4.9 Real-time Syndromic Surveillance

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4.9.1   Learning objectives

To understand the key factors underpinning real-time syndromic surveillance systems and the use of syndromic surveillance data in research, including:

1.   The definition of syndromic surveillance;
2.   Data sources for syndromic surveillance;
3.   Governance issues;
4.   Data analysis and statistics;
5.   The application of syndromic surveillance in research.

4.9

4.9.2　Introduction

Syndromic surveillance is the near real-time collection, analysis, interpretation and dissemination of health-related data in order to enable the early identification of the impact (or absence of impact) of potential health threats that may require public health action *(1)*. Although a relatively new field in comparison to more established methods of surveillance (such as using laboratory reports), syndromic surveillance is growing in stature internationally as it becomes recognized as an innovative approach to public health surveillance. The advantages that syndromic surveillance brings to the identification and investigation of public health threats, including those relevant to health emergency and disaster risk management (Health EDRM), include early warning, situational analysis, reassurance and flexibility.

Early warning
Many syndromic surveillance systems operate in near-real-time (daily, for example), allowing the timely identification of, and response to incidents.

Situational awareness
During an incident, syndromic surveillance systems enable further description of healthcare seeking behaviour in near real-time (daily, for example) providing key intelligence to incident managers and response teams (such as identifying particularly affected age groups, geographical clusters).

Reassurance
During mass gatherings and other similar events, syndromic surveillance can often provide reassurance that there have been no widespread acute public health problems, particularly where surveillance is long term and a 'normal' or historical baseline level has been established prior to the event.

Flexibility
By using broad and adaptable syndromes, syndromic surveillance systems can be flexible in responding to a variety of public health demands ranging from infectious disease outbreaks to environmental incidents and mass gatherings, in addition to providing measures of impact of public health interventions – vaccination impact, for example. Syndromic surveillance also has the potential to detect newly emerging threats not covered by existing surveillance systems.

In general, syndromic surveillance makes opportunistic use of anonymized data collected either as part of standard patient care from healthcare service providers, or proxies of population health (for example, information on accessing of health advice from other sources; see also Chapter 2.1). This information is collected by the healthcare provider or advisor, usually during the contact with the patient and before any final confirmation of a diagnosis or cause of illness. The data used for syndromic surveillance therefore contain valuable detail of symptoms, chief complaints, clinical diagnoses, or other proxies for healthcare seeking behaviour. Furthermore, as this information is collected contemporaneously these data can be made available and used for syndromic surveillance purposes very quickly – often the following day, if not sooner *(2)*.

Syndromic surveillance collates the information received and groups it into syndromes of public health relevance (Table 4.9.1). Each syndrome is constructed from the symptoms, chief complaints or clinical diagnoses, as they have been recorded in the patient record. The format of the data is often data provider specific, based on how information is organized and stored in the local patient record, which may use a standardized coding system, a locally used list of clinical terms or even free text. For example, general practitioners (GPs) managing a patient with acutely presenting asthma use clinical codes (such as ICD-10, SNOMED-CT or Read codes *(3–5)*) to record the clinical management of the patient. Asthma monitored in a syndromic surveillance system would be based on the identification of those patient contacts including clinical asthma codes.

Table 4.9.1 Examples of syndromic surveillance syndromes that are flexible in responding to a range of public health threats

Syndrome monitored	Related public health threats
Asthma	Respiratory pathogens, air pollution, chemical incidents, wild or industrial fires, severe thunderstorms
Fever	Influenza, respiratory pathogens, heatwave (infants)
Difficulty breathing	Air pollution, respiratory pathogens, chemical incidents, wild or industrial fires
Diarrhoea and vomiting	Gastrointestinal pathogens, flooding
Conjunctivitis	Respiratory pathogens, chemical incidents, wild or industrial fires, allergic rhinitis
Cough	Influenza, respiratory syncytial virus (children aged <5 years), respiratory pathogens, chemical incidents, wild or industrial fires

Syndromic surveillance does not generally monitor laboratory confirmed reports. Although a lack of laboratory confirmation (and therefore the absence of a direct link to a causal pathogen) presents a potential limitation in the *specificity* of reporting (particularly around infectious diseases), it can also be an advantage as the flexibility of the systems enables greater *sensitivity* due to the broadness of data collected and the volume of information available. The flexibility of syndromic surveillance systems enables them to respond to a variety of public health incidents, ranging from infectious diseases *(6–7)* to environmental events *(8)*, mass gatherings *(9–10)*, terrorism *(11)*, recovery from disasters caused by natural hazards *(12–13)* or investigations of vaccination impact *(14)*. A single syndrome may be relevant to several different public health issues (Table 4.9.1). For example, a newly emerging respiratory pathogen may not be detected by existing laboratory tests, but increases in numbers of presentations, or severity of illness, in symptomatic patients presenting to healthcare services would be captured by syndromic data.

Syndromic surveillance systems also have the advantage of providing wider population surveillance, covering whole regions or countries, at different levels of patient care (from those requesting advice only, to those requiring urgent emergency treatment), providing a picture of the levels of
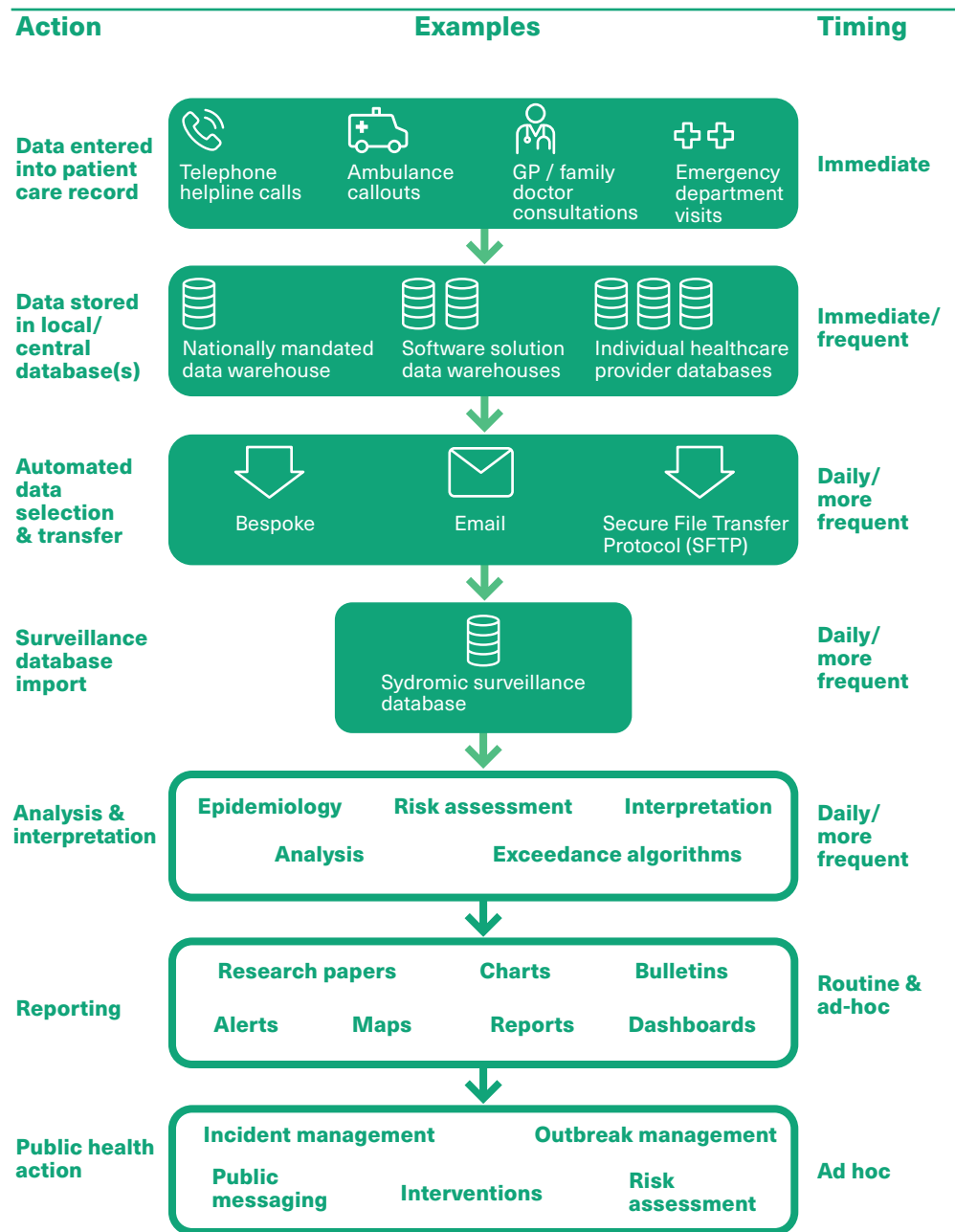
4.9

severity of disease within the community. Laboratory-based surveillance, however, is often biased, based upon only those sampled for testing, which is often limited to patients with ongoing illness, who are more severely ill or hospitalized, or are considered to be at-risk of complications or death. Laboratory surveillance therefore monitors only a fraction of the total burden of disease.

While there are fundamental differences between syndromic and laboratory-based surveillance, it is important that both are synergistic, complementing each other to ensure the delivery of a functioning public health surveillance programme. Without laboratory surveillance, it is difficult to determine the underlying pathogens driving seasonal trends in syndromic data; without syndromic surveillance, it is difficult to establish representative community-based estimates of burden.

The collection of information for syndromic surveillance is normally automated, with electronic transmission of anonymized data from healthcare service providers to public health organizations. Figure 4.9.1 illustrates how health data might flow in a multi-partite syndromic surveillance system. The automation of data collection removes the requirement to ask data providers to undertake additional time-consuming tasks or to remember to flag individual records for inclusion in a syndromic surveillance system. Automation is critical to the success of such systems, especially those based upon healthcare services. Data are collected as part of the usual patient care or advice process. No extra steps or changes to working practices are required by the data providers for syndromic surveillance to be possible.

Figure 4.9.1 Example data flow for a multi-partite syndromic surveillance service

Action	Examples	Timing
Data entered into patient care record	Telephone helpline calls — Ambulance callouts — GP / family doctor consultations — Emergency department visits	**Immediate**
Data stored in local/ central database(s)	Nationally mandated data warehouse — Software solution data warehouses — Individual healthcare provider databases	**Immediate/ frequent**
Automated data selection & transfer	Bespoke — Email — Secure File Transfer Protocol (SFTP)	**Daily/ more frequent**
Surveillance database import	Sydromic surveillance database	**Daily/ more frequent**
Analysis & interpretation	Epidemiology — Risk assessment — Interpretation — Analysis — Exceedance algorithms	**Daily/ more frequent**
Reporting	Research papers — Charts — Bulletins — Alerts — Maps — Reports — Dashboards	**Routine & ad-hoc**
Public health action	Incident management — Outbreak management — Public messaging — Interventions — Risk assessment	**Ad hoc**

Source: Public Health England Real-time Syndromic Surveillance Team.

337

4.9

4.9.3   Data sources for syndromic surveillance

Data for syndromic surveillance are commonly sought from a range of healthcare services including primary care providers or GPs, emergency departments (EDs), telehealth services and ambulance services.

Primary care/general practitioners/physicians/family doctors
Primary care surveillance is often considered a gold standard for assessing community morbidity. Syndromes are usually constructed using clinical diagnoses as recorded by the treating physician at the time of the consultation.

Emergency departments
EDs are frequently used for syndromic surveillance, particularly in countries where access to primary care data may not be readily available. ED surveillance provides a metric for more severe presentation of disease or conditions. Syndromes may be constructed from chief or presenting complaints, or clinical diagnoses, depending on the timescale at which the information is available.

Telehealth services
Telehealth surveillance can provide access to populations not captured through ED or primary care surveillance, such as those who are less ill and require advice, rather than urgent care. Traditionally considered to provide early warning over other systems, the syndromes used are based on patient reported symptoms and may have the lowest specificity.

Ambulance services
Monitoring ambulance dispatch calls can provide an additional measure of acute, potentially more severe presentation of diseases or conditions in public health surveillance.

Outside the healthcare setting, many additional data sources have been used for syndromic surveillance. School absenteeism, employee absenteeism and over the counter pharmacy sales are examples where data represent proxies for disease. These sources have been usefully adopted for monitoring the health of the population *(15)*.

In recent years, with the advent and increasing use of digital platforms to access healthcare and advice, more public health resource has focused on assessing the potential benefits of using 'digital data' such as web searches (such as Google *(16)*), social media activity (such as Twitter *(17)*) and online health services (an online 'symptom-checker', for example *(18)*). The methods used for accessing and collecting data continue to develop, evolving from platforms such as messaging services (for example, HL7 *(19)*) to techniques suited for trawling big data (for example, data mining or natural language processing *(20)*.

4.9.4   Governance

Although it is often overlooked in the published syndromic surveillance literature, the adherence to good governance and data security practices around the collection, storage, processing and use of healthcare data for syndromic surveillance is important. Establishing a syndromic surveillance system (either at national or subnational level) requires multiple phases undertaken by a multi-disciplinary group. This has previously been described by experienced exponents of syndromic surveillance *(1)*. However, one of the key areas that will determine the sustainability of a system is establishing appropriate governance arrangements with data providers to assure the correct use and secure storage of data, as well as the competence of trained specialist staff accessing, analysing and interpreting data. Without such assurances, data are unlikely to be made available for syndromic surveillance.

The governance arrangements underpinning syndromic surveillance systems are equally essential for the long-term success of systems. Without appropriate governance, these surveillance systems are not fit for purpose and are likely to fail. Alongside governance, appropriate management and oversight of syndromic surveillance systems is important for their success, with collaboration between data providers and public health intelligence teams to steer the development and management of the systems. Management through steering or strategic groups, including senior members from all organizations involved in delivering the system is crucial to long term success, fruitful outputs and assurance of the public health benefits of the surveillance system. Collaboration may involve a wide range of organizations including data providers, technology firms providing data collection or transfer systems, public health bodies, clinical groups, academics and professional bodies. Furthermore, these steering groups might be used as a conduit to ensure that research undertaken using the syndromic surveillance data is appropriate (that is, with a public health focus), undertaken with appropriate rigour and, most importantly, that it does not undermine any organization involved in the collaborative surveillance system.

4.9.5   Analysis of syndromic surveillance data

There are many methods used to routinely analyse syndromic surveillance data. The underlying principle of syndromic surveillance is the analysis of trends, rather than identifying individual cases. Traditional descriptive epidemiological methods can be used to examine patterns in disease over time, by person and place, and formal statistical tests can be used to detect anomalies (Figure 4.9.2).

Time
Syndromic surveillance data are analysed over time to identify short term increases in syndromes (suggesting outbreaks of disease, for example), environmental impacts (air pollution, for example) and long-term changes in trend (suggesting changes in disease burden).

Person
Data can be broken down by patient demographics (such as age or gender) to identify changes in burden, which may be indicative of public health threats.

4.9

Place

Where possible, links to the location of the patient (either area of residence or place of healthcare consultation) can be used to identify clusters or map the spread of activity.
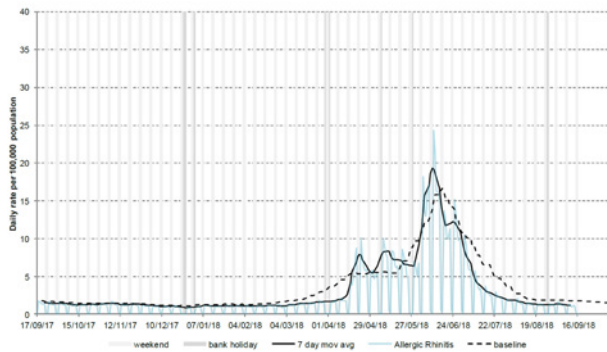
Anomaly detection

Statistical algorithms are used to automatically identify unusual activity. Statistical tests can also be used for anomaly detection or aid interpretation of syndromic data. A wide range of different statistical methods have been used for anomaly detection, including control charts, regression and time series analysis (21–22). Statistical methods can also be applied to the development of historical baselines, which can supplement the interpretation of syndromic data by comparing the observed values to historically expected levels (23).

A further important consideration is the translation of complex information (as produced by epidemiological or statistical analyses) into public health action, a core component of the definition of surveillance (24). This element of syndromic surveillance is not well described in the literature but there are examples available of risk assessment processes designed to assess statistical exceedances by examining relevant epidemiological information and assigning an appropriate response – for example, whether no further action is required, or whether the information needs to be sent to a relevant public health expert for further action (25).

Figure 4.9.2 Analysis of syndromic surveillance data using A) time, B) person, C) place and D) anomaly detection
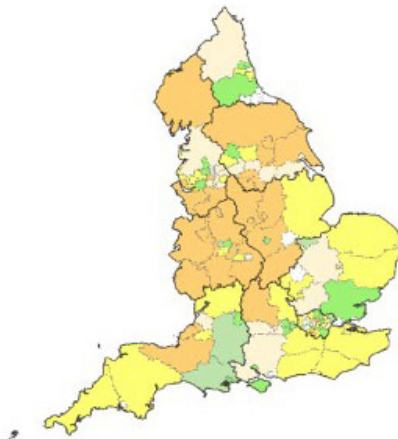
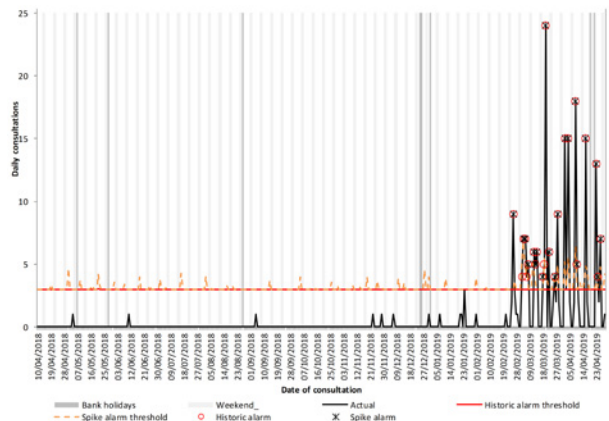**A. Time:** daily GP consultation rate for allergic rhinitis

B. Person: telehealth calls for eye problems by age group
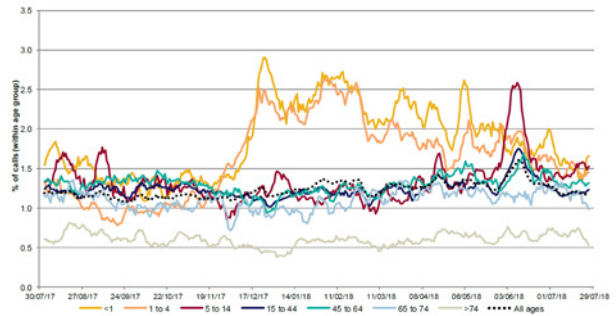
C. Place: map of GP consultations for influenza-like illness (England)

D. Anomaly detection: daily statistical exceedances for mumps

Source: PHE Real-time Syndromic Surveillance Team
Map contains Ordnance Survey data. ©Crown copyright and database right 2018. Contains National Statistics data.

4.9

4.9.6   Using syndromic surveillance in research

The collection of health data to deliver real-time syndromic surveillance can provide a rich resource for Health EDRM researchers to address important public health questions. Alongside the use of other sources of public health data, a wide range of research methods outlined elsewhere in this book can be used alongside syndromic surveillance data. However, syndromic surveillance data are not collected specifically for research purposes and therefore when considering the use of syndromic surveillance data in research, it is important to understand several key limitations of these data, which might limit their application in certain research projects (Table 4.9.2).

Table 4.9.2 Limitations of syndromic surveillance data that need to be assessed when considering its use in research projects

Limitation	Detail
Anonymized records	Syndromic data tend to be anonymised and therefore patient-level data cannot be linked to other records or databases and cannot be used to trace patients or undertake further studies (for example, selecting controls for case-control type analysis)
Population level	Syndromic data tend to be aggregated to population level and often cannot be used for secondary analyses on an individual level
System coverage	Some syndromic systems do not have full or representative coverage geographically (country or region), or person level (such as different age groups: paediatric or adult EDs) or other limitations on access to healthcare
Coding	Clinical coding used to define syndromes can be limited or very generic or, if free text is provided this might require additional analytical skills
Symptom based	Syndromic data are not based on confirmed laboratory reports and, therefore, are not directly attributable to specific pathogens
Data quality	Syndromic data are not 'cleaned' before being used for surveillance. Consequently, compared to other health data sources used by researchers, there is a greater risk of data errors (for example, duplications, miss-entry of age data, incorrect coding or incomplete data fields)
Incomplete data	Syndromic data only uses data available in real-time, taking a 'snapshot' of daily activity. Therefore some data will be excluded due to transfer issues or time taken to confirm diagnoses. For example, most GP pneumonia diagnoses occur after laboratory confirmation and are not available in a next-day extract.

Case Studies 4.9.1, 4.9.2 and 4.9.3 describe examples of published research projects where syndromic surveillance data have been used to respond to a public health problem.

Case Study 4.9.1
Assessing potential health impacts of mass gatherings and sporting events *(26)*

Mass gatherings can impact on the health of the public, including both infectious and non-communicable diseases or conditions. Specifically, the increased risk from infectious diseases includes importation, exposure of visitors to endemic diseases in the host country and increased disease transmission across large populations gathered in one location. Surveillance during mass gatherings is needed to identify and quantify any impact (or reassure that there is an absence of impact) on public health in a timely manner. Subsequently, research on specific areas following an event can inform priorities for healthcare providers and public health organizations at future events.

Large sporting events (for example, the Olympics or world or continental football championships) have the potential to influence the behaviour of the population, and increase (or decrease) demand on health services around the timings of individual events. Of particular note, the impact of sporting events on ED attendances has been documented *(26)*. The 2016 European Football Championship (Euro 2016) was hosted in France, involving 24 nations with 51 matches during a four-week period. To assess the potential impact of Euro 2016 on healthcare seeking behaviour in different nations, syndromic surveillance ED data from four participating countries (England, France, Northern Ireland and Wales) were analysed retrospectively to identify any relevant impacts of matches played. This study focussed on hourly ED attendances across each country. In the four hours before matches were played by the national team, attendances were statistically significantly lower than would be expected in all countries, and reduced further during matches. Following the completion of matches, there was no consistent significant increase in attendances. However, these observed impacts were highly variable between individual matches. For example, in the four hours after the final match, involving France, the number of ED attendances in France increased significantly. Overall, these results indicated relatively small impacts of major sporting events upon ED attendances.

4.9

Case Study 4.9.2
Assessing the impact of air pollution on health using syndromic surveillance *(27, 28)*

Globally, air pollution is the biggest environmental risk to health, carrying responsibility for about one in every nine deaths annually. It is estimated that 91% of the world's population lives in places where air quality exceeds WHO guideline limits *(29)*. Syndromic surveillance systems present an opportunity to assess the acute impact of air pollution on the health of the population. The utility of syndromic surveillance for this purpose has been demonstrated by the identification and monitoring of healthcare seeking behaviour during periods of poor air quality (air pollution). In this scenario, research involving syndromic surveillance data would require a methodological approach to determine whether existing data collected prospectively over a defined time period can be assessed against air quality data. Different research methods may include using numbers or rates for each syndrome or statistical exceedance data to identify periods of unusual syndromic activity. These events can then be compared to air quality data highlighting periods of poor air quality to identify concurrent activity.

More complex research approaches may incorporate the inclusion of further variables and confounders, which might influence the outcome of the relationship between healthcare seeking behaviour and air quality. For example, meteorological variables (such as temperature), environmental variables (such as pollen and spore counts) or pathogen activity (such as influenza laboratory reports) can all be included in models which explore the relationship between air quality and syndromic data. The results of this research can be used to assure prospective surveillance during air pollution incidents by providing baselines for future interventions and adding to the knowledge base. Furthermore, this research provides information on the specificity and sensitivity of syndromic surveillance systems and uses syndromic surveillance data to explore which pollutants drive changes in healthcare seeking behaviours *(28)*.

Case Study 4.9.3
Determining the likely impact of a new vaccine programme using syndromic surveillance *(14)*

Syndromic surveillance can contribute to research investigating the impact of public health interventions, for example, the impact of the introduction of new vaccines on the health of the population. Whilst national vaccination programmes will employ large scale evaluations to assess the impact of the new vaccine on confirmed outcomes, syndromic surveillance can contribute a rapid assessment of the impact. An anticipated outcome of the introduction of a new vaccine might be reduced disease incidence and thus fewer healthcare visits, something which is measured by syndromic surveillance as standard.

Interrupted time series and 'before-after' study methods (Chapter 4.1) can be used to assess the impact of a new vaccine on the demand for healthcare services. These research methods involve measuring the outcome of interest before and after the programme, service or intervention has been implemented. Syndromic data collected before the introduction of the intervention are compared to equivalent data collected after the event. Statistical comparisons of syndromic surveillance data, for example, in pre- and post-vaccine periods, can inform the interpretation of the likely impact of the intervention or vaccine.

In the United Kingdom, rotavirus vaccine was introduced in 2013 and integrated into the routine immunization schedule for young infants. Syndromic surveillance was used to provide an early indication of the potential impact of the introduction of the rotavirus vaccine. Syndromes were chosen based on the anticipated outcome affected by the introduction of the vaccine: GP and ED gastroenteritis, diarrhoea and vomiting syndromes were retrospectively assessed across different age groups, but particularly focussed on young children. Incidence rate ratios (IRRs) were used to compare (statistically) the period of activity pre-vaccine introduction with activity post-vaccine. IRRs showed an approximate 30% decrease in gastroenteritis incidence in infants and children aged 1 to 4 years.

Syndromic surveillance thus revealed a marked decline in gastroenteritis, coinciding with the introduction of the new rotavirus vaccine programme in England (*14)*. This model for contributing to the assessment of the impact of vaccine has been applied to other areas including the live attenuated influenza vaccine *(30)* and meningococcal B vaccine *(31)*, and will be applied to future vaccines as and when they are licensed and introduced (such as respiratory syncytial virus, norovirus).

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4.9.7 Conclusions

Syndromic surveillance can complement existing public health surveillance programmes, introducing new intelligence for identifying and managing incidents. The flexibility of these systems supports a range of public health issues, including infectious disease activity to Health EDRM. Healthcare service data have traditionally underpinned syndromic surveillance systems, however, novel sources including social media and internet-based data are being explored for their potential added benefit.

4.9.8 Key messages

o **Syndromic surveillance systems can augment existing public health surveillance programmes, providing early warning and introducing real-time intelligence and reassurance at a national, regional and local level.**

o **Compared to traditional surveillance systems, syndromic surveillance can provide a more flexible approach to surveillance, enabling multi-purpose surveillance including emerging threats.**

o **Adherence to good governance and data security practices around the collection, storage, processing and use of syndromic surveillance data is essential for the long-term success of systems.**

o **Syndromic surveillance data are a valuable resource for public health research, including in Health EDRM, but specific limitations of syndromic surveillance for research need to be considered.**

o **Syndromic surveillance systems gain value in research data sources when operated consistently over time enabling comparison to historical data.**

4.9.9 Further reading

Conway M, Dowling JN, Chapman WW. Using chief complaints for syndromic surveillance: a review of chief complaint based classifiers in North America. Journal of Biomedical Informatics; 2013: 46: 734-43.

Josseran L, Fouillet A, Caillere N, Brun-Ney D, Ilef D, Brucker G, et al. Assessment of a syndromic surveillance system based on morbidity data: results from the Oscour network during a heat wave. PLoS One;2010: 5: e11984.

Smith GE, Elliot AJ, Ibbotson S, Morbey R, Edeghere O, Hawker J, et al. Novel public health risk assessment process developed to support syndromic surveillance for the 2012 Olympic and Paralympic Games. Journal of Public Health;2017: 39: e111-e7.

Triple-S: Syndromic Surveillance Systems in Europe. Guidelines for designing and implementing a syndromic surveillance system. 2013. https://webgate.ec.europa.eu/chafea_pdb/assets/files/pdb/20091112/20091112_d08_giss_en_ps.pdf (accessed 15 January 2020).

Yoon PW, Ising AI, Gunn JE, editors. Syndromic surveillance: the value of real-time data for public health action. Public Health Reports; 2017: 132: 1S-126S.

4.9.10 References

1. Triple-S: Syndromic Surveillance Systems in Europe (2013). Guidelines for designing and implementing a syndromic surveillance system https://webgate.ec.europa.eu/chafea_pdb/assets/files/pdb/20091112/20091112_d08_giss_en_ps.pdf (accessed 15 January 2020).

2. Henning KJ. What is syndromic surveillance? MMWR Supplements; 2004: 53: 5-11.

3. de Lusignan S. Codes, classifications, terminologies and nomenclatures: definition, development and application in practice. Informatics in Primary Care; 2005: 13: 65-70.

4. International Health Terminology Standards Development Organisation. SNOMED-CT. 2012 http://www.ihtsdo.org/snomed-ct (accessed 15 January 2020).

5. International Classification of Disease – version 10 (ICD-10). WHO. 2016. https://www.who.int/classifications/icd/icdonlineversions/en (accessed 15 January 2020).

6. Olson DR, Heffernan RT, Paladini M, Konty K, Weiss D, Mostashari F. Monitoring the impact of influenza by age: emergency department fever and respiratory complaint surveillance in New York City. PLoS Medicine; 2007: 4: e247.

7. Hughes SL, Morbey RA, Elliot AJ, McEwen SA, Greer AL, Young I, et al. Monitoring telehealth vomiting calls as a potential public health early warning system for seasonal norovirus activity in Ontario, Canada. Epidemiology and Infection; 2019: 147: e112.

4.9

8. Josseran L, Fouillet A, Caillere N, Brun-Ney D, Ilef D, Brucker G, et al. Assessment of a syndromic surveillance system based on morbidity data: results from the Oscour network during a heat wave. PLoS ONE; 2010: 5: e11984.

9. Fleischauer AT, Gaines J. Enhancing surveillance for mass gatherings: the role of syndromic surveillance. Public Health Reports; 2017: 132: 95S-8S.

10. McCloskey B, Endericks T, Catchpole M, Zambon M, McLauchlin J, Shetty N, et al. London 2012 Olympic and Paralympic Games: public health surveillance and epidemiology. Lancet, 2014: 383: 2083-9.

11. Vandentorren S, Paty AC, Baffert E, Chansard P, Caserio-Schonemann C. Syndromic surveillance during the Paris terrorist attacks. Lancet; 2016: 387: 846-7.

12. Griffith MM, Yahata Y, Irie F, Kamiya H, Watanabe A, Kobayashi Y, et al. Evaluation of an ad hoc paper-based syndromic surveillance system in Ibaraki evacuation centres following the 2011 Great East Japan Earthquake and Tsunami. Western Pacific Surveillance and Response Journal; 2018: 9: 21-7.

13. Tante S, Villa E, Pacho A, Galvan MA, Corpuz A. Which surveillance systems were operational after Typhoon Haiyan? Western Pacific Surveillance and Response Journal; 2015: 6: 66-70.

14. Bawa Z, Elliot AJ, Morbey RA, Ladhani S, Cunliffe NA, O'Brien SJ, et al. Assessing the likely impact of a rotavirus vaccination program in England: the contribution of syndromic surveillance. Clinical Infectious Diseases; 2015: 61: 77-85.

15. Heffernan R, Mostashari F, Das D, Besculides M, Rodriguez C, Greenko J, et al. New York City syndromic surveillance systems. MMWR Supplements; 2004: 53: 23-7.

16. Nuti SV, Wayda B, Ranasinghe I, Wang S, Dreyer RP, Chen SI, et al. The use of google trends in health care research: a systematic review. PLoS ONE; 2014: 9: e109583.

17. Gesualdo F, Stilo G, Agricola E, Gonfiantini MV, Pandolfi E, Velardi P, et al. Influenza-like illness surveillance on Twitter through automated learning of naive language. PLoS ONE; 2013: 8: e82489.

18. Elliot AJ, Kara EO, Loveridge P, Bawa Z, Morbey RA, Moth M, et al. Internet-based remote health self-checker symptom data as an adjuvant to a national syndromic surveillance system. Epidemiology and Infection; 2015: 143: 3416-22.

19. Health Level 7 International. HL7 International. 2019. http://www.hl7.org/about (accessed 15 January 2020).

20. Ye Y, Tsui FR, Wagner M, Espino JU, Li Q. Influenza detection from emergency department reports using natural language processing and Bayesian network classifiers. Journal of the American Medical Informatics Association; 2014: 21: 815-23.

21. Noufaily A, Morbey RA, Colon-Gonzalez FJ, Elliot AJ, Smith GE, Lake IR, et al. Comparison of statistical algorithms for daily syndromic surveillance aberration detection. Bioinformatics; 2019: 35: 3110-8.

22. Unkel S, Farrington CP, Garthwaite H, Robertson C, Andrews N. Statistical methods for the prospective detection of infectious disease outbreaks: a review. Journal of the Royal Statistical Society Series A (Statistics in Society) 2012: 175: 49-82.

23. Harcourt SE, Morbey RA, Smith GE, Loveridge P, Green HK, Pebody R, et al. Developing influenza and respiratory syncytial virus activity thresholds for syndromic surveillance in England. Epidemiology and Infection; 2019: 147: e163, 1–7.

24. Porta M. A Dictionary of Epidemiology: Oxford University Press, USA; 2008.

25. Smith GE, Elliot AJ, Ibbotson S, Morbey R, Edeghere O, Hawker J, et al. Novel public health risk assessment process developed to support syndromic surveillance for the 2012 Olympic and Paralympic Games. Journal of Public Health; 2017: 39: e111-e7.

26. Hughes HE, Colon-Gonzalez FJ, Fouillet A, Elliot AJ, Caserio-Schonemann C, Hughes TC, et al. The influence of a major sporting event upon emergency department attendances; A retrospective cross-national European study. PLoS ONE; 2018: 13: e0198665.

27. Harcourt S, Izon-Cooper L, Colón-González FD, Morbey R, Smith G, Bradley N, et al. Using real-time syndromic surveillance to monitor the health effects of air pollution. Online Journal of Public Health Informatics 2018: 10(1): e85.

28. Smith GE, Bawa Z, Macklin Y, Morbey R, Dobney A, Vardoulakis S, et al. Using real-time syndromic surveillance systems to help explore the acute impact of the air pollution incident of March/April 2014 in England. Environmental Research; 2015: 136: 500-4.

29. Ambient air pollution: a global assessment of exposure and burden of disease. WHO. 2016 https://www.who.int/phe/publications/air-pollution-global-assessment/en (accessed 15 January 2020).

30. Pebody RG, Sinnathamby MA, Warburton F, Andrews N, Boddington NL, Zhao H, et al. Uptake and impact of vaccinating primary school-age children against influenza: experiences of a live attenuated influenza vaccine programme, England, 2015/16. Eurosurveillance; 2018: 23: pii=1700496.

31. Harcourt S, Morbey RA, Bates C, Carter H, Ladhani SN, de Lusignan S, et al. Estimating primary care attendance rates for fever in infants after meningococcal B vaccination in England using national syndromic surveillance data. Vaccine; 2018: 36: 565-71.