University of Florida College of Public Health & Health Professions
PHC 6937, 2F64: Analytic Methods for Infectious Diseases (Spring 2018)
Monday periods 7-8, Wednesday Period 9, MAT 4

Main Instructor Information:

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Department of Biostatistics

College of Public Health & Health Professions

Office Hours: 2-3 pm, Wednesdays (on-campus students).   Additional help can be made by appointment

Additonal Instructors:

Diana Rojas, M.D., Ph.D.

Tom Hladish, Ph.D.

Yang Yang, Ph.D.

Natalie Dean, Ph.D.

Tim Tsang, Ph.D.

Prerequisites: PHC 6052, PHC 6053, PHC 6937

Course Overview: 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 methods, stochastic processes, network theory, and stochastic and deterministic transmission models. Examples include case studies in influenza, Ebola, dengue, Zika, cholera, and others. Presentations are largely statistical and mathematical, but with a focus on concepts.

Course Objectives: Upon successful completion of the course, students will be able to analyze infectious disease transmission and control from a mathematical and statistical point of view. In addition, they will be able of design and analyze infectious disease interventions including vaccine trials.

Required Textbook: Halloran, M.E., Longini, I.M. and Struchiner, C.J.: *The Design and Analysis of Vaccine Studies*. Springer, New York, 387 pp. (2009) ISBN 978-0-387-68636-3.

E-Learning/Canvas: An E-Learning site in Canvas will be available for the course. Grades, discussion boards, and other information will be available in the E-Learning system. E-learning is accessible at lss.at.ufl.edu or through my.ufl.edu. You must have a valid Gatorlink ID and password. For assistance, call the UF Help Desk at 392-HELP

Course Requirements/Evaluation/Grading: Students will write a single paper based on the knowledge they have gained in the course. Ideally, this will be a research project that they plan to carry out. Alternatively, they give a detailed synopsis of a scientific paper or papers selected by the instructor of the course. This will include an analysis of the methods base on course materials. The paper should be in scientific article format with references, and should be between 6 and 10 single-space pages.

Class Involvement: students are encouraged to be actively engaged in classes.

Topical Outline: Adjustments to this schedule are possible during the semester. The instructor will strive to be informative and fair regarding any changes.

Tentative Outline

Dates	Topic	Professor	Chapter in Halloran, et., al	Additional reading and materials
Jan 8	Introduction	Longini	1, 5	
10	R_0 and deterministic models	Longini	1	Hethcote (1976)
15	Martin Luther King Day Holiday			
17	Binomial and Stochastic Transmission Mod	Longini	4	Longini (2005)
18	Binomial and Stochastic Transmission Mod	Longini	10-12	Longini (1982)
22	Evaluating vaccines	Longini	2, 6, 13	
24	Survival analysis approach infectious diseases	Longini	2.4, 2.5, 2.9	
29	Vaccine action	Longini	7	Longini (1996)
31	Vaccine action	Longini	7	Halloran (1996)
Feb 5	Transmission of arboviruses	Rojas		
7	Estimation of reproductive numbers	Rojas		
12	Model design & contact network epidemiology	Hladish		
14	EpiFire program	Hladish		EpiFire
19	Percolation with interventions	Hladish		Python 2.x
21	Fitting complex models to data	Hladish		
26	Information levels of transmission data	Yang		Rhodes (1996)
28	Evaluation of vaccine efficacy in the presence of missing data	Yang		Yang (2012) Yang (2017)
March 5,7	Spring Break			
12	Analysis emerging infectious disease threats	Longini		WHO
14	Ebola ring vaccine trial in Guinea	Longini		Henao (2015, 2017)

				Dean (2018)
19	Stochastic models for arboviruses	Longini		Chao (2012)
21	Stochastic models for arboviruses	Longini		Hlasdish (2016)
26	Modeling pandemic influenza	Longini		Longini (2005)
28	Analytic method for influenza control	Longini		Yang (2009)
April 2	Transmission and control of cholera	Longini		Huq (2005), Longini (2007)
4	The design and conduct of dengue serosurveys	Dean		Dean (2017)
9	Study designs for evaluating vaccine efficacy	Dean	13	
11	Study designs for evaluating vaccine efficacy	Dean	13	
16	Household studies of influenza transmission	Tsang		Tsang (2016)
18	Estimation of transmission parameters from household studies of influenza transmission	Tsang		Tsang (2014)
23	WHO R&D Blueprint to prevent epidemics	Longini		WHO (2017)
25	Review of important concepts	Longini		

Statement of University's Honesty Policy: At the University of Florida, each student is bound by the academic honesty guidelines of the University and the student conduct code printed in the Student Guide and on the University website. The Honor Code states: "We, the members of the University of Florida community, pledge to hold ourselves and our peers to the highest standards of honesty and integrity." Cheating, lying, misrepresentation, or plagiarism in any form is unacceptable and inexcusable behavior. Students are expected to act in accordance with the University of Florida policy on academic integrity (see Student Conduct Code, the Graduate Student Handbook or this web site for more details**: http://www.dso.ufl.edu/sccr/**).

Academic integrity: Students are encouraged to discuss the material with other members of the class on homework and other assignments. However, the following is NOT allowed:
- Have another person complete any assignment in this course
- Copy another student's work on any assignment in this course
- Use materials provided by a previous student in the course for any purpose

Policy Related to Class Attendance: Class attendance is mandatory. Excused absences follow the criteria of the UF Graduate Catalogue (e.g., illness, serious family emergency, military obligations, religious holidays), and should be communicated to the instructor prior to the missed class day when possible. UF rules require attendance during the first two course sessions. Regardless of attendance, students are responsible for all material presented in class and meeting the scheduled due dates for class assignments. Finally, students should read the assigned readings prior to the class meetings, and be prepared to discuss the material except for the first class session.

Classroom etiquette: Please come to class on time and be prepared to stay until the time scheduled as the end of class. Pagers and cell phones should not be used in class. The use of cell phones, text messaging, and pagers is a common complaint from students. Please turn them off. Another common complaint is "side" conversations among students. Please consider that your conversation may interrupt the attention of someone seated near you. Generally, you should be speaking to the class as a whole or participating in group discussions as directed by the instructor. I welcome in-class questions. Your question will nearly always be one that other students also have.

Policy Related to Make-up Exams or Other Work: Students are allowed to make up work ONLY as the result of illness or other unanticipated circumstances warranting a medical excuse and resulting in the student missing a homework or project deadline, consistent with College policy. Documentation from a health care provider is required. Work missed for any other reason will receive a grade of zero.

Accommodations for Students with Disabilities: If you require classroom accommodation because of a disability, you must first register with the Dean of Students Office (http://www.dso.ufl.edu/). The Dean of Students Office will provide documentation to you, which you then give to the instructor when requesting accommodation. The College is committed to providing reasonable accommodations to assist students in their coursework.

Counseling and Student Health: Students may occasionally have personal issues that arise in the course of pursuing higher education or that may interfere with their academic performance. If you find yourself facing problems affecting your coursework, you are encouraged to talk with an instructor and to seek confidential assistance at the University of Florida Counseling Center, 352-392-1575, or Student Mental Health Services, 352-392-1171. Visit their web sites for more information: http://www.counsel.ufl.edu/ or http://www.shcc.ufl.edu/smhs/help.shtml

The Student Health Care Center at Shands is a satellite clinic of the main Student Health Care Center located on Fletcher Drive on campus. Student Health at Shands offers a variety of clinical services, including primary care, women's health care, immunizations, mental health care, and pharmacy services. The clinic is located on the second floor of the Dental Tower in the Health Science Center. For more information, contact the clinic at 392-0627 or check out the web site at: www.health.ufl.edu/shcc

Crisis intervention is always available 24/7 from Alachua County Crisis Center: (352) 264-6789.

BUT – *Do not wait until you reach a crisis to come in and talk with us. We have helped many students through stressful situations impacting their academic performance. You are not alone so do not be afraid to ask for assistance.*

As Spring semester course syllabi development begins, please include U Matter, We Care information in your course syllabus. Student Senate Resolution 2015-138 recommends the following language for all course syllabi:

Your well-being is important to the University of Florida. The U Matter, We Care initiative is committed to creating a culture of care on our campus by encouraging members of our community to look out for one another and to reach out for help if a member of our community is in need. If you or a friend is in distress, please contact umatter@ufl.edu so that the U Matter, We Care Team can reach out to the student in distress. A nighttime and weekend crisis counselor is available by phone at 352-392-1575. The U Matter, We Care Team can help connect students to the many other helping resources available including, but not limited to, Victim Advocates, Housing staff, and the Counseling and Wellness Center. Please remember that asking for help is a sign of strength. In case of emergency, call 9-1-1.

Reading Materials

Chao, D.L., Halstead, S.B., Halloran, M.E., Longini, I.M.: Controlling dengue with vaccines in Thailand. PLoS Negl Trop Dis.; 6(10): e1876.doi:10.1371/journal.pntd.0001876 (2012)

Dean NE: Informing vaccination programs: a guide to the design and conduct of dengue serosurveys. WHO (2017)
http://www.who.int/immunization/documents/research/WHOhttp://www.who.int/immunization/documents/research/WHO_IVB_17.07/en/_IVB_17.07/en/

Dean NE, Halloran ME, Longini IM: Design of vaccine trials during outbreaks with and without a delayed vaccination comparator. Annals of Applied Statistics (2018 - in print).

Halloran, M.E., Longini, I.M. and Struchiner, C.J.: Estimability and interpretation of vaccine efficacy using frailty mixing models. American Journal of Epidemiology 144, 83-97 (1996).

Henao-Restrepo A-M, Longini IM, Egger M, Dean NE, et al.: Efficacy of a recombinant live VSV-vectored vaccine expressing Ebola surface glycoprotein: Interim results from the Guinea ring vaccination cluster-randomized trial. The Lancet, 38, 857–866 (2015). PMID: 26248676

Henao-Restrepo A-M, Camacho A, Longini IM, et al: Efficacy and effectiveness of an rVSV-vectored vaccine in preventing Ebola virus disease: final results from the Guinea ring vaccination, open-label, cluster-randomised trial (Ebola Ça Suffit!). The Lancet 389, 505-18 (2017).

Hethcotle: Qualitative analyses of communicable disease models. Math Biosci 28, 335-356 (1976).

Hladish TJ, Pearson CAB, Chao DL, Rojas DP, Recchia GL, Gomez HG, Halloran ME, Pulliam JR, Longini IM: Projected impact of dengue vaccination in Yucatan, Mexico. PLoS Neglected Tropical Diseases: http://dx.doi.org/10.1371/journal.pntd.0004661 PMCID: PMC4882069 (2016).

Huq, A., Sack, R.B., Nizam, A., Longini, I.M., et al.: Critical factors influencing the occurrence of Vibrio cholerae in the environment of Bangladesh. Applied and Environmental Microbiology 71, 4645-4654. PMCID: PMC1183289 (2005)

Longini, I.M.: Chain Binomial Model in The Encyclopedia of Biostatistics. http://onlinelibrary.wiley.com/doi/10.1002/0470011815.b2a07008/full (2005).

Longini, I.M. and Halloran, M.E.: A frailty mixture model for estimating vaccine efficacy. Applied Statistics 45, 165-173 (1996).

Longini, I.M., Koopman, J., Monto, A.S. and Fox, J.P.: Estimating household and community transmission parameters for influenza. American Journal of Epidemiology 115, 736-751 (1982).

Longini, I.M., Nizam, A., Xu, S., Ungchusak, K., Hanshaoworakul, W., Cummings, D., Halloran, M.E.: Containing pandemic influenza at the source. Science 309, 1083-1087. PubMed PMID: 16079251 (2005)

Longini, I.M., Nizam, A., Ali, M., Yunus, M., Shenvi, N. and Clemens, J.D.: Controlling endemic cholera with oral vaccines. Public Library of Science (PloS), Medicine 4 (11): e336 doi:10.1371/journal.pmed.0040336. PMCID: PMC2082648 (2007).

Rhodes, P.H., Halloran, M.E. and Longini, I.M.: Counting process models for infectious disease data: Distinguishing exposure to infection from susceptibility. Journal of the Royal Statistical Society B 58, 751-762 (1996).

Tsang, et al.: Household transmission of influenza virus, Trends Microbiol 24, 123–133 (2016).

Tsang, et al.: Association between antibody titers and protection against influenza virus infection within households. J Infect Dis. 210, 684–692 (2014).

WHO: http://www.who.int/blueprint/en/ (2017)

Yang, Y., Sugimoto, JD, Halloran, ME, Basta, NE, Chao, DL, Matrajt, L, Potter, G, Kenah, E, Longini, IM: The transmissibility and control of pandemic influenza A (H1N1) virus. Science 326, 729-33. PMCID: PMC2880578 (2009)

Yang, Y, Longini, I.M., Halloran, M.E., Obenchain, V: A Hybrid EM and Monte Carlo EM Algorithm and Its Application to Analysis of Transmission of Infectious Diseases. Biometrics 68, 1238–49 (2012).

Yang Y, Meng Y, M. Halloran ME, Longini IM: Dependency of vaccine efficacy on pre-exposure and age: A closer look at a tetravalent dengue vaccine. Clinical Infectious Diseases   cix766, https://doi.org/10.1093/cid/cix766 (2017).