NVRL
Annual Reference Virology Report 2016

Introduction

Dear Colleagues

We are delighted to present – albeit somewhat later than intended – the NVRL Reference Virology Report for 2016. Although the delayed publication this year was unavoidable, we would hope to release the 2017 report in the third quarter of this year.

Despite the end of the Ebola outbreak in West Africa, and the failure of MERS Coronavirus (as yet) to circulate widely in global terms, 2015 was another challenging year in Virology with the emergence of Zika virus as a significant pathogen in Caribbean and South American countries, in particular Brazil. In addition, the influenza season of 2015-2016 was probably our most severe since those following the emergence of the novel H1N1 pandemic virus in 2009-2010.

As in previous years, the report covers the calendar year of 2015 for Measles, Mumps, Rubella, Polio and non-polio Enteroviruses, and the 2015-2016 'winter' season for influenza and those viruses causing respiratory and gastroenteric illness. In addition to the Executive Summary, we have included the key messages in summary form at the top of each of the various sections: this measure will hopefully serve to enhance the usefulness of the report.

There have been no new viruses added to the contents for this year: however, we have been able to include more extensive Rotavirus typing data for the first time. In keeping with WHO recommendations, surveillance of circulating Rotavirus strains is intended to compliment the introduction of Rotavirus vaccine to the universal childhood immunisation schedule.

Finally, on behalf of all the staff at the NVRL, we would like to sincerely thank all of you for your support over the last year: our colleagues in hospitals and in community clinics; GP practices and primary care centres; public health; and professional medical societies and organisations, both in Ireland and internationally. Without your assistance, advice, and commitment to sharing clinical knowledge, this work would not have been possible. Our primary collaborators are listed in Section 9 (page 27). We apologise in advance to anyone that has been inadvertently omitted.

Dr Suzie Coughan, Dr Jeff Connell, Deirdre Burke, Dr Joanne O'Gorman, Dr Cillian De Gascun

January 2017

Executive Summary

- Influenza A(H1N1)pdm09 was the most prevalent virus circulating in Ireland in 2015-16. Influenza strains characterised at the NVRL were antigenically and genetically similar to the strain included in the trivalent vaccine used in Ireland.
- A higher proportion of B/Victoria viruses were detected in Ireland and in Europe this season than last. The B/Victoria lineage was not included in the trivalent inactivated influenza vaccine, which may have contributed to a reduced overall effectiveness of the vaccine.
- Norovirus GII.4 Sydney 2012, which is now globally endemic, continues to predominate in Ireland. The newly described GII.17 virus has not yet been detected in infections acquired in Ireland and tested at NVRL.
- Rotavirus vaccination will be included in the national childhood immunisation schedule from October 2016. Rotavirus genotypic surveillance shows a predominance of genotypes G1P[8] and G9[P8] circulating in Irish cases. This surveillance system, currently based on the WHO molecular methodology for VP4 and VP7 genes, will be used to monitor the impact of vaccine introduction on the molecular epidemiology of rotavirus in coming seasons.
- In 2015, Ireland was deemed to have interrupted transmission of endemic rubella virus by the WHO European Regional Verification Commission for Measles and Rubella.
- No endemic cases of rubella have been notified to the Department of Public Health by the NVRL since 2005.
- There are over 100 non-polio enteroviruses implicated in human infection. In 2015, a variety of enterovirus genotypes were detected in patients with enterovirus associated viral meningitis, including EV-71, Echo 6, Echo 9, Coxsackie B1 and Coxsackie A1.
- EVD68, putatively associated with a recent increase in acute flaccid myelitis cases in the US, was detected in a number of paediatric respiratory samples from Irish hospitals. Respiratory samples submitted from patients will be routinely screened for EV from October 2016.

Key Messages:

Influenza A(H1N1)pdm09 was the most prevalent virus circulating in Ireland in 2015-16. Influenza strains characterised at the NVRL were antigenically and genetically similar to the strain included in the trivalent vaccine used in Ireland.

A higher proportion of B/Victoria viruses were detected in Ireland and in Europe this season than last. The B/Victoria lineage was not included in the trivalent inactivated influenza vaccine, which may have contributed to a reduced overall effectiveness of the vaccine.

Influenza Season 2015-16

The influenza season in Ireland began in early January 2016, with continued activity over the next twelve weeks. Incidence peaked in week four, and returned to below baseline levels in late March 2016. Influenza-like illness (ILI) rates remained above the medium threshold (57/100,000 population) for five weeks but never reached the high threshold level (114/100,000 population) [1]. Over the entire season (week 40 to week 20) there were 1,713 laboratory confirmed influenza cases identified at the NVRL. Influenza AH1 and B strains co-circulated with only sporadic cases of AH3 type viruses detected during the season.

Sentinel sampling of community based ILI cases continued this year with 1,155 combined nose and throat swabs investigated from patient's presenting to participating GP surgeries around the country. Overall influenza detection rates of 50% were obtained in this cohort which increased to >65% at the peak of influenza activity (compared with a European average of 53% in similar sentinel surveillance schemes) [1,2]. Detection rates confirmed the sensitivity of the ILI clinical case definition used [3].

Influenza A:

In contrast to 2014-15 season, the predominant virus was A(H1)pdm09-like, and represented 90% of all influenza A viruses detected (Figure 1). The A(H1N1)pdm09 virus was associated with higher

morbidity and an increased number of intensive care admissions which contrasts with the 2014–15 season where the predominant virus was A(H3N2) with an apparently less severe presentation.

Antiviral Resistance:

Influenza neuraminidase inhibitors (NAI) can be used to treat or used in targeted prophylaxis to prevent influenza. Resistance to oseltamivir, the most commonly used NAI, has been described in influenza A (H1N1) pdm09. Therefore, national guidelines recommend antiviral resistance testing in immunocompromised patients with suspected or confirmed influenza A (H1N1) pdm09 if no clinical improvement is seen within 5 days of commencement of treatment [4]. No antiviral resistance was detected at the NVRL for the 5 clinical cases where resistance to NAI was suspected during the 2015-16 season.

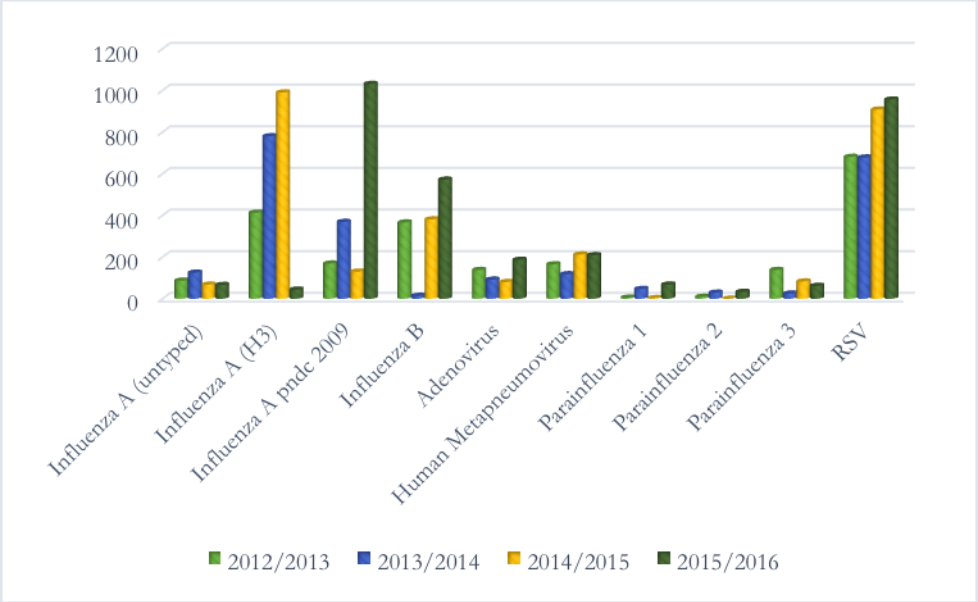


Figure 1. Influenza and other respiratory viruses detected at the NVRL from 2012-2016. Viruses detected from non-sentinel respiratory samples submitted for investigation are represented. Diagnosis was made by RT-PCR.

Influenza B:

The absolute numbers of influenza B laboratory confirmed cases increased significantly (n=572) compared to last year As well , the proportion of B/Victoria-like viruses and B/Yamagata-like viruses was reversed with B/Victoria-like viruses making up the majority of those viruses genetically and

antigenically characterised. (Figure 2). This observation is in accordance with the relative prevalence of influenza B viruses in Europe. Vaccine efficacy may have been compromised considering the trivalent-vaccine for the 2015-16 season used in Ireland did not contain a B/Victoria-like virus.

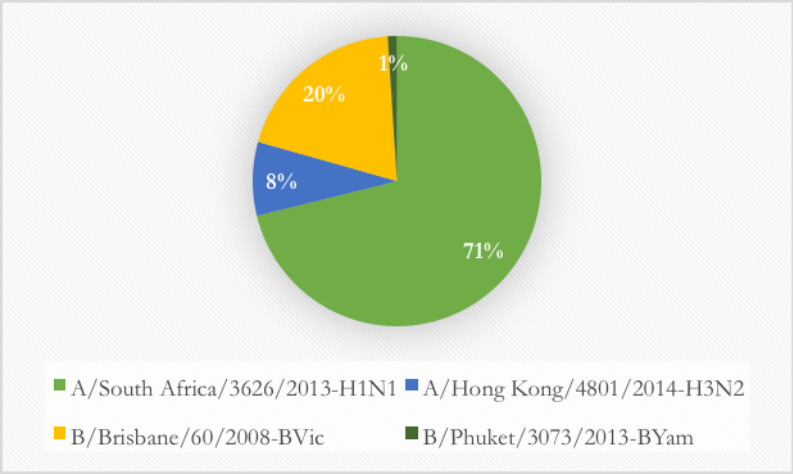


Figure 2: Genetic characteristics of the influenza strains analysed at the NVRL during the 2015-16 season (n=97). The characterisation is based on nucleotide sequence analysis of the HA1 region of the hemagglutinin gene from a representative selection of viruses. A(H3N2) viruses belong to the genetic group 3C. B/Brisbane/60/2008-like viruses are genetically distinct from those in the 2015-16 trivalent vaccine.

More detailed phylogenetic analyses, focused on the HA1 region of the hemagglutinin gene of a representative number of influenza isolates, identified A/California/7/2009-H1N1-like viruses (Figure 3), A/Switzerland/9715293/2013-H3N2-like (Figure 4) and B/Brisbane/60/2008-B-like viruses (Figure 5) as the most commonly circulating strains in Ireland. This pattern is reflective of viruses prevalent in Europe during the season. The AH1 and AH3 viruses identified in Ireland are antigenically similar to the 2015-16 vaccine strains.

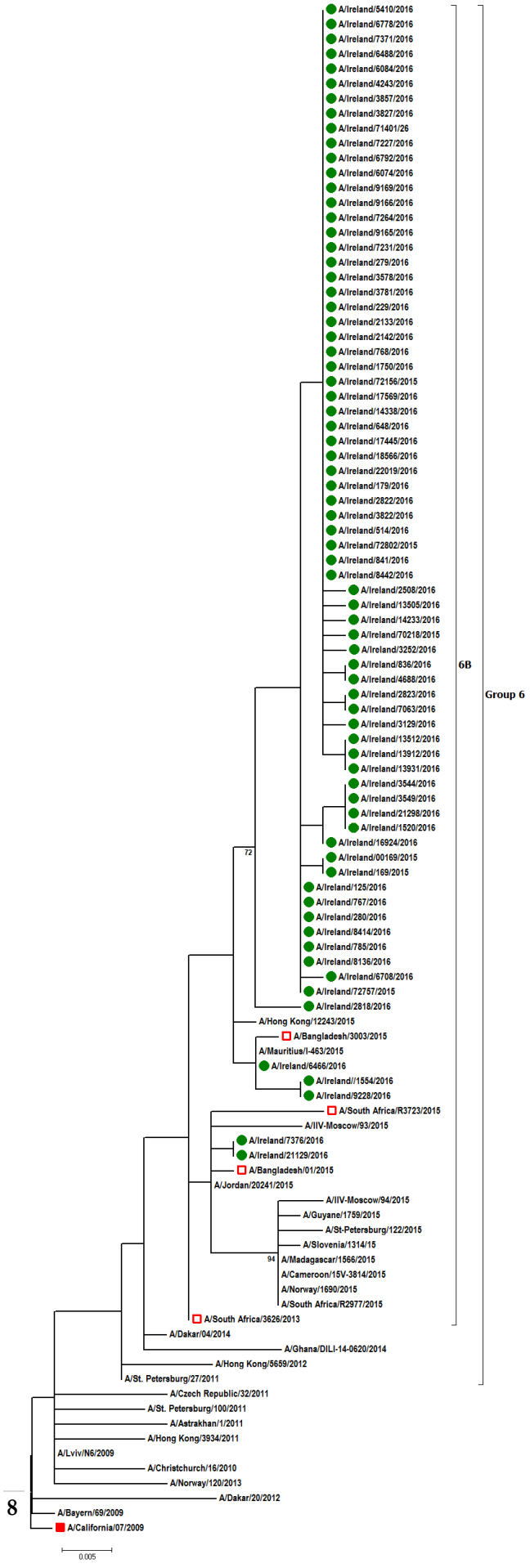


Figure 3: Phylogenetic analysis of the hemagglutinin gene of influenza A(H1). Maximum likelihood trees depicting the genetic relationship between Irish A(H1) strains (green) and reference sequence strains from representative viruses circulating in Europe (red hollow squares). Viruses displayed a high degree of genetic similarity to each other and to the vaccine strain (red closed squares). Relevant bootstrap values over 40% are shown.

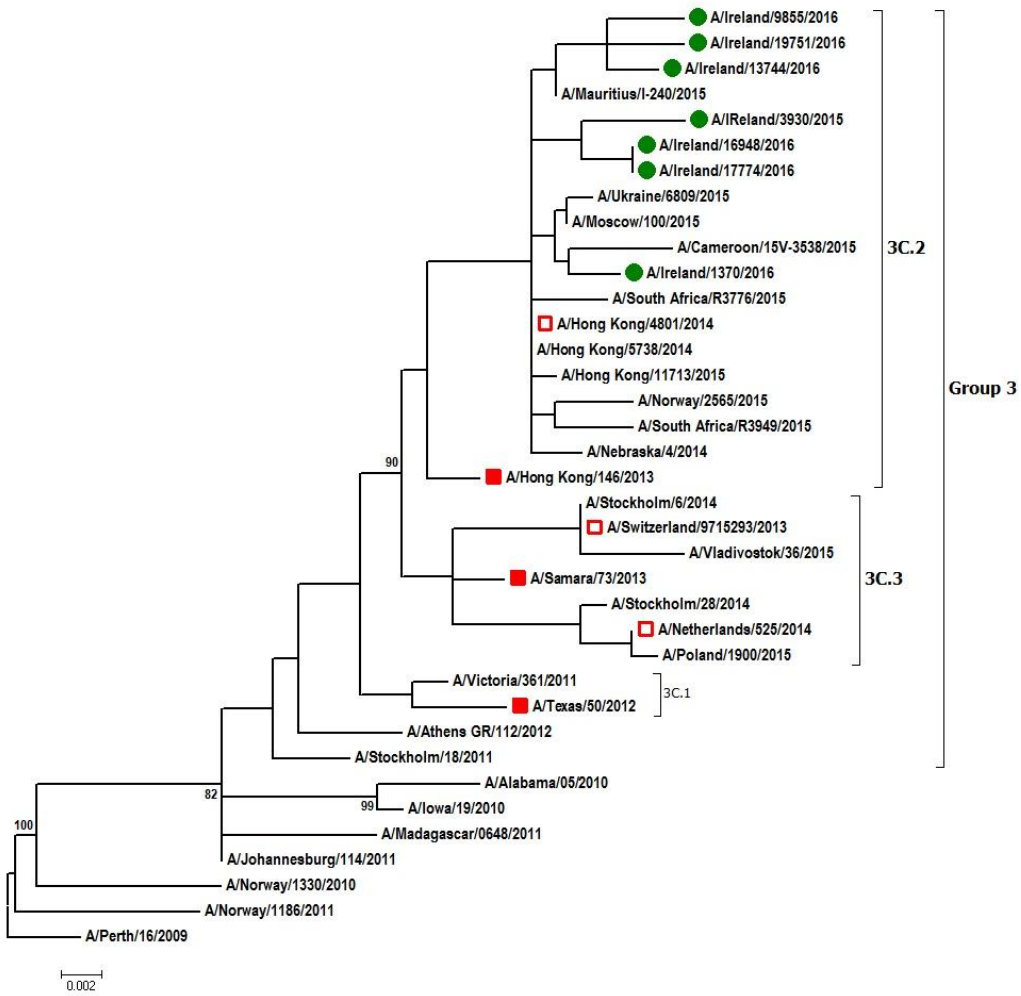
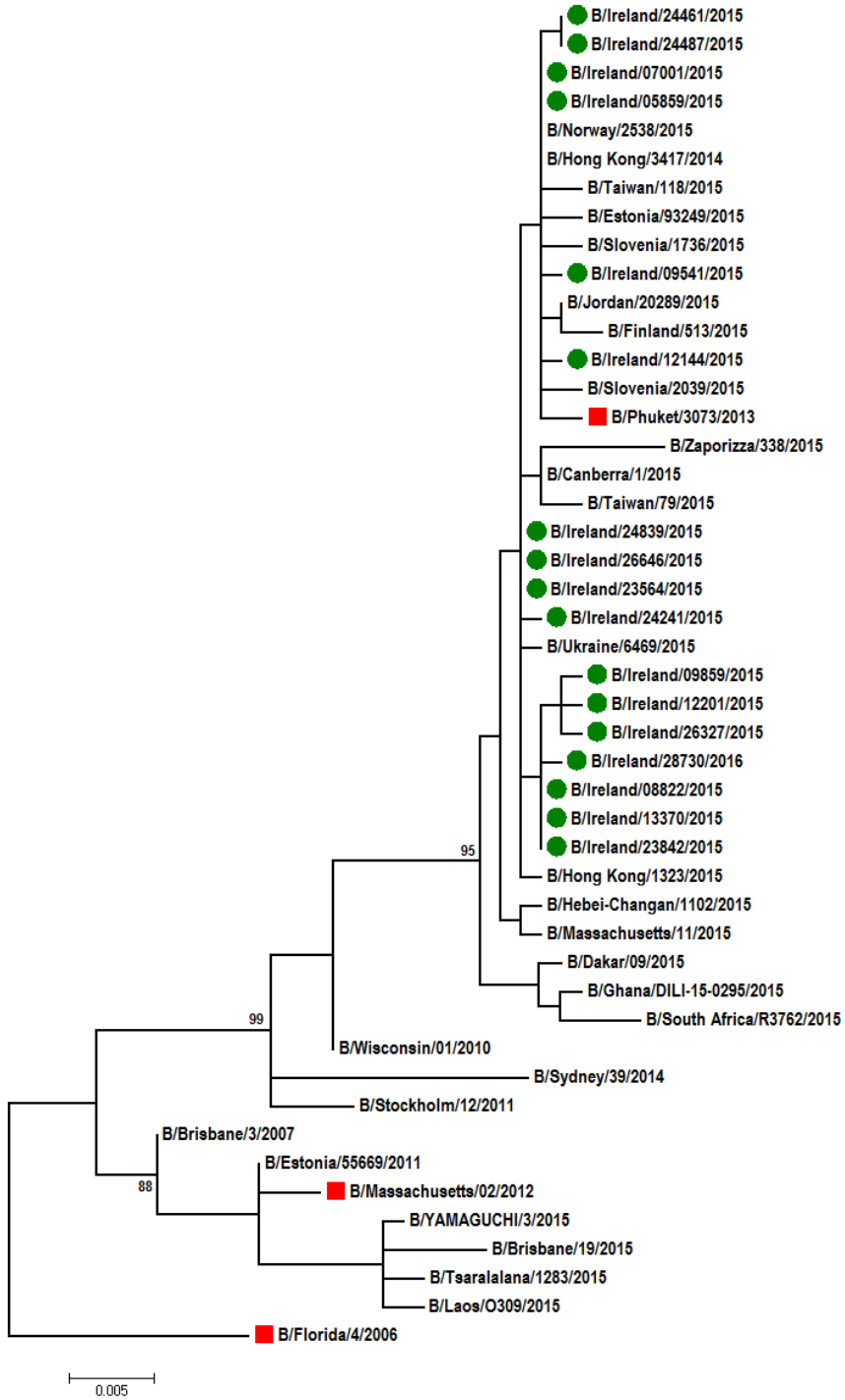


Figure 4: Phylogenetic analysis of the hemagglutinin gene of influenza A(H3). Maximum likelihood trees depicting the genetic relationship between Irish A(H3) strains (green) and reference sequence strains from representative viruses circulating in Europe (red closed squares). Viruses displayed a high degree of genetic similarity to each other and to the vaccine strain (red hollow squares). A/Switzerland/9715293/2013, the H3 component of the 2015-16 trivalent vaccine has been replaced by A/HongKong/4801/2014 strain for the 2016-17 formulation. Relevant bootstrap values of greater than 40% are shown.

Figure 5: Phylogenetic analysis of the hemagglutinin gene of influenza B(Yam). Maximum likelihood trees depicting the genetic relationship between Irish B(Yam) strains (green) and reference sequence strains from representative viruses circulating in Europe (red squares). Viruses displayed a high degree of genetic similarity to each other and to the vaccine strain (B/Phuket/3073/2013). Relevant bootstrap values of greater than 40% are shown.



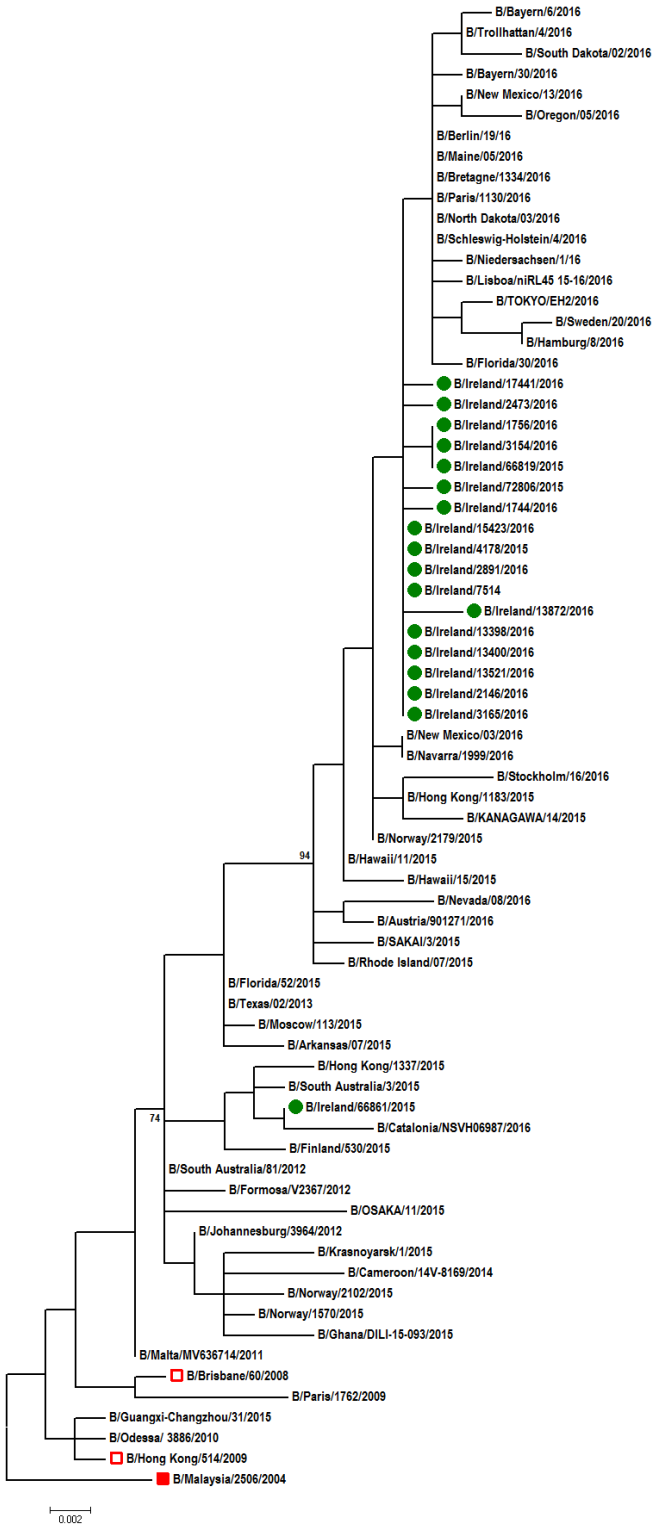


Figure 6: Phylogenetic analysis of the hemagglutinin gene of influenza B(Vic). Maximum likelihood trees depicting the genetic relationship between Irish A(H1) strains (red) and reference sequence strains from representative viruses circulating in Europe (red hollow and closed boxes).

Other Respiratory Viruses:

In addition to influenza viruses, the NVRL notified 956 laboratory confirmed RSV infections this season with a peak of 110 cases diagnosed in week 51 (Figure 1).

Noteworthy among other respiratory viruses was the increase in Parainfluenza viruses (PIV 1-4 inclusive) between this and last season (n=184 in 2015-16 and n=95 in 2014-15) with a predominance of PIV1 and PIV3 types. This reflects the normal seasonal variance of the PIV viruses which tend to circulate toward the end of the season.

The NVRL would like to acknowledge and thank our colleagues in clinical microbiology laboratories for the contribution of influenza viral isolates for culture, antigenic, and genetic characterisation. Data from the NVRL influenza surveillance programme is submitted weekly to the ECDC European Surveillance Database (TESSy) and bi-annually to the WHO Global Influenza Surveillance and Response System (GIRIS) programme (GISAID).

Viral Gastroenteritis – Circulating viruses in 2015-16

Key Message:

Norovirus GII.4 Sydney 2012, which is now globally endemic, continues to predominate in Ireland. The newly described GII.17 virus has not yet been detected in infections acquired in Ireland and tested at NVRL.

Rotavirus vaccination will be included in the national childhood immunisation schedule from October 2016. Rotavirus genotypic surveillance shows a predominance of genotypes G1P[8] and G9[P8] circulating in Irish cases. This surveillance system, currently based on the WHO molecular methodology for VP4 and VP7 genes, will be used to monitor the impact of vaccine introduction on the molecular epidemiology of rotavirus in coming seasons.

Norovirus continued to dominate the viral gastroenteritis season of 2015-16 with 1,321 notifications of infection from the NVRL. This represented >50% of all cases of laboratory confirmed viral gastroenteritis identified (n=2,271 from July 2015 to June 2016). The peak of norovirus activity occurred between weeks 13 and 17 2016 with 723 notifications over those five weeks (55% total NoV notifications).

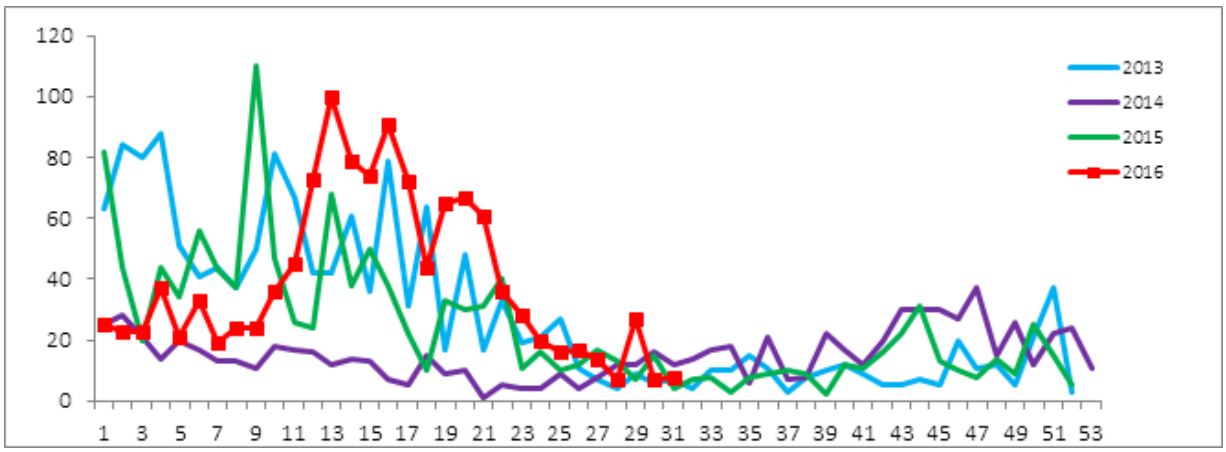


Figure 7: Weekly norovirus notification data from 2013 to 2016. Data produced in collaboration with HPSC and is based on the number of patients with Norovirus RNA positive stool samples. Notification data is disseminated through HPSC weekly infectious disease bulletins.

As with the preceding season 2014-15, Norovirus RNA was detected in patients of all age groups and was associated with 97 outbreaks affecting 1,654 individuals [5]. In addition to the norovirus infections described, Sapovirus, astroviruses and enteric adenovirus (AdVF) continued to cause disease predominantly in children < 5 years, cumulatively causing 538 cases (24% of laboratory confirmed cases). This is the second season of surveillance for Sapovirus – a Calicivirus associated with gastrointestinal illness. Incidence rates remain high with 560 and 390 cases identified in 2015-16 and 2014-15 respectively.

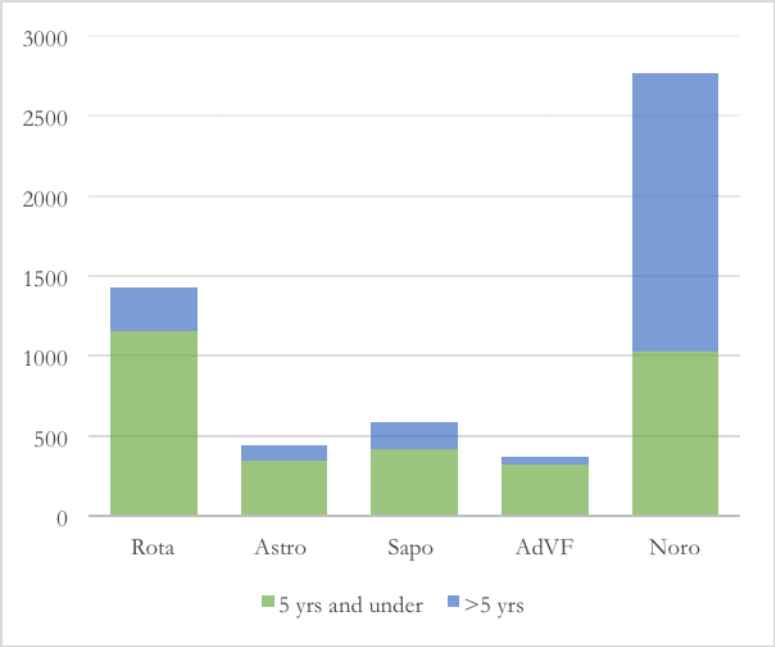


Figure 8: Detection of viral gastroenteritis associated pathogens in stool samples between July 2015 and July 2016 (n = 11,992). Data is analysed in discreet age groups (0-5 years and >5 years). The majority of samples were submitted from acute hospitals and residential healthcare facilities.

Genetic characterisation of the noroviruses responsible for outbreaks confirmed observations from previous years of a predominance of the GII.4 Sydney 2012 virus, which is now globally endemic. Investigations did not reveal the presence of the newly described GII.17 virus in infections acquired in Ireland. Food associated outbreaks showed greater genetic diversity than those associated with person to person spread (Figure 9)

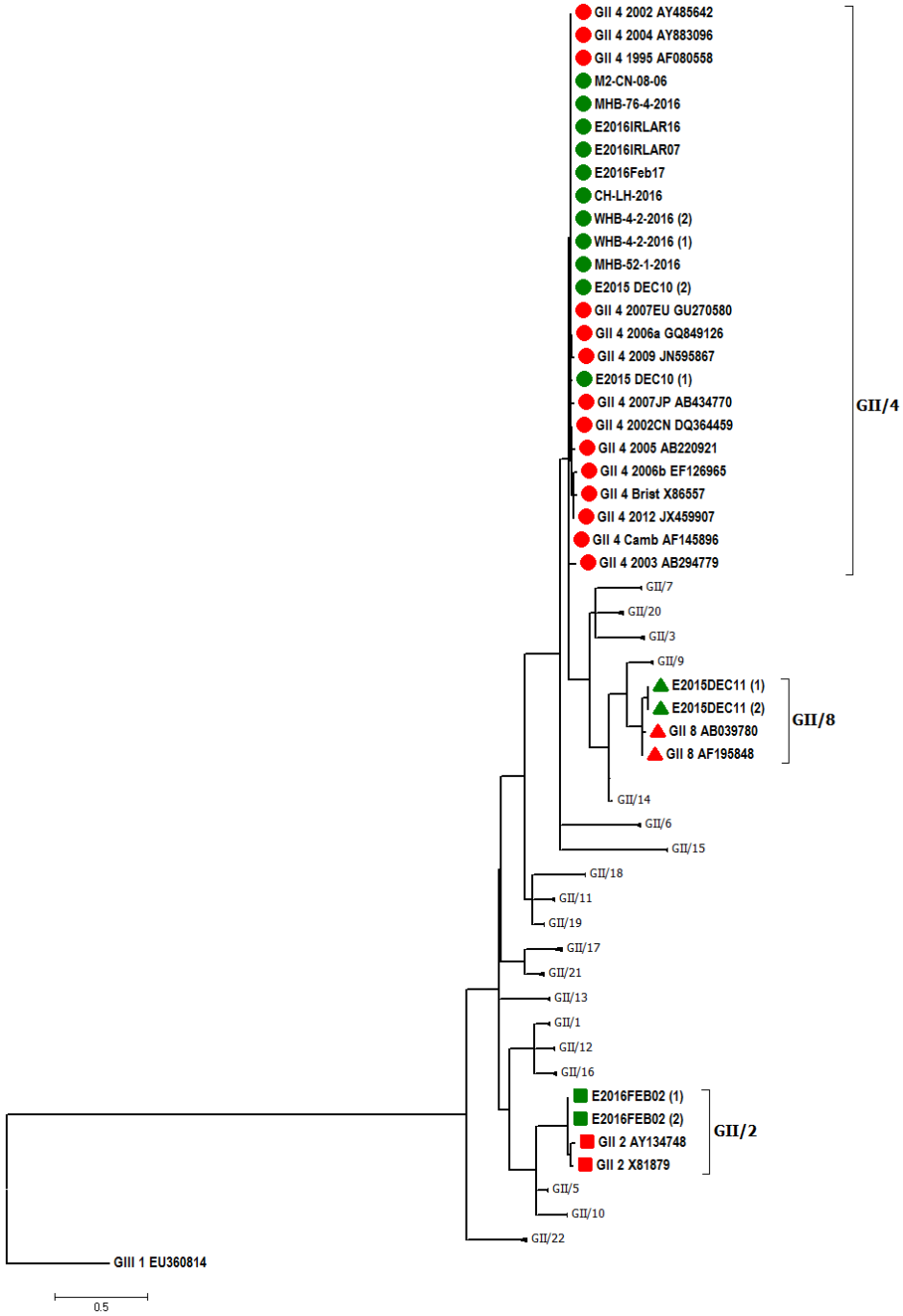


Figure 9: Phylogenetic analysis of norovirus associated outbreaks. Maximum likelihood ML tree of 600bp fragment from the ORF 1-2 capsid gene of the norovirus genome. Noroviruses associated with outbreaks in Ireland are shown in green. Nomenclature is assigned by Department of Public Health Outbreak Surveillance System eg E20156FEB02 (1). Numbers in brackets denote samples from the same outbreak. Analysis included reference strains from the RIVM Noronet database (red squares). NVRL wishes to acknowledge its collaboration with DPH and RIVM.

Rotavirus:

Peak rotavirus activity occurred later this season than last year with the majority of infections notified by the NVRL in April and May 2016. This was confirmed by the timing of clinical notifications of infection to the HPSC [6].

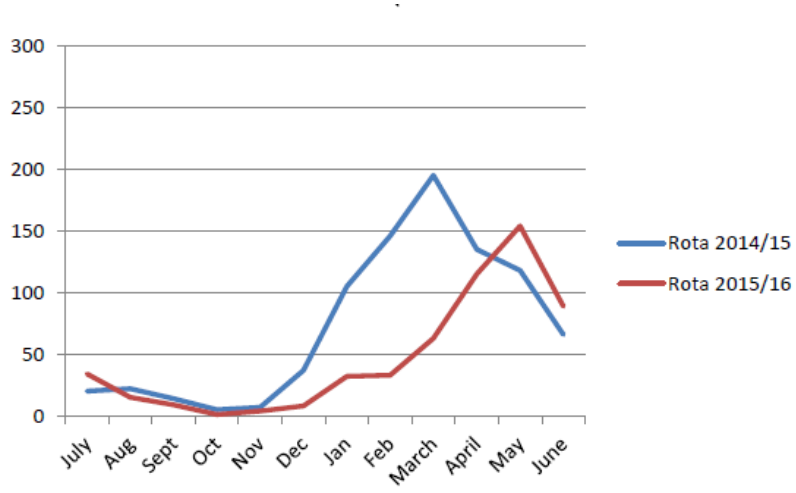


Figure 10: Comparative timeline of rotavirus detections at NVRL in 2014-15 and 2015-16 seasons. Absolute numbers of stool samples with norovirus RNA detected are presented

With the introduction of the Rotavirus vaccine in October 2016 to the childhood immunisation schedule in Ireland, it is likely that the incidence of rotavirus will decline dramatically and the normal seasonality of the virus infections may not be apparent. Prior to the introduction of the vaccine the NVRL has genotyped circulating viruses (n=111) to generate the pre-vaccine baseline characteristics of circulating rotavirus. Rotavirus strains detected during this analysis reflect those circulating in other European countries with a predominance of G1 P[8] (Figure 11). Of note is the higher than expected prevalence of the G9 P[8] strain which constitutes 35% of the viruses typed, a significantly higher proportion than reported elsewhere. The effect of vaccination on the dynamics of the rotavirus in Ireland will be presented 12 months post vaccine introduction. As the GSK Rotarix vaccine, which is a monovalent G1 P[8] modified vaccine, is likely to be the vaccine of choice for infants in Ireland, the NVRL will introduce an assay to discriminate vaccine or wild-type rotavirus strains.

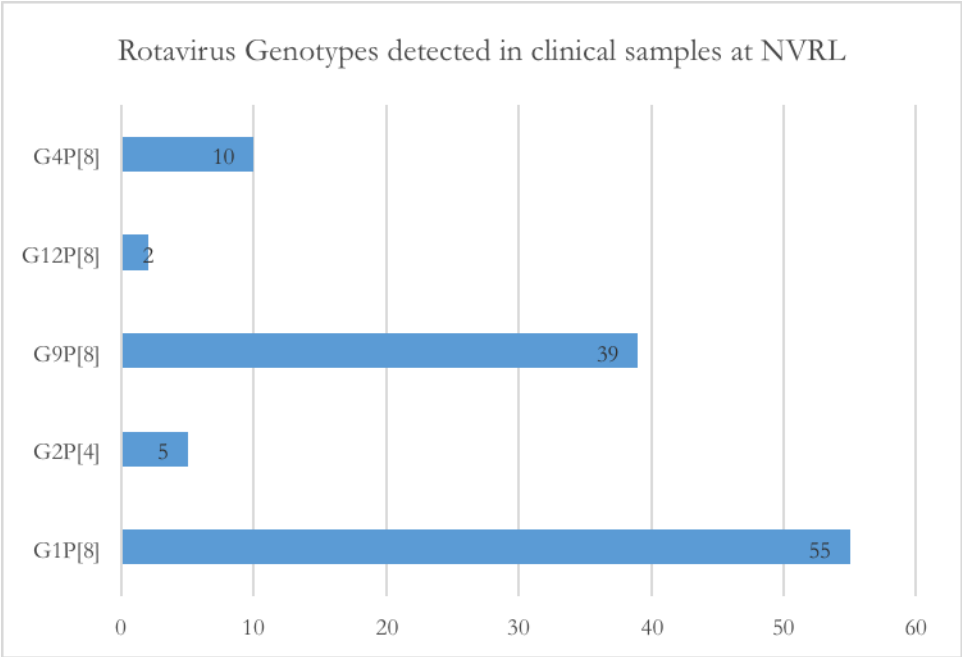


Figure 11: Genotype analysis of the VP4 and VP7 genes (encoding outer capsid proteins) of the rotavirus genome (n =111). Nomenclature and typing methods as defined by WHO technical bulletin.

Please contact the NVRL if you would like Rotavirus typing performed on specific isolates from your institution as the surveillance programme will not type all positive isolates.

Key Message:

In 2015, Ireland was deemed to have interrupted transmission of endemic rubella virus by the WHO European Regional Verification Commission for Measles and Rubella. No endemic cases of rubella have been notified to the Department of Public Health by the NVRL since 2005.

Measles and Rubella

Eliminating measles and rubella is a core goal of the European Vaccine Action Plan 2015–2020 and an important part of global efforts to improve population health. In April 2015, significant advances were announced by the WHO European Regional Verification Commission for Measles and Rubella Elimination, with 32 countries successfully eliminating endemic transmission of measles and/or rubella infection. Ireland was among the 20 member states declared to have successfully interrupted rubella transmission. High-quality surveillance to detect cases and monitor chains of virus transmission and very high immunization coverage with two doses of vaccine against measles and rubella were essential in attaining this goal.

In 2015 the NVRL tested, 333 and 1638 clinical specimens for measles and rubella IgM respectively. However, the majority of rubella IgM investigations are linked to non-specific TORCH requests on infants, neonates and mothers . Therefore the actual number of rubella investigations, performed to investigate a rash illness, are significantly lower. This compromises the surveillance for acute rubella infections. Conversely, probably due to the more frequent cases of measles, the surveillance for and investigation of a measles like rash is more successful.

Current protocols for the investigation of measles and rubella infection are based upon the collection of oral fluid samples using the OraCol collection device. This sample type, especially when collected within 10 days and 3 days for measles and rubella, respectively, is suitable for the detection of viral RNA and subsequent genotyping of the virus. To detect measles or rubella specific IgM, the OraCol specimen needs to collected after 7 days. OraCol collection devices can be obtained from the NVRL (www.nvrl.ucd.ie). An IgM antibody can also be detected in blood samples 3- 5 days post rash onset

In total, 31 (9.3%) samples tested positive for measles IgM and 5 (0.3%) for rubella IgM. When taken in conjunction with clinical, epidemiological links, and vaccination history only 1 was laboratory confirmed measles infection and no cases of laboratory confirmed rubella were reported.

As an accredited member of the Global Measles and Rubella Laboratory Network (GMRLN) the NVRL has a remit to ensure timely reporting of results from laboratory testing for measles and rubella to its databases. In 2015, 95% measles cases were reported with 7 days and 85% within 4 days (time to results of serologic testing (IgM) after receipt of the clinical specimen).

Genetic characterisation was carried out on one confirmed measles case. The virus was classified as genotype D8 based on nucleotide sequence analysis of the N-gene (submitted to the MeaNS (WHO Measles Nucleotide Surveillance database)).

Measles outbreak in 2016

Despite the robust surveillance system and high population vaccine coverage, an outbreak occurred in 2016 in predominately unvaccinated susceptible individuals [7]. An outbreak control team was convened by the Department of Public Health and subsequent epidemiological and laboratory investigations support the likely importation of a single case of measles from Romania. The NVRL responded quickly with distribution of appropriate swabs for sample collection and an increased frequency of testing to identify and confirm cases. As of 15th August 2016 there were 38 confirmed cases and 8 possible cases attributed to the outbreak between weeks 18 and 33 [8]. The majority of cases were from HSE-South.

Genetic characterisation of the virus associated with the outbreak confirmed a B3 genotype with 100% similarity between cases (Figure 12). In addition, there was also an imported case of measles genotype D8 and subsequent onward transmission within Ireland to another individual.

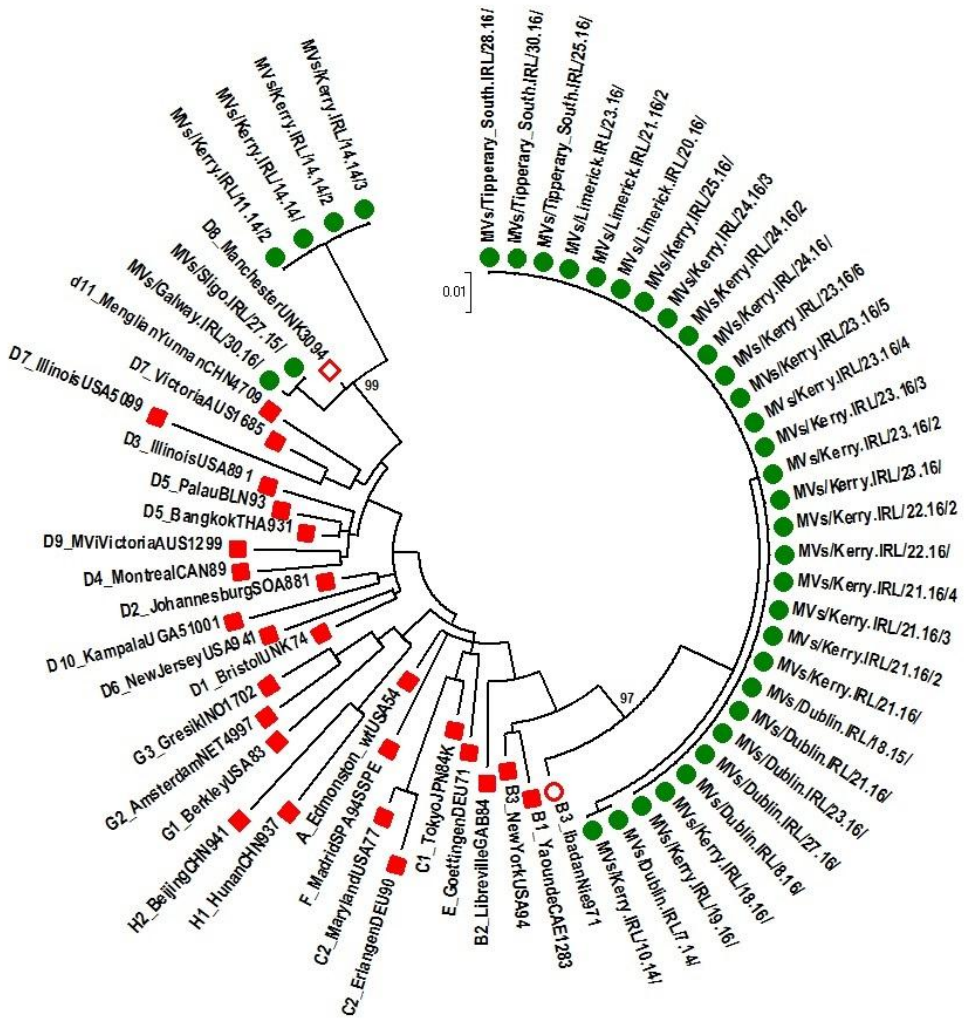


Figure 12. Phylogenetic analysis of the measles 2016 outbreak attributed to genotype B3 virus. Maximum Likelihood tree outlines genetic relationship, based on 439bp fragment on the N-gene of the measles virus genome, between outbreak strains (green) and reference sequences (red) from the WHO MeaNs database. Previously, characterised D8 measles viruses detected in Ireland are also displayed (red). A/Edmonston wtUSA 54 vaccine strain is used to root the tree.

Enterovirus and Picornavirus Surveillance

Key Messages:

There are over 100 non-polio enteroviruses implicated in human infection. In 2015, a variety of enterovirus genotypes were detected in patients with enterovirus associated viral meningitis, including EV-71, Echo 6, Echo 9, Coxsackie B1 and Coxsackie A1.

EVD68, putatively associated with a recent increase in acute flaccid myelitis cases in the US, was detected in a number of paediatric respiratory samples from Irish hospitals. Respiratory samples submitted from patients will be routinely screened for EV from October 2016.

Poliovirus:

The NVRL continues to support the Global Polio Eradication Initiative (GPEI) and the Polio Eradication Endgame and Strategic Plan (2013-2018. The NVRL is the WHO fully accredited national polio laboratory and utilises specific viral culture procedures to ensure the detection and confirmation of poliovirus infection. In September 2015, the Global Certification Committee (GCC) confirmed that wild poliovirus type 2 (WPV2) circulation stopped globally more than 15 years ago. Additionally there have been no WPV3 cases reported since November 2012 anywhere in the world. Interruption of WPV3 would represent another historic milestone for the GPEI and would leave only WPV1 still circulating. However, there is still concern regarding the undetected circulation in the environment of WP1 and also circulating vaccine derived polio 1 and 2 viruses, which can cause acute flaccid paralysis (AFP).

Acute Flaccid Paralysis surveillance, including case investigation and specimen collection is a gold standard method for poliomyelitis surveillance. The expected annual non-polio AFP rate <15 years of age in Ireland is ≥1/100 000 population. In 2015, 5 cases of AFP were notified to the HPSC; however, none was attributable to poliovirus infection. The notification rate fell far short of the expected threshold of reporting which was achieved for the first time in 2014 [8]. Clinicians are recommended to urgently consider polio and enterovirus infection in cases of AFP in children under 15 and to notify these cases to the HPSC. Laboratory investigation of AFP requires submission of two stool specimens collected 24-28 hours apart from all suspected cases.

Non-Polio Enterovirus:

Increased numbers of EV-A71 and EV-D68 detections reinforce the need for vigilance for enterovirus infections, especially cases that present with more severe clinical syndromes. Clinicians should be encouraged to obtain stool and respiratory specimens for enterovirus detection and characterisation from all patients presenting with symptoms suggestive of meningitis; encephalitis; hand, foot and mouth disease (HFMD); acute flaccid myelitis (AFM) or acute flaccid paralysis (AFP).

The diagnosis of EV based on real-time reverse-transcription PCR (RT-PCR) is a sensitive and rapid diagnostic method which has become the standard method over virus isolation. EV-specific primers targeting the conserved 5' untranslated region (UTR) are used to perform real-time RT-PCR directly from clinical specimens, on respiratory or rectal swabs, vesicle fluid, stool sample and cerebrospinal fluid (CSF).

In 2015, 3,653 CSF samples were tested for EV as part of the clinical investigation of suspected meningoencephalitis, 207 of which had detectable EV RNA (5.6% positivity rate). When throat swab and stool samples are included, 5937 samples from patients with suspected enterovirus infection were tested at NVRL. 497 samples had detectable EV RNA (8.4% positivity rate). The majority of these patients were ≤ 1 year of age.

The NVRL employs a combination of genetic and serological characterisation techniques to identify circulating strains. Viruses are chosen for typing from a representative number of clinical specimens, the majority of which were derived from patients presenting with CNS manifestations. Characterisation of these viruses (n=63) was undertaken either directly from CSF or from a stool or throat swab sample which was submitted at the time of the CSF investigations. Results showed a wide variety of enteroviruses to be associated with disease in these patients including 9 cases of EV-71 (Figure 13). From early 2017 results of EV characterisation will be disseminated through the HPSC quarterly reports on Invasive Meningococcal Disease, Bacterial/Viral Meningitis and Haemophilus influenzae in Ireland.

EV-71, primarily associated with hand, foot and mouth disease, can also be associated with brain stem encephalitis [9]. In the 9 cases described here, all were in children ≤ 1 year of age and all resulted in hospitalisation with at least 1 admission to ICU. The subgenogroup of EV-71 was C2 as determined by phylogenetic analysis of the VP1 gene (Figure 14). The NVRL in collaboration with microbiology and paediatric colleagues in Temple Street Children's University Hospital are currently involved in clinical research to assess the impact of EV infections in these children.

EV-D68 has recently been associated with outbreaks of severe respiratory disease in USA, Canada and throughout Europe [10]. A putative association between EV-D68 infection and an increase in cases of acute flaccid myelitis is currently under investigation. Results of pilot studies conducted at NVRL have indicated that a significant proportion of infections in children are attributable to EV-D68. From week 40 2016, the NVRL intends to extend its frontline respiratory screen to include EV testing.

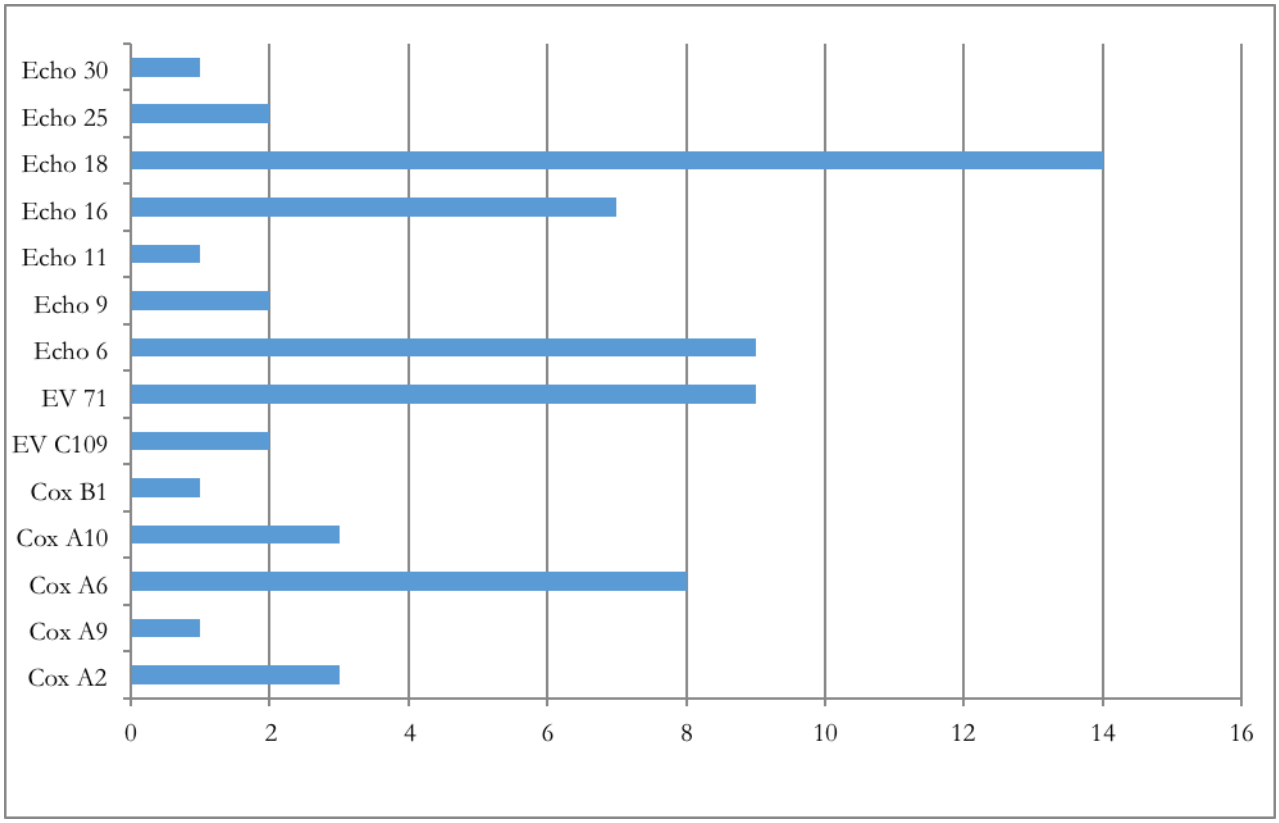


Figure 13. Genetic characterisation of representative EV strains detected samples during 2015 (n=63). Typing was based on a 350bp fragment of the VP1 gene. Analysis of nucleotide sequences was carried out using the RIVM Enterovirus Genotyping tool (www.rivm.nl/mpf/enterovirus/typingtool).

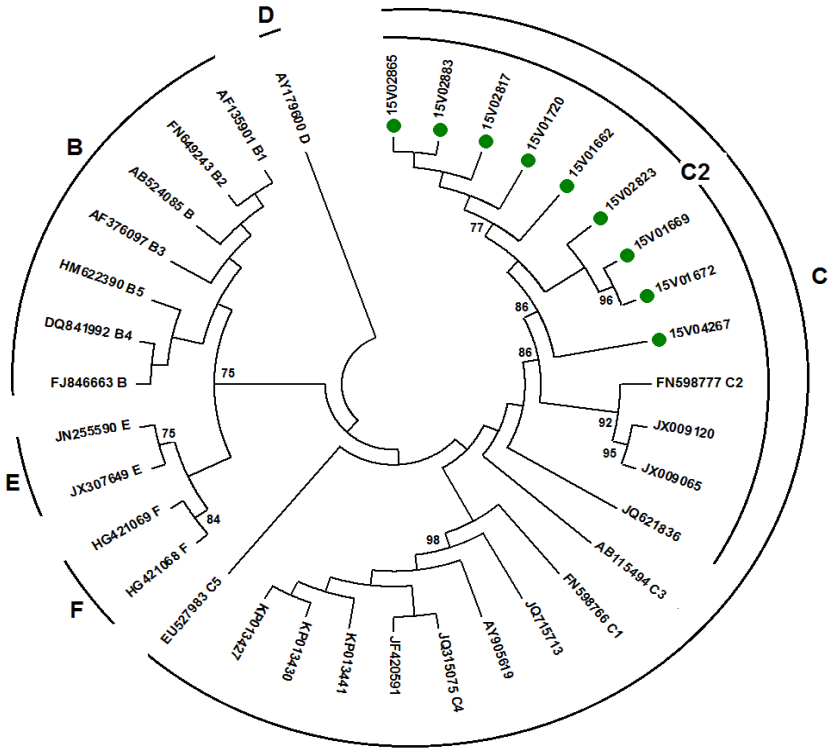


Figure 14: Genetic characterisation of representative EV71 strains detected in clinical samples during 2015 (n=9). Maximum Likelihood tree outlines genetic relationship, based on a fragment on the VP1 gene of EV 71 (B-F) strains. Viruses detected in Irish patients are all within the C2 lineage which is consistent with data emerging from Europe.

Developments in 2015-16

Hepatitis C virus - Antiviral Susceptibility Testing:

Treatment of hepatitis C virus (HCV) infection has progressed considerably with the addition of interferon-free, direct-acting antiviral (DAA)-based combination therapies to management options for those infected. Most treated patients achieve virological cure, however, HCV resistance to DAAs plays an important role in the failure of these interferon-free treatment regimens. Although universal resistance testing is not recommended, it is reasonable to investigate virological failure at least in NS3 and NS5A containing regimens [11]. Specific genotypic antiviral assays have been developed at the NVRL for the NS3, NS5A and NS5B HCV gene fragments which encode the protein targets for this group of drugs. Results from NS3 sequence analysis of a cohort of genotype 1 infected patients (n=681 patients) showed 42% patients contained the Q80K mutation which reduces sustained virological response rates to Simeprevir. Preliminary data for the NS5A genes of a small number of patients treated with an NS5A/B combination regimen displayed a significant number of resistance associated substitutions (RAS). Conversely, there was no evidence of RAS in the NS5B gene in these patients. All assays are genotype dependent and require 1ml serum sample. Information on test requesting is available on the NVRL website.

Rhinovirus Screening and Genotyping Capability:

The NVRL will introduce Rhinovirus screening assays in 2016-17 to investigate RV associated pneumonia. RV detection using bronchoalveolar lavage (BAL) fluid specimens from severe pneumonia patients may be used as an indirect indicator for the pathogenic role of RV. Characterisation of HRV from this cohort will provide insights into genotype specific manifestations of infection.

This service is being developed in response to the increased number of RV infections being identified by new diagnostic platforms. To date the molecular epidemiology of RV in Ireland has not been described.

Verification and Validation of Virus Detection Assays in the Acute Setting:

The NVRL participated in a number of inter laboratory comparisons this year with microbiology colleagues to facilitate the verification or validation of assays for near patient testing. This increase in capacity in hospital microbiology laboratories is welcomed and will facilitate better and more

timely patient management. Details on how to participate in these projects are available from the Quality Department of the NVRL.

Laboratories are also encouraged to continue to send a representative number of isolates to the NVRL for characterisation. The antigenic and genetic data generated will be submitted to the WHO GIRIS so that representative viruses circulating in Ireland can be considered for future vaccine formulations.

Key Message:
The NVRL would like to sincerely thank all those who have contributed to the work performed at the NVRL in recent years, including our colleagues in hospitals, clinics, GP practices, public health and in the community throughout the country. We are also extremely grateful to the professional medical societies and organisations, both in Ireland and internationally, who continually provide advice and support and without whose assistance this work would not have been possible.

Collaborators:

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- Department of Health
- Health Service Executive (HSE)
- Health Protection Surveillance Centre (HPSC)
- Departments of Public Health
- Irish College of General Practitioners (ICGP)
- Irish Society of Clinical Microbiologists (ISCM)
- Infectious Disease Society of Ireland (IDSI)
- National Immunisation Advisory Committee (NIAC)
- National Polio Certification Committee
- Irish Paediatric Surveillance Unit (IPSU)
- World Health Organisation (WHO)
- European Centre Disease Control (ECDC)
- European Society of Clinical Virology (ESCV)
- Virus Reference Department, PHE Colindale, UK
- WHO Collaborating Centre for Reference and Research on Influenza, National Institute for Medical Research, UK
- WHO Global Specialised Poliovirus and Regional Reference Laboratory, National Institute for Biological Standards and Controls (NIBSC), UK
- WHO European Regional Laboratory for Measles/Rubella PHE-VRD, Colindale, UK
- National Institute for Public Health and the Environment (RIVM), Bilthoven, The Netherlands
- Rare and Imported Pathogens Laboratory (RIPL) PHE, Porton
- European Network for Diagnostics of Imported Viral Diseases (ENIVD)

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