Until Death Do We Part

Learning Objectives
After completing this problem, students should be able to:

Identify the modes of transmission of HIV
Define window period as it relates to exposure to disease causing agents and clinical detection of the disease
Define and perform calculations of sensitivity, specificity
Discuss the trade-offs between sensitivity and specificity;
Describe ethical principles in public health.
Apply basic disease transmission knowledge and ethical principles to problem solving activity.

You are engaged to be married in six months. Your state has just passed a new law requiring all persons to show proof of having a test to determine HIV status. You and your fiancé decide to find out as much as possible about the virus and the testing procedures before you have the test done.

You will research HIV and work thorough the background material below in preparation for in class discussion describing your understanding of the virus and test, your concerns and options based on the facts in regards to the test itself and your plans for marriage if you or your fiancé test positive. Cover all objectives, embedded questions, and ethical principles in the discussion.

This problem was adapted from a case study developed in 1987 for the Centers for disease Control and Prevention.

PART I: Understanding the facts (The Research)

Background

In December 1982, a report in the *MMWR* described three persons who had developed acquired immunodeficiency syndrome (AIDS) but who had neither of the previously known risk factors for the disease. These three persons had previously received whole-blood transfusions. By 1983, widespread recognition of the problem of transfusion-related AIDS led to controversial recommendations that persons in known high-risk groups voluntarily defer from donating blood.

Question: What are “known risk factors” for HIV? Who are considered “high-risk groups? (Research to answer this question).

In June 1984, after the discovery of the human immunodeficiency virus (HIV), five companies were licensed to produce enzyme-linked immunosorbent assay (EIA, then called ELISA) test kits for detecting HIV antibody. A Food and Drug Administration (FDA) spokesman stated that, "...getting this test out to the blood banks is our No. 1 priority...." Blood bank directors were anxiously waiting to start screening blood with the new test until March 2, 1985, the date the first test kit was approved by the FDA.

Question: What are other tests for detecting HIV? What exactly do these tests detect? Give a rationale for testing for the item that is detected by the test.

In the pre-licensure evaluation, sensitivity and specificity of the test kits were estimated using blood samples from four groups: those with AIDS by CDC criteria, those with other symptoms and signs of HIV infection, those with various autoimmune disorders and neoplastic diseases that could give a false-positive test result, and those presumed to be healthy blood and plasma donors.

Numerous complex issues were discussed even before licensure. Among them were understanding the magnitude of the problem of false-positive test results, and determining whether test-positive blood donors should be notified.

The sensitivity of test kit A is 95.0% (0.95) and the specificity is 98.0% (0.98). These and related measures are reviewed below.

NOTES ON SENSITIVITY AND SPECIFICITY

	Actual antibody status		
Test result	Present	Absent	Total
Positive	True positive (A)	False positive (B)	All positive tests (A+B)
Negative	False negative (C)	True negative (D)	All negative tests (C+D)
Total	All with antibody (A+C)	All without antibody (B+D)	Total (A+B+C+D)

The above is a Two-by-two table.

Sensitivity - the probability that the test result will be positive when administered to persons who actually have the antibody.
= true positives / all with antibody
Algebraically, sensitivity = A / (A+C)

Specificity - the probability that the test result will be negative when administered to persons who are actually without the antibody.
= true negatives / all without antibody
Algebraically, specificity = D / (B+D).

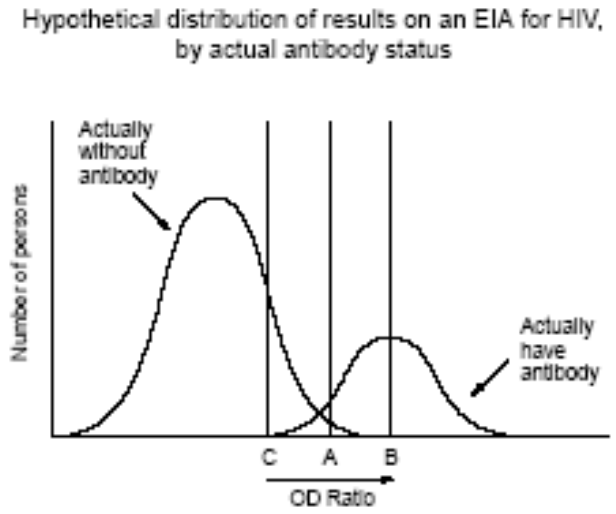
Predictive-value positive (PVP) - the probability that a person with a positive screening test result actually has the antibody.
= true positives / all with positive test
Algebraically, PVP = A / (A+B).

Predictive-value negative (PVN) - the probability that a person with a negative screening test result actually does not have the antibody.
= true negatives / all with negative test
Algebraically, PVN = D / (C+D).

Question : With this information, by constructing a 2-by-2 table, calculate the predictive-value positive and predictive-value negative of the EIA in a hypothetical population of 1,000,000 blood donors. Using a separate 2-by-2 table, calculate PVP and PVN for a

population of 1,000 drug users. Assume that the actual prevalence of HIV antibody among blood donors is 0.04% (0.0004) and that of intravenous drug users is 10.0% (0.10).

Question : If sensitivity and specificity remain constant, what is the relationship of prevalence to predictive-value positive and predictive-value negative?



Establishing the cutoff value to define a positive test result from a negative one is somewhat arbitrary. Suppose that the test manufacturer initially considered that optical density ratios greater than "A" on the above figure would be called positive.

Question: In terms of sensitivity and specificity, what happens if you raise the cutoff from "A" to "B"?

Question: In terms of sensitivity and specificity, what happens if you lower the cutoff from "A" to "C"?

Question: From what you know now, what is the relationship between sensitivity and specificity of a screening test?

Question: Where might the blood bank director want the cutoff point to be?

The Western blot test identifies antibodies to specific proteins associated with the human immunodeficiency virus. The Western blot is the most widely used secondary test to detect HIV antibody because its specificity exceeds 99.99%; however, it is not used as a primary screening test because it is expensive and technically difficult to perform. Its sensitivity is thought to be lower than that of the EIA. Another option to the Western blot test to confirm positive results is to conduct the test a second time on persons that have

EIA-positive results and by considering persons to have the antibody only if results of both tests are positive.

PART II: The real problem

A bill to establish a premarital HIV screening program was just passed by the state legislature in your home state. An estimated 60,000 people will get married in the state in the next year, you are one of them. The legislation requires that each prospective bride and groom submit a blood sample for EIA testing. Samples that test positive by EIA will undergo confirmatory second EIA or Western blot testing. The legislation describes the goal of the screening program to be to decrease inadvertent perinatal or sexual HIV transmission by determining who among those to be married are probably infected with the virus.

You have read the local paper about contaminated blood transfusions but you have never received a blood transfusion. You have however, engaged in sexual intercourse. Your fiancé seems particularly worried about the test. You and your fiancé decide to learn as much as possible about the virus to determine if you have anything to worry about. You want to know what it is, how it is transmitted, how it is cured, what the test actually measures and when is the best time to take the test for the greatest possible correct results. After researching the HIV you realize that you might have been exposed to it just two weeks earlier (you fill in the details based on the mode of transmission of HIV as to how exactly you were exposed). You discuss with your fiancé your concerns about possible exposure, when to be tested and why and options if either receives a positive test result on the first test. You will want to also discuss your plans if either or both receive negative test results on the first test.

Be prepared to discuss the issues above in class.

Ethical Principles in Public Health:

Research ethical issues by going to this website; **Markkula Center for Applied Ethics at Santa Clara University** http://www.scu.edu/ethics/homepage.html . You will be able to explore codes of ethics from professional societies related to public health. Choose societies that represent your interest (public health, health education, epidemiology...). Identify key ethical principles and search for theories to get an in-depth understanding of the topic. Be prepared to discuss the underlying ethical issues in class.

A very important competency of health professionals is advocacy. After completing the research on HIV and ethics in public health, write a letter disclosing all you have learned about the transmission, screening and ethical issues related to mandatory testing. The letter should be written from the perspective of a person planning to be married in the state that the screening program is being proposed. The letter should be addressed to the governor of the state giving factual support for or against the proposed legislation for mandatory testing. Consider the criteria to be used to determine if the screening program is feasible and ethical. Make the final recommendation based on factual evidence considering ethical principles in public health practice.