

INCIDENCE OF PAEDIATRIC ROTAVIRUS GASTROENTERITIS IN EUROPE: THE REVEAL* STUDY

*Rotavirus Gastroenteritis Epidemiology and Viral Types in Europe Accounting for Losses in Public Health and Society

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INTRODUCTION

- Rotavirus is the most common cause of severe acute gastroenteritis (AGE) in young children worldwide, accounting for an estimated 39% of deaths due to diarrhoea in children <5 years old.¹ Almost all children are infected by 5 years of age.² In industrialised countries, mortality rates from rotavirus gastroenteritis (RVGE) are low, but morbidity and hospitalisation rates are high.³
- Now that effective rotavirus vaccines are available, immunisation strategies should be developed based on the incidence of RVGE by age, the causative serotypes and total disease burden. Such comprehensive data, however, were previously lacking in Europe. With rare exceptions,⁴ only national studies of RVGE burden have been reported for Europe, and different methodologies make comparisons difficult.
- The primary objective of the Rotavirus Gastroenteritis Epidemiology and Viral Types in Europe Accounting for Losses in Public Health and Society (REVEAL) Study was to assess the annual incidences of AGE and RVGE in children <5 years old seeking medical attention in primary care, emergency care, and hospital settings in 7 European countries. The study findings have been reported recently.⁵⁻⁸

METHODS

- Study design:**
 - Prospective, 1-year observational study conducted in the 2004–2005 season using a common protocol in Belgium, France, Germany, Italy, Spain, Sweden and the UK.
- In each country, a study area was selected to include both urban and rural communities with ~255,000 inhabitants (Table 1). For each study area, all hospitals and emergency rooms that might see children with AGE were included, along with a sample of primary care physicians (general practitioners and/or paediatricians).
- Inclusion criteria:**
 - Children <5 years old seeking medical care for AGE during the study period (1 October 2004 to 30 September 2005)
 - AGE was defined as an episode of at least 3 loose stools, at least 3 watery stools, or forceful vomiting associated with gastroenteritis, in a 24-hour period in the 7 days before the medical visit; the episode must have been preceded by a 14-day symptom-free period.
- Exclusion criteria:**
 - Previously diagnosed chronic gastrointestinal tract disease with symptoms compatible with the definition of AGE
 - Prior participation in rotavirus vaccine trial
 - Nosocomial AGE.
- If a child visited >1 healthcare setting during the AGE episode, they were included in the study at the highest level of care, in increasing order: primary care, emergency room, hospital. Children presenting more than once were considered as separate cases.
- Children were classified as having RVGE if a stool sample, obtained within 14 days of symptom onset, was rotavirus positive by ELISA performed at a central laboratory.
- For each study area, overall annual incidences of AGE and RVGE were estimated by extrapolating data from the included children to children who were eligible but not included, and adjusting for participation rates and the primary care sampling fraction.



RESULTS

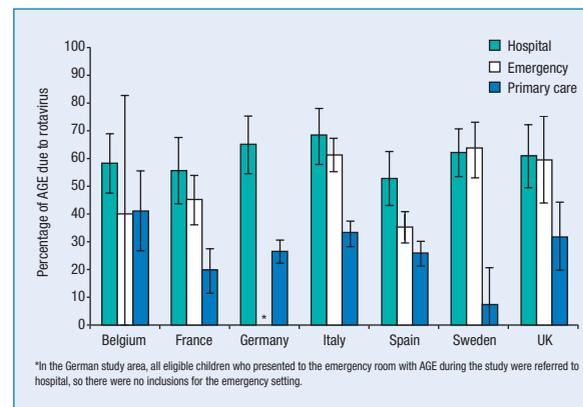
- 2846 children with AGE were included, and ELISA results were available for 2712 children.
- 1102 (40.6%) children were rotavirus positive.
- Overall, RVGE was estimated to account for 27.8% to 52.0% of AGE cases, and was responsible for up to two-thirds of hospitalisations and emergency room consultations, and one-third of primary care consultations for AGE (Figure 1).

Table 1. Study area populations and number of participating hospitals, emergency rooms and primary care physicians.

	Belgium	France	Germany	Italy	Spain	Sweden	UK
Study area	Antwerp	Dijon and surroundings	Rostock and surroundings	Padua and surroundings	Gandia, Denia and surroundings	Västerbotten County	Wirral Peninsula
Population	250,243	242,073	432,740	392,827	305,000	256,875	312,293
No. of children <5 years old (%)	14,193 (5.7)	13,108 (5.4)	15,844 (3.7)	16,000 (4.1)	14,856 (4.9)	12,763 (5.0)	17,488 (5.6)
No. of hospitals	2	2	2	1	2	2	1
No. of emergency rooms	2	6	2	1	3	3	1
No. of primary care physicians	22	22	34	13	23	13	12
Sampling fraction for primary care (%) ^a	37.83	20.54	35.18	39.61	46.82	37.48	17.22

^aPercentage of children seen by study primary care physicians.

Figure 1. Observed percentage (and 95% confidence interval) of AGE due to rotavirus by study area and setting.



^aIn the German study area, all eligible children who presented to the emergency room with AGE during the study were referred to hospital, so there were no inclusions for the emergency setting.

Table 2. Estimated annual incidences, with 95% confidence intervals, of RVGE per 100 children by setting and by study area.

	Hospital	Emergency room	Primary care	Total
Belgium	0.99 (0.79–1.18)	0.79 ^a	1.59 (1.05–2.19)	3.38 (NC)
France	0.87 (0.66–1.05)	2.65 (2.12–3.19)	1.45 (0.95–2.11)	4.96 (3.73–6.35)
Germany	0.50 (0.42–0.57)	– ^b	4.18 (3.53–4.91)	4.68 (3.95–5.48)
Italy	0.52 (0.44–0.60)	1.90 (1.70–2.07)	2.28 (1.94–2.63)	4.70 (4.08–5.30)
Spain	0.65 (0.52–0.77)	1.89 (1.61–2.20)	2.19 (1.81–2.58)	4.73 (3.94–5.55)
Sweden	0.77 (0.66–0.88)	1.37 (1.14–1.57)	0.06 ^{a,c}	2.19 (NC)
UK	0.29 (0.24–0.35)	0.19 (0.14–0.23)	1.59 (1.00–2.29)	2.07 (1.37–2.87)

NC, confidence interval not calculated.

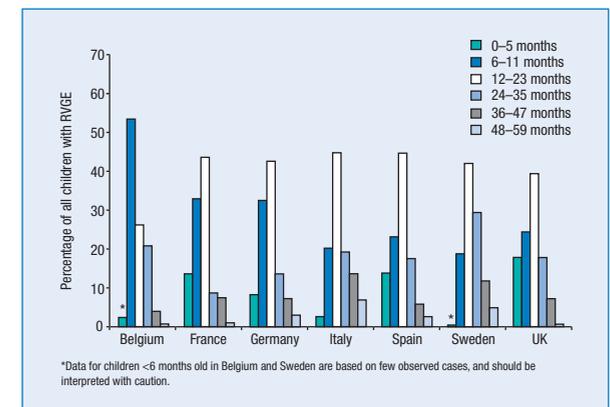
^a Confidence intervals not estimated because low numbers of children were included in these settings.

^b In the German study area, all eligible children presenting to the emergency room with AGE were referred to hospital, so there were no inclusions in the emergency setting.

^c In the primary care setting in the Swedish study area, parents generally called a nurse advice service located in the same medical centre as the primary care physicians. Therefore, following the nurses' advice, most children with AGE were referred to higher care or treated at home.

- The estimated annual incidence of AGE ranged from 4.22 to 16.82 per 100 children <5 years old.
- The estimated annual incidence of RVGE ranged from 2.07 to 4.96 per 100 children <5 years old (Table 2).
- The estimated age-specific annual incidences for RVGE were consistently higher in the 6–11 month and 12–23 month age groups, with 56.7% to 74.2% of all RVGE cases occurring in the 6–23 month age group (Figure 2).
- The greatest burden of AGE was between October and May in all countries, peaking between January and March; whereas for RVGE, the period was shorter (December to April), although the peak was also generally between January and March.

Figure 2. Estimated age-specific distribution of RVGE cases by study area.



^aData for children <6 months old in Belgium and Sweden are based on few observed cases, and should be interpreted with caution.

CONCLUSIONS

- The REVEAL Study was the first large, prospective, international study to investigate systematically the burden of paediatric AGE and RVGE across Europe in 3 clinical settings (hospital, emergency room and primary care) using a common protocol.
- Rotavirus infection accounts for a high proportion of AGE cases in children <5 years old in Europe.
- The peak incidence of RVGE is 6 to 23 months of age. This observation may be explained by the protective effect of maternal antibodies in infants <6 months of age and the development of natural immunity after repeated infections in children >2 years of age.
- The high hospitalisation rate due to RVGE over a short period coincides with the peaks for other winter diseases (e.g. influenza or respiratory syncytial virus infection), which places a considerable burden on hospital services.⁹
- These data suggest that routine rotavirus vaccination in infants <6 months old could significantly reduce the substantial burden of this frequent, potentially serious childhood disease.
- The REVEAL Study has provided essential data that will help to guide immunisation strategies for paediatric RVGE in Europe.

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