http://www.premed.fudan.edu.cn







Secondary Prevention



Sha Tao





Department of Preventive Medicine, School of Public Health, Fudan University



- What is secondary prevention and screening
- What are the principles of screening
- Potential bias for screening analyses
- US Preventive Services Task Force
- Recommendations for screening



What is Secondary Prevention

 Secondary Prevention is concerned with early detection of disease, through either screening or case finding, followed by treatment.





What is Screening



- Screening is the testing of apparently healthy populations to identify previously undiagnosed diseases or people at high risk of developing a disease.
- Screening aims to detect early disease before it becomes symptomatic.
- Screening is an important aspect of prevention, but not all diseases are suitable for screening.



The Principles of Screening



- The choice of disease for which to screen;
- The nature of the screening test or tests to be used;
- The availability of a treatment for those found to have the disease;
- The relative costs of the screening.



8 March 2018



The Principles of Screening



8 March 2018

The condition should be an important health problem.

There should be a latent stage of the disease.

The natural history of the disease should be adequately understood.

There should be a test or examination for the condition.

The test should be acceptable to the population.

There should be a treatment for the condition.

Facilities for diagnosis and treatment should be available.

There should be an agreed policy on whom to treat.

The total cost of finding a case should be economically balanced in relation to medical expenditure as a whole.

Case-finding should be a continuous process, not just a "once and for all" project.



- The disease must be an important health problem.
- There should be a recognizable latent or early symptomatic stage.
- The natural history of the disease, including latent to declared disease, should be adequately understood.
- Facilities for diagnosis and treatment should be available.
- There should be a test or examination for the condition and the test should be acceptable to the population.



• A suitable disease for screening

• Why?



Colorectal Cancer

- CRC is the third leading cause of cancer death worldwide
- A slow progression from detectable and curable precancerous lesions, advanced adenoma
- ◆ 5 years survival rate depends on the stage at diagnosis
 - Stage I > 90 %
 - Stage II 70-85%
 - Stage III 25-65%
 - Stage IV < 10%



Lead time bias



8 March 2018



Length bias



8 March 2018



Other bias

- Selection bias
 - Health conscious
 - High risk individuals
- Over-diagnosis
 - Aging population



- There should be a suitable test or examination.
- The test should be acceptable to the population.



8 March 2018

13/80



Screening test

- Reliability get same result each time
- Validity get the correct result
 - Sensitive correctly classify cases
 - Specificity correctly classify non-cases

[screening and diagnosis are not identical]



Reliability

- ♦ Repeatability get same result
 - Each time
 - From each instrument
 - From each rater
- If don't know correct result, then can examine reliability only.



- Probability (proportion) of correct classification of cases
- Cases found / all cases



- Probability (proportion) of correct classification of noncases
- Non-cases identified / all non-cases







Interpreting test results: predictive value

- Probability (proportion) of those tested who are correctly classified
 - positive predictive value, (PPV)
 - Cases identified / all positive tests
- negative predictive value,(NPV)
 - Non-cases identified / all negative tests







• There should be an acceptable treatment for the patients with recognized disease.

- There should be facilities for diagnosis and treatment.
- There should be an agreed policy on whom to treat as patients.





- The cost of case finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.
- Program: Case finding should be a continuing process and not a "once for all" project.





- Screening is the testing of apparently healthy populations to identify previously undiagnosed diseases or people at high risk of developing a disease.
- Principles of Screening (10): disease, test, treatment and cost



(program)

Some important concept:

Lead time, Lead time bias, Length bias

8 March 2018 Sensitivity, Specificity, PPV, NPV



A 40-year-old woman presents to your clinic for a periodic health examination. She is healthy and has no risk factors for any particular diseases. She does not smoke, is sexually active and is not pregnant.

You note that the US Preventive Services Task Force recommends screening for the following diseases: cervical cancer, hypertension, alcohol misuse and obesity. Routine mammography is not recommended.

She has read about the mammography controversy and wants to know more about the benefits and harms.

8 March 2018



Introduction

- Controversies common in determining: when to begin, when to end, screening frequency and use of newer screening technologies
- Devising recommendations for prevention can be complicated at all steps.
- Determining the appropriate balance between benefits and harms is challenging.
- USPSTF (US Preventive Service Task Force): widely recognized as setting the standard for evidence-based recommendations related to prevention

8 March 2018

Sawaya GF *N Engl J Med* 2009 361;26 2503-2505 27/80



What is the US Preventive Services Task Force Mission?

- To evaluate the benefits of individual services based on age, gender, and risk factors for disease;
- To make recommendations about which preventive services should be incorporated routinely into primary medical care and for which populations;
- To identify a research agenda for clinical preventive care.



What are US Preventive Services Task Force activities?

- Develops recommendations for primary care clinicians and health systems on a broad range of clinical preventive health care services (e.g., screening, counseling, and preventive medications)
- NOT consider costs, medical-legal issues or insurance coverage in deliberations
- Recommendations graded to convey two major elements: certainty and magnitude of net benefit of the service 8 March 2018



8 March 2018

USPSTF Grades of Recommendations

| Certainty of Net Benefit | Magnitude of Net Benefit | | | |
|---|--------------------------|----------|-------|---------------|
| | Substantial | Moderate | Small | Zero/negative |
| High | Α | В | С | D |
| Moderate | В | В | С | D |
| Low | Insufficient | | | |

http://www.uspreventiveservicestaskforce.org/uspstf/grad30/80m



What the Grades Mean: Suggestions for Practice

| Grade | Suggestions for practice |
|-------------|--|
| Α | Offer or provide this service. |
| В | Offer or provide this service. |
| С | Offer or provide this service only if other considerations support the offering or providing the service in an individual patient. |
| D | Discourage the use of this service. |
| I statement | Read the clinical considerations section of USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms. |

8 March 2018

31/80 http://www.uspreventiveservicestaskforce.org/uspstf/grades.htm



Devising Breast Cancer Screening Recommendations: The USPSTF Approach

http://www.uspreventiveservicestaskforce.org/uspstf09/breastcancer/brcanupappfig1.htm 8 March 2018 32/80



Analytic Framework: Screening for Breast Cancer



2 major key questions (see next slide)

8 March 2018



Analytic Framework: Screening for Breast Cancer: Key questions

1a. Does screening with mammography (film and digital) or MRI decrease breast cancer mortality among women age 40–49 years and ≥70 years?
1b. Does clinical breast examination screening decrease breast cancer mortality? Alone or with mammography?
1c. Does breast self-examination practice decrease breast cancer mortality?



Analytic Framework: Screening for Breast Cancer: Key questions

2a. What are the harms associated with screening with mammography (film and digital) and MRI?2b. What are the harms associated with clinical breast examination ?2c. What are the harms associated with breast self-examination?



Breast Cancer Screening: Benefits

- Decreased breast cancer mortality and total mortality
- Decreased morbidity from breast cancer (reduction of late-stage breast cancer)


Breast Cancer Screening: Harms

- Radiation exposure
- Pain during procedures
- Anxiety, distress, and other psychological responses
- False-positive and false-negative mammography results, additional imaging, and biopsies



Evidence of Benefit: Mammography by Age Group

| Age | Trials included, n | RR for Breast Cancer Mortality (95% CI) | NNI to Prevent 1 Breast Cancer Death (95% CI) |
|---------|-----------------------|---|--|
| 39-49 y | 8 | 0.85 (0.75-0.96) | 1904 (929-6378) |
| 50-59 y | 6 | 0.86 (0.75-0.99) | 1339 (322-7455) |
| 60-69 y | 2 | 0.68 (0.54-0.87) | 377 (230-1050) |
| 70-74 y | 1 | 1.12 (073-1.72) | Not available |



Evidence of Harms:

False Positive Testing with Mammography

- Estimated risk of false positive testing after 10 mammograms (all ages): 21-49%
- Estimated risk of false positive testing after 10 mammograms in women aged 40-49: 56%



Judging Evidence of Benefit of Mammography

There is convincing evidence that screening with film mammography reduces breast cancer mortality, with greatest benefit among women aged 60 to 69 years.



Judging Evidence of Harm of Mammography

Adequate evidence that the overall harms associated with mammography are moderate for every age group considered...

False-positive results are more common for women aged 40 to 49 years.



Balancing Benefits and Harms of Mammography

Benefits:

Percentage of mortality reduction

Cancer deaths averted per 1000 women

Life years gained

- "life-year": a measure of the quantity of life lived
- may be expressed as "life years expected per 1000 people" for an intervention strategy



Balancing Benefits and Harms of Mammography

Harms:

- False-positive results per 1000 women
- Unnecessary biopsies per 1000 women



Balancing Benefits and Harms of Mammography

Conclusions (all ages): biennial screening produced 70% to 99% of the benefit of annual screening, with a significant reduction in the number of mammograms required and therefore a decreased risk for harms.



Balancing Benefits and Harms of Mammography

- Screening between the ages of 50 and 69 years produced a projected 17% (range, 15% to 23%) reduction in mortality (compared with no screening)
- Extending the age range produced only minor
 improvements (additional 3% reduction from starting at age 40 years and 7% from extending to age 79).



Estimation of Certainty and Magnitude of Evidence of Net Benefit of Mammography

Benefit Minus Harm

 For biennial screening mammography in women aged 40 to 49 years, there is moderate certainty that the net benefit is small.



Estimation of Certainty and Magnitude of Evidence of Net Benefit of Mammography

 For biennial screening mammography in women aged 50 to 74 years, there is moderate certainty that the net benefit is moderate.



- The USPSTF recommends biennial screening mammography for women aged 50 to 74 years.
 Grade: <u>B recommendation</u>.
- The decision to start regular, biennial screening mammography before the age of 50 years should be an individual one and take patient context into account, including the patient's values regarding specific benefits and harms. Grade: C recommendation.

8 March 2018 http://www.uspreventiveservicestaskforce.org/uspstf09/breastcancer/brcanrs.htm



Back to the Case: Talking to Patients About Mammography

- "The precise age at which the benefits from screening mammography justify the potential harms is a subjective judgment and should take into account patient preferences."
- "Clinicians should inform women about the potential benefits (reduced chance of dying from breast cancer), potential harms (for example, false-positive results, unnecessary biopsies), and limitations of the test that apply to women their age."

http://www.uspreventiveservicestaskforce.org/uspstf09/breastcancer/brcanrs.htm 49/80



- Devising recommendations for prevention can be complicated at all steps.
- While screening benefits are often cited and widely promulgated, the USPSTF gives equal attention to screening harms.
- Determining the appropriate balance between benefits and harms is challenging.



Screening Recommendations General Population

- Alcohol Misuse
- Breast Cancer
- Cervical Cancer
- Colorectal cancer
- Depression

- High Blood Pressure
- Lipid disorders
- Obesity
- Rubella



Alcohol Misuse

- Recommend screening and behavioral counseling interventions to reduce alcohol misuse. B recommendation
 - good evidence that screening can accurately identify patients whose levels or patterns of alcohol consumption do not meet criteria for alcohol dependence, but place them at risk for increased morbidity and mortality
 - good evidence that brief behavioral counseling with follow-up produce small to moderate reductions in alcohol consumption that are sustained over 6 to 12 month periods or longer
 - some evidence that interventions lead to positive health outcomes 4 or more years post-intervention, but limited evidence that screening and behavioral counseling reduce alcohol-related morbidity



Alcohol Misuse

Tools to identify alcohol misuse and abuse or dependence

- ♦ CAGE
 - feeling the need to Cut down
 - <u>Annoyed</u> by criticism
 - Guilty about drinking
 - need for an Eye-opener in the morning
- Alcohol Use Disorders Identification Test (AUDIT)

Screening tools are available at the National Institute on Alcohol Abuse and Alcoholism Web site: <u>8http://www.niaaa.nih.gov/publications/instable.htm</u>. 53/80



Breast Cancer

Clinical breast examination

- Insufficient evidence to recommend for or against routine clinical breast examination alone to screen for breast cancer. I recommendation
 - No screening trial has examined the benefits of CBE alone (without mammography) compared to no screening.
 - USPSTF could not determine the benefits of CBE alone or the incremental benefit of adding CBE to mammography.



Breast Cancer

Breast self-examination

- Insufficient evidence to recommend for or against teaching or performing routine breast selfexamination. I recommendation
 - poor evidence to determine whether BSE reduces breast cancer mortality.
 - fair evidence that BSE is associated with an increased risk of false-positive results and biopsies.



Cervical Cancer

- Strongly recommend screening for cervical cancer in women who have been sexually active and have a cervix (women ages 21-65). A recommendation
 - found good evidence that screening with cervical cytology (Papanicolaou smears) reduces incidence and mortality
 - indirect evidence suggests beginning screening within 3 years of onset of sexual activity or age 21 (whichever comes first) and screening at least every 3 years
 - Ages 30-65:Screen with cytology every 3 years or contesting (cytology/HPV testing) every 5 years



Cervical Cancer

- Recommend against screening women > 65 years for cervical cancer if they have had adequate recent screening with normal Pap smears and are not otherwise at high risk for cervical cancer. D recommendation.
- Recommend against screening women who have had a total hysterectomy for benign disease. D recommendation
 - fair evidence that the yield of cytologic screening is very low in women after hysterectomy
 - poor evidence that screening to detect vaginal cancer improves health outcomes



Colorectal Cancer

- Strongly recommend screening men and women 50-75 years of age for colorectal cancer. Grade A recommendation
 - fair to good evidence that several screening methods are effective in reducing mortality from colorectal cancer
 - the quality of evidence, magnitude of benefit, and potential harms vary with each method



Colorectal Cancer

- Fecal occult blood testing
 - guaiac-based test cards from three consecutive stool samples
 - good evidence that annual testing reduces mortality
- Sigmoidoscopy
 - fair evidence that alone or with fecal occult blood testing reduces mortality
 - every 5 years recommended but some studies suggest that every 10 years may be as effective
- Colonoscopy
 - 10-year interval recommended based on the natural history of adenomatous polyps

Double-contrast barium enema

- no direct evidence that it is effective in reducing mortality rates, less sensitive than colonoscopy
- every 5 years recommended
- 8 March 2018



Depression

- Recommend screening for depression in practices that have systems in place to assure accurate diagnosis, effective treatment and follow-up. Grade B recommendation
 - good evidence that screening improves the accurate identification of depressed patients and that treatment of depressed adults decreases clinical morbidity



Depression

- Many formal screening tools
 - Zung Self-Assessment Depression Scale, Beck Depression Inventory, General Health Questionnaire, and Center for Epidemiologic Study Depression Scale [CES-D]
- Asking two simple questions about mood and anhedonia may be as effective as using longer instruments
 - Over the past 2 weeks, have you felt down, depressed, or hopeless?
 - Over the past 2 weeks, have you felt little interest or pleasure in doing things?
 61/80



Hypertension

- recommend screening for high blood pressure in adults aged 18 and older. A recommendation
 - Hypertension: in adults systolic blood pressure (SBP) of 140 mm Hg or higher, or diastolic blood pressure (DBP) of 90 mm Hg or higher.
 - Due to variability in individual blood pressure measurements, it is recommended that hypertension be diagnosed only after 2 or more elevated readings are obtained on at least 2 visits over a period of 1 to several weeks.
 - Screening every 2 years with BP <120/80. Screening every year with SBP of 120-139 mmHg or DBP of 80-90 mmHg.
 8 March 2018 62/80



Hypertension

- Normal blood pressure: systolic <120 and diastolic <80
- Prehypertension: systolic 120-139 or diastolic 80-89
- Hypertension:
 - Stage 1: systolic 140-159 or diastolic 90-99
 - Stage 2: systolic ≥ 160 or diastolic ≥ 100
- ♦ hypertension should be diagnosed only after ≥2 elevated readings obtained on ≥2 visits over a period of 1 to several weeks



Lipid Disorders

- ♦ Strongly recommend screening men ≥ 35 years and women ≥ 45 years. A recommendation
- Recommend screening men 20 to 35 years and women 20 to 45 years if they have other risk factors for coronary heart disease. B recommendation
 - Risk factors:
 - Diabetes
 - Family history of CVD (< 50 years in male relatives or < 60 years in female relatives)
 - Family history suggestive of familial hyperlipidemia

– Multiple CHD risk factors (eg, tobacco use, hypertension, ^{8 March 2018} Obysuty) ^{64/80}



- Recommend screening all adult patients for obesity and offering intensive counseling and behavioral interventions to promote sustained weight loss for obese adults. B recommendation
 - good evidence that body mass index (BMI), calculated as weight (kg) divided by height (meters)², is reliable and valid for identifying adults at increased risk for mortality and morbidity due to weight.
- fair to good evidence that high-intensity counseling (diet, exercise) together with behavioral interventions aimed at skill development, motivation, and support strategies produces modest, sustained weight loss (typically 3-5 kg for 1 year or more) in obese adults (BMI ≥30 kg/m 2).
 8 March 2018 65/80



Screening Recommendations High Risk Populations

DiabetesTB

- Chlamydia test
- ♦ Gonorrhea
- HIV
- Syphilis



- Recommend screening for type 2 diabetes in adults with sustained blood pressure (either treated or untreated) greater than 135/80 mm Hg. B recommendation
 - adults with hypertension benefit from knowing their diagnosis of diabetes because the BP target changes. The lower BP target is associated with lower incidence of cardiovascular events and cardiovascular mortality.
- ◆ Insufficient evidence to recommend for or against routinely screening asymptomatic adults with blood pressure of <a>≤135/80 mm Hg. I statement



Diabetes

Screening tests

- fasting plasma glucose (FPG)
 - Abnormal if $\geq 126 \text{ mg/dL}$
 - Easier, faster and less expensive than other screening tests
 - Recommended by American Diabetes Association
- 2-hour post-load plasma glucose
 - May lead to more individuals being diagnosed as diabetic
- hemoglobin A1c
 - Less sensitive in detecting lower levels of hyperglycemia than FPG



Tuberculosis

 Recommend screening with tuberculin skin testing for high risk persons. A recommendation

Groups with higher prevalence of TB infection

- close contacts of person with known or suspected TB
- health care workers
- recent immigrants from countries with high TB prevalence
- HIV positive individuals
- alcoholics, injection drug users
- residents of long term care facilities (correctional facilities, nursing homes, group homes)
- 8 Marmedically underserved low income people (homeless persons)80



Tuberculosis

Mantoux test

- Positive Interpretation: cut-offs for different risk group
 - ≥ 15 mm- low risk patients
 - ≥ 10 mm- high risk patients
 - - ≥5mm- very high risk patients (HIV, immunosuppresed, abnormal CXR, recent contact with infected person)
- Prior BCG vaccination should not alter interpretation of results



Strongly recommend screening adults at increased risk for HIV infection. A recommendation

Increased risk for HIV infection if:

- risk factors
 - men who have had sex with men after 1975
 - unprotected sex with multiple partners
 - past or present injection drug users
 - exchange sex for money or drugs or have sex partners who do
 - sex partners were HIV-infected, bisexual or injection drug users
 - being treated for STDs
 - history of blood transfusion between 1978-85
 - persons who request an HIV test despite reporting no individual risk factors
 - receive health care in high-risk settings: STD clinics, correctional facilities, homeless shelters, TB clinics, clinics serving men who have sex with men
 - high-prevalence settings: defined by the CDC as those known to have a $\geq 1\%$ prevalence of HIV infection in the patient population

8 March 2018



- no recommendation for or against routinely screening for HIV in adults who are not at increased risk for infection.
 C recommendation
 - the yield of screening persons without risk factors would be low, and potential harms associated with screening have been noted
 - USPSTF concluded that the benefit of screening adults without risk factors for HIV is too small relative to potential harms to justify a general recommendation.


- A 45-year-old man presents to your clinic for an annual examination.
- His only complaint is occasional elbow pain that he attributes to using a new tennis racquet.
- He reports no medical illnesses and his only prior surgery is a hernia repair 10 years ago. He reports no family history of early heart disease or cancer. Last year, his total cholesterol (TC) and high-density lipoprotein cholesterol (HDL-C) were normal.
- He takes one low-dose aspirin per day, does not smoke and reports having an occasional alcoholic beverage.

8 March 2018



- He is married and in a monogamous relationship. Since testing negative for STIs (including HIV) many years ago, he reports no potential for new exposures.
- On examination, he is not overweight and not hypertensive.
- He wants to know about prevention, and you wonder about the appropriate preventive services to recommend.



Question 1: What prevention services would you recommend?



For this 45-year-old sexually active man who takes aspirin and has had prior normal testing for HIV, lipid disorders and syphilis and an otherwise average-risk profile, the USPSTF Grade A and B recommendations are fairly few:

| 11 - Recommended (A,B) | | | |
|------------------------|---|------------|---------|
| Grade | Title | Risk Info. | Details |
| A* | Aspirin to Prevent CVD: Men age 45 to 79 to prevent myocardial infarctions | | |
| Α | HIV: Screening - Adults and Adolescents at Increased Risk | | |
| A* | High Blood Pressure: Screening - Adults 18 and Over | | |
| Α | Lipid Disorders in Adults: Screening - Men 35 and Older | | |
| Α | Syphilis: Screening - Men and Women at Increased Risk | | |
| В | Alcohol Misuse: Screening and Behavioral Counseling - Men, Women and Pregnant Women | | |
| B* | Depression: Screening - Adults age 18 and over - When staff-assisted depression care supports are in place | | |
| В | Healthy Diet: Counseling - Adults with Hyperlipidemia and Other Risk Factors for CVD | | |
| В | Obesity: Screening and Intensive Counseling - Obese Men and Women | | |
| B* | Sexually Transmitted Infections: Behavioral Counseling - Sexually Active Adolescents and Adults at Increased Risk | | |
| B* | Type 2 Diabetes Mellitus: Screening Men and Women - Sustained BP 135/80+ | | |

For this 45-year-old sexually active man who takes aspirin and has had prior normal testing for HIV, lipid disorders, and syphilis and an otherwise average-risk profile, the 2011 recommendations are fairly few.

The goal of this exercise is to illustrate where to find this information, not to discuss the rationale behind each recommendation. Students can read the full reports on-line. Instruget bogged down in the details of each recommendation.

Question 2: He was told at a local health fair that the American Diabetes Association (ADA) recommends that he be screened for diabetes. He wonders why he is not being tested. Based on your search using the ePSS tool, what is the USPSTF recommendation for diabetes screening in this patient? What is their rationale behind not screening? (15 minutes)

From the ePSS tool search, the USPSTF gives diabetes screening a "B" recommendation among men with hyperlipidemia and/or hypertension; this patient has neither. The US "I" statement for all other average-risk adults, meaning that evidence is insufficient to make a recommendation for or against routine testing.



• Question 2: He was told at a local health fair that the American Diabetes Association (ADA) recommends that he be screened for diabetes. He wonders why he is not being tested. What is the USPSTF recommendation for diabetes screening in this patient? What is their rationale behind not screening?



 the USPSTF gives diabetes screening a "B" recommendation among men with hyperlipidemia and/or hypertension; this patient has neither. The USPSTF gives diabetes screening an "I" statement for all other average-risk adults, meaning that evidence is insufficient to make a recommendation for or against routine testing.



