Understanding statistics can be challenging. Unfortunately, familiarity with some statistics are necessary to help you understand your genetic test results.

One statistical term that is important in prenatal genetics, particularly with cfDNA, is **positive predictive value (PPV)**. PPV answers the question:

If my test comes back 'high-risk' or 'abnormal', what are the chances that someone in my exact position (same age, background risk, etc.) will have a baby with the condition that I tested positive for?

In other words, what are the chances that my positive test result is a true or actual positive?

The equation that is used to calculate PPV is:

Sensitivity X Prevalence / [Sensitivity X Prevalence + (1 – Specificity)(1 – Prevalence)]

Let's break all of these terms down:

- Sensitivity measures the proportion of babies WITH a condition who are correctly identified. For example, if 100 babies have Down syndrome and the test detects 60 of the babies who have it, then the test would have a sensitivity of 60% for Down syndrome.
  - For Down syndrome specifically, most labs quote a greater than 99% sensitivity. This means that for most people who take the test, there is over a 99% chance that if the baby has Down syndrome the test will come back 'positive' or 'high-risk'. When a lab says there is a greater than 99% sensitivity, it does NOT mean that if you receive a 'positive' or 'high-risk' result there is a 99% chance that your baby has that condition.
- Specificity measures the proportion of babies WITHOUT a condition who are correctly identified. For example, if testing was done for 100 babies that do not have a chromosome condition, and 80 received a 'normal', 'negative', or 'low-risk' result, then the specificity of the test would be 80%. This would also mean that 20% of the babies would have a false positive result, meaning the result was 'positive' or 'high-risk', but the baby does not actually have the condition.
  - For Down syndrome specifically, most labs quote a greater than 99% specificity. This means that if a pregnancy does NOT have Down syndrome, there is a greater than 99% chance that the test will come back 'negative' or 'low-risk'.

- Prevalence is how common the condition is in the selected population. For example, chromosome conditions such as Down syndrome tend to happen more frequently as women get older. The chance for a 25-year-old woman to have a baby with Down syndrome is approximately 1 in 1250, while the chance for a 30-year-old woman is 1 in 840. A 35-year-old woman has a 1 in 356 chance to have a baby with Down syndrome.

To put this all in practice, let's calculate the PPVs for our 25-, 30-, and 35-year-old patients above for their cfDNA testing. Most cfDNA testing labs report that they have an approximate 99.9% sensitivity and specificity.

For the 25-year-old:

Sensitivity (0.999) X Prevalence (1/1041 = 0.00096061) / Sensitivity (0.999) X Prevalence (0.00096061) + [1 – Specificity (0.999)][1 – Prevalence (0.00096061)]

So, we're left with:

0.999 X 0.00096061 / 0.999 X 0.00096061 + (**1 – 0.999**)(**1 – 0.00096061**)

0.999 X 0.00096061 / 0.999 X 0.00096061 + **(0.001)(0.99903939)**

0.999 X 0.00096061 / **0.999 X 0.00096061** + 0.00099904

0.999 X 0.00096061 / 0.00095965 + 0.0009904

0.00095965 / **0.00095965 + 0.0009904**

0.00095965 / 0.00195005

0.492

So, if a 25-year-old woman has a 'positive' or 'high-risk' cfDNA result for Down syndrome, there's only a 49.2% chance that her pregnancy actually has Down syndrome.

For the 30-year-old woman, using the same formula outlined above:

(0.999) X (1/701 = 0.00142653) / (0.999) X (0.00142653) + (**1 – 0.999**)(**1 – 0.00142653**)

0.999 X 0.00142653 / 0.999 X 0.00142653 + **(0.001)(0.99857347)**

0.999 X 0.00142653 / **0.999 X 0.00142653** + 0.00099857

0.999 X 0.00142653 / 0.0014251 + 0.00099857

0.0014251 / **0.0014251 + 0.00099857**

0.0014251 / 0.00242367

0.588

So, if a 30-year-old woman has a 'positive' or 'high-risk' cfDNA result for Down syndrome, there's only a 58.8% chance that her pregnancy actually has Down syndrome.

For the 35-year-old woman, using the same formula again:

(0.999) X (1/297 = 0.003367) / (0.999) X (0.003367) + (**1 – 0.999**)(**1 – 0.003367**)

0.999 X 0.003367 / 0.999 X 0.003367 + **(0.001)(0.996633)**

0.999 X 0.003367 / **0.999 X 0.003367** + 0.000996633

0.999 X 0.003367 / 0.003363633 + 0.000996633

0.003363633 / **0.003363633 + 0.000996633**

0.003363633 / 0.004360266

0.771

So, if a 35-year-old woman has a 'positive' or 'high-risk' cfDNA result for Down syndrome, there's only a 77.1% chance that her pregnancy actually has Down syndrome.

***These are just examples using hypothetical sensitivities and specificities.

As these calculations show, as the chance (prevalence) of the condition increases along with mom's age, the PPV also increases. The more rare the condition is, the lower the PPV likely is (despite very high sensitivity and sensitivity).

Many labs do not provide a PPV calculation, but your genetic counselor or other provider should be able to help you calculate the PPV.

Click here to learn more about scheduling a genetic counseling appointment for pregnancy-related questions.