

Bayes Theorem and Clinical Tests

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Introduction to Bayes Theorem

Bayes Theorem is a mathematical formula that accounts for the concept of conditional probability. A conditional probability is the likelihood or probability of an outcome occurring based on a previous outcome having already occurred. This means that both events are dependent from each other.

In short, Bayes Theorem uses prior probability distributions in order to generate posterior probabilities:

- a) *Prior probability*: probability of an event to occur before new data is collected. For example, the probability of having liver disease in a specific population.
- b) *Posterior probability*: updated probability of an event to occur after new data is collected. For example, the probability of having liver disease if the patient is an alcoholic. As it includes more information, it is a better reflection of the underlying truth.

Inferring Bayes Theorem formula: now, we will try to infer the Bayes formula from simple examples.

Independent events: suppose a situation in which we want to calculate the probability of two independent events, A and B, happening. The probability of both events happening $P(A \cap B)$ can be calculated as the multiplication of the probability two events $P(A)$ and $P(B)$:

$$P(A \cap B) = P(A) \cdot P(B)$$

For example, imagine that we want to compute the probability of obtaining a head and a tail in two coin tosses. The probability of obtaining either face of the coin is 0.5, and thus that probability can be represented as:

$$P(\text{head} \cap \text{tail}) = P(\text{head}) \cdot P(\text{tail}) = 0.5 \cdot 0.5 = 0.25$$

Therefore, there is a 25% chance of obtaining a head after a tail, as both tosses are independent.

Dependent events: however, in some situations, the second event is dependent on what happened before. When A and B are dependent, we cannot assume that $P(A \cap B) = P(A) \cdot P(B)$, but we need to compute that probability in other way. For example, imagine that we want to calculate the probability of picking a king and an ace from a card deck. Both events are dependent as there is a limited number of cards in a deck and that number is reduced every time, we pick a card.

In this case, we can compute the probability of picking an ace and a king, $P(\text{ace} \cap \text{king})$, as the probability of picking an ace, $P(\text{ace})$, multiplied by the probability of picking and king provided that an ace was already picked, $P(\text{king}|\text{ace})$:

$$P(\text{ace} \cap \text{king}) = P(\text{ace}) \cdot P(\text{king}|\text{ace})$$

Note that if the two events are independent, then $P(\text{king}|\text{ace}) = P(\text{king})$ and we are in the previous situation. This will be the case if we return the ace to the deck.

In any case, the probability of picking an ace if no other card has been picked from a card deck is:

$$P(\text{ace}) = \frac{4 \text{ aces}}{40 \text{ cards}} = 0.1$$

After picking the ace, the probability of picking a king is influenced by the previous event, as now there are fewer cards in the deck from which we can pick, and is computed as:

$$P(\text{king}|\text{ace}) = \frac{4 \text{ kings}}{39 \text{ cards}} = 0.103$$

Here, the probability of choosing a king after a card has already been picked slightly higher than picking a king from a new deck ($P(\text{king}) = 0.1$), as there are fewer cards to choose from. At the end, the probability of picking an ace and a king is:

$$P(\text{ace} \cap \text{king}) = 0.1 \cdot 0.103 = 0.0103$$

However, we can also compute the probability of picking a king and an ace, $P(\text{king} \cap \text{ace})$, as the probability of picking an ace after a king has already been picked. This is the same probability as before: $P(\text{ace} \cap \text{king}) = P(\text{king} \cap \text{ace})$, and is the step needed to reach the Bayes Theorem formula. In this case, we can calculate the probability as before:

$$P(\text{king} \cap \text{ace}) = P(\text{king}) \cdot P(\text{ace}|\text{king})$$

$$P(\text{king}) = \frac{4 \text{ kings}}{40 \text{ cards}} = 0.1$$

$$P(\text{king}|\text{ace}) = \frac{4 \text{ aces}}{39 \text{ cards}} = 0.103$$

$$P(\text{king} \cap \text{ace}) = 0.1 \cdot 0.103 = 0.0103$$

Important: this does NOT mean that $P(\text{ace}|\text{king})$ is equal to $P(\text{king}|\text{ace})$, but in this toy example it does. For example, it is not the same probability of having cough provided that the subject smokes $P(\text{cough}|\text{smoker})$ and the probability of being a smoker provided that the subject has cough $P(\text{smoker}|\text{cough})$. In reality, it is much more probable the first situation.

What this dissertation tries to explain is that: $P(\text{ace} \cap \text{king}) = P(\text{king} \cap \text{ace})$. This means that both equations can be bound as:

$$P(\text{ace}) \cdot P(\text{king}|\text{ace}) = P(\text{king}) \cdot P(\text{ace}|\text{king})$$

Moving some terms, we reach the Bayes theorem and can calculate the conditional probability of picking a king after an ace has been picked as:

$$P(\text{king}|\text{ace}) = \frac{P(\text{king}) \cdot P(\text{ace}|\text{king})}{P(\text{ace})}$$

We can generalize the formula as:

$$P(A|B) = \frac{P(A) \cdot P(B|A)}{P(B)}$$

where:

$P(A)$: probability of A.

$P(B)$: probability of B.

$P(A|B)$: probability of A happening, provided that B has occurred. What we are trying to calculate.

$P(B|A)$: probability of B happening, provided that A has occurred.

Clinical example: imagine we are in a specific hospital, and we are trying to calculate the probability of a patient having a liver disease if he is an alcoholic. This can help to decide recommendations for patients in certain circumstances. Therefore, we can mathematically represent the information as:

$P(A) = P(\text{liver disease})$: probability of having liver disease. This is the prevalence of the disease in a certain population.

$P(B) = P(\text{alcoholism})$: probability of being an alcoholic.

$P(A|B) = P(\text{liver disease}|\text{alcoholism})$: probability of having liver disease, provided that the patient is an alcoholic. What we are trying to determine here.

$P(B|A) = P(\text{alcoholism}|\text{liver disease})$: probability of being an alcoholic provided that the patient has a liver disease.

Introducing this data in the Bayes formula, we obtain:

$$P(\text{liver disease}|\text{alcoholism}) = \frac{P(\text{liver disease}) \cdot P(\text{alcoholism}|\text{liver disease})}{P(\text{alcoholism})}$$

Knowing the prevalence of liver diseases, $P(\text{liver disease})$, the prevalence of alcoholism in patients with liver disease, $P(\text{alcoholism}|\text{liver disease})$, and the prevalence of alcoholism, $P(\text{alcoholism})$, we can compute the probability of an alcoholic patient to develop liver disease.

For instance, given a prevalence of liver disease $P(\text{liver disease}) = 0.1\% = 0.001$; prevalence of alcoholism $P(\text{alcoholism}) = 2\% = 0.02$; and prevalence alcoholism in patients with liver diseases $P(\text{alcoholism}|\text{liver disease}) = 3.5\% = 0.035$; then the probability of developing liver disease provided that they are an alcoholic would be:

$$P(\text{liver disease}|\text{alcoholism}) = \frac{0.001 \cdot 0.035}{0.02} = 0.7 = 70\%$$

Clinical tests

In the clinical practice, the Bayes theorem is used to determine the conditional probability of having the suggested condition after performing a test. For example, the probability of having HIV after a positive result in a blood test. These calculations take into account the prevalence of the disease and the specificity and sensibility of the test to determine the real probability of a patient to have the disease. Therefore, we must first define the discriminatory capacity of a test by defining specificity and sensibility.

Specificity and sensibility: tests are not completely infallible as the values of a certain biomarker between the healthy and sick populations usually overlap. Therefore, for each test implemented in the clinical practice, we must determine its discriminatory capacity. For that, we can construct a contingency table of the four possible outcomes:

	Sick	Healthy
Positive Test	True Positive (TP)	False Positive (FP)
Negative Test	False Negative (FN)	True Negative (TN)

Taking into account this information, we can mathematically define:

a) Specificity = $P(\text{test} - |\text{healthy}) = \frac{TN}{TN+FP}$ or the rate of correctly identified healthy individuals.

b) Sensibility = $P(\text{test} + |\text{sick}) = \frac{TP}{TP+FN}$ or the rate of correctly identified patients.

c) False Positive rate = $P(\text{test} + |\text{healthy}) = 1 - \text{specificity}$ or not correctly identifying a healthy subject.

d) False Negative rate = $P(\text{test} - | \text{sick}) = 1 - \text{sensibility}$ or not correctly identifying a sick subject.

With these parameters we are trying to calculate the probability of a positive or negative result provided that we know if the subject is healthy or not. However, in the real clinical practice we don't know the real condition of the patient and that is why we use the predictive values.

Predictive values: the predictive values apply the Bayes theorem to determine the real probability of having a condition provided a specific test result. In this situation we are reversing the previous question, we don't ask ourselves the probability of a test result provided a subject condition (that is for checking the test parameters), as in the clinical practice we do not know the subject's condition, but rather the probability of the subject being healthy, or sick provided a test result.

The predictive values gather the information provided by the specificity, sensibility, and the prevalence of the disease. As before, we can construct a contingency table as:

	Sick (prevalence)	Healthy (1-prevalence)
Positive Test	TP: probability of disease and a positive test: $P(+ \cap \text{sick}) = P(+ \text{sick}) \cdot P(\text{sick}) = \text{Sensibility} \cdot \text{Prevalence}$	FP: probability of healthy and positive test: $P(+ \cap \text{healthy}) = P(+ \text{healthy}) \cdot P(\text{healthy}) = (1 - \text{Specificity}) \cdot (1 - \text{Prevalence})$
Negative Test	FN: probability of disease and negative test: $P(- \cap \text{sick}) = P(- \text{sick}) \cdot P(\text{sick}) = (1 - \text{Sensibility}) \cdot \text{Prevalence}$	TN: probability of healthy and negative test: $P(- \cap \text{healthy}) = P(- \text{healthy}) \cdot P(\text{healthy}) = \text{Specificity} \cdot (1 - \text{Prevalence})$

Positive predictive value (PPV): the probability of having the disease provided that the test was positive. We just apply Bayes Theorem:

$$\text{PPV} = P(\text{sick} | +) = \frac{P(+|\text{sick}) \cdot P(\text{sick})}{P(+)}$$

The probability of a positive result is both, the probability of having a positive result and the subject being sick and the probability of having a positive result and the subject being healthy:

$$\text{PPV} = \frac{P(+|\text{sick}) \cdot P(\text{sick})}{P(+ \cap \text{sick}) + P(+ \cap \text{healthy})} = \frac{P(+|\text{sick}) \cdot P(\text{sick})}{P(+|\text{sick}) \cdot P(\text{sick}) + P(+|\text{healthy}) \cdot P(\text{healthy})}$$

In other terms:

$$\text{PPV} = \frac{\text{sensibility} \cdot \text{prevalence}}{\text{sensibility} \cdot \text{prevalence} + (1 - \text{specificity}) \cdot (1 - \text{prevalence})}$$

https://www.youtube.com/watch?v=JX4Je4bO4Zw&ab_channel=MichelvanBiezen

Negative predictive value (NPV): the probability of being healthy provided that the test was negative. Again, we apply Bayes Theorem:

$$\text{NPV} = P(\text{healthy} | -) = \frac{P(-|\text{healthy}) \cdot P(\text{healthy})}{P(-)}$$

The probability of a negative result is both, the probability of having a negative result and the subject being healthy and the probability of having a negative result and the subject being sick:

$$NPV = \frac{P(-|healthy) \cdot P(healthy)}{P(- \cap healthy) + P(- \cap sick)} = \frac{P(-|healthy) \cdot P(healthy)}{P(-|healthy) \cdot P(healthy) + P(-|sick) \cdot P(sick)}$$

In other terms:

$$NPV = \frac{\text{specificity} \cdot (1 - \text{prevalence})}{\text{specificity} \cdot (1 - \text{prevalence}) + (1 - \text{sensitivity}) \cdot \text{prevalence}}$$

In conclusion, with the predictive values we can estimate the probability of the subject's condition based on the probability of a test being positive if the subject is sick (sensitivity), the probability of the test being negative if the subject is healthy (specificity) and the probability of the disease (prevalence).

Clinical examples

We are going to analyse two possible situations, one in which the test has a high specificity and low sensitivity, and the other in which the test has a low specificity and high sensitivity provided a constant disease prevalence. We normally want a test to present high specificity and sensitivity, but in reality, if there is some overlapping between the distribution of the values of a biomarker, increasing one will decrease the other.

Test with high specificity and low sensitivity: the prevalence is $100/1100 = 0.09$

	Sick	Healthy	Total
Positive Test	68	20	88
Negative Test	32	980	1012
Total	100	1000	1100

In this case, we can calculate the specificity and sensitivity as:

$$\text{a) Specificity} = \frac{TN}{TN+FN} = \frac{980}{980+20} = 0.98 \text{ or } 98\%$$

$$\text{b) Sensitivity} = \frac{TP}{TP+FP} = \frac{68}{68+32} = 0.68 \text{ or } 68\%$$

With that we may ask ourselves if a patient has a positive result, what is the probability of them being actually sick. For that we calculate the positive predictive value as:

$$PPV = \frac{\text{sensitivity} \cdot \text{prevalence}}{\text{sensitivity} \cdot \text{prevalence} + (1 - \text{specificity}) \cdot (1 - \text{prevalence})} = \frac{0.68 \cdot 0.09}{0.68 \cdot 0.09 + (1 - 0.98) \cdot (1 - 0.09)}$$

$$PPV = 0.77 \text{ or } 77\%$$

This means that there is a chance in four that the patient is actually healthy after a positive test result. In the same manner, we can calculate the probability of the patient being healthy after a negative test. For that we calculate the negative predictive value as:

$$NPV = \frac{\text{specificity} \cdot (1 - \text{prevalence})}{\text{specificity} \cdot (1 - \text{prevalence}) + (1 - \text{sensitivity}) \cdot \text{prevalence}} = \frac{0.98 \cdot (1 - 0.09)}{0.98 \cdot (1 - 0.09) + (1 - 0.98) \cdot 0.09}$$

$$NPV = 0.97 \text{ or } 97\%$$

Consequently, with high specificity and low sensibility we have more confidence in predicting a subject to be healthy than to be sick after a test result.

https://www.youtube.com/watch?v=QFScbw9WKpM&ab_channel=MichelvanBiezen

Test with low specificity and high sensibility: the same prevalence as before, $100/1100 = 0.09$

	Sick	Healthy	Total
Positive Test	98	320	418
Negative Test	2	680	682
Total	100	1000	1100

In this case, we can calculate the specificity and sensibility as:

$$\text{a) Specificity} = \frac{TN}{TN+FN} = \frac{680}{680+320} = 0.68 \text{ or } 68\%$$

$$\text{b) Sensibility} = \frac{TP}{TP+FP} = \frac{98}{98+2} = 0.98 \text{ or } 98\%$$

With that we may ask ourselves if a patient has a positive result, what is the probability of them being actually sick. For that we calculate the positive predictive value as:

$$PPV = \frac{\text{sensibility} \cdot \text{prevalence}}{\text{sensibility} \cdot \text{prevalence} + (1 - \text{specificity}) \cdot (1 - \text{prevalence})} = \frac{0.98 \cdot 0.09}{0.98 \cdot 0.09 + (1 - 0.68) \cdot (1 - 0.09)}$$

$$PPV = 0.23 \text{ or } 23\%$$

This means that there is a four in five chance that the patient is actually healthy after a positive test result. In the same manner, we can calculate the probability of the patient being healthy after a negative test. For that we calculate the negative predictive value as:

$$NPV = \frac{\text{specificity} \cdot (1 - \text{prevalence})}{\text{specificity} \cdot (1 - \text{prevalence}) + (1 - \text{sensitivity}) \cdot \text{prevalence}} = \frac{0.68 \cdot (1 - 0.09)}{0.68 \cdot (1 - 0.09) + (1 - 0.98) \cdot 0.09}$$

$$NPV = 0.099 \text{ or } 9.9\%$$

Consequently, with high sensibility and low specificity we have more confidence in predicting a subject to be sick than to be healthy after a test result. Although the reduction in specificity greatly diminishes the discriminatory capacity of the test, as small percentages changes in specificity translates in great change in absolute values because in a normal population, the prevalence of the disease is usually very small.

For further reading:

Prior and posterior probability

https://www.investopedia.com/terms/p/prior_probability.asp

<https://www.investopedia.com/terms/p/posterior-probability.asp>

Bayes theorem:

<https://www.investopedia.com/terms/b/bayes-theorem.asp>

<https://towardsdatascience.com/bayes-theorem-the-idea-behind-naive-bayes-algorithm-f7068834a4d7>

<https://www.statisticshowto.com/probability-and-statistics/probability-main-index/bayes-theorem-problems/>

<https://towardsdatascience.com/bayes-theorem-for-medical-test-f1fb12b579c6>

Predictive values

[https://www.jclinepi.com/article/S0895-4356\(20\)31225-7/fulltext](https://www.jclinepi.com/article/S0895-4356(20)31225-7/fulltext)