流行病學建模與分析
Modeling and Analysis of Infectious Disease Epidemiology

0. Course Introduction and Fundamental Concepts

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個人網站: http://mail.cmu.edu.tw/~hsieh/

Course Overview

- The course covers selected topics and techniques in the use of mathematical models to study the transmission dynamics of infectious diseases, including 2009 **A(H1N1) flu pandemic**.
- Use of mathematics and statistics to analyze and evaluate the effectiveness and impact of intervention measures for infectious disease outbreaks.
- Particular attention will be given to the underlying model assumptions and to biological understanding and epidemiological interpretation that can be obtained from the modeling.

Course Contents

- Class sessions will primarily consist of lectures, a mid-term exam, and a course report/project. Introduction of basic ideas of elementary mathematics tools used, including difference equations, linear algebra, and calculus, will be given.
- Topics include design and construction of appropriate mathematical models, and determination and interpretation of important parameters, such as basic reproduction number (感染基數) R_0 of an infectious disease.

Course Contents (cont)

- The course is designed for graduate students in public health or in applied mathematics and statistics who wish to understand mathematical models relating to their research or to develop models for their own work.
- A course project of building a “simple” infectious disease model is required for students, either individually or in group.
- **For master students**, the model need not be original, but can be taken from literature in the form of a paper report.

Purpose of the Course

- **1st Semester**: To learn to understand and appreciate models, and also to understand the inadequacies of modeling

- **2nd Semester**: To learn to analyze infectious disease outbreaks with models and to construct models for research

Similar Courses in the World

- Oxford University/Imperial College: An Intensive 2-3 weeks Short Course: epidemiology and control of Infectious Diseases (since 1990)
- Harvard School of Public Health: Mathematical Modeling of Infectious Diseases; Infectious Disease Dynamics
- Johns Hopkins SPH: Modeling of Infectious Disease
- UC/Berkeley: Modeling the Dynamics of Infectious Disease Processes
- Yale University: Modeling the Epidemiology and Evolution of Infectious Diseases

Background requirements

- High school mathematics (e.g., sequences 數列, rate of change 變率, matrix 矩陣)
- Some (very little) knowledge of elementary calculus and statistics
- Some knowledge of computing software, Matlab, Maple, Mathematica, Phaser, SAS. Etc.

第一學期教學進度表(1)

	時間	主題	負責人
1	9/13	Course Introduction and Fundamental Concepts (lecture 0)	謝英恆
2	9/20	Exponential and logistic growth: simple examples of difference and differential equation models (lecture 1)	"
3	9/27	A Simple Model for Real-time Prediction of Outbreak Severity (lecture 2)	"
4	10/4	Introduction to epidemic models: Some Simple Epidemics (lecture 3)	"
5	10/11	SIS and SIR models (lecture 4)	"
6	10/18	"	"
7	10/25	Mass action and Standard Incidence (lecture 5)	"
8	11/1	Basic reproduction number, R_0 (lecture 6)	"
9	11/8	Course Project Proposals due	"

第一學期教學進度表(2)

	時間	主題	負責人
10	11/15	期中考試	"
11	11/22	Ross-MacDonald Malaria Model (lecture 7)	"
12	11/29	(Tutorial) Fundamental Concepts II (lecture 8)	"
13	12/6	An Overview on Mathematical Models (lecture 9)	"
14	12/13	"	"
15	12/20	Public health-related modeling: Evaluation of interventions measures (lecture 10)	"
16	12/29	"	"
17	1/5	Project Presentations	"
18	1/12	Project Presentations	"

- **參考書籍:**

1. Anderson, R., and May, R. (1991) Infectious Diseases of Humans: Dynamics and Control. Oxford University Press, Oxford.
2. Brauer, F., van den Driessche, P., and Wu, J. (2008) Mathematical Epidemiology. Springer-Verlag, Berlin.

- **評量標準：**

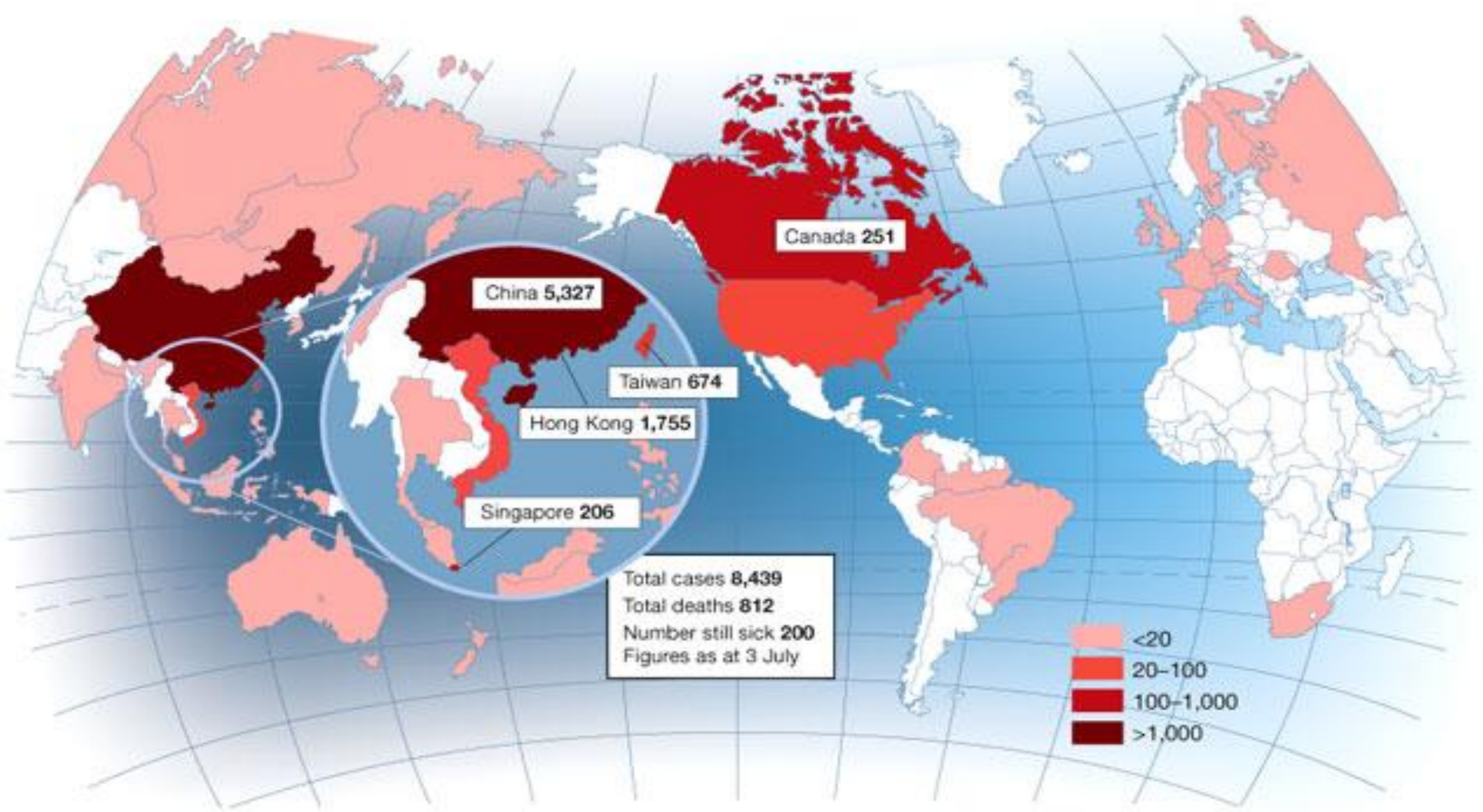
博士班: 期中考試 30%, Course project 70%.

碩士班: 期中考試 50%, Course project 50%.

流行病學建模與分析
Modeling and Analysis of Infectious Disease Epidemiology

Fundamental Concepts and Historical Notes

Geographical map of 8439 SARS cases as of 7/3, 2003 (# deaths later adjusted to 774) (WHO website)



Early Spatial Spread of SARS

(From "Learning from SARS: Preparing for the next disease outbreak" 2003 IOM SARS workshop summary)

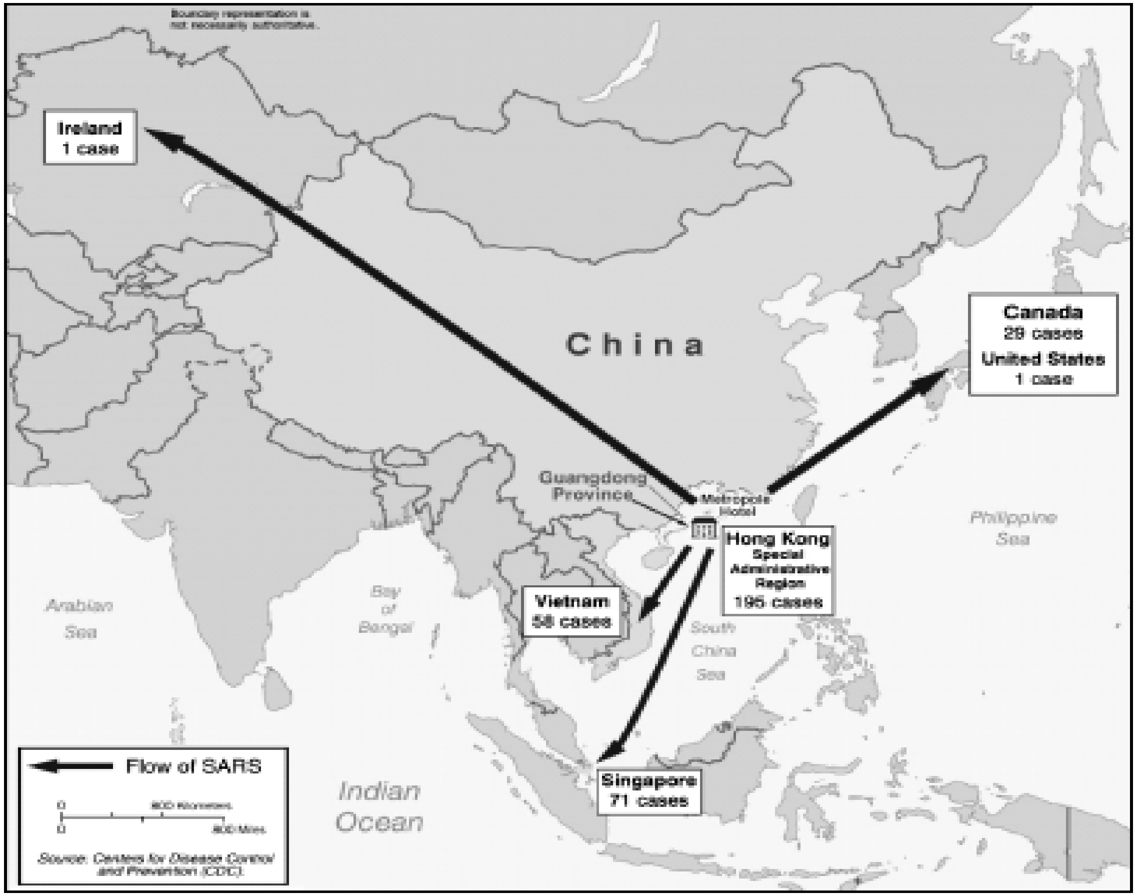


FIGURE S-2 Portrait of a superspreader: spread of SARS from the Metropole Hotel in Hong Kong as of March 28, 2003.

To put things in perspective!

Time for 774 deaths to occur in 2003 due to:

SARS - November, 2002 – July, 2003

HIV – 6 hours

TB – 3 hour

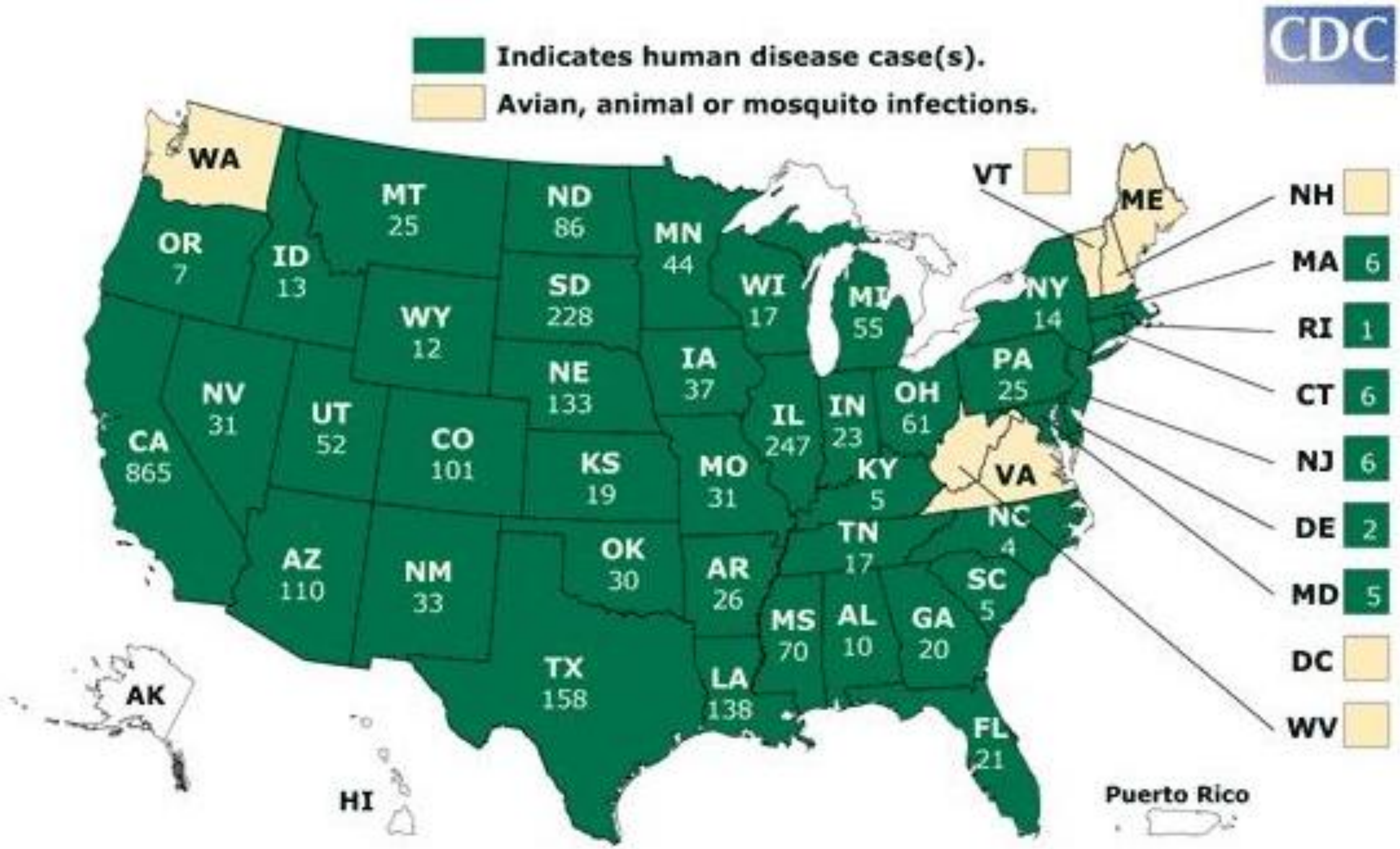
註: 1. HIV and TB highly correlated.

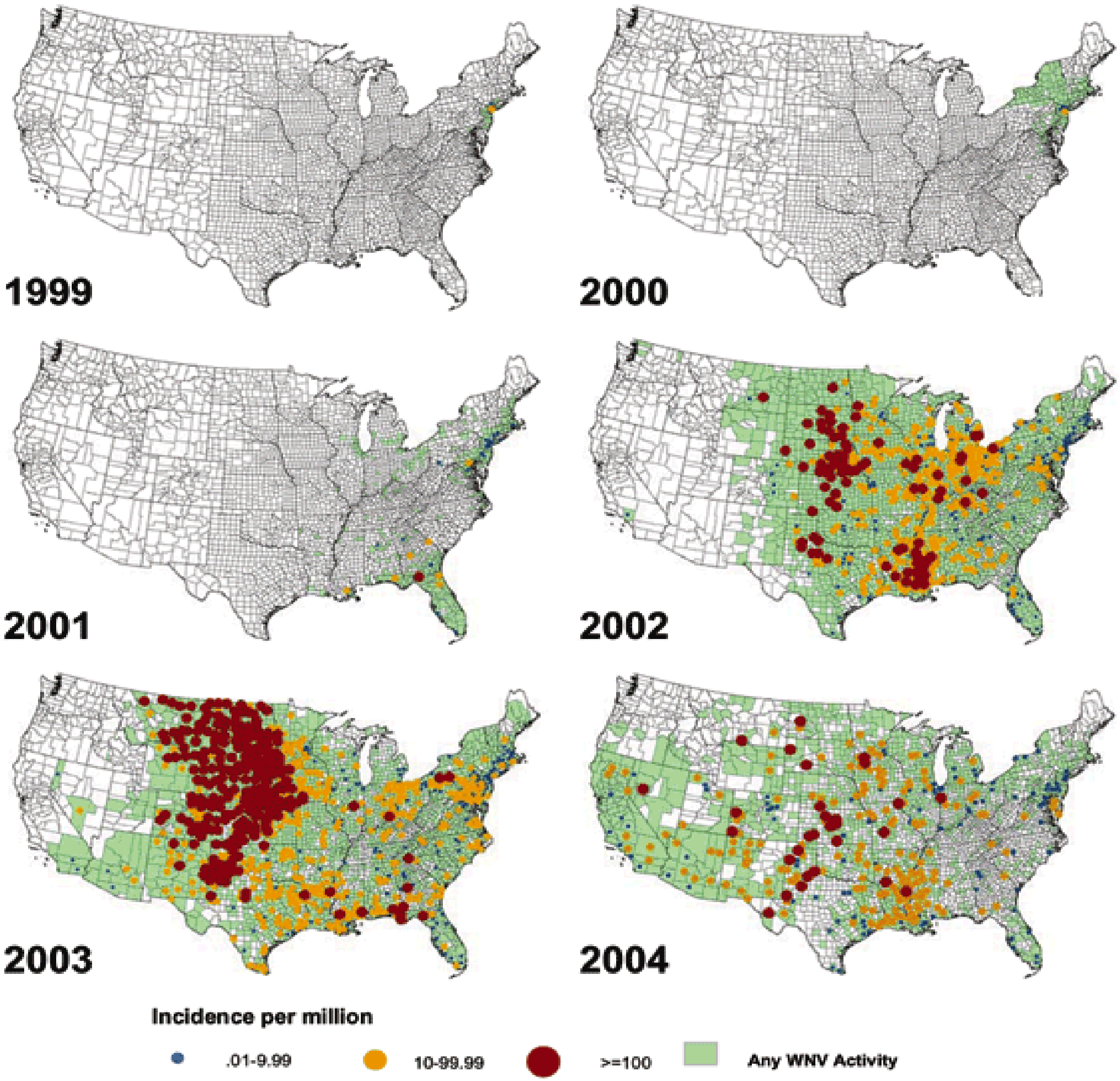
2. 11% of ADI (AIDS-defined illness) deaths due to TB.

Culprits or victims of Avian flu?

牠們是禽流感(H5N1)的罪魁禍首,還是受害者?

West Nile Virus (西尼羅河病毒) in U.S.
2799 cases/102 deaths (1999-2005)

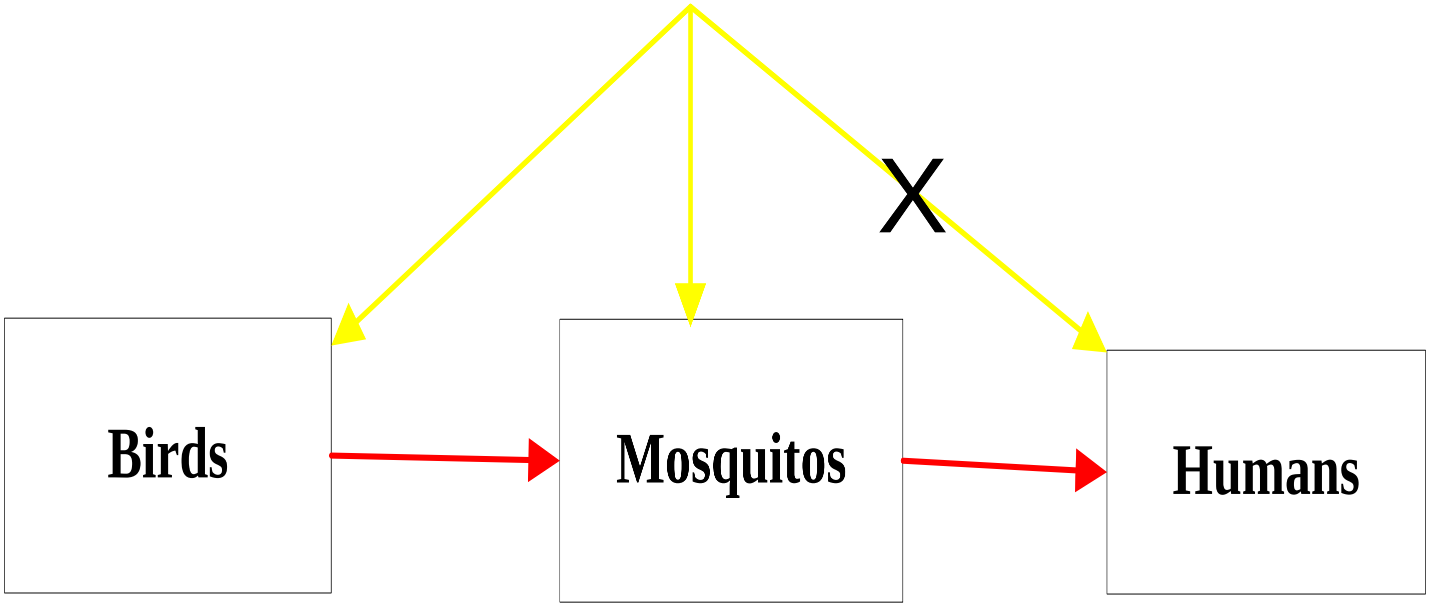


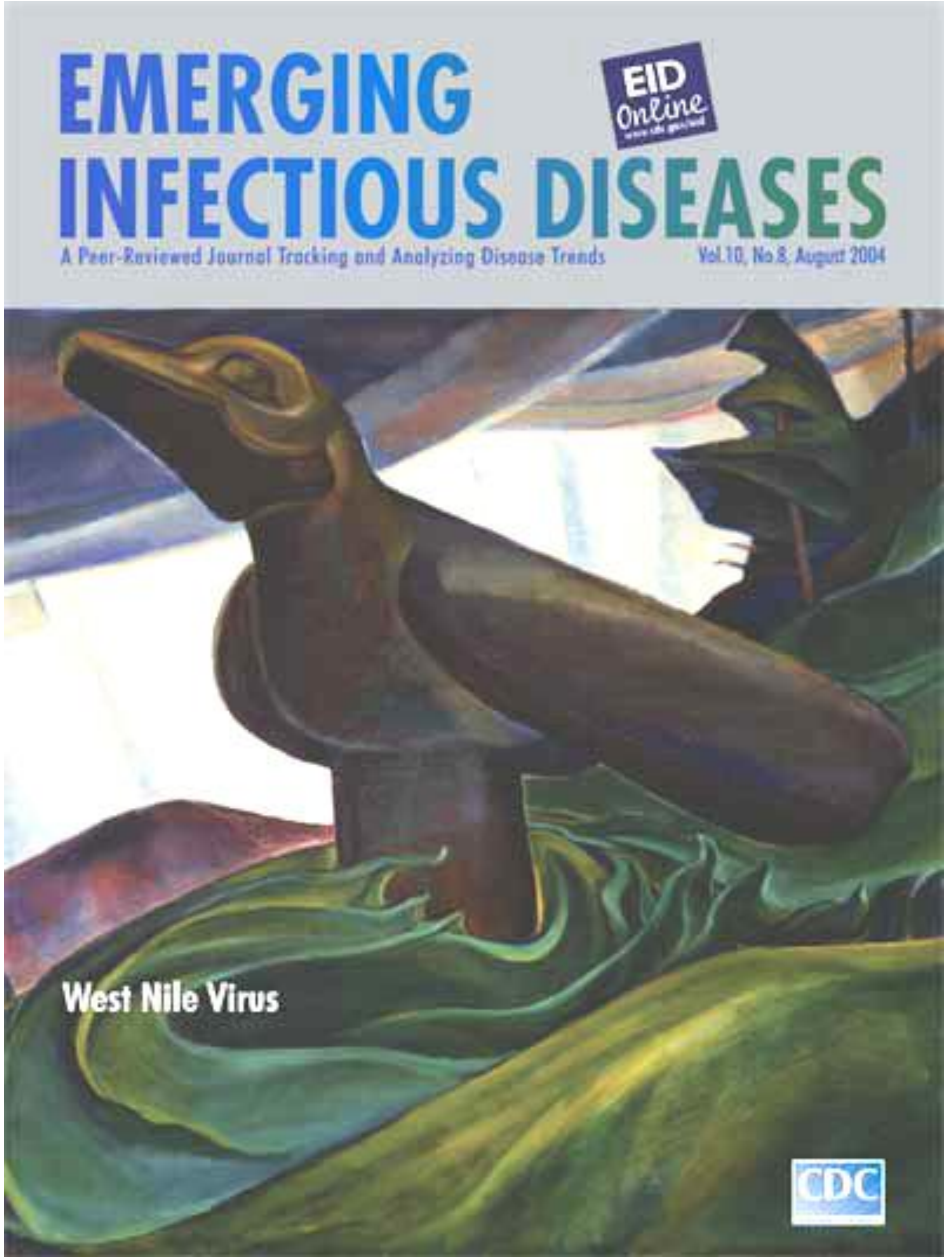


1999
2000
2001
2002
2003
2004
Incidence per million
.01-9.99
10-99.99
>=100
Any WNV Activity

如何防止
West Nile Virus (西尼羅河病毒)?

Which species to cull (撲殺)?





Did Alexander the Great (亞歷山大大帝) died of 西尼羅河病毒 (WNV) in 323 BC at age of 32?

-Marr and Calisher, *EID* (新興傳染病) 2003

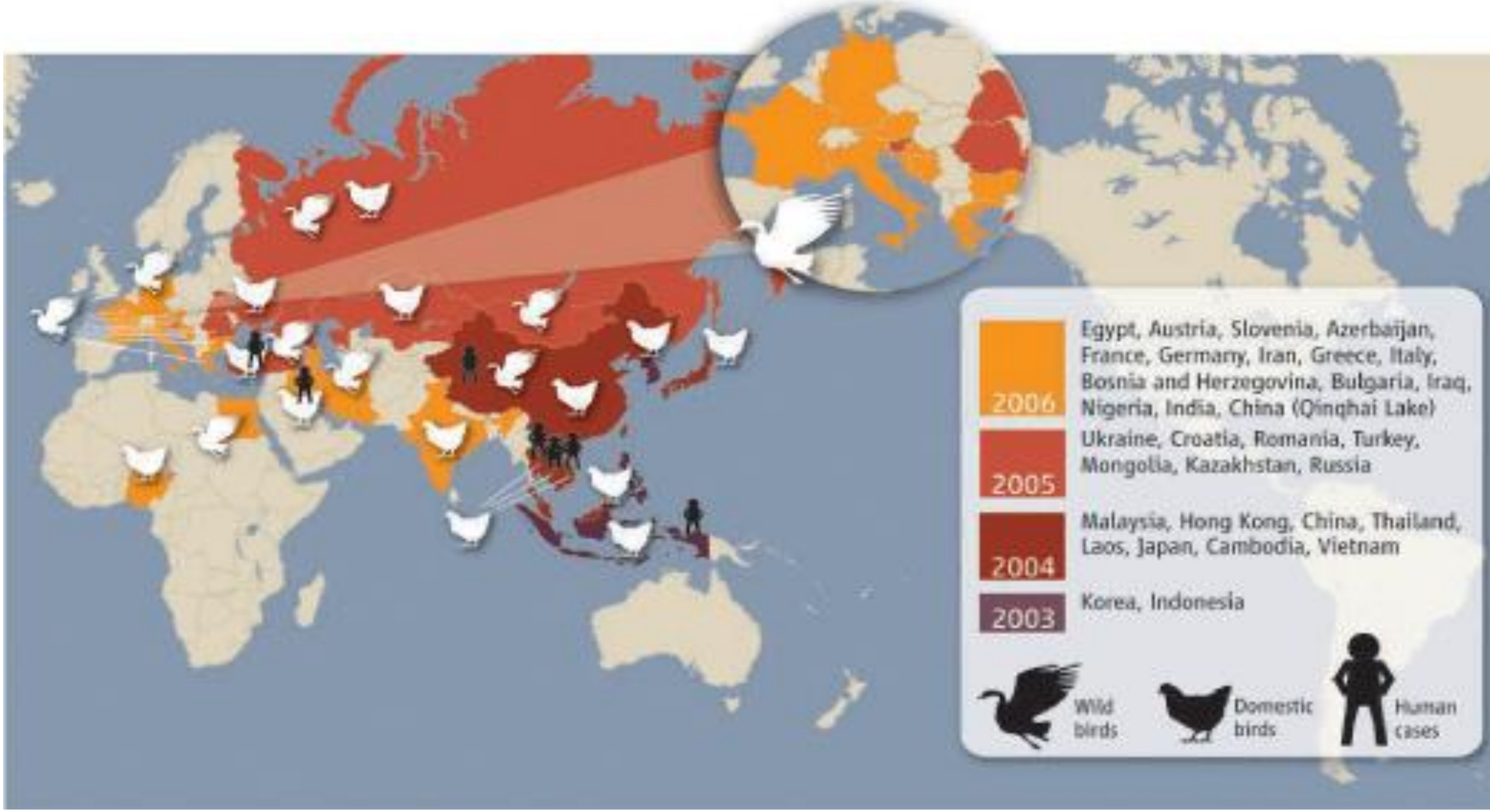
Big Raven (1931) by Emily Carr

Phylogenetic Analysis
（基因系統發生分析）

- Galli, Bernini, and Zehender (*EID*, 2004):

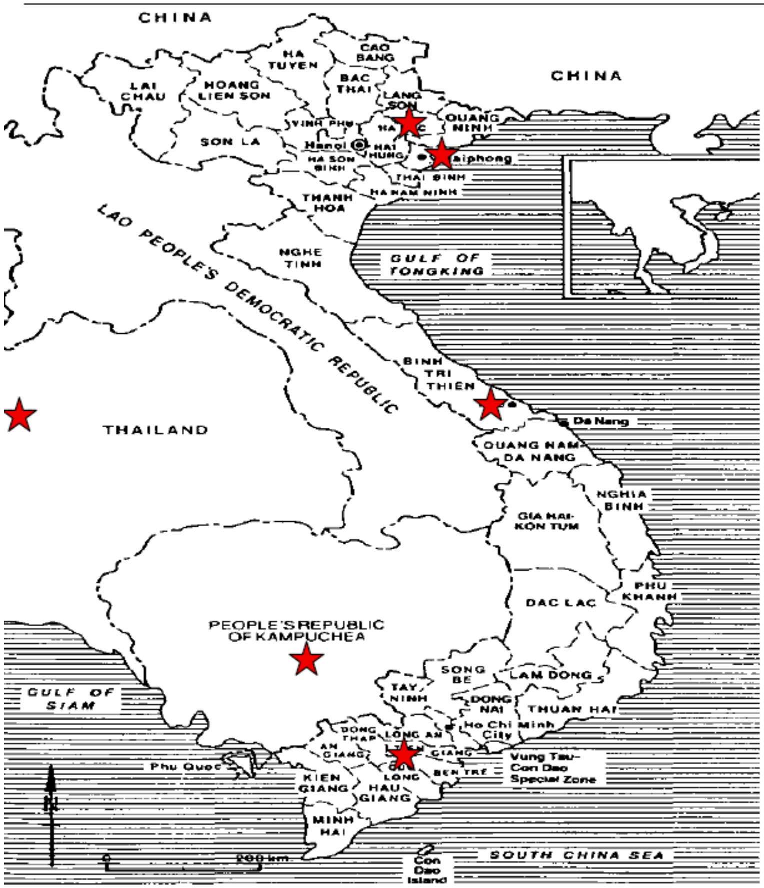
the most recent common ancestor (MRCA) for WNV can be dated back to 8th century (1,159 years ago) only

Spread of avian flu (H5N1) as of February of 2006 (Science 2006)



Geographical map of H5N1 human infections in Southeast Asia as of May 2005 (K. Ungchusak briefing at 2005 WHA Assembly)

Family clusters in Mekong countries



Thailand

- daughter- mother –aunt
  Kamphengphet

Vietnam

- **3 brothers at Thai Binh-Hanoi**
- **Dongthap**
- **Bac Lieu**
- **Haiphong :5 family member with one infant**
- **Health care worker**

Cambodia

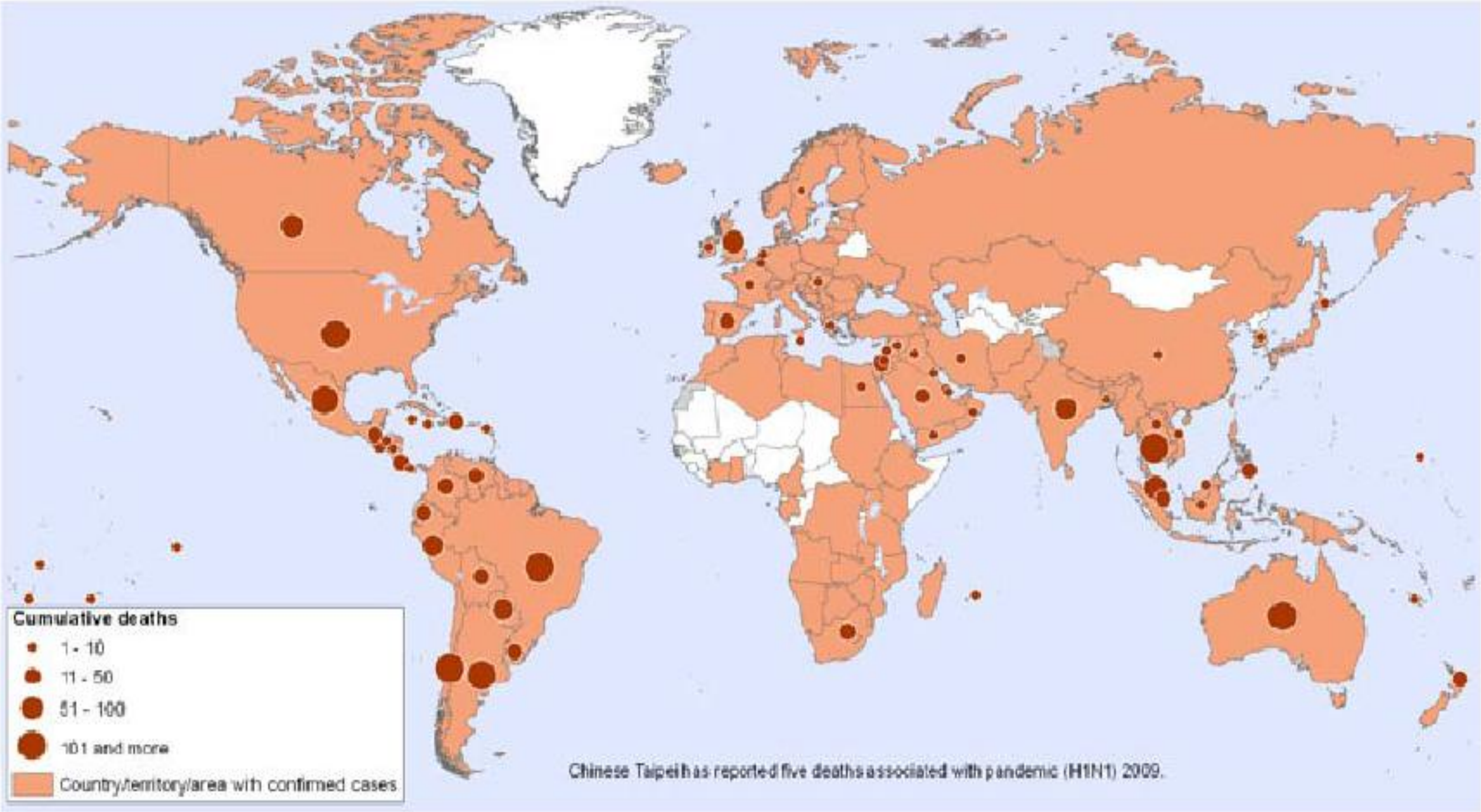
- **Kampot province (Sister— brother)**

Timeline (22 July 2009 onwards)
Pandemic (H1N1) 2009 laboratory confirmed cases
And number of deaths as reported to WHO

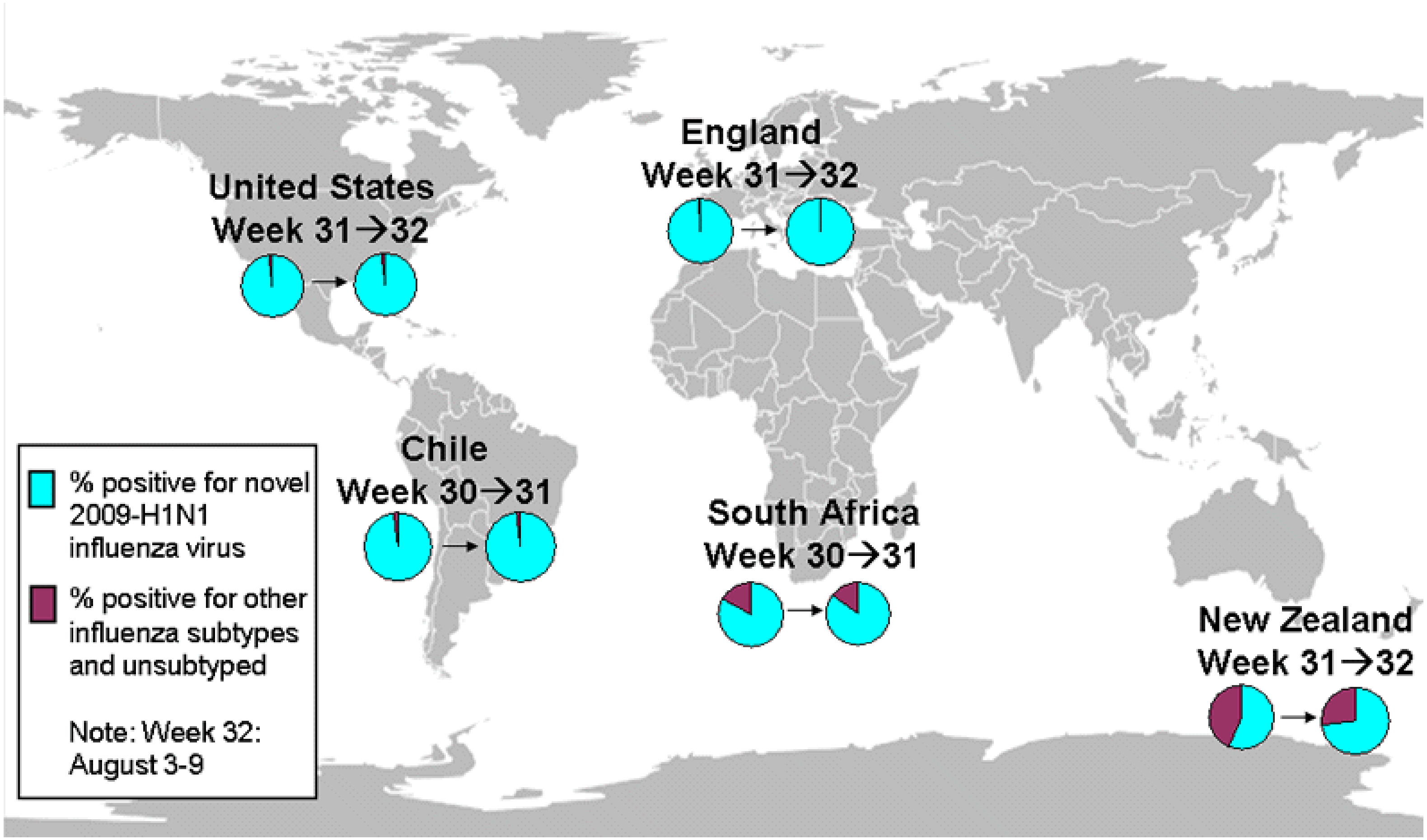
World Health Organization

Status as of: 06 September 2009

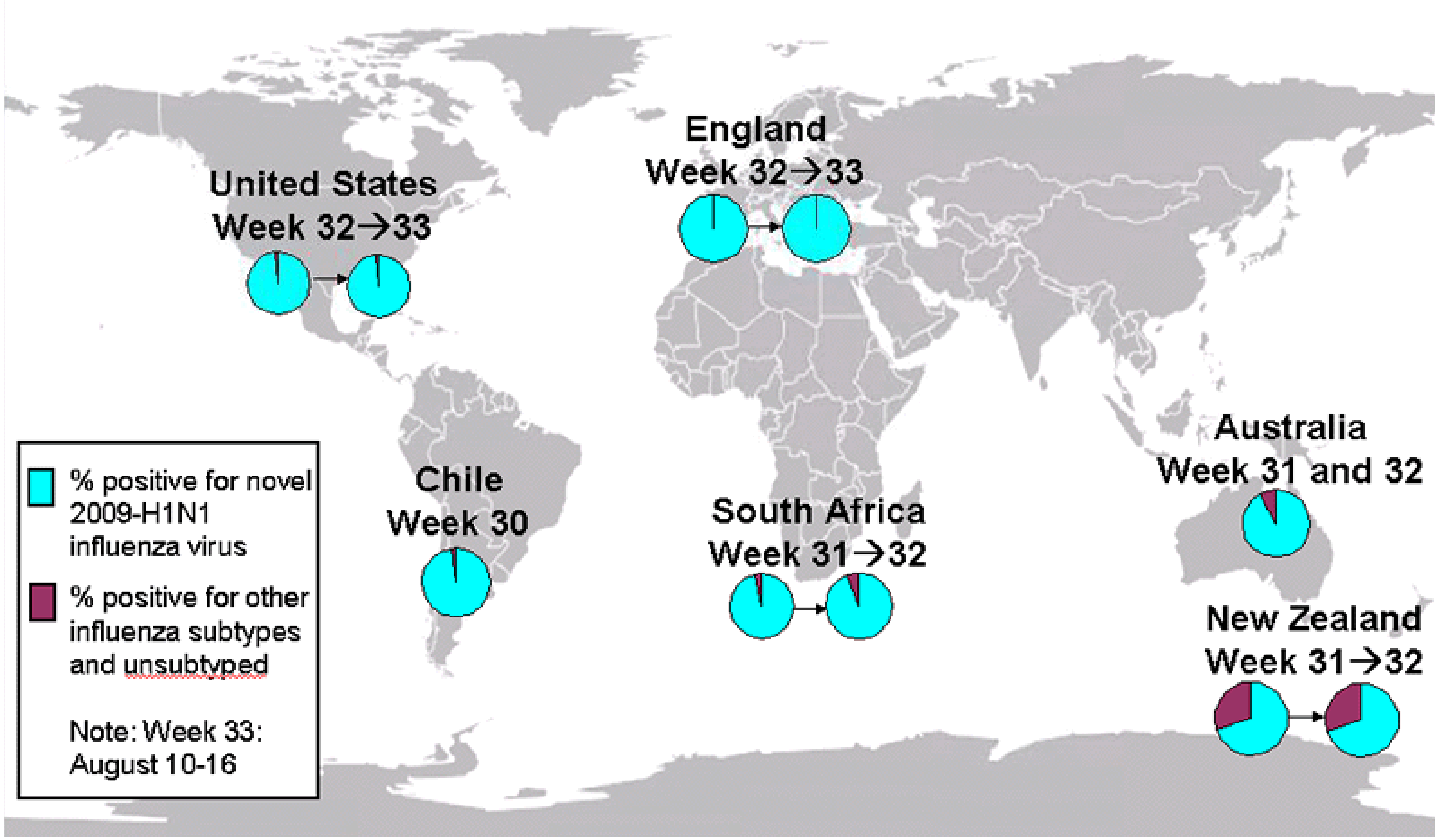
Previous



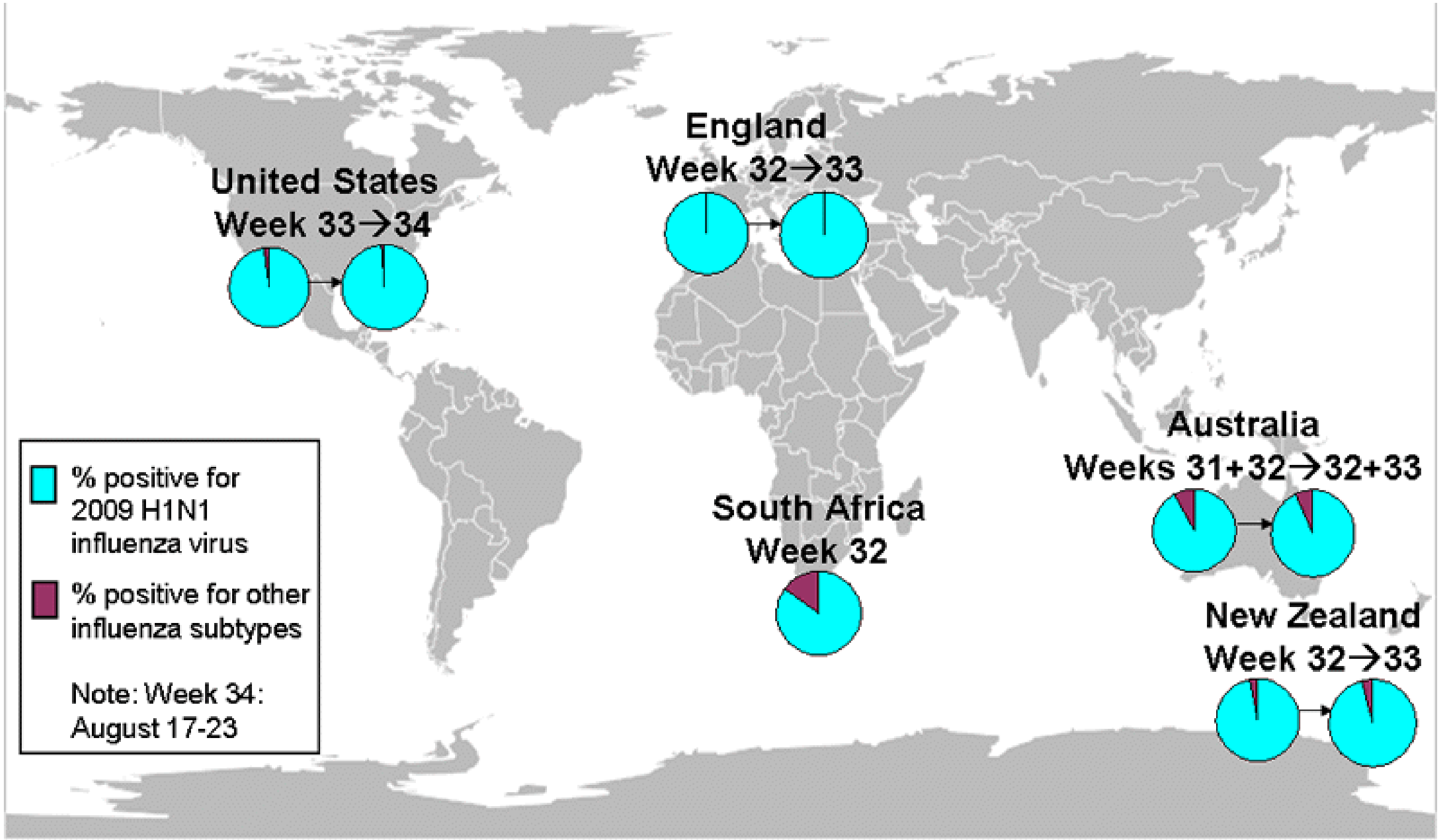
International Co-circulation of 2009 H1N1 and Seasonal Influenza (As of 8/14; posted 8/14 by USCDC)



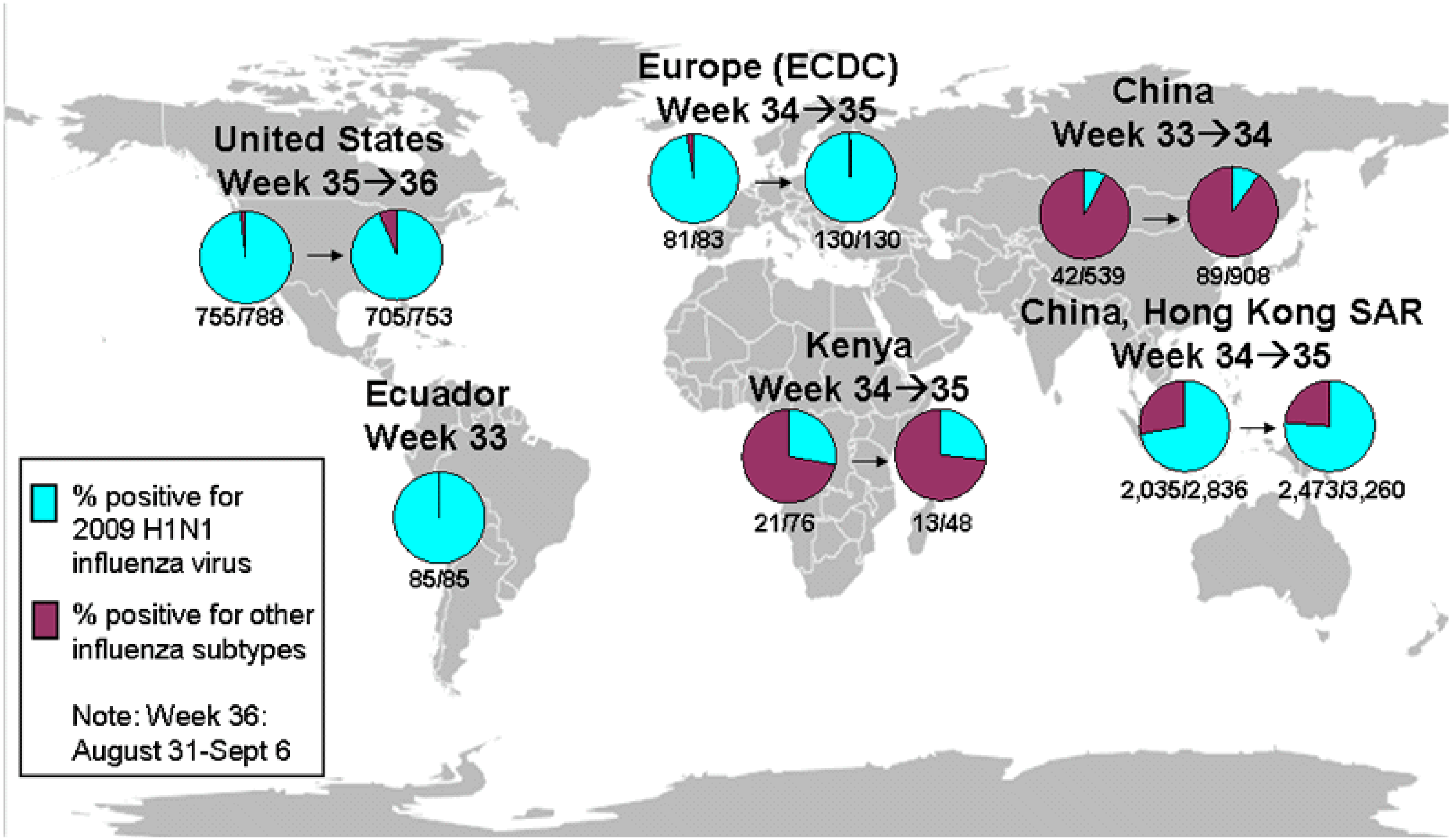
International Co-circulation of 2009 H1N1 and Seasonal Influenza (As of 8/21; posted 8/21 by USCDC)



International Co-circulation of 2009 H1N1 and Seasonal Influenza (As of 8/23; posted 8/28 by USCDC)

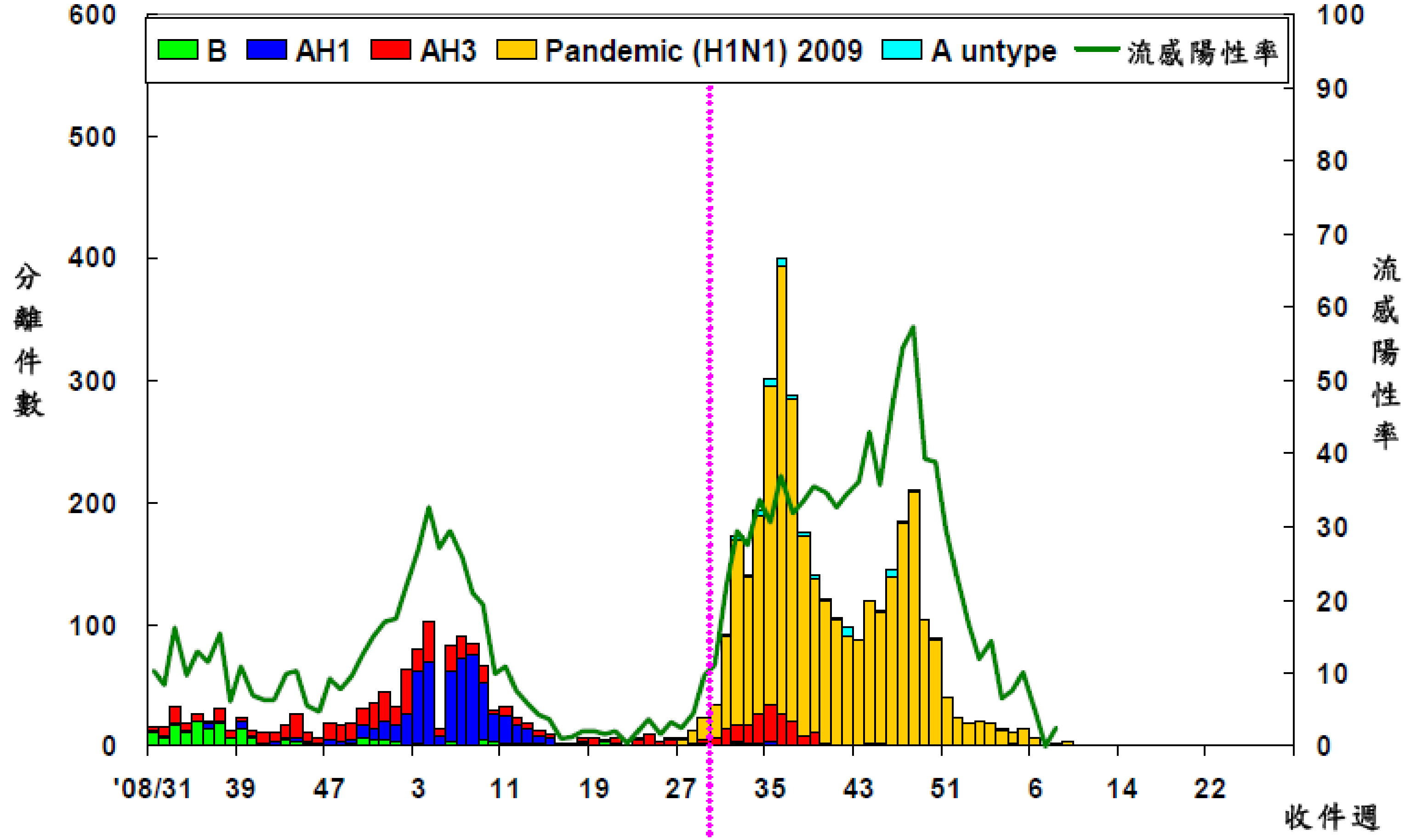


International Co-circulation of 2009 H1N1 and Seasonal Influenza (As of 9/4; posted 9/11 by USCDC)



2009 pH1N1 epidemic in Taiwan (by the end of February 2010)

全國病毒合約實驗室 2008–2010 流感病毒分型趨勢圖



Mathematical Epidemiology
（數理流行病學）

Definition:
"The application of mathematics to the study of infectious disease"

In: "*Infectious Diseases of Humans: Dynamics and Control*" by Anderson and May, 1991.

*Includes, but not restricted to, statistics.

Advances in Mathematical Epidemiology I

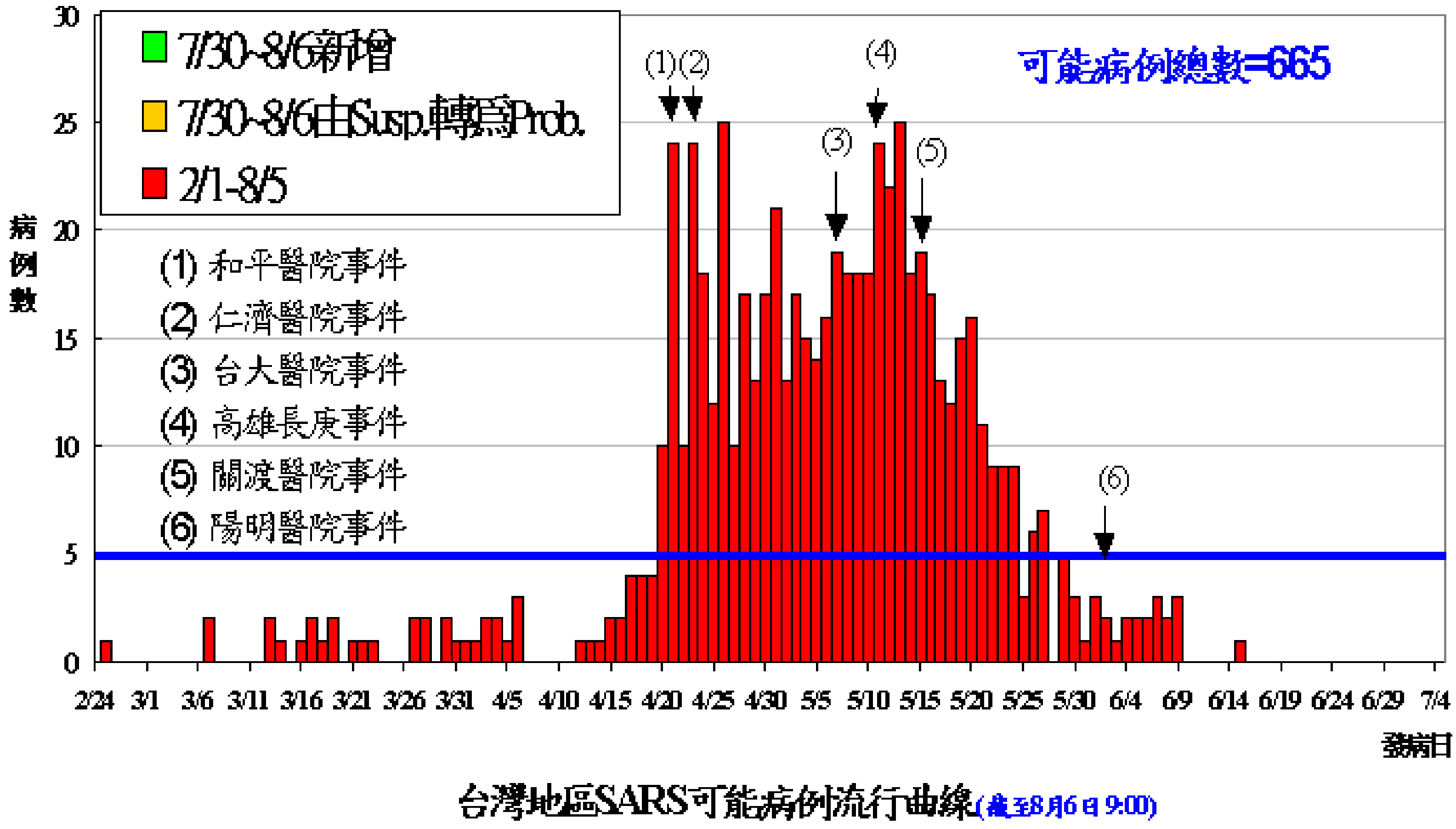
- 1684/1687 – Birth of Calculus due to Newton and Leibniz
- 1690 – Jakob Bernoulli solved a differential equation
- 1760 - Daniel Bernoulli (nephew of Jakob) used mathematical model with differential equation to study effectiveness of inoculation as a public health policy against smallpox.

Advances in Mathematical Epidemiology II

Empirical study of smallpox (1800’s):

- 1840 – William Farr fitted a normal curve to the smoothed quarterly mortality data from smallpox in England and Wales between 1937-9.

2003 Taiwan daily SARS cases by onset date



Advances in Mathematical Epidemiology III

- 1908-1917 - Sir Ronald Ross (MD and Nobel Prize laureate): continuous-time mathematical modeling of malaria.
- 1927 - Epidemic threshold theory (Kermack and McKendrick)
- 1930 - Net reproductive value (R. A. Fisher, *Genetic Theory of Natural Selection*): basic concepts for basic reproduction number R_0

Advances in Mathematical Epidemiology IV

- 1957 - George MacDonald furthers the work of Ross (Ross-MacDonald malaria model).

- 1979-1996 - Roy Anderson and Robert May developed a comprehensive framework for infectious disease transmission, including that of HIV/AIDS.

Origin of the term "Mathematical Epidemiology" (數理流行病學)

- 1985 – The first use of "Mathematical Epidemiology" in publication by Nakasuji et al. *J. Appli. Ecology*, 22(3) 839-847
- 1991 – The term "Mathematical epidemiology" was formally described in book by Anderson and May.

Mathematical Epidemiology

Google 學術搜尋 BETA

mathematical epidemiology 搜尋

進階學術搜尋
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學術搜尋 所有文章 - 最新文章 約有**69,300**項符合**mathematical epidemiology**的查詢結果，以下是第 **1-10**項。 共費**0.17** 秒。

[書籍] Mathematical Epidemiology of Infectious Diseases: Model Building, Analysis and Interpretation
O Diekmann, JAP Heesterbeek - 2000 - igitur-archive.library.uu.nl
Title: Mathematical Epidemiology of Infectious Diseases: model building, analysis and interpretation. Author: Diekmann, O. Heesterbeek, JAP. Year: 2000. Publisher: John Wiley & Son. URL publisher: http://eu.wiley.com. Document type: Book (monograph ...
被引用 495 次 - 相關文章 - 頁庫存檔 - 網頁搜尋 - 查看中國醫藥大學館藏 - 在NBINet（臺灣）尋找 - 全部共 3 個版本

[引言] Mathematical Epidemiology of Infectious Diseases: Model Building
O Diekmann, JAP Heesterbeek - Analysis and Interpretation, Wiley, New York, 2000
被引用 110 次 - 相關文章 - 網頁搜尋

[HTML] ▶ Mathematical structures of epidemic systems
V Capasso, V Capasso - 1993 - cwi.nl
... The main aim of mathematical epidemiology remains the same as it was at the very beginning of the subject in 1760, when Bernoulli wrote a paper on smallpox, that is to evaluate the effects on the infectious agent and the host population of ...
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[HTML] ▶ Vertically transmitted diseases: models and dynamics
SN Busenberg, KL Cooke - 1993 - cwi.nl
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Mathematical Epidemiology

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提示： 如只要搜尋中文（繁體）的結果，可使用學術搜尋偏好.指定搜尋語言。

[書籍] Mathematical epidemiology of infectious diseases: model building, analysis and …
O Diekmann, JAP Heesterbeek - 2000 - books.google.com
WILEY SERIES IN **MATHEMATICAL** AND COMPUTATIONAL BIOLOGY EDITOR-IN-CHIEF Simon Levin, Princeton University, USA **Mathematical Epidemiology** of Infectious Diseases ...
被引用 703 次 - 相關文章 - 查看中國醫藥大學館藏 - 全部共 4 個版本

[引言] **Mathematical Epidemiology** of Infectious Diseases: Model Building
O Diekmann, JAP Heesterbeek - Analysis and Interpretation, Wiley, New York, 2000
被引用 139 次 - 相關文章

► Vertically transmitted diseases: models and dynamics
SN Busenberg, KL Cooke - 1993 - cwi.nl
... The main aim of **mathematical epidemiology** remains the same as it was at the very beginning of the subject in 1760, when Bernoulli wrote a paper on smallpox ...
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[引言] Generalized kinetic (Boltzmann) models: **Mathematical** structures and applications
L Arlotti, N Bellomo, E De Angelis - **Mathematical** Models and Methods in Applied …, 2002 - WORLD SCIENTIFIC
被引用 71 次 - 相關文章

Basic ideas of mathematical epidemiology
F Brauer - **Mathematical** Approaches for Emerging and Reemerging … - books.google.com
Page 43. BASIC IDEAS OF **MATHEMATICAL EPIDEMIOLOGY** FRED BRAUER* 1. Introduction. Communicable diseases are an important part of modern life. ...
被引用 12 次 - 相關文章 - 全部共 2 個版本

[引言] **Mathematical epidemiology** of infectious diseases
O Dieckmann, JP Heesterbeek - 2000 - Wiley, New York
被引用 16 次 - 相關文章

*Search result on September 16, 2009

Mathematical Epidemiology “Forecast”

~100% increase in number of items per year

<==> Two-fold increase in 1 year

<==> 2^{10}=1024-fold increase in 10 years

Mathematical Epidemiology

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mathematical epidemiology [搜尋] 進階學術搜尋

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[書籍] Mathematical epidemiology of infectious diseases — cwi.nl 提供的 [PDF]
O Diekmann... - 2000 - oai.cwi.nl
Images of SMC Research 1 996 Mathematical Epidemiology of Infectious Diseases O. Diekmann 1. Introduction Epidemiology is concerned with patterns in space and time of the occurrence of disease. From the patterns one may infer causes, predict the future and decide about ...
被引用 1166 次 - 相關文章 - 查看中國醫藥大學館藏 - 全部共 10 個版本

[書籍] Mathematical epidemiology
F Brauer, P Van den Driessche, J Wu... - 2008 - books.google.com
Editors Fred Brauer Department of Mathematics University of British Columbia Vancouver, BC V6T 1Z2, Canada brauer@ math. ubc. ca Jianhong Wu Center for Disease Modeling Department of Mathematics and Statistics York University Toronto, Ontario M3J 1P3, Canada wujh@ ...
被引用 51 次 - 相關文章 - 查看中國醫藥大學館藏 - 全部共 2 個版本

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O Dieckmann... - 2000 - Wiley, New York
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RM Anderson... - 2004 - Oxford, UK: Oxford University Press
被引用 40 次 - 相關文章 - 查看中國醫藥大學館藏

Molecular and mathematical epidemiology of Staphylococcus aureus and Streptococcus uberis mastitis in dairy herds
RN Zadoks - 2002 - igitur-archive.library.uu.nl
Molecular and mathematical epidemiology of Staphylococcus aureus and Streptococcus uberis mastitis in dairy herds. authors, Zadoks, Ruth Nicolet. source, Diergeneeskunde proefschriften (2003). full text, [Full text]. document type, Dissertation. disciplines, Diergeneeskunde. ...
被引用 12 次 - 相關文章 - 頁庫存檔 - 全部共 6 個版本

*Search result on September 14, 2011

Why Mathematical Epidemiology Now?

- 衛生環境的改善: Cleaner environment (polio: emerge in Europe in 19th century, first major outbreak in US in 1916)
- 快速全球化: Fast Globalization (HIV 1959? WNV 1999, SARS 2003)
- 生物科技進步: Modern advances in science and technology on understanding of infectious diseases. E.g., Molecular biology: Is 1918 flu epidemic due to a strain of swine flu? (Taubenberger and Morens 2006)

Purposes of Mathematical Modeling

- Reconstruct history, design simple model, and "predict" future
- Study sensitivity to parameters changes
- Compare effectiveness of control strategies
- Design more refined models to improve accuracy

-Fred Brauer
"Current Science of SARS Symposium, 2003"

Important Principles

1. Start with a basic general model and then tailor it to specific disease.
2. Simple model with few parameters may be better than more refined models with many parameters, especially if data is sparse or unreliable.
3. Qualitative results are more reliable than numerical predictions.

Important Principles (cont)

4. Refine model when more reliable data becomes available.
5. Compare models.
6. For future epidemics, it is preferable to use simple models.
7. Sensitivity to parameter changes is vital.

Albert Einstein:

- Models should be as simple as possible, but not more so.

- "When the solution is simple, God is answering."

The KISS method

Keep It Simple and Stupid

-A mathematical biologist

More Quotes

- “There are no right model, but there are certainly lots of wrong ones.”
- “All models are wrong, some are less so than others.

"Mathematics is a way of thinking clearly, no more, but no less."

– Lord Robert M. May of Oxford, President of Royal Society, United Kingdom, in *Virus Dynamics* (2000 Nowak and May).

“The mathematical method of treatment (using mathematical model of malaria transmission) is really nothing but the application of careful reasoning (細心推理) to the problems at issue"

-Sir Ronald Ross (1911)

"I have deeply regretted that I did not proceed far enough at least to understand something of the great leading principles of mathematics; for men thus endowed seem to have an extra sense."

"我深悔沒有深入了解數學的原理，以建立了解事物的特殊官感"

-Charles Darwin（達爾文）in late 19th Century

‘I simply wish that, in a matter which so closely concerns the well-being of the human race, no decision shall be made without all the knowledge which a little analysis and calculation can provide’

-Daniel Bernoulli (1760) explained his motivation to use mathematical model to analyze the mortality caused by smallpox and the advantages of inoculation to prevent it.

"Tell me and I forget, teach me and I may remember, involve me and I learn."

~Benjamin Franklin

References

1. Marr and Calisher, Alexander the Great and West Nile virus encephalitis. Emerg Infect Dis. 2003 Dec;9(12):1599-603.
2. Bernoulli D. Essai d’une nouvelle analyse de la mortalite causee par la petite verole. Mem Math Phy Acad Roy Sci Paris 1766.
3. W. Farr, (1840). Progress of epidemics, Second report of the registrar General of England, 91-8.
4. R. Ross, *The Prevention of Malaria*, (2nd edition), Murray, London (1911).
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6. R. A. Fisher, *The Genetical Theory of Natural Selection*, Clarendon, Oxford (1930).

References (cont)

7. R. M. Anderson and R. M. May, *Infectious Diseases of Humans*, Oxford University Press, Oxford (1991).

8. R.M. Anderson. (1999) Phil.Trans. R. Soc. Lond. B (1999) 354, 689-690

9. Anderson, R. M., Gupta, S., May, R. M.: Potential of community-wide chemotherapy on immunotherapy to control the spread of HIV-1. Nature 350, 356-359 (1991)

10. Taubenberger JK, Morens DM. 1918 influenza: the mother of all pandemics. Emerg Infect Dis. 2006;12:15–22.12.

11. 謝英恆,數理流行病學與SARS數理模式:跨領域的學術研究,國科會自然科學簡訊, 2004,第十六卷第三期, 82-85.□