Epidemiological Thinking and Population Health

An Open Source-like Curriculum

The curriculum for the course is organized around a sequence of basic ideas in thinking like epidemiologists, especially epidemiologists who pay attention to possible social influences on the development and unequal distribution of diseases and behaviors in populations. Contributions, using http://bit.ly/EpiContribute, are welcome in the form of:

- suggested revisions and additions to the ideas and their description;
- additional or replacement readings related to any of the ideas; and
- annotations of the current or suggested readings.

The contributions are inserted by the wikimeister (i.e., the instructor of the course) into the separate wikipages for each session of the curriculum, accessible via http://ppol753.wikispaces.umb.edu . In this appendix I extract from the syllabus and wikipages the key ideas for each session, my initial notes to students, and references to the readings.

The operation of the course is described in the online syllabus and wikipages, but let me set the scene by noting a few features. Each class includes a discussion of the readings, a workshop period, and a mini-lecture to introduce the topic and readings for the week to come. The aim of the workshop is that each student prepares a sketch of ways that the concepts, methods, and problems of that week might be applied to a research or policy question in their own area of interest. The workshop period allows for one-on-one interaction with instructor and peer input/support/coaching. The sketches are assembled by the student into an evolving portfolio, which also include required annotations of at least one reading each week and additions to a personal glossary of terms from chapters of the text—Gordis, L. Epidemiology. Philadelphia, Saunders/ Elsevier—illustrated by examples from the student's field. At the end of the course, students select highlights from their portfolio and introduce them with an essay that explains the development of their thinking to an outside reader.

The conventional notion of teaching as transmission of knowledge from instructor to students has some place in this course. The instructor provides (through the mini-lectures and course wikipages) an introduction to and motivation of each session's readings and cases. The instructor

also provides assistance with technical questions of concern either to the whole class or to individual students, refering to relevant sections of Gordis and Kirkwood, B. R. and J. A. C. Sterne (2003). Essential Medical Statistics. Malden, Blackwell, or helping students create a network of specialists they can consult with during and the semester and after the course is over. At the same time, it is expected that students (and the instructor) will have to employ strategies of reading that allow us to extract take-home lessons from readings even as we skip sections that become too technical. The course as a whole aims to cultivate skills and dispositions of critical thinking and of life-long, cooperative learning facilitated by the resources of the internet. The use of controversies follows an idea central to critical thinking that we understand ideas better by holding them in tension with alternatives.

Week 1. The course as a learning community

Idea: Developing epidemiological literacy requires collaboration with others (of differing skills and interests) and reflection on personal and professional development.

Students identify and share personal, intellectual, professional interests in relation to central themes about inequality, pathways of development, and policy.

Idea: Developing epidemiological literacy requires establish our own practices of learning from material we don't fully grasp at first reading/hearing.

Activities on reading/learning strategies

Idea: Non-specialists need to become comfortable with the fundamental ideas and basic vocabulary of epidemiology in order to converse intelligently with specialists in epidemiology and biostatistics. One way to move in that direction is to practice making the ideas accessible to the layperson.

Preparation of a glossary of terms with examples drawn from the student's area of research.

2. Phenomena: Exploring the "natural history" of disease

Idea: Detailed observation (like a naturalist) or detective work--albeit informed by theoretical ideas--may be needed before we can characterize what the phenomenon is we are studying, what questions we need to ask, and what categories we need for subsequent data collection and analysis.

The initial motivation for this class was to highlight that epidemiology does not necessarily begin with data sets to analyze. There may be exploratory, investigative, detective, anthropological, and naturalist inquiries before

phenomena are even noticed, categories are defined, questions are framed. Good examples of this seemed to be provided by John Snow's work on cholera, by Barker's* (1971) research in Uganda, and on "clues from geography" of infant mortality and heart disease (1998), and the three Lancashire towns, and by Oxford's account of the conditions that provided a source for a global pandemic of the 1918 flu (40 million died from flu, while 8.5m died from war). Even Barker's (1999) speculation about anomalous French cardiovascular disease rates looks like someone who is able to connect dots of diverse kinds and that are spread out in time.

Brody's paper, in addition to drawing attention to the role of maps in this exploratory research, makes the Snow story more complicated and interesting. Snow had clear hypotheses that guided his mapping and his advocacy of stopping the water supply from the Broad Street pump -- he was certainly not simply noticing patterns in the data and hypothesizing about the causes. This account opens up broader questions in philosophy of science. E.g., where do hypotheses that get assessed by research come from in the first place?

(* Barker is a recently retired but still active epidemiologist whose reputation is linked to the "Barker hypothesis" that chronic diseases of later life are associated with fetal or early-life conditions. We'll address this hypothesis within the frame of "life course epidemiology" in week 10.)

• Barker, D. J. P. (1971). "Buruli disease in a district of Uganda." Journal of Tropical Medicine and Hygiene 74: 260-264.

• Barker, D. J. P. (1998). Mothers, Babies, and Health in Later Life. Edinburgh, Churchill Livingstone, pp1-12, 167-172.

• Barker, D. J. P. (1999). "Commentary: Intrauterine nutrition may be important." British Medical Journal 318: 1471-1480. (http://www.bmj.com/cgi/content/full/318/7196/1471#resp2)

• Brody, H., M. R. Rip, et al. (2000). "Map-making and myth-making in Broad Street: the London cholera epidemic, 1854." The Lancet 356: 64-68.

• Oxford, J. S., R. Lambkin, et al. (2005). " A hypothesis: the conjunction of soldiers, gas, pigs, ducks, geese and horses in northern France during the Great War provided the conditions for the emergence of the "Spanish" influenza pandemic of 1918-1919." Vaccine 23(7): 940-945.

• PBS Home Video. (2004). "Killer flu"

3. The scope and challenges of epidemiology

Idea: The uses of epidemiology are many, but shift over time, and are subject to recurrent challenges from inside and outside the field.

The articles provide a variety of historical perspectives and opinion statements on this idea.

On Davey-Smith (2001), see Davey-Smith's conversation with Jerry Morris, the author of the Uses of Epidemiology, http://bit.ly/g9DDHz)

Brandt and Gardner's title conveys the point: physicians have often opposed an increasing role of public health. Epidemiology might be needed for quantitative assessment of new interventions and evaluating patient safety and

healthcare quality, but its role beyond evaluation and assessment, especially in regards to social, cultural, and economic factors of diseases, is contested.

Pearce argues that modern epidemiologists have little concern for the socioeconomic factors that may affect health. He contrasts "bottom-up" and "top-down" approaches. The latter begins at the population level in order to determine the primary factors that effect health, and it uses a structural model of causation. The bottom-up approach, e.g., molecular epidemiology, begins on the individual level and aims to proceed upward toward the population level.

• Davey-Smith, G. (2001). "The uses of Uses of Epidemiology." International Journal of Epidemiology 30: 1146-1155.

• Brandt, A. M. and M. Gardner (2000). "Antagonism and accommodation: interpreting the relationship between public health and medicine in the United States during the 20th century." American Journal of Public Health 90: 707-715

• Caldwell, J. C. (2001). "Population health in transition." Bulletin of the World Health Organization 79(2): 159-160.

• Pearce, N. (1996). "Traditional epidemiology, modern epidemiology, and public health." American Journal of Public Health 86: 678-683

• Schwartz, S., E. Susser, et al. (1999). "A Future for Epidemiology?" Annual Review of Public Health 20: 15-35.

Idea: In advising on the most effective measures to be taken to improve the health of a population, epidemiologists may focus on different determinants of the disease than a doctor would when faced with sick or high-risk individuals.

Rose (1985) promotes the population health focus, but this is not universally accepted by healthcare practitioners and policy makers. If someone asks you the question Rose's mentor posed, "Why did this patient get this disease at this time?," how do you answer? Can you identify areas in your own life and/or work when you would take a population view and other areas where your focus would be individually-centered?

Road accidents and alcohol consumption may be a good illustration of Rose's argument. Most of us know of getting home safely when we've drunk too much "risk factor," but we also know that a substantial fraction of people in accidents have high alcohol levels. We also sense that some people are more susceptible to having their judgement and reaction times impaired by alcohol so we could imagine doing further epidemiological and biological research to develop multivariable risk factor formulas. Would a more refined knowledge of riskiness help us prioritize our risk-prevention efforts, or would that pale into insignificance relative to a Rosean drink-don't-drive efforts?

Controversy over vaccination of girls for HPV, given the physical side effects (at a low rate — see http://www.usatoday.com/news/health/2009-08-31-hpv-gardasil_N.htm) and promiscuity-inducing side effects (no data for this). Question: What would Rose propose?

Question: Why isn't a population an aggregation of individuals and thus population risk = sum of individual risks?

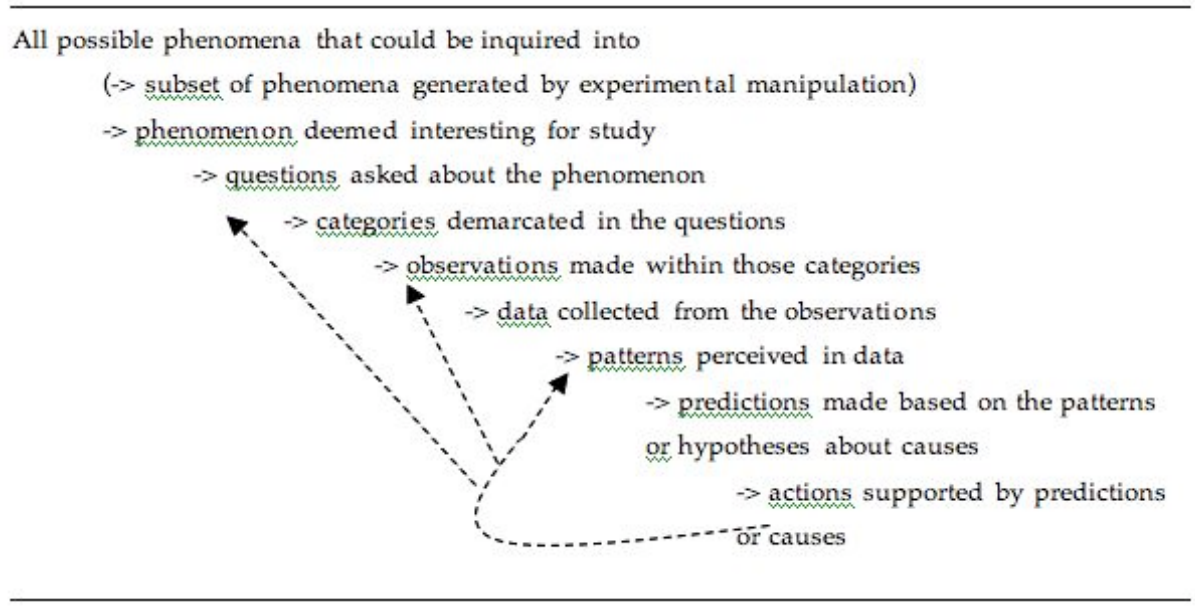
My response: 1. It is necessary to think of different meaning of "treatment." A sick individual is treated by a physician to cure or reduce the effects of the disease. Population health policies do not treat a large group of sick people, but attempt to reduce the incidence in the next generation.
2. A physician treating sick individuals adjusts the treatment for individuals if it doesn't work well for them. In contrast, public health measures usually discount the heterogeneity in the population and apply the same policy to all. Nevertheless, it is possible to imagine that knowledge of heterogeneous responses to treatment of individuals could lead to more effective population health policies (and reduce the kickback that occurs when some individuals claim to have suffered under the population health policy).

• Rose, G. (1985). "Sick individuals and sick populations." International Journal of Epidemiology 14: 32-38. Reprinted in IJE 30: 427-432 (2001)

4. Categories

Idea: Collecting and analyzing data requires categories: Have we omitted relevant categories or mixed different phenomena under one label? What basis do we have for subdividing a continuum into categories? How do we ensure correct diagnosis and assignment to categories? What meaning do we intend to give to data collected in our categories?

1. We can identify a chain of steps in scientific inquiry in which each step involves assumptions and is open for negotiation and wider influences (Taylor 2005, chapter 2).



Decisions made at early steps influence outcomes at later steps. E.g., if schizophrenia is used as a category as defined by the DSM, it is harder for a clinician to pay attention to the contextual and life history information of patients (Poland 2004). This is not a one-way sequence. There is also the possibility that desired outcomes for the

later stages (especially the actions the researcher favors in advance and would like to be supported by the inquiry) influence decisions made at earlier steps.

2. When reading a study, take note of:

• a) where the categories demarcated seem to favor certain kinds of action over others (e.g., Galton only collected data about similarities among relatives so there was no way he could explore hypotheses about non-hereditary or environmental influences or illuminate action regarding those influences); and

• b) what kinds of remedies you would propose whenever the categories seem limited (e.g., disaggregate the category "approve of Congress," which includes Democrats who want the Democratic majority in the Senate not to accede to filibustering Republicans and Republicans who don't want Democrats to get their way).

Hymowitz (2007) [not a scholarly article] disaggregates divorce rates in the USA, which hide different phenomena and trends in different social classes.

Pickles and Angold (2003) review the debate about whether categories of psychopathology are best thought of as categorical (e.g., one has schizophrenia or doesn't) or dimensional (e.g., there are degrees of schizophrenic behavior).

Poland (picking up on both points above) argues that the category "of schizophrenia and the associated received view [does not] have anything useful to add to clinical practice concerned with severe mental illness."

George Brown (UK) and Bruce Dohrenwend (USA) have done research for decades on the relationship between mental illness and life events or difficulties. Brown (as described by Birley and Goldberg 2000) developed methods that tried to expose the meaning of an event for the person and was critical of the US emphasis on "objective" surveys (where the same event, e.g, death of a spouse, might have very different meanings and significance for the subject). Dohrenwend describes his group's eventual realization of this issue, but they still wanted to measure events without having the context fused into the rating of the event.

Davey-Smith et al. (2000) consider comparative methods for studying socioeconomic position and health in different ethnic communities, e.g., — Does socio-economic status (SES) mean the same thing for different communities? If not, what is our proposed remedy?

3. Classifying problems with categories:

Have we omitted relevant categories?

Have we mixed different phenomena under one label?

What basis do we have for subdividing a continuum into categories?

Have we divided the continuum at the right point?

How do we ensure correct diagnosis and assignment to categories?

What meaning do we intend to give to data collected in our categories?

Is our category correctly named?

Identify an example of a problem related to each question. What can be done in practice to overcome the problem? In what ways does the problem illustrate #1 above.

• Birley, J. and D. Goldberg (2000). George Brown's contribution to psychiatry: The effort after meaning. Where Inner and Outer Worlds Meet. T. Harris. London, Routledge: 55-60.
• Brown, G. W. and T. O. Harris (1978). Sociology and the aetiology of depression; Depression and Loss; A Model of Depression; Summary and conclusions. Social Origins of Depression: a Study of Psychiatric Disorder in Women. New York, Free Press: 3-20; 233-293.
• Davey-Smith, G. et al. (2000). Ethnicity, health and the meaning of socio-economic position Pp. 25-37 In Graham, H., Ed. Understanding health inequalities. Buckingham [England], Open University Press.
• Dohrenwend, B. P., K. G. Raphael, et al. (1993). The structured event probe and narrative rating method for measuring stressful life events. Handbook of Stress: Theoretical and Clinical Aspects. L. Goldberg and S. Breznitz. New York, Free Press: 174-199.
• Hymowitz, K. S. (2007). "Marriage and Caste in America: Separate and Unequal Families in a PostMarital Age." Heritage Lecture #1005.
• Pickles, A. and A. Angold (2003). "Natural categories or fundamental dimensions: On carving nature at the joints and the rearticulation of psychopathology." Development and Psychopathology 15: 529-551.
• Poland, J. (2004). "Bias and schizophrenia." Pp. 149-161 in P. J. Caplan and L. Cosgrove, eds. Bias in Psychiatric Diagnosis. Lanham, MD: Rowman & Littlefield.
• Taylor, P. J. (2005). Unruly Complexity: Ecology, Interpretation, Engagement. Chicago, University of Chicago Press.

5. Associations, Predictions, Causes, and Interventions

Idea: Relationships among associations, predictions, causes, and interventions run through all the cases and controversies in this course. The idea introduced in this session is that epidemiology has two faces: One from which the thinking about associations, predictions, causes, and interventions are allowed to cross-fertilize, and the other from which the distinctions among them are vigorously maintained, as in "Correlation is not causation!" The second face views Randomized Control Trial (RCTs) as the "gold-standard" for testing treatments in medicine. The first face recognizes that many hypotheses about treatment and other interventions emerge from observational studies and often such studies provide the only data we have to work with. What are the shortcomings of observational studies we need to pay attention to (e.g., systematic sampling errors leading to unmeasured confounders-see next class)?

Ridker et al. show that the conventional risk factors for heart disease in women (as combined in the Framingham score) identify many women as of intermediate risk who are higher or lower risk. The new Reynolds Risk Score does a much better job, primarily it seems by including the risk marker cReactive Protein. Both scores are based on observations not randomized trials. (But see Shunkert for recent assessment of the role of CRP.)

The case of hormone replacement therapy as a protection against heart disease (Stampfer 1990) is another, more significant instance of mismatch of observational results and RCTs — see Stampfer 2004 & Pettiti for analyses of the discrepancy. It is important to get a handle on the different kinds of explanation for this and other discrepancies, including physician bias in who gets prescribed a treatment, residual confounders, and reverse causation.
Jick presents evidence that statin treatment was associated with lowered risk of dementia but the Alzheimer Research Forum presents the more recent assessment (using RCTs) that statins are not protective against dementia. The discrepancy seems to be undetected bias in which patients get prescribed statins.
Davey-Smith & Ebrahim (2007, pp.2-8) provide a quick review of a number of cases.

• Alzheimer_Research_Forum (2004). "Philadelphia: All Is Not Well with the Statin Story." http://www.alzforum.org/new/detailprint.asp?id=1046.
• Davey-Smith, G. and S. Ebrahim (2007). "Mendelian randomization: Genetic variants as instruments for strengthening causal influences in observational studies. Pp 336-366 in Weinstein, M., Vaupel, J. W., Wachter, K.W. (eds) Biosocial Surveys. Washington, DC, National Academies Press.
• Jick, H., G. L. Zomberg, et al. (2000). "Statins and the risk of dementia." Lancet 356: 1627-1631.
• Petitti, D. B. and D. A. Freedman (2005). "Invited Commentary: How Far Can Epidemiologists Get with Statistical Adjustment?" American Journal of Epidemiology 162: 415-418.
• Ridker, P. M., J. E. Buring, et al. (2007). "Development and Validation of Improved Algorithms for the Assessment of Global Cardiovascular Risk in Women: The Reynolds Risk Score." Journal of the American Medical Association 297: 611-619.
• Schunkert, H. and N. J. Samani (2008). "Elevated C-Reactive Protein in Atherosclerosis – Chicken or Egg?" New England Journal of Medicine 359(18): 1953-1955.
• Stampfer, M. J. and G. A. Colditz (1991). "Estrogen replacement therapy and coronary heart disease: a quantitative assessment of the epidemiologic evidence." Preventive Medicine 20: 47-63.
• Stampfer, M. J.(2004) "Commentary: Hormones and heart disease: do trials and observational studies address different questions?" International Journal of Epidemiology 33: 545-455.

6. Confounders & conditioning of analyses

Idea: Statistical associations between any two variables generally vary depending on the values taken by other "confounding" variables. We need to take this dependency (or conditionality) into account when using our analyses to make predictions or hypothesize about causes, but how do we decide which variables are relevant and real confounders?

When reading the articles, make notes on how the readings address the topic of adjusting for confounding variables (which includes age-standardization) and identify controversies or discordant views about how to do this.
Cases:

Immunization levels (Egede): Note the conclusion about racial/ethnic inequality even after adjusting for other variables thought to correlate with race/ethnicity. Do you agree with the three implications p. 326ff) drawn from the results?

SES gradients in disease (Krieger): The abstract states that "for virtually all outcomes, risk increased with CT [census tract] poverty, and when we adjusted for CT poverty, racial/ethnic disparities were substantially reduced." Where can the result of adjustment be seen in the paper? (This paper also fits in week 7 on inequalities.)

Hormone replacement therapy (Prentice vs. Petitti): Notice the adjustments used by the first paper that bring the clinical component of the WHI hormone replacement trial into line with the observational component. Do Pettiti acknowledge and rebut this in concluding that it was wrong to think that hormone therapy prevents CV disease?

Birth weight and blood pressure (Huxley vs. Davies): Along with Huxley et al's general argument that the birthweight-adult blood pressure association may well be an artifact of selective publication of studies with small sample size, they criticise the adjustment of the association for adult weight. (In other words, the association holds for people in the same stratum or slice of weight.) Try to form an opinion about whether you agree or disagree with such an adjustment. Davies et al. provide counter-evidence to Huxley et al. -- how does their study differ in methods, results, and interpretation?

Control at work and mortality (Davey-Smith 1997): This simple study shows that "control at work" is not the cause of SES gradients in health outcomes. What method(s) do they use to undermine previous claims about control at work?

Mendelian randomization to analyze environmental exposures (Davey-Smith & Ebrahim 2007): The approach introduced in this paper is cutting edge "epidemiology in the age of genomics" and has led to funding of a major new Research Center under Davey-Smith at Bristol. I suggest that you summarize for yourself the logic of this approach so you can explain it to someone who's never heard of it.

• Davey-Smith, G. and S. Harding (1997). "Is control at work the key to socioeconomic gradients in mortality?" Lancet 350: 1369-1370.

• Davey-Smith, G. and S. Ebrahim (2007). "Mendelian randomization: Genetic variants as instruments for strengthening causal influences in observational studies. Pp 336-366 in Weinstein, M., Vaupel, J. W., Wachter, K.W. (eds) Biosocial Surveys. Washington, DC, National Academies Press.

• Davies, A., G. Davey-Smith, et al. (2006). "Association between birth weight and blood pressure is robust, amplifies with age, and may be underestimated." Hypertension 48: 431-436.

• Egede, L. E. and D. Zheng (2003). "Racial/Ethnic Differences in Adult Vaccination Among Individuals With Diabetes." American Journal of Public Health 93(2): 324-329.

• Hernan, M. A. (2002). "Causal Knowledge as a Preequisite for Confounding Evaluation: An Application to Birth Defects Epidemiology." American Journal of Epidemiology 155: 176-184.

• Huxley, R., A. Neil, et al. (2002). "Unravelling the fetal origins hypothesis: is there really an inverse association between birthweight and subsequent blood pressure?" Lancet 360(9334): 659-65.

• Krieger, N., J. T. Chen, et al. (2005). "Painting a truer picture of US socioeconomic and racial/ethnic health inequalities: The Public Health Disparities Geocoding Projec." American Journal of Public Health 95: 312-323.
• Lawlor, D. A., G. Davey-Smith, et al. (2004). "Those confounded vitamins: what can we learn from the differences between observational versus randomised trial evidence?" The Lancet 363: 1724-1726.
• Lynch, J. (2007). Video, http://cpheo4.sph.umn.edu/ramgen/vcontent/healthdisparities/lynch/lynch.smil
• Petitti, D. B. and D. A. Freedman (2005). "Invited Commentary: How Far Can Epidemiologists Get with Statistical Adjustment?" American Journal of Epidemiology 162: 415-418.
• Prentice, R. L., R. Langer, et al. (2005). "Combined Postmenopausal Hormone Therapy and Cardiovascular Disease: Toward Resolving the Discrepancy between Observational Studies and the Women's Health Initiative Clinical Trial." American Journal of Epidemiology 162(5): 404-414.

7. Variations in health care (by place, race, class, gender)

Idea: Inequalities in people's health and how they are treated are associated with place, race, class, gender, even after conditioning on other relevant variables.

The issues here are not only variations or disparities, but also how to measure, track, and talk about those variations.
Krieger et al. started the the Public Health Disparities Geocoding Project because socioeconomic data is often lacking in US public health surveillance systems. Socioeconomic deprivation contributes to racial/ethnic health disparities in more than half of the cases studied.
Davey Smith advises against using ethnicity as a proxy for socioeconomic position and advocates for incorporating both in quantitative models.
Alter et al. conclude that despite Canada's Universal Health Care System a individual's socioeconomic status affected access to cardiac services and increased the prevalence of mortality.
Gawande describes how medical costs can be high even in poor areas; this results from the overuse of medicine from over-treating patients and over-prescribing tests and procedures.
Marmot and Wilkinson argue that researchers should look beyond material privation to examine psychosocial effects on variation in health outcomes, particularly relative deprivation concerning individual agency and control.
Wright et al.'s study of asthma among children in low-income urban settings found a correlation between asthma, stress, and exposure to violence that suggests the need for addressing these intervening variables. However, smoking was not found to be associated with asthma attack incidence.

• Alter, D. A., C. D. Naylor, et al. (1999). "Effects of socioeconomic status on access to invasive cardiac procedures and on mortality after acute myocardial infarction." New England Journal of Medicine 341: 1359-1367.
• Bassuk, S. S., L. F. Berkman, et al. (2002). "Socioeconomic Status and Mortality among the Elderly: Findings from Four US Communities." American Journal of Epidemiology 155: 520-533.
• Davey-Smith, G. (2000). "Learning to live with complexity: Ethnicity, socioeconomic position, and health in Britain and the United States." American Journal of Public Health 90: 1694-1698.
• Dunn, J. R. and S. Cummins (2007). "Placing health in context." Social Science & Medicine 65: 1821-1824

• Egede, L. E. and D. Zheng (2003). "Racial/Ethnic Differences in Adult Vaccination Among Individuals With Diabetes." American Journal of Public Health 93(2): 324-329.
• Gawande, A. (2009). "The cost conundrum: What a Texas town can teach us about health care." The New Yorker (1 June).
• Krieger, N., J. T. Chen, et al. (2005). "Painting a truer picture of US socioeconomic and racial/ethnic health inequalities: The Public Health Disparities Geocoding Projec." American Journal of Public Health 95: 312-323.
• Marmot, M. and R. G. Wilkinson (2001). "Psychosocial and material pathways in the relation between income and health: a response to Lynch et al " British Medical Journal 322: 1233-1236.
• Roger, V. L., M. E. Farkouh, et al. (2000). "Sex Differences in Evaluation and Outcome of Unstable Angina." Journal of the American Medical Association 283: 646-652.
• Wright, R. J., H. Mitchell, et al. (2004). "Community Violence and Asthma Morbidity: The Inner-City Asthma Study " American Journal of Public Health 94: 625-632.

8. Heterogeneity within populations and subgroups

Idea: How people respond to treatment may vary from one subgroup to another--When is this a matter of chance or of undetected additional variables? How do we delineate the boundaries between subgroups?

Lagakos provides a statistician's cautions about the significance of results derived from subgroups of the whole population, especially if the subgroups were only defined after exploring the data.
The opposite caution is that treating everyone as if they were from the same population (for good statistical reasons) distracts our attention from the clues that might lead us to seeing that the population is not one uniform whole, but is a mixture of types. This can have significant health care implications -- see case studies about different kinds of breast cancer (Regan) and aspirin resistance.

• Eikelboom, J. W. and G. J. Hankey (2003). "Aspirin resistance: a new independent predictor of vascular events?" Journal of the American College of Cardiology 41: 966-968.
• Gum, P. A., K. Kottke-Marchant, et al. (2003). "A prospective, blinded determination of the natural history of aspirin resistance among stable patients with cardiovascular disease." Journal of the American College of Cardiology 41: 961-965.
• Kahn, J. (2007). "Race in a Bottle." Scientific American(July 15).
• Lagakos, S. W. (2006). "The challenge of subgroup analysis--Reporting without distorting." New England Journal of Medicine 354: 1667-1669.
• Nelson, M. R., D. Liew, et al. (2005). "Epidemiological modelling of routine use of low dose aspirin for the primary prevention of coronary heart disease and stroke in those aged >=70." British Medical Journal 330: 1306-1311.

• Regan, M. M. and R. D. Gelber (2005). "Predicting response to systematic treatments: Learning from the past to plan for the future." The Breast 14: 582-593.

9. Placing individuals in a multileveled context

Idea: Different or even contradictory associations can be detected at different levels of aggregation (e.g., individual, region, nation), but not all influences can be assigned to properties of the individual—Membership in a larger aggregation can influence outcomes even after conditioning on the attributes of the individuals.

Prepare for class as follows:

Ecological & atomistic fallacies:

Bring one example of an ecological fallacy not in the readings and be ready to explain it to the other students.

Extract one example of an effect that is obscured by focusing only on one level, i.e., all individuals in a population. This example may come from the readings. Be ready to explain it to the other students (and to explain where you get confused, if applicable).

Neighborhood effects:

Diez-Roux (2002a) notes in her commentary that "…many of the analytic issues that arise when examining neighborhood effects on health are present throughout the continuum from society to molecules. These analytic issues include, for example, nested data structures, variables and units of analysis at multiple levels, contextual effects, distal causes, and complex causal chains with feedback loops and reciprocal effects" (p.516).

Do you find that the issues referenced above have been successfully addressed in the studies by Balfour & Kaplan (2002) and Coulton, Korbin & Su (1999)?

Income inequality, stature, and obesity:

Describe (and evaluate) the proposed pathway from income inequality to weight gain in the study by Marcelli (2006).

• Balfour, J. L. and G. A. Kaplan (2002). "Neighborhood Environment and Loss of Physical Function in Older Adults: Evidence from the Alameda County Study." American Journal of Epidemiology 155: 507-515.

• Coulton, C. J., J. E. Korbin, et al. (1999). "Neighborhoods and Child Maltreatment: A Multi-Level Study." Child Abuse & Neglect 23(11): 1019–1040.

• Diez Roux, A. V. (2002a). "Invited Commentary: Places, People, and Health." American Journal of Epidemiology 155: 516-519.

• Diez Roux, A. V. (2002b). "A glossary for multilevel analysis." Journal of Epidemiology and Community Health 56: 588-594.

• Dunn, J. R. and S. Cummins (2007). "Placing health in context." Social Science & Medicine 65: 1821-1824

• Korbin, J. E., C. J. Coulton, et al. (2000). "Neighborhood Views On The Definition And Etiology Of Child Maltreatment." Child Abuse & Neglect 24(12): 1509–1527.

• Lawlor, D. A., G. Davey-Smith, et al. (2005). "Life-Course Socioeconomic Position, Area Deprivation, and Coronary Heart Disease: Findings From the British Women's Heart and Health Study." American Journal of Public Health 95: 91-97.
• Marcelli, E., C. Jencks, et al. (2005). "The Impact of Family Socioeconomic Status and Income Inequality on Stature in the United States." Paper for Meeting of the Population Association of America, Philadelphia, PA.
• Marcelli, E., D. M. Cutler, et al. (2006ms). "An Estimate of the Effects of Income Inequality, Racial Segregation, and Food Prices on Adult Obesity in the United States."
• Marmot, M. and R. G. Wilkinson (2001). "Psychosocial and material pathways in the relation between income and health: a response to Lynch et al " British Medical Journal 322: 1233-1236.
• Oakes, J. M. (2004). "The (mis)estimation of neighborhood effects: Causal inference for a practicable social epidemiology." Social Science & Medicine 58: 1929-1952.

10. Life course epidemiology

Idea: How do we identify and disentangle the biological and social factors that build on each other over the life course from gestation through to old age?

The readings mostly relate to "life course epidemiology," that is, Fetal & developmental origins of diseases in late life (Barker being generalized by Ben-Shlomo=common reading 1), in some tension with development over the life course (incl. Berney reviewing lifetime accumulation of hazards in relation to health in old age). In contrast to this approach, we have Brown on life course influences on depression (not necessarily in old age)=common reading 2. In what ways could either side usefully draw methods, data, results from the other?

• Barker, D. J. P. (1998). Mothers, Babies, and Health in Later Life. Edinburgh, Churchill Livingstone.
• Ben-Shlomo, Y. and D. Kuh (2002). "A life course approach to chronic disease epidemiology: Conceptual models, empirical challenges and interdisciplinary perspectives." International Journal of Epidemiology 31: 285-293.
• Berney, L., D. Blane, et al. (2000). Life course influences on health in old age. Understanding health inequalities. H. Graham. Buckingham [England], Open University Press: 79-95.
• Brown, G. W. and T. O. Harris (1978). Sociology and the aetiology of depression; Depression and Loss; A Model of Depression; Summary and conclusions. Social Origins of Depression: a Study of Psychiatric Disorder in Women. New York, Free Press: 3-20; 233-293.
• Davey-Smith, G. (2007). "Life-course approaches to inequalities in adult chronic disease risk." Proceedings of the Nutrition Society 66: 216-236.
• Krieger, N., J. T. Chen, et al. (2005b). "Lifetime socioeconomic position and twins' health: An analysis of 308 pairs of United States women twins." PLoS Med 2(7): e162.
• Kuh, D., Y. Ben-Shlomo, et al. (2003). "Life course epidemiology." Journal of Epidemiology and Community Health 57: 778-783.

• Lynch, J. and G. Davey-Smith (2005). "A Life Course Approach to Chronic Disease Epidemiology." Annual Review of Public Health 26: 1-35.

11. Multivariable "structural" models of development

Idea: Just as standard regression models allow prediction of a dependent variable on the basis of independent variables, structural models can allow a sequence of predictive steps from root ("exogeneous") through to highest-level variables. Although this kind of model seems to illuminate issues about factors that build up over the life course, there are strong criticisms of using such models to make claims about causes.

Cases: Kendler et al. 2002 on pathways to depression in women: Notice the high R^2 and the way the authors tease out different kinds of pathways to depression from the model they fit to their data.
Freedman 2005 is a statistician who questions whether structural models can be thought of as causal models and tries hard to make his questioning accessible (i.e., with a minimum of technical language [not zero however]).
Ou's 2005 synthesis of pathways from pre-school programs to later outcomes: Notice the different kinds of networks Ou reviews in the literature before presenting her own analysis.
During the class, we might look first at Kendler's and Ou's diagrams,
then do Q&A on the technical aspects of path analysis and SEM primed by the notes on a non-technical introduction to path analysis and structural equation modeling (see http://ppol753.wikispaces.umb.edu/Epi_11),
then work our way through Freedman's critique.

• Chandola, T., P. Clarke, et al. (2006). "Pathways between education and health: a causal modelling approach." Statistics in Society 169(2): 337-359.
• Freedman, D. A. (2005). Linear statistical models for causation: A critical review. Encyclopedia of Statistics in the Behavioral Sciences. B. Everitt and D. Howell. Hoboken, NJ, Wiley.
• Kendler, K. S., C. O. Gardner, et al. (2002). "Towards a comprehensive developmental model for major depression in women." American Journal of Psychiatry 159: 1133-1145.
• Ou, S.-R. (2005). "Pathways of long-term effects of an early intervention program on educational attainment: Findings from the Chicago longituidinal study." Applied Developmental Psychology 26: 478-611.
• Rini, C. K., C. Dunkel-Schetter, et al. (1999). "Psychological adaptation and birth outcomes: The role of personal resources, stress, and sociocultural context in pregnancy." Health Psychology 18: 333-345.

12. Heritability, heterogeneity, and group differences

Idea: As conventionally interpreted, heritability indicates the fraction of variation in a trait associated with "genetic differences." A high value indicates a strong genetic contribution to the trait and "makes the trait a potentially worthwhile candidate for molecular research" that might

identify the specific genetic factors involved. I contest the conventional interpretation and contend that there is nothing reliable that anyone can do on the basis of estimates of heritability for human traits. While some have moved their focus to cases in which measurable genetic and environmental factors are involved, others see the need to bring genetics into the explanation of differences among the averages for groups, especially racial groups.

Common readings = Taylor 2009 (skepticism about the estimation and interpretation of heritability); Moffitt 2005 (Interaction of measured genes and measured environments)

There are many supplementary readings. Get the overall idea, concepts, and evidence first for these articles, going back to go through the equations only if you have time and aptitude/perseverance.

a. Heritability & critique

Heritability is a quantity derived from analysis of variation in traits of humans, other animals, or plants in ways that take account of the genealogical relatedness of the individuals whose traits are observed. Such "quantitative genetic" analysis does not require any knowledge of the genes or "measurable genetic factors" involved.

Turkheimer is "on the left" of behavioral genetics, being much less gung ho about the implications of its findings. Here he gives a clear overview of what the field has shown.

Plomin articulates the confident consensus of behavior genetics, namely, that they've debunked the supposed environmentalist orthodoxy in social science that says that everything is social and have established a basis for connecting with molecular genetics to identify the actual genetic factors.

Rutter, a senior psychological researcher (who once worked with Brown on social determinants of mental illness), tries to moderate the "polarizing claims" and "unwarranted extrapolations."

Taylor 2010 casts doubt on the findings that underlie both Turkheimer and Plomin's articles by exposing problems with the concepts and methods used to arrive at those findings. Taylor ends with a nudge towards methods that use measured genetic factors as well as measured environmental factors (the latter being the staple of social epidemiology).

b. Interaction of measured genes and measured environments

Moffitt 2005 provides a review of what's involved in trying to identify interactions between measured genetic and environmental factors. (Use Taylor 2010 to get clear about the difference between this kind of interaction and the classical genotype x environment interaction in quantitative genetics.) Caspi 2002 is one of two 2002 papers that caused a lot of splash. Davey-Smith picks up on the current consensus that the 2002 studies have been hard to replicate and invokes Mendelian randomization as a way to strengthen causal inference about interactions between measured genetic and environmental factors.

c. Data & models about heritability & change (or lack of it)

Dickens 2001 provides a resolution of the paradox that heritability of IQ test scores is reported to be high, but there has been a large increase in average IQ test scores from one generation to the next. We know that genes haven't changed from one generation to the next, so Dickens' account is also exposing a flaw in the logic that because

heritability of IQ test scores is high within racially defined groups and because there is a large difference in average IQ test scores between whites and blacks, genetic factors are probably involved in that difference.
Rushton 2005 however thinks that 30 years of research has validated that idea.
Taylor 2010 refers to Dickens 2001, but gives a somewhat different spin on its implications.

• Caspi, A., J. McClay, et al. (2002). "Role of Genotype in the Cycle of Violence in Maltreated Children." Science 297(5582): 851-854.
• Davey-Smith, G. (2009). "Mendelian randomization for strengthening causal inference in observational studies: Application to gene by environment interaction." Perspectives on Psychological Science, in press.
• Dickens, W. T. and J. R. Flynn (2001). "Heritability estimates versus large environmental effects: The IQ paradox resolved." Psychological Review 108(2): 346-369.
• Moffitt, T. E., A. Caspi, et al. (2005). "Strategy for investigating interactions between measured genes and measured environments." Archives of General Psychiatry 62(5): 473-481.
• Plomin, R. and K. Asbury (2006). "Nature and Nurture: Genetic and Environmental Influences on Behavior." The Annals of the American Academy of Political and Social Science 600(1): 86-98.
• Rushton, J. P. and A. R. Jensen (2005). "Thirty years of research on race differences in cognitive ability." Psychology, Public Policy, and Law 11: 235-294.
• Rutter, M. (2002). "Nature, nurture, and development: From evangelism through science toward policy and practice." Child Development 73(1): 1-21.
• Taylor, P. J. (2010). "Three puzzles and eight gaps: What heritability studies and critical commentaries have not paid enough attention to." Biology & Philosophy, 25:1-31. (DOI 10.1007/s10539-009-9174-x).
• Turkheimer, E. (2000). "Three laws of behavior genetics and what they mean." Current Directions in Psychological Science 9(5): 160-164.

13. Genetic diagnosis, treatment, monitoring, and surveillance

Idea: Genetic analysis has begun to identify genetic risk factors. We need to consider the social infrastructure needed to keep track of the genetic and environmental exposures with a view to useful epidemiological analysis and subsequent healthcare measures. Even in cases where the condition has a clear-cut link to a single changed gene and treatment is possible, there is complexity in sustaining that treatment.

For a few years this decade, genome-wide association studies seemed to hold promise for detecting genes related to diseases and and the invention of drug-based treatments.
But, in November 2009,
http://www.nytimes.com/2009/11/18/business/18gene.html?_r=1&scp=1&sq=decode&st=cse , A Genetics Company Fails, Its Research Too Complex. See also 2010 commentaries on low yield from GWAs, e.g., Couzin-Frankel , J.: 2010, Major Heart Disease Genes Prove Elusive. Science 328(5983),1220-1221.

In 2009, Khoury et al. were concerned that the promises were not over-stated. Look at the table giving their quality control proposal.
In 2005, Frank cautions that epidemiology needs as much data about environmental factors as genes, but observes that the playing field is not level. (Give credit if you ever cite this powerpoint.)
Even for (rare) diseases governed by single genes, the path from genetic diagnosis to therapy is complicated as the poster-child case of PKU shows. From Taylor (2009):
Diane Paul's (1998) history of PKU screening describes, the certainty of severe retardation has been replaced by a chronic disease with a new set of problems. Screening of newborns became routine quite rapidly during the 1960s and 70s, but there remains an ongoing struggle in the USA to secure health insurance coverage for the special diet and to enlist family and peers to support PKU individuals staying on that diet through adolescence and into adulthood. For women who do not maintain the diet well and become pregnant, high levels of phenylalanine adversely affect the development of their non-PKU fetuses. This so-called maternal PKU is a public health concern that did not previously exist. In short, a more complex picture of development in a social environment is needed for anyone to make use of the knowledge that the fate of individuals with the PKU gene is not determined at birth.

• Bowcock, A. M. (2007). "Guilt by association." Nature 447: 645-646.
• Frank, J. (2005). "A Tale of (More Than ?) Two Cohorts – from Canada." 3rd International Conference on Developmental Origins of Health and Disease.
• Khoury, M. J., J. Little, M. Gwinn and J. P. Ioannidis (2007). "On the synthesis and interpretation of consistent but weak gene-disease associations in the era of genome-wide association studies." International Journal of Epidemiology 36: 439-445.
• Paul, D. (1998). The history of newborn phenylketonuria screening in the U.S. Final Report of the Task on Genetic Testing. Baltimore, Johns Hopkins University Press: 1-13.
• Taylor, P. J. (2009). "Infrastructure and Scaffolding: Interpretation and Change of Research Involving Human Genetic Information." Science as Culture, 18(4):435-459.

14a. Popular epidemiology and health-based social movements

Idea: The traditional subjects of epidemiology become agents when: a. they draw attention of trained epidemiologists to fine scale patterns of disease in that community and otherwise contribute to initiation and completion of studies; b. their resilience and reorganization of their lives and communities in response to social changes displaces or complements researchers' traditional emphasis on exposures impinging on subjects; and c. when their responses to health risks displays rationalities not taken into account by epidemiologists, health educators, and policy makers.

Brown: Popular epidemiology (USA)

Davison: Lay epidemiology (UK)
Compare & Contrast these works from early 1990s.
(Brown 2006 provides a more recent contribution to popular epidemiology, and Lawlor 2003 to lay epidemiology.)
Epstein: AIDS activists influence AIDS science—AZT vs. AIDSVAX
Schienke: Possibilities for citizen surveillance of exposures
Black discusses evidence-based policy (which provides us a contrast)

• Black, N. (2001). "Evidence based policy: proceed with care," BMJ 323: 275-279.
• Brown, P. (1992). "Popular Epidemiology and Toxic Waste Contamination: Lay and Professional Ways of Knowing." Journal of Health and Social Behavior 33: 267-281.
• Brown, P., S. McCormick, et al. (2006). "'A lab of our own': Environmental causation of breast cancer and challenges to the dominant epidemiological paradigm." Science, Technology, & Human Values 31(5): 499-536.
• Davison, C., G. Davey-Smith, et al. (1991). "Lay epidemiology and the prevention paradox: The implications of coronary candidacy for health education." Sociology of Health and Illness 13: 1-19.
• Epstein, S. (1995). "The construction of lay expertise: AIDS activism and the forging of credibility in the reform of clinical trials." Science, Technology, & Human Values 20(4): 408-437.
• Lawlor, D. A., S. Frankel, et al. (2003). "Smoking and Ill Health: Does Lay Epidemiology Explain the Failure of Smoking Cessation Programs Among Deprived Populations?" American Journal of Public Health 93(2): 266-270.
• Schienke, E. (2001). Bill Pease/ An original developer of scorecard.org / 2001. Troy, NY, Center for Ethics in Complex Systems.

14b. Taking Stock of Course: Where have we come and what do we need to learn to go further?

Idea: In order to move ahead and continue developing, it is important to take stock of what went well and what needs further work.

Comparison of initial plans and current position. Revision of plans for personal and professional development.