My reservoir is like the distance between Aden and Amman in al-Balqa

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الوبائيات والإحصاء الحيوي (31505204)

Lecture 18

Screening tests and result interpretation

By

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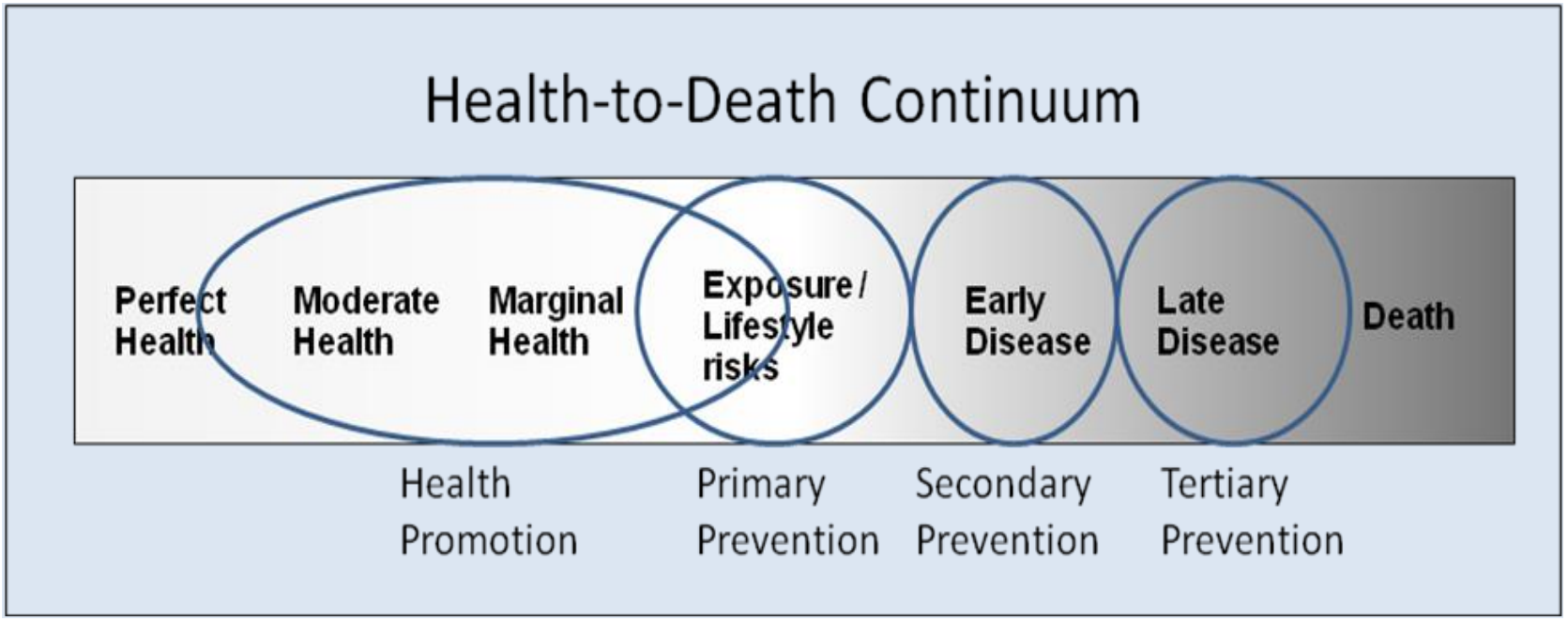
Relationship between Continuum and Health Promotion & Disease Prevention

- **Health Promotion** – **optimize overall health**. LEFT side
- **Disease Prevention** – **reduce occurrence and impact of specific diseases.** RIGHT side



Secondary Prevention

- ***Defn**: measures available for the **early detection and prompt treatment of health problems.***

- **Objectives:**
  - To reduce the consequences of disease (death or morbidity) by ***screening*** **asymptomatic** patients to identify disease in its early stages and intervening with a treatment which is more effective because it is being applied earlier.
  - **It cannot reduce disease incidence**

Screening for diseases: **definition** ***and*** **objectives**

- "*the presumptive* ***identification*** *of* ***unrecognized defect or disease*** *by the application of tests, examinations or procedures which can be applied rapidly, to* ***sort out apparently well persons who probably*** *have a disease, from those who probably do not".*

- **Screening** is the testing of **apparently healthy populations to identify previously undiagnosed diseases.**

Screening for diseases: **definition** ***and*** **objectives**

- To ensure **early detection of a disease** among individuals, so that prompt treatment may be instituted; e.g. screening for cervical cancer, breast cancer, hypertension etc. This is also called **"Prescriptive Screening"**.

- To **protect the community from disease** that the person being screened has, also called "**Prospective Screening**"; e.g. screening the blood units for HIV.

- For **entry into certain forms of occupations** (armed, industries, etc.) with a view to "weed out" those who are **unfit or whose existing** health status may be adversely affected by occupational conditions.

Definitions

1. **Screening program:**

- ***Comprehensive disease control activity*** based on the identification and treatment of persons with either unrecognized disease or unrecognized risk factors for disease.

2. **Screening test -- *specific technology*:**

- (survey questionnaire, physical observation or measurement, laboratory test, radiological procedure, etc.) used to help identify persons **with unrecognized disease or unrecognized risk factors** for disease.

Screening – two different approaches

- **Population-level screening**
  - National level policy decision to offer ***mass screening*** to a **whole sub-group of a population**
    - e.g., mammography screening (women 40+)
    - e.g., Vision and hearing screening of all Michigan 2nd graders

- **Individual-level screening**
  - Occurs at the **individual patient-physician level**
  - Also refereed to **case finding**
    - e.g., BP screening every time you visit MD
    - e.g., PSA screening
  - *Focus is on identifying existing disease in patients **who don't know** they have it.*

Generalities

1. Screening often **implies a public health related activity involving asymptomatic or healthy subjects coming from the general population.**

2. **Case-finding** refers to **special clinical efforts to recognize disease among persons** who consult a health professional.

3. **Screening is an important aspect of prevention, but not all diseases are suitable for screening.**

- **Effective screening** involves **both *diagnostic* and *treatment*** components.
- Screening differs from diagnostic testing:

Screening	Testing
Healthy non-patients	Sick patients
No diagnostic intent	Diagnostic intent
Very low to low disease prevalence	Low to high disease prevalence

Screening and case finding

Screening:

- **Testing for disease** in average (or low) risk, **asymptomatic population**
- may be considered a form of primary prevention
- goals:
  - early detection
  - treating to reduce morbidity or mortality
- **no diagnostic intent**
- average prevalence (by definition)

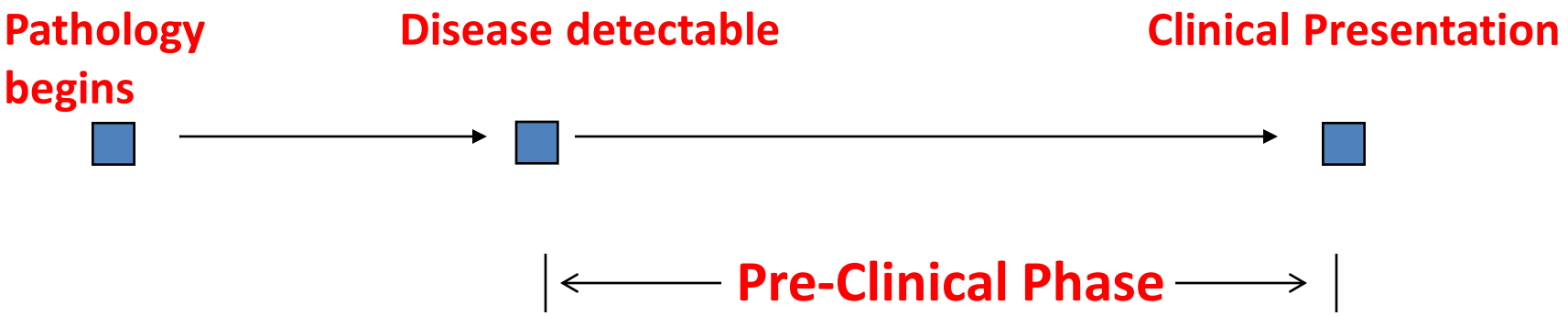
Case-finding:

- Testing **in patients at higher risk**
  - patients seeking medical care because of a complaint
  - patients with familial risks / exposures / other diagnosis
- **may be a form of secondary prevention**
  - disease present, reduce mortality / recurrence rate
- **diagnostic intent**
- usually higher than average disease prevalence

Important Concepts in Screening

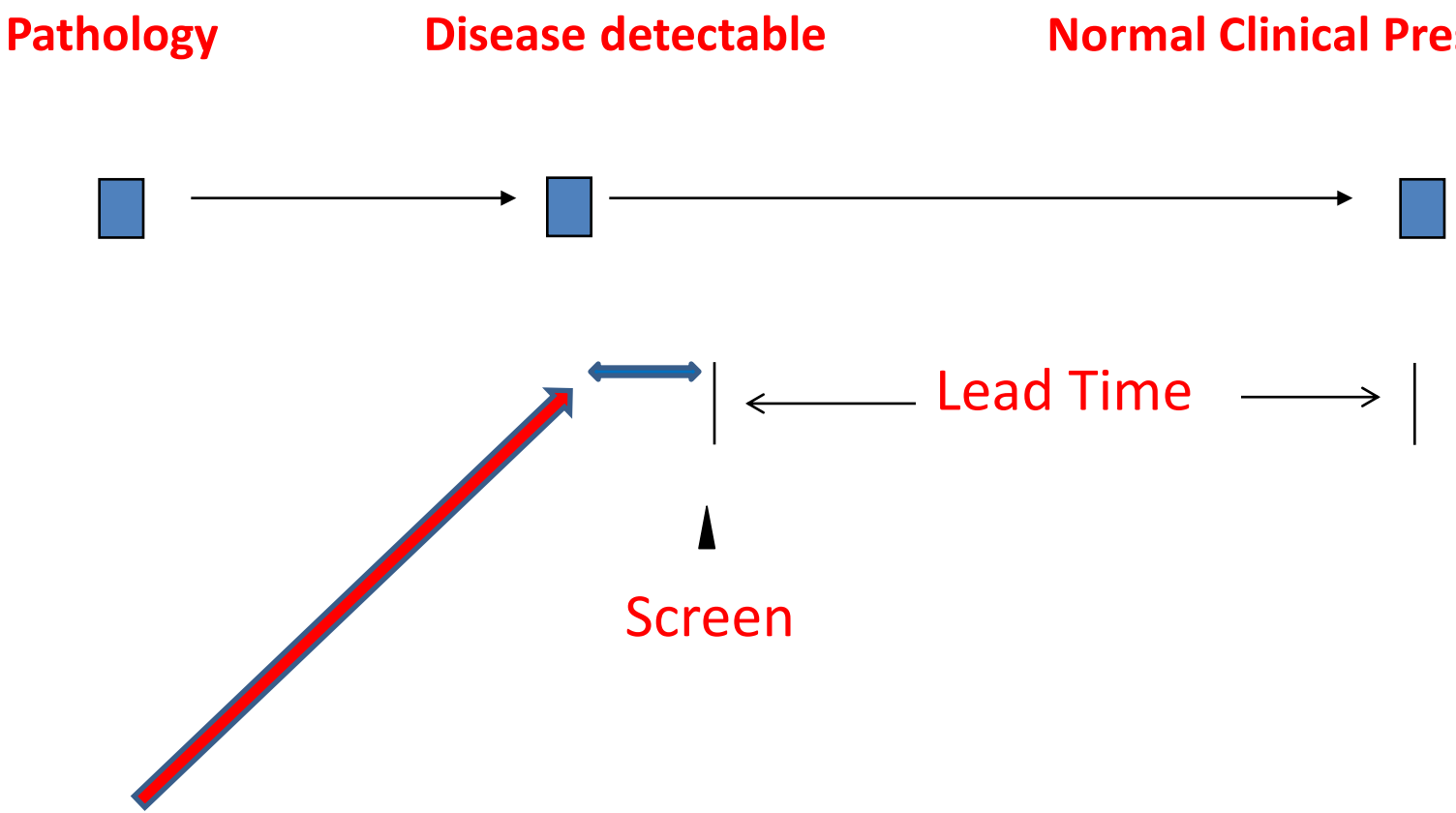
The Pre-Clinical Phase (PCP)

- The period between when **early detection by screening is possible and when the clinical diagnosis would normally have occurred.**



Lead Time

Lead time = amount of time by which diagnosis is advanced or made earlier



Lead Time

- Equals the **amount of time by which treatment is advanced or made "early"**

- **Does not imply improved outcome!!!!!!!!!!!!**

- ***Necessary but not sufficient condition* for effective screening.**

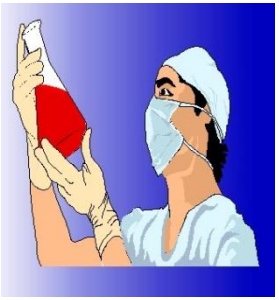
Requirements of Tests used for Screening

- **Valid : It should be "accurate", i.e. should measure correctly** what it intends to. It should have high sensitivity, specificity, and positive & negative predictive values.

- **Reliable (Precise) : It should give consistent results when** repeated applications are made.

- **Yield : It should give enough number of cases to commensurate** with the expenditure and inputs involved.
  - Yield ***will depend on***: **Sensitivity of the test**, **Prevalence of the disease** (If screening is applied to a high risk group, the yield will be better) and **availability of medical** care (if medical care has not been available to the community being screened, a large number of people with the disease will be diagnosed).

Requirements of Tests used for Screening



- **Practical : The test should be easily administered by even** persons with ordinary training, should be innocuous, **acceptable and should give fairly quick results.**

- **Efficient : The amount of inputs (in terms of expenses and time**) should result in reasonable amount of **outputs in terms of improved health & satisfaction.**

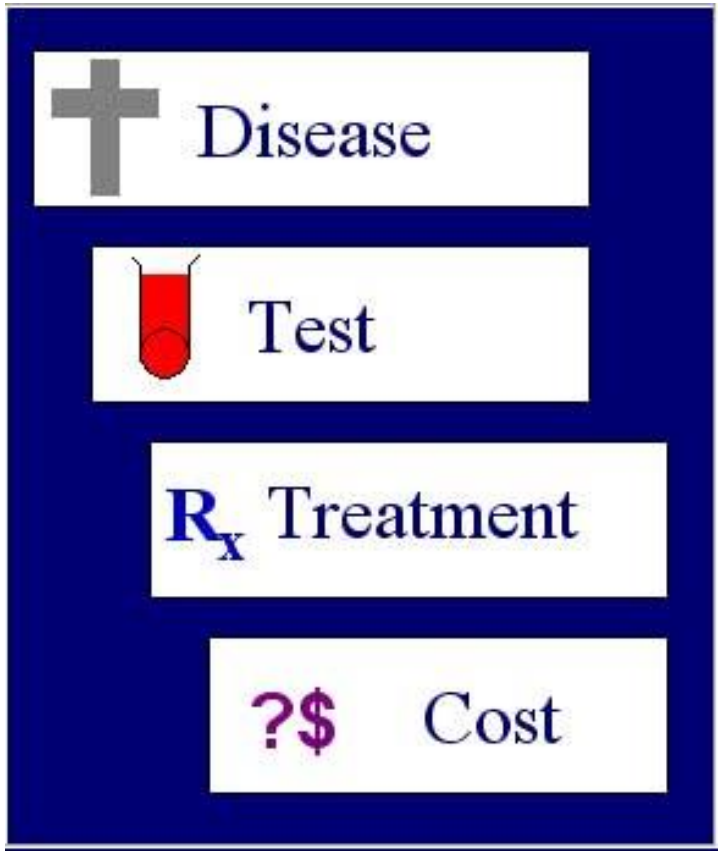
Considerations before Launching a Screening Program for any Disease

- The condition should be an important health problem.
- There should be an acceptable and effective treatment.
- Facilities for confirming the diagnosis and for treatment should be available.
- There should be recognizable latent / early symptomatic stage.
- There should be a suitable screening test or examination available.
- The test should be acceptable.

Considerations before Launching a Screening Program for any Disease

- The **natural history of the condition**, including development from latent to apparent disease, should be **adequately understood.**
- There should be an **agreed policy regarding whom to treat as patients.**
- The ***cost*** of case finding (including final diagnosis and treatment) should be economically balanced vis - a – vis the expenditure on medical care as a whole.
- **Case finding** should be a **continuing process and not "once and for all" project.**

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.**

Summary

- **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: disease, test, treatment and cost.**

What is the next step?

Define the validity of the screening test and put screening to use in the population.

Screening

- **Screening** is the process in which we use a test to determine whether an individual likely has a particular health indicator or not or is likely to develop a particular health indicator or not.
- Screening **is not the same as diagnosis**; screening tests give us information about whether the disease is ***likely to be present.***
- A **screening test** assesses the **presence of an underlying marker that is associated with outcome of interest**.

Screening, examples

- Women receive regular screening tests beginning in young adulthood for cervical cancer ***(Pap smear***).

- Physicians assess **blood pressure and cholesterol** as screening tools for the development of cardiovascular disease.

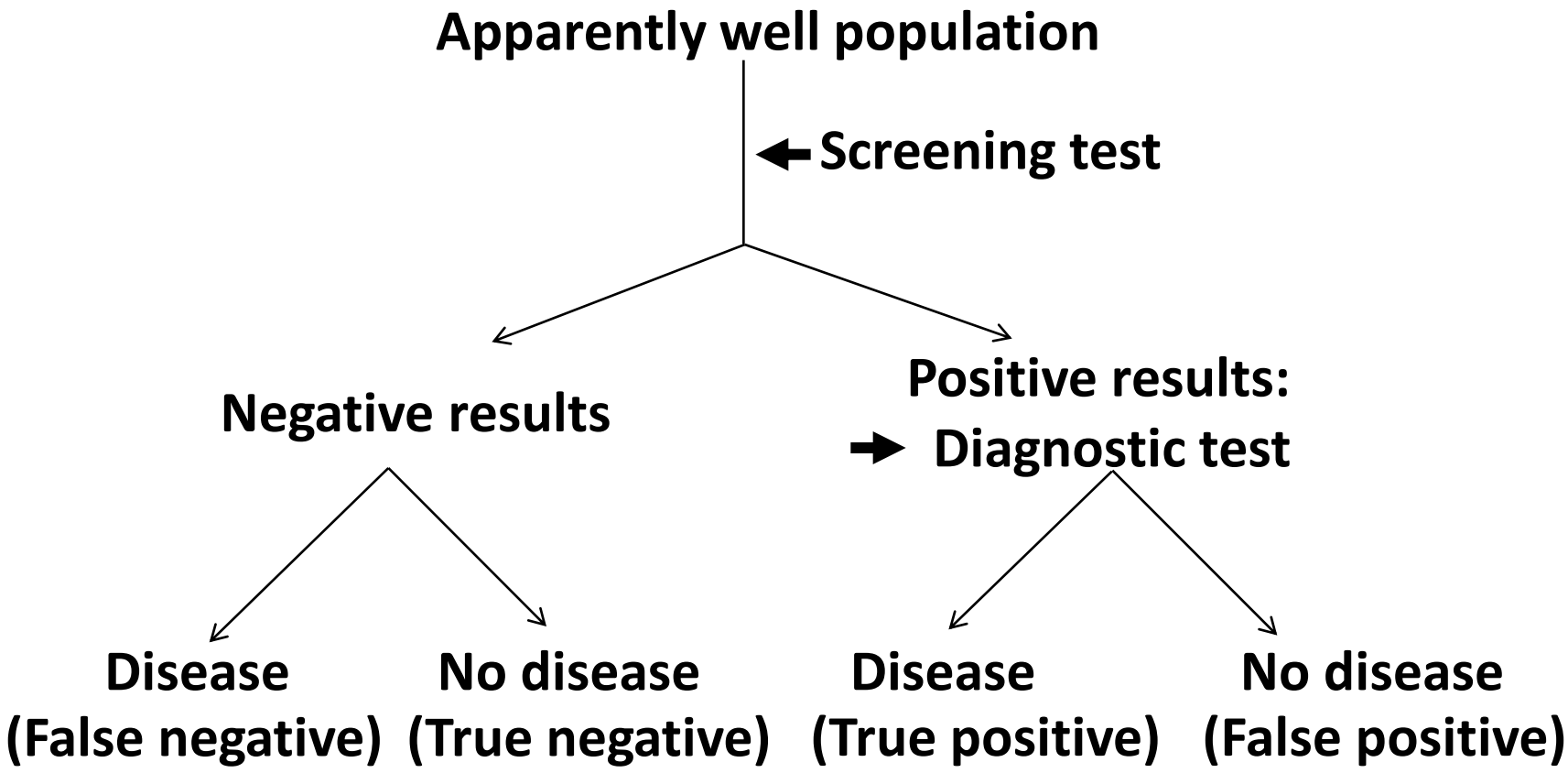
- Women use home **pregnancy tests** to screen for presence of an embryo or fetus.

When should we screen?

- **Screen when:**

- **It is an important health problem (think about how to define 'important'?).**
- **There is an accepted and effective treatment.**
- **Disease has a recognizable latent or early symptomatic stage.**
- **There are adequate facilities for diagnosis and treatment.**
- **There is an accurate screening test.**

Logic of screening



How good is the test?

Test result	Disease present? Yes	Disease present? No
Positive	True positive	False positive
Negative	False negative	True negative

Sensitivity = $\dfrac{\text{True positive}}{\text{True positive + False negatives}}$

Specificity = $\dfrac{\text{True negative}}{\text{True negative + False positives}}$

Screening test evaluation

1. **Sensitivity**
2. **Specificity**
3. **Positive predictive value**
4. **Negative predictive value**

Sensitivity

- **Sensitivity** : This is the frequency of **positive** test results in patients **with** a particular disease , e.g. 95% sensitivity implies 5 % false negative.

- *Sensitivity* = $\frac{\text{Total number } \mathbf{positive} \text{ results}}{\text{Total number } \mathbf{infected} \text{ patients}}$

Specificity

- **Specificity :** The frequency of **negative** test results in patients **without** that disease , e.g. 95% specificity implies 5% false positives.

- *Specificity*= $\frac{\text{Total number } \mathbf{negative} \text{ results}}{\text{Total number } \mathbf{uninfected} \text{ patients}}$

Positive & Negative Predictive Value

- **Positive predictive value**: The percentage of patients with a positive test who actually have the disease.

- **Negative predictive value**: The percentage of patients with a negative test who actually do not have the disease.

Outcomes of a Screening Test

True Disease Status

Screening Test	**Positive**	**Negative**	Total
Positive	True Positives (TP) 	False Positives (FP) 	TP+FP
Negative	False Negatives (FN) 	True Negatives (TN) 	FN+TN
Total	TP+FN	FP+TN	TP+FP+FN+TN

Diagnostic and Screening Tests

Test properties

		DISEASE (+)	DISEASE (Š)	Total
TEST	(+)	A (TP)	B (FP)	A+B (all positives)
	(Š)	C (FN)	D (TN)	C+D (all negatives)
Total		A+C (All ill)	B+D (All healthy)	A+B+C+D (Grand Total)

Diagnostic and Screening Tests

Test properties

		DISEASE (+)	DISEASE (Š)	Total
TEST	(+)	A	B	A+B
	(Š)	C	D	C+D
Total		A+C	B+D	A+B+C+D

(True) prevalence: Proportion of persons with disease in the population. **Prevalence = (A+C)/(A+B+C+D)**

Of 1000 kids, 78 have head lice. Prevalence = 7.8%

Diagnostic and Screening Tests

Test properties

		DISEASE (+)	DISEASE (Š)	Total
TEST	(+)	A (TP)	B (FP)	A+B
	(Š)	C (FN)	D (TN)	C+D
Total		A+C	B+D	A+B+C+D

Sensitivity: Likelihood a diseased person will have a positive test Sensitivity = TP/All disease = A/(A+C)

Of 100 men with prostate cancer, 90 have (+) PSA.
Sensitivity=90%

Diagnostic and Screening Tests

Test properties

		DISEASE (+)	DISEASE (Š)	Total
TEST	(+)	A (TP)	B (FP)	A+B
	(Š)	C (FN)	D (TN)	C+D
Total		A+C	B+D	A+B+C+D

Specificity: Likelihood a healthy person will have a negative test **Specificity = TN/All healthy = D/(B+D)**

Of 100 healthy kids, 3 have a false (+) strep test.
Specificity = 97%

Diagnostic and Screening Tests

- **Sensitivity and specificity** give us ***likelihood*** of the test result among persons **known to be diseased or healthy.**

- As clinicians, we **need to know the opposite**: the **likelihood of being diseased or healthy among persons with a known test result.**

Diagnostic and Screening Tests

Test properties

		DISEASE (+)	DISEASE (Š)	Total
TEST	(+)	A	B	A+B
	(Š)	C	D	C+D
Total		A+C	B+D	A+B+C+D

Predictive value of (+): Likelihood that a person with a positive test actually has the disease

PV(+)=TP/All positives=A/(A+B)

Two-thirds of patients with a (+) Exercise Stress Test will have atherosclerosis on angiography PV(+)=66%

Diagnostic and Screening Tests

Test properties

		DISEASE (+)	DISEASE (Š)	Total
TEST	(+)	A	B	A+B
	(Š)	C	D	C+D
Total		A+C	B+D	A+B+C+D

<u>Predictive value of (–):</u> Likelihood that a person with a negative test is free of the disease

PV(–)= TN/All negatives = D/(C+D)

99 of 100 patients with a (–) syphilis test are free of syphilis
PV(–)=99%

Diagnostic and Screening Tests

Consider: What is the likelihood that a person with a positive test will actually have the disease (**i.e., what is the PV+)** when. . .

Prevalence=20% in a population of 10^4

Sensitivity=90%

Specificity=90%

Diagnostic and Screening Tests

		DISEASE (+)	DISEASE (Š)	Total
TEST	(+)	*Sens x 2000* 1800	800	2600
	(Š)	200	*Spec x 8000* 7200	7400
Total		2000	8000	10,000

Population: 10,000
Prevalence: 20%
Sensitivity: 90%
Specificity:90%

PV(+)=TP/All Positives= **1800/2600=69.2%**

Conclude: Only 69.2% of persons with a positive test actually have the disease. (Tests isn't perfect!)

Diagnostic and Screening Tests

Let's see what happens when we make this a **rare disease**. Test properties stay the same. . .

Prevalence=0.1% in a population of 10^4

Sensitivity=90%

Specificity=90%

Diagnostic and Screening Tests

		DISEASE (+)	DISEASE (Š)	Total
TEST	(+)	*Sens x 10* 9	999	1,008
	(Š)	1	*Spec x 9,990* 8,991	8,992
Total		10	9,990	10,000

Population: 10,000
Prevalence: 0.1%
Sensitivity: 90%
Specificity:90%

PV(+)=TP/All Positives= **9/1,008=0.89%**

Conclude: Less than 1%(!!) of persons with a positive test actually have the disease.

Overall

- **Accuracy = percentage correct overall**
- **TP+TN/(TP+TN+FP+FN)**

Diagnostic and Screening Tests

- **Two other test attributes:**

- **Validity = Accuracy: The likelihood that a test result will be correct, *on average.***

- **Precision = repeatability = reliability: The likelihood that repeated measures on the same sample or subject will yield the same result.**

- **Ideal tests have high validity and high precision.**

Consider validity and precision for five repeated measurements where the true value is 120

Results of five measurements	Validity	Precision
120, 120, 119, 121, 120	High (average is 120)	High (results all very close together
120, 100, 140, 90, 150	High (average is still 120!)	Low (results all over the place)
100, 100, 99, 101, 100	Low (average is way off at 100)	High (results all very close together)
100, 80, 120, 70, 130	Low (average is way off at 100	Low (results all over the place)

A Question:

The sensitivity and specificity of blood factor X for disease Z are 80% and 90% respectively.

The prevalence of disease Z in the general population is 1%.

If blood factor X is found in someone from the general population, the likelihood that he or she has disease Z is closest to:

A. 1% B. 7.5% C. 80% D. 99.8%

Prevalence= 1% Sensitivity= 80% Specificity = 90%

n= 1000

	Disease	No Disease	Total
Positive Test	a= 8	b= 99	107
Negative Test	c= 2	d= 891	893
Total	10	990	1000

If blood factor X is found in someone from the general population, the likelihood that he or she has disease Z is closest to:

Test + ➔ Probability of having the disease

= Positive Predictive Value !

= (8 / 107) * 100 = 7.48%