RISK OF HOSPITALISATION FOR CHILDREN WITH ROTAVIRUS GASTROENTERITIS AND NON-ROTAVIRUS ACUTE GASTROENTERITIS: THE REVEAL* STUDY

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

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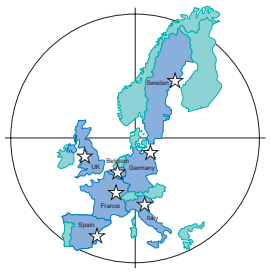
INTRODUCTION

- Rotavirus is the leading cause of severe diarrhoea in children <5 years old.[1] Children with severe rotavirus gastroenteritis (RVGE) may have up to 20 episodes of diarrhoea and vomiting each day, which can lead to dehydration and, in some cases, death.[2]
- Although mortality rates from RVGE are low in industrialised countries, morbidity and hospitalisation rates are high.[3]
- It is estimated that RVGE accounts for approximately 700,000 outpatient visits, >87,000 hospitalisations and 231 deaths annually in the European Union, with 1 in 54 children <5 years old being hospitalised with RVGE.[4]
- Recently available rotavirus vaccines offer an effective means of preventing RVGE. Immunisation strategies should be based on the incidence of RVGE, the causative serotypes and the total disease burden. Until now, comprehensive Europe-wide data have been lacking.
- The Rotavirus Gastroenteritis Epidemiology and Viral Types in Europe Accounting for Losses in Public Health and Society (REVEAL) Study has assessed the annual incidence rates of acute gastroenteritis (AGE) and RVGE in children <5 years old seeking medical attention in primary care, emergency care, and hospital settings in 7 European countries. The findings of the REVEAL Study have been reported recently.[5–8]
- We present REVEAL Study data on the risk of hospitalisation due to paediatric RVGE and non-rotavirus AGE.

METHODS

- This was a prospective, 1-year observational study, which was conducted in the 2004–2005 season using a common protocol in Belgium, France, Germany, Italy, Spain, Sweden and the UK.

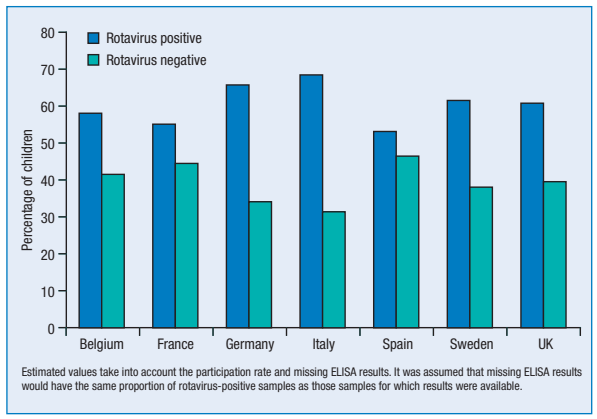


- In each country, a study area was selected to comprise a population of approximately 255,000. For each study area, all hospitals and emergency rooms that might see children with AGE, and a sample of primary care physicians (general practitioners and/or paediatricians), were included.
- All children <5 years old presenting with AGE during the 1-year study period were eligible.
- 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 symptom-free period of at least 14 days. Children with nosocomial AGE were excluded.
- 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, hospitalisation rates were estimated by extrapolating data from the included children to children who were eligible but not included, and adjusting for participation rates.

RESULTS

- 2846 children with AGE were included in the study. ELISA results were available for 2712 children, and 1102 (40.6%) were rotavirus positive.
- Rotavirus infection was responsible for up to two-thirds (range 53.0% to 68.9%) of hospitalisations for AGE (**Figure 1**).
- The mean duration of hospitalisation was similar for children who had RVGE (range 2.5 to 5.0 days) and those who had rotavirus-negative AGE (range 2.4 to 5.2 days).
- The estimated percentage of children with RVGE admitted to hospital ranged from 10.4% to 36.0%, compared with 2.1% to 23.5% of children with rotavirus-negative AGE (**Figure 2**).

Figure 1. Estimated percentages of children who were rotavirus positive or rotavirus negative among hospitalised children with AGE, by study area.



Estimated values take into account the participation rate and missing ELISA results. It was assumed that missing ELISA results would have the same proportion of rotavirus-positive samples as those samples for which results were available.

Figure 2. Estimated percentages of children with rotavirus-positive AGE or rotavirus-negative AGE who were hospitalised, by study area.

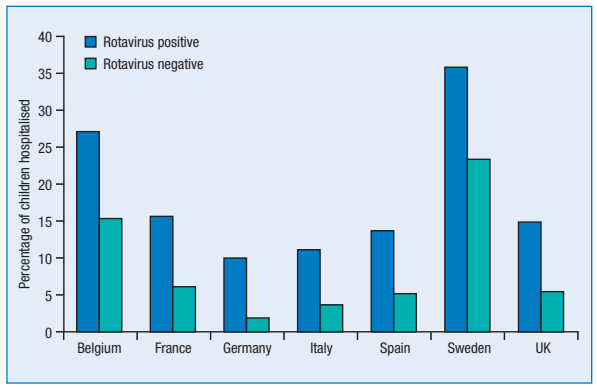
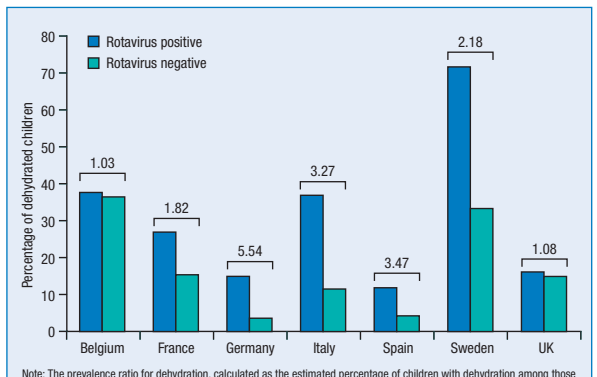


Figure 3. Estimated percentages of children with dehydration among those with rotavirus-positive AGE or rotavirus-negative AGE, by study area.



Note: The prevalence ratio for dehydration, calculated as the estimated percentage of children with dehydration among those with RVGE divided by the estimated percentage of children with dehydration among those with rotavirus-negative AGE, is indicated for each study area above the bars.

- The risk of hospitalisation after an initial consultation in primary care was higher for children with RVGE than for those with rotavirus-negative AGE (range of relative risk [RR] 1.62–3.66), and this difference achieved statistical significance in France, Germany, Italy, Spain and the UK (**Table 1**). A similar effect was observed for the risk of referral to an emergency department (range of RR 1.32–3.38; statistically significant in France and Italy).
- The greater risk of hospitalisation for children with RVGE than for those with rotavirus-negative AGE was accompanied by greater disease severity among children with RVGE, as evidenced by higher frequencies of symptoms, particularly dehydration (**Figure 3**) and vomiting, but also fever and lethargy.

Table 1. Observed numbers of children with rotavirus-positive AGE or rotavirus-negative AGE first seen in the primary care setting who were referred to hospital.

Study area	Number first seen in primary care	Referral to hospital n	(%)	RR	(95% CI)
Belgium					
RV positive	33	15	(45.5)	1.62	(0.83–3.15)
RV negative	32	9	(28.1)	1.00	
ELISA result not available	7				
France					
RV positive	64	16	(25.0)	2.63	(1.27–5.43)
RV negative	105	10	(9.5)	1.00	
ELISA result not available	10				
Germany					
RV positive	121	16	(13.2)	2.21	(1.17–4.15)
RV negative	317	19	(6.0)	1.00	
ELISA result not available	14				
Italy					
RV positive	239	31	(13.0)	3.37	(1.77–6.43)
RV negative	312	12	(3.9)	1.00	
ELISA result not available	17				
Spain					
RV positive	159	22	(13.8)	3.66	(1.92–6.96)
RV negative	370	14	(3.8)	1.00	
ELISA result not available	17				
Sweden					
RV positive	14	8	(57.1)	2.10	(0.92–4.75)
RV negative	22	6	(27.3)	1.00	
ELISA result not available	1				
UK					
RV positive	42	19	(45.2)	1.81	(1.02–3.22)
RV negative	52	13	(25.0)	1.00	
ELISA result not available	12				

CI, confidence interval; RR, relative risk; RV, rotavirus.
ELISA results were not available either because there were insufficient samples or the test results were not interpretable.
The reference group for RR calculations is RV-negative patients, for whom risk is equal to 1.00.

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 using a common protocol.
- Rotavirus infection was the underlying cause of illness in the majority of children hospitalised with AGE.
- Dehydration was up to 5.5 times more likely in children with RVGE than in those with rotavirus-negative AGE. RVGE follows a more severe disease course than rotavirus-negative AGE, often requiring earlier, more intensive treatment in hospital.
- Hospitalisation was up to 3.7 times more likely among children with RVGE compared with children with rotavirus-negative AGE, which is consistent with the results of other studies.[9,10]
- The REVEAL Study has shown that the greatest burden of RVGE occurs from December to April, peaking between January and March.[5] The high rate of hospitalisation due to RVGE over such a short period coincides with peak incidences of other potentially serious winter diseases, such as influenza and respiratory syncytial virus infection, thus increasing the burden on hospital services.
- The burden of RVGE, including the high hospitalisation rate, could be reduced by routine rotavirus vaccination of infants. The REVEAL Study has provided essential data that support the introduction of routine rotavirus immunisation for children in Europe.

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The REVEAL Study is published as a supplement to The Journal of Infectious Diseases, which is available at the Sanofi Pasteur MSD stand.