Impact factor 6.15

Eurosurveillance

Europe's journal on infectious disease epidemiology, prevention and control

Vol. 17 | Weekly issue 31 | 2 August 2012

ecdc EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

www.eurosurveillance.org

New endemic West Nile virus lineage 1a in northern Italy, July 2012

L Barzon[1,2], M Pacenti[2], E Franchin[1,2], E Lavezzo[1], T Martello[2], L Squarzon[1], S Toppo[1], F Fiorin[3], G Marchiori[3], F Russo[4], M Cattai[2], R Cusinato[2], G Palù (giorgio.palu@unipd.it)[1,2]

1. Department of Molecular Medicine, University of Padova, Padova, Italy
2. Regional Reference Laboratory for Infectious Diseases, Microbiology and Virology Unit, Padova University Hospital, Padova, Italy
3. Department of Transfusion Medicine, Venetian Area, Venice, Italy
4. Department of Public Health and Screening, Veneto Region, Venice, Italy

Citation style for this article:
Barzon L, Pacenti M, Franchin E, Lavezzo E, Martello T, Squarzon L, Toppo S, Fiorin F, Marchiori G, Russo F, Cattai M, Cusinato R, Palù G. New endemic West Nile virus lineage 1a in northern Italy, July 2012. Euro Surveill. 2012;17(31):pii=20231. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20231

Article submitted on 26 July 2012 / published on 2 August 2012

We report here the first blood donation positive for West Nile virus (WNV) by nucleic acid amplification testing collected in north-eastern Italy in July 2012. Partial sequencing of the WNV RNA demonstrated identity with a WNV lineage 1a genome identified in the same area in 2011 and divergence from the strain responsible for the outbreak in northern Italy in 2008–09. These data indicate that WNV activity in northern Italy is occurring earlier than expected and that different WNV strains are circulating.

As part of the screening of blood, tissue, and organ donations, performed in Italy according to the national plan in the period between 15 July and 30 November, West Nile virus (WNV) was detected by nucleic acid amplification test (NAAT) in a blood donation on 15 July 2012. NAAT was performed at the Department of Transfusion Medicine in Venice Province using the automated Procleix TIGRIS System (Novartis Vaccines and Diagnostics, Inc., Emeryville, CA, USA). At the time of the donation the WNV-positive donor was asymptomatic and remained asymptomatic during follow-up. The Regional Reference Laboratory demonstrated low viral load in plasma by real-time quantitative RT-PCR (approximately 1,000 genome equivalents/mL) and the absence of WNV IgM and IgG at the time of donation (tested by WNV IgM Capture DxSelect and WNV IgG DxSelect; Focus Diagnostics Inc., Cypress, CA, USA).

Two days after the donation, fresh blood and urine samples were taken from the donor and tested by the Regional Reference Laboratory using the Cobas TaqScreen West Nile Virus Test (Roche, Basel, Switzerland) and two different real-time RT-PCR methods, as reported [1]. In these specimens, WNV RNA was demonstrated in serum and plasma but not in urine, and the presence of WNV IgM in serum. Follow-up testing nine days after the donation demonstrated that plasma, leukocytes, and urine specimens were WNV RNA-negative. Unfortunately, virus isolation in cell culture was not successful.

Epidemiology of West Nile virus in Italy

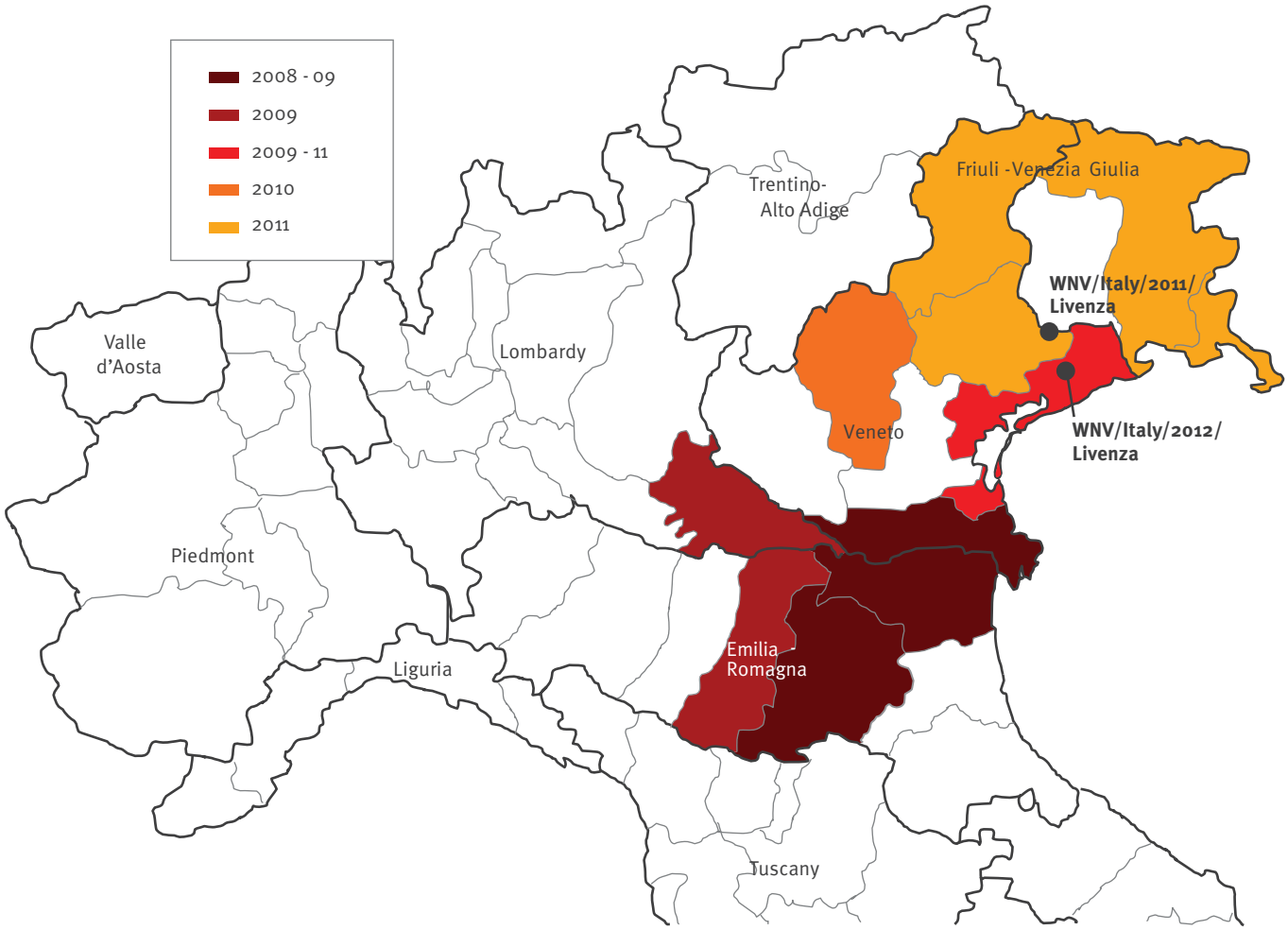
WNV has emerged in recent years in central European, eastern European and Mediterranean countries, and epidemics in these areas have become increasingly frequent [2]. In Italy, the virus was first identified in horses in 1998 in Tuscany, but no human cases were identified at the time [3]. The first human cases of WNV disease were identified in 2008, in north-eastern Italian regions surrounding the delta of the river Po [4,5]. In these areas, in 2008 and 2009, several human cases of WNV disease were identified, large outbreaks occurred among horses, and widespread WNV circulation was demonstrated by screening of birds and mosquitoes [6,7]. Genome sequence analysis of WNV strains isolated in Italy in 2008 and 2009 showed they were closely related [6,8,9], suggesting the virus had overwintered and established an endemic cycle in Italy. Provinces affected by WNV circulation are indicated in Figure 1. In 2010, human cases of WNV disease were reported only in the region Veneto (Figure 1), where special surveillance programmes for West Nile fever had been activated [1,10], and virus circulation was recorded in more northern areas than those affected in previous years [1]. In two blood donations from Veneto in 2010, typing was possible and WNV lineage 1 was identified by specific real-time RT-PCR, but due to the low viral load, viral genome sequencing was unsuccessful [1]. In 2011, increased WNV activity was observed in Italy, involving a larger geographic territory in north-eastern regions (Figure 1) as well as the regions Sardinia and Marche, where WNV circulation had not been reported before [11].

Phylogenetic analysis

WNV RNA was amplified and sequenced from the plasma of the positive donor identified in July 2012. Fragments of the WNV E (278 nt), NS2B-NS3 (721 nt), and NS5 genes (182 nt) (GenBank accession number JX417422) demonstrated 100% sequence identity with the WNV Livenza genome (GenBank accession no. JQ928174) that was detected in September 2011

Figure 1

Provinces in northern Italy with confirmed human cases of West Nile neuroinvasive disease, Italy, 2008–2011



The area where the 2012 case of WNV infection was detected is indicated by a black dot. The WNV/Italy/2012/Livenza RNA sequence obtained from this case was deposited in GenBank (accession number JX417422). The site where WNV/Italy/2011/Livenza (GenBank accession number JQ928174) was identified is also indicated.

in a blood donor resident in a nearby village, and fully sequenced (Figure 2). Both genome sequences belonged to lineage 1a and were related to WNV strains of the western Mediterranean subtype.

A further lineage 1a WNV genome sequence, WNV Piave (GenBank accession numbers JQ928175), had been obtained in 2011 from biological samples collected from a transplant recipient. However, the two WNV genomes from 2011 had a high nucleotide and amino acid sequence divergence from each other and from the WNV strain circulating in Italy in 2008–09 (Figure 2).

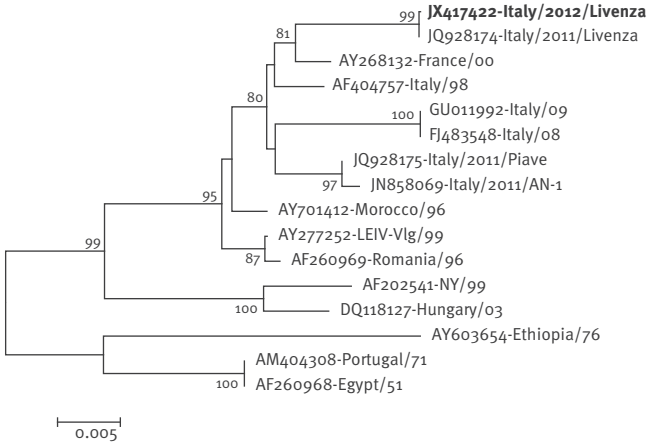
Discussion

The WNV-positive donor identified in July 2012 was resident in a village in Venice Province, located near the Livenza River (Figure 1). Sequence analysis of viral RNA from the donor demonstrated 100% sequence identity with a WNV genome that was fully sequenced the year before from a blood donor resident in a nearby village (Figure 2). This finding strongly suggests overwintering of the so-called WNV Livenza strain in the wetland area surrounding the Livenza River in north-eastern Italy, where it has probably established an endemic cycle.

In 2012, as in previous years [1,11], the surveillance period for human cases of WNV disease in affected areas in Italy lasts from 15 June to 30 November, while the period for WNV nucleic acid amplification test (NAAT) screening of blood, tissue, and organ donations lasts from 15 July to 30 November. Since most human cases of WNV infection detected in Italy so far have been identified during September, when mosquito activity is highest, and fewer cases in August and October, it was unexpected to find a WNV NAAT-positive blood

Figure 2

Molecular phylogenetic comparison of the West Nile virus strain isolated in Italy in 2012 with older strains



The phylogenetic tree was inferred using the maximum likelihood method based on the Jukes–Cantor model [12] on a fragment of 721 nt covering a genomic region across the NS2B and NS3 genes. The percentage of successful bootstrap replicates (n=1,000) is shown on the nodes (only values ≥80 are shown). Evolutionary analyses were conducted in MEGA5 [13]. The bootstrap value of 99 (instead of 100) is due to an approximation made by the phylogenetic software when performing bootstrapping. The phylogenetic trees constructed with a fragment of 278 nt of the E gene and a fragment of 182 nt of the NS5 gene gave similar results.

donation as early as on the first day of blood screening on 15 July 2012.

Such an early detection of a human case of infection during the 2012 season might predict increased WNV activity, requiring strengthened surveillance. It is conceivable that the warm spring and very hot summer in north-eastern Italy may have favoured WNV spread due to increased mosquito density. This year, early detection of human cases of WNV disease has been reported also in Sardinia*, in Greece, Israel, and the occupied Palestinian territory [14], and this trend might predict increased viral activity in the Mediterranean area.

In conclusion, this study reports a new endemic WNV strain detected in north-eastern Italy responsible for a human case of infection early in the summer 2012. This study also indicates the importance of WNV NAAT screening for the safety of blood, tissue, and organ donations.

Funding

This research was funded by Veneto Region, by the EU (FP7 project WINGS, grant no. 261426), and by the University of Padova (grant no. CPDA108383/10) to Giorgio Palù.

* Addendum:

The WNV case from Sardinia, Italy, reported by the European Centre for Disease Prevention and Control (ECDC) on the ECDC website July 26, 2012 [14] was not confirmed by the National Reference Laboratory and after case review was identified as a false positive result by the Italian Ministry of Health. This was stated in the ECDC situation update of August 2, 2012, that was published on the ECDC website on 2 August 2012 (http://ecdc.europa.eu/en/healthtopics/west_nile_fever/West-Nile-fever-maps/Pages/index.aspx).

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Did public health travel advice reach EURO 2012 football fans? A social network survey

J Janiec (jjaniec@pzh.gov.pl)[1], A Zielicka-Hardy[1,2], A Polkowska[2,3], J Rogalska[2,4], M Sadkowska-Todys[1]
1. Department of Epidemiology, National Institute of Public Health- National Institute of Hygiene, Warsaw, Poland
2. European Programme for Intervention Epidemiology Training (EPIET), Surveillance and Response Support Unit project on mass gatherings support, European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden
3. National Institute for Health and Welfare (THL), Helsinki, Finland
4. Health Protection Surveillance Centre, Dublin, Ireland

Citation style for this article:
Janiec J, Zielicka-Hardy A, Polkowska A, Rogalska J, Sadkowska-Todys M. Did public health travel advice reach EURO 2012 football fans? A social network survey. Euro Surveill. 2012;17(31):pii=20238. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20238

Article submitted on 26 July 2012 / published on 2 August 2012

We posted a survey on the Union of European Football Associations (UEFA)'s EURO 2012 Facebook profile to evaluate whether public health travel advice, specifically on the importance of measles vaccination, reached fans attending EURO 2012. Responses suggested that these messages were missed by 77% of fans. Social networks could serve as innovative platforms to conduct surveys, enabling rapid access to target populations at low cost and could be of use during upcoming mass gatherings such as the Olympics.

During the European football tournament (EURO 2012) held between 8 June and 1 July 2012, approximately 1 million people travelled to Poland and Ukraine. Mass gatherings of this scale provide an environment for potential rapid spread of infectious diseases [1,2]. The current prevalence of measles in Europe and the ongoing measles outbreak in Ukraine [3] lead to prioritisation of this disease as a potential threat to visitors of the event. Pre-travel health advice issued by international organisations such as the World Health Organization (WHO) and the European Centre for Disease Prevention and Control (ECDC) as well as national health authorities recommended measles vaccination to all Euro 2012 visitors [4]. Public health messages were released via a number of different platforms including leaflets, official public health websites, other websites and the media.

Although often a lot of effort is invested in the preparation of travel health advice during mass gatherings, little published information is available to date on the degree to which messages reach the general public during such events. The aim of this study was to determine whether public health messages reached persons travelling to EURO 2012.

Methods

We conducted a cross-sectional study among EURO 2012 fans. We set up an anonymous, self-administered, internet-based survey on the Union of European Football Associations (UEFA)'s EURO 2012 Facebook profile [5]. The questionnaire was designed using Survey Monkey (www.surveymonkey.com/). It consisted of 10 questions on personal characteristics (country of residence, sex, age), hosting countries visited during the tournament, and sources of travel health advice received, if any. We divided travel health advice into two categories: actively seeking information *(Did you actively seek any travel health advice before coming to Poland and/or Ukraine for EURO 2012? And if yes where did you find it?)* versus passively receiving information. i.e. hearing/receiving information by chance *(Aside from information you found yourself, did you see or hear any health advice related to EURO 2012? and Where did you see or hear this health advice?)*. The choice of possible answers was different for these two categories, but some answers were possible in both, e.g. public health websites, which may have been browsed by people seeking information related to EURO 2012 or by people seeking unrelated information who may have seen the travel health advice only by chance.

We predominantly used closed-ended questions. Some questions were added to detect errors and inconsistencies, e.g. respondents were asked twice, in different parts of the questionnaire, whether they travelled to any of the hosting countries. Our sampling frame consisted of approximately 1 million people who travelled to matches in Poland or Ukraine. We attempted to reach these fans through the UEFA's Facebook profile (http://www.facebook.com/uefaeuro2012), and also through the Google+ UEFA.com profile (https://plus.google.com/s/uefa%20survey; https://plus.google.com/105904468979374711712/posts), the WHO immunization week blog (http://eiw.euro.who.int/) and Facebook page (apps.facebook.com/afbcaad/), and EU_Health twitter (https://twitter.com/EU_Health). The survey was posted three days after the final match and kept active for a period of two weeks. Analysis was mainly restricted to respondents who visited at least one of the hosting countries during EURO 2012. The analysis also included people residing in Poland or Ukraine. In order to determine differences between fan

groups, we used uncorrected chi-square and Fisher's exact tests.

Results

We received responses from 313 people from 67 countries. Nearly all questions were answered by a different number of respondents. The question with the lowest response rate was answered by 256 people (82%). Comparisons between sexes and the category of country people travelled from were restricted to the 111 individuals who actually attended EURO 2012 in either or both of the hosting countries (Table). These individuals had a median age of 27.4 years (range: 9–57 years), and 79% were male. Of this group, 111 answered the question about actively seeking information, 27 reported they did seek information, and 84 answered that they did not. The question about receiving health information passively was answered by 107 individuals, and 32 answered that they did, 57 answered that they did not, and 18 that they did not remember. There were no significant differences in the responses on travel health advice with regard to the respondents' sex or the country they travelled from, including countries outside Europe (Table). Based on the 304 who answered the question whether they travelled to Euro 2012 or not, respondents who did not attend the tournament were less likely to recall any form of travel health advice, compared with those who attended.

Among fans who actively sought travel health advice, General Practitioners/doctors were the most common source of information. For those who passively received information, the media was the most frequent channel of communication (Figures 1 and 2).

Information regarding the importance of measles vaccination had reached 23% of 108 respondents who attended the tournament and answered this question. There was no statistically significant difference between people from countries with rates of measles notification of over one per 100,000 population [3] compared with those below this threshold (Table).

Discussion

Among the respondents attending EURO 2012, 24% recalled actively seeking any kind of travel health advice, and 30% reported they received it passively. This can indicate either that it was not a priority for all fans or that advice was not appropriately disseminated. Despite the efforts made by public health organisations to raise awareness regarding measles vaccination and the continuous media coverage, both before and during EURO 2012, messages went unnoticed by a significant number of fans attending the tournament. It may be that people travelling to or within Europe have a false sense of security when it comes to health. To effectively disseminate health messages to the general public and capture their attention, new communication strategies need to be adjusted to today's society.

Our study showed that social networking sites, particularly Facebook, serve as innovative platforms for

Table

Comparison of information seeking behaviour among surveyed fans, European football tournament 2012

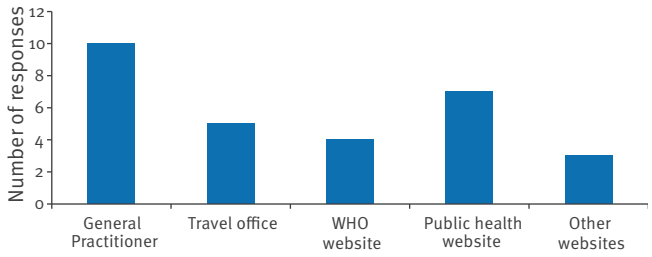
	Did you actively search for travel health information?			Did you passively receive travel health information? (i.e by chance)			Did you receive information on the importance of measles vaccination?		
Comparison between:	Total answers	Answered yes (%)	p value	Total answers	Answered yes (%)	p value	Total answers	Answered yes (%)	p value
Females	24	2 (8)	0.06[a]	23	8 (35)	0.6	23	5 (22)	0.9[a]
Males	87	25 (29)		84	24 (29)		85	20 (24)	
People arriving from:									
European countries	91	23 (25)	0.9[a]	87	29 (33)	0.2	88	22 (25)	0.5[a]
Non-European countries	20	4 (20)		20	3 (15)		20	3 (15)	
Countries competing in EURO 2012	78	21 (27)	0.3	74	26 (35)	0.08	75	20 (27)	0.3[a]
Other countries	33	6 (18)		33	6 (18)		33	5 (15)	
Countries with measles rate >1 per 100,000	n/a	n/a	n/a	n/a	n/a	n/a	48	15 (31)	0.07
Other countries	n/a	n/a	n/a	n/a	n/a	n/a	60	10 (17)	
People who:									
Visited EURO 2012	111	27 (24)	<0.0001[a]	107	32 (30)	<0.001	108	25 (23)	0.03
People who did not visit EURO 2012	193	4 (2)		178	21 (12)		176	27 (15)	

n/a: non applicable

[a] Fishers exact test: used for pairs of comparison with five or less responses.

Figure 1

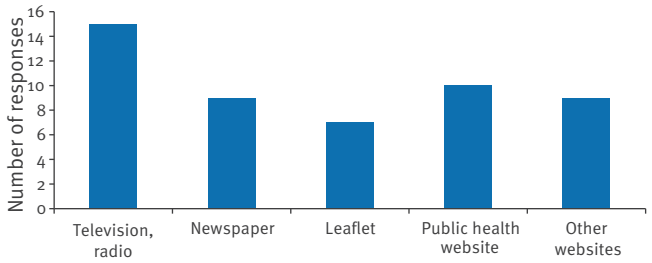
Information sources accessed by fans who actively looked for travel health advice, European football tournament 2012



WHO: World Health Organization.

Figure 2

Information sources for fans who passively received travel health advice, European football tournament 2012



surveys enabling easy and rapid access to target populations at relatively low costs (the first post was "liked" by 325 people and the second post by 684). In epidemiology studies, social media should not be disregarded as basic tools to engage the public as demonstrated by other studies [8]. However, usage of social networks for public health purposes is still in its infancy [9]. In our study the majority of respondents were young, English-speaking users of the UEFA Facebook page. We believe that the response rate could have been higher if the survey had been posted not after but also during the tournament, which was not feasible at that time due to organisational procedures. Furthermore responses received in online questionnaires cannot be validated, unless cross-checking questions are included, which increase the length of the survey and thereby may make it less attractive specifically to respondents recruited via social media. Studies are needed to evaluate the type of groups that are likely to respond and whether they are representative of the population of interest.

Our survey could be adopted for rapid evaluation of the effectiveness of public health campaigns, for example during upcoming mass gathering such as the Olympics. The effectiveness of communication strategies should be constantly validated and adjusted as required.

Acknowledgments

We would like to thank WHO and ECDC for their comments to our initial questionnaire and assistance in disseminating the survey through their social networking channels. We would like to also thank EPIET coordinator Dr. Pawel Stefanoff for his helpful comments.

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Infectious disease surveillance for the London 2012 Olympic and Paralympic Games

E Severi[1,2,3], E Heinsbroek[2,3,4], C Watson[3,4], M Catchpole (mike.catchpole@hpa.org.uk)[4], HPA Olympics Surveillance Work Group[5]
1. Health Protection Agency, South East Regional Epidemiology Unit, London, United Kingdom
2. European Programme for Intervention Epidemiology Training (EPIET), European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden
3. These authors contributed equally to this work
4. Health Protection Agency, Colindale, London, United Kingdom
5. Members of the group are listed at the end of the article

Citation style for this article:
Severi E, Heinsbroek E, Watson C, Catchpole M, HPA Olympics Surveillance Work Group. Infectious disease surveillance for the London 2012 Olympic and Paralympic Games. Euro Surveill. 2012;17(31):pii=20232. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20232

Article submitted 5 July 2012 / published on 2 August 2012

The London 2012 Olympic and Paralympic Games will be one of the largest mass gathering events in British history. In order to minimise potential infectious disease threats related to the event, the Health Protection Agency (HPA) has set up a suite of robust and multi-source surveillance systems. These include enhancements of already established systems (notification of infectious diseases, local and regional reporting, laboratory surveillance, mortality surveillance, international surveillance, and syndromic surveillance in primary care), as well as new systems created for the Games (syndromic surveillance in emergency departments and out-of-hours/unscheduled care, undiagnosed serious infectious illness surveillance). Enhanced existing and newly established surveillance systems will continue after the Games or will be ready for future reactivation should the need arise. In addition to the direct improvements to surveillance, the strengthening of relationships with national and international stakeholders will constitute a major post-Games legacy for the HPA.

Introduction

Few sports events match the scale of the Olympic Games, and few mass gatherings capture such international attention. The London 2012 Olympic and Paralympic Games run from 27 July to 9 September, and involve the participation of 15,000 athletes, 70,000 volunteers, 20,000 journalists and over 10 million ticketed spectators. Games events are taking place across England, Scotland and Wales, with the majority of venues based in the Olympic Park in Stratford, east London (Figure 1) [1].

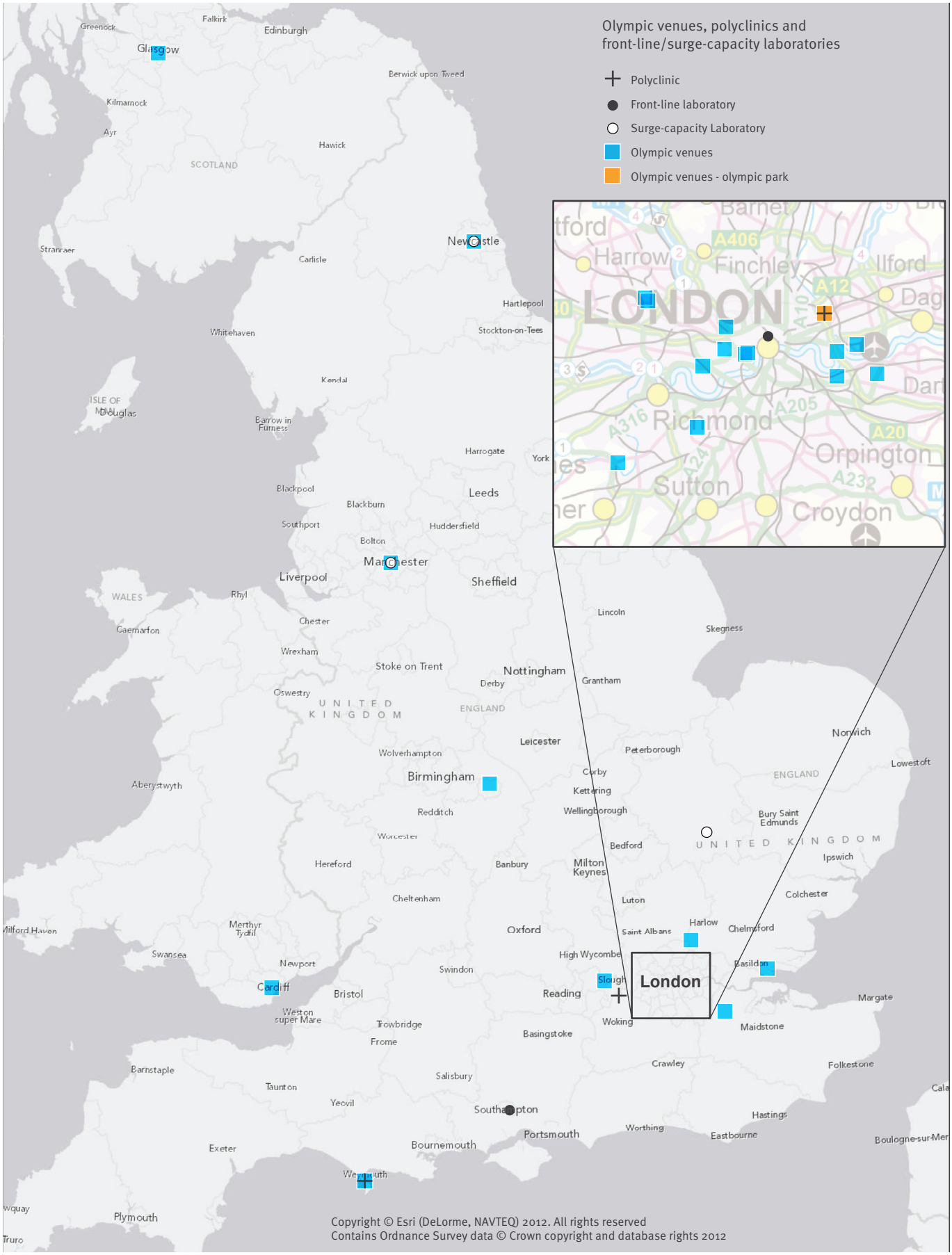
Although the Games last just a few weeks, long-term health aspirations are on a grand scale. London organisers anticipate that the Games will result in economic and social regeneration of East London and a wider health legacy, predicting 'the nation will be healthier, happier and more active' [2]. A more immediate Olympic public health legacy will be the enhancement of communicable disease surveillance systems [3]. A number of surveillance systems that have been developed to meet particular epidemic requirements during the Games will continue to run after this period, or be available for reactivation should the need arise.

The United Kingdom's (UK's) Health Protection Agency (HPA) performed a risk assessment of the potential health threats to the 2012 Games, concluding that serious infectious disease outbreaks associated with the Games are unlikely. No major communicable disease outbreaks were reported associated with the previous four Olympic Games, in Atlanta, Sydney, Athens and Beijing [4-6]. Nonetheless mass gatherings events have been found to be associated with the occurrence of clusters of infectious diseases, particularly of respiratory infections and gastrointestinal illness [7]. International travel to mass gatherings has been associated with the possibility of susceptible residents or visitors being infected by pathogens either imported to or endemic in the country hosting the mass gathering [8]. During the Games, athletes and spectators are expected to arrive from over 200 nations [1], including areas where the incidence of infectious diseases is much higher than in the UK [9]. Given the potentially increased concentration of visitors, the possibility of infectious disease spread through international travel and the public and political profile of the Games, enhanced epidemiological surveillance is considered an essential component of public health preparedness [10]. In this paper, we outline the communicable disease surveillance systems established in preparation for the London Games.

The main features of the surveillance systems described below are outlined in Table 1. Information collected through different systems and arrangements will be conveyed in daily situation reports to the HPA Olympic Coordination Centre for inclusion in a daily public health report to the London Organising Committee of the Olympic and Paralympic Games and the Department of Health (Figure 2). Daily reports also include non-infectious environmental hazards of

Figure 1

London 2012 Olympic and Paralympic Games venues, Olympic polyclinics and front-line and surge-capacity laboratories



Olympic venue location data are supplied by the Olympic Delivery Authority and used in accordance with their data terms and conditions (agreement with the Health Protection Authority; 15/02/2012).

Table 1

Overview of Health Protection Agency infectious disease surveillance systems for London 2012 Olympic and Paralympic Games

System	New/pre-existing	Purpose	Data sources	Olympic relevance
Health protection event-based surveillance	• Pre-existing; adapted for daily reporting and Olympic link risk-assessment • New: HPZone[a] daily screening to identify significant infectious disease events	To accelerate the reporting and the risk assessment of Health Protection events	Infectious diseases reports validated at HPU or regional level	• Daily risk assessment of all Health Protection events
Notifications of infectious diseases	Pre-existing; adapted for daily reporting and telephone notifications	To report infectious diseases notifiable under public health legislation	Medical practitioners	• Daily analysis both at HPU and national level • Notifications available also from Olympic policlinics • Notifications form includes questions about possible Olympic links
Laboratory surveillance	Pre-existing; adapted for daily reporting, new tests	To provide enhanced microbiological testing, risk assessment and expert advice	NHS laboratories, 21 HPA reference laboratories, 8 regional PH laboratories and 5 FWE laboratories	• Data analysed daily for key gastrointestinal and respiratory diseases • New enhanced diagnosis of leptospirosis • New multiplex PCR assay for gastrointestinal pathogens
Syndromic surveillance	• NHSDirect[b] and GP-based: pre-existing; adapted for daily reporting • EDSSS and GP OOHSS: new	To enable the early identification of the impact (or absence of impact) of potential public-health threats and to reassure about lack of wider impact in the event of an incident	NHSDirect, GPs, GP OOHs, EDs	• 'Real-time': no delay in reporting • Daily data available, including during weekends, public holidays and evenings
Undiagnosed serious infectious illness surveillance	New	To detect possible new or emerging infections presenting as undiagnosed serious infectious illness	Sentinel ICU/PICUs	• Data collected on risk factors, including Olympic attendance • Limited delay in reporting • Weekly nil notifications
Mortality surveillance	Pre-existing; adapted for daily reporting	To detect excess all-cause mortality that can result from infectious and non-infectious events	General Register Office	• Close to real-time detection of excess deaths
International surveillance	Pre-existing; adapted for daily reporting	To analyse the global infectious disease situation	WHO (including GOARN and IHR); EWRS; and a wide range of other sources including both official reports (e.g. from other countries' health agencies) and open access unofficial information, including media reports	• Daily communications between international partners • Risk assessment of events related to the Games, travels to/from the UK, media or public concern • Attention to changes in diseases epidemiology and potential for transmission

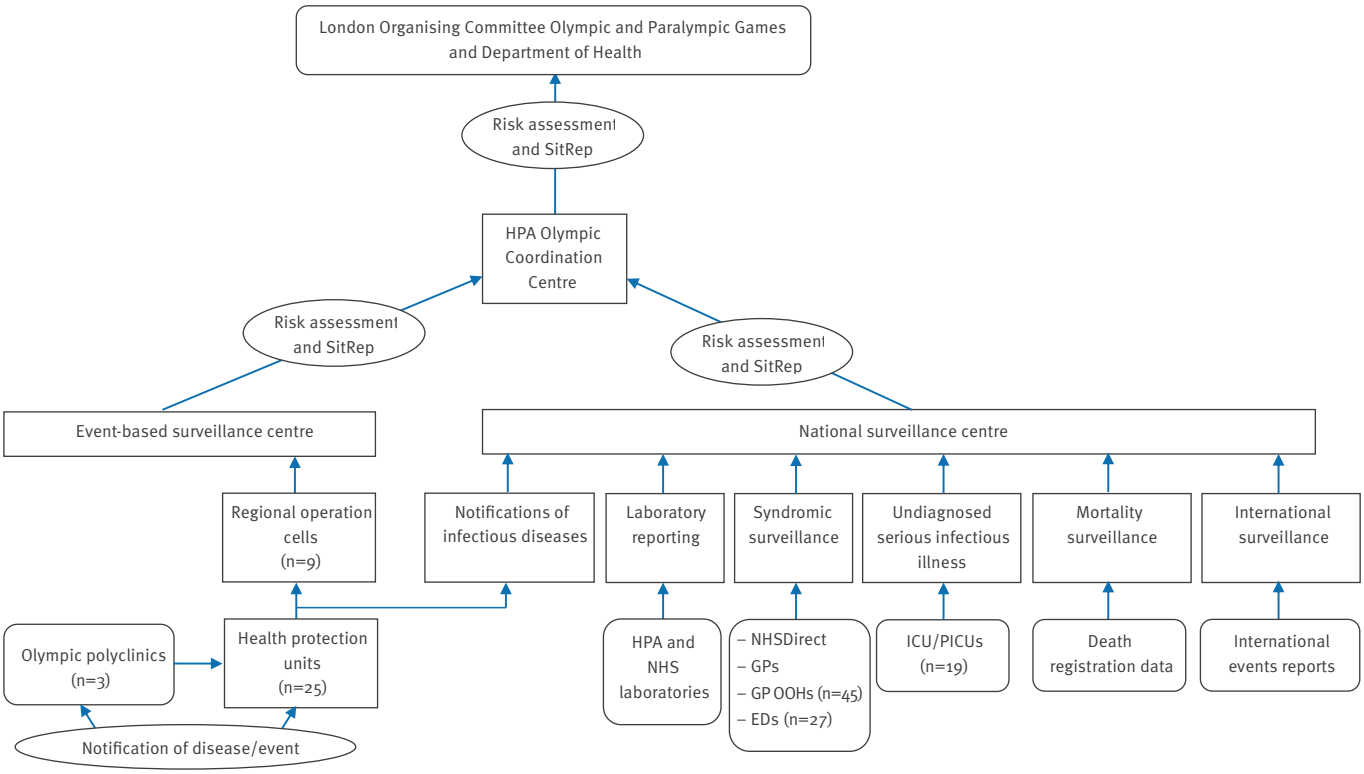
ED: emergency department; EDSSS: emergency department syndromic surveillance system; EWRS: European Early Warning and Response System; FWE: food, water and environment; GOARN: Global Outbreak Alert and Response Network; GP: general practitioner; HPA: Health Protection Agency; HPU: health protection unit; ICU/PICU: adult/paediatric intensive care unit; IHR: International Health Regulations; NHS: National Health Service; OOH: out-of-hours service/unscheduled care; OOHSS: out-of-hours/unscheduled care surveillance system; PCR: polymerase chain reaction; PH: public health; UK: United Kingdom; WHO: World Health Organization.

[a] The HPA's electronic public health management system.

[b] National telephone health helpline.

Figure 2

Flowchart of Health Protection Agency infectious disease surveillance systems for London 2012 Olympic and Paralympic Games



ED: emergency department; GP: general practitioner; HPA: Health Protection Agency; ICU/PICU: adult/paediatric intensive care unit; NHS: National Health Service; OOH: out-of-hours service; SitRep: situation report.

concern to the Games, such as air pollution. Specialist teams of HPA national experts in the different disease areas will support risk assessments and situation reports compilation. Other public health concerns, such as injuries and alcohol-associated morbidity are reported by the National Health Service (NHS) to the Department of Health.

Olympics and Paralympics-related infectious disease event surveillance

Local and regional surveillance of infectious diseases in England has been enhanced to rapidly detect and report any event that could possibly have a link with or an impact on the Games.

The statutory notifications of infectious diseases (NOIDs) system has been modified to ensure registered medical practitioners include specific information about possible Olympics and Paralympics-related exposures when reporting notifiable infectious diseases, such as pertussis or food poisoning in resident and visitor populations [11,12]. NOIDs reports will be analysed at local and regional units and by specialist teams at the national surveillance centre on a daily basis. The HPA maintains a 24/7 system for receiving notifications from clinicians through front-line local health protection unit (HPU) on-call teams, who can provide immediate risk assessment and advice on public health control measures for communicable diseases and non-infectious environmental hazards. Major public health concerns can be escalated by HPUs to regional or national level at any time of day or night. Specific 24/7 escalation arrangements have been established for Games-associated incidents.

To monitor infectious diseases among overseas athletic teams and avoid under-reporting, infectious disease notification was made a compulsory component of the temporary General Medical Council registration for overseas team doctors. Three polyclinics provide care for athletes and officials: the Olympic Village Polyclinic in London, the Weymouth Polyclinic in Dorset and the Royal Holloway Polyclinic in Surrey. Information on infectious diseases and clinical syndromes suggestive of infection is collected daily from the polyclinics. An HPA representative is in the Olympic Village Polyclinic in London to monitor data collection, offer public health advice and provide an initial response to any incident. All information is reported daily to the HPA in London.

Table 2

Risk assessment criteria for infectious disease events during London 2012 Olympic and Paralympic Games

Standard factors	Olympic factors
• The population affected (e.g. children vs adults, immunocompromised persons) • The number of individuals affected by the occurrence (e.g. large vs small outbreaks) • The severity of the disease • The transmissibility of the pathogen, especially in the general community (e.g. influenza virus vs HIV) • The ease of control • Whether the source of an outbreak is known (e.g. *Salmonella* outbreak associated with a particular food outlet vs community outbreak with no identified source) • Community or a closed group (e.g. care home) • The background rate of disease in the community • The seasonality of the disease • The potential for media attention • The potential for public concern	• Involving Olympic athletes, staff, visitors • The geographical location e.g. within an Olympic area • Proximity to an Olympic venue • Proximity to a training site • Proximity to a major Olympic transport hub • Nosocomial infection in an Olympic polyclinic • The time of the occurrence in relation to the Olympic event

Information on outbreaks and incidents is collected by local HPUs and can be reported to the Olympic Coordination Centre through the Health Protection event-based surveillance (EBS) system. EBS is the organised process to detect, validate, analyse, rapidly assess and report on significant infectious disease events of potential public health risk that may have an impact on the Olympic and Paralympic Games. A significant infectious disease event is defined as any event related to an infectious agent affecting an individual or a group of individuals that may put the health of those participating, visiting or working at the Games at considerable risk or may result in widespread public concern. The reporting process in England is coordinated by the national EBS team in London and involves all HPA units at local and regional level. On a daily basis, the 25 HPUs in England perform a preliminary risk assessment of infectious disease events using criteria shown in Table 2 and electronically report significant infectious disease events, or the absence of such events, to the EBS team in London via nine regional operation cells. Similar events occurring in Scotland, Wales and Northern Ireland are reported to the HPA national surveillance centre.

In addition, the EBS team screen the characteristics of events entered into HPZone – the HPA's electronic public health management system – three times a day to identify potential significant infectious disease events. Any case or situation entered onto HPZone with a link to an Olympic venue triggers an email alert to the EBS team. The EBS team use the information from the regional reporting and from HPZone to compile and send a daily situation report to the Olympic Coordination Centre.

Laboratory surveillance

HPA Microbiology Services (MS) Division consists of 21 reference laboratories, eight regional public health laboratories and five food, water and environmental laboratories spread across England. During the Games period, HPA-MS are providing enhanced microbiological testing, risk assessment and expert advice. Coordination across the network during the Games period is through an HPA-MS Olympic national operational cell. The cell is led on a rotational basis by a senior medical microbiologist and is based at the HPA national surveillance centre. A daily national review of ongoing laboratory activity is held to provide an early warning of unusual outbreaks or incidents. All samples from Games athletes or visitors with a suspected infectious disease are tested by or referred to one of two designated HPA front-line laboratories, with surge capacity provided by a further three regional laboratories. Key reference laboratories provide enhanced typing services seven days a week.

Following a gap analysis performed by HPA-MS, microbiological assay development took place to enhance diagnostic capacity. A multiplex polymerase chain reaction (PCR) assay for gastrointestinal pathogens has been introduced in the HPA front-line and surge-capacity laboratories, allowing the rapid diagnosis of a wide range of bacterial, viral and parasitic pathogens from a single sample. Another multiplex PCR was developed for the early diagnosis of leptospirosis, considered an important pathogen for athletes participating in outdoor water sports.

During the Games, HPA-MS will link directly with the agency's epidemiology intelligence on a daily basis, informing part of the public health situation report. Furthermore, laboratory data will be analysed by disease-specific epidemiologists on an ongoing basis. Since October 2010, statutory reporting by clinical and public health diagnostic laboratories for a range of infectious pathogens is included in health protection legislation [12]. Laboratory reports are submitted electronically to the HPA. Reported data are used to calculate exceedance scores to detect an increase in infectious diseases. This is done by using a statistical algorithm to compare observed occurrence with that expected, based on data from the previous five years for the three weeks either side of the reporting date [13]. During the Games period, these data will be analysed and interpreted on a daily basis.

Syndromic surveillance

Syndromic surveillance is defined as 'a real-time (or near real-time) collection, analysis, interpretation, and dissemination of health-related data to enable the early identification of the impact (or absence of impact) of potential human or veterinary public health threats that require effective public health action' [14]. Syndromic surveillance of human illness will play a major role in the surveillance for the Games. Based on non-specific health indicators such as 'vomiting', 'fever', 'impact of heat' or 'rash' rather than laboratory-confirmed diagnoses of a disease, syndromic surveillance can be more rapid and flexible than other systems, particularly in the case of unexpected threats [14].

The UK has several established syndromic surveillance systems including a national general practitioner (GP) surveillance system dating back to 2004 [15] and a nationwide surveillance system using data from the NHSDirect national telephone health helpline, which has been operational since 1999 [16]. During the Games period, the NHSDirect and GP systems will be analysed and interpreted on a daily basis.

The HPA risk assessment identified two shortcomings in the current surveillance systems: (i) lower data availability during weekends, evenings and public holidays; and (ii) different health-seeking behaviour of international visitors as compared with that of UK residents. Two new syndromic surveillance systems have been set up to address this. The GP out-of-hours/unscheduled care surveillance system (GP OOHSS) monitors daily out-of-hours/unscheduled primary care activity provided by NHS-commissioned services and therefore complements existing GP surveillance systems by monitoring activity during evenings, overnight, weekends and public holidays. Currently 45 out-of-hours/unscheduled primary care providers provide daily data for patient-care episodes in 119 of 145 primary care trusts (PCTs) in England, including 30 of 31 PCTs in London and those hosting the rowing and sailing events taking place outside London. The second system, the emergency department syndromic surveillance system (EDSSS), monitors the daily numbers of attendances in a network of sentinel emergency departments across England [17]. Currently 27 sentinel emergency departments provide daily data on a range of generic clinical indicators. Triage data are also monitored, providing an indication of the severity of the presentations. As the syndromic surveillance systems are diverse and at different stages of development, with differing amounts of historical data, statistical analyses are tailored to the specific systems. The in-hours GP surveillance rates are based on practice-registered populations, while other systems use a dynamic denominator (calls made to NHSDirect, emergency department attendances, GP out-of-hours/unscheduled care contacts) and report the proportion of these due to a particular syndrome [18]. The GP OOHSS and EDSSS will remain operational after the Games.

Undiagnosed serious infectious illness surveillance

The influx of international visitors during the Games has the potential to increase the risk of introduction of new and emerging infections, which may present as 'undiagnosed serious infectious illness' (USII) [19]. The HPA risk assessment identified this as a gap and therefore a new surveillance system was established to detect possible new or emerging infections presenting as USII during the Games.

A USII case is defined as 'any adult or child admitted to an adult or paediatric intensive care unit (ICU/PICU) with a serious illness suggestive of an infectious process where the clinical presentation does not fit with any recognisable clinical picture or there is no clinical improvement in response to standard therapy and initial laboratory investigations for infectious agents are negative or do not establish a diagnosis.'

The surveillance system involves sentinel ICU/PICUs reporting USII cases online or, where no cases have occurred, providing weekly nil notifications. Cases are reported using a restricted-access web-based reporting tool, and are investigated for epidemiological links, including temporal and spatial clustering. Results from a pilot study undertaken between January and July 2011 indicate that this system is feasible and able to detect cases, allowing for investigation of clusters of USII in a timely manner [19]. Based on these results, the system was expanded to cover a total of 12 ICUs and seven PICUs in London and the south-east of England, where the majority of the Games venues are based.

Following the Games, an evaluation of the USII surveillance system will take place in which the potential for extending this system across England will be explored. Reporting of USII cases could continue through the established sentinel network of ICUs and PICUs as a public health legacy of the Games [19].

Mortality surveillance

Weekly mortality monitoring in the UK has previously allowed quantification of excess deaths associated with health threats such as influenza and heatwaves [20,21]. Throughout the London 2012 Games, the General Register Office is providing daily data on the total number of deaths for England each weekday to the HPA for Games-time mortality surveillance by age group and region. This daily monitoring enables close to real-time detection of excess deaths, after correcting for reporting delays and accounting for time from exposure or illness onset to death (typically three days for heat exposure at national level) [20-22].

The output from this surveillance will be interpreted with that of other surveillance systems, depending on the incident, such as laboratory or meteorological reports and syndromic surveillance of influenza-like illness or heat illnesses, contributing to a more complete picture of the impact on the health of the population.

International surveillance

International infectious diseases surveillance and collaboration with overseas and international health agencies has been a feature of public health preparedness at recent summer Olympic and Paralympic Games, with the World Health Organization (WHO) as the main collaborating partner [4-6].

Global infectious disease scanning and risk assessment for relevance to the London 2012 Games is being undertaken daily throughout the summer by collaboration between various parts of the HPA that have a routine role in international surveillance, the European Centre for Disease Prevention and Control (ECDC) and the HPA-commissioned National Travel Health Network and Centre (NaTHNaC). Sources of information include those provided by WHO (such as through the Global Outbreak Alert and Response Network (GOARN) and under the International Health Regulations (IHR)), the European Early Warning and Response System (EWRS) and a wide range of other sources including both official reports (e.g. from other countries' health agencies) and open access unofficial information, including media reports. A number of exercises have been used to test and refine the surveillance process, with a secure web-based database and daily teleconferences used for coordination.

While global infectious disease situational analysis for public health protection is routine work for specialists in the three organisations, additional criteria were developed for Olympic risk assessment. These included potential for impacting on the running of the Games or travel to and from the UK, incidents that may attract particular media or public concern, and those that may require specific advice for clinicians or port health or public health measures to be implemented. Consideration is given to significant changes in disease epidemiology, potential for transmission within the UK and degree of uncertainty surrounding potentially emerging infections.

In addition to scanning for international incidents of local significance, reporting of any UK incidents of international significance will continue throughout the Games through routine IHR and EWRS communications.

Discussion

The HPA has built robust systems for the surveillance of infectious diseases in preparation for the London 2012 Olympic and Paralympic Games. Pre-Olympic exercises were performed to test the different surveillance systems' ability to detect infectious disease events of potential significance to the Games and resulted in refinement of reporting criteria and processes for risk assessment.

Communication between the HPA and environmental health officers, microbiologists from the laboratory network, hospital consultants, medical practitioners and international partners has been strengthened in order to fulfil the Agency's commitment to the Olympics. Enhanced pre-existing systems and new arrangements will be operated during the Games for the effective management of infectious disease risks due to the large number of visitors and to the high visibility of the event.

With both a simultaneous influx of Games visitors and potential efflux of the resident population during this holiday period, the precise increase in the London population is not readily measureable. While some surveillance systems, such as emergency department syndromic surveillance, use dynamic denominators, others, such as laboratory case count 'exceedance scores' assume a relatively static population, and so outputs from such systems require further interpretation. Providing reassurance that there is not a need for public action can be as important as the rapid detection of events that do require such action during mass gatherings, when increased media attention can generate public and political concern regarding incidents of low or no public health concern. While real-time surveillance and rapid laboratory services (for infection-related concerns) are important in providing such reassurance, robust arrangements for rapid expert threat assessment are also required. Finally, despite a robust information technology business continuity plan to support surveillance operations, major electronic or telecommunication disruptions could impede several core activities in an era where IT dependency is the norm. Evaluations of the overall infectious disease surveillance and of the different surveillance systems have been planned after the Games, which will consider how such issues have been handled and any lessons learned.

The Olympics and Paralympics legacy for the HPA will not only be the reinforcement of UK infectious disease surveillance systems, but also the strengthened partnerships with ECDC and the London-based WHO Collaborating Centre on Mass Gatherings and High Visibility/High Consequences Events. These partnerships will enable the knowledge and experience gained from the London 2012 Games to be shared with those planning infectious disease surveillance for future mass gathering events.

Members of the Olympics Surveillance Work Group

Colin S. Brown; Meera A. Chand; Duncan Cox; Paul Crook; Alex Elliot; Tina Endericks; James Freed; Helen K. Green; Jonathan Green; Jane Jones; Catherine Keshishian; Hilary Kirkbride; Chris Lane; Joanne Lawrence; Richard Pebody; Kulsum J. Rampling; Bengü Said; Nandini Shetty; Gillian Smith; Deborah Turbitt.

Acknowledgements

We would like to thank Tina Endericks, HPA Olympics Programme Director, Sean Kelleher and all those who have contributed to the work of the Olympics Surveillance Work Group, including all data providers and NHS collaborators. We would also like to thank James Lewis for producing the Olympic venues map. We are grateful for the comments of EPIET coordinators Helen Maguire, Biagio Pedalino and Pawel Stefanoff.

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A new surveillance system for undiagnosed serious infectious illness for the London 2012 Olympic and Paralympic Games

E Heinsbroek[1,2], B Said[1], H Kirkbride (usii@hpa.org.uk)[1], On behalf of the HPA USII Steering Group[3]
1. Health Protection Agency, Colindale, London, United Kingdom
2. European Programme for Intervention Epidemiology Training (EPIET), European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden
3. Members of the group are listed at the end of the article

Citation style for this article:
Heinsbroek E, Said B, Kirkbride H, On behalf of the HPA USII Steering Group. A new surveillance system for undiagnosed serious infectious illness for the London 2012 Olympic and Paralympic Games. Euro Surveill. 2012;17(31):pii=20237. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20237

Article submittefd on 4 July 2012 / published on 2 August 2012

A new surveillance system was developed to detect possible new or emerging infections presenting as undiagnosed serious infectious illness (USII) for use during the London 2012 Olympic and Paralympic Games. Designated clinicians in sentinel adult and paediatric intensive care units (ICU/PICUs) reported USII using an online reporting tool or provided a weekly nil notification. Reported cases were investigated for epidemiological links. A pilot study was undertaken for six months between January and July 2011 to evaluate the feasibility and acceptability of the system. In this six-month period, 5 adults and 13 children were reported by six participating units (3 ICUs, 3 PICUs). Of these 18 patients, 12 were reported within four days after admission to an ICU/PICU. Nine patients were subsequently diagnosed and were thus excluded from the surveillance. Therefore, only nine cases of USII were reported. No clustering was identified. On the basis of the pilot study, we conclude that the system is able to detect cases of USII and is feasible and acceptable to users. USII surveillance has been extended to a total of 19 sentinel units in London and the south-east of England during the London 2012 Olympic and Paralympic Games.

Introduction

Global travel in recent decades has increased the potential for spread of new and emerging infections worldwide [1]. Examples, including the international spread of severe acute respiratory syndrome (SARS) and the influenza A(H1N1)pdm09 pandemic, illustrate that new and emerging infections can spread through major transport hubs in a matter of days [2,3]. Such new and emerging diseases can pose difficulties in diagnosis and may present as undiagnosed serious infectious illness (USII) [4]. These could be missed by traditional surveillance, necessitating the development of new infectious disease surveillance systems.

At the time of publication, London is hosting the 2012 Olympic and Paralympic Games and faces an influx of international and national visitors. An estimated 10,490 Olympic athletes and 4,200 Paralympic athletes from 204 nations are expected to participate in the Games [5], with more than 9 million tickets sold to spectators of both visiting and local populations. Athletes and spectators are expected from all continents of the world, including areas where the incidence of emerging infections is much higher than in the United Kingdom (UK) [6]. It is therefore crucial to be able to detect and respond to potential emerging disease threats during the Games period.

The Health Protection Agency (HPA) has developed a new surveillance system that aims to identify potential cases and clusters of USII in a timely manner, to allow for appropriate investigation and public health response. Additional objectives were to estimate the annual rate of cases of USII and to develop a system that was both feasible and acceptable to participating clinicians. This surveillance is based on similar systems for detecting cases of new and emerging infections established previously in the United States [4,7] and Taiwan [8]. The HPA-based USII surveillance is part of a range of enhanced existing and new surveillance systems, including syndromic surveillance in primary care, Olympic venues and emergency departments, put in place for the 2012 London Games [9,10].

In this paper we discuss the establishment of the new USII surveillance system and the results from a pilot study undertaken during the first six months of surveillance.

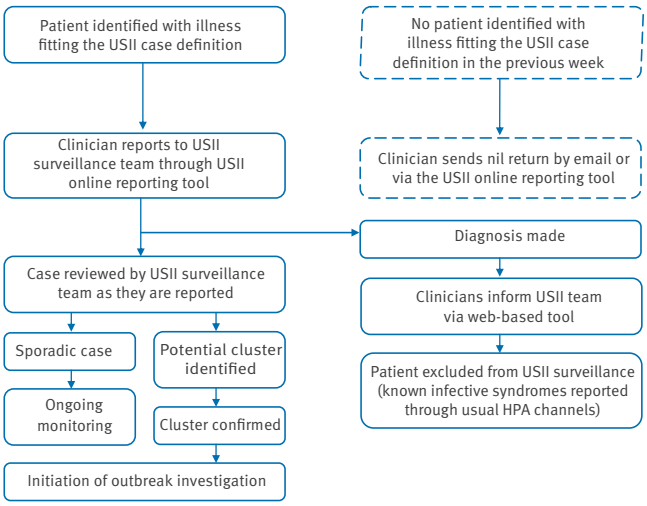
Methods

Design of USII surveillance

We developed a prospective, population-based surveillance system to enable direct reporting of USII cases from sentinel adult and paediatric intensive care units (ICU/PICUs) through a web-based tool. We conducted a six-month pilot in six London units (3 ICUs and 3 PICUs)

Figure 1

Overview of the undiagnosed serious infectious illness surveillance system for London 2012 Olympic and Paralympic Games



HPA: Health Protection Agency; USII: undiagnosed serious infectious illness.

from 10 January to 10 July 2011. Five units were chosen from large teaching hospitals geographically dispersed across London, the sixth unit was chosen because of its proximity to the London 2012 Olympic Park. An overview of USII surveillance is presented in Figure 1.

Case definition and exclusion criteria

The USII case definition was developed and refined in collaboration with clinical and laboratory colleagues. A USII case was defined as any child (≤16 years-old) admitted to a PICU or high-dependency unit (HDU) or any adult (>16 years-old) admitted to an ICU or HDU with a serious illness suggestive of an infectious process where the clinical presentation does not fit with any recognisable clinical picture or there is no clinical improvement in response to standard therapy and initial laboratory investigations for infectious agents are negative. A reported patient remained a USII case until a diagnosis was made. There was no further follow-up of USII cases after discharge from an ICU/PICU.

Indicators suggestive of an infectious process were defined as the following: fever or history of fever, leucocytosis or leucopaenia, raised C-reactive protein levels or other marker of infection, histopathological evidence of an acute infectious process, or a physician-diagnosed syndrome consistent with an infectious aetiology. Each hospital used its own standard laboratory protocols for first-line investigations. Additional advice from HPA experts about further investigations was available on request.

Neonates who had not been discharged from hospital and individuals immunocompromised to a level considered by the attending clinician to render them susceptible to opportunistic infection were excluded from the surveillance.

The case definition was tested by reviewing retrospectively three months' patient records at three units (two PICUs and one ICU) between January and March 2010 and estimating the expected monthly number of cases fulfilling the USII definition. This found an expected maximum of three cases per unit per month, which confirmed that the surveillance system's case definition would detect cases of USII and provided reassurance that reporting into the surveillance system would not place an unreasonable burden on clinicians.

Reporting of cases

Designated clinicians in sentinel ICUs/PICUs were asked to report USII to the HPA-based surveillance team using an online reporting tool. Training on the use of the reporting tool was provided. Clinicians were asked to report as soon as they suspected USII; those patients who were subsequently diagnosed were excluded from the surveillance.

Cases were assigned to one of six predominant clinical syndromes by the attending clinician. The following defined syndromes were developed in collaboration with the participating clinicians: respiratory (pneumonia, bronchiolitis, pneumonitis, acute respiratory distress syndrome (ARDS)); neurological (meningitis, encephalitis); presumed sepsis (sepsis-induced multi-organ failure); jaundice/hepatitis (fulminant hepatitis, hepatic failure, serious illness with jaundice); cardiac (myocarditis, pericarditis, endocarditis); or metabolic syndromes (acidosis, alkalosis). Syndromes that did not fit any of these descriptions were classified as 'other'.

Information was collected on patient demographics, clinical history and course, travel history, possible exposures, antimicrobials given and diagnostic tests performed. Minimal personal identifiable information was collected for each case, e.g. initials, date of birth, sex and postcode. Data were collected through a dedicated password-protected web-based portal. Clinicians could only view cases reported by their ICU/PICU. Approval for the USII surveillance was granted by the Ethics and Confidentiality Committee of the National Information Governance Board.

If no USII was reported, participating clinicians sent weekly nil notifications either by email or via the online reporting tool. The clinicians' response was assessed by the proportion of units providing a weekly response, either through reporting or by providing nil notifications.

Table 1

Information collected through the online reporting tool for the undiagnosed serious infectious illness surveillance system, 10 January-10 July (weeks 2–27) 2011

Temporal indicators	Spatial indicators	Other possible risk factors
• Date of onset • Date of hospital admission • Date of ICU/PICU admission	• Residential and/or hotel postcode • Foreign travel history in last 6 months • National travel history in last 4 weeks • Visiting a mass gathering (e.g. an Olympic event)	• Contact with other sick people with similar presentation • Contact with sick animals or birds • Contact with healthy animals or birds • Recreational exposure • Consumption of unpasteurised or 'unusual' food items, or home-processed foods

ICU: adult intensive care unit; PICU: paediatric intensive care unit.

Investigation of possible clusters

We investigated all reported cases for possible clustering. A potential cluster was defined as two or more cases with the same syndrome and epidemiological links, including spatial and temporal clustering. This definition was kept purposefully broad to maximise sensitivity. As cases of USII are uncommon and by definition there are many unknowns, we reviewed each case individually to determine whether there were any potential epidemiological links between cases. Table 1 shows information collected through the reporting tool. This includes a specific question on attendance at mass-gathering events, designed to enable assessment of potential clusters during the Olympic and Paralympic Games.

Calculation of annual USII rate and coverage

We estimated the coverage of the surveillance scheme separately for adults and children by dividing the number of beds in participating units by the total number of ICU/HDU beds in the London region. For children, the coverage was estimated using the number of beds in participating units divided by the total number of beds in both the London and the South East regions. This is because, in contrast to ICUs, the London PICUs cover London region and most of the South East region [11].

Clinicians in each participating unit provided the number of available beds for their unit. Bed data estimates from published sources were used for other ICU/PICUs in London and the South East regions [11,12]. The population covered by USII surveillance was estimated based on the mid-2010 population estimates for London and the South East regions [13]. The rate of annual USII cases per 100,000 population was extrapolated from the number of cases reported in the pilot study period and the population covered.

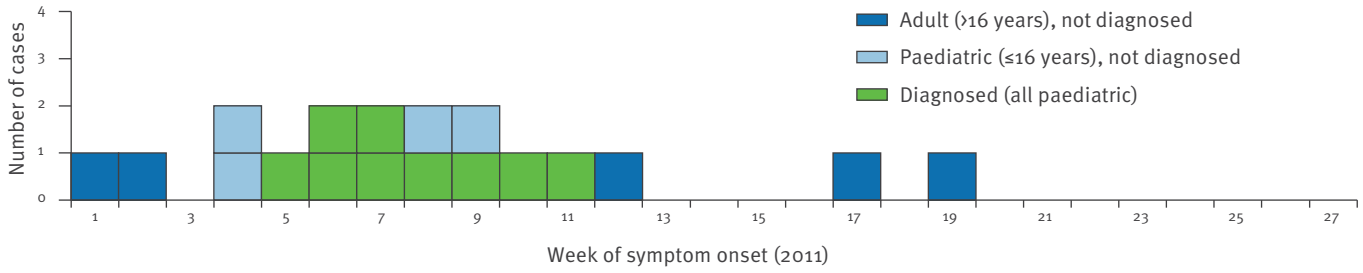
A 95% confidence interval (CI) for the coverage of ICU/PICUs was calculated assuming a binomial distribution, whereas for the rate, a Poisson distribution was assumed. The latter assumes that the denominator is a known quantity whereas it is only an estimate and variable over time, especially when extrapolating for the 2012 Olympic year, when the precise London population is not readily measureable due to a simultaneous influx of Games visitors and potential efflux of the resident population. To capture this extra variability, three CIs for the rate were calculated. One CI used the estimated coverage, another the lower limit of the coverage CI and a third the upper limit. A 95% Bonferroni-type CI was then derived by taking the lowest of the lower limits and highest of the upper limits to be lower and upper limits, respectively.

Assessing timeliness of surveillance

The timeliness of the surveillance system was measured by calculating the mean number of days between

Figure 2

Total reports through undiagnosed serious infectious illness surveillance by week of symptom onset, 10 January–10 July (reporting weeks 2–27) 2011 (n=18)



admission to the participating ICU/PICU and reporting via the web-based reporting tool. From discussions with participating clinicians, we estimated that initial results from laboratory investigations would be received at the ICU/PICU within 72 hours. We therefore defined a timely notification as a report made within 24 hours of this defined 72-hour period, i.e. within four days of admission to the ICU/PICU.

User feedback

We conducted structured face-to-face meetings with all participating units at the end of the pilot study to assess the feasibility and acceptability of the surveillance system and the user-friendliness of the web-based reporting tool.

Results of the six-month pilot study

Cases reported and investigation of possible clusters

A total of 5 adults and 13 children (n=18) were reported from the six units during the six-month pilot period (Figure 2). Of these 18, nine children were subsequently excluded as USII cases because the causative microbiological agents were identified.

The remaining nine USII cases (5 adult, 4 paediatric) presented with presumed sepsis, respiratory or cardiac syndromes (Table 2). Seven of these had co-existing illnesses. One adult case with multiple organ failure secondary to presumed sepsis had travelled to Africa within the last six months, while possible exposures were not identified for the other cases. Symptom onset date was available for all cases; postcode of home address was available for eight of the nine cases. Two paediatric cases with onset date in week 4 both had presumed sepsis of unknown cause. However, no common exposures were reported and there was no evidence of spatial or temporal clustering in these or any of the other reported cases. There was one adult death, but no post-mortem investigation was done. The remaining cases recovered and were discharged from the ICU/PICU without laboratory confirmation of the causative agent of their illness.

Population coverage

The estimated population coverage during the pilot period was 8.4% (95% CI: 6.6–10.5) of the adult population in the London region, and 31.5% (95% CI: 23.5–40.3) of the paediatric population in London and the South East regions. The estimated annual rate for all USII cases was 1.2 per 100,000 population (range: 0.4–3.1 per 100,000 population). For adult cases, this was 1.8 per 100,000 population (range: 0.4–5.6 per 100,000 population) and for paediatric cases, this was 0.8 per 100,000 population (range: 0.2–3.0 per 100,000 population).

Timeliness

Of the 18 patients initially reported, 12 were reported within four days of admission to the ICU/PICU. Four were reported in 5–7 days and two were reported more than a week after admission to the ICU/PICU. The mean reporting time was 3.6 days (median: 2 days; range: 1–12 days).

Table 2

Characteristics of reported cases of undiagnosed serious infectious illness, 10 January–10 July (weeks 2–27) 2011 (n=9)

Characteristic	Adult (n=5)	Child (n=4)
Age	29 to 67 years	1 month to 2 years
Sex	3 male, 2 female	1 male, 3 female
Co-existing illness	2 hypertension 1 polyarthritis 2 none	1 prematurity 1 asthma 2 other
Syndrome	2 respiratory 2 presumed sepsis 1 cardiac	2 respiratory 2 presumed sepsis
Possible exposures	1 travel abroad 4 none identified	4 none identified
Outcome	1 died, 4 discharged	4 discharged

User feedback

Participating clinicians considered that, due to the low incidence of USII cases, participation in the USII surveillance system was feasible and acceptable. They indicated that the online reporting tool was user-friendly, although some improvements for the online data collection were suggested and subsequently implemented. All participating clinicians agreed to continue reporting through the USII surveillance system.

Participating clinicians also found the weekly nil notification requests were acceptable and weekly nil returns were received from all participating units. The overall weekly response rate (either reporting cases or providing a nil notification) ranged from 50% to 100% per week, with a mean response rate of 80.7%.

Discussion

This paper describes a new surveillance system established to detect cases and clusters of USII during the 2012 London Games. Results of the pilot study indicate that USII cases are very rare: only nine USII cases were reported, equivalent to an estimated annual rate of 1.2 per 100,000 population (range: 0.4–3.1 per 100,000 population). Our annual rate is comparable to that reported in the literature from similar surveillance systems in the United States and Taiwan, despite methodological differences such as the inclusion and exclusion criteria and the extent of laboratory investigations. In Taiwan, 0.12 cases per 100,000 population were reported in 2000–05 [8] and in the United States, 0.5 cases per 100,000 population (range: 0.3–2.3 per 100,000 population) were reported during 1995–98 [4].

The majority of USII cases in our pilot study were reported in the first three months of surveillance. The initial surge of reported cases could be because this period coincided with the respiratory virus season in the UK, resulting in more ICU/PICU admissions and thus more cases of USII, especially with respiratory syndromes, during this period. However, given that the majority of children reported were subsequently diagnosed and that no paediatric cases were reported after week 11, the initial surge in cases may reflect a lower threshold of reporting by some of the participating units when the surveillance was first introduced. There is no evidence that this surge may have been the result of initial awareness and motivation of participating clinicians as despite low reporting rates (50%) in two bank holiday weeks, the weekly response rate remained high throughout the six months of the pilot. Participation and response was encouraged through close communication with the units. The high response rate suggests that major incidents are unlikely to have been missed.

Of the 18 patients initially reported, 12 were reported within four days of admission to the ICU/PICU and the mean reporting time was 3.6 days. This indicates that the system allows for close to real-time reporting, which is essential for immediate response to new and emerging infections. In addition, in the event of a serious public health incident, clinicians can make the initial report by telephone at any time, followed by a report via the online reporting tool.

One aim of the USII surveillance system was to identify possible clusters of USII. To meet this aim, spatial and temporal indicators were collected, as well as information on possible risk factors, such as travel or contact with another patient with similar symptoms. As it can be difficult to obtain detailed risk factor information from patients who are seriously ill, it may be necessary to obtain risk factor information from patients' family members as a proxy. Of the nine USII cases, travel to Africa was identified as a possible risk factor for one, while relevant exposures were not identified for the other eight cases. Home postcode was available for eight of the nine cases and the symptom onset date was available for all nine, indicating that cluster analysis based on spatial and temporal indicators is feasible. Although some surveillance systems rely for the detection of possible clusters on the calculation of exceedance scores expressed as a deviation from baseline rates, in USII surveillance, all reported cases are investigated for possible clustering as they are reported. This makes the USII surveillance more sensitive in detecting any possible clustering, and less reliant on accurate population denominators, which are difficult to estimate during the 2012 London Games.

Some limitations have been identified in the USII surveillance system. Given that USII is a diagnosis of exclusion and clinicians usually await initial laboratory results before reporting, there is a risk of delaying public health action. There were variations in reporting between different clinicians and these are likely to reflect a number of factors including lack of certainty in the diagnosis, clinical condition and improvement of the patient, availability of further diagnostics and individual clinical practice. These may have introduced reporting and measurement bias. We are aware that if additional testing had been made available, some USII cases could have had a microbiologically confirmed diagnosis before the patient's death or discharge from the ICU/PICU. Therefore, to facilitate diagnosis of potential USII cases, HPA now provides access to additional microbiological techniques for pathogen identification such as 16S rDNA polymerase chain reaction (PCR).

On the basis of the results of the pilot study and feedback from the six participating units, the USII surveillance system has been extended across London and the South East, with a total of 19 units involved at time of publication. This established sentinel network of ICU/PICUs can be used as a quick way of communicating a public health incident. Similar networks have previously been successfully established by the HPA, for example during the influenza A(H1N1)pdm09 pandemic [14].

To the best of our knowledge, this is the first time that a system to detect cases of USII has been established for a mass gathering event. During the Athens Games of 2004, 'unexplained death with a history of fever' and 'unexplained shock' were criteria included as part of the syndromic surveillance of cases presenting at emergency departments, from Olympic venues and from cruise ships [15,16]. Also during the Beijing 2008 Games and the Sydney 2000 Games, syndromic surveillance was set up in emergency departments, but not in intensive care units [17,18].

The USII surveillance put in place for the 2012 London Games is part of a range of enhanced existing and new surveillance systems, including syndromic surveillance in primary care, Olympic venues and emergency departments [9,10]. It is expected that these systems will complement each other and that surveillance teams will be in regular contact to exchange information, particularly if there is an increase of patients presenting with USII or an increase in the disease severity of patients attending emergency departments. In addition, the USII surveillance weekly nil notification system enables us to provide reassurance in response to enquiries on the emergence of infections, especially during the Games period when HPA is expected to be under increased international media pressure. Following the Games, the USII surveillance system and the sustainability of this approach will be evaluated and the potential for extending this network across England will be explored. The continued reporting of USII cases through the established sentinel network of ICUs and PICUs could be a valuable part of the public health legacy of the Olympic and Paralympic Games.

Members of the HPA USII Steering Group

Barbara Bannister, David Brown, Meera Chand, Tim Dallman, Jaran Eriksen, Saheer Gharbia, Ed Kaczmarski, Rohini Manuel, Dilys Morgan, Gillian Smith, Deborah Turbitt, Amanda Walsh.

Acknowledgments

The following colleagues made a significant contribution to the USII surveillance: Dr Richard Leonard and the AICU team of St. Mary's Hospital; Dr Simon Nadel and the PICU team of St. Mary's Hospital; Dr Jonathan Ball and the ICU team of St George's Hospital; Dr Martin Gray, Dr Linda Murdoch, Emma Wall and the PICU team of St Georges Hospital; Dr Robert Ghosh, Shaun Mcauliffe and the ICU team of the Homerton Hospital; Dr Shane Tibby and the PICU team of Evelina Children's Hospital; Dr Satu Kurkela, European Programme for Public Health Microbiology Training; Neville Verlander, Statistics, Modelling and Economics Department, HPS Colindale; Dr Helen Maguire, EPIET coordinator; and Dr Richard Pebody, EPIET supervisor.

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Is the basic reproductive number (R_0) for measles viruses observed in recent outbreaks lower than in the pre-vaccination era?

P Plans Rubió (pedro.plans@gencat.net)[1]
1. Public Health Agency of Catalonia, Barcelona, Spain

Citation style for this article:
Plans Rubió P. Is the basic reproductive number (Ro) for measles viruses observed in recent outbreaks lower than in the pre-vaccination era?. Euro Surveill. 2012;17(31):pii=20233. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20233

Article submitted 26 July 2012 / published on 2 August 2012

To the editor:

In their recent article on the large outbreak of measles in Merseyside, England, Vivancos et al. [1] obtained a basic reproductive number R_0 of 1.2 in week 3 after the start of the outbreak. This result could suggest that measles viruses are less infectious in recent outbreaks than in the pre-vaccination era, when the basic reproductive number R_0 ranged from 11 to 18 [2]. The basic reproductive number obtained in the study is however the effective basic reproductive number.

The basic reproductive number R_0 is the average number of individuals directly infected by one infectious case (secondary cases) during the entire infectious period, when the infectious agent has entered a totally susceptible population [3]. The effective basic reproductive number R, on the other hand, is the reproductive number observed when of a part of the population is immunised (I) [3]. In this situation, the reproductive number decreases from R_0 to $R=R_0-R_0I$ [3]. Outbreaks can be interrupted when R=1.

The basic reproductive number R_0 in the Merseyside outbreak can be determined from $R_0=R/(1-I)$, where I is the prevalence of protected individuals in the population. Assuming that prevalence of protected individuals was at least equal to 81–87% (85–92% vaccination coverage (V) x 95% vaccine effectiveness (VE)) the value of R_0 necessary to generate the outbreak was 6.2–9.5, only slightly lower than in the pre-vaccination era. The lowest value is obtained taking into account a vaccination coverage of V=85% (two doses of measles-mumps-rubella (MMR) vaccine at five years) and vaccine effectiveness of E=95%: $R_0=R/(1-I)=R/(1-VE)=1.2/(1-0.8075)=6.2$. The highest value is obtained taking into acount a vaccination coverage of 92% (first dose of MMR at 24 months) and 95% vaccine effectiveness: $R_0=1.2/(1-0.874)=9.5$.

Measles is one of the most contagious infectious diseases, and outbreaks can only be prevented by means of achieving a high vaccination coverage. For a $R_0=11–18$, the vaccination coverage required to prevent measles outbreaks is 96–99% [3].

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Authors' reply: An ongoing large outbreak of measles in Merseyside, England, January to June 2012

R Vivancos (roberto.vivancos@hpa.org.uk)[1], A Keenan[1]
1. Cheshire and Merseyside Health Protection Unit, Health Protection Agency, Rail House, Lord Nelson Street, Liverpool, United Kingdom

Citation style for this article:
Vivancos R, Keenan A. Authors' reply: An ongoing large outbreak of measles in Merseyside, England, January to June 2012. Euro Surveill. 2012;17(31):pii=20234. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20234

Article submitted 31 July 2012 / published on 2 August 2012

Authors' reply:

We would like to thank Dr Plans-Rubió for his comments regarding the reproductive number.

It has to be noted that measles is highly infectious and the low estimated reproductive number estimated is likely to be the result of the relatively high levels of vaccination in Merseyside over time [1]. However, the levels have been lower than the 95% recommended by the World Health Organisation needed to prevent outbreaks [2], leaving a pool of susceptible individuals within the population of Merseyside.

Therefore, as we have taken account of the immunised population in Merseyside, our estimate as rightly suggested by Dr Plans-Rubió represents an effective reproductive number (R) rather than the basic reproductive number (R_0) for measles.

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