Severe acute respiratory infections, the missing link in the surveillance pyramid

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CHAPTER 2

Experience of establishing severe acute respiratory surveillance in the Netherlands: evaluation and challenges

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ABSTRACT

The 2009 influenza A(H1N1) pandemic prompted the World Health Organization (WHO) to recommend countries to establish a national severe acute respiratory infections (SARI) surveillance system for preparedness and emergency response. However, setting up or maintaining a robust SARI surveillance system has been challenging. Similar to other countries, surveillance data on hospitalisations for SARI in the Netherlands are still limited, in contrast to the robust surveillance data in primary care.

The objective of this narrative review is to provide an overview, evaluation, and challenges of already available surveillance systems or datasets in the Netherlands, which might be used for near real-time surveillance of severe respiratory infections.

Seven available surveillance systems or datasets in the Netherlands were reviewed. The evaluation criteria, including data quality, timeliness, representativeness, simplicity, flexibility, acceptability and stability were based on United States Centers for Disease Control and Prevention (CDC) and European Centre for Disease Prevention and Control (ECDC) guidelines for public health surveillance. We added sustainability as additional evaluation criterion.

The best evaluated surveillance system or dataset currently available for SARI surveillance is crude mortality monitoring, although it lacks specificity. In contrast to influenza-like illness (ILI) in primary care, there is currently no gold standard for SARI surveillance in the Netherlands.

Based on our experience with sentinel SARI surveillance, a fully or semi-automated, passive surveillance system seems most suited for a sustainable SARI surveillance system. An important future challenge remains integrating SARI surveillance into existing hospital programs in order to make surveillance data valuable for public health, as well as hospital quality of care management and individual patient care.

INTRODUCTION

Surveillance is a vital tool to monitor shifts in the occurrence and burden of infectious diseases in the population, which is necessary for prevention and control.[1,2] Most European countries have a well-established weekly near real-time surveillance system of influenza-like illness (ILI) and/or acute respiratory infections (ARI) in primary care, reported weekly in the bulletin Flu News Europe.[3] Arguably, influenza is the best organised infectious disease surveillance program that exists today. However, during the 2009 influenza A(H1N1) pandemic, it became apparent that countries had very limited historic and real-time data on hospitalised patients with severe respiratory infections, such as pneumonia as a complication of influenza. In response, the World Health Organization (WHO) recommended to establish national severe acute respiratory infection (SARI) surveillance systems to gain insight in the severity of epidemics and enable earlier detection of potential epidemics and pandemics.[4-6] According to the WHO, a severe acute respiratory infection is defined as an acute respiratory infection requiring hospitalisation with a history of fever (≥38°C), cough, and onset within the last 10 days.[7] SARI surveillance data would be essential for guiding healthcare interventions, such as additional vaccination, and communication with healthcare professionals and the public.[8]

Over the past decade, many countries have piloted some type of severe respiratory infection surveillance, but only few countries have established a robust SARI surveillance system.[9-11] In Europe, these are mainly eastern European countries, while in western Europe, Germany [12] and Belgium maintain a syndromic sentinel SARI surveillance system, which is complemented with influenza testing in Belgium.[13,14] Since 2013, the United Kingdom (UK) publishes weekly national influenza reports, including incidence estimates of influenza-confirmed hospitalisations.[15] Other European countries merely report the absolute number of influenza positive patients admitted to general wards or intensive care units (ICUs), i.e. without any denominator data.[16-18] Insight in the spectrum of surveillance systems and datasets that could potentially be used for SARI surveillance is scarce. In addition, studies which focus on challenges and main lessons learned for establishing a robust SARI surveillance system are lacking.

In the Netherlands, several initiatives aim at setting up a severe infectious disease surveillance system.[19,20] Our objective is to provide an overview, evaluation, and challenges of the available surveillance systems or datasets in the Netherlands, which could potentially be used for near real-time surveillance of severe respiratory infections. Our lessons learned could be valuable to other countries aiming to establish a robust SARI surveillance system.

AVAILABLE SURVEILLANCE SYSTEMS OR DATASETS

QUALITY OF CARE MONITORING SYSTEM IN INTENSIVE CARE

To date, 90 adult ICUs report to National Intensive Care Evaluation (NICE), reaching 100% coverage in the Netherlands. The catchment population therefore represents the total Dutch population in 2018 (17.2 million inhabitants). The syndromic, aggregated data are only available retrospectively with a time lag of one to three months and without microbiological test results. All ICUs participating in the NICE registry have adopted the Acute Physiology and Chronic Health Evaluation IV (APACHE IV) model.[21] The APACHE IV scoring system contains codes for several respiratory syndromes that could potentially be used for SARI surveillance, such as pulmonary sepsis and pneumonia due to bacteria, viruses, fungi, parasites, and/or other causative agents.[22,23]

NATIONAL REGISTER OF HOSPITAL DISCHARGE DIAGNOSES

In the Netherlands, Dutch Hospital Data (DHD) maintains a national register consisting of discharge diagnoses of hospitalised patients in the Netherlands. Annually, 90 hospitals report to DHD, but their exact catchment populations are unknown. Reaching 90% coverage in 2014, this dataset is updated annually for participating hospitals with a one-year time lag.[24,25] International Classification of Diseases and Related Health Problems (ICD-9 & 10) registration are used for coding discharge diagnoses and are reported in DHD. Discharge diagnosis with ICD-10 codes, J00-J22, could be defined as a SARI case.

MORTALITY MONITORING

Deaths are notified to municipalities and reported to Statistics Netherlands (CBS). During the 2009 influenza A(H1N1) pandemic, the National Institute for Public Health and the Environment (RIVM) and CBS initiated a prospective, syndromic surveillance system, reporting aggregated all-cause mortality data weekly. Deaths from all causes are further stratified by age group and region. The presence of excess mortality (i.e. above a pre-defined threshold obtained from historical data) is verified weekly.[26] The catchment population comprises the total population in the Netherlands.

SARI SENTINEL SURVEILLANCE

SARI sentinel surveillance is a prospective, case-based, surveillance system with lab-confirmed outcomes and currently only implemented in one Dutch hospital, Jeroen Bosch Hospital (JBH) (catchment population 323,000 persons). The SARI sentinel surveillance was part of a pilot study initiated in 2015 with the main objective to set up SARI surveillance in the Netherlands.[19] In this pilot study different strategies were tested to assess which hospital data were best suited for a sustainable real-time SARI surveillance system. In JBH, an active, case-based surveillance system was set up, with registration by medical staff of any patient fulfilling the SARI case definition. A SARI case is defined as a hospitalised patient with at least one systemic symptom or deterioration of general condition *and* at least one respiratory symptom *and* symptoms started within a week from admission.

FINANCIAL CODING SYSTEM

In Leiden University Medical Center (LUMC), SARI surveillance was embedded in an automated cluster detection system, which was operational since 2013.[27] This passive, prospective, syndromic SARI surveillance system was based on financial claim codes corresponding to diagnoses related to the clinical syndrome SARI. These clinical syndromes include upper respiratory infections, lower respiratory infections and other respiratory infections. The aggregated data were reported real-time by LUMC (catchment population 183,000 persons).

AMBULANCE DISPATCH CALLS DATA

Ambulance dispatch calls data could be used as syndromic data for an early warning system for respiratory infectious disease.[28] The Advanced Medical Priority Dispatch System (AMPDS) or Netherlands Triage Standard (NTS) are used to determine the medical urgency. Specific emergency signs, such as breathing difficulties, are protocolled in AMPDS and provided with specific triage codes. NTS further subdivides medical emergencies according to presenting symptom with a triage code. Retrospective ambulance dispatch calls data are analysed for potential use for a real-time, syndromic surveillance system of acute respiratory infections.[29] A SARI case is detected if the patient adheres to specific triage codes related to respiratory syndrome calls. The data are provided in aggregated format. Data of 4 dispatch centers using AMPDS are available to the RIVM, covering 4.2 million inhabitants in 2016 distributed over 5 provinces.

VIROLOGICAL LABORATORY SURVEILLANCE

Currently, about 20 laboratories, with an unknown catchment population, report weekly the number of laboratory-confirmed, positive test results of various pathogens to the virological laboratory surveillance. No distinction can be made between specimens from primary and hospital care and information on the diagnostic methods is absent. Aggregated data are reported without patient medical history and/or clinical data and therefore a SARI case definition cannot be established.[30] Positive test results are available for influenza virus, RSV, para-influenza (type 1-4), human metapneumovirus, coronavirus, rhinovirus, adenovirus, bocavirus, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Chlamydia psittaci* and *Coxiella burnetii*.

Examples of each surveillance system or dataset are given in supplemental file, figure S1-7.

EVALUATION SURVEILLANCE SYSTEM OR DATASET

Available infectious disease surveillance systems or datasets in the Netherlands were reviewed for evaluation as a potential SARI surveillance system. The 4 authors assessed the 7 surveillance systems or datasets by using 8 evaluation criteria.

EVALUATION CRITERIA

The selected evaluation criteria, based on United States Centers for Disease Control and Prevention (CDC) and European Centre for Disease Prevention and Control (ECDC) guidelines for public health surveillance [31,32] are:

- data quality: the completeness and validity of the data recorded in the surveillance system, including the addition of microbiological diagnostics;
- timeliness: the speed between steps in a surveillance system, from event occurrence, recognition, report, to control and prevention activities;
- representativeness: the ability to accurately describe the occurrence of an event over time, place and person;
- simplicity: the system's structure and ease of operation;
- flexibility: the ability to adapt to changing information needs or technological operating conditions;
- acceptability: the willingness of persons and organisations to participate in the system;
- stability: the system's reliability (ability to collect, manage and provide data without failure) and availability (ability to be operational when needed).

We added one additional evaluation criterion:

- sustainability; the ongoing maintenance and support of a routine epidemiologic and/or microbiologic surveillance system.

EVALUATION METHOD

To asses each evaluation criterion, the 4 authors (2 infectious disease consultants, 1 medical doctor/epidemiologist, 1 senior epidemiologist) independently assigned the qualification 'good', 'moderate', or 'poor'. A semi-quantitative score for the surveillance system or dataset was obtained by attributing three points for each evaluation criterion rated 'good', two points for each evaluation criterion rated 'moderate' and one point to each evaluation criterion rated 'poor'. If the opinions of the 4 experts diverged, the assessment was re-evaluated in order to reach consensus. The total evaluation score was calculated as the sum of 8 evaluation criteria scores. Descriptive statistics were used for reporting the score per surveillance system or dataset, such as total number and the percentage of the maximum score.

EVALUATION RESULTS

Crude mortality monitoring scored the best if comparing the 7 surveillance systems or datasets based on the evaluation criteria (Table 1). The SARI sentinel surveillance had the lowest score. In all surveillance systems or datasets data quality and sustainability was moderate to good. The largest contrast in evaluation scores (poor versus good scores) between surveillance systems or datasets were seen for timeliness.

Table 1. Evaluation of available surveillance systems and datasets that could potentially be used for SARI surveillance in the Netherlands

System or dataset	Data quality	Timeliness	Represen-tativeness	Simplicity	Flexibility	Acceptability	Stability	Sustainability	Score (% of maximum score)[a]
Quality of care management system	Good	Poor	Moderate	Moderate	Good	Good	Good	Good	20 (83)
National register discharge diagnoses	Moderate	Poor	Moderate	Good	Moderate	Good	Moderate	Good	18 (75)
Mortality monitoring	Good	Good	Moderate	Good	Good	Good	Good	Good	23 (96)
SARI sentinal surveillance	Moderate	Good	Poor	Poor	Poor	Moderate	Poor	Moderate	13 (54)
Financial coding system	Moderate	Good	Poor	Good	Poor	Good	Moderate	Good	16 (67)
Ambulance dispatch calls data	Moderate	Good	Poor	Good	Good	Moderate	Poor	Poor	16 (67)
Virological laboratory surveillance	Good	Good	Poor	Moderate	Moderate	Good	Good	Good	20 (83)

[a] Score: per evaluation criterion the following scores were attributed: 3 points if rated 'good', 2 points if rated 'moderate', 1 point if rated 'poor'. The total evaluation score was expressed as the sum of all individual evaluation criteria and percentage of the total maximum score.

DISCUSSION

The best evaluated surveillance system or dataset currently available for SARI surveillance is crude mortality monitoring, although it is still not sufficient. This system is well-established in the European Union (EU) region with weekly country reports on the EuroMOMO and on the RIVM website.[26,33] However, crude mortality surveillance reports only all-cause mortality and therefore lacks specificity for SARI. Within the EuroMOMO network, models are now being developed to attribute mortality to influenza.[34] Crude mortality monitoring is also providing crucial data in the COVID-19 pandemic, in addition to the reported deaths from laboratory-confirmed SARS-CoV-2 infection. If disease-specific mortality, such as respiratory mortality, could be reported, a more sensitive endpoint for SARI surveillance would be reached. However, it is not expected that cause-of-death statistics will become available near real-time in the foreseeable future.

In ICUs a large amount of patient data is collected for quality assurance. In the Netherlands, these data are available in the NICE database and selected variables could provide a robust, syndromic SARI surveillance system, if timeliness could be improved together with maintaining current coverage. An exploratory query indicated that reporting frequency could be improved to every six weeks. However, to be better optimised for a SARI surveillance system for preparedness and emergency control, timeliness has to be improved to at least a weekly reporting frequency. During the current COVID-19 pandemic NICE was quickly modified for COVID-19 monitoring with several updates per day.

The financial coding system comprised a passive, syndromic SARI surveillance system, which is evaluated as good for timeliness, simplicity and acceptability. Passive surveillance systems, such as fully automated cluster detection systems, are the preferred design for SARI surveillance, because they minimize administrative burden and increase sustainability.

National register of hospital discharge diagnoses with specific ICD-10 codes related to respiratory infections are available with a one-year time lag, which precludes its use for SARI surveillance. Efforts are underway to improve timeliness, which could make these data potentially valuable for SARI surveillance. In Germany, weekly SARI surveillance was established based on ICD-10 discharge codes from a large number of hospitals.[12] A relative drawback of DHD is the unknown denominator estimate of participating hospitals, which could be compensated by using the proportion of respiratory-related and total number of hospital admissions instead.

Ambulance dispatch calls data are available real-time, but contain a high background incidence of non-infectious causes of respiratory disease, and have high variability if attributed to ILI.[29,35] If representativeness could be improved, it could potentially complement other available respiratory infectious disease surveillance systems.

Ideally, severe respiratory infectious disease surveillance would consist of sentinel syndromic SARI surveillance with virological testing of a subset of cases, comparable with ILI surveillance in primary care. Such sentinel SARI surveillance is still in a pilot phase in the Netherlands, contributing to poor current scores on simplicity, flexibility and stability. By extending to five or more, evenly geographically-distributed hospitals, a sentinel SARI surveillance system with relatively good coverage in the Netherlands could be achieved. Currently, Dutch sentinel SARI surveillance of patients, aged 65 years and older with influenza test results, also has international scientific value by sharing data with the European influenza monitoring vaccine effectiveness study (I-MOVE+).[36] By pooling data from ten European countries, the seasonal influenza vaccine effectiveness against laboratory-confirmed SARI among elderly is calculated.[37]

The virological laboratory surveillance, as it is available in the Netherlands and several other European countries, lacks linked-patient data, catchment population estimate, and distinction between primary and secondary care, which makes it less suitable for use as SARI surveillance on its own. However, it could be of potential value in complementing another surveillance system or dataset, such as syndromic SARI sentinel surveillance. In comparison, Denmark has a national microbiology database available, with national legislation that allows for linkage with other patient data.[38]

LIMITATIONS OF THE EVALUATION

Established public health surveillance systems may be more extensively evaluated based on other surveillance system attributes, such as level of usefulness, sensitivity, and positive predictive value.[8] We chose a limited amount of evaluation criteria which are applicable and available for the current surveillance systems and datasets that could potentially be used for SARI surveillance in the Netherlands. In addition, costs for developing a SARI surveillance system are not included in this evaluation. With limited public health funding in many countries, this might be a critical first obstacle in setting up SARI surveillance.[8,39] We have also not considered possible legal constraints for national public health agencies in obtaining data for surveillance. For example, because of the implementation of General Data Protection Regulation (GDPR) in the EU in 2018, DHD stopped providing case-based hospital discharge data to the RIVM and other organisations.

SARI SURVEILLANCE IN EUROPE

Based on literature, online reports, and personal communication, we made an overview of 15 available SARI surveillance systems in Europe (Supplemental material, Table S8). If recent data on a SARI surveillance system were unavailable, countries were not included in this overview. Available SARI surveillance systems in Europe show great diversity, ranging from syndromic SARI to laboratory-confirmed severe influenza surveillance in ICU. When comparing SARI surveillance between European countries various methodological challenges are encountered. Firstly, multiple different SARI case or severe influenza case definitions exist, with possibly different sensitivities and specificities. Secondly, the representativeness of the surveillance data between countries is different, because catchment population sizes vary substantially. Only two countries lacked catchment population estimates and reported absolute numbers. Thirdly, the number of pathogens under surveillance is diverse between countries, but influenza virus is reported the most. Fourthly, variation in threshold for hospitalisation may exist due to differences in healthcare systems between countries.

2

CURRENT AND FUTURE CHALLENGES

MICROBIOLOGICAL DIAGNOSTICS

Besides virological laboratory and SARI sentinel surveillance, all evaluated surveillance systems or datasets have in common that they lack diagnostic specificity. Adding microbiology diagnostics to syndromic surveillance improves both timeliness and completeness of a SARI surveillance system.[8] For identification of epidemics, causative pathogen detection is essential for implementing timely healthcare interventions.[40] Firstly, adding microbiological diagnostics to syndromic SARI surveillance is challenging, because SARI could be caused by multiple, different pathogens.[9,41] Influenza and *Streptococcus pneumoniae* were chosen for inclusion in our SARI sentinel surveillance system, because they are common causative pathogens of SARI with a high burden of disease.[42,43] Introduction of point-of-care tests and multiplex PCR in microbiology laboratories in the last decade, offers a great opportunity to expand the number of pathogens under surveillance in the future.[44,45] Secondly, another challenge when adding microbiological diagnostics is to decide which sampling strategy to implement. An option is to upscale baseline microbiological diagnostics, based on differential diagnosis, if an elevation of SARI incidence occurs above a predefined threshold. To facilitate a more systemic testing policy in SARI patients and minimize the amount of testing bias in the Netherlands, hospital or national guidelines would have to be improved. Currently, microbiological diagnostics often occur at the discretion of the treating physician and hospital or national guidelines regarding microbiological diagnostics are scarce. The Infectious Diseases Society of America/American Thoracic Society (IDSA/ATS) clinical guidelines state that testing for at least influenza should be considered in adult patients admitted with suspected respiratory infection during local epidemics.[46] However, there are no recommendations for respiratory virus testing, besides influenza virus, in SARI patients admitted to regular ward or ICU.[46]

SUSTAINABILITY OF SURVEILLANCE SYSTEMS

Based on our experience and evaluation, improving sustainability is crucial for establishing a robust SARI surveillance system. In terms of sustainability, several challenges play an essential role. Firstly, the administrative burden associated with surveillance should be addressed. In a demanding hospital setting with increasing registration burden for hospital staff [47], our experience from SARI sentinel surveillance indicated that additional workload associated with surveillance should be decreased as much as possible. Thus, to improve timeliness, simplicity, and acceptability of a SARI surveillance system, we believe that implementation of a passive, fully or semi-automated, SARI surveillance system is required. This is underlined by high scores evaluations scores for mortality monitoring and virological laboratory surveillance, which are largely automated surveillance systems as well. Secondly, a different appreciation of the value of epidemiological surveillance data by data providers, such as clinicians, laboratories or hospitals, should be taken into account. We experienced that stakeholders withdrew their participation in SARI surveillance after a year, because of different appreciation of the value of epidemiological surveillance data. Therefore, we believe it is essential that a SARI surveillance system serves both a public health and a patient care goal.[48] This could be achieved by integrating SARI surveillance in existing hospital programs in order to make surveillance data valuable for public health as well as patient care.[49] SARI surveillance data could for example be utilised for monitoring antibiotic or antiviral use and resistance and lead to targeted antibiotic stewardship programs (ASP) interventions in patient care.[50] Embedding SARI surveillance in a quality of care program for SARI patients is a strategy that was pursued in our SARI sentinel surveillance.[8,51] Being part of routine quality care helped improve efficiency of our SARI sentinel surveillance system and increased the commitment of the participating hospital.

FUTURE DIRECTIONS SARI SURVEILLANCE IN THE NETHERLANDS

Our aim is establishing a fully or semi-automated passive SARI surveillance system in the Netherlands based on financial codes. The advantages are the limited administrative burden and the data availability based on financial coding is (near) real-time. Based on our experience with SARI sentinel surveillance, it is currently not possible to easily combine syndromic SARI data with microbiological diagnostics due to information communication technology (ICT) difficulties. Therefore, we aim to establish a separate laboratory surveillance system for influenza, RSV, *S. pneumoniae* and SARS-CoV-2, parallel to passive syndromic surveillance. In the long term, our goal is establishing an integrated, automated, passive SARI surveillance system with laboratory outcomes in sentinel hospitals evenly geographically distributed across the Netherlands.

CONCLUSION

Multiple surveillance systems or datasets are available in the Netherlands with potential use for SARI surveillance. In contrast to ILI in primary care, there is currently no gold standard for SARI surveillance in the Netherlands. Based on our experience from sentinel SARI surveillance, a potential sustainable SARI surveillance system for the long-term is a fully or semi-automated, passive surveillance system. In addition to increased timeliness, and simplicity of the surveillance system, the acceptability is improved by reducing unnecessary administrative burden of hospital staff. An important future challenge remains integrating SARI surveillance into existing hospital programs in order to make surveillance data valuable for both public health and patient care.

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2

SUPPLEMENTARY MATERIAL

Quality of care monitoring system intensive care unit

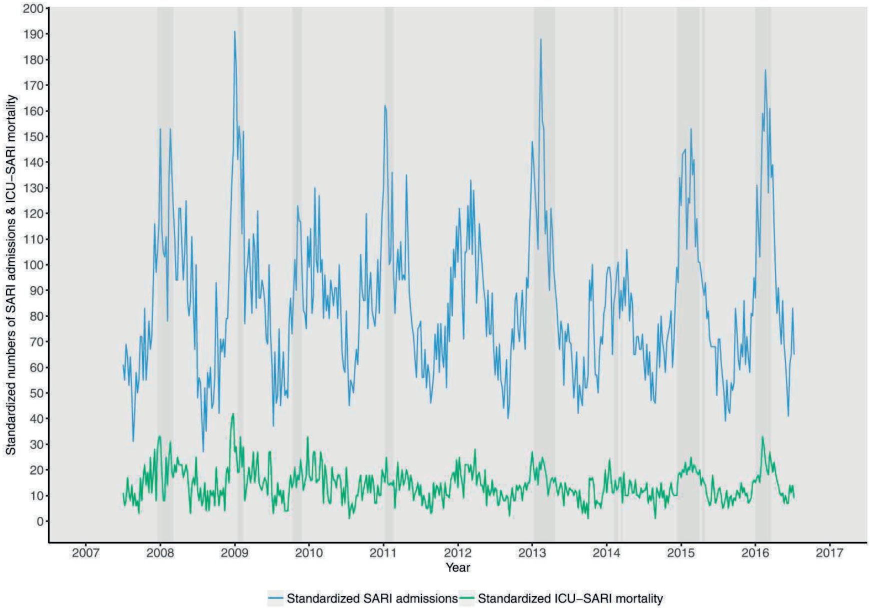

Figure S1. Standardized number of SARI admissions and standardized in-ICU SARI mortality per year (2007-2017)[1]

The utilisation of data derived from the quality-of-care monitoring system in the ICU in the Netherlands is illustrated by comparing the trend of SARI admissions in the ICU to standardized SARI mortality in the ICU over a period of ten years. If available near real-time, these data could be used for in-ICU SARI mortality surveillance and provide a more disease-specific insight than the longer existing all-cause mortality surveillance in the Netherlands.

National register of hospital discharge diagnoses

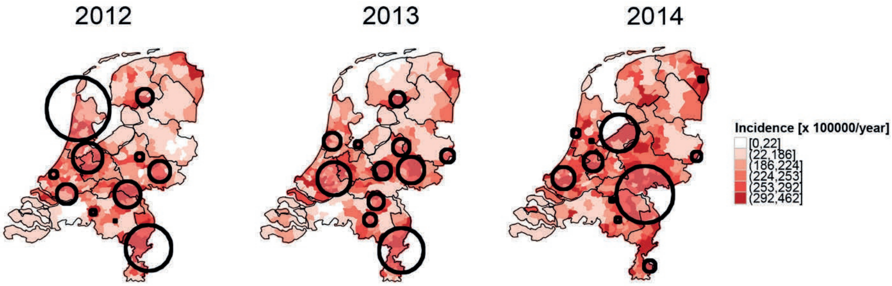

Figure S2. Maps of age adjusted incidence of unspecified pneumonia cases at municipality level for the years 2012, 2013 and 2014. Black circles represent significant clusters (p<0.05) identified whilst imposing a 10% upper limit and choosing a non-overlapping criterion. The incidence intervals in the color bar represent the quantiles of the pneumonia incidence in 2014[2]

This figure illustrates that surveillance of ICD-10 codes related to SARI could be used for giving insight in SARI incidence and geographical distribution in the Netherlands by accurately identifying SARI patients in person, time and place. In a SARI surveillance system for action and control these data could trigger specific healthcare interventions, such as upscaling diagnostics, additional vaccinations in specific patient groups, directing antibiotic treatment if a causative pathogen is identified.

Vital statistics

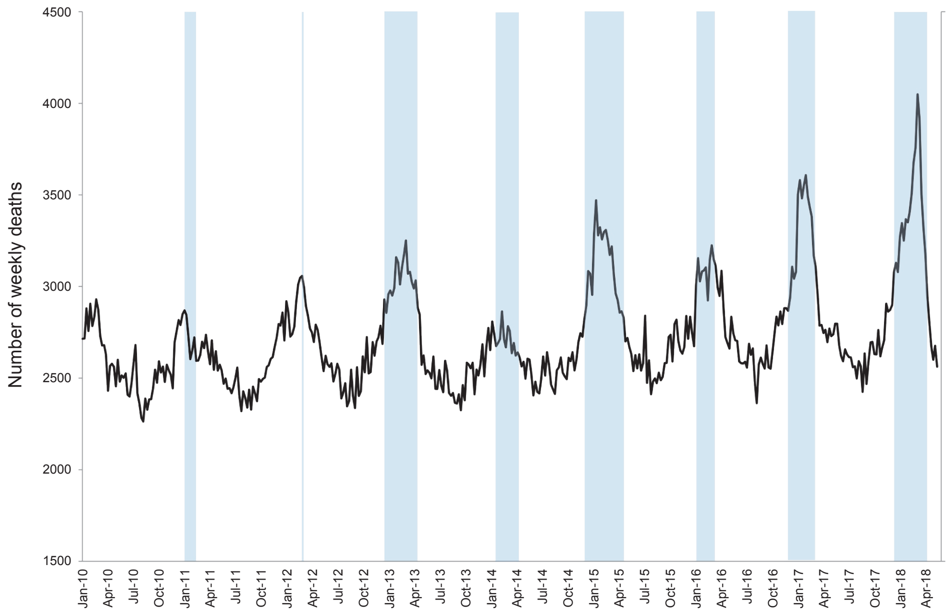

Figure S3. Weekly number of deaths per week from January 2010 through April 2018, with the influenza epidemic depicted by blue shading, provided by the crude mortality surveillance. Blue shading depict the influenza epidemic period[3]

All-cause mortality surveillance is a longstanding near real-time surveillance system with ten years of historical data. This figure shows clear peaks in all-cause mortality during the influenza epidemics. In addition, an increasing trend of all-cause mortality is observed, which is probably caused by an aging population.

SARI sentinel surveillance

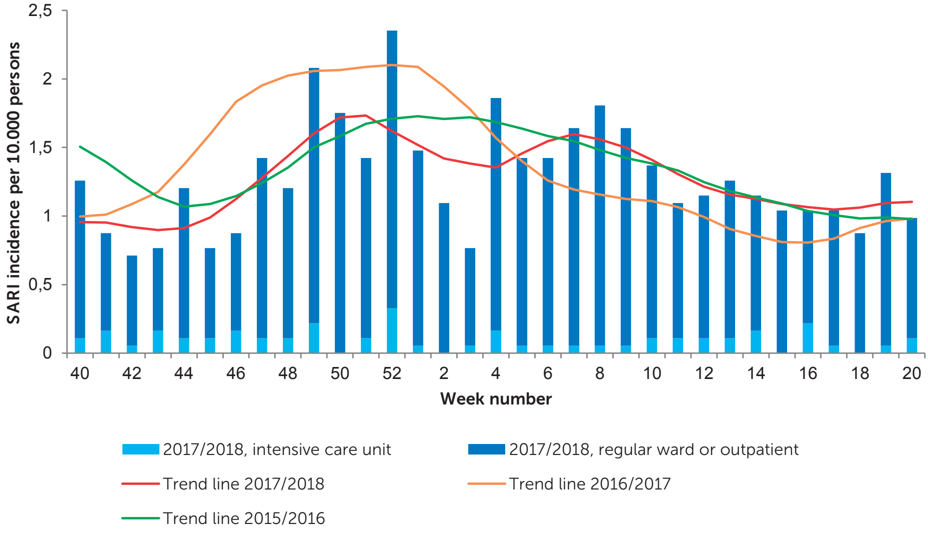

Figure S4a. SARI incidence at the Jeroen Bosch Hospital during influenza season 2017-2018, 2016-2017 and 2015-2016[3]

Although limited historical data on SARI incidence are available from the sentinel surveillance, figure S4a. illustrates that 2017-2018 was a more severe SARI season compared to season 2016-2017 and 2015-2016. The peak of SARI incidence in 2017-2018 was reached in week 10 of 2018, which coincided with the peak in influenza-like illness surveillance (ILI) in primary care.

2

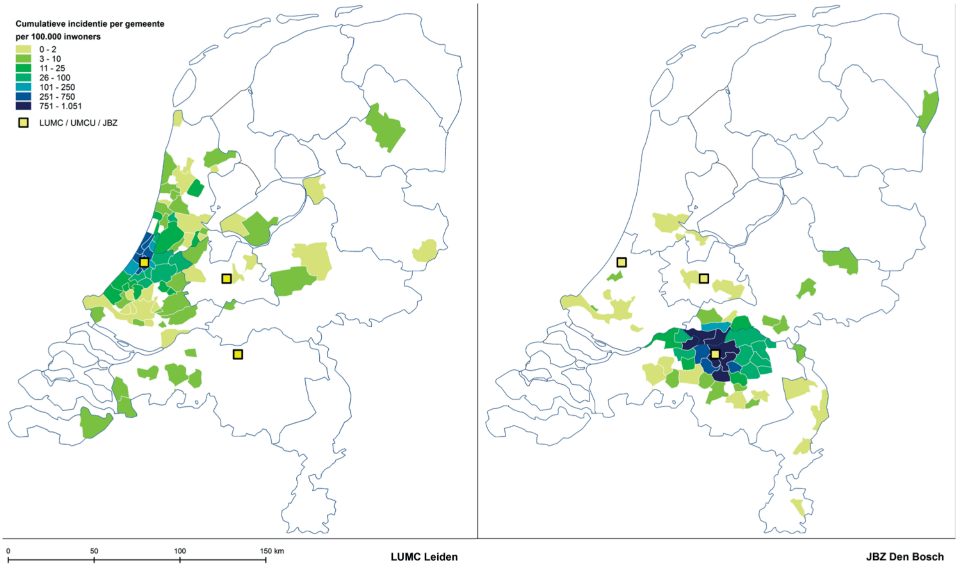

Figure S4b. Catchment population for SARI in Leiden University Medical Center and Jeroen Bosch Hospital

The catchment population was determined by a selection of International Statistical Classification of Diseases and Related Health Problems (ICD-10) codes related to SARI (J00-J22, A15, A16, A48.1, A70 and A78) for each hospital for the years 2014, 2015 and 2016. The largest catchment population belonged to Jeroen Bosch Hospital (323,000 persons) and was less geographically scattered than Leiden University Medical Center (183,000 persons).

Financial coding system

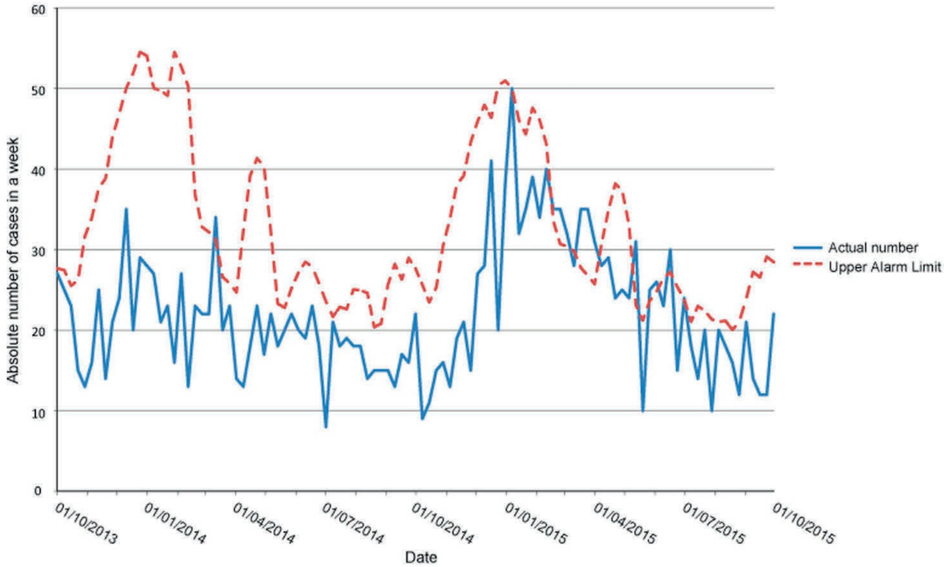

Figure S5. Absolute number of SARI cases per week during 2013-2015 using financial claim codes[4]

The cluster detection system compares real-time data to historical data in the nearest current time window using a cumulative sum method for a moving seven-day period. The threshold for the upper alarm limit (red dotted line) is reached if the incident ratio is more than 1.40. In March-May 2015 an alert was reached, which was part the longest influenza epidemic (21 weeks) recorded in the Netherlands.

Ambulance dispatch calls data

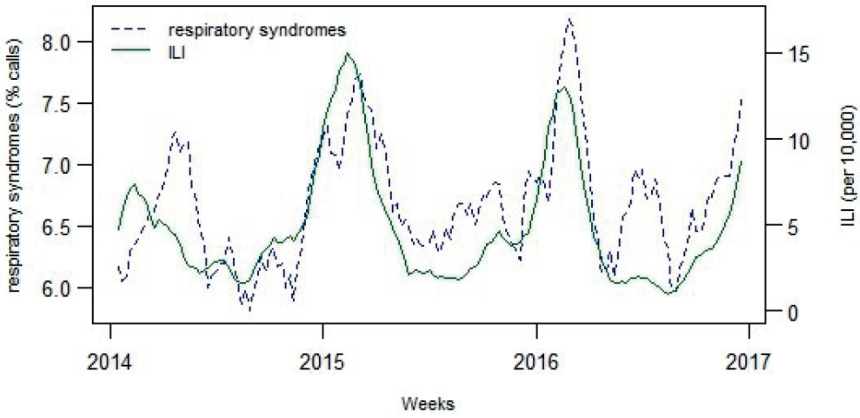

Figure S6. Trends of influenza-like illness in primary care versus respiratory syndromes in ambulance dispatch calls (5-week moving average of the current ±2 weeks; proportion of respiratory syndromes relative to all included calls) in the period 2014-2017[5]

The proportion of respiratory syndromes in ambulance dispatch calls showed a periodic trend with high peaks in winter and lower inter-seasonal peaks. On visual inspection, the winter peaks of respiratory syndromes in ambulances dispatch calls coincide with ILI incidence peaks in 2014-2015 and 2015-2016.

Virological laboratory surveillance

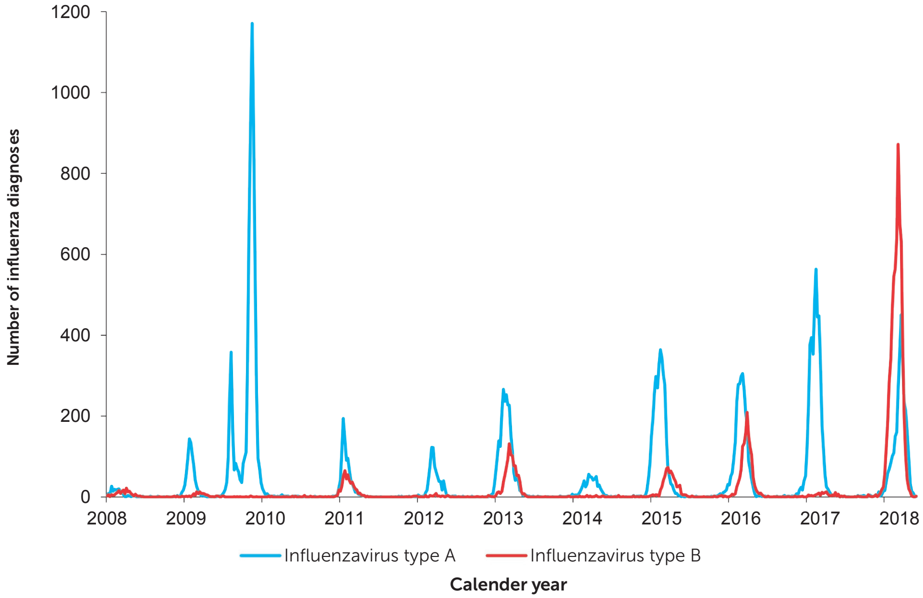

Figure S7. Total number of positive influenza test results in the period 2008-2018 provided by the virological laboratory surveillance[6]

The virological laboratory surveillance comprises multiple pathogens, among which influenza virus is a pathogen with a high burden of disease. These historical data show the variation in detected influenza type virus per season and the number of detected positive influenza virus samples. During the 2009 influenza A(H1N1) pandemic the number of positive influenza virus samples was the highest, taking into consideration that the total number of requested influenza tests was unknown. These laboratory surveillance data would ideally complement a SARI sentinel surveillance system.

Table S8. Severe acute respiratory surveillance systems in Europe

Country	Surveillance type	Reporting facilities	Case definition	Microbiological sampling	Data availability	Data format	Catchment population	Reporting platform
Belgium	SARI sentinel	6 hospitals	Adjusted SARI case definition WHO*	• influenza virus • RSV • parainfluenza • rhino/enterovirus • human metapneumovirus • parechovirus • bocavirus • adenovirus • coronavirus • enterovirus D68	Weekly	Case-based	915,000	[7]; ECDC, WHO
Croatia	SARI sentinel	3 hospitals	Adjusted SARI case definition§	• influenza virus (sub)typing	Weekly	Case-based	1 million	None
Czech Republic	Severe influenza	±180 hospitals (including all ICUs)	Adjusted SARI case definition (WHO)**	• influenza virus	Daily (district) Weekly (national)	Case-based	10.6 million (general population)	[8];ECDC
France	Severe influenza	192 ICUs	Lab-confirmed influenza or probable case of influenza according to clinicians' judgement	• influenza virus	Weekly	Case-based	67 million (general population)	[9]; ECDC
Germany	SARI sentinel	73 hospitals	Primary or secondary ICD-10 codes: J09-J22	None	Weekly	Aggregated	±5 million	[10, 11]
Lithuania	Severe influenza	59 hospitals	Influenza case§§	None	Weekly	Aggregated	Unknown	National
Montenegro	SARI sentinel	9 hospitals	Adjusted SARI case definition WHO§	• influenza virus • RSV	Weekly	Case-based	620,000	[12], ECDC
Norway	Severe influenza	7 hospitals	Lab-confirmed influenza in hospitalised patient	• influenza virus	Weekly	Aggregated	3.6 million	[13, 14]
Portugal	Severe influenza	24 hospitals (33 ICUs)	Lab-confirmed ICU influenza patient	• influenza virus	Weekly	Case-based	Unknown	[15]; ECDC
Republic of Ireland	Severe influenza	44 hospitals (29 ICUs)	EU influenza case definition (only lab-confirmed)	• influenza virus	Near real-time	Case-based	4.8 million (general population)	[16]; ECDC

Table S8. Continued.

Country	Surveillance type	Reporting facilities	Case definition	Microbiological sampling	Data availability	Data format	Catchment population	Reporting platform
Romania	SARI sentinel	19 hospitals	Adjusted SARI case definition WHO†	• influenza virus Sporadically: • RSV • hMPV • parainfluenza • coronavirus • *S. pneumoniae*	Weekly	Case-based	3.6 million	[17]; ECDC
Spain	Influenza sentinel	100 hospitals	SHCIC case definition††	• influenza virus	Weekly	Case-based	24.3 million	[18]; ECDC
Sweden	Severe influenza	±50 ICUs	Lab-confirmed influenza patient in ICU	• influenza virus	Daily	Case-based	Unknown	[19]; ECDC
The Netherlands	SARI sentinel	1 hospital	Financial claim coding related to SARI	None	Weekly	Case-based	323,000	[20]
United Kingdom	Severe influenza	All NHS acute hospital trusts in England, Northern-Ireland, and Scotland	Laboratory confirmed influenza infection	• influenza virus	Weekly	Aggregated	66 million (general population)	[21]

*Acute respiratory infection with onset in the last 7 days, and fever of ≥38 °C, and cough, or dyspnoea, requiring hospitalisation of 24 hours or longer. The first symptoms should have a symptom onset before date of hospitalisation and respiratory swabs should be taken within 10 days of symptom onset.

**An acute respiratory infection with: history of fever or measured fever of ≥38 °C; and cough; with onset within the last 10 days; and requires hospitalization in ICU.

§Acute respiratory disease initiated in the previous 7 days, requiring immediate hospitalization, and includes history of fever or measured fever of ≥38°C and cough, along with shortness of breath or difficulty breathing.

§§Patient must be hospitalised, have a detected diagnosis of influenza, and admitted to the ICU

†Acute respiratory infection having onset in the previous 10 days, which requires hospitalization and includes: history of fever or measured fever of at least 38 °C and cough and shortness of breath or difficulty breathing.

††Any case with clinical features compatible with influenza, requiring hospitalization for clinical severity: at least one of the following criteria: pneumonia, septic shock, acute respiratory distress syndrome, multiple organ dysfunction syndrome, admission to ICU, or death.

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