

Linking Global Surveillance for Human and Animal Diseases: Progress and Pitfalls:



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Biotechnology and Global Health

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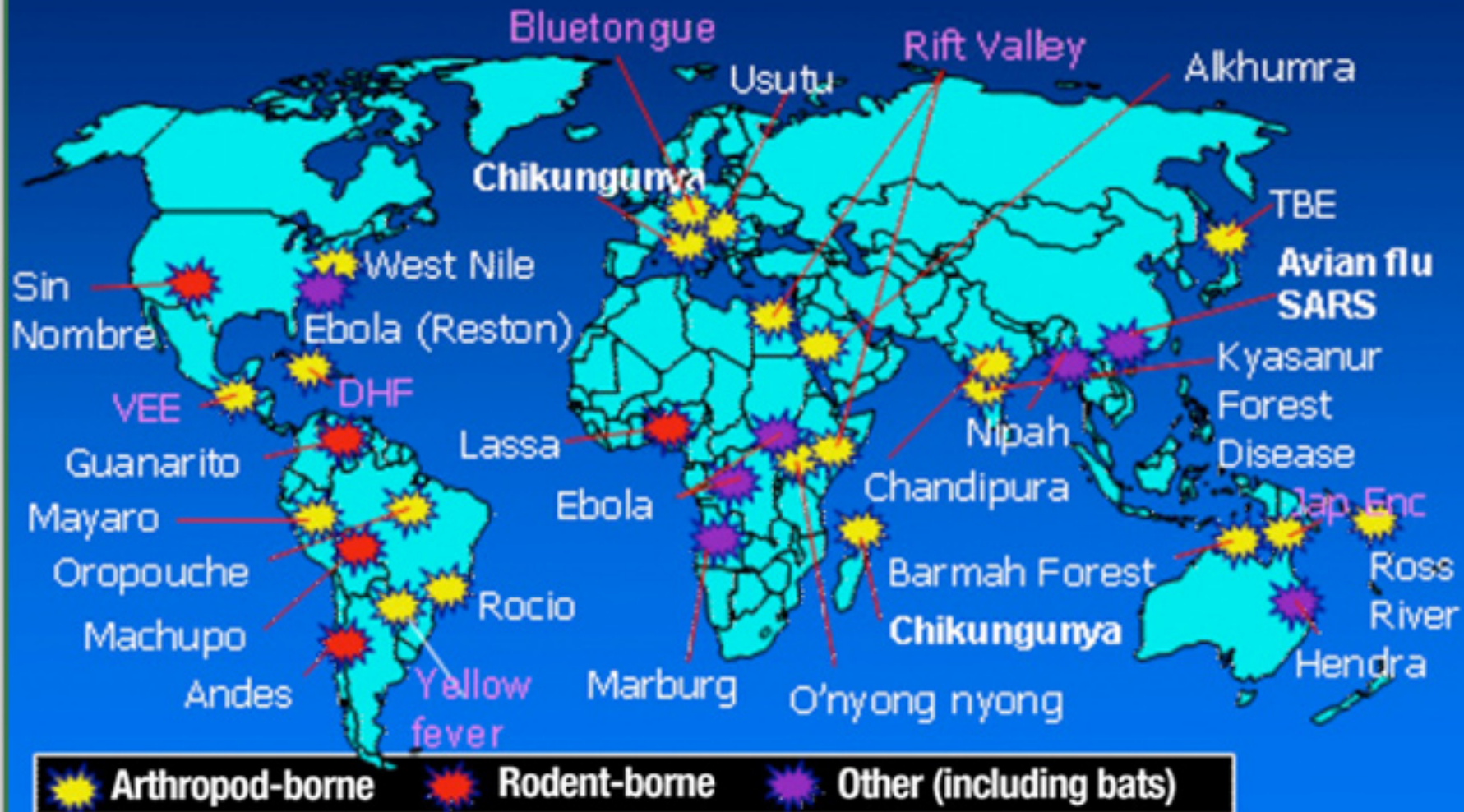
Overview

- Convergence of human and animal health
- Why human health should care about disease in animals
- Why animal health should care about disease in humans
- Current human and animal surveillance for global disease
- Barriers to linking animal and human data
- Avian influenza : lessons learned

Convergence of Human and Animal Health

- Emerging diseases: SARS, West Nile, Monkeypox, avian influenza

Emerging and Reemerging infections - 70% vector-borne or zoonotic



Other Convergence of Human and Animal Health

- Toxic exposures
- Live animal trade
- Food safety

Need for Collaboration between Human and Animal Health



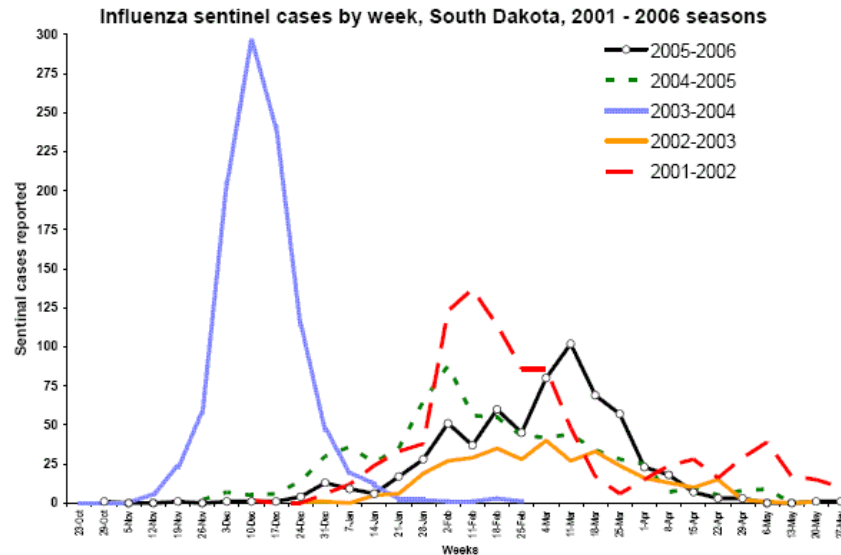
Why Human Health Professionals Need to Care about Animal Disease

- Zoonotic disease threat: infected animals could threaten humans
- “Sentinel” of environmental risk
 - Toxic or infectious
 - Intentional or accidental Release
 - Change in disease ecology

Sentinel Health Events

- “A Sentinel Health Event (SHE) is a preventable disease, disability, or untimely death whose occurrence serves as a warning signal that the quality of preventive and/or therapeutic medical care may need to be improved.”
 - Ruttstein et al Am JI Pub Health 1983

Sentinel Human Influenza Cases



This week's graph presents the influenza sentinel cases by week in South Dakota during the 2001 through 2006 flu seasons. Surveillance for influenza viruses involves a statewide network of sentinels including physician offices with a laboratory, hospital laboratories, large clinical practice labs, college health services, and community health centers that collect throat swabs on patients meeting clinical criteria defined as illness with a fever greater than or equal to 101° F and three or more cold symptoms such as cough, coryza, headache, chills, sore throat, or myalgia. There are 32 influenza surveillance sentinel sites in South Dakota that voluntarily collect and submit influenza isolates for testing at the public health laboratory. In South Dakota, all laboratory confirmed cases of influenza are mandatory reportable events.

During the 2005-2006 influenza season in South Dakota, 636 confirmed influenza cases were reported to the South Dakota Department of Health. The 2005-2006 South Dakota influenza season peaked during mid March (week ending 11 March, 2006) and lasted for a period of 34 weeks. Source of information: South Dakota Department of Health.

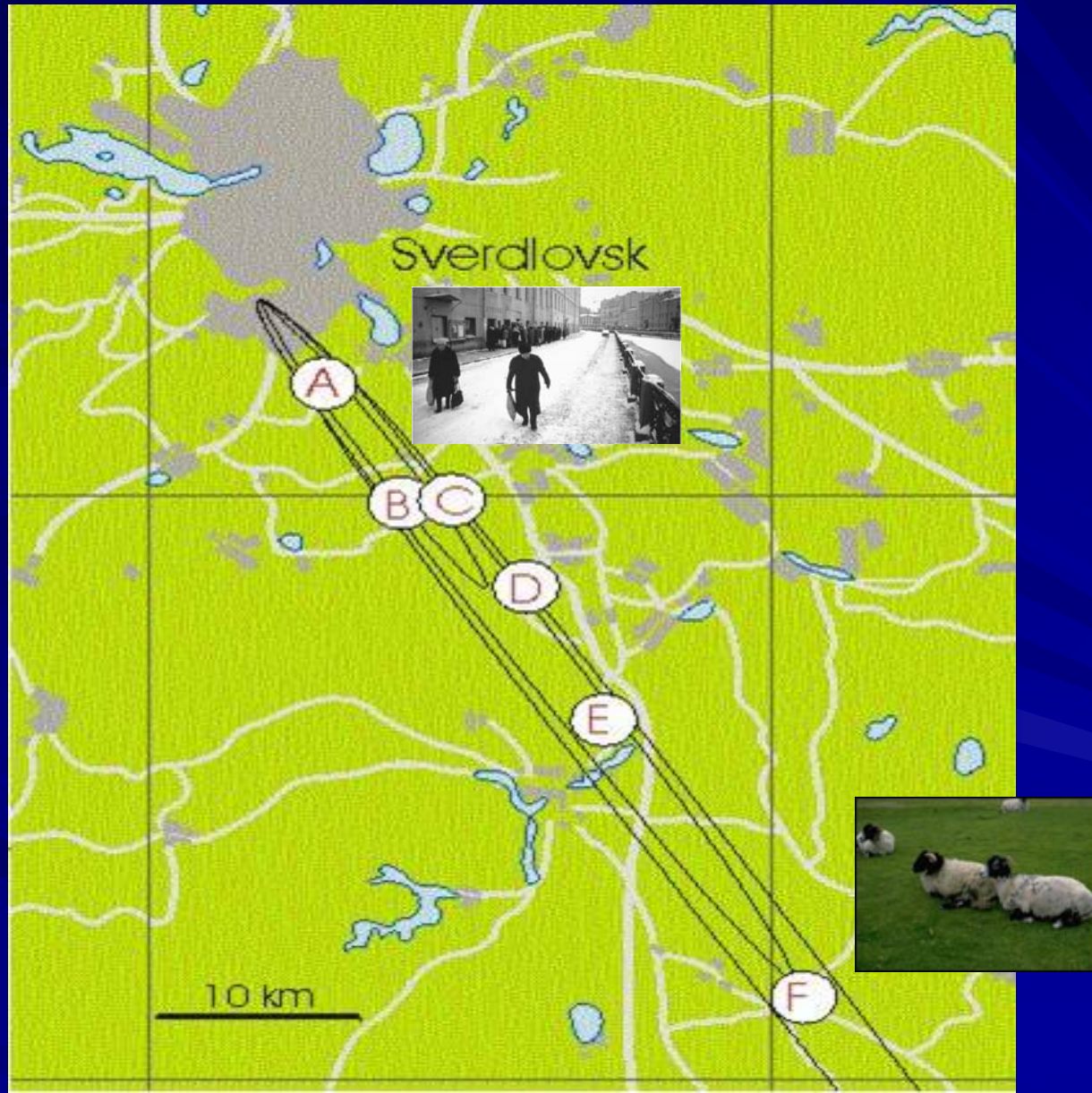
Animals as Sentinels for Humans

- Provide “early warning” about disease risks shared with humans due to some combination of:
 - Increased susceptibility
 - Increased exposure
 - shorter latency
 - Easily recognizable clinical signs

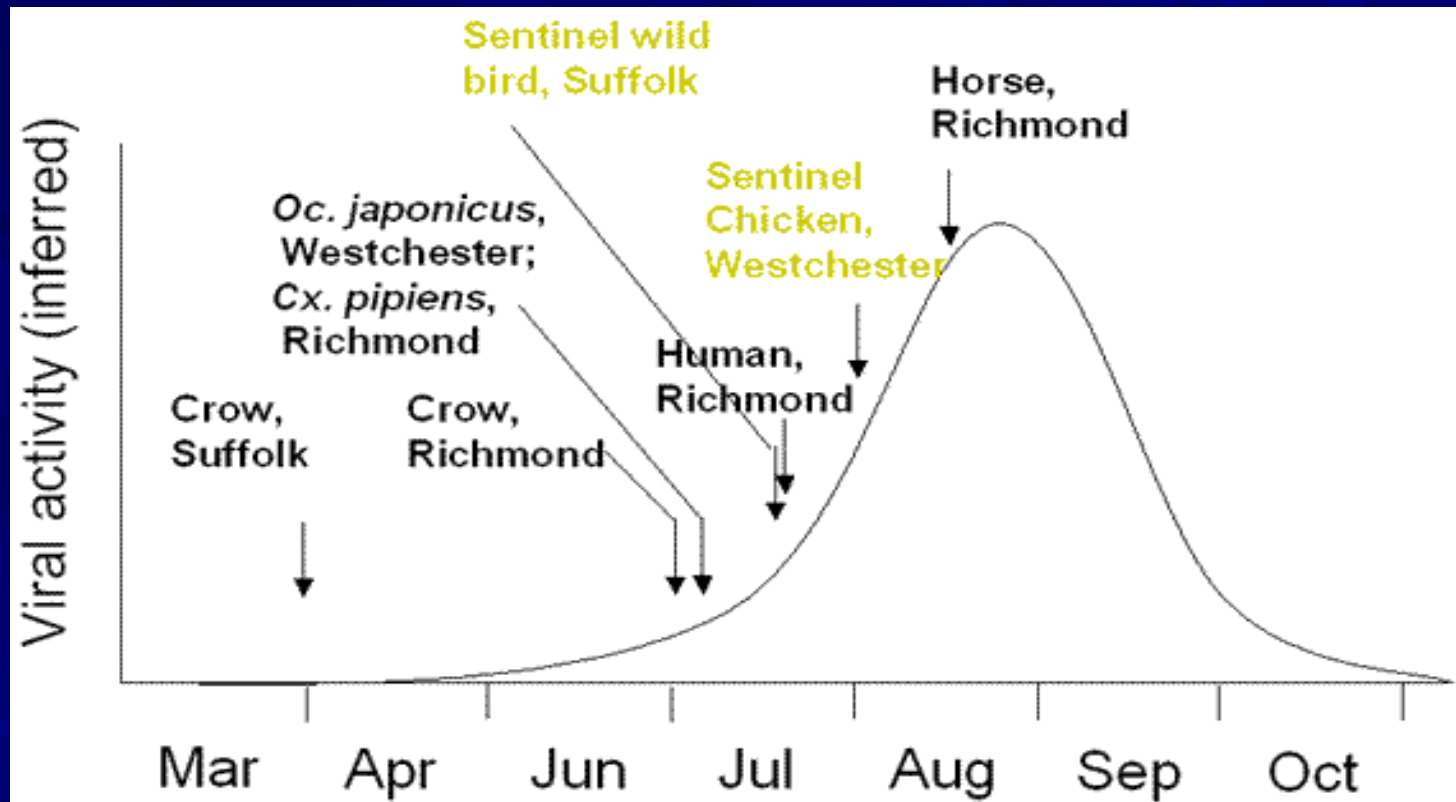
Canaries and Coal Mines



Sverdlovsk: Anthrax and Livestock



Animals as Sentinels for West Nile Virus



Komar N. 2001. Second National Planning Meeting for Surveillance, Prevention, and Control of West Nile Virus in the United States

Why Animal Health Professionals Need to Care About Disease in Humans

- Impact on trade
- Occupational disease risk
- Humans can be sentinels for animal disease risks
 - Toxic or infectious
 - Intentional or accidental release
 - Change in disease ecology
 - Change in biosecurity in agriculture or trade

Humans as Sentinels for Animals

- Due to better detection efforts, disease may first be reported in humans
- Often the case with occupational disease
- Abattoir worker with brucellosis
- Veterinarians with zoonotic disease
- Rift valley fever
- Avian influenza
- Toxic exposures

Disease Surveillance

- Systematic gathering of disease data in humans or other animals
- Should be tied to response efforts and concrete interventions
 - Outbreak response
 - Disease prevention activities/policies
- Active surveillance
 - Surveys in asymptomatic population, outreach to clinicians
- Passive surveillance
 - Required reporting to authorities

Human Disease Surveillance

■ Human:

- CDC, other national systems
- WHO compiles data, estimates
- DOD
- Emerging disease tracking: Promed, GIPHN (Global Public Health Intelligence Network)
 - Monitor websites, news media, clinician networks

Animal Disease Surveillance

- Country level: Departments of agriculture: diseases reportable to agriculture, (US: USDA, NAHMS)
- World Organization for Animal Health (OIE): receives reports from countries (Agriculture departments) for a list of notifiable diseases
- UN Food and Agriculture Organization (FAO): gathers data on food production, disease in food animals
 - EMPRESi: tracks AI in animals, plans for other diseases

Emergency Prevention System for Transboundary Animal and Plant Pests and Diseases

Livestock component



EMPRE
EMERGENCY PREVENTION SYSTEM

FAO AGA

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What is EMPRES-*i*

EMPRES INFORMATION SYSTEM

The EMPRES Global Animal Disease Information System (EMPRES-*i*) has been designed to support national veterinary epidemiologists and facilitate regional and global information sharing and collaboration on the progressive control and eradication of major TADs.

EMPRES-*i* provides five different modules with updated information on global disease distribution, current threats and response to emergencies. It also provides access to training material and resources for veterinary epidemiologists.

EMPRES Information System Modules

- ▶ **Animal Disease Information Systems**
- ▶ **Disease recognition Module**
- ▶ **Disease mapping**
- ▶ **Disease Alerts**
- ▶ **Tools for veterinary epidemiology**

Internet

Animal Disease Surveillance(continued)

■ Wildlife:

no mandate for international tracking

OIE: committee on wildlife

Recent initiatives: Global Avian Influenza
Network for Surveillance(GAINS), Highly
Pathogenic Avian Influenza Early
Detection System (HEDDS)

Case for Linking Human and Animal Disease Data

- Provide early warning of disease outbreaks, but also:
- Identify ecological/environmental “drivers” of disease emergence
 - Land use change
 - Agricultural systems
 - Problems with biosecurity

Challenges to Linkage

- Agriculture and public health with different mandates
- No agency with clear mandate to compare disease trends in humans and animals in a “One Health” manner

Ramification of Animal Disease Reporting

- Countries may ban imports or exports based on animal disease status in a country, affected by OIE reports
- Huge economic consequences and effect on global movement of animals and animal products
- Local measures of control, culling, vaccination

Case Example: Avian influenza H5N1

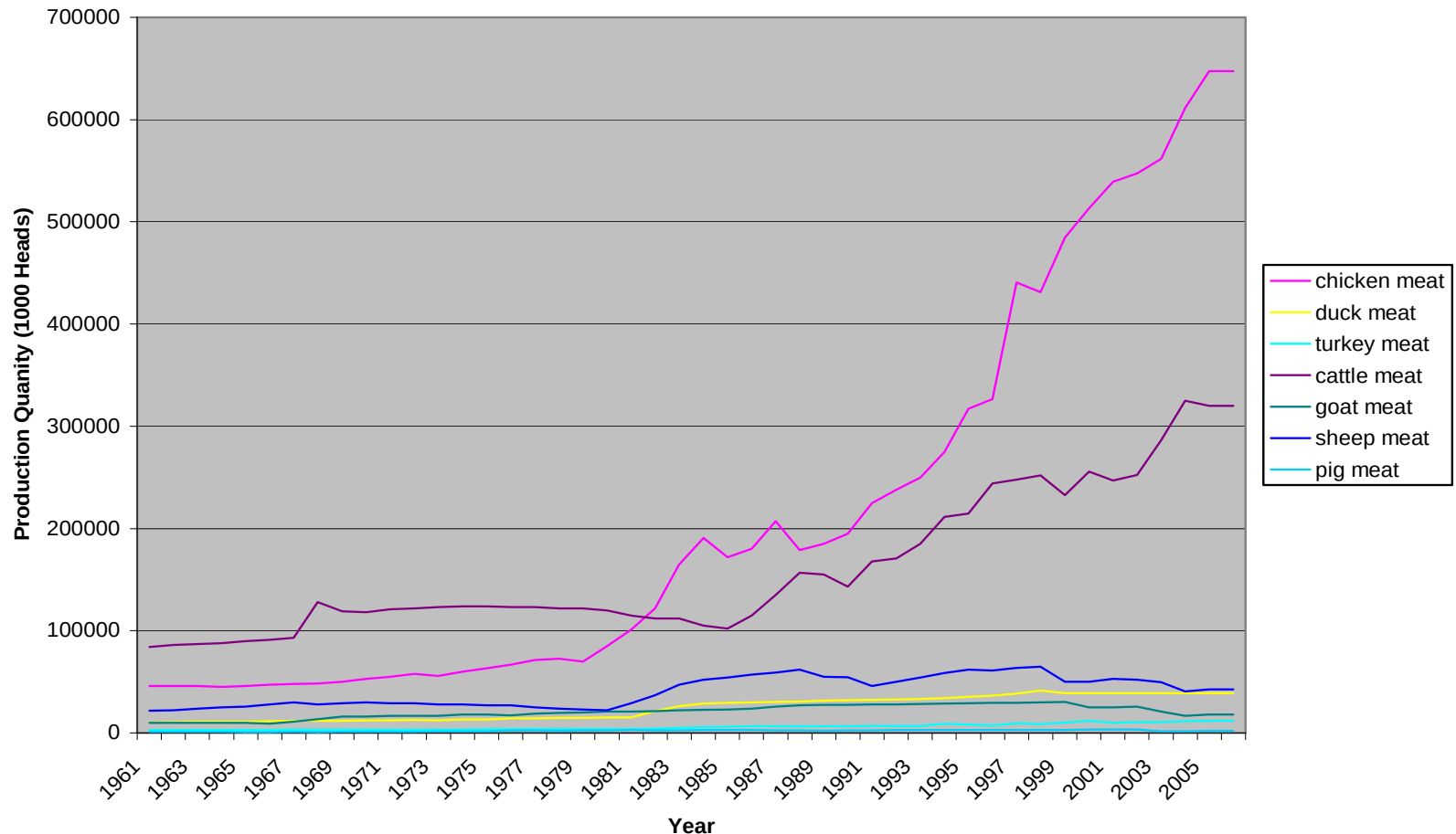
- Global epizootic: hundreds of millions of birds diseased or culled- continuing outbreaks
- Zoonotic transmission
- 387 WHO confirmed human cases, 245 deaths
- Pandemic potential

Intensification of Poultry Production

Contact between Wild and Domestic Birds

Increased Production of Poultry

Production Quantity of Meat Types in Egypt



Highly Pathogenic Avian Influenza Surveillance in Humans

- Detect human cases
- Detect person to person transmission
- Help identify risk factors

Human AI Surveillance

- Human cases diagnosed clinically, confirmed by lab testing
- Country reports cases to regional disease control authorities as well as WHO which determines if lab diagnosis meets WHO standards for confirmation
- Viral isolate if available
- Limited information regarding risk factors

Active Surveillance for AI

- Serosurveys in outbreak or endemic areas
- Surveillance of high risk workers and other groups

Other Types of AI tracking

- GPHIN, Promed monitor news reports, networks of clinicians and public health professionals
- “Rumor Tracking”

Challenges of Avian influenza

- Can you define modifiable risk factors for human infection?
- Can you identify “high risk groups”?
- Can you predict “high risk areas” for human cases?

Animal AI Surveillance

- Disease suspected in poultry or other animal population
- Confirmatory testing
- Reported to national agricultural authorities
- Country reports to OIE on periodic basis

Other Animal Surveillance for HPAI

- FAO/EMPRES monitors Promed, GPHIN, receives reports from country offices, depts. of agriculture
- GAINS, HEDDS, etc. track virus in wild birds

Response to Animal Cases

- Search for more animal and human cases
- Outbreak response: local, regional, national and international level
- Vaccination , culling,restrictions on movement of animals

GLEWS

- “Global Early Warning System for Major Animal Disease”
- Cooperation between WHO, OIE, and FAO

Sharing of Avian Influenza Disease Information between Animal and Human Health

- GLEWS model: HPAI information sharing between WHO, OIE, and FAO: realtime
- Sharing of viral sequence data on both animals and human viral isolates
- Some coordination of outbreak response between WHO and FAO

Ongoing AI Risk Assessment

- Where are high risk areas for human cases?
- What are high risk groups for human cases?
- What are the factors driving animal outbreaks?

Implications of Risk Assessment

- Targeting of public health measures to reduce human risk (including possibility of vaccine)
- Targeting of agricultural methods to control and prevent animal disease

Biosecurity is Key to Link Between Human and Animal Cases

Human disease risk is related to the degree of virus circulation (manifest as cases in animals) and:

Degree of animal-human contact

Degree of domestic animal-wildlife contact also important

FAO Production Sector Concept

Poultry Production Sectors

Sector 1

Industrial integrated system with high level biosecurity and birds/products marketed commercially (e.g. farms that are part of an integrated broiler production enterprise with clearly defined and implemented standard operating procedures for biosecurity).

Sector 2

Commercial poultry production system with moderate to high biosecurity and birds/products usually marketed commercially (e.g. farms with birds kept indoors continuously; strictly preventing contact with other poultry or wildlife).

Sector 3

Commercial poultry production system with low to minimal biosecurity and birds/products entering live bird markets (e.g. a caged layer farm with birds in open sheds; a farm with poultry spending time outside the shed; a farm producing chickens and waterfowl).

Sector 4

Village or backyard production with minimal biosecurity and birds/products consumed locally.

Source: *FAO Recommendations on the Prevention, Control and Eradication of Highly Pathogenic Avian Influenza (HPAI) in Asia*, September 2004

Relationship of Production Sector to Disease Risk

- Bird cases identified in all sectors
- Global growth in sectors 1 and 2
- Human cases more in sector 4

Not Well Known, not Easily Tracked

- Distribution of production sectors within countries
- Maps of production sectors, including
 - Location of intensive production facilities
 - Location of (many) live animal markets
 - Interaction with wildlife

Mapping Biosecurity

- No agreed upon method:
- Large farms
- Small farms
- Movement of animals

Data Sources on Biosecurity

- FAO global livestock production atlas (GLIPHA)
- UN Demographic databases
- OIE WAHID data on animal health-veterinary services
- In-country agricultural censuses and surveys

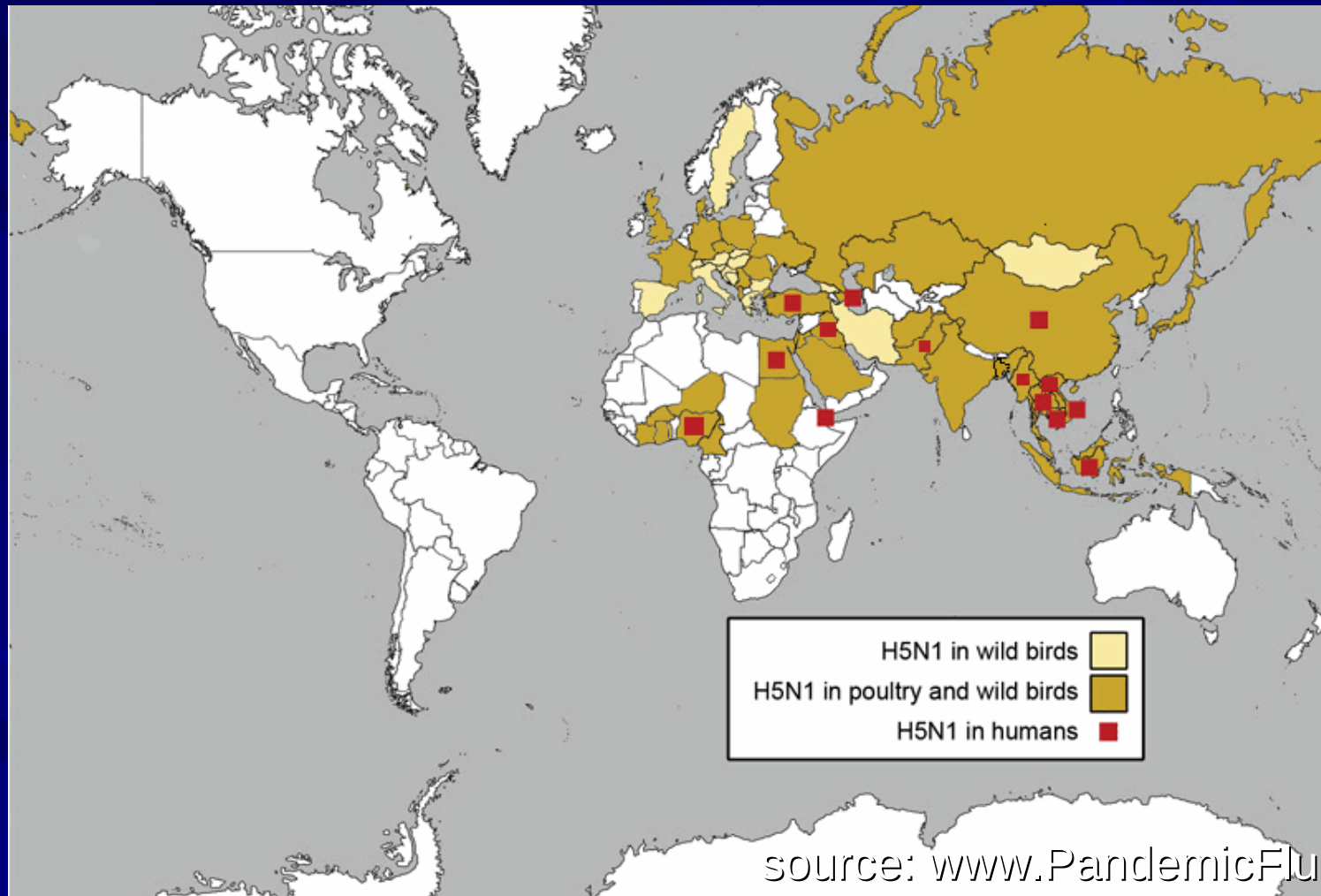
FAO Global Livestock Atlas of the World (GLIPHA)

- Maps of livestock density
- Data on animal census and exports, by country

Can Linking Human and Animal Surveillance Data Shed Light on Human and Animal Risk?

- “One Health” concept in action
- View both human and animal cases as indicators of biosecurity and other environmental risks

Traditional Dot Map to Compare Bird and Human AI Cases



Other Approaches to Data Linkage

- Compare temporal and spatial patterns of disease using quantitative methods
- Use animal data in a predictive model for human cases
- Can other risk variables help explain the relationships?

Previous Analysis of Temporal Relationships

Dynamic patterns of avian and human influenza in east and southeast Asia

Andrew W Park, Kathryn Glass

The seasonal patterns of human influenza in temperate regions have been well documented; however, much less attention has been paid to patterns of infection in the tropical and subtropical areas of east and southeast Asia. During the period 1997–2006, this region experienced several outbreaks of highly pathogenic avian influenza A (H5N1) in hosts including wild and domestic poultry, human beings, and other mammals. H5N1 is thought to be a likely source of a pandemic strain of human influenza. Incidence of both human influenza and avian influenza in human beings shows evidence of seasonality throughout east and southeast Asia, although the seasonal patterns in tropical and subtropical areas are not as simple or as pronounced as those in temperate regions around the world. The possibility of a human being becoming co-infected with both human and avian strains of influenza is not restricted to a short season, although the risks do appear to be greatest during the winter months.

Introduction

In Hong Kong in 1997, an outbreak of highly pathogenic avian influenza A (H5N1) spread from poultry to human beings, causing 18 confirmed cases and six deaths.¹ Between 2001 and 2006, outbreaks of H5N1 occurred in poultry every year in various parts of east and southeast Asia and led to around 200 confirmed human cases in the region.² As yet, the virus has shown very limited ability to spread from person to person. However, if a strain of influenza that is highly pathogenic to human beings acquires the ability to spread easily between human beings, the result could be a global pandemic such as that seen in 1918–19, which killed an estimated 40 million people.^{3,4}

A pandemic strain could arise either by adaptive mutation of a zoonotic influenza A virus during human infection, or by genetic reassortment of a zoonotic virus with a human virus in a person simultaneously infected with both human and avian strains of influenza A. Although H5N1 has now spread more widely, much of the recent activity remains in the region of east and southeast Asia, which is considered to be a “hot spot” for the emergence of pandemic influenza because of the close contact between human beings and poultry in live bird markets and farms.

In many regions around the world, there is a wealth of data on influenza incidence in human beings. These regions tend to be temperate and show a strong seasonality characterised by a single peak in the winter months lasting between 8 and 12 weeks. By contrast, there has been relatively little work looking at the temporal patterns of human influenza A in east and southeast Asia, which contains both tropical and subtropical areas. Although there is some evidence that survival of the H5N1 avian influenza virus is temperature dependent,⁵ there has been limited investigation into the seasonal patterns of incidence. Moreover, there is a pressing need to monitor these data for evidence of changes in the patterns of incidence and for evidence of expanding host range.

In this paper, we present a review of the data on human and avian influenza H5N1 in east and southeast Asia between 1997 and 2006. Not only do these data give valuable insights into the risk of the emergence of a pandemic strain

of influenza, they also show dynamic trends, revealing which patterns are robust and which are changing. Armed with this information, we are able to monitor important changes in avian influenza epidemiology expressed at the population level, aiding strategic planning in surveillance, control, and pandemic preparedness.

Search strategy and selection criteria

To investigate the seasonality of H5N1 virus, outbreaks of H5N1 involving morbidity and mortality of domestic poultry were identified using data from the World Organisation for Animal Health for outbreaks from late 2003 onwards,⁶ and published articles on outbreaks in Hong Kong between 1997 and 2003.^{1,2,4} In some cases, isolates from poultry markets indicated that H5N1 virus was present before mortality was observed;¹⁷ however, because surveillance was not uniform across time and all locations, we included identified outbreaks only. For each region and year in which an outbreak occurred, we classified each month according to the number of outbreaks in that month: none, 1–9 outbreaks, 10–99 outbreaks, and 100 or more outbreaks. Where the data-reporting period included more than 1 month, outbreaks were split between months according to the number of days in the reporting period in that month.

Data on human cases of H5N1 virus from late 2003 onwards were obtained from WHO,² with data on human cases in Hong Kong between 1997 and 2003 taken from published articles.^{1,20} The reference date for each case was taken to be the date of onset of symptoms, if available, otherwise the date of hospitalisation was used. For each region, the presence or absence of (at least) one human H5N1 case was recorded for each 10-day period.

A search using PubMed (using the search terms “avian influenza”, “H5N1”, and “surveillance”) for English language articles with surveillance data extending over at least 1 year identified only one article that included H5N1 isolates. These data were collected from live poultry markets in mainland China from July, 2000, until January, 2004.²¹ Since there is evidence that ducks and geese in central China had an important role in the persistence and

Lancet Infect Dis 2007; 7: 543–48

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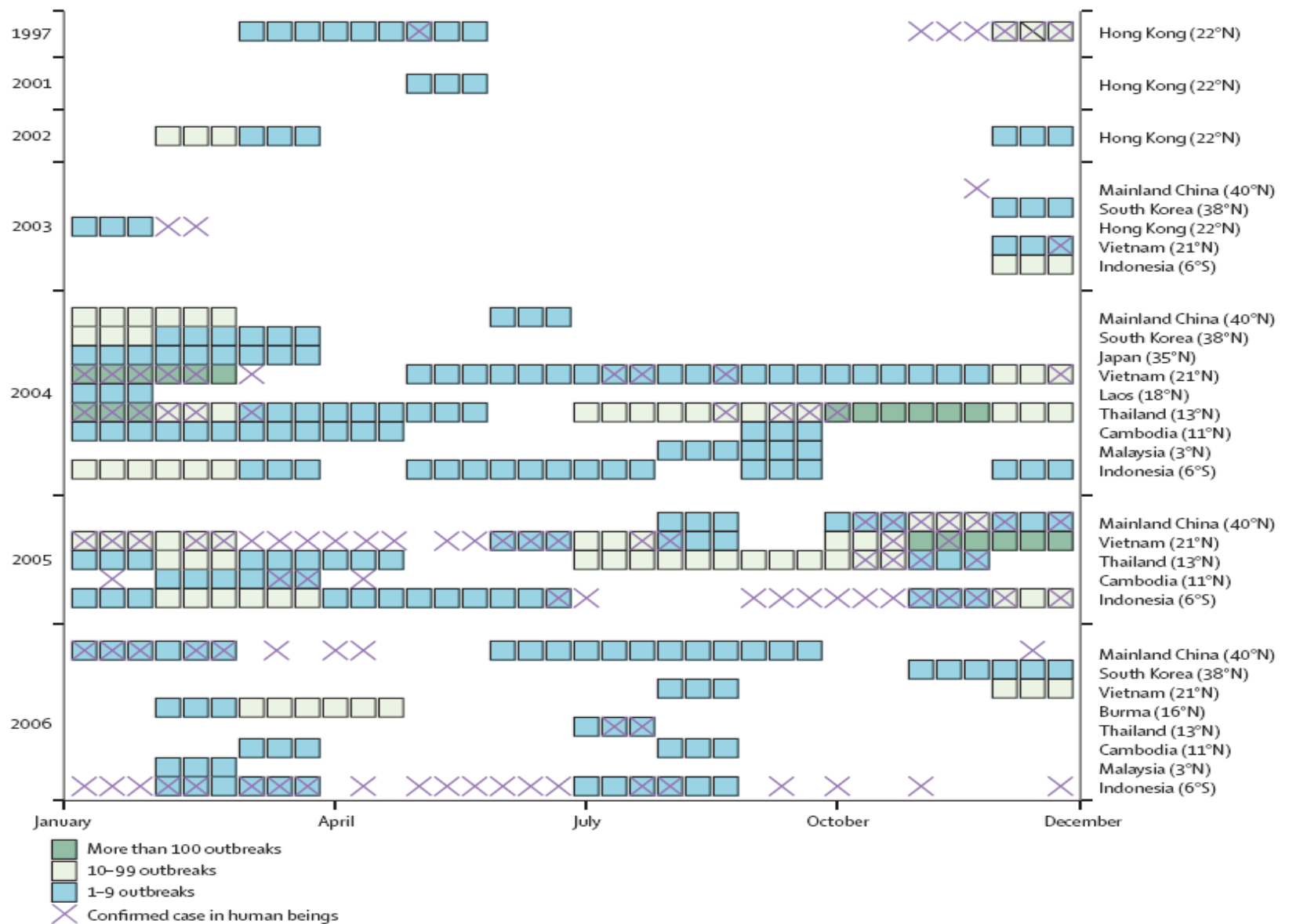


Figure 2: Seasonality of avian influenza A virus (H5N1) outbreaks in poultry and cases in human beings 1997–2006

The number of outbreaks in poultry is classified by month as low (blue), medium-high (pale green), and very high (dark green). A cross indicates the presence of confirmed human cases in any 10-day period. The right vertical axis shows the latitude of the capital city of each country included.

No Previous Use of Bird Data to
Predict Human Cases in
Quantitative Model

Development of Objective Data Model for Human Risk Assessment

- Merge animal and human data (EMPRESi animal cases and WHO human cases (from website))
- Identify variables mediating association between animal and human cases
- Create risk map based on model
- Can it add value ?

Country Level Variables

- Human population
- GDP (UN)
- Prevalence of hunger (FAO)
- Number of veterinarians (WAHID)
- Poultry density (GLIPHA)
- Duck census (GLIPHA)
- Poultry exports (GLIPHA)
- % human population engaged in agriculture (GLIPHA)

Data Analysis Model

- Created, in SAS 9.01, a longitudinal data analysis model that looks at sequential time windows for a particular country and determines
 - Number of animal cases in past 30 days (including species of animal case)
 - Occurrence of human case in current month
 - Other time dependent information (season, temperature, holiday)
 - Adjusts for other risk variables

Application of Risk Model

- Performed bivariate and multivariate analyses of variables to determine which were independent predictors of human risk
- Analyzed collinearity between variables

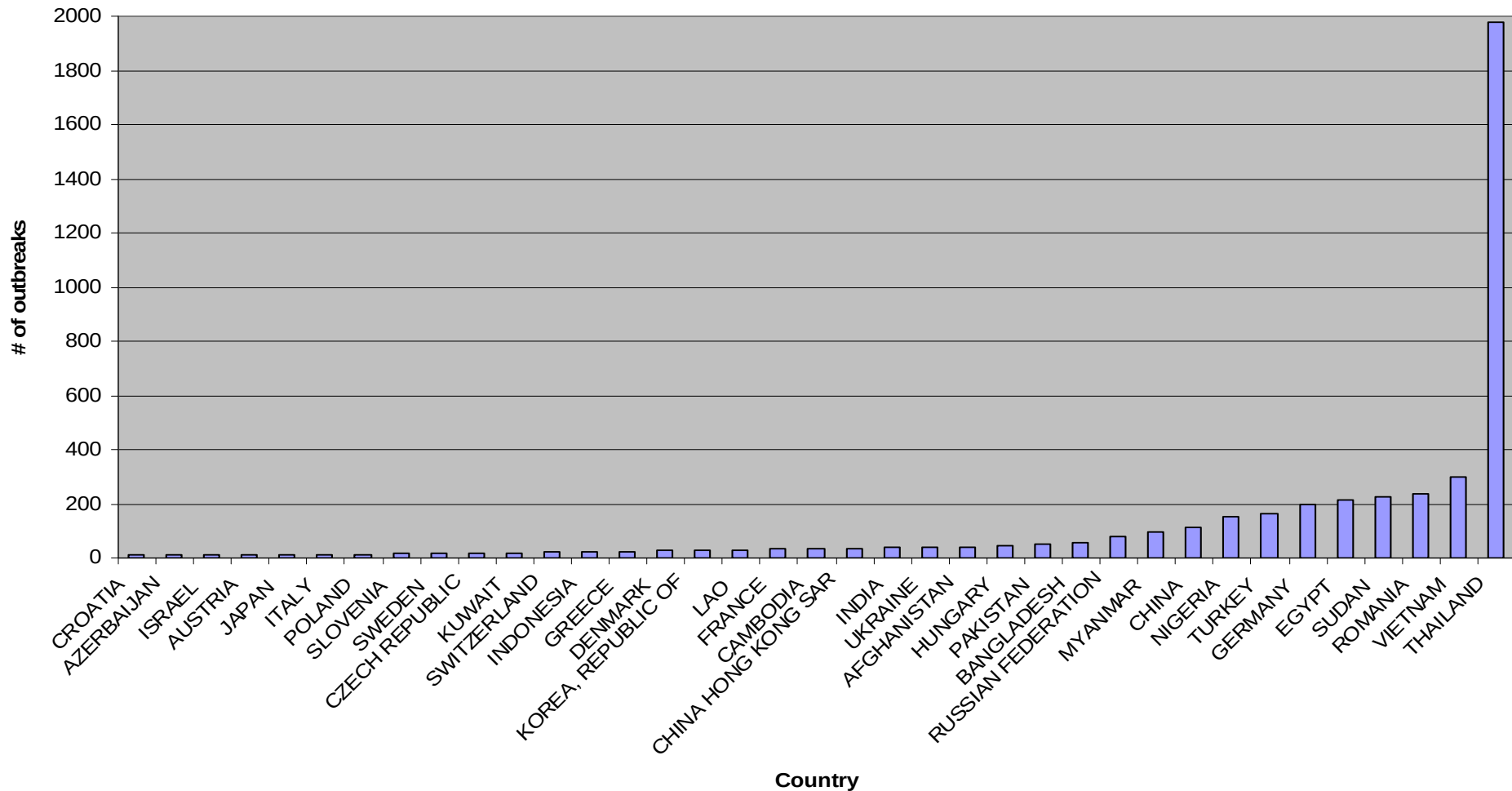
Additional Comparison of Human and Animal Data Streams

- Epidemiological curves for birds and animals
- Time lags between first reported bird case and first reported human case in a country

Results of Preliminary Analyses

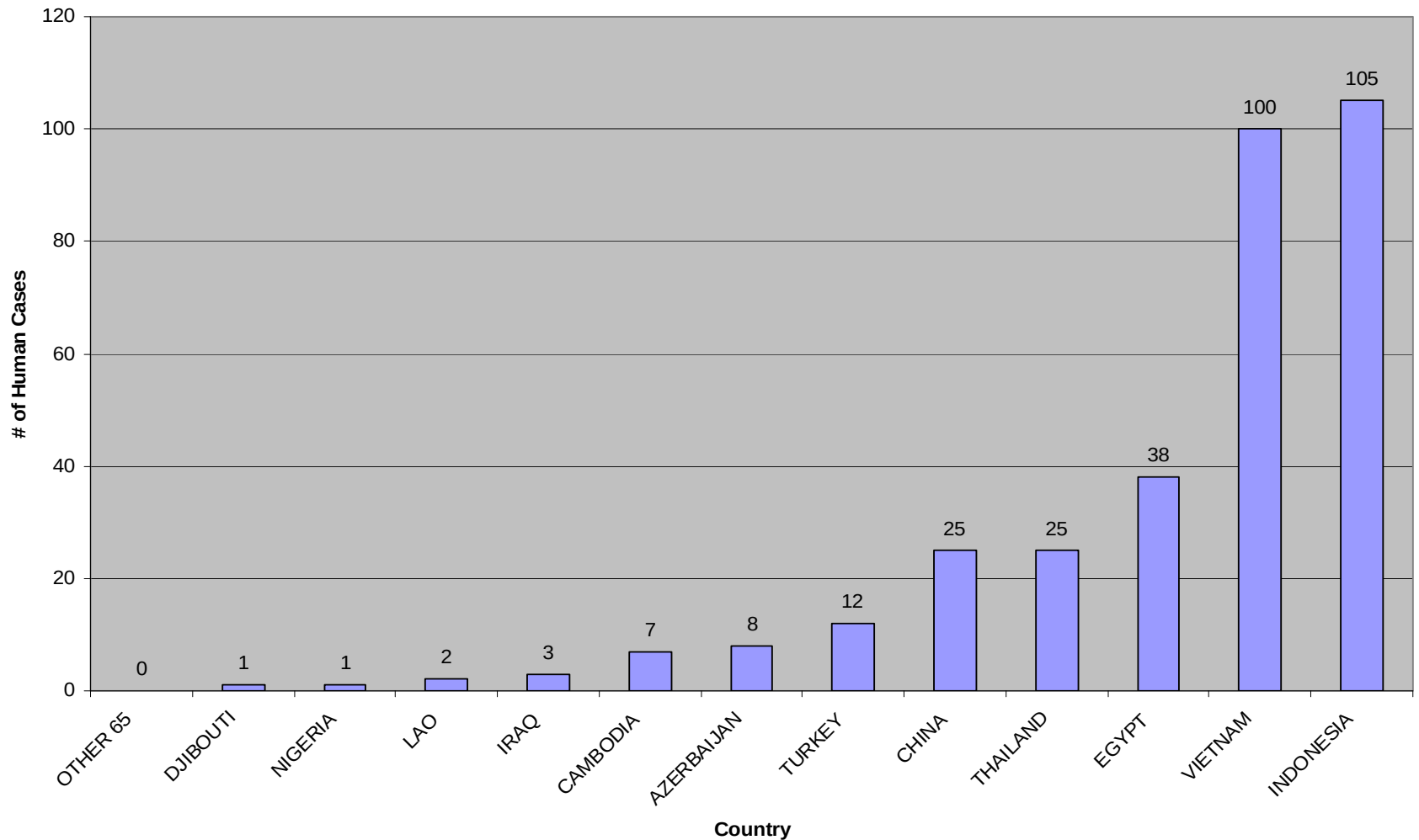
H5N1 Outbreaks in Birds 2003-7

Avian Influenza
Countries with ≥ 10 outbreaks
(N=59 Countries)

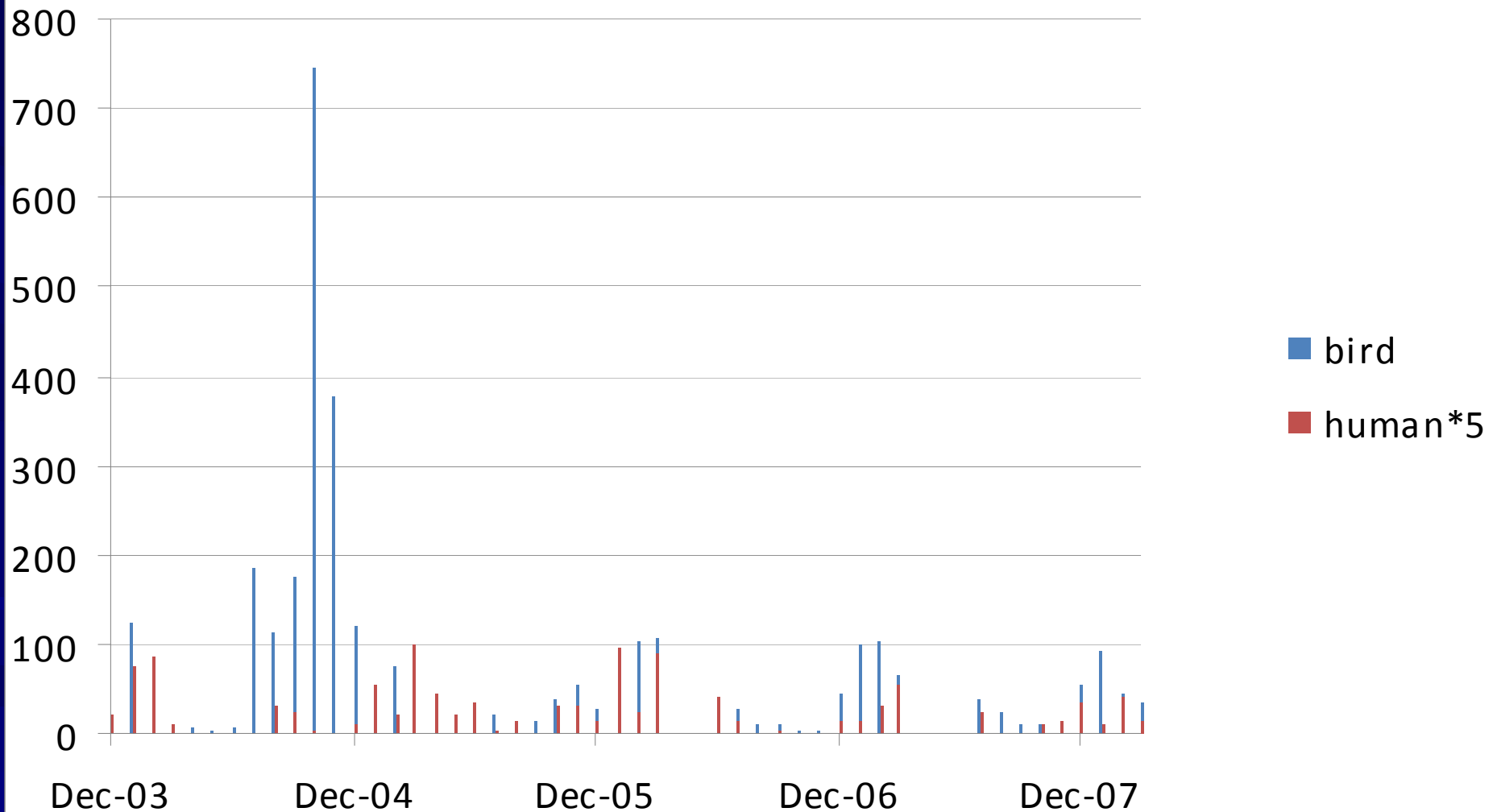


H5N1 Human Cases 2003-7

Human Cases of Avian Influenza
(N=77 Countries)



Epidemiological Curves for Bird (EMPRESi) and Human (WHO Confirmed) HPAI Cases



Time Lags Between First Bird and Human Cases: by Country

- Range between -56 days (humans sentinels for animal risk) to 1122 days (animals sentinels for humans)
- Indicates variability in quality and consistency of surveillance and reporting

Use of Animal Cases in A Predictive Model of Human Risk

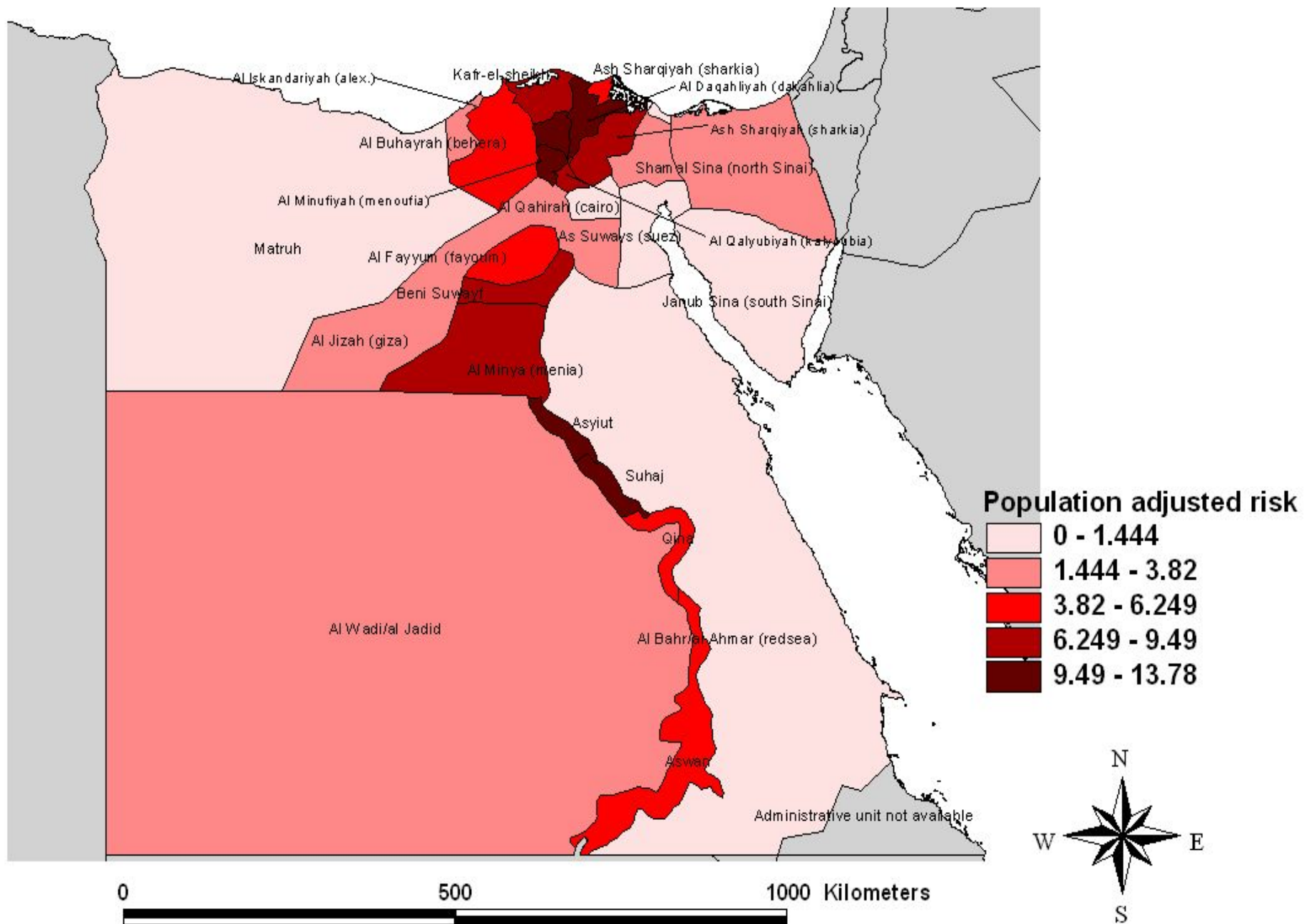
- In initial multivariate analyses, predictive factors include:
 - Poultry density
 - Recent bird cases
 - Cases involving ducks
 - Season

Accuracy of Model

- Country-level model appeared to have an accuracy of approximately 90% when tested in a logistic regression fashion.

Risk Maps

- Can be generated from model
- Will change continuously based on new temporal information (EMPRESi cases, etc.)
- Example: AI risk in Egypt- Map



Conclusions

- Bird cases in EMPRESi provide predictive information for human risk
- Outbreaks involving ducks appear to be associated with increased human risk
- Seasonality and temperature important for human animal transmission risk
- Independent geographic variables (FAOSTAT and other sources) can help explain human animal risk linkages

Additional findings

- Often (but not always) the reported bird cases are providing early warning of human risk for HPAI.
- When human cases precede bird cases- suggests problems with animal surveillance systems

Ways to Improve Linkage of Human and Animal Data

- virus characteristics
 - (clade /molecular markers?)
 - some more infectious to humans than others?
- biosecurity
 - Better information on production sectors
- Wildlife surveillance data

Beyond AI: Other Disease Risks Related to Human-Animal Contact:

- Specific diseases
 - Rift Valley Fever, Brucellosis, etc.
- High Risk settings
 - Bushmeat industry
 - Live animal markets
 - Agricultural practices
- How many exposed and with what degree of exposure and biosafety?

Other benefits of Avian influenza Cooperation

- On local levels, unprecedented contact and cooperation between agriculture/animal health and human health- alliances formed
- Involvement of wildlife health, unprecedented wildlife surveillance
- Attempts for international tracking
- Realization that animal and human outbreaks are connected

If Linking Animal and Human Disease Data Has Value, Who Should Do it?

- Public Health?
- Agriculture/Animal Health?
- GLEWS?
- Need for joint effort in “One Health” Model
- Global mapping of biosecurity risks:
 - Disease reservoirs: wild and domestic
 - Cases in animals and humans
 - Types of human-animal contact

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