

# Costs of Community-Acquired Pediatric Rotavirus Gastroenteritis in 7 European Countries: The REVEAL Study

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**Background.** Morbidity and resource use due to rotavirus gastroenteritis (RVGE) are substantial in Europe, although comprehensive data on the economic impact of the disease are lacking.

**Methods.** A cost study was conducted to assess health care resource use data collected during a prospective epidemiologic study of acute gastroenteritis in children <5 years of age in selected areas of Belgium, France, Germany, Italy, Spain, Sweden, and the United Kingdom. We calculated the average cost (direct and indirect) per episode of confirmed RVGE in primary care, emergency department, and hospital settings.

**Results.** The total societal cost (including direct medical, direct nonmedical, and indirect costs) per episode of RVGE ranged from €166 to €473 in the primary care setting, from €334 to €770 in the emergency department setting, and from €1525 to €2101 in the hospital setting. The majority of hospital-related costs were reimbursed by national health care payers, but the percentage of reimbursed costs declined progressively in the emergency department and primary care settings. The mean number of workdays lost by parents and other relatives varied between study areas and settings, ranging from 2.3 to 7.5 days, and this represented the major cost not reimbursed by national health care payers.

**Conclusions.** RVGE incurs considerable resource utilization in all health care settings and substantial costs for national health care payers, families of patients, and employers. Routine rotavirus vaccination in infants could significantly reduce the health and economic burden of pediatric RVGE.

Rotavirus is a major cause of acute gastroenteritis (AGE) in young children in developing and industrialized countries [1–3], with infections most common in children 6–24 months of age [1, 4, 5]. The majority of children are infected with the virus by 2–3 years of age [6, 7], and most are infected more than once [8]. In a recent study using published data on the burden of rotavirus gastroenteritis (RVGE) in the European Union, it was estimated that 3.6 million episodes of RVGE occur annually among the 23.6 million children <5 years of age in the European Union [9]. It was suggested that RVGE is responsible for 231 deaths,

>87,000 hospitalizations, and ~700,000 outpatient visits annually.

The symptoms of RVGE include diarrhea and vomiting, which may lead to severe dehydration and even death if rehydration therapy is not promptly initiated.

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<sup>a</sup> Further details of the REVEAL Study Group are provided after the text.

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Although death due to RVGE is rare in industrialized regions such as Europe because of access to adequate medical care, the burden of RVGE is substantial, given the high frequency of infection and resulting morbidity among infected children.

A number of studies conducted in individual European countries have described RVGE hospitalization rates [10–17] and the impact of RVGE on primary care centers [18–22]. Studies assessing the medical costs of hospitalizations for RVGE have been published for Austria [23], Scotland [24], Spain [25], Ireland [26], Sweden [13], England [27, 28], Germany [29], and France [30]. In addition, some studies conducted in European countries have reported the costs of outpatient visits for RVGE and the indirect costs to families and society [23, 28, 31–34]. Differences in populations, methods, and outcomes make comparisons between studies 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 prospectively the annual incidence rates of AGE and RVGE in children <5 years of age in primary care, emergency department, and hospital settings, in selected areas of 7 countries [35]. The secondary objectives were to describe the distribution of rotavirus serotypes associated with RVGE [36], to describe the clinical impact of RVGE [37], and, as is reported in the present article, to estimate the medical, nonmedical, and indirect costs associated with RVGE, from the perspectives of both the national health care payer and society.

## MATERIALS AND METHODS

### Study Design

The REVEAL Study was a prospective, multicenter, observational study of AGE in children <5 years of age, performed over a 12-month period (1 October 2004–30 September 2005) in selected areas in 7 European countries, each including both urban and rural populations: Antwerp, Belgium; Dijon, France; Rostock, Germany; Padua, Italy; Gandia and Denia (Valencia), Spain; Västerbotten County, Sweden; and the Wirral, United Kingdom. The methods have been described elsewhere [35].

### Inclusion Criteria

Within each study area, all children <5 years of age presenting to a primary care physician (general practitioner [GP] and/or pediatrician) or an emergency department or requiring hospitalization for AGE during the study period and whose parents gave written, informed consent were eligible for inclusion in the study. AGE was defined as an episode of at least 3 loose stools, 3 watery stools, or forceful vomiting associated with gastroenteritis within a 24-h period during the 7 days before the medical visit; the episode must have been preceded by a symptom-free period of 14 days in the absence of a previously diagnosed chronic gastrointestinal tract disease with symptoms

compatible with the definition of AGE. Children who had participated in a trial of a rotavirus vaccine or who had nosocomial AGE were excluded.

If a child visited >1 health care setting during the AGE episode, the inclusion visit was regarded as the highest level of care received; levels of care, in increasing order, were primary care, emergency department, and hospital. RVGE was defined as AGE (corresponding to the clinical definition) with rotavirus detected in a stool sample by ELISA. Full details of the sampling and analytic methods are reported elsewhere [36].

### Data Collection

Health care resource utilization data (medication, laboratory tests, and health care visits/contacts) and other parameters associated with the cost of RVGE (child care, workdays lost, extra diapers, and transportation) were collected via questionnaires as described elsewhere [35, 37].

### Cost Analysis

The aim of the cost analysis was to calculate the average cost of an episode of confirmed RVGE in each of the 3 health care settings for each country. Because some costs were incurred in >1 health care setting, all costs for each episode were calculated, including resource use related to the inclusion setting and resource use in lower-level health care settings before and after the inclusion visit.

Costs were determined from both the national health care payer and societal perspectives and were calculated using health care resource utilization data collected during the REVEAL Study and the most recent unit costs from official sources (a list of sources for the costs used in the study are available from the authors on request). Costs from the national health care payer perspective included the reimbursed direct medical costs and some nonmedical costs (such as ambulance costs). Costs from the societal perspective included the above costs, as well as some nonmedical costs, such as copayment by parents for costs not covered by the national health care system and indirect costs (e.g., workdays lost by parents).

The cost evaluation was conducted separately for each country because of the differences in the health care systems. The period of the assessment was 1 year, and costs were not discounted. All costs are presented in euros (€). In the Discussion, where comparisons are made with studies reporting costs in UK pounds sterling, an exchange rate of £1 = €1.4765 (7 December 2006) is used.

### Determination of Costs

**Direct medical costs.** Direct medical costs included telephone consultation, consultation in outpatient settings (primary care office/home visit, emergency department/assessment ward visit), or inpatient care (hospitalization); medication (prescribed and

**Table 1. Observed numbers of children with confirmed rotavirus gastroenteritis (RVGE), by study area and setting.**

Setting	Belgium (n = 57)	France (n = 99)	Germany (n = 158)	Italy (n = 336)	Spain (n = 252)	Sweden (n = 124)	United Kingdom (n = 76)
Hospital	39	30	53	55	52	69	39
Emergency department	2	50	0 <sup>a</sup>	148	101	54	22
Primary care	16	19	105	133	99	1 <sup>b</sup>	15

<sup>a</sup> In the German study area, all eligible children who presented to the emergency department with RVGE during the study were referred to hospitals, so there were no inclusions for the emergency department setting.

<sup>b</sup> In the primary care setting in the Swedish study area, parents generally called a nurse advice service located in the same medical center as the primary care physicians. Therefore, on the basis of the nurses' advice, most children with acute gastroenteritis were referred to a higher level of care or treated at home.

over the counter [OTC]); and medical services (nurse surgery/home visits, laboratory tests, and diagnostic procedures). Assessment wards exist only in Sweden, Italy, and the United Kingdom.

The cost of hospitalization was based on the Health-Related Group (HRG; United Kingdom) and Diagnosis-Related Group (DRG; Belgium, France, Germany, Italy, Spain, Sweden) systems. These systems provide average hospitalization costs for defined hospital cases expected to have similar hospital resource use and are inclusive of all consumables and services (e.g., drugs, diagnostic and laboratory tests, and diapers used in the hospital).

The average medication cost was based on the most prescribed or consumed drugs in the REVEAL Study. Drugs were coded according to the Anatomical Therapeutic Chemical (ATC) classification [38]. An average medication cost was calculated per therapeutic class of ATC code level 4. This calculation took into consideration the drugs representing  $\geq 80\%$  of prescribed and OTC products in the ATC classification. For example, if there were 10 drugs in a particular ATC code, and if drug A represented 45% of the prescriptions, drug B represented 40%, and the remaining 8 drugs represented 15%, we used only drugs A and B in the calculation. The average cost for the class was then calculated as follows: (unit cost of A  $\times$  no. of units of A used)  $\times$  (% A in ATC class) + (unit cost of B  $\times$  no. of units of B used)  $\times$  (% B in ATC class).

Tests and procedures that were included in the costs were stool sample analyses, blood tests, abdominal ultrasound examinations, and chest radiography. The costs for the study laboratory tests (ELISA and polymerase chain reaction) were not included in this analysis. Additional consultations before or after the inclusion visit were included in the cost analysis; these included visits to a primary care physician or nurse, emergency department visits (children visiting the emergency department and hospitalized children only), additional hospitalizations (hospitalized children only), and telephone consultations.

**Direct nonmedical costs.** Direct nonmedical costs included costs related to any form of transportation, as recorded on the study questionnaire (based on local cost per kilometer); extra

diapers; and child care. While children were in hospital, diapers were included in the hospitalization costs, so the extra diapers are for the period during the illness outside of hospital. Child care costs specifically related to RVGE episodes were included. These were calculated from the information provided by the parents on the questionnaire (number of hours of extra child care specifically for the gastroenteritis episode) and the local costs, a list of the sources of which is available from the authors on request.

**Indirect costs.** Indirect costs included the number of workdays lost by parents and caregivers (<65 years of age) per RVGE episode. The value of workday losses was determined on the basis of the average wage or average daily absenteeism allowance [39–42].

### Statistical Analysis

No formal statistical analyses were performed.

## RESULTS

A total of 1102 RVGE episodes were included in the cost study (table 1).

**Resource use and costs for hospitalized children with confirmed RVGE.** The average length of hospital stay ranged from 2.5 days in Sweden to 5.0 days in Germany. The percentage of hospitalized children seeking medical attention for their RVGE episode before being admitted ranged from 30% in Germany to 72% in the United Kingdom. The percentage of children seeking medical attention after hospital discharge ranged from 14% in Belgium to 52% in Spain.

Considerable differences were observed between countries in the percentage of hospitalized children receiving intravenous (iv) fluids alone for rehydration, ranging from none in Germany and the United Kingdom to 91% in Italy. Similarly, the percentage of hospitalized children receiving oral rehydration solutions alone varied markedly, ranging from none in Italy to 56% in the United Kingdom. The percentage receiving both iv fluids and oral rehydration solutions ranged from 9% in Italy to 88% in Germany. The percentage of hospitalized children

**Table 2. Cost per episode of confirmed rotavirus gastroenteritis requiring hospitalization.**

Cost type	Belgium		France		Germany		Italy		Spain		Sweden		United Kingdom	
	Payer <sup>a</sup>	Societal <sup>b</sup>												
Direct medical	1253	1343	1270	1349	1481	1484	1255	1269	1249	1263	1515	1519	1217	1220
Direct nonmedical	0	18	0	8	0	4	0	10	0	10	2	23	4	33
Indirect	0	185	0	168	64	597	0	622	0	279	313	559	0	685
Total	1253	1546	1270	1525	1545	2085	1255	1901	1249	1552	1830	2101	1221	1938

**NOTE.** Data are mean costs in euros.

<sup>a</sup> Costs from the payer perspective included direct costs funded by the national health authorities. In Germany and Sweden, the payer funds part of the costs for loss of productivity.

<sup>b</sup> Costs from the societal perspective included all costs (direct medical, direct nonmedical, and indirect costs), whether funded by the national health authorities, families of patients, or employers.

with confirmed RVGE who underwent laboratory tests (stool sample analysis and/or blood tests) was lowest in Belgium (19%) and highest in Spain and Sweden (98% and 97%, respectively). The percentage of children with RVGE who used OTC products was highest in Sweden (56%) and lowest in Spain (27%). On average, patients using OTC drugs or dietary products received 1 or 2 products.

The majority of hospitalized patients required transportation to reach the hospital. The lowest percentage of children with RVGE who needed to use transportation was recorded for Italy (51%), whereas the percentage in all other countries ranged from 78% (Spain) to 98% (Sweden).

The percentage of families in which a parent or other relative took time off work because of a hospitalized child was highly variable across study areas, ranging from 39% in Belgium to 91% in the United Kingdom. The average number of workdays lost per episode of confirmed RVGE was 2.3 days in France, 3.8 days in Sweden, 4.0 days in the United Kingdom, 4.2 days in Belgium, 4.6 days in Spain, 5.4 days in Italy, and 6.4 days in Germany. The highest rates of paid child care use occurred in Sweden (21%) and the United Kingdom (14%), whereas no paid child care was used in Germany and Spain. The majority of hospitalized children required increased use of diapers, with children using diapers requiring an average of 5–7 additional diapers per day.

The total societal costs for children hospitalized with RVGE did not differ greatly between countries, ranging from €1525 per episode in France to €2101 per episode in Sweden. Hospitalization costs represented the largest part of the costs supported by the national health care payer (table 2). The percentage of the total cost reimbursed by the national health care payer was 63% in the United Kingdom, 66% in Italy, 74% in Germany, 83% in France, 87% in Sweden, 81% in Belgium, and 80% in Spain.

Loss of productivity due to work absenteeism among parents and other relatives of patients was the major cost not supported by the national health care payer. The average cost for loss of

productivity as a percentage of the total societal cost was 11% in France, 12% in Belgium, 18% in Spain, 27% in Sweden, 29% in Germany, 33% in Italy, and 35% in the United Kingdom.

**Resource use and costs for children with confirmed RVGE in the emergency department setting.** Germany and Belgium were omitted from this analysis because, in the Rostock area of Germany, all eligible children presenting to emergency departments during the study were referred to a hospital, and because only 2 children with confirmed RVGE were included in the emergency department setting in Belgium.

For children with RVGE in the emergency department setting, additional medical care before or after the inclusion visit included additional emergency department visits, primary care consultations, and telephone consultations. The percentage of children seeking medical attention for their RVGE episode before an emergency department visit ranged from 44% in Spain to 60% in France. The percentage seeking medical attention after their emergency department visit ranged from 8% in Sweden to 54% in Spain.

The percentage of children receiving a prescription for drugs and dietary products at the emergency department visit ranged from 19% in Sweden to 90% in France. The percentage of children for whom laboratory tests were ordered in this setting was highly variable, ranging from 4% and 6% in Spain and France, respectively, to 59% and 61% in the United Kingdom and Italy, respectively.

As was noted for hospitalized children, the lowest percentage of children requiring transportation to the emergency department was found in Italy (45% of children with RVGE). The percentage of children requiring transportation in other countries ranged from 73% in Spain to 98% in Sweden.

Loss of workdays was a substantial burden for families in all countries, with the percentage of families losing workdays ranging from 44% in France and Spain to 64% in Italy. The average number of workdays lost, by country, was 2.5 days in France, 2.9 days in the United Kingdom, 3.9 days in Italy, 4.3 days in Sweden, and 4.4 days in Spain. No paid child care was used

**Table 3. Cost per episode of confirmed rotavirus gastroenteritis requiring an emergency department visit.**

Cost type	France		Italy		Spain		Sweden		United Kingdom	
	Payer <sup>a</sup>	Societal <sup>b</sup>								
Direct medical	80	136	202	222	204	220	129	135	476	477
Direct nonmedical	0	12	0	13	0	17	0	33	0	14
Indirect	0	186	0	364	0	172	259	462	0	279
Total	80	334	202	599	204	409	388	630	476	770

**NOTE.** Data are mean costs in euros. Data for Belgium are omitted because there were only 2 children with confirmed rotavirus gastroenteritis in the emergency department setting. In the German study area, all eligible children who presented to the emergency department with rotavirus gastroenteritis during the study were referred to hospital, so there were no inclusions for the emergency department setting.

<sup>a</sup> Costs from the payer perspective included direct costs funded by the national health authorities. In Germany and Sweden, the payer funds part of the costs for loss of productivity.

<sup>b</sup> Costs from the societal perspective included all costs (direct medical, direct nonmedical, and indirect costs), whether funded by the national health authorities, families of patients, or employers.

in France and the United Kingdom, and rates of child care use elsewhere ranged from 3% in Spain to 14% in Sweden. The majority of children in the emergency department setting required increased use of diapers, with children who were using diapers requiring an average of 5–7 additional diapers per day.

The mean costs per episode of confirmed RVGE in the emergency department setting are presented in table 3. Total societal costs varied across the 5 included countries and were considerably lower than those for hospitalized children (see table 2). They ranged from €334 per episode in France to €770 per episode in the United Kingdom. The percentage of the societal costs reimbursed by the national health care payer was 25% in France, 34% in Italy, 50% in Spain, and 62% in the United Kingdom and Sweden. Lost productivity among parents and other relatives was a major indirect cost in the emergency department setting in all included countries. The average cost for lost productivity as a percentage of the total societal cost was 36% in the United Kingdom, 42% in Spain, 56% in France, 61% in Italy, and 73% in Sweden.

**Resource use and costs for children with confirmed RVGE in primary care.** For children with confirmed RVGE in primary care, additional medical care before or after the inclusion visit included extra primary care consultations or telephone consultations. In all countries except France, medical care was not sought before the inclusion visit to a primary care physician. The percentage of children requiring medical care after the inclusion visit ranged from 9% in Spain to 44% in Germany. For countries with very few patients in this setting, the data should be interpreted with caution. A single child in primary care in Sweden was excluded from the cost analysis.

The percentage of patients receiving a prescription for drugs and dietary products at the primary care visit ranged from 47% in the United Kingdom to 95% in France. The percentage of patients using OTC products was also high in France (58% of children with RVGE). Consistent with findings for the hospital and emergency department settings, in the primary care setting, Spain once again had the lowest consumption of OTC products

(22% of children with RVGE). The percentage of children in primary care undergoing laboratory tests ranged from none in the United Kingdom to 21% in Germany.

There was generally less need for transportation in the primary care setting than in the hospital and emergency department settings, reflecting the closer proximity of primary care physicians to their patients. The percentage of children requiring transportation was lowest once again in Italy (9%) and was highest in Belgium (71%).

The percentage of families losing workdays ranged from 20% in the United Kingdom to 64% in Belgium. The average number of workdays lost was 3.4 days in France, 3.7 days in Italy, 4.2 days in Spain, 4.8 days in Belgium, 5.3 days in Germany, and 7.5 days in the United Kingdom. No paid child care was used in France, and rates elsewhere ranged from 3% in Spain to 11% in the United Kingdom. The majority of children required increased use of diapers, with children who were using diapers requiring an average of 3–5 additional diapers per day.

The mean costs per episode of confirmed RVGE in primary care are presented in table 4. Total societal costs varied across the included countries and were lower than those for children with RVGE in the hospital and emergency department settings (tables 2 and 3); they ranged from €166 in Spain to €473 in Belgium. In all countries, the cost to the national health care payer was a relatively small part of the societal cost because, in the primary care setting, the majority of the societal cost is due to indirect costs that are not reimbursed by national health care payers. Overall, the percentage of the total societal costs reimbursed by the national health care payer was 5% in Belgium, 8% in Italy, 10% in Spain, 11% in France, 15% in the United Kingdom, and 25% in Germany. Loss of productivity as a result of work absenteeism among family members was responsible for a large proportion of the total societal costs for children in primary care, representing 75% of the total societal cost in Spain, 76% in the United Kingdom, 78% in Germany and in France, 82% in Italy, and 85% in Belgium.

**Table 4. Cost per episode of confirmed rotavirus gastroenteritis in the primary care setting.**

Cost type	Belgium		France		Germany		Italy		Spain		United Kingdom	
	Payer <sup>a</sup>	Societal <sup>b</sup>										
Direct medical	23	52	34	70	74	77	22	36	17	27	57	59
Direct nonmedical	0	19	0	8	0	17	0	16	0	14	0	32
Indirect	0	402	0	243	36	338	0	240	0	125	0	284
Total	23	473	34	321	110	432	22	292	17	166	57	375

**NOTE.** Data are mean costs in euros. Data for Sweden are omitted because there was only 1 child with confirmed rotavirus gastroenteritis in primary care.

<sup>a</sup> Costs from the payer perspective included direct costs funded by the national health authorities. In Germany and Sweden, the payer funds part of the costs for loss of productivity.

<sup>b</sup> Costs from the societal perspective included all costs (direct medical, direct nonmedical, and indirect costs), whether funded by the national health authorities, families of patients, or employers.

## DISCUSSION

This cost study evaluating pediatric RVGE in selected areas across 7 European countries is based on epidemiologic data collected using a common protocol and is, to our knowledge, the most comprehensive economic study of this health issue to date. It is the first study to collect resource-use data prospectively and calculate direct and indirect costs for children with confirmed RVGE requiring consultations and treatment in 3 distinct health care settings—hospital, emergency department, and primary care.

Epidemiologic data—and, therefore, the cost analyses based on them—should be interpreted with caution, particularly with rotavirus and especially when attempting to make international comparisons. For example, the available data on the incidence of RVGE and its associated morbidity might underestimate the actual impact of rotavirus infection [43]. Many patients with AGE may not present for medical treatment, and, because detection of rotavirus in stools does not influence treatment, physicians invariably do not collect stool samples from patients; thus, RVGE goes undiagnosed in the majority of children with the disease [9]. Moreover, national differences in medical practice and health care-seeking behavior [21] and differences in study methodologies and populations mean that comparisons of different study results should be made with caution; these differences highlight the importance of collecting country-specific epidemiologic data in assessing the economic burden of RVGE.

The REVEAL Study has demonstrated the substantial burden of RVGE in European countries, in terms of both disease incidence and resource use [35, 37]. Although previous studies have assessed the economic costs of community-acquired RVGE in some of the countries we have studied, including Spain [25], France [30], and the United Kingdom [24, 28], these studies have largely been based on retrospective data. Caution is needed in comparing the results of these studies with the results of our study, because of differences in methodology, patient populations, outcomes, and the years when costs were determined. However, the results of these studies are comparable to ours,

in that they highlight the high direct and indirect costs associated with RVGE. Lengths of hospital stay similar to those that we observed have been reported by others [25], and, where individual patient health care costs have been quoted [28, 30], they are similar to those that we calculated.

Three prospective studies conducted in the United Kingdom and Italy have estimated the outpatient costs associated with community-acquired RVGE. In the United Kingdom, Lorgelly et al. [33] estimated the average total direct and indirect cost (equating to societal cost in our study) to be as high as £169 (approximately €249 per child ≤5 years of age with RVGE). A study of children attending nurseries and GP practices in England found that the mean total direct and indirect cost per pediatric RVGE episode was £173 in nurseries and £167 in general practice (approximately €255 and €246, respectively) [31]. In Italy, Fontana et al. [32] estimated the total direct and indirect cost of an RVGE episode in the outpatient setting at €110 per child <47 months of age. Comparable mean societal costs in the primary care setting in our study ranged from €166 in Spain to €473 in Belgium.

A recent review of the burden of RVGE in children <5 years of age in Europe concentrated primarily on hospitalized children, because data on children treated in the home, primary care, and emergency department settings were limited [44]. The median direct medical cost funded by the national health care payer per hospitalized child with RVGE was estimated to be €1417, which is comparable to the mean direct medical costs associated with hospitalized children funded by the national health care payer in the present study (ranging from €1217 per episode in the United Kingdom to €1515 per episode in Sweden).

In addition to providing incidence and resource use data, our study looked at costs reimbursed by the national health care payer and indirect costs shouldered by families and society as a whole. Despite the wide variability in health care resource use in different countries that reflects the different health care systems, we found these costs to be substantial in all 3 health care settings. In addition to its associated costs in terms of OTC products, extra diapers, and days off work for family members,

pediatric RVGE has wider implications for society, in that it may have an impact on nursery or day care attendance, further exacerbating the burden on families and employers [31].

As with previous studies, a limitation of this study is that it does not fully encompass all children with RVGE in the study areas. Children not seeking medical attention and those with nosocomial infections were not included. It has been reported that nosocomial infections account for ~25% of hospitalizations of children with RVGE [26, 44]. In addition, rotavirus transmission within families was not considered, yet it leads to an additional burden on health care services and society. Families and employers bear the majority of the burden of RVGE in the primary care setting, in the form of indirect costs. This has been clearly demonstrated in a study of RVGE among children in day care centers in France over a 6- to 7-month period, in which ~25% of children with RVGE infected at least 1 other household member [34]. Medical attention was sought for approximately two-thirds of children with RVGE, and, for >50% of these children, at least 1 parent had to miss work for a mean of 2.3 days. For children seeking medical attention, >75% of total costs were indirect costs. Interestingly, in our study, the average number of workdays lost by family members was higher for children in primary care than for hospitalized children in France (3.4 vs. 2.3 days), Belgium (4.8 vs. 4.2 days), and the United Kingdom (7.5 vs. 4.0 days), further demonstrating the significant impact of the disease on family life. The majority of costs associated with hospitalized children with confirmed RVGE were paid by the national health care payer, with lost workdays being responsible for most of the indirect costs.

The potential for selection and information biases in the study design may limit the interpretation and extrapolation of data and have been detailed elsewhere [35]. In particular, although in the REVEAL study we analyzed the resource use of >1000 children, it must be remembered that the children are spread across 7 countries and 3 settings; it is important to be cautious in the interpretation of our findings because, in some settings, there were very few children analyzed, and therefore the data may be unrepresentative. Cost data from different sources were not adjusted for inflation or standardized to a chosen time frame. In Europe, since the introduction of the common currency—the euro—in 2001, there has been only ~2% inflation. Although most cost sources dated from within 3 years of the study and, so, can be considered to be reasonably current, some of the sources for Italy dated back to 1996 (costs for laboratory tests and diagnostic procedures from the Ministry of Health) and 1997 (costs for hospitalization from the Ministry of Health). Use of these conservative costs has led to an underestimation of the current cost of RVGE, particularly in Italy. In addition, the low level of transportation use reported in Italy probably also contributes to the underestimation.

In conclusion, to the best of our knowledge, our study represents the most complete cost study of pediatric RVGE in Europe. The burden of RVGE in Europe is high, because it results in considerable costs in all health care settings, for national health care payers, families of patients, and employers, which suggests that an effective childhood vaccination program would have considerable direct and indirect benefits for society. Meaningful comparisons between countries are difficult because of differences in the management of RVGE and differences in local costs. The data from this cost study will be used as cost inputs for cost-effectiveness analyses of rotavirus vaccination programs in Europe.

Recently, 2 new rotavirus vaccines have been shown to be safe and effective and have been licensed in Europe: a pentavalent reassortant rotavirus vaccine containing G1–G4 and P[8] [45] and an attenuated monovalent G1P[8] human rotavirus vaccine [46]. Our study provides comprehensive, up-to-date epidemiologic and cost-of-illness data for 3 health care settings in 7 European countries, which should prove useful to decision makers when evaluating the public health impact of introducing rotavirus vaccines.

## THE REVEAL STUDY GROUP

### Principal Investigators

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