



Health Protection Surveillance Centre

Decline in rotavirus notifications following vaccine introduction

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Rotavirus infection - background

- Most common cause of paediatric gastrointestinal infection globally
 - 25% of all diarrhoea in <5 years
 - >10,000 deaths in children <5 years annually in WHO European Region
 - In Ireland low mortality but high morbidity and associated costs
- Vomiting, fever and watery diarrhoea lasting 3-7 days
- 3 / 1,000 cases may require hospitalisation, average of 5 days length of stay
- Transmission is usually person-to-person, via the faecal-oral route
- Cases are infectious 2 days before symptoms and 10 days after symptoms begin
- Children <2 years of age are most susceptible to infection, also seen in elderly and immunocompromised adults
- Infection and vaccination confer immunity but re-infection can occur with milder illness



Rotavirus vaccine – background

- Currently 4 rotavirus vaccines available internationally: Rotarix™, RotaTeq™, Rotavac™ and RotaSiil™
- Since 2009 WHO recommendation to include in national immunisation programmes
- By 2018, 98 countries introduced vaccination, including 14 EU countries
- December 2016 vaccine introduced in Ireland in for babies born from October 2016
 - Rotarix™ oral, live, attenuated monovalent vaccine using human G1P[8] strain
 - two doses at 2 and 4 months, completed by 8 months
 - may shed virus for ~2 weeks after vaccination
 - vaccine effectiveness 89% for RV hospitalisation in high income countries
- Rotarix™ vaccination uptake ~90% nationally in Ireland



Rotavirus infection – laboratory diagnostics

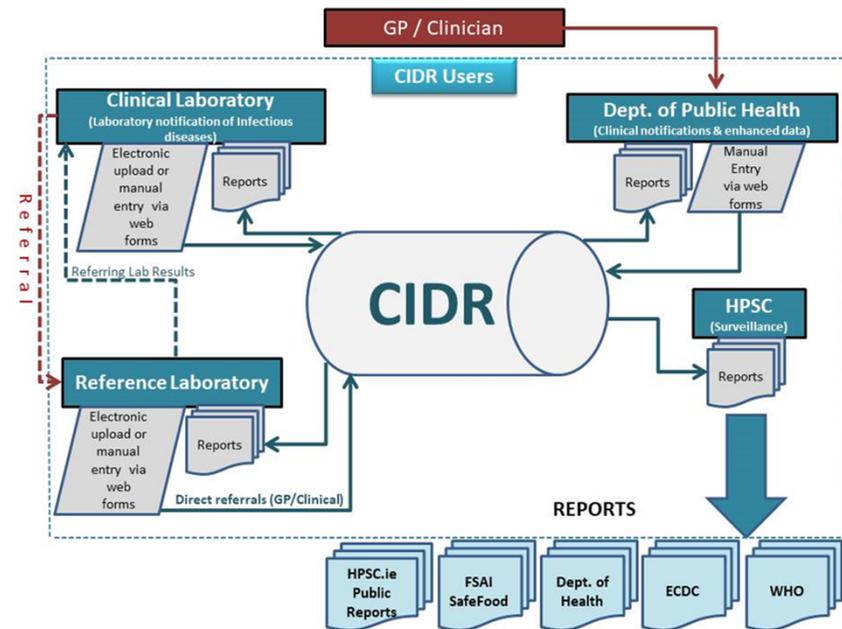
- 2016 HPSC survey of diagnostic methods in microbiology laboratories:
 - Mix of antigen testing and PCR methods in use
- Rotarix™ vaccine RNA is also detectable & indistinguishable from wildtype in many available commercial and “in-house” assays
 - NVRL* introduced RT-PCR assay which discriminates between wildtype or Rotarix vaccine strain in December 2017
 - during first month of testing, 93% of detections in suspected clinical cases from the vaccine eligible age group were vaccine strain
- Genotyping project ongoing in NVRL to monitor strain diversity

*National Virus Reference Laboratory, University College Dublin

Rotavirus infection: sources of data

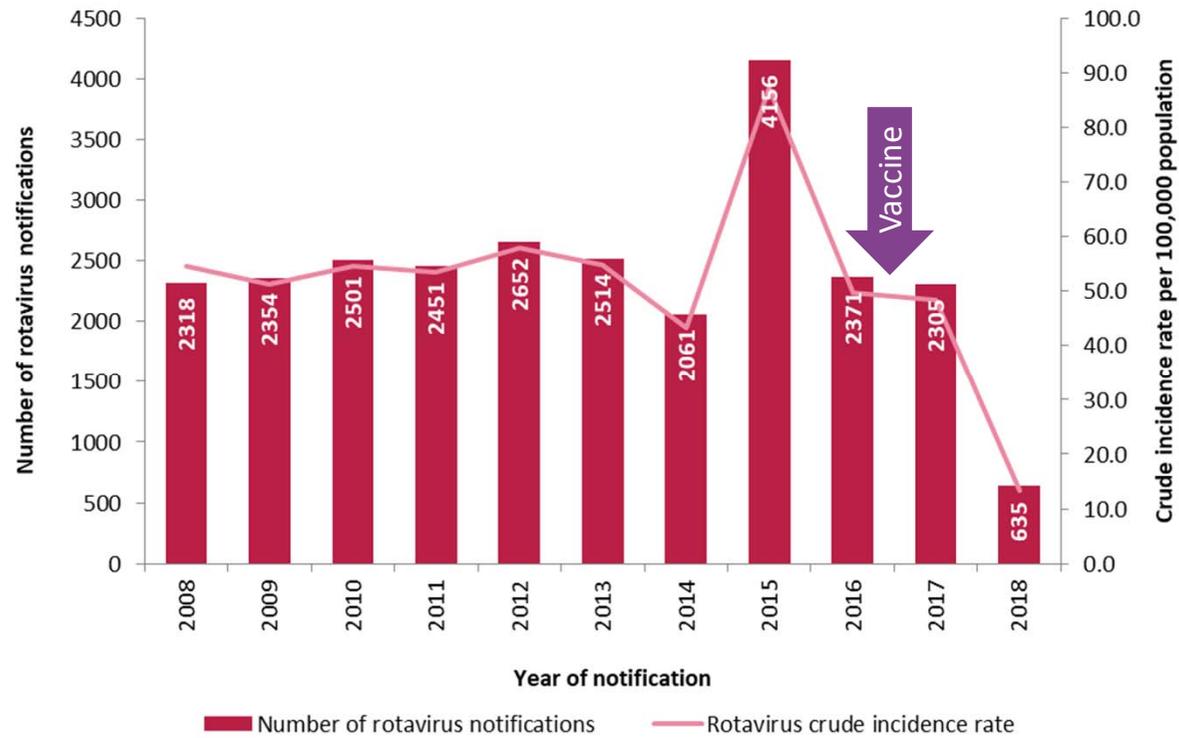


- Notifiable disease under the Infectious Disease Regulations
 - Prior to 2004 “**Gastroenteritis in children under two years**”
 - 2004 to 2010 all age groups under the “**Acute Infectious Gastroenteritis**”
 - 2011 to present day all age groups “**Rotavirus infection**”
 - Germany & Ireland are only EU countries to have as notifiable disease
- Laboratory & clinical data integrated in national web based system
 - ISO accreditation for information security
- Vaccination status is not currently reported on CIDR* for rotavirus cases



*Computerised Infectious Disease Reporting system

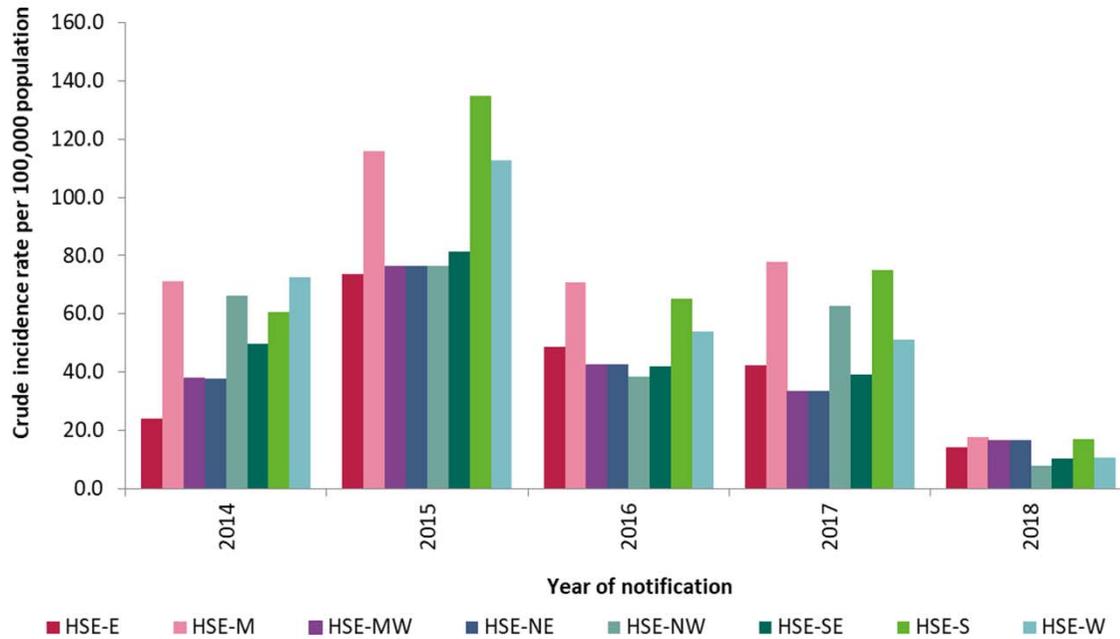
Annual number of rotavirus notifications and rate*, Ireland



*crude incidence rate per 100,000 population

Source: CIDR

Rotavirus annual rate by HSE area, Ireland



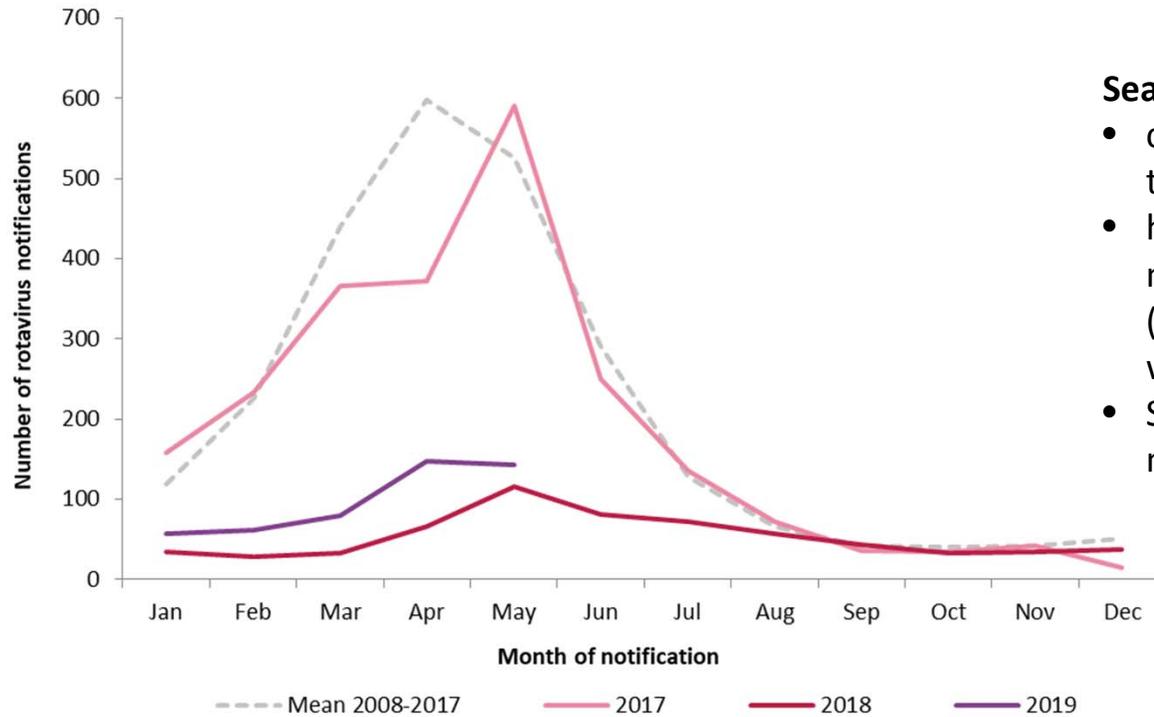
2018 regional rates :

- All HSE areas had >60% decrease
- highest CIR: HSE-M (17.8)
- lowest CIR: HSE-NW (7.8)

*crude incidence rate per 100,000 population

Source: CIDR

Annual number of rotavirus notifications by month of notification, Ireland



Seasonality:

- cases typically peak during March to May in Ireland.
- highest number of rotavirus notifications in 2018 during May (n=116) but the characteristic peak was absent
- Smallest peak: low ratio showing magnitude of seasonality decreased

Source: CIDR



Annual rotavirus rates* in children <10 years old, Ireland



Age groups:

- decrease of >75% in the <1 year old and 1-4 years old ASIRs compared to mean 2008-2017.
- 172 rotavirus notifications in the vaccine eligible cohort**

*ASIR: age specific incidence rate

** defined as having been born after 01/10/2016 and being aged two months or older at the time of notification

Source: CIDR



Conclusions

- High vaccination uptake ~90%
- Decrease observed in 2018 and hopefully sustained in 2019
- Laboratory methods are critical for interpretation of trends



Acknowledgements :

- Sincere thanks are extended to all those who participated in the collection of data used in this presentation. This includes the notifying laboratory staff & clinicians, public health doctors, nurses, surveillance scientists, microbiologists and administrative staff.
- Further information available on HPSC website: <http://www.hpsc.ie/a-z/gastroenteric/rotavirus/>
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References

Vaccine effectiveness:

- **Hungerford et al. 2017.** *Population effectiveness of the pentavalent and monovalent rotavirus vaccines: a systematic review and meta-analysis of observational studies.* BMC. DOI 10.1186/s12879-017-2613-4
 - Vaccine effectiveness RV lab conf hospitalisations 89% in high income, VE 74% in middle income
 - Vaccine effectiveness all cause gastroenteritis community 40%
 - Vaccine effectiveness full dose 81%, partial dose 62%
- **Jonesteller et al. 2017.** *Effectiveness of Rotavirus Vaccination: A Systematic Review of the First Decade of Global Postlicensure Data, 2006–2016.* Clinical Infectious Diseases. DOI: 10.1093/cid/cix369
 - Vaccine effectiveness against RV admission/ ED/ OP by country mortality <5yrs: 84% in low, VE 75% in medium, 57% high mortality
 - Vaccine effectiveness from random effects model 82%
 - partial series effectiveness lower than full but partial of either RV1/5 provided considerable protection against severe RV disease for 1st 2yrs life

Strain diversity:

- **Leshem et al. 2014.** *Distribution of rotavirus strains and strain-specific effectiveness of the rotavirus vaccine after its introduction: a systematic review and meta-analysis.* Lancet. 10.1016/S1473-3099
 - Intro of vaccines “has not altered the regular variation in strains that would suggest selective pressure”
 - “dominance of strains changes fairly regularly”
 - “immunity after rotavirus vaccination and infection is polygenic”

Herd immunity:

- **Pollard et al. 2015.** *Estimating the herd immunity of rotavirus vaccine.* Vaccine DOI: [10.1016/j.vaccine.2015.06.064](https://doi.org/10.1016/j.vaccine.2015.06.064)
 - Evidence that rotavirus vaccination confers a herd immunity effect among children <1yr in the US and Latin America.
 - Observed reductions in all cause diarrhoea hospitalisations were higher than the theoretical maximum reduction

Cost effectiveness:

- **Haider et al. 2018.** *Systematic Review and Meta-Analysis of Cost-effectiveness of Rotavirus Vaccine in Low-Income and Lower-Middle-Income Countries.* OFID. DOI: 10.1093/ofid/ofz117
- **Kotirim et al. 2017.** *Global economic evaluations of rotavirus vaccines: A systematic review.* Vaccine. DOI: 10.1016/j.vaccine.2017.04.051
 - Both found cost –effective for low-middle income, may not be cost effective for high income if vaccine is at market price

<http://rotacouncil.org/vaccine-introduction/global-introduction-status>