Neces-SARI-ly?

Ignacio Martin-Löeches¹,²*, Marcio Soares³ and Antoni Torres⁴,²

Introduction
Over the last decade, several outbreaks have exposed major limitations in healthcare systems around the globe [1]. These outbreaks are characterized by the sudden emergence of an infectious and virulent respiratory pathogen that has the potential to spread rapidly around the world. Severe acute respiratory syndrome (SARS) in 2003, influenza A (H1N1) in 2009, and more recently the emergence of avian influenza A (H7N9) in China and novel coronavirus (e.g., Middle East respiratory syndrome coronavirus (MERS-CoV) have been the major threats to healthcare on a global scale [2]. The World Health Organization (WHO) recommended an increase in the surveillance of respiratory outbreaks and coined the severe acute respiratory infection (SARI) concept for surveillance purposes as well as to help the development of adequate sentinel programs [3]. The SARI definition encompassed a wide array of features including (1) recent onset of respiratory illness (within 10 days) (2) clinical signs and symptoms (fever, cough, and dyspnea), and (3) need for overnight hospitalization.

SARI concept
The imperative to plan for and respond to SARI in the future has been encouraging to provide guidance for public health professionals to both prepare for and respond to known and emerging respiratory pathogens. In this sense, the European Society of Intensive Care Medicine (ESICM) conducted a multicenter, multinational, observational study called The Intensive Care Global Study on Severe Acute Respiratory Infection (IC-GLOSSARI) in order to determine the incidence of SARI in intensive care units (ICU) around the globe. The main finding of this study was that among the patients admitted during the study periods, one out of ten had SARI. The present study has shown that the SARI concept needs to be tailored to account for both regional and seasonal variation. Accordingly the concept of an influenza-like illness (ILI), rather than SARI, may be adopted to characterize seasonal influenza or any respiratory pathogen with the potential to cause outbreaks and epidemics. Incorporating this concept of ILI into future epidemiologic studies might shed light on the burden of such outbreaks. To better report the incidence of respiratory infections, the authors adapted the International Sepsis Forum (ISF) definitions for categorizing SARI as community, healthcare related and hospital acquired. However as the majority of study patients were admitted to European ICUs with community-acquired SARI this study predominantly reflects the burden of respiratory disease in Europe. This study uniquely reported SARI with a 7-day onset of illness in contrast to the accepted SARI definition of 10 days [3]. Furthermore the study was performed in late autumn and winter, which is the peak season for community-acquired pneumonia (CAP) with Streptococcus pneumoniae [4]. However other pathogens are more prevalent in warm seasons, when the incidence of Legionella pneumoniae is known to correlate with increased humidity and rainfall and may have been under-represented in this study [5]. With this seasonal factor in mind it is notable that the recent influenza A (H1N1) pandemic which occurred in the spring and summer 2009 would not have been captured by this study [6]. Interestingly the low rate of viral illness reported in this study (7.7–13.7 %) is not in keeping with the reported seasonality of viral respiratory illness while the rate of fungal infections, almost 1/3 of ICU patients, is highly unexpected [7]. Both these observations will require confirmation.

The 4S concept: seasonality, clinical setting, severity, and sentinel critical care for outbreaks
Although SARI events may appear as a reiteration of an established concept, SARI encompasses a wide spectrum...
of diseases including ILI, CAP, and COPD exacerbations, with or without tracheobronchitis, in patients with certain comorbidities such as diabetes, cancer, and obesity. However, SARI definitions need to include more specific and objective parameters for disease severity such as the presence of organ dysfunction and/or the need for invasive support with vasopressors and mechanical ventilation and to assist in the diagnostic workup to search for underlying treatable causes [8]. Grading the severity of SARI could help to identify patients’ deteriorations at an early and treatable stage to propose a paradigm for diagnostic investigations and to estimate the global need for intensive care with ventilator or cardiovascular support.

The concepts of severity-graduated SARI and ILI will be epidemiologically helpful to determine trends of disease and the impact of disease at institutional and national levels. The impact of seasonality upon disease incidence is an important factor that will be subject to regional variation and which is not adequately addressed by the SARI concept. Lastly the occurrence of community-acquired respiratory co-infection (CARC) [9] during SARI outbreaks should be considered when studying SARI. Tools or strategies might help to identify the presence of CARC, such as a decision-tree analysis based on biomarkers, to correctly stratify patients’ etiology risk [10]. These aforementioned key points are summarized in Fig. 1.

SARI was initially developed to capture prolonged outbreaks of ILI in order to compare the severity of influenza by season and country, and address strengths and weaknesses of current surveillance strategies [11]. Therefore the present study with a 2-week inception cohort design might not achieve the goal of its design. Furthermore, the assessment of possible risk factors for an adverse outcome could be improved by performing the analysis by influenza type and subtype [12]. Continued evaluation and review of surveillance systems will improve our ability to understand the output of these systems and may allow for comparison of the surveillance data for SARI outbreaks in different regions [13]. The SARI concept based on its very wide definition might benefit from improved diagnostics and may also help formulate preventive strategies and empiric treatment guidelines in low-income settings with limited laboratory capacity and where routine testing of samples for pathogen identification is not currently feasible.

**Game wording by institutional bodies**

Over the last few years, we have seen the development of different concepts and nomenclature for emerging diseases data collection for the purpose of epidemiology. For instance, the Centers for Disease Control and Prevention (CDC) devised the term ventilator-associated events (VAEs) to adequately capture data for ventilator-associated pneumonia (VAP). This concept included the increase in need for oxygen or positive end-expiratory pressure (PEEP) instead of the VAP radiographic criterion [14]. The CDC aimed to use the VAE definition algorithm for surveillance purposes and not for use in the clinical management of patients [15]. Similarly the WHO developed the SARI concept to allow healthcare authorities better capture future outbreaks of infectious respiratory diseases, with a major focus on influenza cases and with a sufficient broad definition that can be applied to all settings independently of the laboratory resources. However without an adequate laboratory capacity to detect other pathogens, the SARI concept may be less useful in developed countries, where strategies, classifications and algorithms focusing on community- and healthcare-acquired pneumonia have provided substantial results. As happened with VAE, SARI seems to be an excellent term for the purposes of epidemiology but may not serve for treatment and management.

**Conclusion**

SARI events are not intended to guide day-to-day patient management but are created for sentinel quality tracking and possible public reporting, and could be incorporated into outbreak preparedness initiatives. However, it is helpful for clinicians to understand how their patients and performance are being monitored and reported to outside agencies. Providing a mechanism to monitor trends in the evolution of disease outbreaks and enhancing communication within health systems for the critically ill will improve the disease awareness and buttress healthcare system sustainability during an outbreak. The SARI concept is, therefore, useful for epidemiology purposes but not for assessing treatment and management. Carefully taking this into account would avoid overusing the SARI concept and adding confusion to a complex disease.
Author details
1 Department of Clinical Medicine, Wellcome Trust - HRB Clinical Research Facility. St. James's Hospital, Trinity College, Dublin, Ireland. 2 CIBER de Enfermedades Respiratorias (CIBERES), Barcelona, Spain. 3 D’Or Institute for Research and Education, Postgraduate Program of Internal Medicine and Cancer, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil. 4 Respiratory Disease Department, Hospital Clinic i Provincial de Barcelona, IDIBAPS, Barcelona, Spain.

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References
1. Dunning JW, Merson L, Rohde GGU et al (2014) Open source clinical science for emerging infections. Lancet Infect Dis 14:8–9. doi:10.1016/S1473-3099(13)70327-X
2. Poulakou G, Bassetti M, Timsit J-F (2015) Critically ill migrants with infection: diagnostic considerations for intensive care physicians in Europe. Intensive Care Med 42:245–248. doi:10.1007/s00134-015-4090-9
3. Pan American Health Organization/WHO (2014) Operational guidelines for sentinel severe acute respiratory infection (SARI) surveillance.http://www.paho.org/revelaci-n/wp-content/uploads/2015/10/2015-cha-operational-guidelines-sentinel-sari.pdf. Accessed 22 Jan 2015
4. Cillóniz C, Ewig S, Polverino E et al (2011) Microbial aetiology of community-acquired pneumonia and its relation to severity. Thorax 66:340–346. doi:10.1136/thx.2010.145982
5. Altizer S, Ostfeld RS, Johnson PTJ et al (2013) Climate change and infectious diseases: from evidence to a predictive framework. Science 341:514–519. doi:10.1126/science.1239401
6. Martín-Loeches I, Bermejo-Martin JF, Valles J et al (2013) Macrolide-based regimens in absence of bacterial co-infection in critically ill H1N1 patients with primary viral pneumonia. Intensive Care Med 39:693–702. doi:10.1007/s00134-013-2829-8
7. Terranone S, Ferrer M, Martín-Loeches I et al (2015) Impact of Candida spp. isolation in the respiratory tract in patients with intensive care unit-acquired pneumonia. Clin Microbiol Infect. doi:10.1016/j.cmi.2015.09.002
8. Ewig S, Woodhead M, Torres A (2011) Towards a sensible comprehension of severe community-acquired pneumonia. Intensive Care Med 37:214–223. doi:10.1007/s00134-010-2077-0
9. Martin-Loeches I, Sanchez-Corral A, Diaz E et al (2011) Community-acquired respiratory coinfection in critically ill patients with pandemic 2009 influenza A(H1N1) virus. Chest 139:555–562. doi:10.1378/chest.10-1396
10. Rodríguez AH, Avilés-Jurado FX, Diaz E et al (2015) Procalcitonin (PCT) levels for ruling-out bacterial coinfection in ICU patients with influenza: a CHAID decision-tree analysis. J Infect. doi:10.1016/j.jinf.2015.11.007
11. Budgell E, Cohen AL, McAneney J et al (2015) Evaluation of two influenza surveillance systems in South Africa. PLoS One 10:e0120226. doi:10.1371/journal.pone.0120226
12. Martin-Loeches I, Díaz E, Vidaur L et al (2011) Pandemic and post-pandemic influenza A (H1N1) infection in critically ill patients. Crit Care 15:R286. doi:10.1186/cc10573
13. Meerhoff TJ, Simaku A, Ulqinaku D et al (2015) Surveillance for severe acute respiratory infections (SARI) in hospitals in the WHO European region—an exploratory analysis of risk factors for a severe outcome in influenza-positive SARI cases. BMC Infect Dis 15:1. doi:10.1186/s12879-014-0722-x
14. Boudiaf L, Sonnevile R, Garrouste-Orgeas M et al (2015) Ventilator-associated events: prevalence, outcome, and relationship with ventilator-associated pneumonia. Crit Care Med 43:1798–1806. doi:10.1097/CCM.0000000000001091
15. Klompas M (2013) Complications of mechanical ventilation—the CDC’s new surveillance paradigm. N Engl J Med 368:1472–1475. doi:10.1056/NEJMmp1306633