Epidemiologic Inference in Public Health I

340.721.60
Pablo Martinez Amezcua

Review for Final Examination 2019

Room Assignments for Final Exam
Wednesday, October 23, 10:00am – 12:00pm

<table>
<thead>
<tr>
<th>If your last name begins with:</th>
<th>Go to:</th>
</tr>
</thead>
<tbody>
<tr>
<td>A – F</td>
<td>Becton-Dickinson Lecture Hall (room W1020)</td>
</tr>
<tr>
<td>G – L</td>
<td>Sheldon Hall</td>
</tr>
<tr>
<td>M – Z</td>
<td>Sommer Hall</td>
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</tbody>
</table>

Final Exam

- **Wednesday, October 23**
- 10 am-12 noon (CoursePlus enforces this!)
- Room assignments are posted
- You must complete the exam on your own. The exam is closed notes and books. You must adhere to the academic ethics code.
- Bring a calculator. You may not use the calculator on your cell phone or laptop.
- 20 multiple choice questions

Final Exam, Continued

- Exams are administered via Courseplus; you are required to bring a laptop to class in order to take the exam
- Charge your laptop the night before the exam!
- **You will have a paper copy of the exam that you may use as scratch paper; this exam must be turned in at the end of the exam**

Final Exam, Continued

- Bring to the exam:
  - Pen or pencil
  - Calculator
    - You are not allowed to use the calculator function on your cellphone or tablet.
    - You cannot use Excel or any other computer software.
  - Charged laptop computer

Final Exam

- During the exam:
  - The only application that should be open on your computer is an Internet browser, and the only tab that should be open on that browser is the examination in Courseplus
  - Any failure to follow this rule will be considered an academic ethics violation
Methods of Assessment
• 50% PRE-Activity Questions
• 25% Midterm Exam
• 25% Final Exam (cumulative)

Preparing for the Final Exam
• Consider
  – Reviewing your notes
  – Re-listening to online material
  – Listening to live recordings from lectures
  – Reviewing PRE-Activity Questions
  – Reviewing Activities
  – Reviewing Self-Assessments
  – Reviewing Practice Problems (old exam questions)
  – Re-Reading Textbook readings
  – Going to office hours to ask questions

What you learned in this course, in brief!
MODULE 1: Descriptive Epidemiology: Populations and Measurement
MODULE 2: Analytical Epidemiology: Study Designs
MODULE 3: Analytical Epidemiology: Comparisons and Inferences
MODULE 4: Synthesis and Applications

Module 1: Introduction to Epidemiology (Dr. Celentano)
Provided an overview of the role of epidemiology in disease control and the promotion of health.

1. Define epidemiology
2. Uses of epidemiology
3. Tools of epidemiology

Epidemiology
The study of how disease is distributed in populations and what factors influence or determine this distribution.

Celentano & Szko, 2019: 2

Learning the epidemiologic tools of public health allows us to:
1. Measure disease burden
2. Assess risk factors for disease
3. Evaluate interventions
4. Provide the evidence-base for policy decisions
5. Communicate public health evidence
Module 1: Populations

- Defined target, source and study populations
- Described challenges in establishing a case definition and enumerating at-risk populations
- Defined key concepts for quantifying disease: at risk and person-time

What Does it Mean to be At Risk?

Able to experience the outcome of interest during the follow-up period

At-Risk Individuals Over Time

- What do the circles represent?
- What do the bars represent?
- What do the arrows represent?

The Concept of Person-Years

Module 1: Epidemics

(Dr. Celentano)

- Interpreted epidemic curves from an outbreak investigation
Endemic and Epidemic Disease

Number of Cases

Endemic Epidemic

Time

Three Important Variables in the Investigation of an Epidemic

1. Time of exposure
2. Time of disease onset
3. Incubation period

Module 1: Measures of Morbidity and Mortality (Dr. Deal)

- Defined and calculated indices of **morbidity**:
  - Prevalence
  - Incidence

- Indices of **mortality**:
  - Mortality rate (overall, age-specific mortality, cause-specific mortality rate)
  - Case-fatality “rate”

- **Adjusted rates**:
  - Direct
  - Indirect

Measures of Morbidity and Mortality

- Indices of morbidity:
  - Prevalence
  - Incidence

- Indices of mortality:
  - Cumulative incidence
    - Can be directly calculated in a closed cohort
    - In an open population, need other methods (e.g., Kaplan-Meier)
  - Incidence rate

- Prevalence = Incidence x Duration of disease

Module 2: Validity & Reliability (Dr. Deal)

- Defined and calculated measures of validity, predictive value and reliability
- Described how the use of different cutpoints for a screening test affects the validity of the test
- Defined and calculated measures of reliability (overall percent agreement, positive percent agreement)
- Interpreted Kappa statistic

Measures of Morbidity and Mortality continued

- Indices of mortality:
  - Mortality rate
    - Overall
    - Cause-specific

- To compare 2 populations that differ on one or more characteristics (e.g., age)
  - Direct adjustment
  - Indirect adjustment (SMR, SIR)

- Adjusted rates are useful for comparing populations, but are NOT the true rates
Validity: Sensitivity & Specificity

Validity = the ability of a test to distinguish between individuals who have a disease and individuals who do not have the disease

1. Sensitivity = ability of a test to correctly identify individuals who have the disease
2. Specificity = ability of a test to correctly identify individuals who do not have the disease

Comparing Cutpoints (Activity 3)

Cutpoint of ≥80 mg/dL:
- Sensitivity = 100% (no FN)
- Specificity = low (lots of FP)

Cutpoint of ≥200 mg/dL:
- Sensitivity = low (lots of FN)
- Specificity = 100% (no FP)

Comparing Cutpoints (Activity 3)

Cutpoint of ≥80 mg/dL:
- Sensitivity = 100% (no FN)
- Specificity = low (lots of FP)

Cutpoint of ≥200 mg/dL:
- Sensitivity = low (lots of FN)
- Specificity = 100% (no FP)

Which cutpoint is better?
Depends on the importance of False Positives and False Negatives

Consequences of FP:
- Emotional cost
- Financial cost to re-test
- More invasive test

Consequences of FN:
- Missed opportunity to treat

Predictive Value

- What proportion of individuals who test positive (or negative) actually have (or do not have) the disease?

- Positive & Negative Predictive Value:
  - Are important for the patient
  - Depend on disease prevalence & validity of the test

Validity vs. Reliability

- Validity:
  - Are the test results correct?
  - Analogous to accuracy

- Reliability:
  - Are the test results the same when the same test is repeated in the same individual under similar conditions?
  - Analogous to precision

Public Health Surveillance (Dr. Castillo)

The WHO Definition

1. Surveillance is the "systematic collection and use of epidemiologic information for the planning, implementation, and assessment of disease control" (WHO, 1985)
2. "Public health surveillance is the continuous, systematic collection, analysis and interpretation of health-related data needed for planning, implementation, and evaluation of public health practice" (WHO, 2012)

Module 2: Epidemiologic Study Design I (Dr. Celentano)

- Reviewed ecologic and cross-sectional study designs and appreciate how they inform other types of observational studies
- Described the structure and design of case-control studies, including selection of cases and controls and the process of matching
- Discussed potential sources of bias, and distinguish between nested and non-nested designs

Descriptive Epidemiology

- Distribution of disease and its determinants is the domain of descriptive epidemiology
- Analysis of disease patterns according to the characteristics of the person, place and time

Who is getting the disease?
Where is it occurring?
How is it changing over time?

Analytical Epidemiology

- Determining risk factors and causes of disease
- Evaluating preventive and therapeutic interventions that alter the course of disease

Analytic Study Designs

- Case-control studies
- Cohort studies
- Randomized trials

Matching In Case-Control Studies

Group matching
(frequency matching, stratification)

Individual matching
(matched pairs)
Design of a Nested Case-Control Study

TIME 1
YEARS
TIME 2

Study Population

Develop Disease

Do NOT Develop Disease

CASES

CONTROLS

NESTED CASE-CONTROL STUDY

Obtain interviews, bloods, urines, etc.

Advantages of Nested Case-Control Studies
- Possibility of recall bias is eliminated, since data on exposures are obtained before disease develops.
- Exposure data are more likely to represent the pre-illness state since they are obtained years before clinical illness is diagnosed.
- Costs are reduced compared to those of a prospective study, since laboratory tests need to be done only on specimens from subjects who are later chosen as cases or as controls.

Module 2: Epidemiologic Study Design II (Dr. Celentano)
- Described the basic components and structure of cohort studies
- Described the key features of randomized trials
  - Distinguished experimental from observational designs
  - Described benefits of randomization
  - Described basic design elements of randomized trials

Design of a Cohort Study

Start with:

Exposed

Not Exposed

Then, follow-up:

Disease

No Disease

Disease

No Disease

For a defined standard period of time

Prospective / Retrospective

- Prospective (concurrent)
  - Cohort is assembled NOW and followed into
  - Obtain exposure information prior to determining endpoint status
- Retrospective (nonconcurrent/historical)
  - Cohort was assembled in the PAST and followed forward in time up to the present
  - Obtain endpoint status prior to or at the same time as exposure information

Advantages and Disadvantages of Cohort Studies
- **Advantages**
  - Can assess several outcomes simultaneously
  - Control of time and outcome measurements
  - Less potential for bias than case-control studies but same potential for confounding
- **Disadvantages**
  - Usually requires large samples
  - Often requires long follow-up
  - Not very efficient for rare outcomes if exposure is low
  - Financially costly
  - Cohort members “choose” exposures themselves
Design of a Randomized, Controlled Trial

**Defined Population**

- **NEW Treatment**
  - Improved
  - NOT Improved

- **CURRENT/NO Treatment**
  - Improved
  - NOT Improved

**Randomize**

Types of Outcome Data from Different Study Designs

<table>
<thead>
<tr>
<th>Measures of disease frequency</th>
<th>Type of study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence (risk)</td>
<td>Randomized trial; Cohort study</td>
</tr>
<tr>
<td>Incidence rate</td>
<td>Randomized trial; Cohort study</td>
</tr>
<tr>
<td>Prevalence</td>
<td>Cross-sectional</td>
</tr>
<tr>
<td>Odds</td>
<td>Case-control</td>
</tr>
</tbody>
</table>

Module 3: Measures of Association, Part 1
(Doctor Celentano)

- Described the importance of making comparisons to determine associations
- Learned how to calculate and interpret measures of association
  - Risk or rate difference
  - Relative risk
  - Odds ratio

Comparison Group

- The purpose of selecting a comparison group is to obtain an estimate of the disease risk experience that the exposed group would have had, had they not had been exposed.
  - The comparison group should be as similar as possible to the exposed group on all factors except the exposure

Comparing Risks between Groups

- Identify the exposed and comparison groups.
- Then, make comparisons in the risk experiences between the groups.
  - Calculate measures of association
    - Difference in risks
    - Ratio of risks

Let's Calculate and Interpret RRs

- Use the 2x2 table
- Calculate Measures of Association

1. Difference in Risks
   - \( \text{RR} = \frac{\text{Risk in Exposed}}{\text{Risk in Non-Exposed}} \)

2. Ratio of Risks
   - \( \text{RR} = \frac{\text{Risk in Exposed}}{\text{Risk in Non-Exposed}} \)

*Can also calculate for rates*
Relative Measures of Association

- Relative Risk
  - Calculated in cohort studies
- Odds Ratio
  - Calculated in case-control studies

Module 3: Measures of Association, Part 2 (Dr. Deal)

- Identified when the OR is a reasonable estimate of the RR.
- Reviewed the calculation of the OR for unmatched studies and calculate the OR for matched case-control studies.
- Understood and applied the concepts of attributable risk percent and the population attributable risk percent.

When is the OR a Reasonable Estimate of the RR?

- Both the OR and RR are measures of association.
- What are there circumstances under which the OR approximates the RR?
  - Cases are representative, with regard to history of exposure, of all people with the disease in the source population
  - Controls are representative, with regard to history of exposure, of all people without disease in the source population
  - When the risk of disease is low — “rare disease assumption”

Calculate the OR for a Matched Case-Control Study

In a matched pairs study, we calculate the OR as the ratio of the discordant pairs.

Real study data do not automatically appear in a 2x2 table format!

OR in a Case-Control Study: Unmatched

A study of 10 cases and 10 unmatched controls with the following exposure status (E=exposed, N=non-exposed)

<table>
<thead>
<tr>
<th>CASES</th>
<th>CONTROLS</th>
<th>Exposed</th>
<th>Not exposed</th>
</tr>
</thead>
<tbody>
<tr>
<td>E</td>
<td>N</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>E</td>
<td>E</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>N</td>
<td>E</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>
| E      | N        | ODDS RATIO (unmatched pairs) = \( \frac{6 \times 7}{4 \times 3} = 3.5 \)
| N      | N        |         |             |

OR in a Case-Control Study: Matched

A study of 10 matched pairs with the following exposure status (E=exposed, N=non-exposed)

<table>
<thead>
<tr>
<th>CASES</th>
<th>CONTROLS</th>
<th>Exposed</th>
<th>Not exposed</th>
</tr>
</thead>
<tbody>
<tr>
<td>E</td>
<td>N</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>E</td>
<td>E</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>N</td>
<td>E</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| E      | N        | ODDS RATIO (matched pairs) = \( \frac{4}{1} = 4 \)
| N      | N        |         |             |
Motivating the concept of attributable risk: Risks in the Exposed and Non-Exposed

That is, the “Risk Difference”

Remember, right before this slide we stretched because we were shifting topics!

AR and AR%

Population Attributable Risk

\[
\text{Population Attributable Risk} = \left( \frac{\text{Risk in the Exposed}}{\text{Risk in the Non-Exposed}} \right) - 1
\]

Population Attributable Risk Percent

\[
\text{Population Attributable Risk Percent} = \left( \frac{\text{Risk in the Exposed}}{\text{Risk in the Non-Exposed}} \right) - 1 \times 100\%
\]

Calculating Risk in the Total Group

\[
\text{Risk in the Total Group} = \left( \frac{\text{Risk in the Exposed}}{\text{Risk in the Non-Exposed}} \right) \times \left( \frac{\% \text{ Exposed}}{\% \text{ Non-Exposed}} \right)
\]

PAR and PAR% and Interpretation!

Recall a Goal of Epidemiologic Research

• Goal: To identify exposure and disease associations.
  • Observational epidemiologic methods cannot determine whether an association is causal, though.
  • Several possible explanations exist for any epidemiologic association observed, only one of which is cause.

Possible Explanations for Associations

• Bias
  • Information bias
  • Selection bias
• Confounding
• Chance
• Cause

Module 3: Bias (Dr. Deal)

• Defined and distinguished between non-differential versus differential bias.
• Defined selection bias and information bias in association studies, and identified their sources.
• Described approaches to minimize bias in association studies.
Effects of Bias in Epidemiology

Non-Differential Information Bias
- Misclassification of or measurement error in the exposure and/or outcome, but the extent of the error does not differ between the groups being compared.
  - Cohort study – The extent of the misclassification or measurement error of the disease does not differ between the exposed and the unexposed.
  - Case-control study – The extent of the misclassification or measurement error of the exposure does not differ between cases and controls.

Differential Information Bias
- Differential bias results when the inaccuracy of the classification or measurement differs between:
  - Cases and controls in a case-control study
  - Exposed and nonexposed in a cohort study

Summary of Information Bias

Selection Bias (always differential)

Module 3: Confounding & Effect Modification (Dr. Celentano)
- Identified and learned how to eliminate or reduce confounding in the design and analysis of observational epidemiologic studies.
  - A type of bias
- Identified and learned how to highlight the presence of effect modification.
  - Not bias, possibly biology
**Epidemiologic Inference in Public Health**

10/18/2019

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**Confounder – Classic Definition**

- A confounding variable or confounder is a 3rd factor that is
  1. A risk factor for the disease,
  2. Associated with the exposure, and
  3. Not a factor in the causal pathway from exposure to disease (i.e., not a mediator).

- If any of these criteria is not satisfied, then the 3rd factor is not a confounder.
  
  ![Diagram: Confounder](image)

**Empirical Way to Identify a Confounder**

Using the actual data from your study:

1. Calculate crude RR
   
   $$\text{RR}_{\text{crude}} = \frac{\text{MI+ Alcohol+}}{\text{MI- Alcohol-}}$$

2. Stratify by potential confounder and calculate stratum-specific RRs
   
   $$\text{RR}_1 = \frac{\text{MI+ Smoking+}}{\text{MI- Smoking-}}$$
   
   $$\text{RR}_2 = \frac{\text{MI+ Smoking-}}{\text{MI- Smoking+}}$$

- If they differ by more than 10-20%, then confounding is likely present.

**Ex: Assess Presence of Confounding**

- Is smoking a confounder of the alcohol-MI association?
  
  - Yes, the stratum-specific ORs differ from the crude OR

- Is alcohol drinking associated with MI?
  
  - No, the un-confounded, stratum-specific ORs=1.0

**Methods to Minimize Confounding**

- In the study design
  
  - Restrict
  
  - Match

- In the analysis
  
  - Stratify (or restrict to one stratum)
  
  - Adjust

---

**Effect Modification**

- In contrast to confounding, effect modification is not an error in the design or analysis of the study.

- Effect modification is present when the association between an exposure and outcome differs between categories of a third factor.
  
  - It results due to the biological interaction between two factors

**Your Perfect Example of Effect Modification!**

- Inherit a faulty gene for metabolizing lactose (sugar in milk) and drinking milk in the production of GI discomfort (e.g., gas and bloating).

Lactose intolerance (-)  Lactose intolerance (+)
Your Perfect Example of Effect Modification!

- Inherit a faulty gene for metabolizing lactose (sugar in milk) and drinking milk in the presence of a genetic mutation.

The effect of milk on GI discomfort differs by the presence of a genetic mutation.

<table>
<thead>
<tr>
<th>Lactose intolerance (-)</th>
<th>Lactose intolerance (+)</th>
</tr>
</thead>
</table>

Other Examples of Effect Modification

- The effect of insulin (as a treatment) on hypoglycemia is higher for patients with chronic kidney disease.
- The effect of falling on a bone fracture is stronger for people with osteoporosis.
- The effect of the physical condition of neighborhoods on physical activity differs by age.

Stratifying to Identify Effect Modification

1. Calculate the RR for the exposure-disease association within each stratum of the possible effect modifier.
2. Compare stratum-specific RRs to each other:
   - If the same → no effect modification
   - If different → effect modification
     - How different?
       - That’s the art of epidemiology.

Quantitative vs Qualitative Effect Modification

**Quantitative**

- M+ (RR > 1.0)
- M- (RR < 1.0)

**Qualitative**

- M+ (RR > 1.0)
- M- (RR < 1.0)

Interaction

- Effect modification occurs because of biological interaction between two factors in the production of disease.
- Interaction occurs when the risk of the outcome in people who have two factors is greater or lesser than would be expected based on the independent risks of the outcome in people with one, but not both factors.
  - Greater – positive interaction or synergy
  - Lesser – negative interaction or antagonism

Joint Production of Disease Can be Additive or Multiplicative

- In the absence of interaction, when two factors act together, based on biology they can follow:
  - An additive model – the independent risks from the two factors add to each other
  - A multiplicative model – the independent risks from the two factors multiply each other
Additive Model:
Incidences for participants exposed to neither, one, or both risk factors

\[
\text{FACTOR A} - \quad + \\
3 \quad 9 \\
50 \quad 15 \\
+ \quad +
\]

Under the additive model, expected rate = \((9-3) + (15-3) + 3\) = 21.
Observed 50.
50 > 21, so interaction is present.

Multiplicative Model:
Relative Risks

\[
\text{FACTOR A} - \quad + \\
1.0 \quad 3.0 \\
5.0
\]

Interaction: Multiplicative Model
Under the multiplicative model, expected RR=15, observed RR=40.
40 > 3.0*5.0, so interaction is present.

Key concepts in addressing public health problems using epidemiology
- Recognizing and describing public health problems
- Generate hypotheses
  - Patterns of disease occurrence by person, place, and time
- Develop a research question to address public health problem based on a causal model
  - Define population-at-risk, exposure, outcome
- Test hypotheses based on the causal model using epidemiologic approaches
  - Make comparisons between groups
- Draw inferences and revise the causal model
  - Establish temporality of the exposure-disease relationship
  - Compare results among studies in epidemiology and other fields
  - Determine if risk factors are causal
- Intervene based on revised causal model to prevent the public health problem

What is Causal Inference?
“The thought process and methods that assess or test whether a relation of cause to effect does or does not exist.”

- Miguel Porta, 2008
Causal “Criteria”

- Strength
  - Suggests the observed association is not due to chance
  - Test: Relative risk or odds ratio
  - Test: p-value less than 0.05

- Temporality
  - The cause comes before the effect
  - Causality: Cause to Effect

- Specificity
  - The observed association is not due to confounding

- Dose-Response
  - The observed association is not due to chance

- Coherence
  - The observed association is not due to chance

- Analogical
  - The observed association is not due to chance

Module 4: Evaluating Screening Programs & Health Interventions (Dr. Celentano, online material)

- Described the natural history of disease and screening
- Reviewed criteria to evaluate screening effectiveness
- Reviewed designs to evaluate:
  - Screening programs and outcomes
  - Health services and clinical interventions
- Evaluated sources of bias in screening
- Described how measurement of a health intervention can affect how we determine effectiveness

Natural History of Disease

- Preclinical Phase
  - Biologic Onset
  - Symptoms
  - Diagnosis
  - Therapy

- Clinical Phase
  - Detectable
  - Preclinical (DPCP)
  - Biologic Onset
  - Symptoms
  - Diagnosis
  - Therapy

Assessing the Effectiveness of a Screening Program Using Outcome Measures

1. Reduction of mortality in the population screened
2. Reduction of case-fatality in screened individuals
3. Increase in percent of cases detected at earlier stages
4. Reduction in complications
5. Prevention of or reduction in recurrences
6. Improvement of quality of life in screened individuals
Possible Biases in Evaluating Screening Programs

- **Volunteer bias** - People who choose screening may have health-seeking behaviors in general or may have poorer risk profiles (e.g., family history) when compared to those who do not choose screening. Thus, will bias toward screening appearing beneficial or not appearing beneficial, respectively. Concern in observational studies of screening (not randomized trials). Solution: Randomize.

Possible Biases in Evaluating Screening Programs

- **Length bias** - More likely to screen/detect cases with a longer than shorter detectable preclinical phase (DPCP), and cases with a longer DPCP are likely those that are more slowly progressing and thus, likely have a better prognosis. Concern if compare case-fatality rates or the 5-year survivals between cases that were detected by screening and those not detected by screening. Solution: Compare cause-specific mortality rates.

Health Intervention Evaluation

- **Efficacy** - The extent to which a specific intervention or service produces a beneficial result under usual conditions (based on results of an RCT).

- **Effectiveness** - The extent to which a specific intervention or service, as deployed in the field, does what it is intended to do for a defined population.
Health Outcomes Research

- Morbidity
- Mortality
- Quality of life (Euro-QAL)
- Functional status (ADL, IADL)
- Patients’ perceptions of health status
  - Symptom recognition
  - Patient satisfaction and pain levels (Smiley faces)

Health Outcomes Research – Non-randomized (In vogue right now!)

Adantages of Using Large Data Sets
- Data collected in research populations, so the problem of external validity is minimized
- Analysis can usually be conducted quickly because the data have already been collected
- Sample size is usually not a problem except in specific subgroups

Disadvantages of Large Data Sets - I
- Because data are gathered for final or administrative purposes, they are often not designed for research which may be invasive
- Data on independent and dependent variables may be very limited

Disadvantages of Large Data Sets - II
- Data on disease severity, details of interventions and diagnostic methods may be limited
- Data relating to individual characteristics may be inadequate or missing

Final Exam Emphasis

- The emphasis of the final exam questions will be on concepts/methods covered in greater detail or covered multiple times in the course lectures, Activities, Assignments, textbook and other course materials.

- Cumulative

Genetic Epidemiology

“Most diseases have both genetic and environmental components. Unless we consider both, we will never get it right”!

Multifactorial Traits (Complex Traits)

<table>
<thead>
<tr>
<th>Two genes additive effects</th>
<th>Gene-environment additive effects</th>
<th>Gene-environment interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gene 1</td>
<td>Trait</td>
<td>Environment</td>
</tr>
<tr>
<td>Gene 2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Genetic Epidemiology Questions

| Is there familial clustering? | Where is the disease gene? | How does this gene contribute to disease in the general population? |
|------------------------------|---------------------------|-----------------------------------------------------------------
| Disease                    | SNP4 (rs6)                | SNP4 in exon 2 of Gene X |
| Family history positive    |                           | SNP2 (p8) |
| Family history negative    |                           | SNP1 (b.1) |
| No disease                 |                           |                                                                   |

Good Luck!
Good Luck!