# Medical Screening

## Focusing Treatment on Those Who Need It

Although the COVID19 pandemic highlighted some critical issues with this approach; the underlying basis for medical screening is both as a measure of community morbidity and as a secondary prevention approach. The idea is that if a sufficiently large sample of the population in a given community undergoes screening, it can provide public health officials with vital information about the spread of the disease/disorder within the community and if there are particular segments of the community who are at greater risk. At the same time, individuals who may be unaware that they they are developing an issue can seek early treatment potentially altering the disease/disorder outcome.

**Topics:** Sensitivity — Specificity — Informedness — SnNO — SpPI

**Medical Screening** — A method for detecting disease or dysfunction before an individual would normally seek medical care. Secondary Prevention

**Medical Screening** — A method of tracking the spread of a disease/disorder and/or identifying at–risk segments of the community where a disease/disorder is disproportionately occurring.

The way in which medical screening can and should be used in clinical decisions is dictated by the **Sensitivity** and **Specificity** of the test. These concepts specifically categorize the intersection of if a disease actually exists and if the test is able to identify it. If the disease is actually present and the test identifies it, this is referred to as a **True Positive**. If the disease is actually absent and the test says the disease is absent, this is referred to as a **True Negative**. These are ideal circumstances. Despite our best efforts, no test is perfect. So consider the situation where the patient does not have the disease but the test says they do, this is referred to as a **False Positive**. Alternatively, if the patient actually does have the disease but the test says they do not, this is referred to as a **False Negative**.

Hypothetical Medical Test

| | Disease Present | Disease Absent |
|---|---|---|
| **Test Positive** | True Positive<br>65 | False Positive<br>3 |
| **Test Negative** | False Negative<br>35 | True Negative<br>997 |

$$Sensitivity = \frac{True\ Positive}{True\ Positive\ +\ False\ Negative} = \frac{65}{65+35} = 0.65 = 65.0\%$$

$$Specificity = \frac{True\ Negative}{True\ Negative\ +\ False\ Positive} = \frac{997}{997+3} = 0.997 = 99.7\%$$

Sensitivity refers to how accurate the test is in identifying disease in individuals who truly have the disease. When thinking about sensitivity, focus on the individuals who really were diseased — in this case, the left hand column. In the example above, the test exhibited a sensitivity of 65%. This can be interpreted as the probability of the test correctly identifying diseased individuals was 65%.

**A test with a very high level of sensitivity can be useful in ruling OUT the presence of a disease/disorder when the test is NEGATIVE**. Initially this seems counterintuitive, but consider the example of a friend who always thinks everyone is mad at them. You might refer to them as being very sensitive. Because their sensitivity is high, they often make a lot of false positives — they think someone is mad at them who is not. So you would tend to ignore the times when they think someone is mad at them (i.e., the positive test result). But because their sensitivity is high they would tend to make very few false negatives — thinking someone is not mad when they are. So if your friend thinks someone is not mad at them (i.e., the negative test result), you have pretty good confidence that it is the case. In a medical context, if a test correctly identifies 100% of individuals with the disease/disorder, testing negative would give a high degree of confidence that the individual is free of the disease/disorder. So when a test has high sensitivity, obtaining a negative test enables ruling out the disease/disorder. This idea is often referred to as **SnNO — Sen**sitivity **N**egative test rule **O**ut.

Tests with high sensitivity are **biased for the detection of a disease** while allowing for the possibility of false positives. So they are useful for diseases where we absolutely must identify the disease to contain the spread or start treatment early, even if it means that the same test will result in a large number of false positives. As a result, obtaining a positive test result would not necessarily mean that the individual has the disease/disorder.

**Specificity** refers to the accuracy of the test in correctly classifying truly non-diseased individuals. When thinking about specificity, focus on the individuals who were not-diseased — in this case, the right hand column. In the example above, the test exhibited a specificity of 99.7%. This can be interpreted as the probability that non-diseased subjects will be classified as normal by the test was 99.7%.

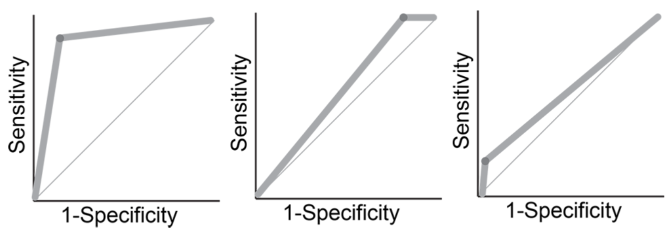
**A test with a very high level of specificity can be useful in ruling IN the presence of a disease/disorder when the test is POSITIVE**. If the test correctly identifies 100% of individuals without the disease/disorder as being normal, testing positive would give a high degree of confidence that the individual has something going on. But it is very likely that the same test will result in a large number of false negatives.

Consider that we might have a test that is designed to be very specific to a particular type of cancer. If the patient tests positive, we know they definitely would have that type of cancer. But what if they have a type of cancer the test was not designed to detect? Because the test was biased for being specific to the disease of interest, obtaining a negative test result could occur if the individual has a disease process that does not perfectly align with what the test is measuring. So obtaining a negative test result would not necessarily mean that the individual is normal. This idea is often referred to as **SpPI** — **Sp**ecificity **P**ositive test rule **I**n.

Ideally a medical test is both highly sensitive and highly specific. Medical tests are rarely perfect and as such it is important to recognize the potential bias that the test has. In practice, tests will trade-off between specificity and sensitivity and the diagnostic power of any given test will be assessed against other potential tests for the disease. Although there are no perfect ways to do this, the **Informedness** of a test — assessed as **Sensitivity + Specificity - 1** — is a straightforward approach as larger numbers indicate superior tests.

It is also important to understand that for most medical screening tests, there is a range of possible values that could be used as the critical value for determining if someone has a disease or disorder. Take for instance a fasting blood glucose test. If your patient's blood glucose is above 100 mg/dL the screening test would flag them as potentially having diabetes. The sensitivity and specificity of the test can be altered by choosing a higher or lower blood glucose level. This is typically visually represented using what is known as a **Receiver Operating Characteristic (ROC) curve** that allows for seeing the relationship between a diagnostic tests sensitivity and specificity across various cut-off values. This approach also allows for quickly visually identifying the quality of a medical screening tool.

**Figure:** Receiver Operating Characteristic curves.




The utility of medical screening also relates to a number of critical questions about how medical tests deployed for screening/diagnostic purposes actually impact the clinical decision making process. If the treatment would be the same regardless of the outcome, then doing such a test is largely irrelevant and can be difficult to justify implementing only for public health monitoring. Similarly, there are ethical debates regarding the use of medical screening for conditions that do not have any effective treatments (such as Huntington's disease and Alzheimer's disease). Informing someone that they have such a disease might alter the way in which they would choose to live their life. Relatedly, is the cost and burden of the test proportionate to the potential benefits? If a test is exceptionally expensive or highly burdensome to the patient, and the information obtained is only marginally better than what could be obtained through a less expensive or burdensome test then why would you choose to use it clinically? Finally there are questions about potential adverse effects and safety/privacy concerns that should always be considered.

## Why do we need medical screening?

### Community Morbidity

With a sufficiently large sample of individuals in a community, screening enables:

- Assessment of the spread of the disease/disorder within the community.
- Identification of 'At-Risk' segments of the community where the disease/disorder is *disproportionately occurring*.

### Secondary Prevention

The Iceberg Principle of Disease Presentation tells us that most people may not be aware that they have a disease/disorder (e.g., latent, subclinical, undiagnosed and carrier states).

Medical screening provides a way of identifying these individuals in hopes early intervention can reduce the morbidity and mortality of the disease.

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HYPOTHETICAL MEDICAL TEST

| | Disease Present | Disease Absent |
|---|---|---|
| **Test Positive** | True Positive 65 | False Positive 3 |
| **Test Negative** | False Negative 35 | True Negative 997 |

**Sensitivity**

The test's accuracy in correctly identifying the disease in individuals who truly have the disease

$$\frac{True\ Positive}{True\ Positive + False\ Negative}$$

$$\frac{65}{65+35} = 0.65 = 65.0\%$$

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HYPOTHETICAL MEDICAL TEST

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| **Test Positive** | True Positive 65 | False Positive 3 |
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**Sensitivity**

The test's accuracy in correctly identifying the disease in individuals who truly have the disease

$$\frac{True\ Positive}{True\ Positive + False\ Negative}$$

$$\frac{65}{65+35} = 0.65 = 65.0\%$$

**Specificity**

The test's accuracy in correctly identifying individuals who do not truly have the disease

$$\frac{True\ Negative}{True\ Negative + False\ Positive}$$

$$\frac{997}{997+3} = 0.997 = 99.7\%$$

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HYPOTHETICAL MEDICAL TEST

| | Disease Present | Disease Absent |
|---|---|---|
| **Test Positive** | True Positive 100 | False Positive 200 |
| **Test Negative** | False Negative 0 | True Negative 800 |

**Sensitivity = 100%**

If the test correctly identifies every individual with the disease/disorder, testing negative would give a high degree of confidence that the individual is free of the disease/disorder.

A negative test would be highly unlikely if the disease was actually present.

Tests with high sensitivity are useful in **Ruling Out** the presence of a disease/disorder when the test is **Negative**

SnNO

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HYPOTHETICAL MEDICAL TEST

| | Disease Present | Disease Absent |
|---|---|---|
| **Test Positive** | True Positive 100 | False Positive 200 |
| **Test Negative** | False Negative 0 | True Negative 800 |

**Sensitivity = 100%**

If the test correctly identifies every individual with the disease/disorder, testing negative would give a high degree of confidence that the individual is free of the disease/disorder.

A positive test does not necessarily mean that the disease was actually present.

The sensitivity is biased for detection.

In order to make sure the disease is detected, we accept the possibility of false positives.

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HYPOTHETICAL MEDICAL TEST

| | Disease Present | Disease Absent |
|---|---|---|
| **Test Positive** | True Positive 10 | False Positive 0 |
| **Test Negative** | False Negative 90 | True Negative 1000 |

A positive test would be highly unlikely if the disease was absent.

Tests with high specificity are useful in **Ruling In** the presence of a disease/disorder when the test is **Positive**

SpPI

**Specificity = 100%**

If the test correctly identifies 100% of individuals without the disease/disorder as being normal, testing positive would give a high degree of confidence that the individual has something going on.

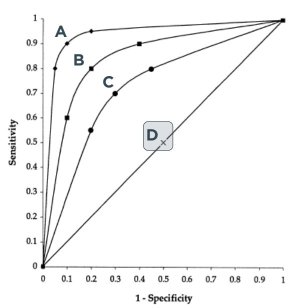
High Sensitivity | High Specificity
Negative Test | Positive Test
Rule Out | Rule In
SnNO | SpPI

HYPOTHETICAL MEDICAL TEST

| | Disease Present | Disease Absent |
|---|---|---|
| **Test Positive** | True Positive 65 | False Positive 3 |
| **Test Negative** | False Negative 35 | True Negative 997 |
| | Sensitivity = 65% | Specificity = 99.7% |

High Sensitivity — High Specificity
Negative Test — Positive Test
Rule Out — Rule In
SnNO — SpPI

A positive test would be unlikely if the disease/disorder were absent. An individual with a positive test very likely has the disease/disorder.




In practice, there is always a tradeoff between sensitivity and specificity.

$$Informedness = Sensitivity + Specificity - 1$$

A = 0.9 + 0.9 – 1 = 0.8

B = 0.8 + 0.8 – 1 = 0.6

C = 0.7 + 0.7 – 1 = 0.4

D = 0.5 + 0.5 – 1 = 0

With continuous data, the sensitivity and specificity of a medical test is determined by where the cutoff point is placed.

Using the concepts of **SpPI** and **SnNO**, we can choose cutoffs optimized for rejection or detection.

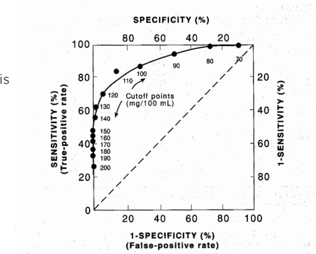



**Figure 3.4.** A ROC curve. The accuracy of 2-hr postprandial blood sugar as a diagnostic test for diabetes mellitus. (Data from Public Health Service. Diabetes program guide. Publication no. 506. Washington, DC: U.S. Government Printing Office, 1960.)

If the goal was to rule in the presence of diabetes with a positive test, what blood sugar cut point would you use?

**SpPI** – Specificity Positive Test Rule In

**150**: Sensitivity = 49%, Specificity = 100%
Informedness = 0.49

**130**: Sensitivity = 62%, Specificity = 98%
Informedness = 0.6

**120**: Sensitivity = 70%, Specificity = 92%
Informedness = 0.62

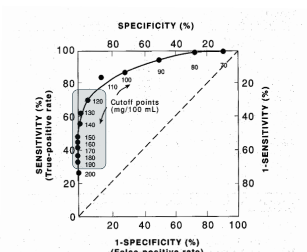



**Figure 3.4.** A ROC curve. The accuracy of 2-hr postprandial blood sugar as a diagnostic test for diabetes mellitus. (Data from Public Health Service. Diabetes program guide. Publication no. 506. Washington, DC: U.S. Government Printing Office, 1960.)

## How does the medical screening impact treatment?

- Ideally the medical screening/diagnosis has a direct impact upon treatment.
  - The screening identifies the issue and the clinician begins treatment of the issue.
  - The screening identifies the absence of the issue so the clinician avoids performing a treatment that could do more harm than good.
    - **Quaternary Prevention**

## How does the medical screening impact treatment?

- Is performing a screening test valuable if the treatment is the same regardless of the outcome?
    - A test indicates the absence of a bacterial infection, but we are going to put the patient on antibiotics anyways.
    - The screening identifies an issue that has no effective treatment or treatments with minimal effectiveness.

## Huntington's disease

- Inherited disorder that causes parts of the brain to gradually break down and die.
- Progressive degeneration of areas involved with:
    - Motor control
    - High level cognition
    - Anxiety, Depression, Psychosis

Screening tests currently identify those with the genetic markers associated with the disease.

If you have the genetic marker, you will develop the disease.

Diagnosis typically occurs in mid-life when an elderly family member presents with symptoms.

## Medical Screening Worksheet

| | Disease Present | Disease Absent |
|---|---|---|
| Test Positive | True Positive | False Positive |
| Test Negative | False Negative | True Negative |

1. What is the formula for sensitivity? What column of the table does sensitivity focus on?

2. What is the formula for specificity? What column of the table does specificity focus on?

3. What is the formula for informedness?

**Test A**

| | Disease Present | Disease Absent |
|---|---|---|
| Test Positive | True Positive: 4230 | False Positive: 410 |
| Test Negative | False Negative: 360 | True Negative: 5700 |

4. What is the sensitivity of Test A?

5. What is the specificity of Test A?

**Test B**

| | Disease Present | Disease Absent |
|---|---|---|
| Test Positive | True Positive: 2991 | False Positive: 850 |
| Test Negative | False Negative: 16 | True Negative: 4621 |

6. What is the sensitivity of Test B?

7. What is the specificity of Test B?

8. What is the informedness of Test B?

**Test C**

| | Disease Present | Disease Absent |
|---|---|---|
| Test Positive | True Positive: 882 | False Positive: 96 |
| Test Negative | False Negative: 289 | True Negative: 3621 |

9. What is the sensitivity of Test C?

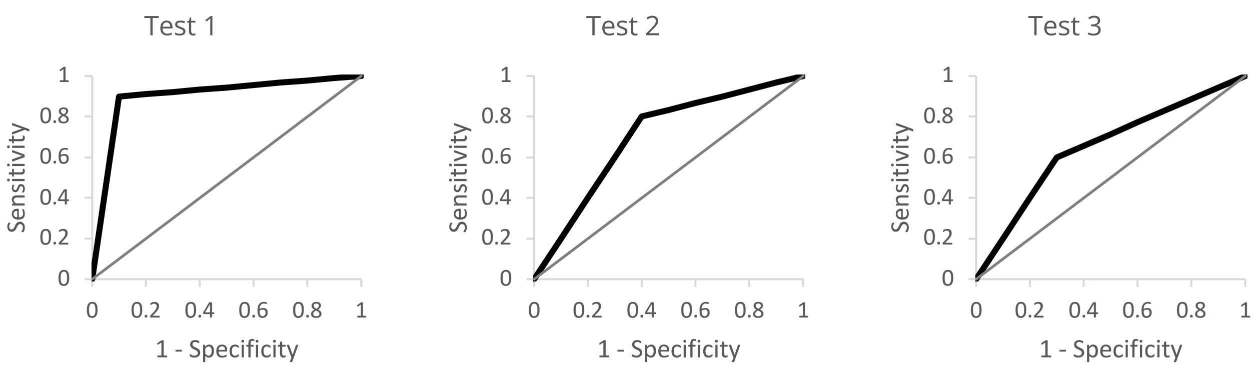
10. What is the specificity of Test C?

11. What is the informedness of Test C?

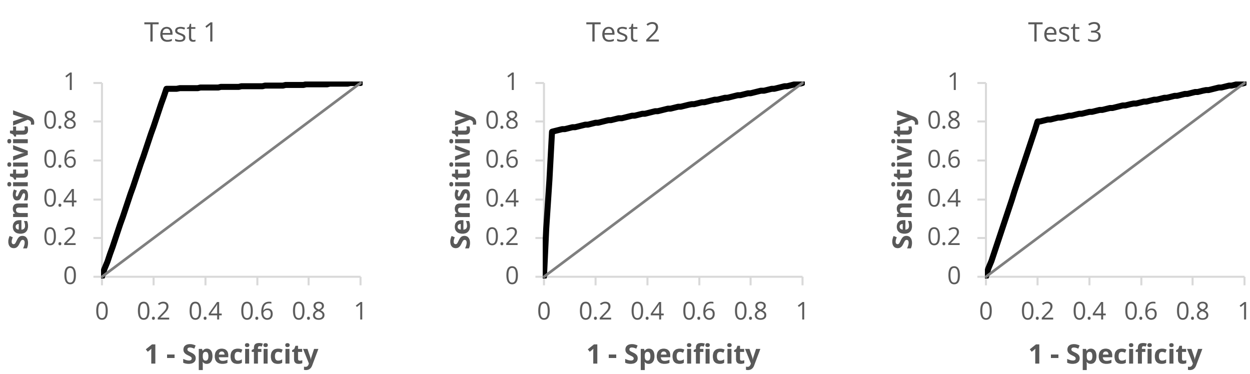
12. Of Tests A, B, and C, which test would you choose if the goal was to rule in the presence of a disease/disorder with a positive test? Why?

13. Of Tests A, B, and C, which test would you choose if the goal was to rule out the presence of a disease/disorder with a negative test? Why?

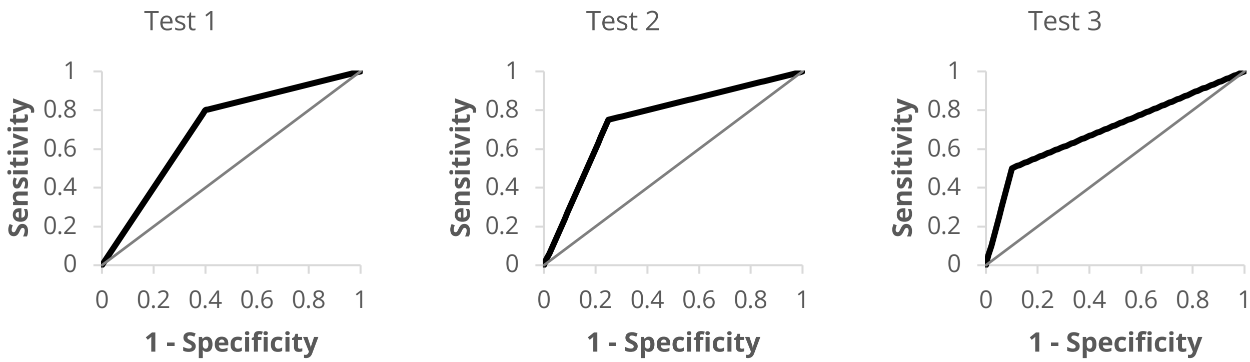
14. Of Tests 1, 2, and 3, which test is the best? Which test is the worst?




15. Of Tests 1, 2, and 3, which test would you choose to use if the goal was to rule out the presence of a disease/disorder with a negative test?



16. Of Tests 1, 2, and 3, which test would you choose to use if the goal was to rule in the presence of a disease/disorder with a positive test?




17. Your friend was just screened for cancer and received a positive test result that cancer was detected. Because of your area of study, you look into the screening tool and find that it is a test with a very high level of sensitivity. What can you conclude from the positive test result?

18. Your uncle was just screened for a respiratory virus and received a negative test result that no virus was detected. Because of your area of study, you look into the screening tool and find that it is a test with a very high level of specificity. What can you conclude from the negative test result?