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A practical approach to designing syndromic surveillance systems for livestock and poultry

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ABSTRACT

The field of animal syndromic surveillance (SyS) is growing, with many systems being developed worldwide. Now is an appropriate time to share ideas and lessons learned from early SyS design and implementation. Based on our practical experience in animal health SyS, with additions from the public health and animal health SyS literature, we put forward for discussion a 6-step approach to designing SyS systems for livestock and poultry.

The first step is to formalise policy and surveillance goals which are considerate of stakeholder expectations and reflect priority issues (1). Next, it is important to find consensus on national priority diseases and identify current surveillance gaps. The geographic, demographic, and temporal coverage of the system must be carefully assessed (2). A minimum dataset for SyS that includes the essential data to achieve all surveillance objectives while minimizing the amount of data collected should be defined. One can then compile an inventory of the data sources available and evaluate each using the criteria developed (3). A list of syndromes should then be produced for all data sources. Cases can be classified into syndrome classes and the data can be converted into time series (4). Based on the characteristics of the syndrome-time series, the length of historic data available and the type of outbreaks the system must detect, different aberration detection algorithms can be tested (5). Finally, it is essential to develop a minimally acceptable response protocol for each statistical signal produced (6).

Important outcomes of this pre-operational phase should be building of a national network of experts and collective action and evaluation plans. While some of the more applied steps (4 and 5) are currently receiving consideration, more emphasis should be put on earlier conceptual steps by decision makers and surveillance developers (1–3).

1. Introduction

Animal health surveillance is no longer restricted to field personnel investigating animal health on farms, but has expanded to include epidemiologists who are "more in touch – electronically – with global animal health developments" and who carry out their surveillance duties on national or sub-national levels (Kellar, 2012). The political and economic drivers of cost-effectiveness and new technologies have fostered new approaches to surveillance systems. Syndromic surveillance (SyS) is one of them. Syndromic surveillance is not based on laboratory confirmed diagnoses of a disease, but on non-specific health indicators including clinical signs and other proxy measures (e.g. absenteeism, drug sales, decrease in animal production etc.) that are potential indicators (or "syndromes") of change in the disease status of a population (Triple-S definition: http://www.syndromicsurveillance.eu). Advances

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in electronic data capture, transfer, storage, analysis and visualization technologies during the past decade have made the collection and storage of large amounts of meaningful health and health-related digital data possible by non-specialists. This has created an opportunity for SyS implementation as SyS is often a secondary use of health-related data which are collected for other primary purposes (e.g. payment of subsidies, calculations of breeding values, managing veterinary practices etc.).

SyS systems have become relatively common in public health surveillance following 2001 when threats of bioterrorism on US soil motivated the creation of such systems (Reingold, 2003). Because SyS can use existing data, SyS may be a more cost-effective alternative for the detection of unexpected disease events when the diseases are believed to be absent in the population or at low prevalence. Studies have shown that SyS can complement traditional surveillance by detecting patterns not visible in passive diagnostic laboratory surveillance (Amezcua et al., 2013); or by detecting outbreaks earlier than conventional surveillance (e.g. Bluetongue in the Netherlands (Elbers et al., 2008)). It is unlikely that SyS will replace more traditional animal disease surveillance such as reportable disease programs, slaughter surveillance or repeated population based disease surveys. However, SyS has the potential to complement these methods by producing different health-related information. SyS can be adapted to data coming from almost any point on a livestock production chain or any point along the continuum from the introduction of a new to pathogen into a naïve population to the production of a disease epidemic (Dórea et al., 2011). SyS can therefore target points along the production chain or disease continuum that are not covered by traditional surveillance, filing in surveillance coverage gaps. Combining SyS and traditional surveillance methods into one system has the potential to broaden the overall coverage of livestock populations, potentially enabling earlier outbreak detection (Elbers et al., 2008).

While the interest in SyS is growing, it is only in the last 5 years that its potential application for animal health surveillance has been explored. Dórea et al. (2011) reviewed SyS systems based on the systematic monitoring of animal populations for outbreak detection and reported 11 animal health SyS systems from 7 countries (Australia, Canada, France, Netherlands, New Zealand, United Kingdom, USA). A more recent inventory of SyS in Europe (Dupuy et al., 2013), based on the wider Triple-S definition of SyS, identified 27 veterinary SyS projects. However, only 12 of these were operational, the rest being in the pilot or exploratory phase, as opposed to 22 (out of 33) active human SyS in Europe (Conti et al., 2012).

Despite the growing interest in SyS, there is little practical information to guide animal health SyS developers in developing and operating a SyS system. There are some publications describing methods for animal health surveillance in general that are relevant to SyS. These include: key terms and concepts for animal-health surveillance (Hoinville et al., 2013); key methods for surveillance (Salman, 2003); a conceptual framework for population health surveillance and foreign animal disease surveillance (El Allaki et al., 2012); surveillance to document freedom from animal diseases (Christensen, 2012) and methods for evaluating animal health surveillance (Hadorn et al., 2008; Hendrikx et al., 2011). The Animal and Plant Health Inspection Services (APHIS) from the US Department of Agriculture have also published standards focused on (1) key components, (2) data, and (3) information management for surveillance systems (Centers for Epidemiology and Animal Health, 2006). Similarly, the Department for Food and Rural Affairs (DEFRA) has published a list of surveillance system requirements for the UK (Defra, 2012). Many SyS resources are available from the public health surveillance sector that may have relevance to animal health SyS. For example there are methods available for the early detection of disease outbreaks (Wagner et al., 2006); recommendations for SyS systems for bioterrorism preparedness (Mandl et al., 2004); many approaches for selecting, fitting and evaluating event detection algorithms (Buckeridge, 2007); and methods for evaluating public health syndromic surveillance (Buckeridge et al., 2004).

To the authors' knowledge, no practical, animal health specific SyS guidelines have yet been published. This is likely because SyS in animals is relatively new and also because there is considerable variation among the approaches to SyS for livestock (Dórea et al., 2011; Dupuy et al., 2013). In this paper, we propose, a practical approach to designing a SyS system for livestock and poultry.

2. Proposed approach

Our 6-step proposed approach (Fig. 1) loosely follows the population health surveillance theory presented in (El Allaki et al., 2012). The latter is made of four sequential interrelated phases: phase (1) recognizing a trigger or a need for surveillance; phase (2) formulating the problem; phase (3) planning the surveillance system; and phase (4) implementing and evaluating the system. Population health surveillance is an activity that targets populations as opposed to individuals; produces information relating to specific diseases of importance (prioritizes diseases for surveillance), and is conducted by organizations of people, therefore requiring group-based decision making (El Allaki et al., 2012). Our process recognizes these attributes, and at the same time provides practical approaches that are specific to designing and implementing SyS for livestock and poultry.

2.1. Define the purpose and goals of a national livestock SyS

In the words of A. Reingold, "If SyS is the answer, what is the question?" (Reingold, 2003). Public health SyS was originally conceived and implemented for the purpose of early detection of a large-scale release of bioterrorist agent (Reingold, 2003). Current public health SyS goals reach beyond bioterrorism preparedness and include detecting the changing incidence of nonspecific mild illnesses (Mostashari and Hartman, 2003). Similarly, many livestock SyS systems currently focus on the early detection of emerging diseases; however other surveillance goals

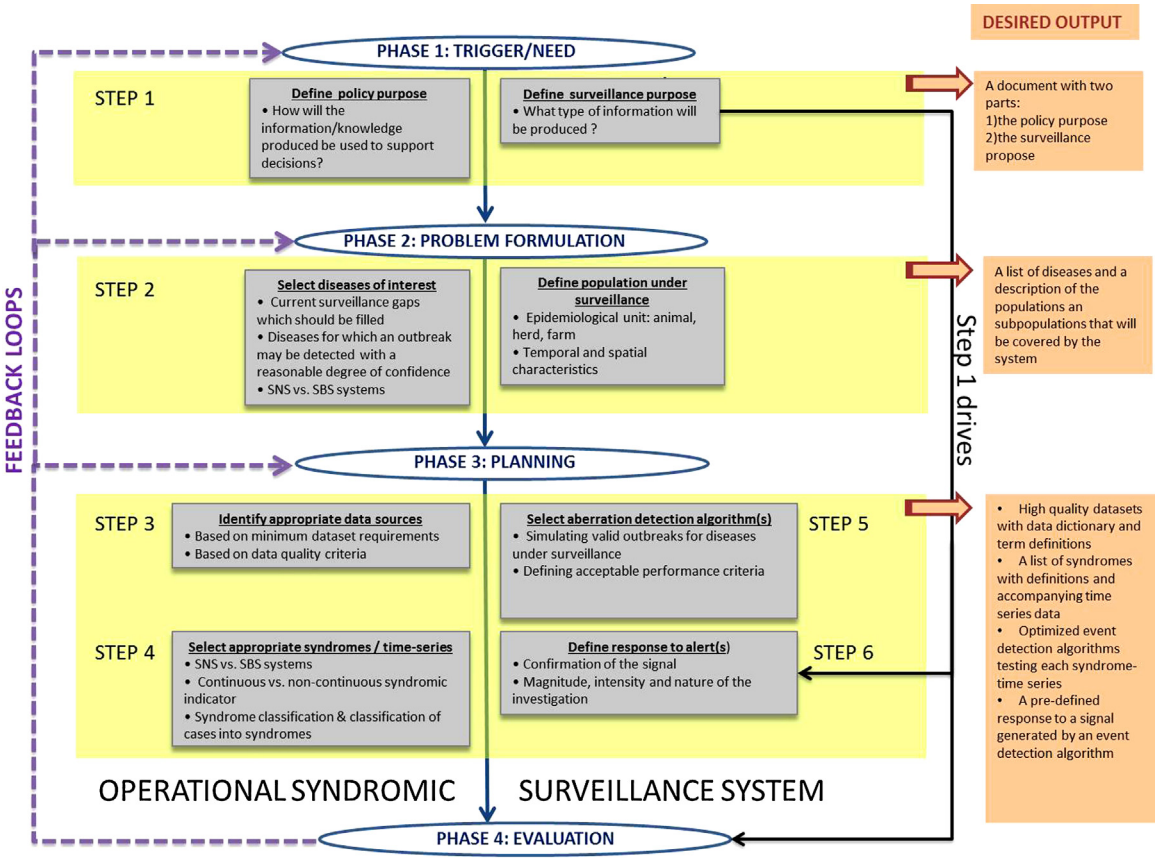

Fig. 1. Proposed conceptual steps to be undertaken before operating a national SyS system.

have been proposed (Table 1). Since livestock SyS is a relatively new addition to the surveillance toolbox, it is likely that the full utility of SyS has yet to be discovered and we expect the range of achievable goals to expand as animal health SyS continues to grow.

The SyS purpose is critically important because it will guide the design of the SyS, define the SyS outcomes and information produced, and provide standards against which the SyS will be evaluated. When defining the purpose it is important to distinguish between the "surveillance purpose", which describes the type of information that will be produced by the SyS, and the "policy purpose" which describes how this information will be used to support decisions (Hoinville et al., 2013). The latter can be thought of as the need that triggered the development process. As pointed out above, public health SyS was originally implemented to address the need for surveillance to detect the release of a bioterrorist agent. Animal health policy purposes can include planning disease control and eradication programs (how should different threats be ranked/prioritised); maintaining a healthy and sustainable food and farming industry; documenting disease risk as a basis for trust in international trade in animals and animal products; providing situational awareness during disease outbreaks; or supporting national economic development (Hoinville et al., 2013). Since surveillance aims to produce information that will be used by decision or policy makers, it will be the policy purpose that drives the type of information that is expected to be produced by the surveillance activity, and ultimately the nature of the surveillance activity.

The first step in our proposed approach is to develop a process for establishing reasonable and achievable goals for SyS. We do so by defining the need or policy purpose and then use it to define more specific surveillance goals. We expect both the need and policy purpose of SyS systems to be different for systems operated by livestock industry groups versus government agencies. While government and industry share many common animal health goals, there are some differences. For instance, government SyS activities might be restricted to diseases that affect trade or public health, whereas industry groups might be interested in SyS for a broader range of diseases, including those that affect productivity, in addition to those that affect trade. In the same way, goals may not be the same at the local, regional or national level. Finally it is likely that decision makers and system designers will have different views of the purpose and goals for the SyS. At the very least, we could expect SyS designers to be more interested in the surveillance purpose and decision makers to be more interested in the policy purpose.

All influential stakeholders should be engaged in the process of defining the purpose and goals, and ideally consensus should be achieved. This is essential to avoid future

Table 1
Conceivable SyS goals for animal and public health. Human and livestock SyS systems currently focus on the early detection of emerging diseases or on situational awareness. Syndrome-based systems (SBS) and syndromic-non-specific systems (SNS) will seek to monitor different variables. Examples from human and animal public health SyS systems are provided.

		Variable monitored	Examples from human public health	Examples from animal public health
Early detection	SBS system	Changes in endemic diseases (including zoonotic)	Detecting influenza epidemics (Ginsberg et al., 2009)	Identifying changes in endemic diseases in companion animals (Glickman et al., 2006)
		Transboundary diseases	Detecting the inhaled anthrax epidemic in the USA (Buckeridge et al., 2006)	Detecting transboundary vector-borne disease incursions in livestock (Madouasse et al., 2013)
	SNS system	New/emerging diseases	Potential use but not established	Identifying an outbreak of a novel swine disease (O'Sullivan et al., 2012)
		Changes in health data quality	Detecting health information technology system failures (Ong et al., 2013)	Management of the diagnostic process (potential use but not established)
Situational awareness	SBS system	Identify changes in risk factors	Potential use but not established	Surveillance of pets to detect increased risk of enteric disease in people (Anholt et al., 2014a)
		Potential for antimicrobial resistance	Potential use but not established	Monitoring of antimicrobial compounds sold for use in animals (Stege et al., 2003)
		Pathogen activity/Movement of disease to new areas during outbreak	Surveillance to create information to support decision-making during the H1N1 pandemic (Chu et al., 2012)	Potential use but not established
	SNS system	Absence of disease (freedom from?)	Reassurance that no bioterrorism-related epidemics is ongoing (Buehler et al., 2003); health impact of the Icelandic volcanic ash plume (Elliot et al., 2010)	Potential use but not established
		Non-specific changes in the population (e.g. increase in mortality)	Evaluate the effectiveness of treatments and intervention programmes (Chretien et al., 2008)	Using surveillance to produce information to improve production management & animal welfare (Wallberg, 2013)

conflict and to ensure that the SyS system being built is based on realistic and mutually acceptable expectations that will establish a framework for further research and development and for the evaluation of the SyS system after it has been implemented. The stakeholder group should include those who provide data for the system, those who design and operate the system and those who will use the information generated by the system. The group may be large and will likely be diverse in terms of desired goals and views of SyS capabilities. Reaching consensus may be a challenge.

The agreed goals should be: (1) relevant; (2) detailed, precise and formalised; (3) considerate of stakeholder expectations; and (4) should reflect priority issues (OASIS criteria developed by (Hendrikx et al., 2011)). In addition, they should be technologically achievable within the available budget, and they should be valid scientifically. These should be established by a scoping literature review and consultation with expert surveillance system designers. The International Society for Disease Surveillance (ISDS), via their Meaningful Use Workgroup, recently published an assessment of feasible public health uses of hospital inpatient and ambulatory clinical care data for human SyS (ISDS, 2012), some of which could be transferred to animal health SyS systems including: monitoring population health; informing public health service delivery; and informing intervention, policy and health education development and evaluation.

Considerations for defining the SyS purpose and goals include some of the following:

- What are the primary drivers or most significant needs?
- Who are the intended users of the information that will be produced?
- Who are the potential data providers? What is their relationship to the decision makers, and how will decisions affect them?
- Will the SyS system be used for early outbreak detection, to produce animal health intelligence, or both?
- Will the system be used for specific disease(s), or to detect a non-specific change in the health of a population that will be require further investigation?
- Will the SyS system be designed for short-term, high-risk situations or long-term, continuous use?
- Are there secondary uses for the SyS system or the information produced by the SyS?
- What is the operational scale of the system: small scale (farm-level) vs. large scale (national)?
- What is the context in which the system will operate: will it complement other types of surveillance or will it stand alone?

2.2. Select diseases & populations for surveillance

A national SyS system should target those diseases that are of importance to the national animal health

community. As such, it is important to find consensus on national priority diseases and then to identify current surveillance gaps which should be filled by the future SyS system. Many livestock and poultry diseases could be of interest to SyS system designers (depending on the goals defined in step 1 above). These could include any or all of: OIE listed diseases, endemic diseases, sporadic diseases, exotic diseases, re-emerging diseases, new (emerging) diseases, zoonotic diseases, production diseases, and diseases that affect trade. Many of the diseases that SyS systems attempt to detect occur rarely, if ever. If this is the case, using a random selection of clinical or laboratory records to generate a reference standard set of diseases to be monitored would not be recommended because of the low prevalence of many diseases. An approach using a mixture of literature reviews, other information sources (for example diagnostic laboratory reports, government-funded disease surveys or surveillance reports), and disease expert consultations could highlight suitable disease candidates (Tan et al., 2013). Since there is considerable variation in the clinical presentation of diseases, it is likely that there will be variability in the suitability of each disease for SyS. It would be prudent to evaluate each disease against a defined set of criteria to estimate whether an outbreak of each specific disease could be detected with a reasonable degree of confidence. However, these criteria have yet to be developed.

The surveillance objectives set in step 1 will dictate whether the SyS system will be "syndrome-based" (SBS), "syndromic-non-specific" (SNS) or both (Katz et al., 2011). Whereas SBS focuses on monitoring defined syndromes, diseases or outcomes of interest (e.g. a specific disease(s) or influenza-like illnesses), SNS aims to monitor non-specific indicators such as the number of dead stock picked up by rendering companies, or the sales of antimicrobial pharmaceuticals. SBS would enable situational awareness for defined health threats, and could be used to identify clusters of excess cases with specific disease characteristics that might represent an outbreak with a defined cause. An example is a geographic cluster of samples from aborted material sent to the laboratory for *Brucella* testing. Such data are still syndromic because they are pre-diagnostic (a request for a *Brucella* test does not necessarily mean the sample will be positive). But they are based on clinical suspicion providing some indication of the type of disease occurring in the cluster. On the other hand, a SNS would focus on identifying unexpected excesses of indicators that could be caused by unknown, unspecific or many disease processes, making SNS useful for detecting previously unknown and unseen diseases.

Depending on their nature, diseases will be expressed differently in space, time, and demographic strata of the livestock population. The geographic, demographic, and temporal coverage of the SyS system must therefore be sufficient to support anomaly detection. It may be relatively easy to define the adequate level of aggregation (e.g. age, production type) in a SBS system with known risk factors for specific diseases. However it is often difficult to identify a priori the subpopulation groups for SNS systems which aim to detect unexpected events. Similarly the most suitable spatial scale cannot be easily defined: a system able to identify problems at the herd level could be the most convenient for risk managers, whereas significant abnormal increases in the syndromic indicator may only be possible at the regional or national level (Perrin et al., 2012). The target population about which statistical inference will be made should therefore be defined in terms of (1) animal or group type; (2) epidemiological unit (animal, herd, region, etc.); and (3) administrative unit (e.g. county, region, canton, district etc.).

2.3. Inventory and evaluate available data sources

A data source can be chosen anywhere along the continuum of the disease process, the animal life cycle, or the production chain. It may originate from producer or professional organisations (Madouasse et al., 2013), private practitioners (Zurbrigg and Van den Borre, 2013), diagnostic labs (O'Sullivan et al., 2012), government agencies (Perrin et al., 2012), and businesses such as slaughterhouses (Vial and Reist, 2014) and livestock markets (Van Metre et al., 2009). The relevance of the different data sources will be different for SBS or SNS SyS systems. For the former, clinical pre-diagnostic data will preferentially be used, and for the latter, a combination of pre-clinical and/or clinical pre-diagnostic data will be more appropriate. Data sources with relatively long history will be preferred as the availability of baseline data will make the fitting of aberration detection algorithms (step 5) easier.

The availability of each data source must be established. SyS that is based on existing data is a secondary use of data, meaning that the data are collected for some other, often non-surveillance purpose. Many of these data are in databases controlled by people or organizations that are different from the organization conducting the SyS (Fig. 2). In some cases, the data in these databases may have originated from third parties, and this can have important legal and ethical implications. For example veterinary practices collect and store data about diseases that occur on their clients' farms as part of their medical and billing records. Who has legal ownership of these data will be defined by the laws in the jurisdiction where the farmer and the veterinarian reside. Regardless of who owns the data legally, veterinarians will often wish to keep their clients data confidential if for no other reason than to safeguard the trusting relationships they have built with their clients. A data sharing and use agreement that protects the confidentiality and privacy of all data providers and very clearly defines the terms of use of the data is essential. These should be initiated by the SyS operator as many individuals and organizations that collect or hold data may not have previously dealt with this issue. Negotiating the terms of use of the data and the information generated from it is a worthwhile process as it is an opportunity for the SyS provider to explain the purpose of the SyS, who will benefit from the SyS, how the data will be used and protected, and the risks for participating. It also precipitates discussion about the acceptability by the data provider and all stakeholders of the consequences of an outbreak suspicion. System developers should make sure that the owners and providers of the data are aware of the potential consequences of data sharing. A farmer who is contacted by a team

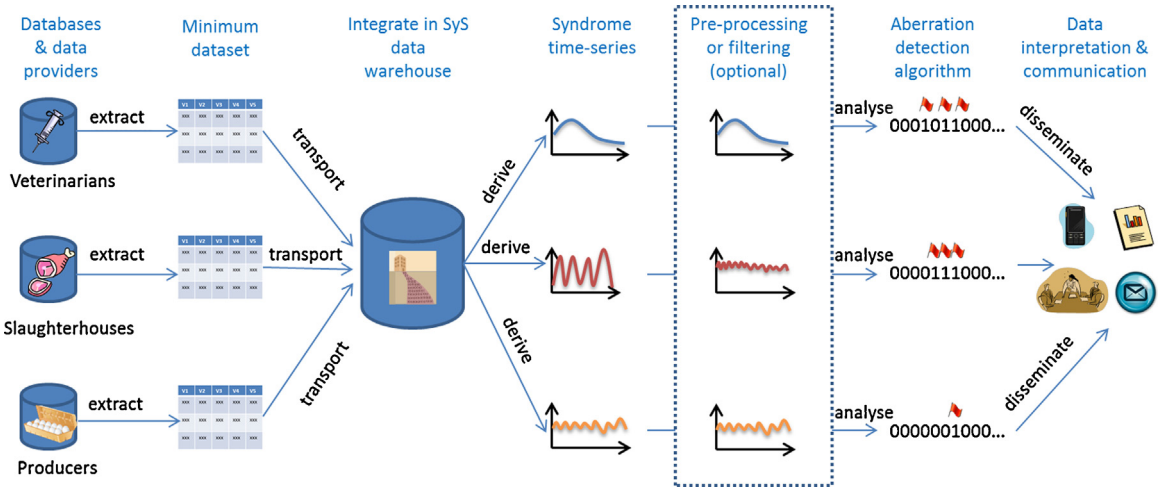

Fig. 2. Schematic representation of animal health data flow in a SyS system.

investigating a potential disease outbreak on his or her farm without being aware that he or she has been contributing data via their veterinarian to a SyS system could harm all parties (farmer, veterinarian, and SyS operator). Data use agreements must also specify the terms of communication of information derived from the data. Communication of any identifying information in a public forum about the occurrence of a sensitive disease can significantly and sometimes irreparably damage a farmers' livelihood or potentially the industry as a whole.

The credibility of the SyS system will be driven by the requirements for data quality. This is particularly important when using data that are pre-diagnostic (and thus, by definition, dealing with suspicions and not cases). Data must be sufficiently accurate and valid to fulfil the system's intended purpose. In cases in which data quality (e.g. coverage, number of records etc.) is low, as may be the case in lower income countries, changes in health patterns may still be detectable (albeit with a lower sensitivity) provided data quality does not dramatically change over time. Both negative and positive feedback should be communicated to the data providers in order to help them rectify the problems and to ensure continued motivation and involvement in the SyS system. The latter is particular relevant in lower income countries where the availability of quantitative animal health information from "traditional" sources (e.g. animal health laboratories) is more patchy or scarce.

A useful endeavour in this phase is to develop minimum data requirements to achieve all surveillance objectives while minimizing the amount of data collected, especially eliminating data with no direct added value for analysis or reporting (Kloeze et al., 2012). One can then compile an inventory of the data sources that are available and evaluate each using the criteria developed. We suggest at a minimum to use the following evaluation criteria:

- Data dictionary and definition of terms in the data: Since many SyS are secondary data uses, it is likely that the data being considered for SyS were collected by someone other than the SyS operator. A data dictionary that is a clearly written, and easily understandable description of the names of the values (terms) in each variable is essential, as is a definition for each term in each variable. It is essential for understanding the data and more importantly for understanding how the data relate to the population under surveillance. Knowing the meaning of the terms used in the data will be necessary for defining the syndromes and time series that will be monitored for detecting disease outbreaks. Finally having well defined terms will allow comparison of SyS results between different data sources, SyS systems and across jurisdictions. This would be further facilitated by having internationally agreed upon standards for SyS terminology; however these have not yet been established.
- Recording: The description of the system's data management should address who is allowed to enter the data, how and at what levels the data can be edited, and what checks are in place to ensure data quality (spelling, missing fields etc.). Training may have to be put in place to ensure that all data providers are aware of data quality requirements.
- Compliance: It is important to assess the completeness of the data as this will have a direct bearing on the value of the data for SyS especially in terms of the validity of SyS signals. This can be done by estimating the proportion of missing values for each variable and eliminating those data sources with too many missing values.
- Transmission: The minimum dataset then needs to be extracted and transferred to a central unit. A well-integrated system should seek to increase timeliness by meeting the specific primary data collection needs of the providers while avoiding duplication of effort. In non-integrated reporting systems, the compliance of the data provider to timeliness will depend on their primary use of data and their motivation for reporting it. Automated systems are most favoured since they minimize the amount of work required by the data provider. However they may be difficult to install in some proprietary software and some software providers may not allow additions to their software. In some cases it may be necessary to

seek assistance directly from the software provider to construct data export software for software extraction (Anholt et al., 2014b).

- Compilation: In situations in which data from several providers needs to be simultaneously considered, a further step of data compilation must be undertaken. Issues of data privacy and data sharing may then become apparent. Customised data extraction and compilation software may need to be developed (Anholt et al., 2014b) to automatize the process of data standardisation between providers and potential linking of animals or animal premises between the various databases using universal identifiers.
- Accuracy of the compiled/received data: Once the data have been compiled in the SyS database it is essential to confirm that the data in the SyS database is in fact the same as the data that is present in the data providers' database. This can be done by selecting a random sample of cases in the SyS database and comparing them to those same cases as they are recorded within the data providers' database (Anholt et al., 2014b).
- Epidemiological evaluation: Criteria and methods for evaluating data sources for disease surveillance have been developed for human systems and are thoroughly discussed in the public health literature (Buehler et al., 2004; CDC guidelines working group, 2001). One important consideration is how well these data match the required coverage defined in step 2 in terms of catchment area/population for surveillance. Does the data adequately cover the populations, subpopulations or production types and the geographic regions that are required? Another consideration is timeliness; some data even if they are collected in real time may not be reported to a central database for days or weeks and will have little value for early disease detection.

The technological infrastructure available for the SyS must at some point be considered. Institutional constraints on software availability and Information Technology (IT) infrastructure will affect the functionality of the SyS and may make it impractical to deal with some data. Each institution is likely to have made organization-wide decisions about the software that is permitted for use for data bases, data transfer, data analyses, data reporting, as well as rules about using open source versus proprietary software. In addition, human resources may be limited, making it difficult to complete certain tasks such as building tools to transfer data to the SyS database from external databases.

We have discussed SyS based on the secondary use of data that is already being collected for other purposes. However, there may be situations where there are insufficient data sources available to allow the SyS to achieve the defined purpose and goals. If this is the case the SyS designer will be faced with the additional task of developing data collection tools and enrolling the appropriate data providers. Designing the data collection tools provides the SyS designer with control of the data that will be collected and enables collecting data that meets the purpose and goals of the SyS. However there are many additional factors that will need to be considered when designing purpose-built data collection tools. While a detailed description of these is beyond the scope of this manuscript there are a few things that should be mentioned including: determining the best vehicle for data collection (e.g. paper, web page, smart phone app, etc.) that best aligns the purpose of surveillance with the technical abilities of the data providers; following best practices for questionnaire design, especially with respect to keeping the burden of data entry in terms of time and difficulty to a minimum; and developing strategies for timely and sustainable data submission. The last point is extremely important because it will affect not only the sensitivity of the system, but also the long term sustainability of the surveillance. Strategies include payment (Berezowski et al., 2011) for timely data submission and returning valued information to the data providers (Klopfenstein et al., 2012).

2.4. Identify, evaluate and select syndrome-time series

This step consists of two consecutive phases which are needed in order to have the required set of syndrome-time series ready for the fitting and evaluation of aberration detection algorithms (step 5): a syndrome definition phase followed by a case classification phase.

Based on the output of step 3, a list of syndromes should be produced for all data sources whose monitoring is considered potentially useful for the SyS being developed. The inventory should not necessarily be exhaustive, but rather tempered by an understanding of how the diseases selected for SyS could be expressed in each syndrome and the characteristics of each syndrome. The syndromes defined should ideally lead to high performance outbreak detection (i.e. high specificity for the disease(s) under surveillance and highly sensitive for early detection of outbreaks of those diseases)

A syndrome has been defined as "a set of non-specific pre-diagnosis medical or other information that may indicate the release of a bioterrorism agent or natural disease outbreak" (Katz et al., 2011). Public health SyS is based on the premise that a significant change in the health of a population will result in an accompanying change in the behaviour of the population (Mandl et al., 2004). Similarly, a significant change in the health of an animal population should be expected to result in an accompanying change in the behaviour of the animal population and, or, the human population that cares for the animal population. Therefore, for animal health SyS, a syndrome can be any indicator originating from the animal population, animal care giver population or other source, that accompanies a significant change in the health of the animal population.

The syndromes most often used in SyS are categorical variables (continuous variable SyS is much less common and will not be considered here). For analyses, syndromes are converted into time series, which are counts of the syndrome occurrence per unit of time. A working definition for a particular syndrome should include the syndrome being counted, the unit of time, as well as other contextual information such as the geographic region, production type, sex, age, or other important information. An example is the number of occurrences of acute diarrhoea in pigs per week in Switzerland. The syndrome that is counted is diarrhoea. The time units are counts per week. The contextual

information includes the species: pigs, and the geographic region: Switzerland.

Syndromes vary considerably, from non-specific surrogates for disease to very specific case definitions that could be used for detecting an outbreak of a single disease or for disease intelligence during an outbreak. Defining syndromes will be dependent on purpose of the SyS and the contextual information present in the data. For SNS SyS, the syndromic information is by definition non-specific. In addition, the contextual information in the data may be limited and this may restrict the range of available syndromes. In the example of the counts of dead animals picked up by a rendering company, the only syndrome available in the data may be the count of dead animals per unit of time. For data that are used for SBS SyS such as veterinary practitioner data there may be a lot of contextual information present and it may be possible to subset the data into more specific syndromes-time series. In the diarrhoea example above, if the age of the pigs were available the specificity of the syndrome could be increased by monitoring the counts of acute diarrhoea in neonatal piglets less than 2 weeks of age. Since many gastrointestinal pathogens of pigs are age related this would narrow the number of diseases detected by the syndrome-time series considerably. If information about the within litter prevalence of diarrhoea in neonatal piglets was available, it could be possible to be even more specific by including only farms where neonatal piglets had diarrhoea with very high prevalence. This would further restrict the number of pathogens that could potentially be detected by the syndrome-time series. Other factors that may be used to subset the data include the production type, for instance dairy versus beef for cattle, or the geographic region (county, versus province, versus country).

It should be noted that event detection algorithms are statistical tests that are run on each time series with each time unit of analysis. Most importantly, they are subject to error. Sub-setting the data into more narrowly defined syndrome-time series may have the desired effect of increasing the specificity of each syndrome-time series by reducing the number of diseases detected, but it will increase the total number of syndrome-time series that must be tested. For a fixed value of statistical significance, increasing the number of tests run every time period will increase the number of false positive results generated by the whole system. Raising the level of statistical significance for each algorithm may not be the best solution as this will reduce the sensitivity of each individual algorithm

Using well defined and accepted terminology for defining syndromes is important for all stakeholders including those who enter the data, surveillance epidemiologists, and the decision makers who use the information generated from the data. In addition commonly accepted definitions for syndromes and other terms are necessary for comparing SyS findings across jurisdictions. Case definitions might exist for a variety of health-related events under surveillance (e.g. in the Systematized Nomenclature of Veterinary Medicine SNOVET) as they do in public health surveillance (CDC, 1997). If an official definition does not exist, one must be agreed upon by the system users (a sort of gold standard).

Data have been screened, high quality data have been selected and transported to the SyS database in step 3. In step 4, syndromes have been defined and each case (record) in the data has been classified into one of the defined syndromes. For some data sources, cases will have already been classified into syndromes. An example is a veterinary practitioner SyS where veterinarians are required to classify each sick animal (or group of animals) they examine into one of the syndromes defined for the SyS. However, many data will arrive without the cases having been classified into syndromes. For these data each case (record) will have to be classified into a syndrome class using text-mining and logic rules. Both supervised, such as diagnostic learning and rule-based methods as in (Buckeridge et al., 2005; Dórea et al., 2013), and unsupervised methods, such as multiple factor and cluster analysis as in (Woodall, 2006), are available. Even automatized syndromic case classifiers are not 100% reliable. A note of caution regarding the substantial heterogeneity of findings constituting the syndromic case definition can be found in (Shmueli and Burkom, 2010).

The next step is to convert the data into time series. Each syndrome that is included in the SyS must be converted to a single time series. This is a relatively simple process that can be easily automated. Difficulties may arise due to different formats for recording time, and these should be considered when evaluating data for inclusion in the SyS (step 3) and may be dealt with in data pre-processing (step 5).

2.5. Fit event detection algorithms to each time series & report

Based on the characteristics of the syndrome-time series coming out of step 4, the length of historic data available and the type of outbreak the system must detect, different aberration detection algorithms can be tested. There is abundant literature reviewing (Unkel et al., 2012) and/or applying such algorithms available in both human (Buckeridge et al., 2005) and veterinary (Dórea et al., 2013) literature. Most syndromic surveillance systems apply variants of the standard univariate statistical process control (SPC) methods, for example Shewhart, cumulative sum or exponentially weighted moving average charts (Woodall, 2006). SPC approaches rely on cumulative differences between observed and expected data in a time window when compared with a threshold. A suspicious increase in the observed data over the theoretical mean is evidence for an unspecified outbreak. Other approaches involve comparing observed patterns with those predicted by a model. Typical models for temporal data include regressions and time-series methods, explicitly accounting for seasonality in syndrome incidence for example (Shmueli and Burkom, 2010). Spatial and spatio-temporal data are more suited to analyses using generalised linear mixed models (Kleinman et al., 2004) or scan statistics (Kleinman et al., 2005). Syndromes, like diseases, may cluster in space or time. The automated process of cluster identification, using scan statistics for example, can help identify areas or sub-populations that require further epidemiological investigations.

Different algorithms will require different levels of pre-processing. This is the process of identifying and removing explainable patterns, such as temporal dependence (e.g. daily autocorrelation) or seasonality, which may obscure unexplained outbreak events, and whose presence in the data violates standard control-chart assumptions (Dórea et al., 2013; Lotze et al., 2008). Pre-processing can also be used to deal with the inherent biases, confounders, and missing records which may have been identified in steps 3 and 4.

Relevant algorithms should then be parameterized and optimized for each time series based on achieving or exceeding performance goals based on the disease(s) that must be detected, the smallest outbreak size that must be detected, and the time frame within which detection must occur (Wagner et al., 2006). Algorithm evaluation will be based on historical outbreak data if available or on the simulation of outbreaks for the disease(s) under surveillance. The performance criteria of these algorithms (sensitivity, specificity, false positive rates or other parameters) may vary with the type of disease under surveillance. Choices will have to be made (often based on decision theory (Wagner et al., 2011)) regarding the alarm thresholds of the algorithms, i.e. above what level of excess syndrome counts is an epidemiological investigation instigated to confirm/identify the health event behind the statistical signal (unlike monitoring systems). Similarly, the frequency of analysis needs to be agreed upon and should be based on the practical possibilities: can the pre-processing and analysis process be automated and run on a daily basis or does it have to be done "manually" by an operator with a statistical background? Even in an automatized system, a process for scheduled evaluation of the performance of the algorithms and re-parameterization (as may be required) should be developed as the baseline behaviour of the time-series (mean, variance...) may change periodically or over a longer time scale. When this happens, the system developers should investigate why it is changing and re-evaluate algorithm performance by injecting outbreaks into the new baseline.

Stakeholders must agree on a communication strategy for the SyS system. Mere accumulation of knowledge without any relevant output is useless. Data interpretation must provide timely and relevant information that meets surveillance objectives. The exact content of the information disseminated will depend on the audience (e.g. general public, system users, decision-makers etc.) but should always include a brief description of how the system works and how the data were analysed; information about the system's performance (e.g. mean/variance of time-series to detect possible change in the baseline) and the degree of confidence in these results; and some epidemiological intelligence (e.g. summary graphs and maps). Such knowledge should then be quickly and effectively disseminated. The dissemination of output to system users and epidemiologists should be done in almost real-time in order for them to assess the potential implications. This is most efficiently done through electronic interchange (e.g. reports can be automatically sent by email to a list of users after each analysis). Such users also have the possibility to access and drill down into the raw data to support a field investigation (see step 6). During non-acute situations, communication to decision-makers may be limited to quarterly reports or meetings, debriefing about the latest observed trends and possible data issues encountered. Dissemination of epidemiological knowledge to other stakeholders (e.g. animal health professionals or researchers) and/or the general public may be done via the Internet, press releases or newsletters. During acute situations (following the confirmation of an alarm in step 6), the analytical output produced by the system should be rapidly presented to the decision makers with advice and recommendations for multiple public health action options. Wider communication should strictly follow the guidelines in place in the relevant animal health authority/ministry. These may include the publication of official statements to the general public and professionals and the use of social media (or more traditional media) to convey the message to a wide audience in a short time.

2.6. Define an appropriate response for detected signals

Finally, it is essential to develop a minimally acceptable response protocol for each signal or alarm produced (Duchin, 2003). The first step in investigating an alarm is confirmation of the signal. The individual cases that triggered the alarm must be examined to obtain geographic (and potentially demographic) data. Then if the signal is determined to not be a consequence of duplication of individual case data or data entry error, the specificity of the signal may be increased by:

- Evaluating the absolute number of cases leading to the alarm.
- Validating the alarm using data from other surveillance systems covering the same population (sentinel veterinarian network, pathology data etc.).
- Speaking directly to the individuals who entered the case data.
- Using email lists to query animal health specialists about specific conditions relating to the excess cases in question.
- Requesting additional testing of animals to rule specific diseases in or out.
- Initiating an outbreak investigation.

The nature and magnitude of the event will influence the intensity of the response (from a phone call to veterinarians at the reporting sites to dispatching a team of epidemiologists in the field etc.). This will also depend on the relationship between the indicator and the real health status of the population under surveillance. Statistical alarms produced by systems based on the monitoring of non-specific data should thus be carefully interpreted before being converted into epidemiological alerts and transmitted to field investigators. An in-depth study of the variation factors of the monitored health parameter should be carried out before running the system for surveillance, in order to facilitate the rapid interpretation of anomalies detected day-to-day.

Since both SBS and SNS monitor pre-diagnostic indicators, a signal from either type of SyS will require an

immediate investigation to determine whether there is an ongoing outbreak in the population and to identify the cause. However the magnitude, intensity and nature of the investigation will likely be different depending on whether the SyS is an SBS or SNS system. Because SBS monitors a specific disease or group of related diseases, SBS provides some information on which to focus an outbreak investigation (i.e. an increase in submissions for *Brucella* testing would suggest at *Brucella*-like disease outbreak). SNS however may provide little additional information to guide an outbreak investigation. An unexpected increase in the number of dead stock picked up by a rendering company could be caused by an outbreak of any one of a large number of candidate diseases. In the case of a signal from a SNS outbreak investigation would by necessity cast a large net and be very nonspecific.

3. Discussion

The steps presented here relate to the design of an operational livestock SyS. We have reported practical approaches from our field experiences and from the literature. These steps are not intended to be a complete set of directions; rather, they are intended to be the starting point for further discussion. It is our hope that other animal health surveillance researchers and designers will augment these recommendations based on their research and experience, leading ultimately to a more informed guide to the design and implementation of livestock SyS.

The adaptation of SyS to livestock surveillance is new (Dórea et al., 2011; Dupuy et al., 2013), and at this time there is much to be learned and many issues to be addressed. The issue that is perhaps of greatest importance is justifying the effort and expense required to implement a functioning livestock SyS. The potential benefits and advantages of SyS have been reported briefly in this paper, and more extensively elsewhere (Dórea et al., 2011). These benefits could be strong motivators for the implementing a SyS, however, most have not yet been proven in the field (Dórea et al., 2011; Dupuy et al., 2013). Proving these benefits requires observation of functioning livestock SyS, of which there are few at this time. At this early stage it is imperative that organizations operating functional livestock SyS critically evaluate their SyS and report their findings.

All SyS systems should be evaluated periodically to assess whether the surveillance goals (established in step 1) are met; whether steps 2–6 of the system are functional; and what the users' perspective of the system (i.e. is the system useful) is. The actual evaluation process should be carried out by an independent party who is not associated with the SyS and who will be more likely to provide an unbiased evaluation. Evaluation indicators for public health systems in general, or public health SyS systems in particular have been extensively presented in the literature (Buehler et al., 2004; CDC guidelines working group, 2001; Drewe et al., 2013; Hendrikx et al., 2011; Hoinville et al., 2013; Salman, 2003). Indicators such as data quality, compliance, costs, acceptability, usefulness, validity and timeliness will also apply when evaluating animal SyS. It is important to note that evaluation indicators may vary for systems with different surveillance purposes (Drewe et al., 2013). The evaluation indicators may be measured through focus groups or interviews involving system users and decision makers (Del Rocio Amezcua et al., 2010; Reeder et al., 2011). System reliability may be measured during or immediately after significant health events (Josseran et al., 2010); or at the very least through outbreak simulations (to specifically evaluate algorithms as in step 5). The outcomes of the evaluation process are critically important since they will include recommendations for actions to improve quality, efficiency, and usefulness which should be widely communicated to all stakeholders (Del Rocio Amezcua et al., 2010). Such recommendations should be fed back into steps 1–6 of our proposed approach (Fig. 1) and set standards for the next round of evaluation.

Within disease control organizations, the fundamental purpose of all surveillance, regardless of type, is to provide accurate and timely information upon which to make decisions about how to control disease (El Allaki et al., 2012). If the purpose of surveillance is information production, then it follows that the motivation for implementing new surveillance should be a need for more or better information. Information needs will be highly variable between disease control organizations, and a detailed discussion is beyond the scope of this paper. However these should be well known within each organization. It will be the responsibility of the surveillance system designers within each organization to select the type of surveillance that is most likely to produce the information they require. For most types of traditional surveillance such as disease surveys, this well-known, making it relatively easy to evaluate the effectiveness of these approaches. This is not the case for livestock SyS. Because it is still new and there are only a small number of livestock SyS systems in operation, the information that livestock SyS can produce has not been fully explored. It is expected that as more SyS systems become implemented this will be more fully explored and reported.

Important outcomes of this pre-operational phase should include building a national network of experts in animal SyS; and of a collective action plan that identifies activities, task division and resource allocation (El Allaki et al., 2012). The following questions, and many others (see (Centers for Epidemiology and Animal Health, 2006; Defra, 2012)), should be considered:

- Is there a legal basis for implementing the SyS?
- Are the central & field institutional infrastructures in place?
- Who will finance the system?
- Are there possible synergies with other animal, human or environment surveillance systems?

All aspects of the operation of the SyS system should be described and documented in detail. This is necessary in order for stakeholders to fully understand the complexity and resources needed to operate such a system; and to highlight areas in the process flow which may become relevant when considering variations in system performance during the evaluation phase.

Strong effort and emphasis should be put on steps 1–3 of our proposed conceptual approach: identifying realistic goals for SyS, selecting diseases for SyS and evaluating data sources available based on the first two steps. Abundant literature on methods for the classification of human health data into syndromic groups and the retrospective application of aberration detection algorithms (steps 4 and 5) exists and more literature is emerging on these topics within the animal health community. However, surprisingly little discussion appears to have taken place on defining the goals of planned national animal disease SyS systems. Early detection of emerging diseases constitutes the main justification for most animal SyS systems. However, for many of them, current limitations for early detection of unknown events are inherently associated with the non-specific properties of the syndromic data sources available.

As the field of veterinary SyS is still relatively new, most systems in development are fitting aberration detection algorithms retrospectively using historical syndromic data. However, as the field moves towards a prospective application of these methods in real-time (operational phase), decision makers and surveillance developers will need to agree beforehand on investigative methods and responses to detected alarms by the SyS system. Developing international terminology standards for surveillance has never been needed more. The data that are used by SyS are entered into databases by many different people, often with very different backgrounds and with very different reasons for collecting and using the data. The terms and concepts that are used to capture information within the data can thus be highly variable. Converting these to standard terms that allow combining information from different data sources is a challenge within a single country. Comparing and sharing information across borders considering the differences in native languages is an even greater challenge. We make a strong plea for an international process to define the standardized terminology for SyS. Finally, valuable lessons for the future of animal health SyS may be learned from discussing with the public health sector and collaborating with them on the development of analytical methods and of joint SyS applications across our surveillance domains (One Health SyS).

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