Course Syllabus
BIOST/STAT 578 A Statistical Methods in Infectious Diseases
Winter 2009

Instructors: M. Elizabeth Halloran and Ira M. Longini, Jr.
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Time: TTh 10:30–11:50 am; Begin: January 6, 2009
Office hours: TBN
Location: Health Sciences T–531
Credits: 3 hours, CR/NC

Course Description: This course will introduce concepts of infectious disease epidemiology and study designs and analytic methods for evaluating interventions. Especially the relation between the underlying transmission dynamics and the design and evaluation of interventions will be discussed. Special emphasis will be on the design and evaluation of vaccination and vaccination programs. We will present methods for real-time statistical evaluation of interventions of emerging infectious diseases. Statistical and mathematical methods include survival analysis, likelihood and Bayesian methods, smoothing methods, stochastic processes, network theory, and stochastic and deterministic transmission models. We will discuss causal inference for interventions in infectious diseases. Examples include case studies in influenza, HIV, measles, cholera, rubella, dengue, and malaria, among others. Presentations are largely statistical and mathematical, but with a focus on concepts.

Learning Objectives: At the end of this course, the student should be able to

1. Describe the relation between the underlying transmission dynamics and the design and evaluation of interventions.
2. Define direct, indirect, total, and overall effects and the general types of study designs to estimate them
3. Define, estimate, and interpret the basic reproductive number, R_0
4. Define the generation time and serial interval of an infectious disease
5. Formulate simple deterministic models of infectious disease transmission
6. Distinguish VE_S, VE_I, VE_P, and VE_{SP} and the study design and statistical methods to estimate them.
7. Compute the probability of no spread and final-size distribution for a stochastic Reed-Frost model
8. Distinguish three time lines of infection: transmission, disease, and behavior
9. Contrast the leaky with the all-or-none mechanism of vaccine protection and compare their implications for interpreting vaccine trial results and for population dynamics

10. Estimate in real-time R_0 for an emerging infectious disease
11. Discuss applications of causal inference in infectious diseases
12. Design studies and community trials to evaluate indirect, total and overall effects of vaccination
13. Analyze household secondary attack rate studies
14. Distinguish different methods for analyzing studies of households assumed to be in communities
15. Evaluate the effects of vaccines on post-infection outcomes
16. Explain the elements of a stochastic simulation model
17. Describe the application of mathematical transmission models to describe the indirect and overall effects of intervention programs.
18. Describe the application of statistical methods such as survival analysis, likelihood and Bayesian methods to problems in infectious diseases
19. Use validation sets for outcomes in infectious disease studies
20. Discuss different methods for evaluating immunological surrogates of protection

Students: This course is open to PhD and Master's students with a wide variety of backgrounds, including Biostatistics, Statistics, Epidemiology, Biology, and others. Post-docs and faculty are welcome to participate.

Evaluation: Class participation and a written project depending on the background and interest of the student.

Text:

- *Design and Analysis of Vaccine Studies* (book draft), M. Elizabeth Halloran, Ira M. Longini, Jr., and Claudio J. Struchiner, Springer Verlag, 2009 (will be available for download from the web for course participants)
- journal articles and supplementary notes.

Website: http://courses.washington.edu/b578a

1. January 6
    - Halloran: Introduction to the course: population biology, micro- versus macro parasitic diseases, R_0, generation time, time lines of transmission and disease, transmission probability, dependent happenings, dynamic models: epidemic versus endemic models, basic immunology

- Readings: Halloran, Longini, Struchiner (2009) Chapters 1 and 3
- Further: Ross (1916); Fraser et al (2004)
- Software: http://www.berkeleymadonna.com

2. January 8

- Longini: Reed-Frost model, Greenwood model, chain-binomial model
- Readings: Halloran, Longini, Struchiner (2009) Chapter 4
- Further: Bailey (1975); Becker (1989); Fox and Elveback (1975); Longini (1998)
- Software: small simulator

3. January 13

- Halloran: Dependent happenings; direct, indirect, total and overall effects of interventions; VE_S, VE_I, VE_P; overview of study designs for different effects; herd immunity
- Readings: Halloran, Longini, Struchiner (2009) Chapter 2 and 6
- Further: Greenwood and Yule (1915); Rhodes, Halloran, Longini (1996); Halloran (2001b); Halloran and Struchiner (1991); Halloran et al (1997), Basta et al (2008) Fine (1993);

4. January 15

- Halloran: Deterministic models I; simple insights from R_0; SIR, SEIR, SIS, and SI models
- Readings: Halloran, Longini, Struchiner (2009) Chapter 5
- Further: Halloran (2001a); Fraser et al (2004); Anderson and May (1991)

5. January 20

- Longini: Vaccine efficacy and models of vaccine mechanisms; time-to-event and final value data
- Readings: Halloran, Longini, Struchiner (2009) Chapter 7
- Further: Smith, Rodriguez, Fine (1984); Longini and Halloran (1996); Durham et al (1999); Halloran, Longini, Struchiner (1999), Durham et al (1998)

6. January 22

- Longini: Estimating R_0 for emerging infectious diseases in real time
- Readings: Wallinga and Teunis (2004); Yang et al (2007)
- Further: Cauchemez et al (2006)

7. January 27

- Halloran: Households studies I; dynamics, study designs, and estimation; secondary attack rate, community probability of infection, estimating VE_S and VE_I, households within communities, independent households
- Readings: Halloran, Longini, Struchiner (2009) Chapters 10 and 12

- Further: Longini, et al (1988), Halloran, Préziosi, Chu (2003) Longini and Koopman (1982); Becker (1989); O'Neill et al (2000); Longini, Datta, Halloran (1996); Addy et al (1991); Préziosi and Halloran (2003); Fine et al (1988); Halloran et al (2006)

8. January 29

   - Longini: Stochastic epidemic models: Pandemic influenza I
   - Readings: Halloran, Longini, Struchiner (2009) Chapter 4
   - Further: Longini et al (2005); Germann et al (2006); Ferguson et al (2005); Ferguson et al (2006); Halloran and Longini (2006); Longini et al (2004); Halloran et al (2002); Patel et al (2005)

9. February 3

   - Longini: Stochastic epidemic models: Pandemic influenza II
   - Readings: See previous class

10. February 5

    - Guest Lecture: Dr. Yang Yang
    - Households within a community II; Estimating (A)VE$_I$ and (A)VE$_S$ from time of onset data
    - Readings: Halloran, Longini, Struchiner (2009) Chapter 11
    - Further: Yang et al (2006); Rampey et al (1992); Cauchemez et al (2004);

11. February 10

    - Halloran: Evaluating indirect, total, and overall effects before and after vaccination, mini-community design
    - Readings: Halloran, Longini, Struchiner (2009) Chapter 13
    - Further: Halloran and Struchiner (1991)

12. February 12

    - Guest lecture: Professor Herb Hethecote
    - Deterministic models II: Rubella Vaccination Strategies in China
    - Readings: TBN

13. February 17

    - Halloran: Community trials for estimating vaccine effects
    - Readings: Halloran, Longini, Struchiner (2009) Chapter 13
    - Further: Longini et al (2002); Struchiner and Halloran (2007); Hayes and Moulton (2009); Hayes et al (1995); Moulton (2004); Gambia Hepatitis Study Group (1987).

14. February 19

    - Halloran: Evaluating immunological surrogates of protection

- Readings: Halloran, Longini, Struchiner (2009) Chapters 15 and 3
- Further: Gilbert and Hudgens (2008), Qin et al (2007)

15. February 24

- Longini: What exactly is R_0 anyway? Theory of heterogeneous mixing; critical vaccination fraction; R_0 as the eigenvalue of the next generation matrix, flu optimization
- Readings: Hill and Longini (2002)
- Further: Dieckmann et al (1990)

16. February 26

- Longini: Cholera: ecological determinants and vaccination
- Readings: Halloran, Longini, Struchiner (2009) Chapter 4
- Further: Hartley et al (2006); Longini et al (2002); Huq et al (2005)

17. March 3

- Halloran: Estimating efficacy of vaccination on post-infection outcomes, VE_P
- Readings: Halloran, Longini, Struchiner (2009) Chapter 9
- Further: Gilbert et al (2003a); Hudgens and Halloran (2006); Préziosi and Halloran (2003);

18. March 5

- Longini: Estimation of subtype-specific infectiousness of HIV
- Readings: Hudgens et al (2002);
- Further: Hudgens et al (2001)

19. March 10:

- Halloran: Validation sets for outcomes in vaccine studies
- Readings: Halloran, Longini, Struchiner (2009) Chapter 8
- Further: Halloran et al (2003); Halloran and Longini (2001); Scharfstein et al (2006)

20. March 12: last class

- Guest lecture: Dr. Eben Kenah
- How do we discover contact structures and what do they tell us about epidemic outcomes? Network-based analysis of stochastic SIR models.
- Readings: Wallinga et al (2006); Halloran (2006); Keeling and Eames (2005); Newman et al (2001)
- Further: Kenah and Robins (2007a,2007b); Andersson (1998)

21. March 16–20

- Exam week

References

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