Rotavirus
Burden of disease

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Rotavirus

* Overview of burden
  * Worldwide
  * New Zealand

* Vaccination impact
  * International evidence
  * Intussusception
  * New Zealand intuss data

* Prelim NZ data of impact of rotavirus vaccination
* Research in pneumococcal vaccine and otitis media
  * GSK funded laboratory consumables
  * Travel to pneumococcal conference Pfizer
* Diarrhoeal disease is second leading cause of death in children under 5 years (\(\frac{3}{4}\) million per year)

* Rotavirus is commonest cause of severe diarrhoeal disease and dehydration in infants and young children throughout the world

* Rotavirus associated with 1/3 of all diarrhoeal deaths (250,000 children)

* Highest burden of deaths and severe disease occur in low income countries
Rotavirus: very frequent pathogen of childhood gastroenteritis and hospital morbidity

* Rotavirus gastroenteritis occurs in all infants and children, at least once in early life - first symptomatic infection generally happens between 2 months to 2 years

* REGARDLESS of sanitation, high income or resource poor setting

* One of the **leading** causes of hospitalisation in young children in Australia and New Zealand

*Parashar et al., Emerg Infect Dis, 2003, Galati et al., Aust NZJ Public Health, 2006*
Burden of gastrointestinal infection in NZ

* Increasing hospitalisations for infectious illnesses in NZ
  * Increase by 50% 1989-2008 compared with non-infectious disease 7.3%

* GI infections (along with LRTI and skin soft tissue) accounted for 57% total infectious disease admissions between 2004-8

* GI infection admissions nearly doubled 1989-2008

* ID admissions (include GI infections) associated with deprivation and ethnicity

Rotavirus disease burden in New Zealand

* Gastroenteritis (D&V) most common medically preventable cause of acute hospital admission in NZ kids
  * Accounts for 5,200 admissions/year
  * Amongst all cause acute admissions is only exceeded by injury/poisoning

* NZ: rotavirus account for 42%+ of gastro admissions in children aged <3 years

* Rotavirus gastroenteritis is most severe in infants in the first year, and in particular the first months of life

* In NZ rotavirus admissions are significantly more likely in areas of socioeconomic deprivation

Craig E et al. The Health Status of Children and Young People in the Midland Region. NZ Child and Youth Epi, Dunedin, 2011.
Rotavirus disease burden in New Zealand

Number of rotavirus events per year

- ?deaths since 2001
- ~ 1,000 Hospitalisations
- ~ 2,000 ED visits
- ~ 10,000 GP Visits


= 1 in 52 children hospitalised by age 3 years with rotavirus

Milne and Grimwood. Value in Health 2009;12:888

Grimwood K et al. Rotavirus hospitalisation in NZ children under 3 years of age. J Paeds Child Health. 2006; 42: 196-203

National hospitalisation rate for rotavirus diarrhoea in children <3yrs = 634/100,000.

Figure 19.1 Hospitalisations from rotavirus in children aged less than two years, 2000–2010

Source: Ministry of Health

Notes: Publicly funded hospital discharges with a primary diagnosis of enteritis due to rotavirus (ICD-9 code 008.61)

What does rotavirus look like?

* Symptoms usually about 2-3 days after infectious contact
  * projectile vomiting and very watery diarrhoea (>3 loose/liquid stools/day)
  * often with fever and abdominal pain

* Severe diarrhoea leads to fluid loss, and may be life-threatening, particularly in young children

* Seasonal in NZ (winter/spring twice as common as summer/autumn)

* Children with rotavirus more likely to be dehydrated compared with other forms of acute gastroenteritis (NZ data)
<table>
<thead>
<tr>
<th>Severity</th>
<th>Symptoms</th>
<th>Physical signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>thirsty, restless</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Slightly dry mouth/ mucosa</td>
</tr>
<tr>
<td>Moderate</td>
<td>lethargic, irritable</td>
<td>Dry mouth mucosa, absent tears</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sunken eyes &amp; fontanelle</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Decreased urine output</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Altered skin elasticity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Signs of ketosis (rapid shallow breathing, smell of ketones)</td>
</tr>
<tr>
<td>Severe</td>
<td>limp, drowsy</td>
<td>Drowsiness</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Shock (tachycardia, poor volume pulses, cool to touch)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Skin retraction time &gt; 2 seconds</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Capillary refill time &gt; 3 seconds</td>
</tr>
</tbody>
</table>
Treatment

* No drug treatment (no antivirals)

* Oral rehydration solution

* Virus spreads rapidly, presumably through person-to-person contact, airborne droplets, or contact with contaminated objects (fomites)

* The first infection is usually the worst one
Available Rotavirus vaccines

* Rotarix (GSK) - monovalent rotavirus vaccine (RV1)
* RotaTeq** (CSL Biotherapies/Merck) - pentavalent vaccine (RV5)

* Both are live attenuated and oral

* Introduced
  * USA 2006
  * Australia 2007
  * UK 2013
Global and local support for Rotavirus vaccination

* WHO's Strategic Advisory Group of Experts (SAGE)
  “recommended that rotavirus vaccination should be included in all national immunization programmes to protect against virus responsible for >500,000 diarrhoeal deaths and 2 million hospitalizations/year among children.”


* 2012 Paediatric Society endorsed nationally funded vaccination

Pharmac-funded rotavirus for all eligible infants born from July 2014 (rotateq (3 dose RV5))
“More jabs in store for Kiwi babies”

Kiwi babies look likely to get free vaccinations against rotavirus later this year - up to six years after Australia.

The Paediatric Society has issued a position statement urging the Government to give "urgent priority" to vaccinating all babies against rotavirus, which can cause serious vomiting and diarrhoea.

Starship paediatrician Dr Emma Best, who chairs the society's infection and immunisation group…said priority had gone to raising immunisation rates for established vaccines against diseases such as tetanus, polio, hepatitis and measles.

…..Rotavirus vaccines are both given to babies as liquid medicines, rather than by injections.
Uptake, Impact, and Effectiveness of Rotavirus Vaccination in the United States

Review of the First 3 Years of Postlicensure Data

FIGURE 3. Rates of acute gastroenteritis hospitalization by year and rotavirus season among children <5 years of age, 18 states, January 2000 through June 2008. Adapted from J Infect Dis. 2010;201:1617–1624.28

Pediatric Infect Dis Journal Tate et al. 2011; 30
Sustained decrease in lab detection of rotavirus after vaccine implementation; 2000-2014

Now 7 years post vaccine
* 58-90% reduction in each post vaccine year
* Biennial pattern, low/erratic ongoing cases


MMWR April 2015 64 (13)
Reduction in admission due to gastroenteritis in Australia

Figure 4.17.1: Rotavirus-coded hospitalisations per month, Australia, 2001 to 2010

National Immunisation Program

Australian Immunisation Handbook 2013
* Westmead Children’s hospital
* Pre-vaccine period 2001-2006
* Vaccine introduced 1st July 2007
* 84% coverage by end 2008
* 75% reduction in hospitalisations 2008-2009
* 93% in <12 months old
* Reduction across all age groups
Previous 20% of RV nosocomial acquisition

**Fig. 1** Mean rotavirus hospitalisations at The Children’s Hospital at Westmead, 2001–2006 compared with three subsequent years, in children <18 years of age.
* Vaccine introduced in 2012
* 2013-2014 showed **77% decline** in laboratory confirmed RV in infants
* **26% decline** in all-cause gastroenteritis hospitalisations
  * =11,000 RV admissions and over 50,000 diarrhoeal admission prevented in UK in 1 year
* Reductions also seen in older children and adults
RV vaccine coverage and weekly rate (per 1,000,000) of laboratory-confirmed RV infections (A) and all-cause gastroenteritis hospitalisations (B) 2000-2015.

Table 17.1: Cochrane review: percentage of severe rotavirus and all-cause diarrhoea cases prevented in children by RV1 and RV5, compared to placebo (low mortality rate countries)

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Percentage of cases prevented</th>
<th>Risk ratio (95% confidence interval)</th>
<th>Number of participants (number of trials)</th>
<th>Quality of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Severe rotavirus diarrhoea: infants aged under 1 year</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV1</td>
<td>86</td>
<td>0.14 (0.07–0.26)</td>
<td>40,631 (6)</td>
<td>High</td>
</tr>
<tr>
<td>RV5</td>
<td>87</td>
<td>0.13 (0.04–0.45)</td>
<td>2344 (3)</td>
<td>Moderate</td>
</tr>
<tr>
<td><strong>Severe rotavirus diarrhoea: children aged under 2 years</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV1</td>
<td>85</td>
<td>0.15 (0.12–0.2)</td>
<td>32,854 (8)</td>
<td>High</td>
</tr>
<tr>
<td>RV5</td>
<td>82</td>
<td>0.18 (0.07–0.5)</td>
<td>3190 (3)</td>
<td>Moderate</td>
</tr>
<tr>
<td><strong>Severe all-cause diarrhoea: infants aged under 1 year</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV1</td>
<td>40</td>
<td>0.60 (0.5–0.72)</td>
<td>17,867 (1)</td>
<td>Moderate</td>
</tr>
<tr>
<td>RV5</td>
<td>72</td>
<td>0.28 (0.16–0.48)</td>
<td>1029 (1)</td>
<td>Low</td>
</tr>
<tr>
<td><strong>Severe all-cause diarrhoea: children aged under 2 years</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV1</td>
<td>37</td>
<td>0.63 (0.56–0.71)</td>
<td>39,091 (2)</td>
<td>Moderate</td>
</tr>
<tr>
<td>RV5</td>
<td>96</td>
<td>0.04 (0.00–0.70)</td>
<td>5916 (1)</td>
<td>Low</td>
</tr>
</tbody>
</table>


**World**

RV vaccine reduces:
* Vaccine prevents 70% of cases RV diarrhoea
* Vaccine prevents 80% of severe episodes that occur in first 1 or 2 years of life
* Reduce severe All Cause diarrhoea by at least 40%
* Wanes 1-3 years following last dose
**TABLE 1. Region-specific Pooled Effect Estimates of Rotavirus Vaccination on Select Outcomes**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Study Design</th>
<th>MDG Region</th>
<th>Effect Size (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rotavirus diarrhea</strong></td>
<td>RCT (vaccine efficacy)</td>
<td>Developed</td>
<td>75.9 (72.4, 78.9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Southern Asia</td>
<td>34.6 (21.6, 45.3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sub-Saharan Africa</td>
<td>55.4 (27.6, 72.6)</td>
</tr>
<tr>
<td></td>
<td>Observational (vaccine</td>
<td>Developed</td>
<td>86.8 (60.7, 95.6)</td>
</tr>
<tr>
<td></td>
<td>effectiveness)§</td>
<td>Latin America and Caribbean</td>
<td>29.6 (−53.5, 67.7)</td>
</tr>
<tr>
<td></td>
<td>Observational (percent</td>
<td>Developed</td>
<td>61.4 (60.2, 62.6)</td>
</tr>
<tr>
<td></td>
<td>change)§</td>
<td>Latin America and Caribbean</td>
<td></td>
</tr>
<tr>
<td><strong>Severe rotavirus diarrhea</strong></td>
<td>RCT (vaccine efficacy)</td>
<td>Eastern Asia/SE Asia</td>
<td>90.6 (82.3, 95.0)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Latin America and Caribbean</td>
<td>88.4 (67.1, 95.9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sub-Saharan Africa</td>
<td>79.6 (71.3, 85.5)</td>
</tr>
<tr>
<td></td>
<td>Observational (vaccine</td>
<td>Developed</td>
<td>68.8 (55.8, 77.9)</td>
</tr>
<tr>
<td></td>
<td>effectiveness)§</td>
<td>Latin America and Caribbean</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Observational (percent</td>
<td>Developed</td>
<td>61.9 (55.7, 68.1)</td>
</tr>
<tr>
<td></td>
<td>change)§</td>
<td>Latin America and Caribbean</td>
<td></td>
</tr>
<tr>
<td><strong>Rotavirus hospitalizations</strong></td>
<td>RCT (vaccine efficacy)</td>
<td>Eastern Asia/SE Asia</td>
<td>94.3 (72.8, 98.8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Latin America and Caribbean</td>
<td>93.8 (81.5, 97.9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sub-Saharan Africa</td>
<td>83.8 (74.6, 89.6)</td>
</tr>
<tr>
<td></td>
<td>Observational (vaccine</td>
<td>Developed</td>
<td>88.9 (80.9, 93.5)</td>
</tr>
<tr>
<td></td>
<td>effectiveness)§</td>
<td>Latin America and Caribbean</td>
<td>67.6 (54.8, 76.7)</td>
</tr>
<tr>
<td></td>
<td>Observational (percent</td>
<td>Developed</td>
<td>57.0 (40.0, 68.0)</td>
</tr>
<tr>
<td></td>
<td>change)§</td>
<td>Latin America and Caribbean</td>
<td>76.7 (75.6, 77.7)</td>
</tr>
<tr>
<td><strong>Diarrhea hospitalizations</strong></td>
<td>RCT (vaccine efficacy)</td>
<td>Sub-Saharan Africa</td>
<td>10.0 (−22.3, 33.9)</td>
</tr>
<tr>
<td><strong>Severe diarrhea</strong></td>
<td>RCT (vaccine efficacy)</td>
<td>Developed</td>
<td>49.6 (39.8, 57.8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Eastern Asia/SE Asia</td>
<td>30.3 (13.1, 44.2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Latin America and Caribbean</td>
<td>35.8 (24.1, 45.7)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Southern Asia</td>
<td>18.6 (1.9, 32.3)</td>
</tr>
<tr>
<td></td>
<td>Observational (vaccine</td>
<td>Developed</td>
<td>83.2 (41.7, 95.1)</td>
</tr>
<tr>
<td></td>
<td>effectiveness)§</td>
<td>Latin America and Caribbean</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Observational (percent</td>
<td>Developed</td>
<td>71.5 (53.4, 82.9)</td>
</tr>
<tr>
<td></td>
<td>change)§</td>
<td>Latin America and Caribbean</td>
<td>28.9 (16.3, 39.6)</td>
</tr>
<tr>
<td><strong>Diarrhea mortality</strong></td>
<td>Observational (percent</td>
<td>Developed</td>
<td>41.5 (32.5, 50.5)</td>
</tr>
<tr>
<td></td>
<td>change)§</td>
<td>Latin America and Caribbean</td>
<td>41.2 (39.9, 42.4)</td>
</tr>
</tbody>
</table>
Differences in environmental influences, other pathogens, maternal antibodies

BUT WAIT

THERE'S

MORE!
Rotavirus is linked to childhood seizures both febrile and afebrile - about 5% of young children with rotavirus infection experience a seizure.

Cohort of US infants Vaccine Safety Datalink & Hospitalisation/ED visit

Looked at the first year after the last dose vaccine

250,601
  186,502 fully vaccinated
  64,099 not vaccinated

Protective association between full rotavirus vaccination and childhood seizures for the year after vaccination

20% reduction in risk of seizure

Protective association between rotavirus vaccination and childhood seizures in the year following vaccination in US children Payne et al, 2014, CID
Aimed to show similar effect in Queensland, Aus as had been seen in US

RotaTeq (RV5) introduced mid-2007 (Queensland)

Preexisting linked data with febrile (but not afebrile) seizures presenting to ED
### Table 1. VE of Rotavirus Vaccine Against ED Presentations and Hospital Admissions for Febrile Convulsions According to Age

<table>
<thead>
<tr>
<th>Birth Cohort</th>
<th>Age Range</th>
<th>No. of Vaccinated Cases</th>
<th>Total No. of Cases</th>
<th>PPV Range (%)</th>
<th>VE (%) [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any ED presentation/hospital admission</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any ED presentation</td>
<td>May 2007–April 2008; May 2008–April 2009; May 2009–April 2010</td>
<td>8 mo–2 y 7 mo</td>
<td>1301</td>
<td>1530</td>
<td>87.7–90.9</td>
</tr>
<tr>
<td></td>
<td>May 2007–April 2008; May 2008–April 2009; May 2007–April 2008</td>
<td>1 y 8 mo–3 y 7 mo</td>
<td>454</td>
<td>544</td>
<td>86.7–90.3</td>
</tr>
<tr>
<td></td>
<td>2 y 8 mo–4 y 7 mo</td>
<td>92</td>
<td>137</td>
<td></td>
<td>85.8</td>
</tr>
<tr>
<td>Any hospital admission</td>
<td>May 2007–April 2008; May 2008–April 2009; May 2009–April 2010</td>
<td>8 mo–2 y 7 mo</td>
<td>389</td>
<td>460</td>
<td>87.7–90.9</td>
</tr>
<tr>
<td></td>
<td>May 2009–April 2010</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>May 2007–April 2008; May 2008–April 2009; May 2007–April 2008</td>
<td>1 y 8 mo–3 y 7 mo</td>
<td>110</td>
<td>142</td>
<td>86.7–90.3</td>
</tr>
<tr>
<td></td>
<td>2 y 8 mo–4 y 7 mo</td>
<td>23</td>
<td>33</td>
<td></td>
<td>85.8</td>
</tr>
<tr>
<td>First presentation/admission in the year</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First ED presentation</td>
<td>May 2007–April 2008; May 2008–April 2009; May 2009–April 2010</td>
<td>8 mo–2 y 7 mo</td>
<td>1065</td>
<td>1266</td>
<td>87.7–90.9</td>
</tr>
<tr>
<td></td>
<td>May 2009–April 2010</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>May 2007–April 2008; May 2008–April 2009; May 2007–April 2008</td>
<td>1 y 8 mo–3 y 7 mo</td>
<td>384</td>
<td>461</td>
<td>86.7–90.3</td>
</tr>
<tr>
<td></td>
<td>2 y 8 mo–4 y 7 mo</td>
<td>78</td>
<td>114</td>
<td></td>
<td>85.8</td>
</tr>
<tr>
<td>First hospital admission</td>
<td>May 2007–April 2008; May 2008–April 2009; May 2009–April 2010</td>
<td>8 mo–2 y 7 mo</td>
<td>326</td>
<td>392</td>
<td>87.7–90.9</td>
</tr>
<tr>
<td></td>
<td>May 2009–April 2010</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>May 2007–April 2008; May 2008–April 2009; May 2007–April 2008</td>
<td>1 y 8 mo–3 y 7 mo</td>
<td>93</td>
<td>120</td>
<td>86.7–90.3</td>
</tr>
<tr>
<td></td>
<td>2 y 8 mo–4 y 7 mo</td>
<td>20</td>
<td>28</td>
<td></td>
<td>85.8</td>
</tr>
</tbody>
</table>
The trade-off

- Colon
- Intussuscipens
- Intussusceptum
- Ileum
- Cecum
* Association between intussusception and rotavirus vaccine seen 1998 with RotaShield vaccine in US
  * 37 x incr risk first week after first vaccine dose
  * 1 excess case of intussusception per 10,000 vaccine recipients
  * Vaccine withdrawn 1999

* Peak age for intussusception known to be first 6-8 months of life

* Associations noted with IS and both RV1 and RV5 but is an uncommon occurrence
Vaccine introduced in Australia in 2007 - split between states as to whether used RV1 or RV5
Findings

* Both vaccines give increased risk of IS in 1st 3wks after 1st dose - risk greatest 1st wk

  * Risk also slightly increased in 1st week after 2nd dose

* Excess of 14 cases intuss/year with 85% coverage

* RV1 4/100,000  RV5 7/100,000

  * (Rotashield 1999 - 10/100000)

* Also prevents 6500 hospitalisations for rotavirus illness in for <5yrs

Clinical Infectious Diseases 2013 Carlin et al.
Does incr risk post vaccine actually mean an overall increase in cases of intussusception for population.....?

Vaccine triggers IS earlier in those who are ‘susceptible’ anyway.....?

Is wild RV infection on of the causative agent in IS (therefore overall lessening in IS may be seen after vaccination?)
* Variable geographic and ethnic incidence

* Variable over time

* No seasonality

Rates in infants < 1 year
* Worldwide incidence of 74 per 100,000
* 9/100,000 in Bangladesh (2001-2006)
* 328/100,000 in South Korea
* 40/100,000 in USA
* 80 -100/100,000 in Australia
How Common in NZ?

* One prior estimate
* NZHIS data, Jan 1998-June 2003
* Children < 3yrs
* 207 cases with discharge diagnosis of intussusception
* Incidence rates:
  * < 1 year, 65/100,000 child years
  * 1-2 years, 18/100,000 child years
  * 2-3 years, 6.7/100,000 child years

Chen, Y.E. Beasley, S. Grimwood, K. and the New Zealand Rotavirus Study Group. Arch Dis Childhood 2005
* Need to quantify NZ’s background intussusception rate before the vaccine

* Enables rotavirus vaccine-associated changes or increases in intussusception rate to be recognised

Epidemiology of Intussusception in New Zealand Pre Rotavirus Vaccination

Rosie B, Dalziel S, Wilson E, Best EJ

New Zealand Medical Journal Accepted June 2016
Results

* 794 cases in children aged 0-36 months Jan 1998 - Dec 2013

* Average of 50 cases per year (range 39-62)

* Incidence varied from 21/100,000 child years in 2009, to 37 in 2002

* No increasing or decreasing trend over study period

* Rosie B, Dalziel S, Wilson E, Best EJ. Epidemiology of Intussusception in NZ Pre RV Vaccination

NZMJ 2016
Incidence of Intussusception by Year (NZ Children 0-36 Months, 1998-2013)

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Incidence (Cases/100,000 Child Years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 year</td>
<td>56.1 / 100,000</td>
</tr>
<tr>
<td>1-2 years</td>
<td>18.6 / 100,000</td>
</tr>
<tr>
<td>2-3 years</td>
<td>9.2 / 100,000</td>
</tr>
</tbody>
</table>

Rosie B, Dalziel S, Wilson E, Best EJ. Epidemiology of Intussusception in NZ Pre RV Vaccination
NZMJ 2016
Average Annual Incidence of Intussusception by Age
(Children 0-36 Months, 1998-2013)

Kruskal Wallis, p < 0.001

Rosie B, Dalziel S, Wilson E, Best EJ. Epidemiology of Intussusception in NZ Pre RV Vaccination
NZMJ 2016
Age at Intussusception by Ethnic Group
(Children 0-36 Months, 1998-2013)

(Kruskal Wallis, p=0.03).

Rosie B, Dalziel S, Wilson E, Best EJ. Epidemiology of Intussusception in NZ Pre RV Vaccination
NZMJ 2016
Summary

* Age adjusted incidence rate 56/100,000 child-years - Wide variation between years, but no overall trend
* Occurs at younger age in Maori and Pacific infants but not more frequently

- Extrapolating Australian rates & assume birth cohort of 60,000 & vaccination rate 95% (Health Target)

- NZ might expect 3 extra intussusception cases per year

- Ethnicity differences in timing of intussusception +/- later immunisation delivery in Maori means vaccine might occur closer to peak incidence of intussusception ?trigger more..

- Need to keep watching this space for NZ

How do we use this information

* Vaccine contra-indications - prior intussusception or congenital abnormality that predisposes to IS
  * Risk of recurrence of IS (unrelated to RV vaccination) is about 10%

* Complete rotavirus vaccine on time; this will be well before peak age of intussusception

* Immunisation providers should inform parents and carers of the rare risk of intussusception and how to be alert for the signs and symptoms of the condition

Intussusception symptoms include baby having intermittent crying/screaming episodes, curling up or pulling up knees to chest, vomiting +/- passing bloody, pink or red coloured jelly-like stools

Risk is highest 1 week after vaccine (1st dose maybe second)
Comparison of virus shedding after rotavirus vaccine

* 87 infants vaccinated with rotavirus vaccine
* 80-90% detection of RV by PCR
* 20-30% by EIA
* 1-28 days after vaccination
* Peak detection day 4 to day 7 post vaccine

What does this mean?

**Laboratory comments on results:**
Low levels of rotavirus may be detected in asymptomatic children and following vaccination

Hsieh YC, Vaccine, 2013
Norovirus and Medically Attended Gastroenteritis in U.S. Children


* NV in 21% children seeking medical attention for acute gastroenteritis

* Rotavirus in 12%

* Norovirus now leading cause gastro post RV vaccine
Auckland, CMDHB, WDHB and Waikato data show impressive impact of RV vaccine already

Both direct and indirect benefits in hospital and community infection rates (less diarrhoeal disease in those up to age 5 years, not just the vaccinated infants)

Changes in laboratory testing techniques will happen (antigen less useful, PCR increasingly used)

With a shift to molecular testing for NV/RV in children: low false positives will occur in healthy, vaccinated children

NV likely to become more common detected cause of GE in children, this is not replacement of disease burden though
* Rotavirus - a huge morbidity burden for New Zealand’s young children
* Vaccine is highly effective
* Extra benefits becoming apparent internationally
  * decrease in seizure presentations
  * less nosocomial infections
  * herd effects
* Risk versus benefit of vaccine favours the vaccine
  * Changes in intussusception rate will be difficult to detect as is very uncommon
  * Need clear information for providers and parents about small intussusception risks
Clinical questions about rotavirus vaccine

* Can baby have it in hospital?
* Can baby have it in NICU?

* Can newborn have receive vaccine if mother/siblings are on immunosuppressants like cancer treatment?

* Can newborn have the vaccine if mother had immunosuppression in pregnancy?


* Australian Immunisation Handbook 10th Edition