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A note from the editors: changes and stability – looking back to 2012 and forward to 2013

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At the end of every year, editors reflect on their activities, count their successes and check if they met the goals set for their journals. When we think about 2012, one of our achievements stands out – our first impact factor (for 2011). With the allocated 6.15, we shot far beyond our expectations and were placed among the top-10 leading journals in our field [1]. Interestingly, most of the competing journals have profit-oriented business models, different from *Eurosurveillance*, which has a non-commercial publisher, the European Centre for Disease Prevention and Control (ECDC).

The attention gained through the impact factor resulted in a steep increase in the number of articles submitted to the journal. This increase concerned mainly regular articles (462 compared with 247 in 2011). While the vast majority of submissions were from Europe, considerably more articles came also from Asia and Africa. We are thankful that authors consider *Eurosurveillance* a good channel to disseminate their research findings.

Of course, the high number of submissions has impacted on our daily routines and on those who collaborate with us. In 2012, more experts than in previous years were contacted and agreed to support us with their scientific judgment about the merits of papers submitted. Some 500 experts (2011: some 380, 2010: some 330) from across the world dedicated time, often on short notice and with tight deadlines, to review for us. We are grateful for their assistance in the evaluation of submissions. In this issue, we publish a list with the names of our peer reviewers in 2012 [2]. We continue to receive informal guidance from our board members, both associate editors and editorial advisors, numerous colleagues at ECDC and other scientists. Even though they remain unnamed here, we highly appreciate their willingness to help and inspire us.

While we had more contacts with our reviewers and authors in 2012, we worked hard to keep up with timely publication and short turnover times. We published 100 rapid communications, 86 regular papers, 14 editorials, and 42 letters and other content. The rejection rate 43% for rapid communications and 76% for regular papers. However, this should not discourage those who have important data and research from submitting them to us because one of our main objectives remains to contribute to a balanced scientific evidence-base in the fields of epidemiology, surveillance, prevention and control of infectious diseases that are relevant to Europe.

The capability to provide timely peer-reviewed information about relevant events that require rapid public health action is one of the main assets of *Eurosurveillance* and remains high on our agenda. In 2012, when it became known that patients from Saudi Arabia and Quatar with severe respiratory symptoms had been infected with a novel coronavirus [3,4], we were among the first scientific journals to provide authoritative information. In total, we published eight peer-reviewed rapid communications related to the event within three months. Some of them were processed in record speed – 24–48 hours from submission. This was possible with the support of our contributors and reviewers who agree to follow us on a route that is still unusual and sometimes even controversial in the world of scientific publishing. Our intention in providing timely, authoritative, quality-controlled preliminary information relevant for communicable disease control is not to go after headline stories, but to enable public health action. We are well aware that publishing preliminary data needs to be handled with care. Rapid processing may raise questions of quality control and conclusions may change when more evidence becomes available. However, the overall positive experience, gained over 15 years, leads us to conclude that with careful selection and processing, the benefits for public health outweigh the concerns raised and that our approach is justified. This is also confirmed by our authors and dedicated peer reviewers who support the concept actively, with important, good-quality contributions.

Having listed some of our achievements, what can our readers and contributors expect in the coming year? In order to increase transparency, speed up and ease our

interaction with authors and reviewers, we will soon introduce an electronic submission system. Authors and reviewers will be asked to log on to the system and follow the instructions when submitting or reviewing for us. Moreover, as a new editorial policy we will automatically share the reviews for specific papers between the respective referees. This change is in response to repeated requests from many who would like to see the comments from the other reviewer(s) for the paper they commented on, as a learning experience. Another new feature is authors will be expected to outline the contribution of each author to the article – this information will be published at the end of the text. We have also started preparing for a new improved website, taking into account the comments obtained from an earlier reader survey and hope to be able to launch it around the start of 2014.

At the beginning of 2013, there is no need to change the identity of *Eurosurveillance*. Instead, we will stick to our concept of rapid communications and timely publication of regular articles. Relevance for public health, i.e. the control and prevention of infectious diseases, and quality will remain our focus. In addition, we will continue to support dissemination of important and good-quality data from authors in countries with fewer papers in scientific literature databases.

Key points, in our view, for the journal for the coming years are our commitment to open access publishing without author or reader fees and that editors should play a role in safeguarding the credibility, quality and speed of published scientific information. Even if the world of scientific publishing were to change in ways we cannot anticipate today, information provision through mobile platforms, social media and self-service information-gathering has already become a reality. We will watch developments closely and tie in where beneficial for the journal and its readers. We believe that an important task for editors is still to guide experts though the large amount of scientific information available and support them with evidence to make informed decisions, also in the future. Moreover, we will keep an eye on and support new ways of publishing (sharing) large datasets, in particular surveillance data collected at various levels in Europe.

In all our activities, we are supported by our publisher, the ECDC and its Director, to whom we are grateful for continued trust, editorial independence, support and funding. We also hope to be able to rely on our good collaboration with you who are already part of our well-established networks of experts in Europe and beyond, and invite others to join too. Together with our supporters, we look forward to exploring and encouraging new ways of sharing and disseminating data and information for the benefit of public health in the coming years.

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The continued emergence of hantaviruses: isolation of a Seoul virus implicated in human disease, United Kingdom, October 2012

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Following a suspected case of hantavirus in a patient suffering from acute kidney injury, rodents from the patient's property in Yorkshire and the Humber, United Kingdom (UK) were screened for hantaviruses. Hantavirus RNA was detected via RT-PCR in two *Rattus norvegicus*. Complete sequencing and phylogenetic analysis established the virus as a Seoul hantavirus, which we have provisionally designated as strain Humber. This is the first hantavirus isolated from wild rodents in the UK and confirms the presence of a pathogenic Seoul virus in Europe.

In January 2012, as part of routine diagnostic services, the Rare and Imported Pathogens Laboratory (RIPL) at the Health Protection Agency (HPA) Porton, detected a suspected case of hantavirus infection in a patient diagnosed with acute kidney injury (AKI) from Yorkshire and the Humber, United Kingdom (UK). Positive serology by way of indirect immunofluorescence (Euroimmun, Germany) showed evidence of hantavirus antibodies specific to Hantaan virus (HTNV) and Seoul virus (SEOV) with rising IgG titres >1:10,000. The patient disclosed regular exposure to rodents at their home and noted that the rat population had increased in recent months. With permission from the patient, trapping of rodents in the vicinity of the family residence and farm was undertaken in February/March 2012, with the aim of confirming the presence of an aetiological agent in these rodents that might be responsible for the patient's AKI.

Rodent sampling

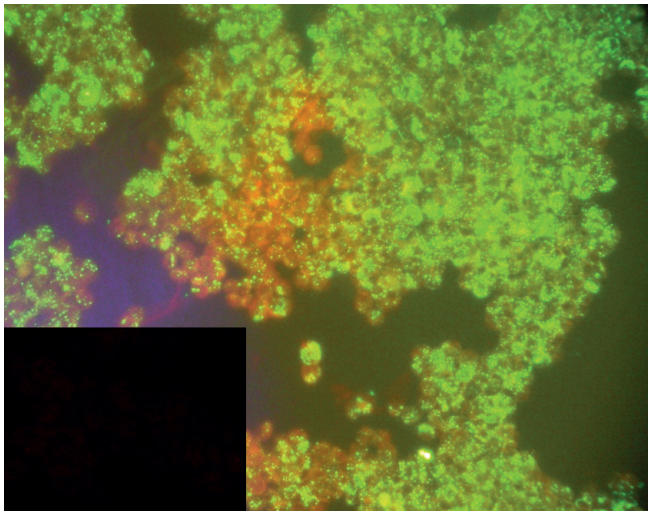
Permission was obtained from the patient and family to trap rodents at their residence. Between 28 February and 1 March 2012, rodents were trapped using a Longworth trap (Penlon Ltd., Oxford) or snap traps and, where necessary, humanely killed via cervical dislocation before being flash frozen on dry ice. Eleven rodents were analysed for the presence of hantavirus RNA: five *Apodemus sylvaticus* (wood mouse), four *Rattus norvegicus* (Norway rat) and two *Myodes glareolus* (bank vole). Following tissue harvest by necropsy, lung tissue was homogenised and total RNA was extracted using QIAamp viral RNA mini kit (Qiagen). RNA from each rodent lung was subjected to a genus-specific RT-PCR assay using hantavirus primers targeting the S segment [1]. Two *R. norvegicus* (RN1 and RN4) samples produced amplicons of the expected size of ca. 850 bp, with SEOV R22 used as the positive control. cDNA from both amplicons was sequenced and showed the highest level of similarity (97%) to Seoul hantavirus IR461 (GenBank accession no. AF329388) in a BLAST analysis. Further evidence the virus was Seoul-like was obtained through virus culture of homogenised lung from RN4. Infected Vero E6 cells (ECACC Vero C1008, clone E6) showed positive staining to a commercial monoclonal antibody (Progen, Germany) against the nucleocapsid protein of SEOV R22 strain after ten days in culture. After a further three passages the majority of cells demonstrated positive staining (Figure 1), the cells were harvested and virus isolated as previously described [2]. The isolate was designated Seoul hantavirus, strain Humber. Attempts to culture virus from RN1 were unsuccessful.

Molecular analysis

Hantaviruses are enveloped viruses with a tripartite, negative-strand RNA genome encoding the small (S), medium (M) and large (L) segments. Following multiple nucleotide sequence alignments of available SEOV sequences in GenBank, primers were designed for each segment spanning overlapping intervals of ca. 500 bp. Between two and seven independent runs were completed for each amplicon with 100% sequence conformity. Complete sequences for all three segments (RN1) were generated using standard Sanger sequencing on

Figure 1

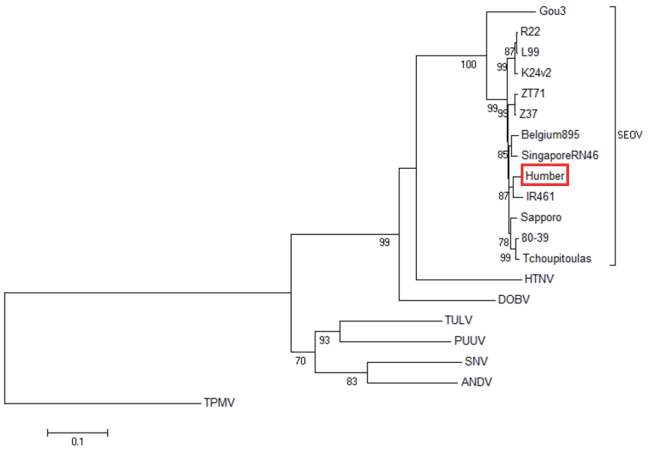
Vero E6 cells infected with Seoul hantavirus, strain Humber showing positive immunofluorescence, United Kingdom, October 2012



Negative and infected cells were stained with mouse monoclonal anti-Seoul N-protein antibody (Progen, Heidelberg, Germany) at 1:2 dilution, a secondary FITC-conjugated anti-mouse antibody at 1:64 (Sigma-Aldrich) and counterstained with 0.1% Evans blue. Viewed at 20x magnification under ultraviolet light; scattered, granular, punctate fluorescence (green) when compared to negative control Vero E6 cells only (inset, red) signified a positive reaction.

Figure 2

Phylogenetic analysis of the complete S segment of Seoul hantavirus, strain Humber, United Kingdom, October 2012



Horizontal distances represent the number of nucleotide differences. Bootstrap confidence limits exceeding 70% are shown for each branch node. Accession numbers for sequences extracted from GenBank: SEOV Gou3 AF288651, IR461 AF329388, K24v2 AF288655, R22 AF288295, L99 AF488708, Sapporo M34881, 80-39 NC005236, SingaporeRN46 GQ27495, ZT71 AY75171, Z37 AF187082, DOBV JF920150, HTNV AB620031, TULV Z49915, PUUV AB433845, SNV L2578, ANDV AF291702 and AY526097.

a 3130xl sequencer (Life Technologies); they comprised 1,768 nt, 3,651 nt and 6,530 nt, each encoding one open reading frame. These sequences were deposited in the GenBank database under accession numbers JX879768-70 designated as Seoul virus, strain Humber. Sequence data from RN4 were compared with deposited sequence data from RN1, this demonstrated 1 nt difference each in the S and M segments at positions 1,264 and 2,458 respectively.

The MEGA5 programme suite [3] was used to perform alignments using ClustalW and phylogenetic analysis. Phylogenetic trees were constructed from complete SEOV sequences using the neighbour-joining method, with bootstrap values obtained with 2,000 replicates. Subsequent genetic analysis of the S and M segments (RN1) confirmed their similarity to SEOV IR461 (Figures 2 and 3), with 63 (3.6%) and 149 (4.1%) nucleotide substitutions, respectively. The high homology and grouping of SEOV Humber with SEOV IR461 is surprising as IR461 is a distinctive strain [4] linked only to infections in laboratory workers in the UK and Belgium [5,6]. IR461 has not been detected in wild rodents.

Sequence data are not currently available for the L segment of SEOV IR461, however enough L segment sequences are available from isolates in the SEOV group to show that the L segment of the Humber strain (RN1) also clusters within the SEOV phylogenetic group of the hantavirus family (Figure 4).

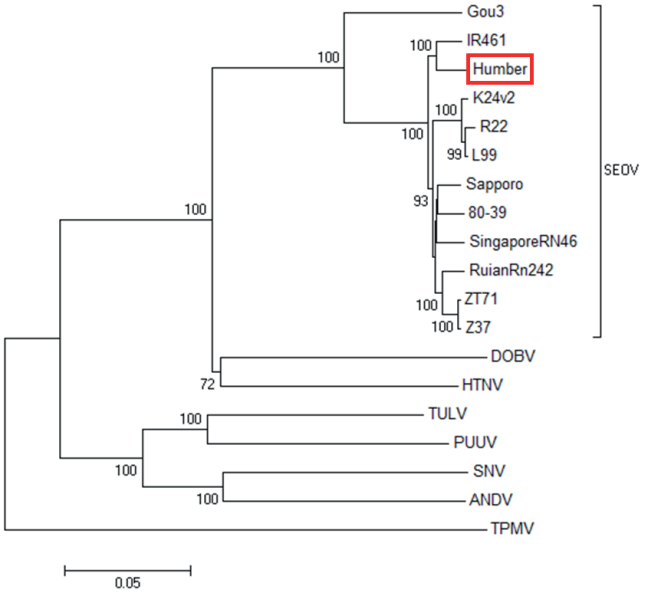
Discussion

Hantaviruses (genus *Hantavirus*, family *Bunyaviridae*) are a group of rodent-borne viruses with a wide global distribution. Human infection most often occurs when breathing in dried aerosolised excreta from infected rodents. Two clinical syndromes are associated with severe disease: haemorrhagic fever with renal syndrome (HFRS) and hantavirus cardiopulmonary syndrome (HCPS) [7]. In the UK there has been growing evidence for human and animal exposure to hantaviruses demonstrated by the detection of specific antibodies and classic HFRS disease.

As hantaviruses are wholly associated with their rodent and insectivore hosts, their distribution is limited to that of their respective host species. SEOV is an exceptional hantavirus in that it has a global distribution owing to the dispersal of its carrier host, rats, through global trade. Outside of Asia, SEOV has been confirmed by molecular methods in rats in Africa [8], the Americas [9] and Europe [10-12]. There are several ports located on the Humber estuary including: the UK's largest port by metric tons, Grimsby and Immingham, Kingston upon Hull, and the UK's most inland port, Goole. It is possible that the importation of infected rats has led to the establishment of SEOV in local populations of *R. norvegicus* in the Yorkshire and Humber region. Few acute human cases caused by infection with SEOV have been confirmed outside of Asia [13] and none have simultaneously reported identification

Figure 3

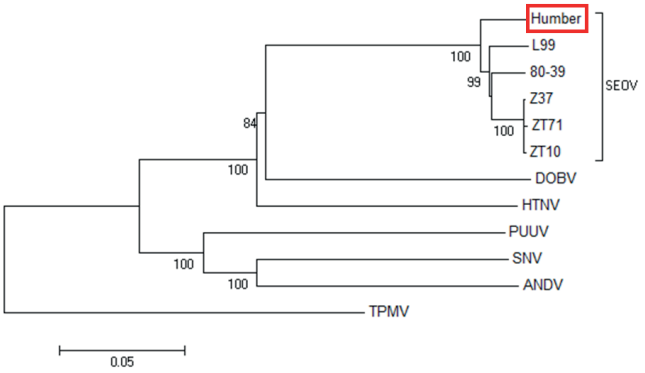
Phylogenetic analysis of the complete M segment of Seoul hantavirus, strain Humber, United Kingdom, October 2012



Horizontal distances represent the number of nucleotide differences. Bootstrap confidence limits exceeding 70% are shown for each branch node. Accession numbers for sequences extracted from GenBank: SEOV Gou3 AF145977, IR461 AF458104, K24v2 AF288654, R22 S68035, L99 AF288298, Sapporo M34882, 80-39 S47716, SingaporeRN46 GQ274943, RuianRn242 GU592928, ZT71 EF117248, Z37 AF190119, DOBV JF920149, HTNV AB620032, TULV NC005228, PUUV AB433852, SNV NC005215, ANDV AF291703 and TPMV NC010708.

Figure 4

Phylogenetic analysis of the complete L segment of Seoul hantavirus, strain Humber, United Kingdom, October 2012



Horizontal distances represent the number of nucleotide differences. Bootstrap confidence limits exceeding 70% are shown for each branch node. Accession numbers for sequences extracted from GenBank: SEOV L99 AF288297, 80-39 X56492, Z37 AF285266, ZT71 EF190551, ZT10 EF581094, DOBV JF920148, HTNV AB620033, PUUV AB574184, SNV L37901, ANDV AF291704 and TPMV DQ825770.

of the causative virus from rodents. Taking into consideration the patient's AKI, typical of SEOV, the high titre of antibodies detected specifically to the SEOV/HTNV group, the isolation of the virus from *R. norvegicus* from the patient's property, and its similarity to other pathogenic SEOV strains, it is highly likely the Humber strain is pathogenic to humans.

Due to the high levels of cross-reactivity between hantavirus species and the lack of viral detection in any published UK study, it has previously been impossible to confirm and identify the presence of a hantavirus in the UK. This represents the first isolation of a UK hantavirus from wild rodents and further confirmation of SEOV as a human pathogen outside of Asia. Given that *R. norvegicus* are ubiquitous in the UK, research is ongoing to determine the extent of human exposure to this virus in the region. Furthermore, with serological evidence specifically for SEOV previously reported in rats in Northern Ireland [14], it is unlikely this virus is restricted to north-east England.

Conclusion

Here we report the first detection and characterisation of a UK strain of Seoul hantavirus from wild rats. We feel it is important to raise awareness of hantavirus as a potential cause of renal disease in the UK, as Seoul hantaviruses are capable of causing moderate HFRS and we have strong indications this virus is linked to human disease. Our findings confirm the existence of a hantavirus in the UK and will allow further studies to evaluate its prevalence as a human pathogen.

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Indications for worldwide increased norovirus activity associated with emergence of a new variant of genotype II.4, late 2012

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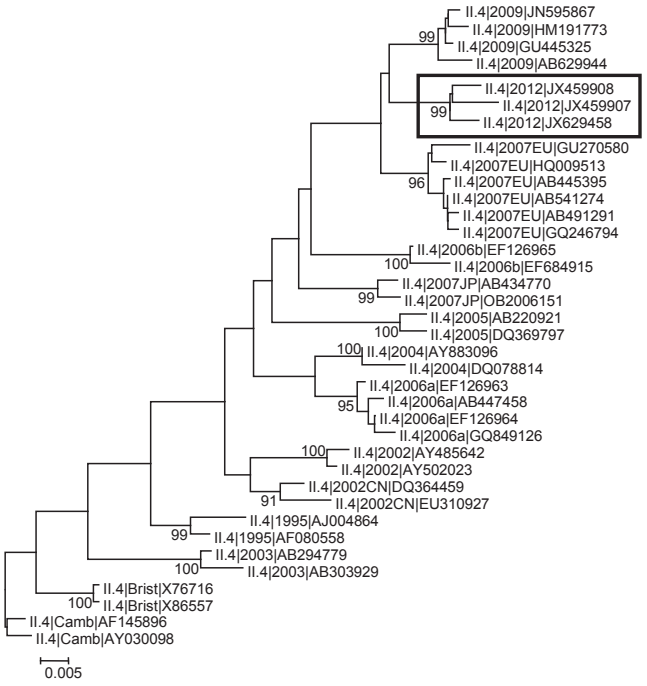
Globally, surveillance systems showed an increase in norovirus activity in late 2012. Molecular data shared through the NoroNet network suggest that this increase is related to the emergence of a new norovirus genotype II.4 variant, termed Sydney 2012. Healthcare institutions are advised to be prepared for a severe norovirus season.

In the United Kingdom (UK), the Netherlands, and Japan, norovirus (NoV) epidemiological and laboratory surveillance systems show increased levels of NoV activity compared to previous seasons, in late 2012 [1-3]. Similarly, increases have been noted in Australia, France and New Zealand (unpublished data). At this stage, and with the limited surveillance of NoV in most countries, it is difficult to conclude if these increases denote early seasonal activity or truly increased incidence, although for the UK the latter has been suggested. On 29 November, and on 4 and 6 December, ProMed (http://www.promedmail.org/) messages reported a dramatic rise in NoV hospital outbreaks in England, a 64% higher number of confirmed NoV laboratory reports (hospital- and community-acquired) in England and Wales, and NoV-related deaths in elderly in Japan. The first molecular data uploaded to the international molecular surveillance database NoroNet from Australia, France, New Zealand and Japan indicate that this increase is associated with emergence of a new variant of genotype II.4 (GII.4). The first report of this variant was from Australia in March 2012 (personal communication P.A. White, September 2012), and the strain sequence was submitted to GenBank (accession number: JX459908.1). In the United States (US), the variant (named Sydney 2012) was detected in September 2012 in five of 22 (23%) laboratory-confirmed outbreaks, and in November in 37 of 71 (52%) laboratory-confirmed outbreaks (recorded in the US norovirus surveillance network CaliciNet) [4]. In two European countries that have not reported any indications of increased activity, the new variant has been found in outbreaks, two in Belgium (September and December 2012) and one in Denmark (November 2012). Other countries participating in NoroNet have not yet reported the new variant.

NoV is the predominant aetiological viral agent of acute gastroenteritis worldwide and is present throughout the year, but most prevalent in the winter season in temperate climates. In the last decade, strains belonging to NoV GII.4 have been responsible for the majority of outbreaks, as well as community cases of acute gastroenteritis. It has been suggested that hospitalisation and deaths occur more frequently during peak seasons associated with new NoV GII.4 variants [5-7]. Since 1995, new epidemic variants of GII.4 have emerged every two to three years, with population immunity and genetic drift as major evolutionary driving forces [8]. Emergence of new variants has been associated with increased NoV activity early in the season [9-11]. The newly found NoV GII.4 Sydney 2012 variant has evolved from previous NoV GII.4 variants (Figure 1) and will be described in detail elsewhere. Briefly, the NoV GII.4 Sydney 2012 variant has a common ancestor with the dominant NoV GII.4 variants Apeldoorn_2007 and NewOrleans_2009, but is phylogenetically distinct. Amino acid changes are seen in the main epitopes located at the P2 domain, consistent with observations from prior epidemics. This may have led to an escape to

Figure

Neighbour-joining tree of norovirus GII.4 capsid amino acid sequences



Representative strains from the variant typing tool were used in this analysis. The taxa are named with genotype|variant name|accession number. Taxa representing the recent NoV GII.4 Sydney 2012 variant are boxed. The bootstrap values in percentage of 500 replicates are shown next to the major branches. The evolutionary distances were computed using the Poisson correction method in the units of the number of amino acid substitutions per site with the exclusion of gaps leaving a total of 536 positions in the final dataset. Phylogenetic analyses were conducted in MEGA4 [12].

existing herd immunity and might explain the observed increased outbreak activity.

The reference set of the Norovirus Typing Tool has been updated to correctly assign GII.4 Sydney 2012 sequences. This web-based tool (http://www.rivm.nl/mpf/norovirus/typingtool) is publicly available for genotyping of NoV sequences and was developed to facilitate standardisation of nomenclature [13].

Conclusion

Various countries around the globe have reported a higher incidence of NoV outbreaks or illness late 2012, and the first molecular data available via NoroNet suggests that this increase is related to emergence of a new variant of NoV GII.4. More data is needed to confirm the association between a higher NoV incidence and the new NoV GII.4 2012 variant. For this, we invite new members to join the NoroNet network (http://www.noronet.nl). Noronet is a worldwide network for NoV molecular and epidemiological surveillance, through which countries in Europe, Asia, and Australasia have shared NoV outbreak data, sequences, and other information. The NoroNet database, including analysis tools, is accessible for all NoroNet members.

With the early signs of a severe NoV season, healthcare institutions are advised to be prepared for NoV introductions. Outbreak management measures, like stringent hygiene measures and quarantine of infected cases, can help to reduce the size of outbreaks [14,15].

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