

Module 2 – Screening

Introduction

Screening is the early identification and treatment of asymptomatic persons who have already developed subclinical (unrecognized) disease by use of periodic tests and examinations. Early detection and treatment is *secondary prevention*. Crucial to the success of a screening program are 1) the accuracy of the screening test and, 2) the effectiveness of treatment early in the course of disease.

Test Accuracy

Sensitivity and specificity are intrinsic properties of a screening test that help determine its accuracy. Test sensitivity indicates the proportion of persons with a disease who test positive when screened. A test with low sensitivity generates many false negative results; persons with subclinical disease may go undetected and medical treatment will be delayed.

Test specificity indicates the proportion of persons without a disease who test negative when screened. A test with low specificity generates many false positive results; healthy persons will be told that they *may* have a disease. This leads to additional testing and procedures that incur unnecessary risk, distress and expense.

The positive predictive value [PPV] of a test is the proportion of patients with positive test results that have disease. Unlike sensitivity and specificity, PPV is not an *intrinsic* property of a test. It is dependent upon the prevalence of the disease in the screened population. As disease prevalence in a population increases, the PPV of a screening test in that population will also increase. Likewise, as disease prevalence decreases, the PPV of a screening test will decrease. (*More on these concepts can be found in chapter 7 of Glaser's book, High-Yield Biostatistics. They will also be explained more fully in class.*)

Effectiveness of Screening

For a screening program to be effective, a clinical intervention that can prevent or delay progression of disease must be available. Furthermore, early detection and treatment must offer some benefit (such as improved survival rate) over conventional diagnosis and treatment when the disease is clinically evident.

In evaluating the effectiveness of a screening program, one must consider several types of bias that could affect the reported results. *Lead-time bias* may result in the appearance of improved survival with screening. Survival will appear to be improved even if screening only identifies cancer earlier. It can lengthen the period between diagnosis and death, without truly prolonging life expectancy. *Length bias* may result in the identification of a disproportionate number of slowly progressive cancers

but miss aggressive cases that are present only briefly. If slowly progressive cases do not generally become clinically significant diseases, then the screening program may not provide a benefit.

When considering the benefits of screening, one must ask about the effect of a program on an entire population (population benefit). If the disease in question is of low prevalence or morbidity, then even a highly sensitive screening test will have little impact on the population as a whole. Likewise, screening with even modestly sensitive tests may have dramatic impact on the total population if the disease is of high prevalence or morbidity.

Finally, the effectiveness of any a screening program should also take into consideration the potential adverse effects of screening. There may be physical harm from the test itself, from misdiagnosis, and from treatment for non-aggressive disease. Cost-effectiveness must also be considered. From a population standpoint, the benefits must be weighed against the costs of implementation (especially since those resources could have been used for other interventions). 'Years of life saved' and 'quality-adjusted life years' are some of the measures used in a cost-benefit analysis.

Quality of the Evidence about the Effectiveness of Screening

Randomized controlled trials (and well constructed meta-analyses of such trials) provide the highest level of evidence. The random assignment of volunteers should result in the equal distribution of potential confounding variables (known or unknown) among the intervention and control groups. These are prospective studies and thus require large sample sizes and years of observation.

A cohort study provides the next best level of evidence. These observational trials examine the outcome of individuals who received an intervention and those who did not. They are subject to multiple confounding variables, which must be accounted for. These studies also require large sample size and years of observation.

A case-control study is retrospective. Persons known to have disease are compared to a control group without disease. Data about exposure to the intervention is sought retrospectively. It is more difficult to control for confounding variables in these studies. Furthermore, case control studies may be subject to both observer bias and recall bias.

Overall Learning Objectives for the Screening Module

1. Define screening. Understand the role it should play in primary care practice.
2. Define and be able to utilize the following terms when reading a study about a screening test: sensitivity, specificity, positive predictive value, cutoff point.
3. Recognize the characteristics of diseases that are suitable for screening and the characteristics of a good screening test.

4. Understand the rationale behind the most recent US Preventive Services Task Force (USPSTF) and American Cancer Society (ACS) recommendations for breast, colon, prostate and cervical cancer screening.
5. Understand the rationale behind the most recent USPSTF recommendations on screening for lipid disorders, hypertension, coronary artery disease, and STDs.

Small Group Forum

Reading Assignment

1. Chapter 7: “Statistics in Medical Decision Making” in Glaser, A. High Yield Biostatistics, 3rd Edition. Lippincott Williams and Wilkins. 2005
2. Look at the Grading Definitions used by the U.S. Preventive Services Task Force (USPSTF): <http://www.uspreventiveservicestaskforce.org/uspstf/grades.htm>
3. USPSTF (summary) and ACS recommendations for breast cancer screening
4. USPSTF (summary) and ACS recommendations for colon cancer screening
5. USPSTF (summary) and ACS recommendations for cervical cancer screening
6. USPSTF (summary) and ACS recommendations for prostate cancer screening
7. USPSTF recommendations for hypertension screening (summary)
8. USPSTF recommendations for lipid disorders screening (summary)
9. USPSTF recommendations for Chlamydia screening (summary)

The **USPSTF recommendations** can be found from their recommendations page (<http://www.uspreventiveservicestaskforce.org/recommendations.htm>). The **ACS recommendations** can be found at (<http://www.cancer.org/Healthy/FindCancerEarly/CancerScreeningGuidelines/index>)

Case Vignettes for Discussion

Case 1

A 60-year old man has had no medical problems. He was made the president of a local corporation and is in your office for an “executive physical”.

1. What should be done on physical examination? Is there any evidence that a complete physical exam on a well patient is beneficial?
2. What screening tests and/or procedures will you recommend? Do you need additional history to determine which tests you should recommend? (*Consult the above reading assignments to answer these questions. The consumer oriented site <http://www.ahrq.gov/ppip/healthymen.htm> may also help.*)

3. You note that his blood pressure is elevated. He wants you to order a stress test because his 66-year old brother just had coronary artery bypass surgery done after an angina episode and a stress test. He does not have any chest pain but he is mildly obese and does not do much exercise. How would you respond? Are there other tests that you would suggest?
4. He would like a PSA (prostate specific antigen) test to check for prostate cancer. What will you tell him about the test? How will you proceed if the test result is elevated?

Case 2

A 52-year old woman has recently moved to your city and you are listed as part of her health plan. She comes to your office because she feels she is in need of a general “check-up”. She does not have any complaints but she has a long tobacco history and this is what she is most concerned about. She has not seen a physician (nor has she had any testing) since she was treated for pyelonephritis 7 years ago.

1. What should be done on physical examination? Is there any evidence that a complete physical exam on a well patient is beneficial?
2. What screening tests and/or procedures will you recommend? Do you need additional history to determine which tests you should recommend? (*Consult the above reading assignments to answer these questions. The consumer oriented sites <http://www.ahrq.gov/ppip/healthywom.htm> may also help.*)
3. During the visit you find out that she has not had a pelvic exam or Papanicolou smear since the birth of her last child. She reports that she has not had a period in several years, is not currently sexually active, and so she does not see any reason to go through the discomfort and embarrassment of a pelvic exam. How would you counsel her? What is the likelihood of a false positive test on a Pap smear and what are the consequences of such a result?
4. When you recommend a mammogram, she reports that she does not have any pain in her breasts and does not see the need for this test. Several of her friends have had to undergo extra ultrasounds and biopsies because they had abnormal mammograms. She does not want something like this to happen to her because of the stress it will cause. She has also heard that the radiation from mammograms can cause cancer. How would you respond? What if she were 60 years old? What if she were 30 years old?

Sample Multiple Choice Questions

1. A 31-year old woman was in good health when she learned that her 60-year old mother died from a massive myocardial infarction. The woman decided to begin an exercise regimen and to maintain a healthy diet. She is now 70 years old and has continued to be in good health. Her serum cholesterol is low, her blood pressure is low, and she has never had any signs of ischemic heart disease. She does not take any medications. This is an example of

- A) Primary prevention
- B) Secondary prevention
- C) Tertiary prevention

2. A rapid serologic test for Lyme disease is tested in 1100 people. 100 are known to have Lyme disease and 95 of them test positive by this new assay. Of the remaining subjects who did not have Lyme disease, 200 also test positive. Which of the following statements about this assay are correct?

- A) It has 95% sensitivity and 20% specificity
- B) It has 80 % sensitivity and 95% specificity
- C) It has 95% sensitivity and 80% specificity
- D) It has 20% sensitivity and 95% specificity

3. A screening test has 90% sensitivity and 90% specificity for disease X. If disease X has a prevalence rate of 10% in the population being screened, what is the positive predictive value of a positive screening test?

- A) 40%
- B) 50%
- C) 60%
- D) 70%

Plan your Group Project and Presentation

Your group will develop a presentation on one of the four following topics for a symposium to be held in several weeks. Group assignments begin on the following page.

Small Groups 1, 5, 9 and 13

Study Topic #1: Screening for Sexually Transmitted Diseases

*Instructions: Give a 15-minute PowerPoint presentation on the above topic using the following questions as a guide. Consult the USPSTF and CDC websites as well as other resources. **At least one part of your presentation should involve the summary of a primary study or meta-analysis.** Send a copy of your PowerPoint presentation and the primary study you will use to Dr. DiCarlo (rdicar@lsuhsc.edu) at least one day prior to your presentation.*

- 1 **Briefly** review the U.S. and Louisiana incidence rates of gonorrhea, syphilis, and chlamydia. For each of these diseases, discuss any significant disparities in the rates based on ethnicity, geography, gender, and sexual orientation.
<http://www.cdc.gov/std/stats09/default.htm>
- 2 Briefly review the USPSTF recommendations and rationale for chlamydia, gonorrhea, herpes simplex, and syphilis screening. Briefly report on any data you can find relating to the rates of screening for chlamydia in the U.S. Does the USPSTF recommend chlamydia screening for adolescent boys and men? Explain the rationale.
- 3 Briefly review the USPSTF recommendations about screening for HIV infection. How do the more recent (2006) CDC recommendations for HIV screening (<http://www.cdc.gov/hiv/testing/HIVStandardCare/science.htm>) differ from those listed by the USPSTF? What is the rationale for the expanded screening recommendations?
- 4 *Find a primary study or meta-analysis on the efficacy of screening for Chlamydia or HIV and report on the study and its findings. If you would prefer, you may present a primary study that provides efficacy data about screening for a different STD such as gonorrhea, syphilis, or genital herpes. (Send the reference to Dr. DiCarlo prior to your presentation)*

Small Groups 2, 6, 10 and 14

Study Topic #2: Cardiovascular Screening

*Instructions: Give a 15-minute PowerPoint presentation on the above topic using the following questions as a guide. Consult the USPSTF website as well as other resources. **At least one part of your presentation should involve the summary of one or more primary journal articles.** Finally, email a copy of your PowerPoint presentation to Dr. DiCarlo (rdicar@lsuhsc.edu) at least one day prior to your presentation.*

1. **Briefly**, review the morbidity and mortality from coronary heart disease in the United States. If possible, compare rates in Louisiana to those of the nation. Are there differences based on ethnicity or socio-economic groups?
2. Review the major risk factors for coronary heart disease? What are the contributing (minor) risk factors?
3. Review the USPSTF recommendations about screening for coronary heart disease, hypertension, abdominal aortic aneurysm, carotid artery disease, and hyperlipidemia.
4. What is the current rate of screening and treatment for lipid disorders and hypertension?
5. Discuss additional screening for coronary artery disease in asymptomatic patients with risk factors. What is the utility of tests such as EKG, exercise treadmill tests, electron-beam CT, and CRP? Can you find data about the sensitivity and specificity of these tests? Does the USPSTF recommend the use of these tests in asymptomatic individuals? *Report on one primary study or meta-analysis* that investigates the efficacy of a one of these tests in screening for coronary disease. Use the data to argue for or against making this part of routine screening. *(Send the reference to Dr. DiCarlo prior to your presentation)*

Small Groups 3, 7, 11 and 15

Study Topic #3: Cancer Screening in Men

*Instructions: Give a 15-minute PowerPoint presentation on the above topic using the following questions as a guide. Consult the USPSTF and ACS websites as well as other resources. **At least one part of your presentation should involve the summary of a primary study or meta-analysis.** Send a copy of your PowerPoint presentation and the primary study you will use to Dr. DiCarlo (rdicar@lsuhsc.edu) at least one day prior to your presentation.*

1. Briefly review the incidence and mortality of colon, prostate and testicular cancer in U.S. men (in the case of colon cancer, use U.S. men and women). How does Louisiana compare to the national average? *You may want to use the CDC Cancer Data and Statistics website or the National Cancer Institute (NCI) SEER (Surveillance Epidemiology and End Results) database.*
2. Briefly review the USPSTF recommendations about cancer screening in men (include colon cancer screening). Include the sensitivity, specificity and (if available) the predictive values of recommended tests.
3. Briefly report on any data you can find relating to the rates of screening for the diseases discussed above in the U.S. Are there differences based on ethnicity or socioeconomic status?
4. Briefly discuss the possibility of screening for lung cancer. Are there effective screening tests or strategies? What are the current USPSTF recommendations?
5. Discuss screening for prostate cancer in more detail. What are the risks of screening and subsequent treatment? What are arguments for and against screening using PSA or other methods? Do the American Cancer Society recommendations differ from those of the USPSTF? What do you recommend? *Find a primary study or meta-analysis on the efficacy of PSA screening and report on the study and its findings. (Send the reference to Dr. DiCarlo prior to your presentation)*

Small Groups 4, 8, 12 and 16

Study Topic #4: Cancer Screening in Women

*Instructions: Give a 15-minute PowerPoint presentation on the above topic using the following questions as a guide. Consult the USPSTF and ACS websites as well as other resources. **At least one part of your presentation should involve the summary of one or more primary journal articles.** Finally, email a copy of your PowerPoint presentation to Dr. DiCarlo (rdicar@lsuhsc.edu) at least one day prior to your presentation.*

1. Review the incidence and mortality of breast, cervical and ovarian cancer in U.S. women. How does Louisiana compare to the national average? *You may want to use the CDC Cancer Data and Statistics website or the National Cancer Institute (NCI) SEER (Surveillance Epidemiology and End Results) database.*
2. Review the USPSTF recommendations about cancer screening in women. Include the sensitivity, specificity and (if available) the predictive values of recommended tests. *(Note: while colon cancer screening is recommended for women and men, a more detailed discussion will be presented by the group presenting cancer screening in men. Your group should mention that women should be screened, but you do not need to discuss the specific recommendations and the performance characteristics of colonoscopy or fecal occult blood testing.)*
3. Discuss screening for breast cancer in more detail. In particular, discuss the pros and cons of screening mammograms beginning at age 40 as opposed to delaying routine mammography until age 50. What is the role of testing for *BRCA 1* and *BRCA 2* testing?
4. Report on any data you can find relating to the rates of screening for the diseases discussed above in the U.S. How does Louisiana compare to the national average? Are there differences based on ethnicity or socioeconomic status?
5. Discuss the recommendations of the USPSTF and National Cancer Institute (NCI) regarding ovarian cancer screening. Is there any evidence that routine screening for ovarian cancer is beneficial? *Report on a primary study or meta-analysis and present an argument for or against routine ovarian cancer screening using the data you find. (Send the reference to Dr. DiCarlo prior to your presentation)*