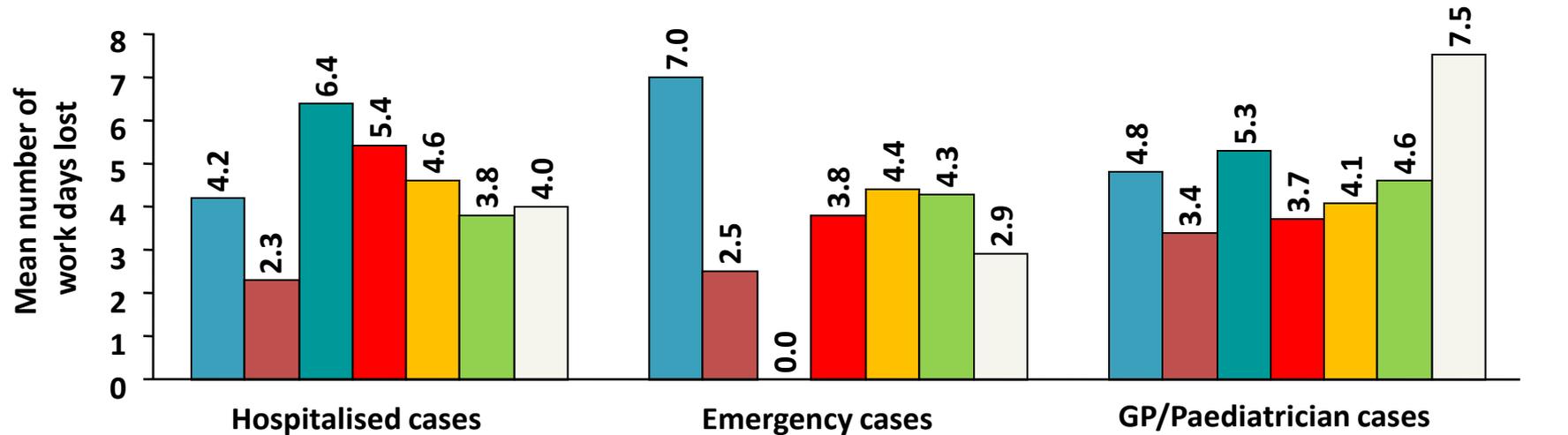


Symptoms in purple are most commonly reported (63% of patients report all three)<sup>3</sup>  
Symptomatic adults with rotavirus frequently report additional symptoms in blue<sup>2</sup>

1. Raebel MA and Ou BS. *Pharmacotherapy* 1999; **19**: 1279–95; 2. Anderson EJ and Weber SG. *Lancet Infect Dis* 2004; **4**: 91–9;  
3. Staat MA et al. *Pediatr Infect Dis J* 2002; **21**: 221–7

# Average number of work days lost by parents due to their child being ill with RVGE

- Mean number of work days lost by parents due to child's RVGE in seven European countries
  - hospitalised cases: 4 days
  - emergency cases: 4 days
  - primary care cases: 5 days

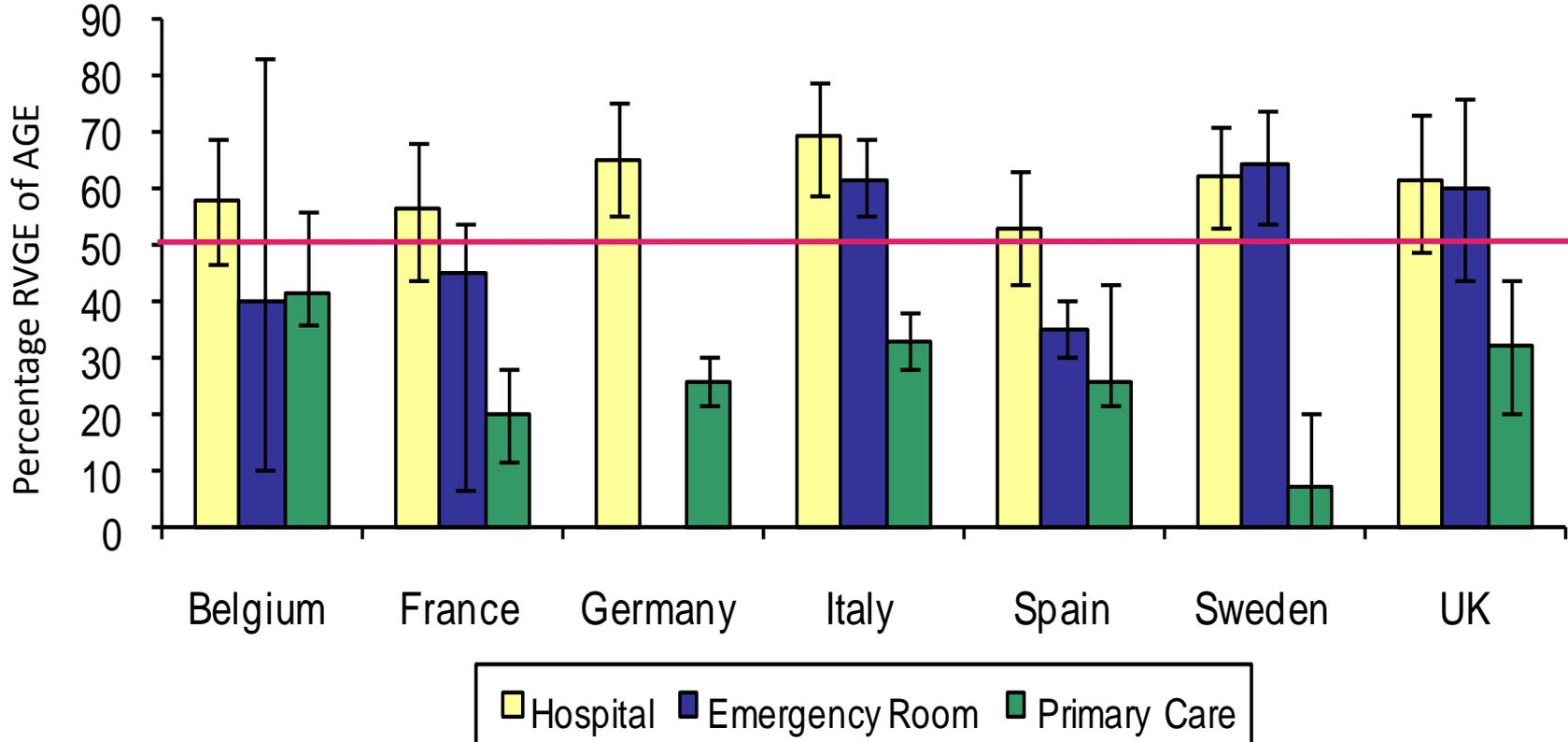


# Global Rotavirus burden

- 25 million clinic visits per year
- 2 million hospitalisations per year
- >527,000 deaths per year in children < 5 years (15% of deaths in children <5 yrs)
- Burden probably underestimated

# REVEAL study: percentage of RVGE among AGE cases in each study area stratified by setting

- More than 50% of hospitalisations for AGE are due to RV
- Around 30% of children seen in primary care for AGE have RV

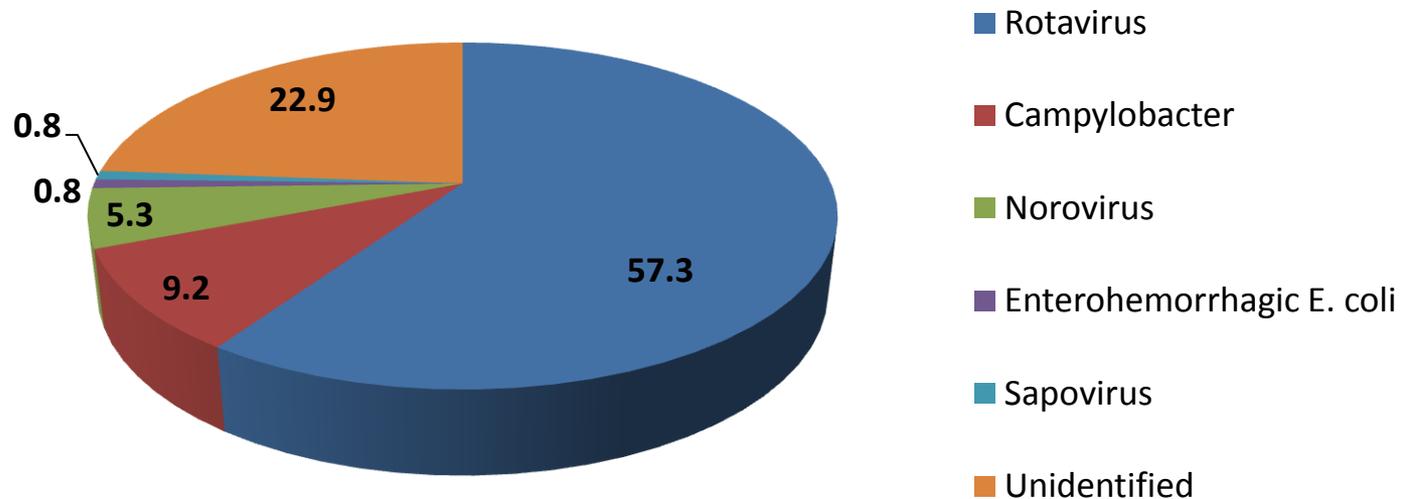


# NZ Rotavirus Epidemiology

- Annually for those age less than 3 years  
657 hospitalised/100,000
- Highest rate those aged 12 -23 months.
- One in 52 admitted by age 3 years
- One in 43 by age 5
- One in 5 will attend GP by age 5
- Rotavirus more likely to cause dehydration than other infections
- Peaks in winter when health burden at greatest

# Rotavirus is the most common cause of severe gastroenteritis in NZ

- Rotavirus is the most common cause of GE resulting in hospitalisation of NZ children and is most severe in children aged <2 years<sup>1</sup>



Licensed products

# Protection from Infection

## Rationale for vaccination

- Repeated infections throughout life but cumulative immunity provides broad protection
- Community study of Mexican infants
  - Initial (2<sup>nd</sup>) infection provided protection
  - 38% against asymptomatic infection (60%)
  - 73% against mild diarrhoea (83%)
  - 87% against moderate to severe illness (100%)

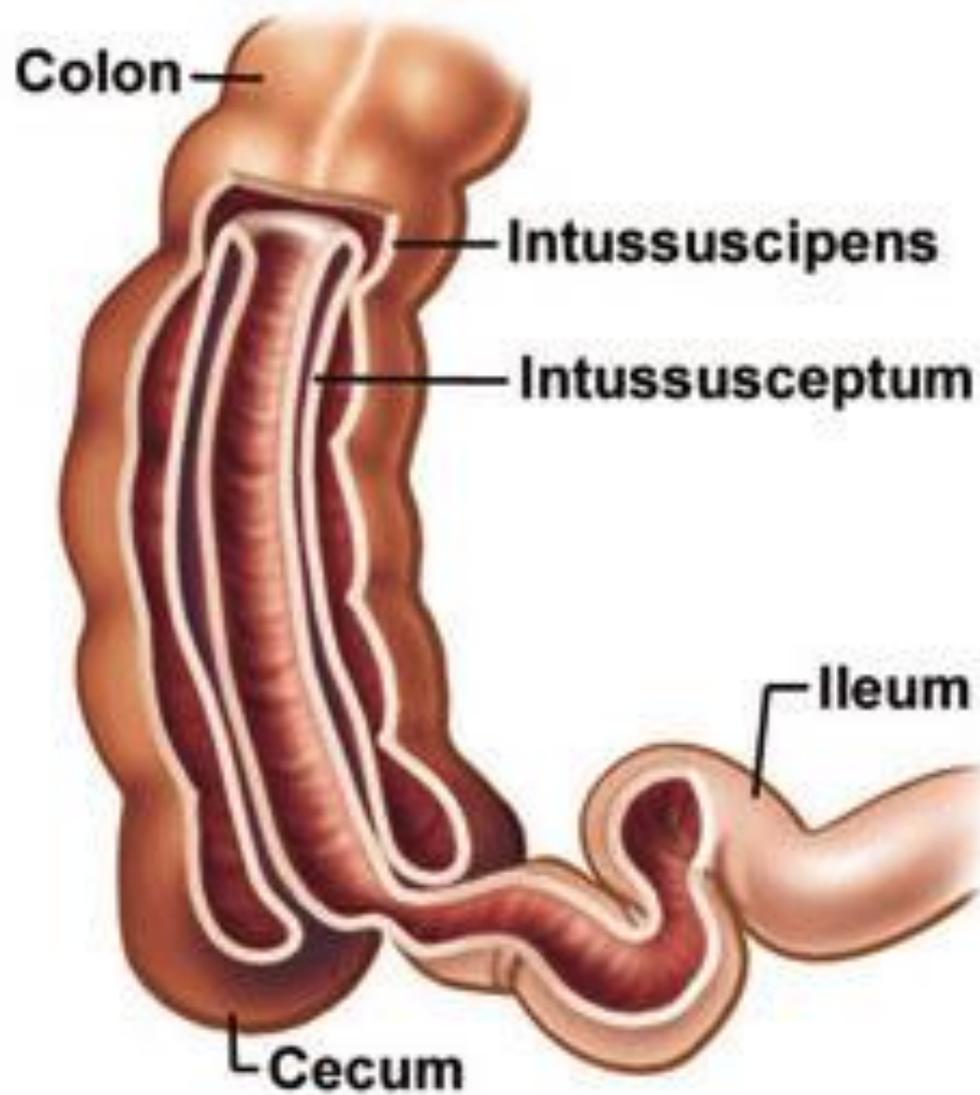
# Rotavirus Vaccine history

- Rotashield - 1<sup>st</sup> rotavirus vaccine
- Highly efficacious
- Incidence of Intussusception in clinical trials
  - 5/10,054 vaccine recipients
  - 1/4,633 placebo recipients

Rennels MB. Pediatrics 2000;106:123-5. Murphy TV, et al GN Engl J Med 2001; 344:564-572.

Kramarz P, et al Pediatr Infect Dis J 2001;20:410-416. Chang H-G, et al Pediatrics 2001;108:54-60.

Simonsen L et al Lancet 2001;358:1224-1229.



# RotaShield

- 10 months post licensure 15 cases reported to VAERS - 13 after first dose
- Vaccine use suspended - case control study - then vaccine withdrawn by company
- 1/10,000 - overall risk estimate
  - RR 1<sup>st</sup> dose - 37.27 (P<0.001)
  - 2<sup>nd</sup> dose - 3.8 (P=0.05)

Risk highest when 1<sup>st</sup> dose after 3 months of age

# Summary: EFFICACY of Rotavirus vaccines

- The two currently licensed rotavirus vaccines, *human RV vaccine* and *bovine-human reassortant RV vaccine*, have undergone large-scale, worldwide clinical development programmes
- Both vaccines have demonstrated efficacy:
  - against RVGE, severe RVGE and RVGE-hospitalisations
  - against diverse rotavirus serotypes
  - sustained over the first few years of life
  - in co-administration with other routinely used infant vaccines
  - in challenging study settings in the developing world
  - in pre-term infants

# What about intussusception?

- 2 large pre-licensure studies (each >60,000 children) showed no increase
- Population figures from active follow-up of intussusception cases in Australia found **NO OVERALL INCREASE** in intussusception after rotavirus vaccine but a slightly higher risk after the first dose
- Mexican population figures (*Rotarix*) suggest a slightly higher risk after the first dose overall but a similar study in Brazil did not demonstrate an overall risk
- Intussusception is a rare condition, with an annual incidence under 12 months of age in Australia of 80 per 100,000. The increased risk estimated at approximately 2 additional cases per every 100,000 infants vaccinated<sup>1</sup>

1. <http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/immunise-rotavirus>

# Recommendations about intussusception<sup>1</sup>

- As a precaution, healthcare professionals should follow-up on any symptoms indicative of intussusception
  - *Severe abdominal pain, persistent vomiting, bloody stools, abdominal bloating and/or high fever.*
- Inform parents/caregivers of the *rare* risk of intussusception and advise them to promptly report such symptoms.
- Do not give rotavirus vaccine outside the recommended age limits or to an infant with any history of chronic gastrointestinal disease including uncorrected congenital malformation
- Report any cases of intussusception following rotavirus vaccination to CARM: [carmnz@stonebow.otago.ac.nz](mailto:carmnz@stonebow.otago.ac.nz)  
<https://nzphvc-01.otago.ac.nz/carm-adr>

# Experience in other countries

- Post licensure data (introduced 2006) from USA suggest high efficacy and possible herd protection
- Aboriginal Australians high efficacy during outbreak
- Studies from Mexico (introduced 2007)
  - 41% reduction diarrhoea related deaths in vaccine recipients during 2008
  - 29% reduction in 1-2 year olds few of whom were vaccinated

# Fit with Schedule

- *Rotarix* - 2 doses
  - First dose at 6 weeks - no later than 14 weeks
  - Minimum 4 week gap,
  - 2<sup>nd</sup> dose by 24 weeks
- *RotaTeq* - 3 doses
  - Start at 6 weeks - no later than 12 weeks
  - Minimum 4 week gap,
  - 3<sup>rd</sup> dose by 32 weeks
- **Great potential to improve on time coverage**

# Rotavirus vaccine should be offered to infants because

- It should be on the schedule
- Rotavirus causes a serious illness in many children
- Parents lose time off work ~ 5 days
- It is challenging because it has to be given by 12 weeks of age
- But warn parents about low risk of intussusception

# Rotavirus vaccine summary

- No hesitation about recommending either
- Which one?

# Questions for you

- Is there an obligation to inform parents of the availability of non schedule vaccines for their children?
- If so when? And how?
- How are parents to be informed about rotavirus vaccine in a timely manner? (first dose has to be administered by 12 weeks)

# Suggested approach

- Send letter to pregnant women possibly in pregnancy pack covering routine schedule and non funded vaccines
  - Rotavirus, Varicella and cocoon pertussis
- Follow up phone call in 2<sup>nd</sup>/3<sup>rd</sup> trimester to discuss - offering appt. if required

# Excellent Summary Article

Grimwood K, Lambert SB, Milne RJ.  
Rotavirus Infections and Vaccines  
Pediatr Drugs 2010;12(4):1-22

# Acknowledgements

- Colleagues on ITF and Ministry of Health who taught me so much
- Sharon Wong, Lesley Voss and David Graham who shared slides with me
- Colleagues at Ropata Medical Centre who critiqued this presentation



UNATTENDED  
CHILDREN  
WILL BE GIVEN  
AN ESPRESSO  
AND A FREE PUPPY

The End

# Cost benefit

- Depends on
- Efficacy of vaccine
- Cost of vaccine
- Burden of disease - incidence and severity
  
- WHO suggests a cost effective intervention is one which averts a DALY at < 3 per capita GDP