

7.1 Rotavirus infection

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7.1.1 Key points

- In 2014, the rotavirus season was exceptional low.
- G9P[8] was the most prevalent genotype in 2014.
- The relative prevalence of G2P[4] shows a slight, but steady increase since 2011.

7.1.2 Epidemiology

The Working Group Clinical Virology reports the number of rotavirus positive results weekly. In 2014, the rotavirus season was exceptionally low and delayed in the winter/spring in the Netherlands (Figure 7.1.1). In total, 607 diagnoses were reported in 2014, compared with 1,487 diagnoses in 2013 and 1,287 in 2012 (Table 7.1.1). After the low season of 2014, an extra high season was expected in the winter of 2014-2015. However, up to July 2015, the season was comparable to 2012, which had been a low season (see Figure 7.1.1). All-cause gastroenteritis in children under the age of 5 was examined using routine health record data from general practices in the Nivel Primary Care Database for comparison with the weekly rotavirus reports [1]. These data correlated well with the weekly number of rotavirus positive results, with a significant decrease occurring between August 2013 and August 2014. The cause of this drop in rotavirus in the Netherlands in 2014 is unknown. Some potential contributing mechanisms mentioned in the literature are the mild winter of 2013/2014, the relatively high rotavirus epidemic season of the winter of 2012/2013, declining birth rates over the years, thus decreasing the group of susceptible individuals, and rotavirus vaccination programmes in neighbouring countries [1-4].

Recent studies suggest that there is a slight increase in the risk of intussusception among babies after receiving the first dose of rotavirus vaccine [5-9]. After the second and third doses, this risk is marginally elevated. As a result of these findings, baseline incidences of intussusception are calculated for the Netherlands to observe a possible increase after the introduction of rotavirus vaccination (see Chapter 5, Table 5.3 and Table 5.4).

7.1.3 Pathogen

IDS/RIVM received 137 faeces samples that tested positive for rotavirus in peripheral laboratories, 130 of these samples could be typed (Table 7.1.1). G1P[8] was no longer the most prevalent genotype in 2014. The most prevalent genotype in 2014 was G9P[8]. Worthy of note is the slight, but steady increase of relative prevalence of G2P[4] since 2011 (Figure 7.1.2). Mixed rotavirus infections are known to occur in approximately 5% of the cases, but will not readily be detected by this sequence-based method.

7.1.4 Research

IDS/RIVM participates, together with 14 other countries, in EuroRotaNet. This European Rotavirus Network was established in January 2007; IDS joined the project in June 2008. Within this project, Dutch microbiological laboratories can send rotavirus-positive faeces

samples to IDS for typing using sequencing. EuroRotaNet combines the results of the participating countries to create an overview of circulating serotypes of rotavirus in consecutive rotavirus seasons in Europe. The results for the Netherlands for 2009–2014 are given in Section 7.1.3 and Figure 7.1.2.

This multicentre study, Risk-Group Infant Vaccination Against Rotavirus (RIVAR), started in December 2014. This Phase IV study assesses the effectiveness, impact and feasibility of a rotavirus vaccination programme organised through secondary paediatric care and targets high-risk infants, including children born prematurely, with low birth weight or severe congenital pathology. The study pilots implementation of the RIVAR programme in several hospitals in a step-wedged design, combined with an observational before-after cohort study of high-risk infants. Enrolment of implementation across several hospitals covers a period of 3 years. The mechanisms contributing to the rotavirus epidemic pattern and explaining the unanticipated drop in detected rotavirus cases in the 2014 season are further explored in a project initiated by the Epidemiology and Surveillance Department of the RIVM on temporal associations between rotavirus detections, birth rate and weather conditions.

7.1.5 International developments

As of April 1st 2015, 77 countries worldwide have implemented universal rotavirus vaccination, including 12 European countries (Armenia, Austria, Belgium, Estonia, Finland, Georgia, Germany, Latvia, Luxembourg, Moldavia, Norway and the United Kingdom) [10]. Several other countries are at various stages of issuing national recommendations or integrating rotavirus vaccination into their national immunisation programmes. In the Netherlands, a recommendation by the Health Council about including rotavirus vaccination in the NIP is expected at the end of this year. In France, however, because of three infant deaths and many serious side effects, rotavirus vaccines are no longer recommended for routine childhood immunisation (see Chapter 5) [11].

Both the orally administered live monovalent Rotarix vaccine and the orally administered live pentavalent Rotateq vaccine are marketed internationally. The monovalent live attenuated vaccine Rotavac is currently only licensed for the Indian market. Local development of other rotavirus vaccines is ongoing in the USA, Finland, India, Brazil, Australia and Vietnam [12]. These include other live (neonatal) rotavirus vaccines, as well as inactivated (subunit) rotavirus vaccines suitable for intramuscular or intradermal administration.

Post-implementation studies on the real-world impact of rotavirus vaccination now include data covering up to 7 years post-implementation. A systematic review summarised the impact of universal rotavirus vaccination in European countries and reported an effectiveness of between 68 and 98% and reductions in rotavirus-related hospitalisations of between 65 and 84% [13]. Another meta-analysis assessed strain-specific effectiveness in high and middle-income countries globally and the impact on rotavirus strain distribution using data covering up to 6 years post-implementation [14]. In high-income settings, the effectiveness of Rotarix and Rotateq was comparable, ranging from 83% to 94% for fully homotypic strains and from 71% to 87% for partly or fully heterotypic strains. Prevalent strains in countries using Rotarix were G2P[4] (2,198 of 4,428, 50%) and G1P[8] (953, 22%), and prevalent strains in countries

using Rotateq were G1P[8] (1,280 of 3,875, 33%) and G2P[4] (1,169, 30%). Sustained predominance of a single strain was not recorded. The US reported sustained reductions in rotavirus detections up to 7 years post-implementation in the CDC passive laboratory reporting system, the National Respiratory and Enteric Virus Surveillance System (NREVSS) [15]. The decline compared with pre-vaccination ranged between 58% and 90% in each of the 7 post-vaccine years. The biennial pattern of rotavirus activity that emerged in the post-vaccine era in the US was sustained, with years of low activity and highly erratic seasonality alternating with years of moderately increased activity and seasonality similar to that seen in the pre-vaccine era. Annual rotavirus-coded hospitalisation rates in the US also declined by 63-94% in the post-vaccine years 2008-2012 [16].

The European Society for Paediatric Infectious Diseases updated their consensus recommendations for rotavirus vaccination in Europe [17]. The recommendation to vaccinate all infants against rotavirus and that the first dose of oral rotavirus vaccine should be given between 6 and 12 weeks of age has been sustained, but with an emphasis toward the lower range of the recommended age, that is, preferably between 6 and 8 weeks of age in order to minimise the risk of rotavirus vaccination induced intussusception. An update of literature on intussusception and other AEs of rotavirus vaccination is given in 5.3.2.5.

7.1.6 Tables and Figures

Table 7.1.1 Number of reported laboratory diagnoses of rotavirus, and number of positive samples sent to and typed at the RIVM, 2009-2014

Year	Laboratory diagnoses	Samples at RIVM		Samples typed at RIVM	
		N	% of diagnoses	N	% of samples at RIVM
2009	1,935	869	44.9	830	95.5
2010	2,180	578	26.5	547	94.6
2011	1,504	414	27.5	400	96.6
2012	1,287	276	21.4	265	96.0
2013	1,487	299	20.1	280	93.6
2014	607	137	22.6	130	94.9

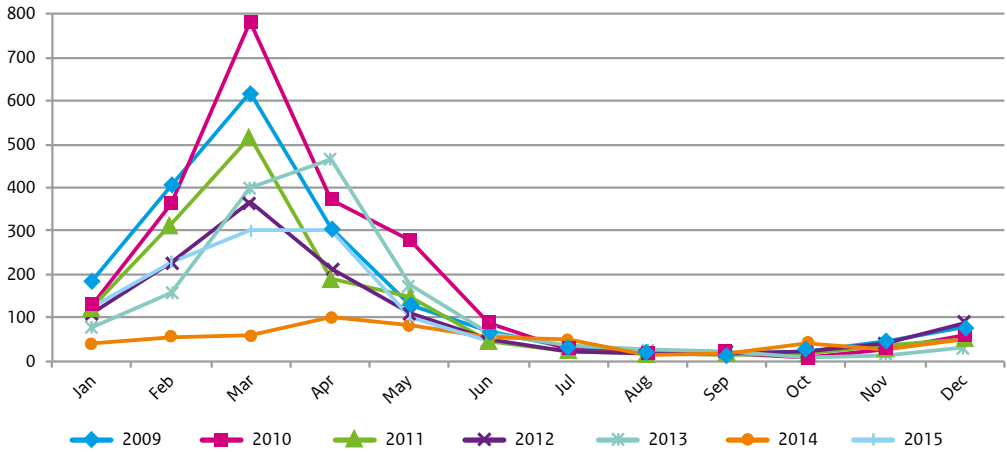


Figure 7.1.1 Reported laboratory diagnoses of rotavirus per month, 2009-2014

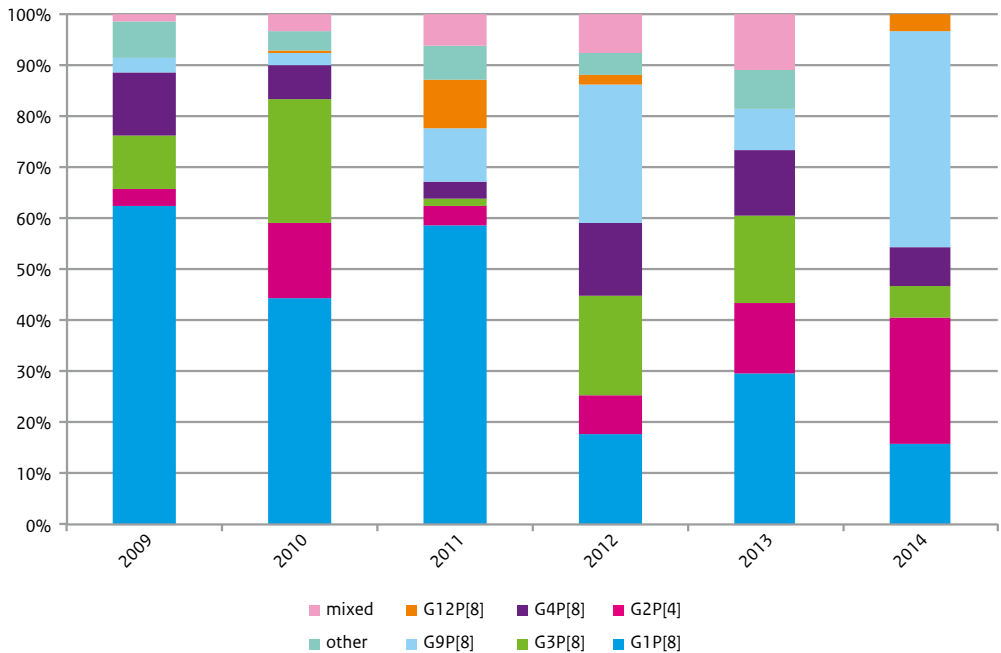


Figure 7.1.2 Rotavirus types as genotyped at the RIVM, 2009-2014

7.1.7 Literature

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* RIVM publication