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A PROPOSED TAXONOMY FOR CHARACTERIZATION AND ASSESSMENT OF AVIAN INFLUENZA OUTBREAKS

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Abstract

Purpose—The speed and high potential impact of Avian Influenza’s (AI) on local bird populations, poultry economies and human health make timely and coordinated characterization, assessment and response to possible threats essential. To achieve effective collaboration, stakeholders (public health, medical, veterinary, and agricultural professionals) must be able to communicate and record findings, assessments, and actions in a standard fashion. We seek to discern a taxonomy of concepts and relationships that are important to the stakeholder community when sharing information about the characterization and assessment of an AI outbreak, according to a consistent and common perspective, interpretation, and level of detail.

Methods—To derive concepts relevant to AI characterization and assessment, we reviewed selected journal articles, reporting and laboratory forms, and public health Websites associated with AI case reporting. We mapped concepts to existing medical terminologies when possible, using the Unified Medical Language System MetaMap.

Results—From 54 distinct information sources, we extracted 1113 concepts, of which 533 mapped to 15 medical terminologies; 580 did not map to specific terminologies. Using a combination of semantic type-relationship matching and expert consensus, we constructed the proposed taxonomy, with linkages to existing terminologies where pragmatic.

Conclusion—The proposed taxonomy describes core knowledge, data and communication needs for the characterization and assessment of AI outbreaks in the context of existing medical terminologies across different domains. We also describe areas for further work.

Keywords

Avian Influenza; Disease Notification; Classification; Zoonoses; Disease Attributes; Concept Formation

1. Introduction

Avian Influenza (AI), a disease caused by a virus of the family Orthomyxoviridae, genus Influenzavirus A, affects both avian and mammalian species (including humans). Its pathogenicity is categorized as low or high, with low pathogenic AI (LPAI) causing morbidity and mortality in birds and high pathogenic AI (HPAI) causing high fatalities in both birds and

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humans. Its antigenic categorization depends on biochemical assays for viral surface glycoproteins hemagglutinin (H) and neuraminidase (N). To date, 16 H and 9 N subtypes have been associated with AI [1–4]. Generalized AI diseases are associated with subtypes H5 and H7 (in birds and humans) and fatal human AI infections appear to be associated with the H5N1 subtype (as a causative agent). Its natural hosts are wild birds, in which the viruses are believed to be antigenically stable. In new hosts, however, it is believed that the viruses undergo antigenic shift and drift leading to differential virulence [5].

The World Office for Animal Health (Office International des Epizootics, OIE) classifies HPAI as Class A because of its high mortality, its efficient transmissibility and pathogenicity [6] and the serious socioeconomic or public health consequences associated with it (in international trade of animals and animal products). The World Health Organization (WHO) believes a sustained and widespread HPAI epidemic (especially due to H5N1) in poultry increases the risk of a human influenza pandemic [7]. Because of the variable mutagenic potential of LPAI (H5N1) into HPAI, its short incubation period (3–5 days), increasing resistance to current therapies [8] and the increasing vulnerability of other mammals (pigs, tigers, horses, sea mammals and cats among others) [9–12], there is a need for timely and coordinated public health approach to understand, detect and control outbreaks.

2. Background

2.1. Information model of the public health response to AI outbreaks

The public health response to a disease such as HPAI is a collaboration of local, federal and international agencies, private groups and the public to achieve the multiple objectives including [13]:

1. determination and control of immediate health threats,
2. prevention of spread,
3. mitigation of human suffering and
4. minimization of negative impacts on trade and travel.

Public health agencies information requirement to meet these objectives include [13]:

1. up-to-date knowledge of the disease pathogenesis and transmission,
2. real-time surveillance and report data from clinical and veterinary sources and
3. facilitated and timely collaboration and coordinated response among stakeholders on horizontal (commercial and private bird owners, public health and wildlife agencies, clinical laboratories, medical and veterinary practices) and vertical (local, national, regional and global) dimensions.

Stakeholder information tasks within the collaboration include [14]:

1. detection: reporting and investigation of cases;
2. analysis: characterization and assessment of cases in terms of potential threat and spread;
3. response: treatment/prevention of morbidity and mortality, containment of regional/national/international spread and minimization of impact to the public, trade and travel.

Each task requires communication within agencies or between agencies and health entities for detection (sentinel workers, local public health data collection agencies, laboratories) and response (health facilities, agriculture and food service regulatory agencies, law enforcement

and military). Appropriate public health response depends on timely and effective analysis (characterization and assessment) by public health officials/agencies of reported cases as outbreaks.

Characterization of an outbreak is the discernment of attributes of a reported case that are important for identifying its threat potential [15]. Potential cases are identified by clinical or pathological data or through surveillance (routine cultures for avian influenza, for example). Follow up investigation includes collection of clinical and laboratory data to identify causative agents (for the clinical or surveillance data), their sources and routes of transmission.

Assessment of an outbreak patterns to the integration of data (from characterization) by decision makers to derive measures of risks and/or disease burden that determine actions and allocation of resources necessary to optimize public health in the context of the characterization data [15]. The urgency with which decisions and actions (including resource allocations for response) are required may be influenced by current and predicted local morbidity and mortality [16–17], estimations of current and projected economic losses (due to bird death), and problem scope [18]. Assessments may provide a combination of qualitative (expert opinion) and quantitative (rates and biostatistical) measures that may be of help to decision makers [6,19–20].

2.2. Decision maker's information needs

To facilitate an informed and effective public health response, the decision/policy maker must integrate information from a variety of sources including abstractions from case characterization and assessment in a timely fashion. Information sources include: surveillance of current incoming data, historical records of past data and previous decisions, responses and outcomes, evidence-based knowledge of disease and behavior patterns and other relationships and current hypotheses (based on observed patterns and logical inference) [21]. The development and use of statistical packages, analytical processing tools and conceptual bridging tools such as clinical and business dashboards [22] and controlled terminologies and description logic have been useful in bringing together heterogeneous biomedical information on syntactic and semantic levels for incorporation into decision tools.

2.3. Need for sharable terminology/vocabulary

The potential widespread severity and urgency of an AI outbreak and the need for timely management necessitate a consistent and common ground for rapid and accurate communication among all stakeholders in AI characterization and assessment. There is currently no common formal vocabulary for human understanding and electronic processing for this across the breadth of domains of stakeholders (the health community, veterinary care, farming, wildlife workers, food industry and the military).

We describe our effort to discern structural, administrative and descriptive data and metadata needs to characterize and assess AI outbreaks. The goals of this research include:

1. determination of terms and concepts common to AI literature and work,
2. identification of existing terminologies that contain such concepts and
3. identification of gaps between existing terminologies and the data/metadata needs of AI workers.

3. Methods

3.1. Taxonomy development

Using a published model for creation, use, and management of ontologies [23], we created use cases on which the development of a taxonomy was based (see Appendix A); an information model for the use cases was also developed to further aid clarification of the process of AI outbreak characterization and assessment (see figure 1). Publicly accessible documents related to AI (public health reporting forms, public and professional educational information documents and research articles (reviews and case reports)) were selected and reviewed. Terms were extracted from each document type until saturation [24] across all document types occurred. Extracted terms were mapped to UMLS concepts and terminologies and concepts were arranged into a hierarchical taxonomy, suggested by UMLS semantic types and relationships, using an expert consensus approach.

3.2. Modeling public health AI data processes: use cases

Use cases were developed to represent the information/data needs of AI stakeholders, using the public health worker as the central user, who communicates with sentinel (front-line) persons (farmers, veterinarians, physicians, the public, laboratories and government agencies) in association with reported clinical cases of AI. These use cases formed the basis of AI characterization. Public health workers and public health decision makers also use biomedical and epidemiologic knowledge to analyze and interpret collected data from reported clinical cases. These use cases also form the basis of AI assessment.

3.3. Approximating public health AI data needs: document types

Experts in the field of public health and infectious diseases were consulted about sources of concepts and terms to describe public health data needs with respect to AI. Recommended sources included human experts, medical journal articles, and Web-based public health and infectious diseases data collection and reporting forms. For this pilot, we limited our search to reporting forms for suspected cases of AI as an approximation for characterization and to journal articles (case reports, reviews) as an approximation of assessments of AI outbreaks.

Forms were collected from US public health departments' websites for reporting cases of AI or for AI-related laboratory requests. Eligibility criteria included online availability of forms and attribution of the sponsoring public health department. Websites of public health, agricultural and animal health departments of all 50 states were reviewed, and 16 eligible forms were collected and used as source of concepts.

Published articles discussing characterization and assessment of AI outbreak in humans, birds, and other mammals were reviewed. Articles were retrieved from literature searches in PubMed, Biological Abstracts, Agricola, and ScienceDirect [1,3,4,6,9–12,16,18–20,25–66]. The first search strategy in PubMed used the keywords “influenza in birds”, “avian influenza”, and “disease outbreaks”; this resulted in 685 hits, 40 of which were reviewed. A second search in PubMed that used the keywords “influenza in birds”, “hemagglutinin”, “avian influenza A virus”, and “case reports” resulted in 22 hits, of these 16 were reviewed. Biological Abstract was searched using the keywords “avian influenza”, “influenza in birds”, and “outbreak”; the search returned 136 records, of which 42 were reviewed. The search in Agricola with the keywords “avian”, “influenza”, and “outbreak”, returned 68 records and 21 of the records were reviewed. ScienceDirect was searched using the keywords “avian influenza”; the search returned 298 articles, of which 40 were reviewed. The reviewed articles had abstracts that were: 1) strongly suggestive of the subject of AI outbreak characterization and assessment; 2) written only in English Language; 3) and not focusing primarily on prevention including vaccination. All the reviewed articles were re-reviewed and a final selection of 13 articles was made from

ScienceDirect, 11 from PubMed, 6 from Biological Abstracts, and 2 from Agricola. Final article selection was based on: 1) the comprehensiveness of the article; 2) the provision of a sufficient level of detail description of AI outbreak attributes; 3) and the subject scope and relevance of the article to the subject of characterization and assessment of AI outbreak. (See Table 1)

3.4. Identifying concepts: extracting terms

Experts in informatics and veterinary science (SLM) and clinical medicine (HPL, GRK) performed the extraction of AI-related terms and concepts from the articles and forms. The extraction process included the identification of atomic concepts and multi-term concepts (e.g. pathogenicity index). All articles, documents, and forms were read and reoccurring terms and concepts highlighted. Two investigators (SLM and either GRK or HPL) reviewed each document, and highlighted terms and concepts they considered were necessary for the process of AI characterization and/or assessment. A term was accepted if it was highlighted by either reviewer. A second reading was done to recapture terms and concepts that were omitted in the initial reading but subsequently found to be reoccurring in later articles, documents or forms.

3.5. Finding linkage to existing terminologies: mapping concepts to the UMLS

Extracted terms and concepts were mapped to concepts (and their associated terminologies) in the Unified Medical Language System (UMLS) using the MetaMap application adapted by the Advanced Technology Information Services at Johns Hopkins University, Baltimore (UMLS version 2006AD, moderate restriction setting) to determine semantic type, home terminologies and concept relationships. UMLS contains over 100 controlled medical vocabulary sources and 1.2 million concepts. The initial retrieval was followed by a manual process of mapping terms and concepts that were either not mapped to a UMLS concept by the MetaMap or that had synonyms, this is to verify the adequacy of the mapping with regard to the process of AI characterization and assessment. Mapped concepts were then grouped according to their home terminologies. Compound concepts (of atomic concepts found in the UMLS) were identified; and in addition appropriate multi-concepts (e.g. bird proventriculus mucosa hemorrhage) were composed in order to further clarify the somewhat ambiguous nature of some terms and concepts. A proposed taxonomy structure based on concepts, their semantic type and relationships to the other terms and concepts was then constructed.

4. Results

4.1. Concept mapping to UMLS terminologies

From 54 different information sources, comprising of 32 peer-reviewed articles, 6 Web-based documents and 16 public health disease reporting forms, 1113 human-extracted concepts related to AI characterization and assessment were derived. The level of saturation or completeness was assessed by the rate of emergence of new concepts with each additional information source; a significant drop in emergence of concepts with 6 consecutive additional information sources or the absence of new concepts after 5 information sources were regarded as measures of saturation, as depicted by Figure 2, showing saturation at source #48. Of the human-extracted concepts that mapped to UMLS terminologies, 533 were associated with 15 terminology homes, and of these, 158 belonged to numerous (more than 3) terminology homes. By terminology, 190 concepts mapped to SNOMED CT®, 42 to the NCI thesaurus, 38 to the Metathesaurus terms, 37 to the Medical Subject Headings (MeSH), and 28 to Health Level Seven (HL7). Other terminologies to which concepts mapped included NCBI, LOINC, AOD, READ CODES, and CRISP (see appendix B). Of the human-extracted concepts, 580 were not mapped to UMLS concepts by MetaMap.

Thirty-four of the extracted concepts were used in conjunction with the rest 1079 concepts in composing additional multi-concepts. The 1,079 explicit concepts were then used in forming a proposed taxonomy for characterization and assessment of AI outbreak as depicted in figure 3. Characterization and assessment were used as the two top hierarchical levels of the taxonomy (See appendix C).

AI outbreak characterization¹ concepts are those used in discerning attributes of an outbreak that are important for its control. These concepts were classified into 4 categories:

1. AI outbreak index case concepts, which are related to describing the initial occurrence of an AI outbreak that eventually leads to further investigation, and includes specific, pathologic, and associated disease findings concepts, as well as concepts related to differential diagnosis, signs or symptoms, laboratory or test results, and infected host attributes (see table 2);
2. management of characterization concepts, which are related to knowledge and intellectual assets useful for accomplishing the goals of characterization, including temporal and functional concepts for management, and outbreak staff concepts that comprises of professionals reporting disease and diseases detection activities. The category also includes concepts related to laboratory procedures, materials requirements, specimens, and laboratory regulatory and services concepts.
3. AI outbreak etiologic agent concepts, which are useful in ascertaining the causative organism or agent of the disease and its mode of transmission. This category of concepts includes concepts for subtypes names, subtyping, chemical, pathological, and genetic attributes of the organism. Other concepts in this category includes those of AI outbreak etiologic agent transmission that pertains to the concepts related to transferring of AI disease etiologic agent from an infected host to an uninfected host; these concepts includes those of epidemiological risk factors and sources of infection comprising of animate, inanimate, and potential sources;
4. and species affected concepts, which refer to concepts related to the host infected by the AI etiologic agent, and includes the concepts of mammals, birds, and humans.

The hierarchical concepts of AI outbreak assessment are those used in the quantification or measurement or estimation of the associated risk of disease burden. The concepts were categorized into 3 groups:

1. AI outbreak consequences including:
  - a. concepts related to economic significance that are important for issues of production, distribution, and consumption of goods and services in relation to avian influenza;
  - b. disease mortality concepts which are concerned with expressing the number of deaths associated with the disease;
  - c. and morbidity concepts that are useful in expressing the proportion of the population infected with the disease during an outbreak

¹“Typewriter” font indicates concepts in the hierarchy.

2. geographic concepts for assessment are those related to describing the geographic size of an outbreak; these include directional, qualitative, and quantitative concepts, as well as concepts of geographical areas (see table 3).
3. biostatistical concepts are useful in the collection, summarizing, and analyses of biological data related to AI outbreak, and includes qualitative, quantitative, and biostatistical activity concepts.

5. Discussion

The purpose of this project was to discern a common set of concepts across domains according to a consistent perspective, interpretation and granularity to aid in public health surveillance and analysis of AI outbreaks. To date there is no specific terminology, taxonomy or classification that captures this common ground. Challenges of this task include the wide assortment of stakeholders in different domains (medical, veterinary, infectious disease prevention and control, public health and epidemiology, poultry farming, agriculture, food industry, military domains, and government regulatory agencies) who have varied areas of expertise and differing terminologies, and must all work together in a timely and coordinated fashion. The finding that only half of the discovered concepts mapped to the UMLS (primarily related to human health) reflects this difficulty in finding an existing terminology for the purposes of AI characterization and assessment. Most of the unmapped classes of concepts included: temporal and functional concepts for characterization management; epidemiological risk factors and sources of infection concepts; laboratory agencies, specimens, materials, and procedures concepts; organism subtyping and subtypes names; biostatistical concepts; and directional, qualitative, and quantitative concepts of geography related to AI characterization and assessment. Existing taxonomies that will be useful in bridging this missing link include the Food and Agricultural Organization's Agriculture Information Management Standards, the Gene Ontology, the USGS GIS Database, and the NCBI Taxonomy Browser; specific taxonomies are however needed for considerations of biostatistics, veterinary medicine, and public health, particularly epidemiology.

This exploration of the UMLS and its subsets, particularly SNOMED CT (see Appendix D), as sources of descriptive information on AI concepts suggests that existing terminologies may provide only part of the desired solution. Doyle and colleagues found that SNOMED CT provides extensive domain coverage of reportable diseases (89%), infectious agents (97%), and substances (94%), but less so for population findings especially disease outbreaks (19%) and reportable procedures (33%) [67]. Mougin and colleagues had earlier found the UMLS being inadequate in meeting public health data requirements [68].

The proposed taxonomy offers a systemic categorization of concepts needed at appropriate granularities for characterization and assessment of AI outbreak. Its scope includes:

- biological and clinical concepts that describe findings relevant to characterization of cases and outbreaks including signs and symptoms (of humans and birds), laboratory and test results and diseases and syndromes;
- epidemiological and biostatistical concepts that describe the extent and potential of an outbreak necessary for assessment including species affected, sources and modes of transmission of infection, geographic concepts, and temporal and functional concepts;
- case specific concepts that support the structural and administrative aspects of AI detection and control including case-specific identifiers, agencies involved and linkage to specific data from cases.

Strengths of this approach include the incorporation of both general knowledge from the diverse fields that comprise the study, detection, understanding and control of AI as well as generic data from case and outbreak specific reports. Such an approach has been described for medical information needs [69] and has potentials for use in case identification in electronic health records and ontologic and natural language support of bio-surveillance [70]. The use of textual corpus for modeling the taxonomy also offers it some strength since textual corpus has been described as the best source for modeling ontologies [71].

The proposed taxonomy is presented, not as the basis for yet another ontology, but to serve as a specification list for an AI sub-domain ontology. This ontology could then be integrated into a larger bio-surveillance taxonomy that links vocabularies from other domains such as virology as part of standards-based public health information sharing [72]. Integration of the proposed taxonomy into the UMLS can facilitate and enable interoperability among disparate systems and formalize inter-concept relationships [73] as may be required for more sophisticated models of medical knowledge representation, such as the Health Level 7 Reference Information Model (HL7 RIM) [74]. As such, further work in the area of AI characterization/assessment taxonomy development will require consensus among the community of AI workers as well as with the owners of other terminologies with which the taxonomy may need to interoperate [75].

An example of the use of the proposed taxonomy concerns geography. The taxonomy points to several attributes of geography, including directional, qualitative, and quantitative as important. These attributes in addition to a systematic and worldwide atlas-dictionary of locations to fine levels of detail and using multiple criteria (latitude, longitude, jurisdiction, travel routes and connection points) with relevant associated knowledge (real-time weather maps, bird migration routes, traffic and trade patterns), will meet the administrative data needs of AI characterization and assessment. By means of an appropriate GIS standard, the proposed taxonomy can be linked to a standard geographic taxonomy such as the USGS Global GIS Database that empowers the use of geographical information systems (GIS) for visualization and prediction of outbreak extension [76].

Limitations of our approach include inadequate coverage of scope. The reduction in the number of new concepts with additional information source was used as measure of saturation and was considered adequate, however, the taxonomy may lack important concepts since only articles in English were used as source of information. Other limitations include: non-inclusion of other potential information sources (such as interviewing experts on the subject of AI characterization and assessment) as well as the need for more experts within the field of AI study with diverse perspectives. Further development of this project will include: the expansion of use cases, validation through consensus and expert opinion, as knowledge of AI grows and design and evaluation of its use in field work (i.e. the characterization and assessment of real-time cases).

Conclusion

We have, based on documents in current use for characterizing AI, assembled a taxonomy of concepts. These concepts provide specifications for future work in choosing available vocabularies, filling them in, or creating novel ones to help in supporting the work of communication surrounding the important task of characterizing and assessing AI outbreaks.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Avian Influenza Outbreak Information Processes. Arrow indicates direction of information

Figure 2.

Saturation Graph showing emergence of concepts with additional information sources.

Figure 3.

Proposed taxonomy for characterization and assessment of avian influenza outbreak with links to other taxonomies; arrow connotes “part-of” superclass.

Table 1

Summary of articles search results.

Database Name	Records Returned	Records Reviewed	Records Selected
PubMed	707	56	11
Biological Abstracts	136	42	6
Agricola	68	21	2
ScienceDirect	298	40	13
Total	1,209	159	32

Table 2

Definitions of hierarchical concepts associated with characterization of avian influenza outbreak.

Class	No	Concepts	Role Type	Definition
Index case	1	Specific findings	attribute	Precise and detailed information from the outbreak investigation
	2	Pathologic findings	attribute	Changes in structure and function of organs associated with AI infection
	3	Associated disease	association	Described pathologic processes with characteristic signs or symptoms
	4	Differential diagnosis	association	Other diseases or conditions having similar signs or symptoms as AI
	5	Signs or symptoms	attribute	Elicited or subjective indicators of illness in a host due to AI
	6	Lab or test results	association	Findings of a specific test aimed at measuring a patient or bird Attribute
	7	Host attributes	attribute	Properties, roles, or associations of an AI-infected human or bird
Characterization Management	8	Temporal concepts	association	Time-point or interval- related concepts used in characterizing AI
	9	Functional concepts	association	Workflow concepts related to the process of characterizing AI
	10	Professionals reporting	class	Personnel responsible for reporting cases of AI to regulatory agencies
	11	Detection activities	association	Actions by which professionals perceive, discern, discover, or identify AI
	12	Laboratory procedures	association	Procedures for generating, assuring, and recording the test of a sample or bodily substance in the laboratory
	13	Materials	class	Materials, beside specimens, used in laboratory procedures
	14	Specimens	class	Preparation of tissues or bodily fluid needed for laboratory procedures
Etiologic agent	15	Regulatory organizations	class	Agencies that make and oversees regulations for AI outbreak reporting
	16	Services organizations	class	Labs associated with procedures for determining the AI etiologic agent
	17	Subtype names	class	Standard names for the AI agent
	18	Subtyping	association	Process of identifying the genetic identity of the AI agent
	19	Chemical attributes	attribute	Substances within AI agent having defined atomic or molecular structure
	20	Pathologic attributes	attribute	Properties of AI agent associated with producing diseases
	21	Genetic attributes	attribute	Properties of AI agent resulting from or related to genes
	22	Methods of transmission	association	Ways of transferring AI from an infected host to an uninfected host
	23	Risk factors for transmission	association	Epidemiologic factor known to be associated with AI occurrence
	24	Sources of infection	association	Geographic point or specie from where AI infection spreads
Species affected	25	Mammals	class	Warm-blooded vertebrate animals belonging to the class Mammalia
	26	Birds	class	Warm-blooded vertebrates belonging to class Aves

Class	No	Concepts	Role Type	Definition
	27	Humans	Class	Mammal in species Homo sapiens

*
AI = Avian Influenza

Table 3

Definitions of hierarchical concepts associated with assessment of avian influenza outbreak.

Class	No	Concepts	Role Type	Definition
AI Outbreak Consequences	1	Economic consequences	attribute	Concepts related to the production, distribution, and consumption of goods and services affected by AI outbreak
	2	Disease mortality	attribute	Concepts expressing the number of deaths associated with AI outbreak
	3	Disease morbidity	attribute	Concepts concerned with expressing the proportion of the population infected in an AI outbreak
Geographic	4	Directional	association	Concepts concerned with directional descriptions
	5	Quantitative	association	Concepts relating to geographical measures or values during AI outbreak
	6	Qualitative	association	Concepts relating to the quality or character of AI outbreak's magnitude
	7	Geographic areas	class	Demarcated area of the earth that is significant for epidemiological studies during an AI outbreak
Biostatistical	8	Quantitative	association	Relating to the amount or number of findings associated with analyzing AI outbreak data
	9	Qualitative	association	Relating to the quality or character of findings associated with analyzing AI outbreak data
	10	Biostatistical activity	association	Statistical undertakings used in analyzing AI outbreak observations or phenomena

* AI = Avian Influenza