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

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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.

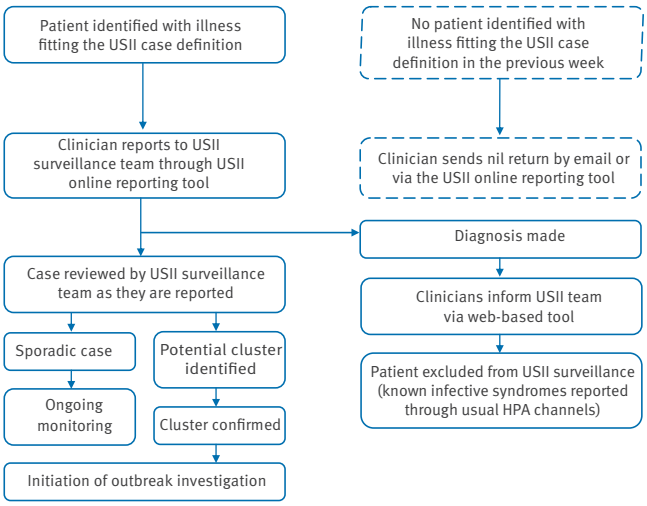
Methods

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.

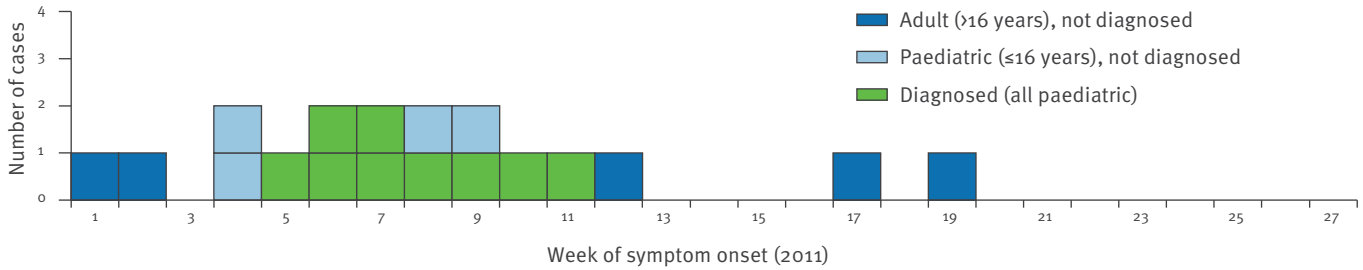
A 95% confidence interval (CI) for the coverage of ICU/PICUs was calculated assuming a binomial distribution, whereas for the rate, a Poisson distribution was assumed. The latter assumes that the denominator is a known quantity whereas it is only an estimate and variable over time, especially when extrapolating 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

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