

Exceptionally low rotavirus incidence in the Netherlands in 2013/14 in the absence of rotavirus vaccination

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An unexpected drop in rotavirus (RV) detections was observed in the Netherlands in 2014, without RV vaccination. The estimated decrease in RV detections and gastroenteritis consultations in under five year-olds, in January–April 2014, compared to the same months in previous years, was 72% and 36%, respectively. The low birth rate, mild winter, high RV incidence in the previous year and the introduction of RV vaccination in neighbouring countries may have contributed to this decrease.

We describe an unexpected and large decrease in rotavirus (RV) detections in the Netherlands in the winter of 2013/14 compared to previous years. We corroborated this finding with our analysis of syndromic disease data on acute gastroenteritis (GE) in children under five years old, in which we also found a reduction and no sign of the usual peak in March. We believe that our findings are of great importance to the European public health community to alert other countries on the unusual RV epidemiology of the 2013/14 winter.

Background

RV is a leading cause of GE in infants and young children. A number of European countries have recently implemented universal RV vaccination, including neighbours of the Netherlands (Belgium in 2006, UK (UK) and Germany in 2013) [1]. In the Netherlands, however, RV vaccination is not part of the national vaccination programme and a national recommendation for its use has not been issued so far. On average, only 41 doses were distributed per year between 2011 and 2014 (personal communication, Truus Maessen, IP International Pharmacy GmbH, September 2014).

RV incidence in the Netherlands usually follows the typical seasonal pattern observed in temperate climates

with an annual epidemic during winter months, peaking in February–March [2]. Up to 2014, RV was responsible for 3,300–4,800 hospitalisations annually in children under five years old, of which 85% occurred between January and April with the highest incidence in those aged between six months and two years [3,4].

Virological surveillance data showed an unexpected low number of RV detections in the Netherlands in the winter of 2013/14. We studied this observation to assess whether it reflects a decreased circulation of RV and to discuss implications for the control of RV in the Netherlands and beyond.

Epidemiological surveillance for rotavirus infection, data collection and analysis

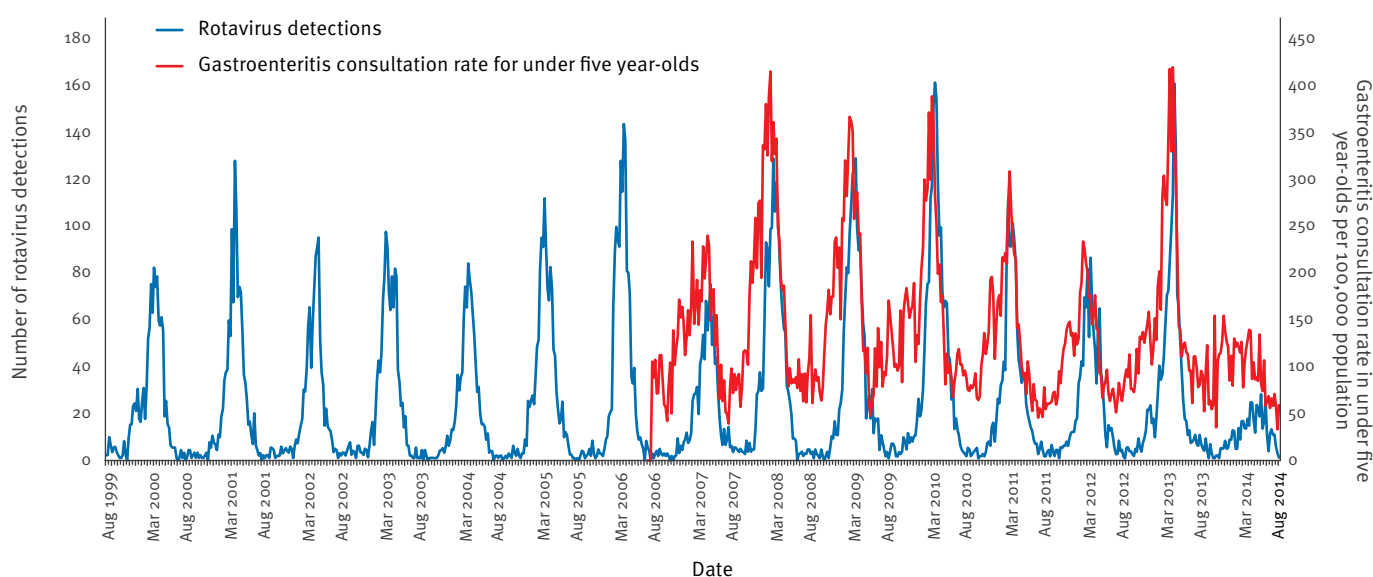
We studied RV laboratory detections from virological laboratory surveillance and all-cause GE consultations in under five year-olds from a Dutch sentinel General Practice (GP) network.

The virological surveillance collects weekly numbers of virus detections from between 17 and 21 virological laboratories registered with the Dutch Working Group for Clinical Virology (NWKV), serving primary care, hospitals and long-term care facilities. RV diagnostic testing is not routinely recommended for suspected infectious GE, but stool tests are performed in approximately two-thirds of children admitted for GE and in 10% of children with GE visiting primary care [3]. We analysed data from 1999 to 2014 by RV epidemiological year, defined as running from August to July of the following year.

We analysed GP consultations for all cause GE in under five year-olds using routine electronic health record data from general practices participating in the NIVEL

FIGURE

Weekly rotavirus detections^a (August 1999–August 2014) and general practice gastroenteritis consultation rate for children under five years old (August 2006–August 2014), the Netherlands



^a Adjusted for the weekly number of reporting laboratories by multiplying the number of rotavirus detections by the average number of reporting laboratories / the number of laboratories reporting that week.

Primary Care Database (NIVEL-PCD). Here, data were available from August 2006 to July 2014. Consultations are coded according to the International Classification of Primary Care (ICPC) [5]. Data are provided by 240 general practices covering a population of 1 million people, ca 5.5% of the Dutch population. Every Dutch citizen is obliged to be registered with a general practice. The GP acts as a gatekeeper for specialised, secondary healthcare. The electronic medical records kept by the GP, therefore, provide the most complete picture of the population's health.

Descriptive statistics were used to summarise data by RV epidemiological year and by seasonal month. Time-series analysis was performed to assess trends in weekly counts of RV detections and in GE consultations in under five year-olds, and to compare the 2013/14 RV season (January–April) to the same months in previous years. Negative binomial regression models were fitted to each data source separately. We adjusted the models for seasonal patterns (adding an indicator variable for month), for potential long-term linear trends and for variations in the number of reporting laboratories or person-time under observation, respectively. Both models were corrected for residual autocorrelation by adding lagged residuals.

Results

The weekly number of RV detections and the all-cause GE consultation rate in children under five year-old correlate well and were both much lower between August 2013 and August 2014 than in previous years (Figure).

Between August 1999 and July 2013, the average annual number of RV detections in virological surveillance, adjusted for the number of reporting virological laboratories, was 1,362 (range: 1,001–2,000). The adjusted number of RV detections between August 2013 and July 2014 was 570 (a 58% drop). This RV epidemiological year registered by far the lowest number of RV detections in the entire time series. Reductions were most pronounced during February and March 2014 when the number of adjusted RV detections were down by 75% and 88%, respectively. In contrast, an elevated number of RV detections was observed in July 2014 compared to previous years (Table). The peak in weekly RV detections in 2014 was shifted to May, whereas the peak was usually observed in March in previous years.

The mean weekly GE consultation rate in under five year-olds in the GP sentinel surveillance for the RV epidemiological years 2006–2013 was 152 per 100,000 person-weeks in under five year-olds (range: 111–201). The mean consultation for the 2013/14 season was 97 per 100,000 (a 36% decrease). In accordance with RV laboratory detections, the decrease in GE consultations was most pronounced during February (55%) and March (61%) (Table). Furthermore, there was no sign of the usual peak in February–March in GE consultations.

In time-series analyses, both the model for RV detections and for the GE consultation rates confirmed significantly lower activity in the 2013/14 season compared to previous years ($p < 0.0001$). The mean estimated decrease in RV detections for the 2014 winter season (January–April) compared to the same period in

TABLE

Weekly rotavirus detections and general practice gastroenteritis consultation rate by month, the Netherlands, 2013/14 (August–July) compared to previous years

| Month | Weekly mean number of RV detections ^a | | | | Weekly mean rate of GE consultations ^b in children under five years old per 100,000 population | | | |
|-------|--|-----------------------|--------------------------|----------------------|--|-----------------------|--------------------------|----------------------|
| | Aug 1999– Jul 2013 | Aug 2013– Jul 2014 | Change in 2013/14 (%) | P-value ^c | Aug 2006– Jul 2013 | Aug 2013– Jul 2014 | Change in 2013/14 (%) | P-value ^c |
| Aug | 3.0 | 5.3 | +80 | 0.0910 | 90.6 | 69.4 | -23 | 0.0218 |
| Sep | 3.3 | 5.4 | +63 | 0.3299 | 86.2 | 79.7 | -8 | 0.6515 |
| Oct | 3.2 | 1.8 | -44 | 0.0626 | 89.7 | 83.3 | -7 | 0.8065 |
| Nov | 5.0 | 3.7 | -26 | 0.2408 | 139.3 | 99.4 | -29 | 0.0703 |
| Dec | 11.9 | 6.9 | -42 | 0.0046 | 171.4 | 135.3 | -21 | 0.0059 |
| Jan | 25.7 | 8.8 | -66 | <0.0001 | 180.7 | 105.7 | -42 | 0.0001 |
| Feb | 58.2 | 14.1 | -76 | <0.0000 | 269.8 | 122.3 | -55 | <0.0001 |
| Mar | 85.2 | 15.0 | -82 | <0.0001 | 277.2 | 107.4 | -61 | <0.0001 |
| Apr | 70.4 | 19.8 | -72 | <0.0001 | 205.4 | 117.5 | -43 | 0.0006 |
| May | 31.3 | 21.4 | -32 | 0.0103 | 112.3 | 95.3 | -15 | 0.1996 |
| Jun | 12.5 | 14.3 | +15 | 0.7158 | 95.3 | 75.5 | -21 | 0.1675 |
| Jul | 5.1 | 11.7 | +131 | <0.0001 | 88.5 | 62.3 | -30 | 0.0001 |

GE: gastroenteritis; RV: rotavirus.

The usual RV season (January–April) is highlighted.

^a Adjusted for the weekly number of reporting laboratories by multiplying the number of rotavirus detections by the average number of reporting laboratories / the number of laboratories reporting that week.

^b International Classification of Primary Care (ICPC) code D73.

^c Derived by performing t-tests.

2000–2013 was 72% (95% CI: 59–81%). The estimated decrease in GE consultation rate for the 2013/14 winter season, which was adjusted for the presence of a significant linear time trend, was 36% (95% CI: 17–50%).

Discussion

We observed an exceptionally low number of RV detections and a low primary care GE consultation rate in children under five years of age, with nearly complete absence of winter excess, during the period of the typical RV season in 2014. This is a striking finding in the absence of RV vaccination in the Netherlands. The observation that the decrease was found in both data-sets indicates that the low number of RV detections is not a surveillance artefact, and likely reflects reduced RV circulation. Our RV data did not include the number of RV tests performed. However, there have been no changes in diagnostic guidelines or reimbursement policy that could have impacted RV testing practices in 2014 compared to previous years.

Potential contributing mechanisms for the reduced RV circulation in 2013/14 include the mild winter, the relatively high RV epidemic season in the previous year, a low birth rate and, possibly, RV vaccination programmes in the neighbouring countries [6–8].

RV transmission can be affected by weather-related differences in human behaviour or virus survival. For the Netherlands, it has been estimated that for every degree Celsius rise in temperature above a threshold of

4 degrees the number of symptomatic RV infections in the Dutch population decreases by 9%. Winter 2013/14 was unusually mild in the Netherlands: the average daily temperature was 2.6 degrees above the average of 3.4°C, while four out of five preceding winters were considerably colder than the average [9]. This may have contributed to reduced RV transmission in 2013/14.

The recent history of the intensity of RV-seasons is a likely determinant of the future incidence, through depletion of susceptibles. In our RV time-series, this effect is not clearly discernible in the pattern of high and low epidemic peaks. Nevertheless, the relatively high incidence in 2012/13 is likely to have contributed in this manner to the low incidence in 2013/14. The 2013 introduction of RV vaccination in the UK and Germany may also have contributed to a reduction of RV circulation in the Netherlands by reducing the number of introductions of RV into the Netherlands. In Germany, the RV vaccine has been used in some eastern federal states since 2006, with evidence of local impact [10]. Notifications dropped by 36% in 2014 compared to 2013 [11]. This suggests that coverage increased only moderately since the introduction of a national RV vaccine recommendation. Furthermore, we are unaware of reports of such effects in other countries bordering regions with universal infant RV vaccination and no decline in RV activity in the Netherlands was observed after Belgium introduced RV vaccination in 2006 with immediate high uptake. In France, a country without routine RV vaccination where between

5 and 10% of infants are vaccinated each year in the private sector, the threshold for epidemic GE was, for the first time since 1992, not reached in the winter of 2013/14. This suggests that RV transmission was low in France also (personal communication, Daniel Lévy-Bruhl, September 2014).

Mathematical modelling studies have suggested that recruitment of susceptible infants, as determined by birth rate and RV vaccination coverage, is a main determinant in timing of RV season and in generating annual or biennial epidemics [6]. In the Netherlands, the birth rate has dropped to an all-time low of 10.2 per 1,000 population in 2013 [12]. This may now have reached a level at which timing of epidemics is shifted towards April–May and occur biennially, similar to the pattern observed in the United States, where recruitment of susceptibles is nowadays diminished due to the widespread use of RV vaccination.

Circulation of an unusual RV strain causing relatively mild disease could also result in lower numbers of RV related hospitalisations and GP visits. However, RV genotype surveillance for the 2013/14 season did not demonstrate an abnormal pattern of RV strains in the Netherlands. G1P[8] was the dominant strain until 2012. Since 2012 a varying mixture of G1P[8], G2P[4], G3P[8], G4P[8], G9P[8], and G12P[8] has been observed (unpublished data).

Conclusion

The incidence of RV infections was exceptionally low in the Netherlands in the winter of 2013/14 in the absence of RV vaccination. This finding is relevant to countries assessing the impact of RV vaccination. Data from other European countries with and without RV vaccination and mathematical modelling are needed to provide further insight in determinants of low and high epidemic years. The risk of a compensatory hyperepidemic RV season in the coming year(s) needs to be urgently assessed, to allow adequate hospital bed capacity management and to inform RV vaccination policy [13].

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Conflict of interest

None declared.

Authors' contributions

Designed the study: SH, PB-V, WvP. Collected, synthesised and analysed data: SH, PB-V, MH, AvG. Wrote the first draft: SH, PB-V. Interpreted the results and revised the article: SH, MH, PB-V, JW, AvG, WvP, HV, HdM. All authors read and approved the final manuscript.

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