UZ Leuven

Rotavirus
Surveillance
Network
Belgium

Laboratory of Clinical Virology
National Reference Center Rotavirus
Prof. Dr. Marc Van Ranst
Prof. Jelle Matthijnssens

Dear Colleagues,

We would like to thank you again for your participation in the Rotavirus Surveillance Network Belgium (RSNB), studying rotavirus incidence and the genotype distribution in Belgium. Please find enclosed the results of the analyses for the 2022-2023 rotavirus season as well as the individual rotavirus genotyping results of the samples you have sent us.

Due to the successful introduction of the Rotarix™ and RotaTeq™ vaccines onto the Belgian vaccination scheme, the number of rotavirus positive cases has strongly declined. However, we are still extremely interested in the remaining rotavirus positive cases in Belgium, both from VACCINATED and UNVACCINATED children. Since 2010 the laboratory of clinical and epidemiological virology at the KU Leuven is the national reference center for rotavirus which allows us to maintain the RSNB for the upcoming seasons. Therefore, we hope that you will keep sending us rotavirus positive samples.

As the vaccination status of the rotavirus-positive patient is crucial for the continued monitoring of the effectiveness of the vaccines, we would appreciate if this information could be added to the samples, if available. If convenient for you, you can use the template included with this letter.

Sincerely yours,

Prof. Jelle Matthijnssens
Prof. Dr. Marc Van Ranst

Laboratory of Clinical and Epidemiological Virology
Department of Microbiology, Immunology and ransplantation
Rega Institute
Herestraat 49 bus 1040
B-3000 Leuven, Belgium
Tel: 016/32.11.61, Fax: 016/33.00.26
e-mail: jelle.matthijnssens@kuleuven.be

Yearly report of the Rotavirus Surveillance Network Belgium 2022-2023

Rotavirus surveillance in Belgium

Rotavirus incidence and genotype distribution have been monitored at the UZ Leuven since the 1999-2000 rotavirus season. Rotavirus incidence has strongly decreased since the introduction of Rotarix™ (2006) and RotaTeq™ (2007) (1). The 2022-2023 rotavirus season is the sixteenth season since the establishment of the RSNB and many hospitals, private laboratories and pediatricians across Belgium are cooperating in this surveillance network. We received 530 samples, of which 423 (79.8%) could be (partially) genotyped.

Reduction of rotavirus gastroenteritis after vaccine introduction

In figure 1 the number of hospitalized gastroenteritis cases (orange bars), the number of hospitalized rotavirus gastroenteritis cases (blue bars) and the rotavirus positivity rate (green line) is shown for the UZ Leuven (**figure 1**). Before vaccine introduction the rotavirus positivity rate fluctuated between 15.2% and 23.1%. After vaccine introduction a steep drop in the rotavirus positivity rate was observed and the rotavirus positivity rate has fluctuated between 3.3% and 8.9% until 2018-2019. These fluctuations were also reflected in the number of samples the RSNB received during this period (between 289 to slightly over 900). For the 2 "COVID-19-seasons" (2019-2021) we received an all-time low number of positive cases through the rotavirus NRC (n=114; n=110, respectively), which was

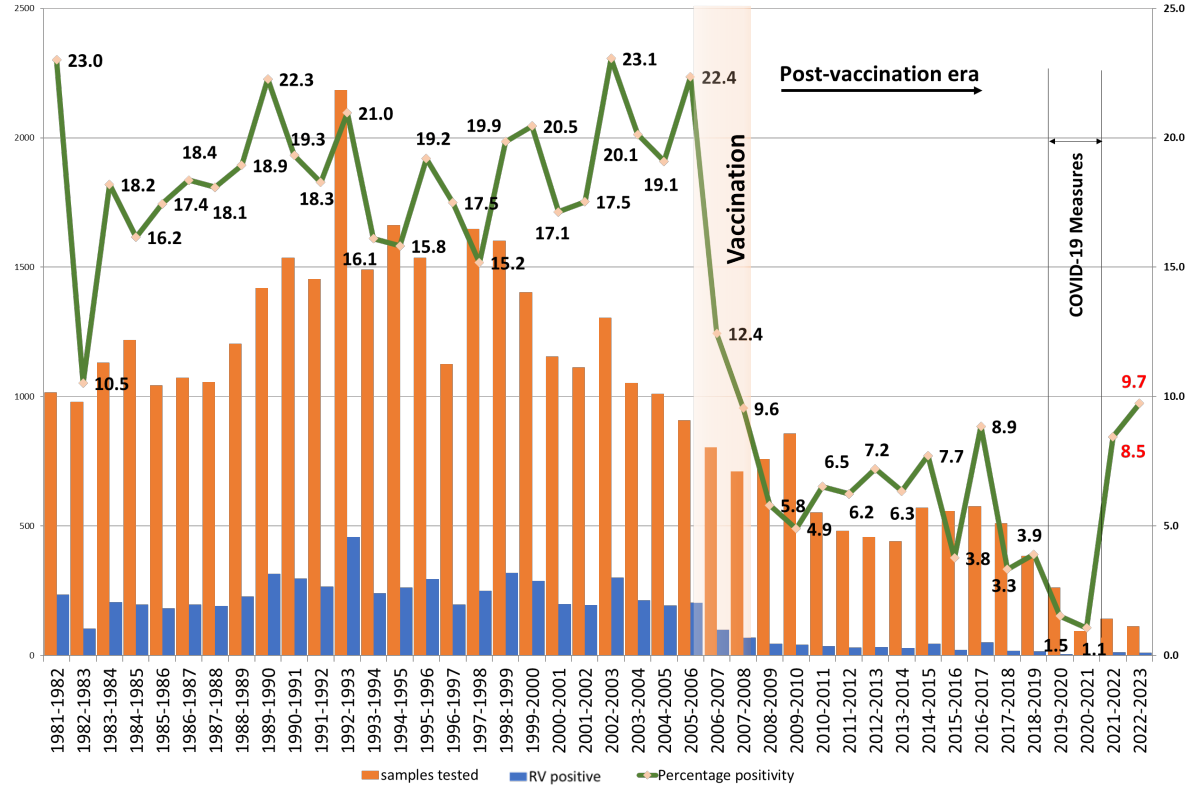


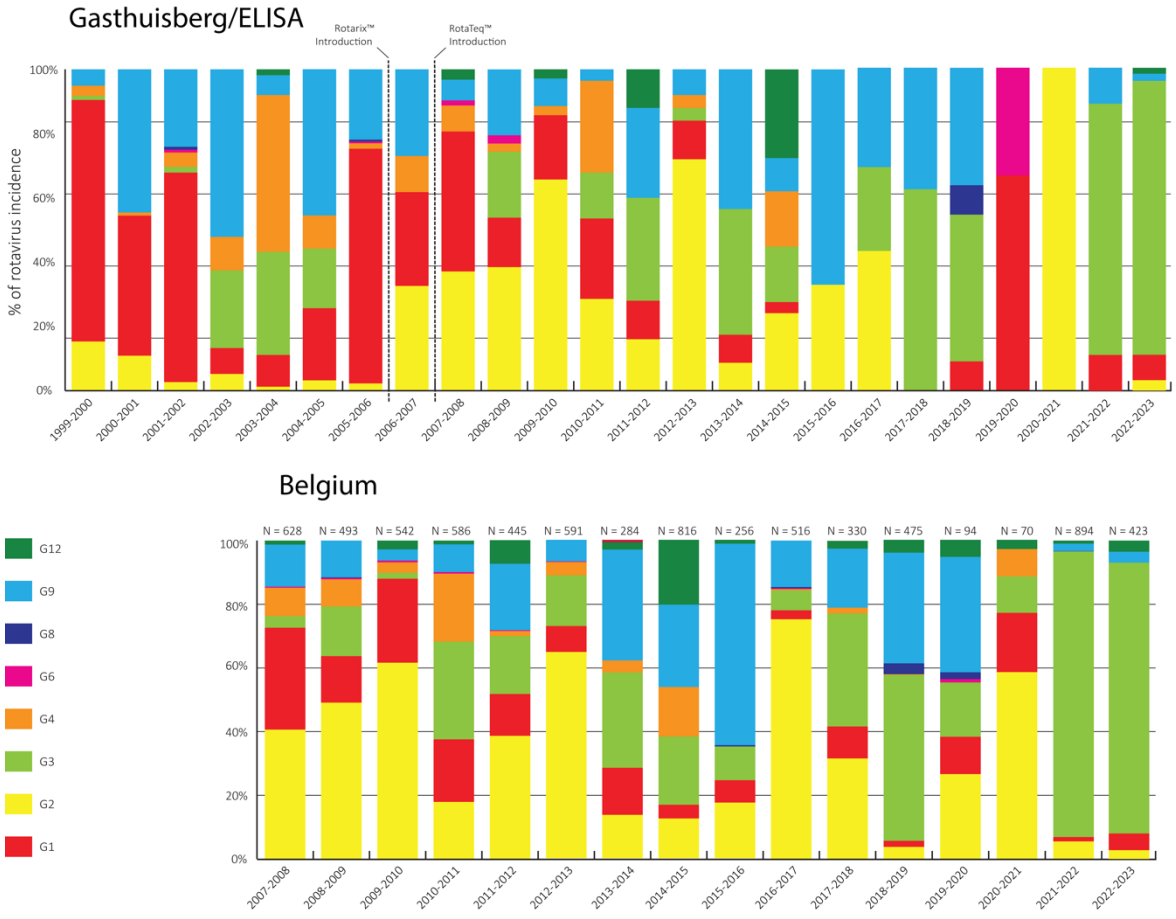
Fig. 1. Number of hospitalized gastroenteritis cases (orange bars) and number of hospitalized GE cases tested rotavirus positive (blue bars) per season at the UZ Leuven from 1981–1982 until 2022–2023. The green line indicates the percentage rotavirus positive tested in a particular season. Shaded orange mirror indicates vaccine introductions in Belgium. Period of most (school closures, lockdowns, mask mandates) COVID-19 measures were in place is shown as "COVID-19 Measures".

also reflected in only 4 and 1 rotavirus positive samples at the UZ Leuven corresponding to a 1.5% and 1.1% positivity rate (4/263, 1/94), respectively (Figure 1). After the COVID-19 seasons, the 2021-2022 season was characterized by a strong rebound in the number of rotavirus positive samples at the UZ Leuven (n=12; 8.5% positivity rate) as well as through the RSNB (n=1045). Interestingly, the 2022-2023

season followed the same trend and with positivity rate of rotavirus tests found to be slightly increased to 9.7% at the UZ Leuven (n=11) despite the total number of samples received through the RSNB being lower than 2021-2022 season (n= 530).

Rotavirus G-genotype distribution

The G-genotype distribution of rotavirus samples collected at the UZ Leuven and by the RSNB are shown in figure 2. Before vaccine introduction a fluctuating pattern of genotype predominance was seen (G1, G4 and G9) in conjunction with a low prevalence of the G2 genotype. After vaccine introduction a prolonged but fluctuating increase in the prevalence of G2 genotypes was observed. In general, the RSNB data display a similar genotype distribution as was observed at the UZ Leuven, although the low number of rotavirus positive cases at the UZ Leuven the last 15 seasons makes this comparison less reliable. The G2 genotype reached its lowest prevalence (3.6%) post vaccine introduction in the 2018-2019 season, after which it increased again to 26.6% and 55.6% in the 2019-2021 seasons. However, the 2021-2022 season was completely dominated by G3P[8] (85.9%).This trend continued in the last season (2022-2023), with the G3P[8] genotype encompassing 70% (14/20) of the cases, followed by G1P[8] (15%, 3/20) at UZ Leuven and 82.4% of the samples being genotyped as G3P[8] at the RSNB.



Seasonality

In addition to a decline in the number of rotavirus positive cases at UZ Leuven, the rotavirus season was found to be shortened and delayed after vaccine introduction. Before vaccine introduction the rotavirus season started in November and the peak incidence of rotavirus infections occurred in February. In the seasons after vaccine introduction, the rotavirus season typically started in the

beginning of a calendar year and the peak incidence was delayed to between March and April (Fig. 3). In the 2021-2022 season a peak was observed in March, while the 2022-2023 season did not show a clear peak, with just a few cases in March-April-May-June at the UZ Leuven. Samples received from across Belgium showed a peak between March-April (365/530). Of note, we received the highest number of samples in June since the NRC activity started (n=72).

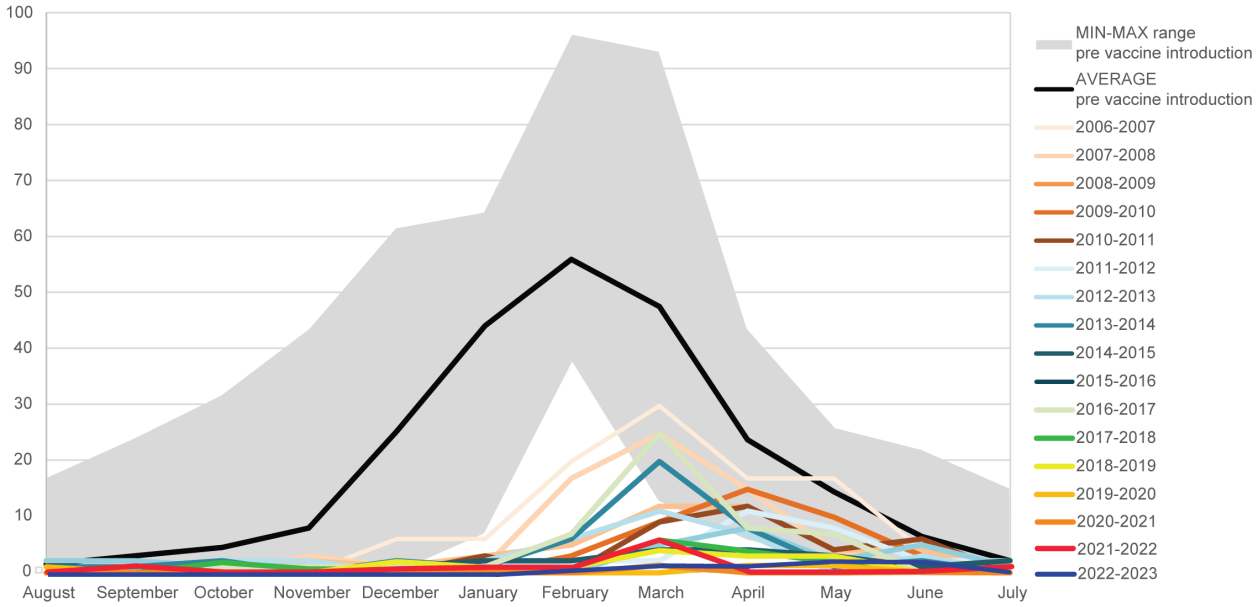


Fig. 3. Number of hospitalized GE cases tested rotavirus positive at the UZ Leuven university hospital per month of year. The black line indicates the median number of rotavirus positive cases in a particular month from 1986–1987 until 2005–2006. The shaded area indicates the minimum and maximum number of rotavirus positive cases in a particular month from 1986–1987 until 2005–2006. The colored lines indicate the number of rotavirus positive cases in a particular month in post-vaccine introduction seasons.

Geographic distribution of genotypes

In figure 4 the geographic G-genotype distribution across Belgium is shown based on the available postcode provided with the samples from the 2022-2023 season. Despite the clear dominance of the G3 genotype some small regional difference could be observed with G2 and G12 being slightly more prevalent in the center of Belgium, whereas G9 was found more frequently in the North-West of Belgium.

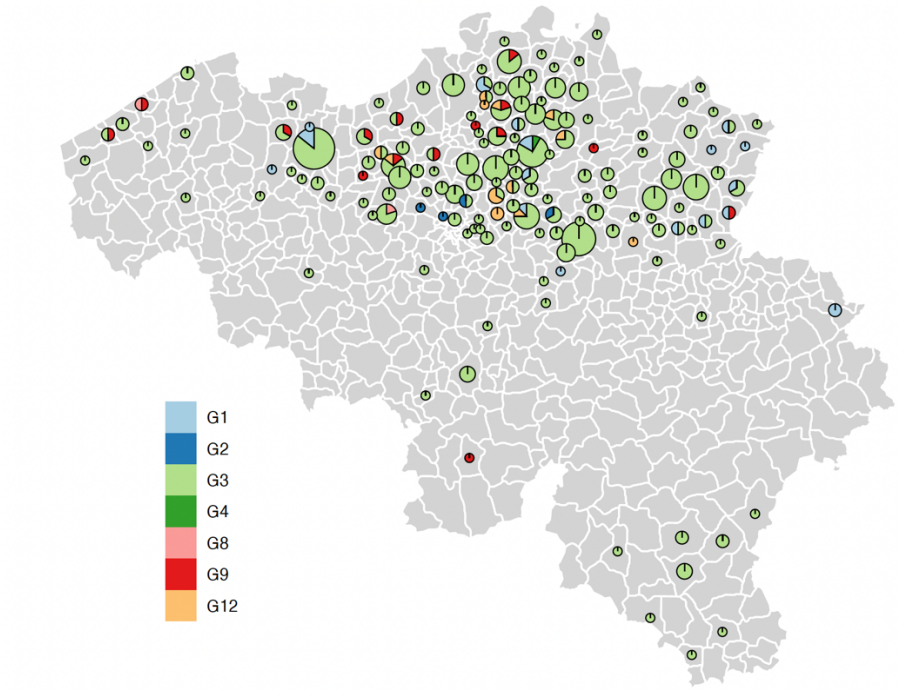


Fig. 4. G-genotype distribution across Belgium based on provided postal area codes of samples.

Conclusions

In our previous report describing the rotavirus epidemiology during the 2019-2020 and 2020-2021 "COVID-19" rotavirus seasons we speculated that "*due to a decreased circulation of rotavirus - due to physical distancing - an increasing number of susceptible infants could be accumulating. This in combination with further relaxations of measures implemented to restrict the pandemic, might results in more severe rotavirus seasons to come*." This speculation has come true, as the 2021-2022 rotavirus season represented the season in which the RSNB received the highest number of samples (n=1045) in its 15 years of existence. This was also reflected in the rotavirus positivity ratio (8.5%) observed at the UZ Leuven (Figure 1). However, the 2022-2023 season, the epidemiological situation seems to have returned to levels seen pre-pandemic.

Interesting to see was the maintained near complete dominance of the G3P[8] genotype in both the 2021-2022 and 2022-2023 seasons. This genotype has been present in each of the 15 rotavirus seasons investigated by the RSNB, usually ranging between a few percent to approximately 50% of the cases (in the 2018-2019 season, Figure 2). However, the observed dominance of G3P[8] (almost 85.9% and 82.4%) has not been observed for any of the 15 past rotavirus seasons for any genotype, and will be further monitored closely.

As described for previous seasons, despite the use of both life attenuated vaccines for more than a decade in Belgium now, there is very little evidence of their circulation in the human population. In the 2021-2022 season 5 Rotarix derived strains were identified, which were all very likely derived from a recent vaccination event, and not from circulation.

In order to keep evaluating the effects of vaccination on the rotavirus population, and to monitor the possible appearance of animal-like genotypes into the human rotavirus population, it will be important to continue the rotavirus surveillance in Belgium. Belgium is one of the few countries in the world with a very long track record of rotavirus genotyping in a country with a very high rotavirus vaccination coverage, which makes it ideally suited to investigate the impact of the vaccines on the rotavirus genotype distribution in the long run.

We would also like to encourage you to take a closer look at the 2 following manuscript which were recently published. In these papers we investigate the presence of other enteric pathogens in alleged "rotavirus break through cases", as well as the presence of other enteric pathogens in infants in which a Rotarix vaccine strains was identified.

High Prevalence of Coinfecting Enteropathogens in Suspected Rotavirus Vaccine Breakthrough Cases. Simsek C, Bloemen M, Jansen D, Beller L, Descheemaeker P, Reynders M, Van Ranst M, Matthijnssens J. J Clin Microbiol. 2021 Nov 18;59(12):e0123621.

Rotavirus vaccine-derived cases in Belgium: Evidence for reversion of attenuating mutations and alternative causes of gastroenteritis. Simsek C, Bloemen M, Jansen D, Descheemaeker P, Reynders M, Van Ranst M, Matthijnssens J. Vaccine. 2022 Aug 19;40(35):5114-5125.

In case you do not have access to this paper, and would like to have an electronic copy, feel free to send an email to: jelle.matthijnssens@kuleuven.be

References

1. Zeller M, Rahman M, Heylen E, De Coster S, De Vos S, Arijs I, et al. Rotavirus incidence and genotype distribution before and after national rotavirus vaccine introduction in Belgium. Vaccine. 2010;28(47):7507-13.