

MACROEPIDEMIOLOGY: ANALYTICAL PAPER

Each student chooses a common disease such as a form of cancer, vascular disease or diabetes of interest to him or her.

Every three weeks a "chapter" is due in draft form with references developed in parallel with material from class that uses colon and lung cancer as principle examples. A "chapter" would be on the order of four-five pages of discussion of the key facts @ the chosen disease. Tables and figures copied from data bases and original papers would also be submitted along with a bibliography annotated when useful by the abstracts of key papers. These will be returned with criticisms and suggestions generally by the following Tuesday. Drafts may be delayed up to one week for "crunch" periods with e-mailed request for delay stating reason. The idea is that each successive chapter is resubmitted with amendments when the next chapter is due so that the effort is spread out over the length of the course.

Chapters with suggested topics:

CHAPTER 1

History of chosen disease rates among male and female European and African Americans and Japanese from <http://epidemiology.mit.edu>. Compari-historical changes in birth cohorts experience to historical changes in human environment/lifestyles. Estimate minimum fraction at risk, age at onset and age-dependent rates in transitional birth cohorts. Compare history of changes of rates for other common forms of mortality identifying mortal diseases with similar historical changes. Offer supportable and/or testable hypotheses as to environmental risk factors. Due February 17.

CHAPTER 2

Use the multiparametric model (CancerFit) to analyze age-specific disease rates in birth cohorts whose lives spanned the 19th and 20th centuries and obtain the following estimates: Fraction (F) at lifetime risk versus fraction of deaths. Fraction (f) accounting risk of mortality with diseases with identical subgroup at risk. Constant describing initiation rate (cancers, other clonal diseases), constant describing growth rate of preclinical lesions, constant representing rate or probability of transition to lethal clinical lesions. Summarize the ranges of these parameters yielding results consistent with clinical observations. Due March 17.

CHAPTER 3

Apply a model of genetic risk in general population and familial risks (Sweden) to narrowing estimates of lifetime risk, F, genetic risk, G and environmental risk, E. Search, organize, and analyse literature pertaining to said risks for your disease. Recalculate of model parameters (CancerFit) with supportable restrictions on estimates of lifetime risks. Due April 7.

CHAPTER 4

Physiology and pathology of disease. From the literature create a quantitative description of histology of organ definition, growth and function from blastula through old age. Summarize studies indicating role of mutations in specific somatic genes with emphasis on information from early onset forms of disease. Estimate stem cell number if possible and apply to estimation of rates for initiation processes. Consider limitation of initiation events to juvenile years. Due April 28.

CHAPTER 5

SUMMARY Prepare and present a quantitative cascade model of your disease indicating limits on values of parameters of lifetime risk and physiological transition rates identifying specific processes, e.g. rate of APC gene mutation in initiation of colon cancer. Outline what additional information is needed to define undefined parameters, genes and environmental factors especially the physiological role(s) of environmental factors interacting with susceptibility genes. Due May 12 as part of final paper.

ORAL PRESENTATIONS

MAY 5, 10 and 12

Ten minute presentation comprising 5-9 PowerPoint slides summarizing key findings of the analytical paper embedded in the quantitative cascade model. Five minutes of questions from class. Order of presentation first by volunteering and then by a lottery in the last class before Spring Vacation. These presentations have been generally excellent in past years. Students are encouraged to invite friends and faculty advisors.

LIST OF POTENTIAL DISEASES FOR ANALYSES

Most "straightforward":

Esophageal cancer
Pancreatic cancer
Prostate cancer
Brain cancers*
Kidney cancers
Lung cancers*
Colon and/or colorectal cancers**
Gastric cancer**

More challenging:

Breast and ovarian cancers
Testicular cancer
Leukemias
Hodgkin's lymphoma
Skin cancers* including melanoma
Leukemias
Non-Hodgkin's lymphomas
Less frequent forms of cancer

Most challenging:

Cardiovascular disease*** or
Cerebrovascular disease*** derived from atherosclerosis
Diabetes mellitus***
Alzheimer's disease***
Multiple sclerosis***
Infectious diseases** , ***

* Genes involved in initiation processes identified.

** Major environmental risk factor identified.

*** Requires original work on cascade model/program. Code available for modification.

Any common disease may be chosen if in discussion with the instructor the student demonstrates strong motivation and reasonable preparation for independent work. Students with sufficient background may also elect to analyze a hypothesis such as, "Growth of preclinical lesions is governed by inflammation." or "The drop in death rates by infectious disease in the early 20th century accounts for the increased rates of cancers thereafter."