

A great challenge, a simple approach: multi-dimensional data, context-specific methods, real-time and cost-effective decisions – a retrospective analysis of avian influenza (H5N1) epidemics

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Summary

At least since the 1993 cholera pandemic (the result of a Pacific Ocean water temperature increase), climate change has been known to facilitate the emergence and propagation of disease. Better and earlier ways to monitor zoonoses are necessary. Like climate change, zoonosis is not a simple entity but a complex interaction. It involves at least 4 dimensions: the host, the microbe, space, and time. By combining these 4 dimensions with new technologies and new methods, the analysis and resolution of zoonotic challenges could be improved.

Here we describe an approach that utilizes disease- and context-specific methods to make, in real time, cost-benefit based decisions that address zoonotic challenges. Using data from an Avian Influenza virus (H5N1) epidemic, it is shown that earlier, less costly or more beneficial decisions can be generated to manage both zoonotic and non-zoonotic diseases.

The (re)discovery of...space?

Until recently, space could not be measured easily, precisely, rapidly, or at low or no cost. Now, by using Geographical Information System software and additional algorithms that facilitate the analysis of epidemic scenarios, we can, once an epidemic occurs, ask questions like **where**, **how**, and **why should we act**, so we can stop it faster and at the lowest cost. To answer those questions, spatial data are necessary. But they are not sufficient. It is not space what is being re-discovered but the value of addressing problems that require decisions on real time. Such challenge requires the creation of (disease- and context-specific) methods.

The problem: Avian Influenza (H5N1) in Nigeria

In January, 2006, highly pathogenic Avian Influenza (HPAI) virus, subtype H5N1, was detected in Nigeria. As of December, 2008, HPAI H5N1 has been reported in 62 countries, resulting in the loss of > 100 million birds and > 245 human deaths.

From old issues to new data and methods

Cost vs. benefit – In exotic and rapidly disseminating infections (e.g., HPAI), the number of cases and the spatial size of the epidemic grow over time. Early decisions are critical.

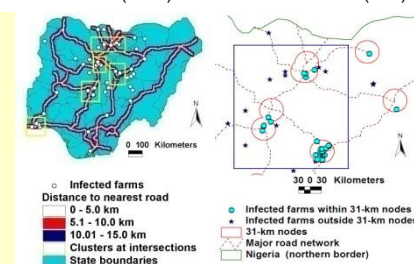
Intervening hosts or vectors? – Classic interventions focus on the host (e.g., vaccination, de-population) and tend to involve large spatial scales (e.g., countries, states). These approaches apply to control endemic (ongoing) diseases, but are less so to control emerging (new) diseases.

Limited data – Classic analytical methods require a rather large volume of data. Because, in emerging diseases the initial number of cases is close to zero, some of those methods (e.g., case-control comparisons) are marginally applicable.

Waiting time – Classic policy-making oriented models use data collected over 2 or more transmission cycles of the infecting agent. Because the transmission period of HPAI H5N1 is ~ 10 days, such models require a ~ 20-day waiting time.

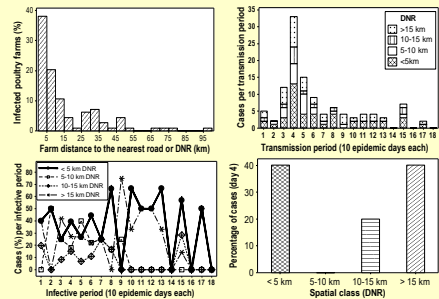
Needs – Could **earlier** factors (e.g., **propagation** vectors) be intervened? Could new methods be **less sensitive to the volume of the data?**

The data – To address these questions, a geo-temporal dataset of the 2006 Nigerian HPAI H5N1 epidemic was created. It included: (a) date and location of 113 infected poultry farms, and (b) the Euclidean distance from each infected farm to the nearest road (DNR) and road intersection (DNI).



The 2006 Nigerian AI H5N1 epidemic. Location of 113 infected poultry farms in relation to DNR (left), and DNI (right).

Thirty-eight percent of all cases were reported at < 5 km DNR, and 57% of all cases were at >31 km DNI. Since epidemic day 1, ~ 40% of all cases were at <5 km DNR. Roads (e.g., human traffic, poultry trade) facilitated epidemic spread.



Without requiring large volumes of data, spatial analysis can generate earlier decisions. Since epidemic day 1, more than one third of all cases were at < 5 km from the nearest road (DNR). When time was expressed in biologically meaningful formats (microbial transmission periods, not days or weeks), the typical, epidemic exponential growth phase was observed. If, spatial-epidemic descriptors are used (e.g., cases contributed by each DNR class at each transmission period), a dissimilar pattern is observed: not all spatial-epidemic classes contributed equally to the epidemic size (e.g., cases at < 5 km DNR generated 40-60% of all cases until the 9th transmission period). If only the data of the first transmission cycle (epidemic day 4) were available, what conclusion (and decision) could be made?

Emerging and rapidly disseminating epidemics are characterized by the "20:80" rule: a small percentage of cases explains most of the epidemic. Epidemic data are neither independent nor identically distributed: (some of the) primary cases generate all later cases, secondary cases generate more cases than tertiary ones and, when epidemics stop, the last cases add nothing.

These features can be considered to make an early (although uncertain) decision: if (a) a spatial variable is identified as a possible transmission factor (e.g., proximity to roads), (b) it is associated with a substantial percentage of cases (e.g., > 20%), and (c) such identification is produced before the first transmission cycle of the invading microbe concludes, then an early intervention, meant to neutralize the vector, can be decided.

In this scenario, by epidemic day 4 (not after 20 days), it could have been suspected that epidemic spread was promoted by proximity to roads: a decision (road blocks) could have prevented poultry trade. Even if erroneous (if roads were not the only transmission vector), the cost of such decision would have been negligible. However, if correct, it would induce larger benefits than those of a scientifically sound but late decision.

Because data on some transmission factors (e.g., road networks) are available for all countries, this approach can be conducted on real time, worldwide.

Detection of interactions

The Avian Influenza example shows how multi-dimensional (geo-temporal-host-microbial) data can help in making decisions.

Each data type may include numerous variables. For instance, host-related data can include leukocyte data (e.g., counts and percentages of lymphocytes, macrophages, and neutrophils). Microbial data can identify microbial strains.

Geo-temporal, host and microbial profiles can now be assessed with up to 120 variables, which can detect *Interactions* (e.g., the effect of a specific spatial class at a specific epidemic transmission period). They tell *what* and also *why*, *how*, *where*, and *when* (an explanatory system also applicable to non-zoonotic diseases).

What is new in this approach?

- It is not limited to the analysis of space and transmissibility (explored by John Snow in 1848).
- It is the set of 3 criteria:

real time implementation, cost-benefit analysis, and worldwide applicability.

Methods are developed to be conducted within minutes, producing measurable evidence of costs vs. benefits, which can be applied without sophisticated equipment or specialized training

- And a set of **means**:

a **"library"** of epidemic data.

A collection of actual geo-temporal-epidemic datasets on both "rapid" and "slow" diseases.

Potential consequences

- new (problem-solving oriented) **educational programs**,
- new **disease monitoring systems**, with population- and individual-based diagnoses and prognoses.

Significance

The prospective creation of epidemic data (with 4 types of data), potentially collected at diagnostic settings, could be the building block of a simple process to improve the analysis and resolution of zoonotic and non-zoonotic challenges.

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