I. Course Description
An observed relative risk (RR_{obs}) can be described mathematically as the product of the causal relative risk (RR_{causal})—a desired effect measure for etiologic epidemiologic studies—and error factors for the impact on study results of imperfections in the design, conduct and analysis of the study (uncontrolled confounding, losses-to-followup, nonrandom subject sampling, subject nonresponse, missing data, exposure and disease measurement error, unjustified statistical model assumptions, and random error). When viewed from this perspective, it becomes clear that RR_{causal} is not identifiable (i.e., cannot be validly estimated) without making assumptions about the values of the error-factor and random-error terms. A standard quantitative analysis does not account for most study imperfections. It therefore implicitly assumes that the product of the error-factor equals 1.0. This standard-practice assumption, however, has neither theoretical nor empirical justification. We therefore advise epidemiologists to replace the standard assumption with more justifiable assumptions about the values of the error-factor terms. These more-justifiable assumptions can be incorporated into a quantitative analysis with uncertainty analysis (also known as bias modeling, probabilistic sensitivity analysis, Monte Carlo sensitivity analysis). We discuss this technique in this class.

II. Course Prerequisites
PubH 8140 or equivalent

III. Course Goals and Objectives
In this course we build on the concepts discussed in PubH 8140, and we discuss how to use the technique of uncertainty analysis to adjust a relative-risk estimate for study imperfections.

IV. Methods of Instruction and Work Expectations
Lecture and discussions. Each student will be required to perform an uncertainty analysis on a study of their choosing. They will be required to give two class presentations related to their uncertainty analysis: (1) early in the semester they will present a brief overview of their chosen study, and they will discuss the implicit no-bias assumptions the authors made in the course of the
published analysis; (2) at the end of the semester each student will present the results of their uncertainty analysis of their chosen study. Students will also be required to write a brief paper that documents their uncertainty analysis, due on the final-exam day.

V. Readings

Required Readings:

- Maldonado G, Greenland S. Estimating causal effects. International Journal of Epidemiology 2002;31:422-429. (Many of the fundamental concepts we will use in our uncertainty analysis of epidemiologic data are explained in this paper.)

- Maldonado G. Adjusting a relative-risk estimate for study imperfections. Journal of Epidemiology and Community Health 2008;62:655-663. (This is a key reading for this course.)


- Lash TL, Fox MP, Fink AK. Applying quantitative uncertainty analysis to epidemiologic data. (In press). (The publisher has given us permission to use this in-press book for this class.)


- Alavanja MCR, Samanic C, Dosemeci M, et al. Use of agricultural pesticides and prostate cancer in the agricultural health study cohort. Am J Epidemiol 2003;157:800-814. (To illustrate uncertainty-analysis methods, during the course we will perform an uncertainty analysis on the association reported in this study between methyl bromide and prostate cancer.)

- Phillips CV, Maldonado G. Using Monte Carlo methods to quantify the multiple sources of error in studies. (Abstract) Am J Epidemiol 1999;149:S17. (I believe this is the first publication in the epidemiologic literature to propose that uncertainty-analysis methods be applied to epidemiologic data.)


- Jurek AM, Maldonado G, Church TR, Greenland S. Exposure-measurement error is frequently ignored when interpreting epidemiologic study results. European Journal of Epidemiology 2006;21:871-876. (We often think that epidemiologic study reports routinely discuss the impact of study imperfections in their discussion sections. This survey shows that this is not true, specifically for exposure measurement error.)

- Jurek AM, Maldonado G, Greenland S, Church TR. Uncertainty analysis: an example of its application to estimating a survey proportion. Journal of Epidemiology and Community Health 2007;61:650-654. (This is a tutorial on the application of uncertainty-analysis methods.)

- Maldonado G, Delzell E, Tyl S, Sever L.E. Occupational exposure to glycol ethers and human congenital malformations. Int Arch Occup Environ Health 2003;76:405-423. (Published example of a full sensitivity (non-probabilistic uncertainty) analysis of an epidemiologic study. This paper actually examines three different studies, all of the same exposure-disease relationship.)


Required Software:

- @Risk (included in The DecisionTools Suite student version. Purchase for $50.00 at http://www.palisade.com/academic/students.asp)
Suggested Readings:


- Lash TL, Silliman RA. A sensitivity analysis to separate bias due to confounding from bias due to predicting misclassification by a variable that does both. Epidemiology 2000; 11:544-549.


- Phillips CV. Quantifying and reporting uncertainty from systematic errors. Epidemiology 2003; 14:459-466.


- Phillips CV. Quantifying and reporting uncertainty from systematic errors. Epidemiology 2003;14:459-466.


• Maldonado G. Quantifying the impact of study imperfections on study results (abstract). Am J Epidemiol 2005; 161:S100.


VI. Course Outline/Weekly Schedule

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<thead>
<tr>
<th>Week</th>
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<tbody>
<tr>
<td>1</td>
<td>• Introduction to the course</td>
<td>• Adjusting a relative-risk estimate for study imperfections</td>
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<tr>
<td>2</td>
<td>• Adjusting a relative-risk estimate for study imperfections (continued)</td>
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<td>3</td>
<td>• Adjusting a relative-risk estimate for study imperfections (continued)</td>
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<td>4</td>
<td>• Adjusting a relative-risk estimate for study imperfections (continued)</td>
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<td>5</td>
<td>• Alavanja et al. (2003) paper on methyl bromide and prostate cancer: implicit no-bias assumptions</td>
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<td>6</td>
<td>• Alavanja et al. (2003) paper on methyl bromide and prostate cancer: implicit no-bias assumptions (continued)</td>
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<td>7</td>
<td>• Using @Risk for sensitivity/uncertainty analysis</td>
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<td>8</td>
<td>• Students present implicit no-bias assumptions in a study of their choosing</td>
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<td>9</td>
<td>• Students present implicit no-bias assumptions in a study of their choosing</td>
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<td>10</td>
<td>• Sensitivity/uncertainty analysis methods: discussion of readings</td>
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<td>11</td>
<td>• Sensitivity/uncertainty analysis methods: discussion of readings</td>
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<td>12</td>
<td>• Alavanja et al. (2003) paper on agricultural pesticides and prostate cancer: uncertainty analysis</td>
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<td>13</td>
<td>• Alavanja et al. (2003) paper on agricultural pesticides and prostate cancer: uncertainty analysis</td>
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<td>14</td>
<td>• Students present uncertainty analyses</td>
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<td>15</td>
<td>• Students present uncertainty analyses</td>
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VII. Evaluation and Grading

Grade based on 50% for general participation in class discussions and 50% for student project.

Incomplete Grade

A grade of incomplete “I” shall be assigned at the discretion of the instructor when, due to extraordinary circumstances, the student was prevented from completing the work of the course on time. The assignment of an incomplete requires a written agreement between the instructor and student specifying the time and manner in which the student will complete the course requirements. In no event may any such written agreement allow a period of longer than one year to complete the course requirements.

University of Minnesota Uniform Grading and Transcript Policy
A link to the policy can be found at onestop.umn.edu.

VIII. Other Course Information and Policies

Grade Option Change (if applicable)
For full-semester courses, students may change their grad option, if applicable, through the second week of the semester. Grade option change deadlines for other terms (i.e. summer and half-semester) can be found at onestop.umn.edu.

Course Withdrawal
Students should refer to the Refund and Drop/Add Deadlines for the particular term at onestop.umn.edu for information and deadlines for withdrawing from a course. As a courtesy, students should notify their instructor and, if applicable, advisor of their intent to withdraw.

Students wishing to withdraw from a course after the noted final deadline for a particular term must contact the School of Public Health Student Services Center at sph-ssc@umn.edu for further information.

Student Conduct, Scholastic Dishonesty and Sexual Harassment Policies
Students are responsible for knowing the University of Minnesota, Board of Regents' policy on Student Conduct and Sexual Harassment found at www.umn.edu/regents/polindex.html.

Students are responsible for maintaining scholastic honesty in their work at all times. Students engaged in scholastic dishonesty will be penalized, and offenses will be reported to the Office of Student Academic Integrity (OSAI, www.osai.umn.edu).

The University’s Student Conduct Code defines scholastic dishonesty as “plagiarizing; cheating on assignments or examinations; engaging in unauthorized collaboration on academic work; taking, acquiring, or using test materials without faculty permission; submitting false or incomplete records of academic achievement; acting alone or in cooperation with another to falsify records or to obtain dishonestly grades, honors, awards, or professional endorsement; or altering, forging, or misusing a University academic record; or fabricating or falsifying of data, research procedures, or data analysis.”

Plagiarism is an important element of this policy. It is defined as the presentation of another’s writing or ideas as your own. Serious, intentional plagiarism will result in a grade of “F” or “N” for the entire course. For more information on this policy and for a helpful discussion of preventing plagiarism, please consult University policies and procedures regarding academic integrity: http://writing.umn.edu/tww/plagiarism/.

Students are urged to be careful that they properly attribute and cite others’ work in their own writing. For guidelines for correctly citing sources, go to http://tutorial.lib.umn.edu/ and click on “Citing Sources”.

In addition, original work is expected in this course. It is unacceptable to hand in assignments for this course for which you receive credit in another course unless by prior agreement with the instructor. Building on a line of work begun in another course or leading to a thesis, dissertation, or final project is acceptable.

If you have any questions, consult the instructor.

Disability Statement
It is University policy to provide, on a flexible and individualized basis, reasonable accommodations to students who have a documented disability (e.g., physical, learning, psychiatric, vision, hearing, or systemic) that may affect their ability to participate in course activities or to meet course requirements. Students with disabilities are encouraged to contact Disability Services to have a confidential discussion of their individual needs for accommodations. Disability Services is located in Suite180 McNamara Alumni Center, 200 Oak Street. Staff can be reached by calling 612/626-1333 (voice or TTY).