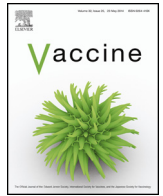




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Reply to Letter to the Editor

The case for ILI surveillance



Beverley Paterson and David Durrheim make five statements in their letter [1]: (1) That a standard universal case definition of ILI would be helpful but “most formal definitions include a measured temperature and this is not always possible, particularly in developing settings where thermometers may not be readily available.” (2) “The spectrum of influenza illness is phenomenal and depends on the characteristics of particular circulating strains.” (3) The use of SARI would “likely cause great confusion.” (4) The Australian FluTracking system provided “real-time evidence of a mismatch between vaccine components and the circulating strains” and (5) that ILI “offers the opportunistic capacity to identify increases in a range of pathogens that can present with ILI symptoms.”

1. ILI definition

The WHO’s 2011 update [2] specifically answers their query about measured temperature. WHO updated the definition of ILI to: “The case definition for influenza-like-illness is: An acute respiratory illness with onset during the past 7 days WITH measured temperature $\geq 38^{\circ}\text{C}$ AND cough.” The notes to the definition state that “Sudden onset of fever” was changed to “acute respiratory illness” as a recognizable clinical syndrome, that many clinicians and record keepers round down a temperature of $38.2\text{--}38^{\circ}\text{C}$, so the criterion temperature was changed to $\geq 38^{\circ}\text{C}$, and that “sore throat” was dropped as it is difficult to assess among infants. The WHO in 2011 also defined Acute Respiratory Infection (ARI) as: “Acute onset of at least one of the following four respiratory symptoms: cough, sore throat, shortness of breath, coryza AND a clinician’s judgment that the illness is due to an infection,” with the note that “ARI may present with or without fever.” ([2], p. 32). Thus there are WHO universally accepted definitions for ILI and ARI (which, however, make case definitions in research studies before and after 2011 not exactly comparable).

2. Is ILI a useful definition for influenza?

(a) The percentage of cases of ILI laboratory-proven to be influenza is small: in the review by Thomas ([3], Table 1) the percentage of cases of influenza-like illness proven on culture or by RT-PCR to be influenza A was $\leq 20\%$ in 9 of 14 studies and for Influenza B was below 10% in all 10 studies. (b) The percentage of ILI cases laboratory-proven to be influenza varies substantially for different years: The Government of Bangladesh conducted national hospital-based influenza surveillance in 12 sentinel

hospitals 2009–2010. Physicians in emergency departments applied ILI criteria using a structured questionnaire, collected nasal and throat swabs and tested them by RT-PCR. The incidence of medically-attended laboratory confirmed seasonal influenza in outpatients varied between 10/100 person years (95%CI 8, 14) in 2008, 6.6 (5, 9) in 2009 and 17 (13, 22) in 2010. These numbers comprise a very small percentage of the cases designated “ILI” and the number in 2010 was 2.5 times larger than that in 2009 [4]. (c) Studies of ILI cases find they include varying percentages of bacterial pathogens and a wide variety of other viruses: in 14 studies of ILI patients, cases of adenovirus were identified in 9, bacterial infections in 4, coronavirus in 7, metapneumovirus in 9, parainfluenza in 7, Picornavirus in 7, rhinovirus in 9, and RSV in 12 ([3], Table 1). (d) ILI patients may have multiple viruses: Galindo-Fraga in Mexico City for 678 patients found combinations of viruses in 70: influenza A with another virus in 45, adenovirus + rhinovirus in 9, adenovirus + metapneumovirus in 8, and Influenza B + metapneumovirus in 8 [5]. Hombrouck in Belgium found 12 of the 139 children with ILI had two viruses and 3 of the 810 adults [6]. Kammerer on the Mexico/US border crossing found of 1855 persons with ILI, 29 had combined viral and bacterial infections and seven had two viruses [7]. Noh in Korea for 1983 ILI patients found 58 had two or more respiratory viruses [8]. Rumoro in the US for 1233 ILI cases found 14 had both bacterial pneumonia and H1N1 [9]. Schnepf in France for 213 ILI cases found 36 had multiple viruses (32 with two viruses, two with 3 viruses, and one with four viruses) [10], and Thiberville in France found five of 286 ILI patients had multiple viruses [11]. (e) Patients with ILI have varying symptoms: When physicians ask about symptoms in ILI patients, they can neither differentiate cases of influenza from rhinovirus nor predict which cases are influenza ([3], Table 3). By analogy, if our automobile mechanics diagnosed “automobile-like illness” in our cars and they were right only 20% of the time, then 80% of our vehicles would remain stalled by the roadside. The mechanics could identify a wide range of other automobile viral pathogens if they tested for them, but 50% of the time they would not be able to identify any pathogen. (3) The WHO SARI definition: has specific usefulness in identifying children with severe respiratory illness as the mortality rate in the developing world is much higher than for ARI and identifies them as needing prompt and more intensive care [12]. (4) The Australian FluTracking system is a weekly online system that asks patients if they had experienced “fever and/or cough and/or muscle aches on any specific day/s and whether they had been absent from usual activities on any specific day/s.” In New South Wales an average 502 individuals participated weekly 3 June to 14 October 2007 [13] and nationally 4827 in 2008 and 10,773 in 2010 [14]. Individuals who access the Internet to report symptoms may be different from those who do not. There is no analysis of whether the participants were representative of cases of ILI presenting to GPs, and there was minimal correlation with national laboratory influenza notifications. Google Flu Trends in the US

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collates searches on the Internet about influenza and ILI by members of the public but correlations with CDC outpatient surveillance network data vary by season and region ([3], p. 2148). (5) ILI as a means of identifying other pathogens: The data in response 2 above indicate that in a large number of studies less than 20% of ILI cases have influenza A and less than 10% Influenza B. It would be much more helpful to identify the other pathogens and stop mislabeling cases as influenza when they are not.

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