



Assessment of intussusception risk in Mexican infants under 9 months of age after administration of pentavalent rotavirus vaccine.

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Background

- During its use in Mexico (2007-2010), RV1 was associated with intussusception
 - Risk: 5.8, (95%CI:2.6–13.0)
- Since 2011, Mexico shifted to RV5.

Objective

- Estimate the risk of intussusception with RV5 in Universal Immunization Program in México in the first 30 days after vaccination

Methods

- Self-Controlled Case Series
- Estimate intussusception risk after each dose of RV5.
- Active surveillance: 14 public hospitals through the country.
- Vaccination status determined by card or immunization records from health facilities.
- Relative incidence as measure of risk comparison
- Analysis in MS Excel, EpiInfo7 and R.

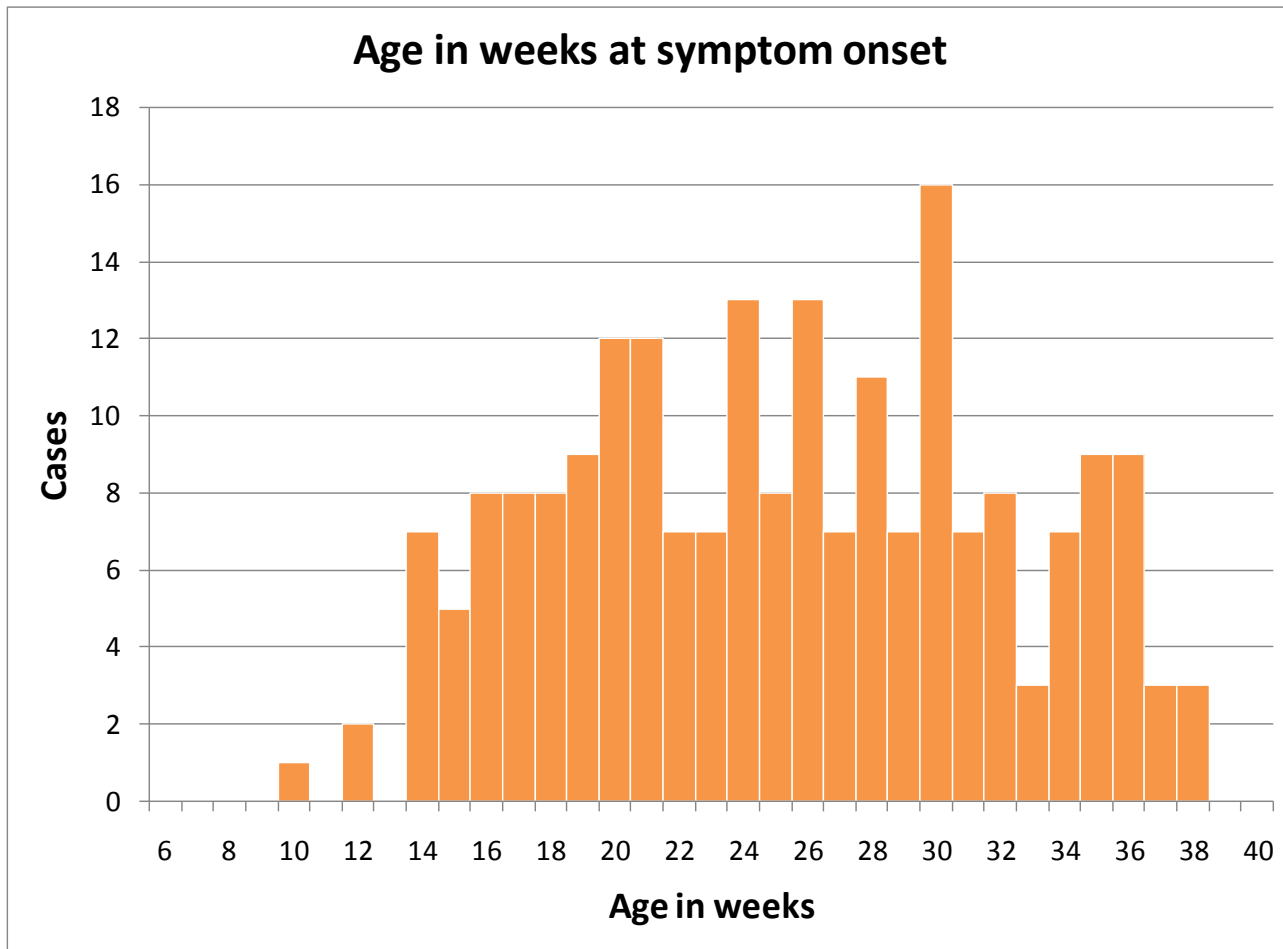
Selection criteria

- Inclusion
 - Age: ≥ 6 weeks & ≤ 8 months 29 days.
 - Brighton Collaboration criteria for definitive diagnosis of intussusception
 - Informed consent by parents
- Exclusion
 - Intestinal anatomical conditions

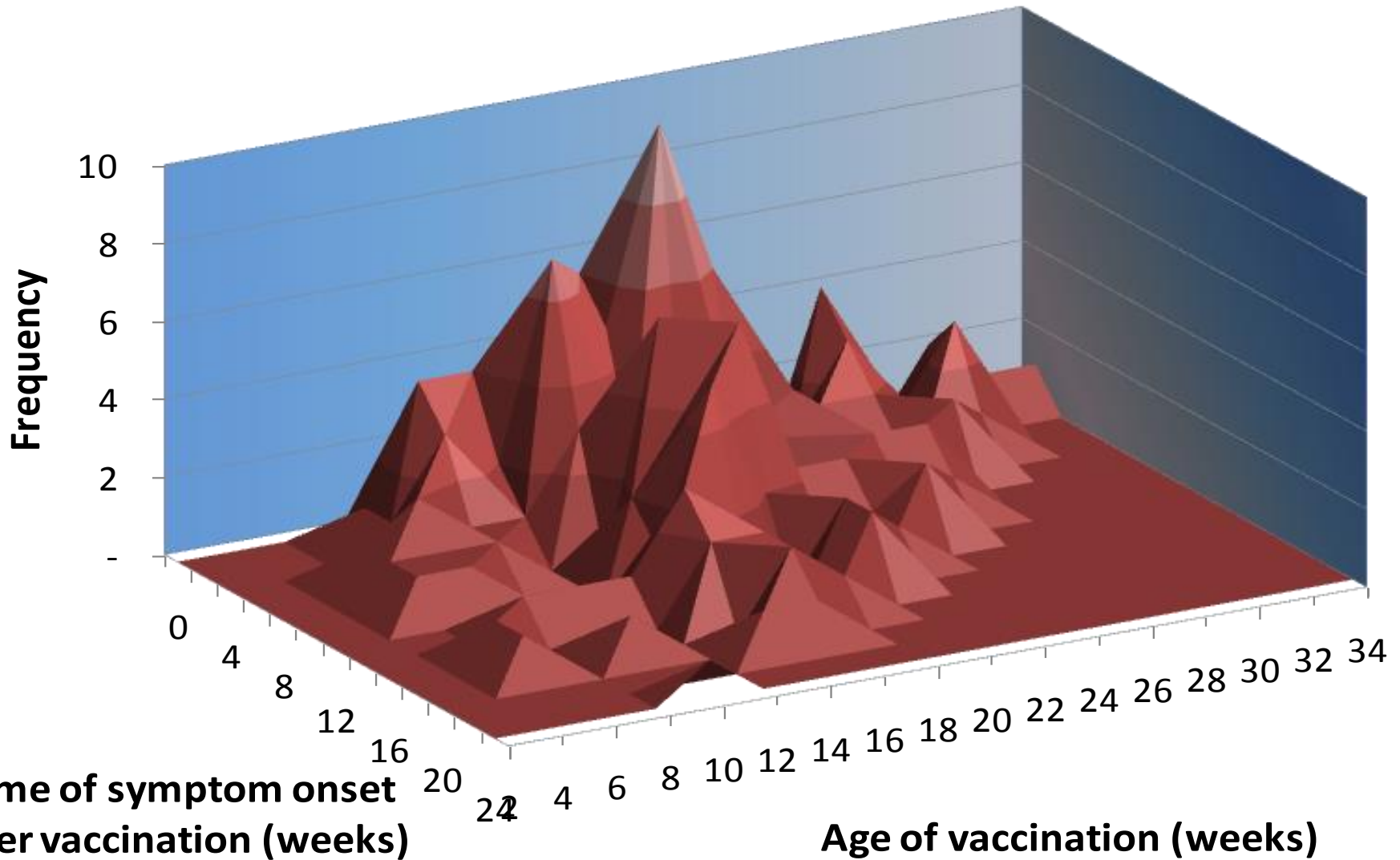
Results

- Included
 - 210 infants
 - 60% male
 - First, second and third RV5 doses received in 94%, 88%, and 78% respectively.
- Excluded
 - Anatomical conditions: 10
 - Meckel's diverticulum 8, malrotation 1, colonic incomplete fixation 1
 - Participation not accepted by parents 5
 - No definitive diagnosis 3

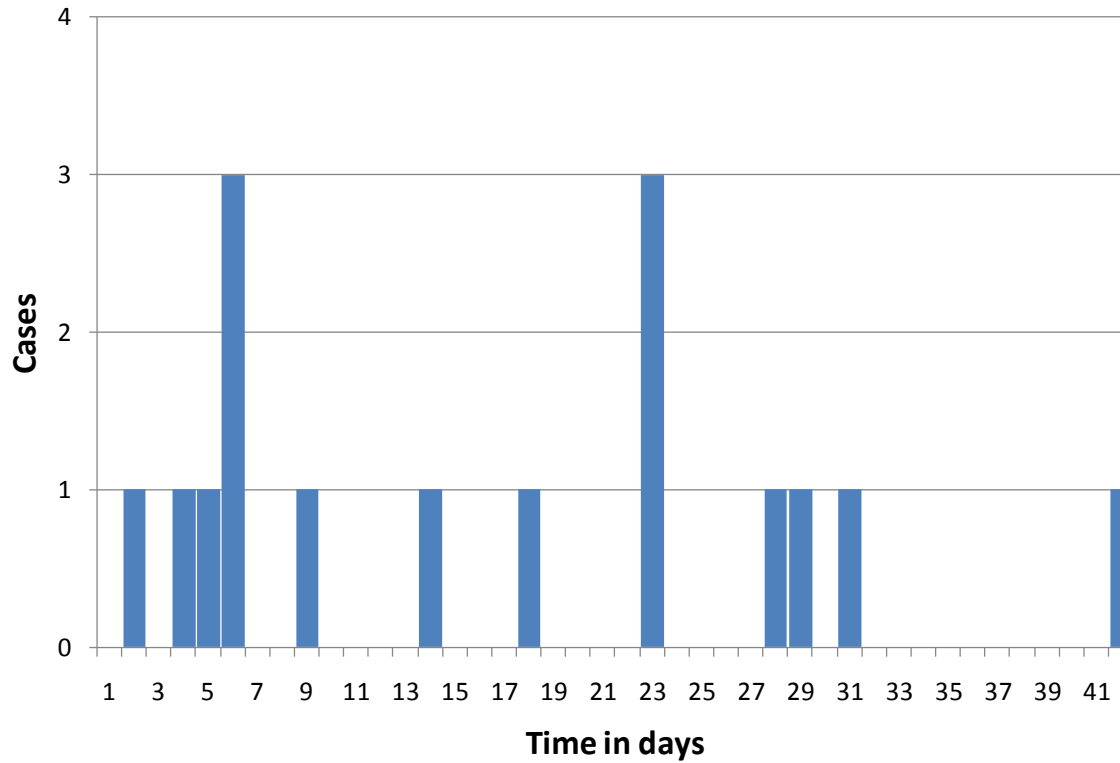
Distribution by age of symptom onset



Number of cases by age at vaccination before symptom onset (any dose) and by time of symptom onset after vaccination



Time from dose 1 to symptom onset

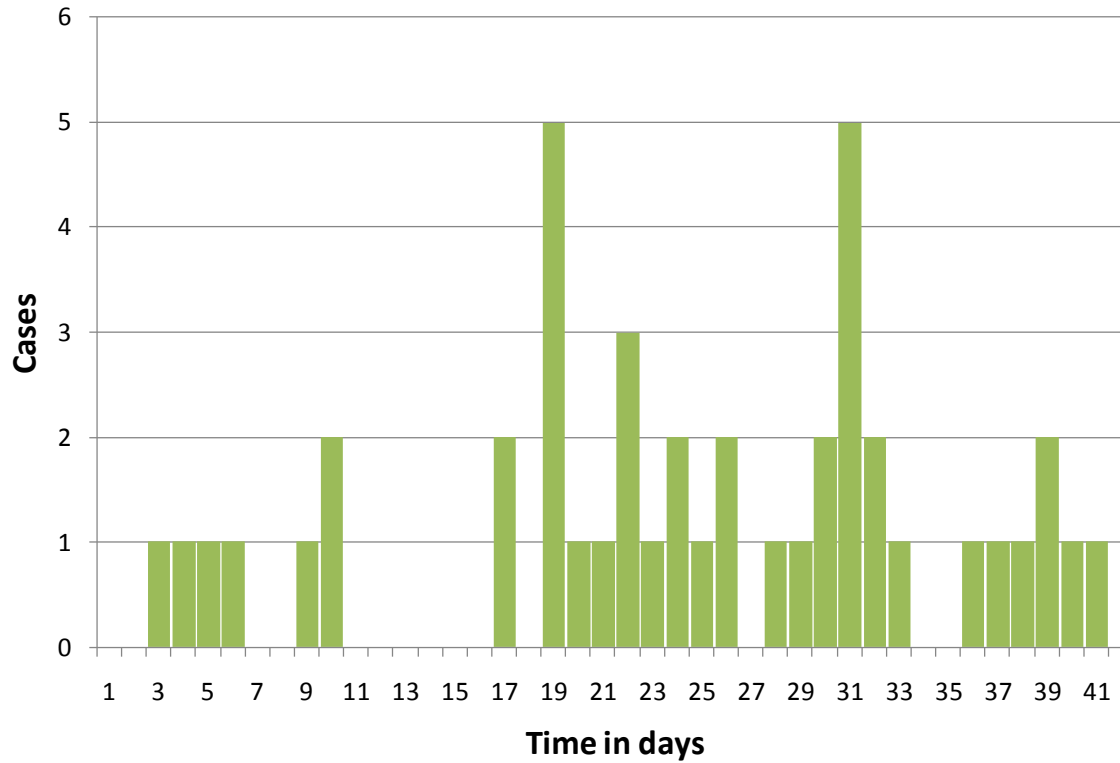


After first dose. 1 to 7 days.

R.I.: 3.6 (95%C.I.:1.4-9.3, p=0.008).

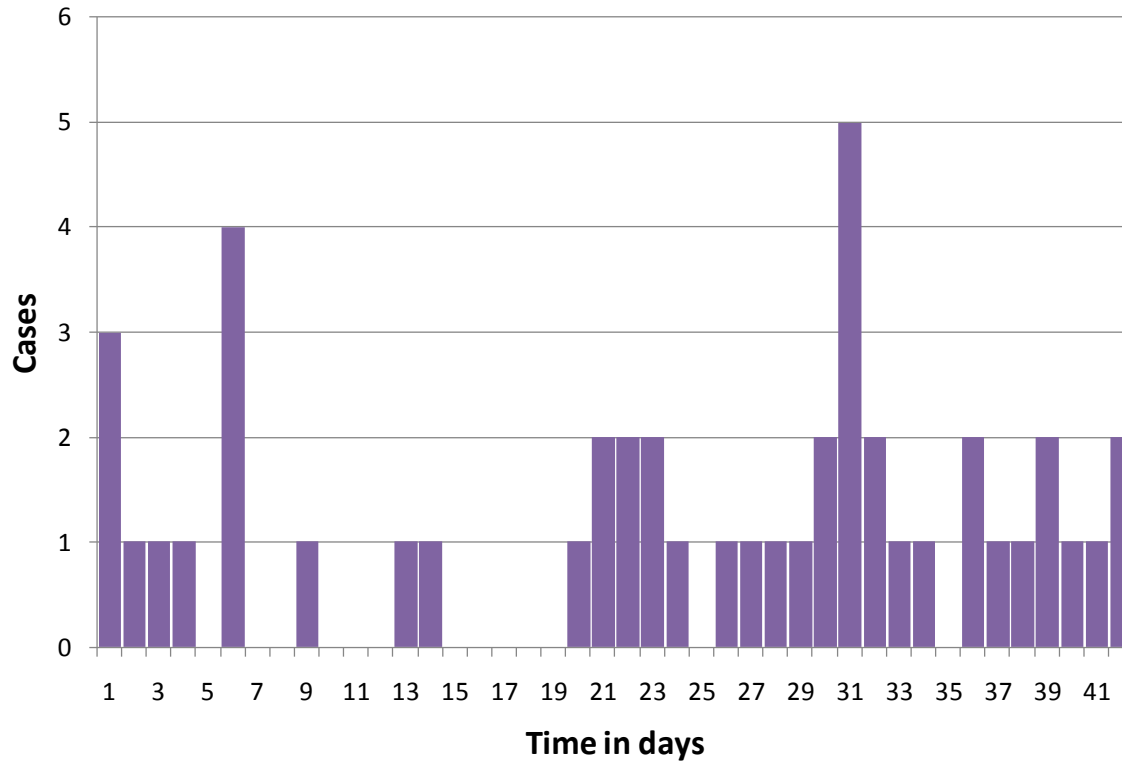
Once adjusted by age effect and the presence of the other doses

Time from dose 2 to symptom onset



**After second dose. 22 to 31 days.
R.I.: 2.6 (95%C.I.:1.5-4.4, p=0.001).**

Time from dose 3 to symptom onset



**After third dose. 22 to 31 days.
R.I.: 2.8 (95%C.I.:1.6-4.9, p<0.001).**

Table 1. Age adjusted intussusception risk estimates by RV5 dose and time of symptom onset after vaccination

	Risk window. Days after Vaccination	Relative Incidence	95%CI	p value	
Dose 1	1 to 7	3.6	1.4-9.3	0.008	**
	8 to 14	1.1	0.3-4.6	0.932	
	15 to 21	0.5	0.6-3.5	0.455	
	22 to 31	1.9	0.8-4.7	0.176	
Dose 2	1 to 7	1.3	0.5-3.5	0.666	
	8 to 14	0.8	0.2-2.4	0.632	
	15 to 21	2.2	1.1-4.4	0.034	*
	22 to 31	2.6	1.5-4.4	0.001	**
Dose 3	1 to 7	2.1	0.9-4.6	0.072	
	8 to 14	0.7	0.2-2.2	0.537	
	15 to 21	0.7	0.2-2.3	0.570	
	22 to 31	2.8	1.6-4.9	<0.001	***
	Age in Days	Relative Incidence	95%CI	p value	
Age effect	113 to 217	12.0	6.4-22.6	<0.001	***
	218 to 274	12.2	6.1-24.7	<0.001	***

Events=210. Rsquare= 0.053 (max possible= 0.266). Likelihood ratio test= 161.5 on 15 df, p=0. Wald test= 103.9 on 15 df, p=<0.0001. Score (logrank) test = 143.6 on 15 df, p=0.000

Applying the risk of three doses

To

- Proportions of intussusception incidence by age group reported for Mexico
 - BMC Gastroenterol. 2013 May 27;13:95.
- For the prevaccine incidence of intussusception in México
 - 2006
- And proportion of infants vaccinated at different ages:
 - 1 additional case / 7508 vaccinated infants,
or
 - 295 vaccine-related cases / cohort of about 2 million

Conclusions

- Slight increase in risk after any dose of RV5.
- Possible reason for the observed risk increase in second and third doses
 - Some children received accelerated schedule: 6 weeks of age and next doses after 4 weeks intervals.
 - None infant with “accelerated” schedule developed intussusception within risk window after first dose.

Conclusions

- Additional cases attributable to RV5 (294 yearly) are surpassed by
 - 205,909 cases,
 - 11,662 hospitalizations and
 - 959 deaths
- Averted in México every year.