



# BayesianReasoning

<https://github.com/gorkang/BayesianReasoning>

An R package to help with medical risks comprehension and decision making in medical contexts.



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@gorkang



# Cognitive mechanisms behind the comprehension of Bayesian reasoning problems



Improve medical risks  
communication

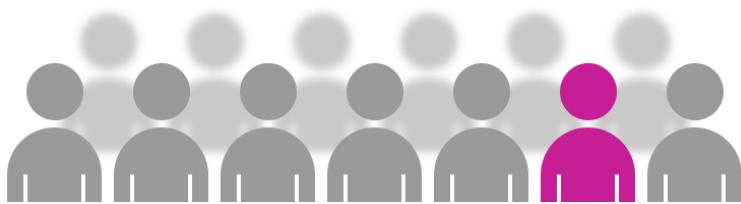


Decision making

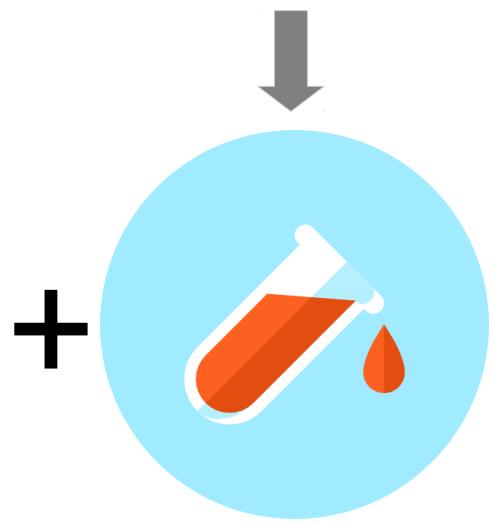


**Fondecyt**  
Fondo Nacional de Desarrollo  
Científico y Tecnológico

Bayesian reasoning is an area inside Cognitive Psychology studying how humans update beliefs after receiving new information

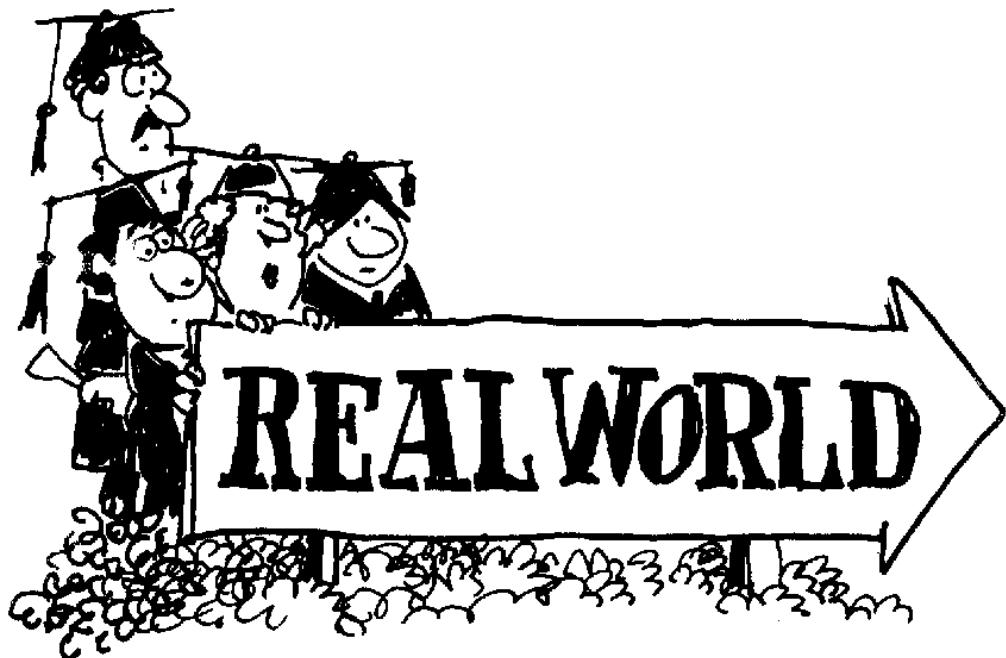


1 out of 1000 have disease X



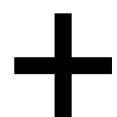
# Consent forms

Shared decision making





Information about the test  
and the medical condition



Medical  
condition?

# How people deal with Consent Forms?



2.3.1 Payment types (child assignment clause): In addition to any monetary payment that the user may make to NameDrop, by agreeing to these Terms of Service, and in exchange for service, all users of this site agree to immediately assign their first-born child to NameDrop, Inc. If the user does not yet have children, this agreement will be enforceable until the year 2050. All individuals assigned to NameDrop automatically become the property of NameDrop, Inc. No exceptions.

Service, and in exchange for service, all users of this site agree to immediately assign  
their first-born child to NameDrop, Inc. If the user does not yet have children, this

<2%  
complained about the Child clause

# Consent forms

Prenatal screening example



## PRENATAL TEST



Clear ANSWERS to  
Questions that Matter

## What is a Trisomy?

Humans have 23 pairs of chromosomes, which are strands of DNA that carry genetic information. A trisomy is a chromosomal condition that occurs when there are three copies of a particular chromosome instead of the expected two.

### Trisomy 21

Trisomy 21 is due to an extra chromosome 21 and is the most common trisomy at the time of birth. Trisomy 21, also called Down syndrome, is associated with mild to moderate intellectual disabilities and may also lead to digestive disease and congenital heart defects. It is estimated that trisomy 21 is present in 1 out of every 800 births in Canada.<sup>1</sup>

### Genetic Test

When you're pregnant, your blood contains fragments of your fetus' DNA. The Prenatal Test is a new type of test that analyzes this DNA in a sample of your blood to determine the risk of trisomy 21.

**A positive result does not necessarily mean that Trisomy 21 is present.**

The Prenatal test has been shown in clinical testing to identify 99% of trisomy 21 cases and to have a false-positive rate of less than 0.1%.

### For Women of Any Age or Risk Category

Traditional screening tests can miss as many as 20% of trisomy 21 cases in pregnant women.<sup>1</sup> The Prenatal Test was developed to be a more accurate prenatal screening test for women of any age or risk category. It is a new DNA-based blood test that has been extensively tested in pregnant women ages 18 to 50.<sup>2,3</sup>

### Minimizes Need for Follow-Up Tests

The greater accuracy and low false-positive rate of the Prenatal test compared to traditional tests minimizes the chance further testing would be recommended due to a positive result. Follow-up testing might include an invasive procedure, such as amniocentesis.

<sup>1</sup>Norton M, et al. *N Engl J Med*. 2015;372:1589-1597.

<sup>2</sup>Nicolaides KH, et al. *Am J Obstet Gynecol*. 2012 Nov;207(5):374.e1-6.

<sup>3</sup>Canadian Down Syndrome Society

## PRENATAL TEST



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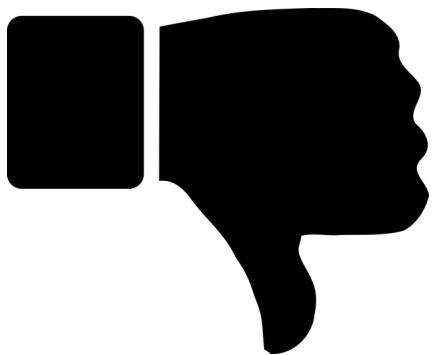
$$p(\text{Trisomy 21} | + \text{test}) =$$

$$(A) \frac{1 \text{ out of } 800 \times 99\%}{(1 \text{ out of } 800 \times 99\%) + (799 \text{ out of } 800 \times 0.1\%)} =$$

$$(B) \frac{0.123}{0.123 + 0.0998} = 0.55$$



But... how bad is it?



# Accuracy

General population

~5 to 25%

Experts

~8 to 32%

+Visual aid

~50%

# 0%

gets what a +  
result means

## PRENATAL TEST



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2Nicolae A, et al. Am J Obstet Gynecol. 2012 Nov;207(5):374.e1-6.  
3Canadian Down Syndrome Society.

Hit rate  
**99%**

False  
positives  
**2%**

Prevalence  
**1 out of 1500**

**p(Disease|+)?**

<25%

25-49%

50%

51-75%

>75%

Hit rate  
**99%**

False  
positives  
**2%**

Prevalence  
**1 out of 1500**

**p(Disease|+)?**

3%

<25%

25-49%

50%

51-75%

>75%

PPV (21): ~1.60%

PPV (18): ~0.48%

PPV (13): ~0.32%

Navarrete, G., Correia, R., & Froimovitch, D. (2014). Communicating risk in prenatal screening: the consequences of Bayesian misapprehension. *Frontiers in Psychology*, 5(1272), 1–4. doi:10.3389/fpsyg.2014.01272

Harmony	
Cost*	\$795.00

\*Subject to change without notice.

**What is a Trisomy?**

Harmony™ PRENATAL TEST

Trisomy 21 is due to an extra chromosome 21 and is the most common trisomy at the time of birth. Trisomy 18, also called Edwards syndrome, is associated with mild to moderate intellectual disabilities and may also lead to digestive disease and congenital heart defects. It is estimated that trisomy 21 is present in 1 out of every 600 births in North America.<sup>1</sup>

**TRISOMY 21**

Trisomy 18 is due to an extra chromosome 18. Trisomy 18, also called Edwards syndrome, is associated with mild to moderate intellectual disabilities and may also lead to digestive disease and congenital heart defects. It is estimated that trisomy 21 is present in approximately 1 out of every 6000 births.<sup>2</sup>

**TRISOMY 18**

Trisomy 13 is due to an extra chromosome 13. Trisomy 13, also called Patau syndrome, is associated with mild to moderate intellectual disabilities and may also lead to digestive disease and congenital heart defects. It is estimated that trisomy 21 is present in approximately 1 out of every 6000 births.<sup>3</sup>

**TRISOMY 13**

The Harmony™ Prenatal Test is based on the newest advances in non-invasive prenatal testing. It is simple and safe blood test that has been shown clinically to detect the risk of fetal trisomies in maternal blood with high accuracy.<sup>4</sup>

**HOW IS THE HARMONY™ PRENATAL TEST DIFFERENT FROM OTHER PRENATAL TESTS?**

The Harmony™ Prenatal Test is based on the newest advances in non-invasive prenatal testing. It is simple and safe blood test that has been shown clinically to detect the risk of fetal trisomies in maternal blood with high accuracy.<sup>4</sup>

1Canadian Down Syndrome Society. National Survey of Down Syndrome in Canada. 2012. Accessed April 2013. URL: <http://www.cdsociety.org/CDSS/CDSS%20National%20Survey%20of%20Down%20Syndrome%20in%20Canada%202012.pdf>

2U.S. National Library of Medicine. Trisomy 18. Last updated: 2012-09-01. Accessed April 2013. URL: <http://www.ncbi.nlm.nih.gov/pubmed/23021229>

3U.S. National Library of Medicine. Trisomy 13. Last updated: 2012-09-01. Accessed April 2013. URL: <http://www.ncbi.nlm.nih.gov/pubmed/23021228>

4Harmonix Medical Research Foundation. The Harmony™ Prenatal Test. Last updated: 2012-09-01. Accessed April 2013. URL: <http://www.harmonixmedical.com/harmony-prenatal-test.html>

**Harmony™ Prenatal Test**

Simple, safe and accurate for you and your pregnancy.

The Harmony Prenatal Test is a non-invasive test that detects the risk of fetal anomalies in pregnant women 10 weeks or more, based on directed analysis of DNA in maternal blood.

WHAT WILL THE HARMONY™ PRENATAL TEST TELL ME AND MY HEALTH CARE PROVIDER?

The Harmony Prenatal Test assesses the risk of three fetal trisomies by measuring the relative amount of chromosomes in maternal blood.

HOW IS THE HARMONY™ PRENATAL TEST DIFFERENT FROM OTHER PRENATAL TESTS?

The Harmony™ Prenatal Test is based on the newest advances in non-invasive prenatal testing. It is simple and safe blood test that has been shown clinically to detect the risk of fetal trisomies in maternal blood with high accuracy.<sup>4</sup>

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**An advance in non-invasive fetal trisomy testing**

**Integrated Genetics**  
LabCorp Specialty Testing Group

# Consequences



# Breast Cancer Early Detection

by mammography screening

Numbers for women aged 50 years or older who participated in screening for 10 years or more

1000 women without screening:

● Women who died from breast cancer:

● Women who died from all types of cancer:

● Women who learned after a biopsy that their diagnosis was a false-positive:

● Women who were diagnosed and treated for breast cancer unnecessarily:

● Remaining women:

1000 women with screening:

● Women who died from breast cancer:

● Women who died from all types of cancer:

● Women who learned after a biopsy that their diagnosis was a false-positive:

● Women who were diagnosed and treated for breast cancer unnecessarily:

● Remaining women:

5

21

—

—

979

4

21

—

100

5

874

Source:

Gøtzsche, PC, Jørgensen, KJ (2013). Cochrane Database of Systematic Reviews (6): CD001877

Numbers in the facts box are rounded. Where no data for women above 50 years of age are available, numbers refer to women above 40 years of age.

[www.harding-center.mpg.de](http://www.harding-center.mpg.de)

# National (USA) Expenditure For False-Positive Mammograms And Breast Cancer Overdiagnoses

Estimated At  
**\$4 Billion A Year**

Ong, M.-S., & Mandl, K. D. (2015). National Expenditure For False-Positive Mammograms And Breast Cancer Overdiagnoses Estimated At \$4 Billion A Year, 4(4), 576–583. <https://doi.org/10.1377/hlthaff.2014.1087>



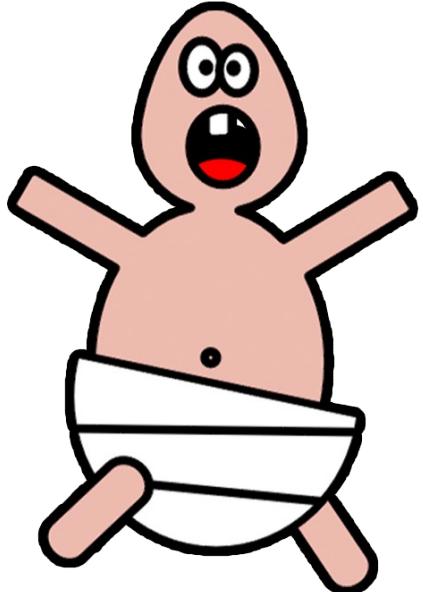
$$p\left(H\left|D\right.\right)\!=\!\frac{p\left(H\right).\,p\left(D\!\left|H\right.\right)}{p\left(H\right).\,p\left(D\!\left|H\right.\right)\!+\!p\left(\bar{H}\right).\,p\left(D\!\left|\bar{H}\right.\right)}$$



# BayesianReasoning

<https://github.com/gorkang/BayesianReasoning>

An R package to help with medical risks comprehension and decision making in medical contexts.



Work in progress with lots of moving parts and **horrible code**.

### Install with:

```
remotes::install_github("gorkang/BayesianReasoning").
```

### Bugs and Issues:

<https://github.com/gorkang/BayesianReasoning/issues>



# BayesianReasoning

Functions to plot and help understand  
Positive and Negative Predictive Values,  
and their relationship with test and  
disease characteristics.

# Epidemiology 101:

## **Positive Predictive Value (PPV)**

## **Negative Predictive Value (NPV)**



The **Positive Predictive Value** of a medical test is the probability that a positive result will mean having the disease →  $p(\text{Disease}|+)$

$$\text{PPV} = \frac{\text{TRUE +}}{\text{ALL +}}$$

(**TRUE +** and **FALSE +**)

The **Negative Predictive Value** of a medical test is the probability that a negative result will mean being healthy →  $p(\text{Healthy} | -)$

$$\text{NPV} = \frac{\text{TRUE } -}{\text{ALL } -}$$

(**TRUE -** and **FALSE -**)



# BayesianReasoning

## **PPV\_heatmap()**

Plot heatmaps with PPV/NPV

## **PPV\_diagnostic\_vs\_screening()**

Plots difference of PPV in diagnostic vs screening context

## **min\_possible\_prevalence()**

How high should the prevalence of a disease be to reach a desired PPV?



# BayesianReasoning

## **PPV\_heatmap()**

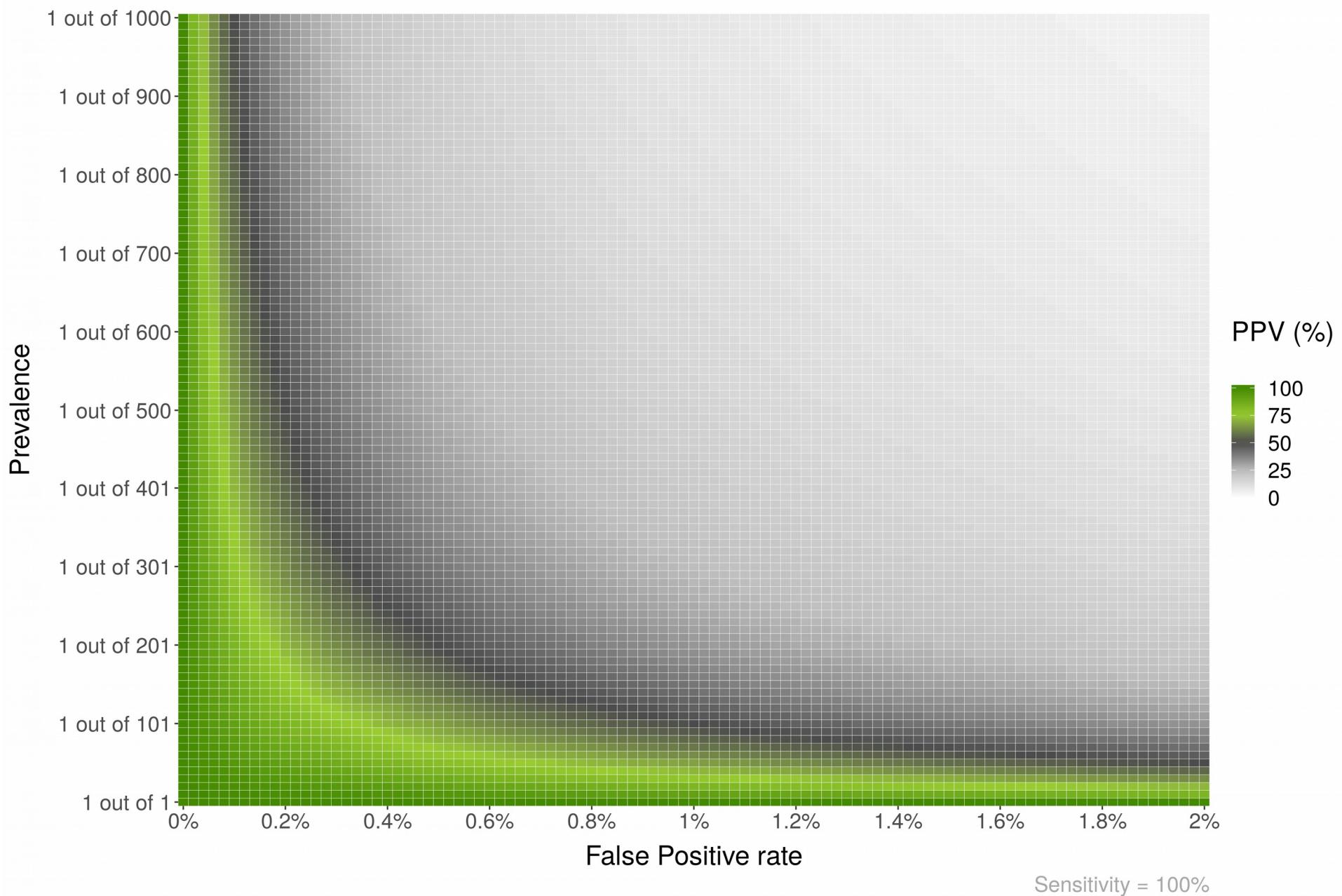
Plot heatmaps with PPV/NPV

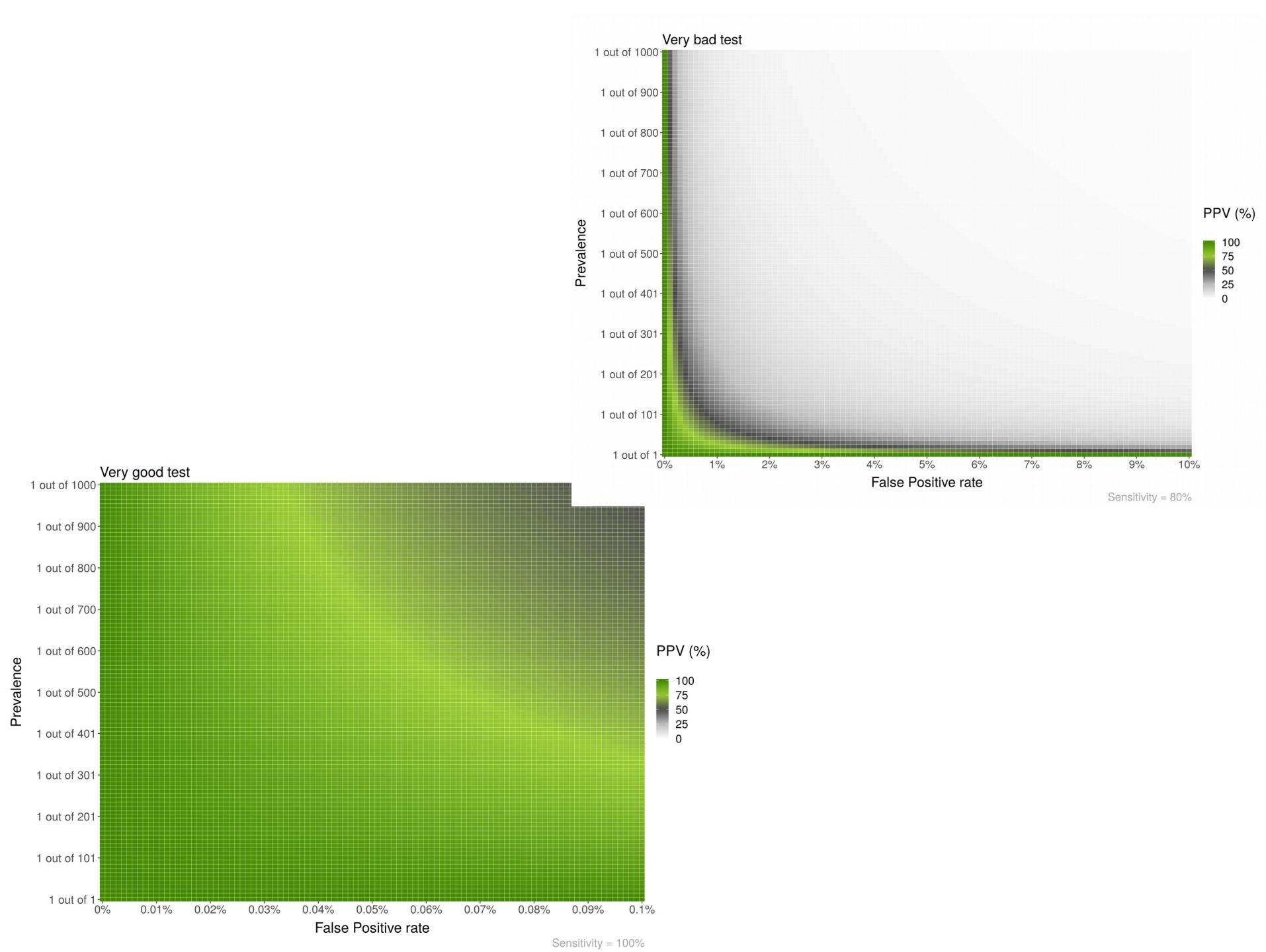
## PPV\_heatmap()

Plot heatmaps with PPV or NPV values for a given specificity and a range of Prevalences and False Positives. The basic parameters are:

- **Max\_Prevalence**: Max prevalence in y axis. "1 out of Max\_Prevalence"
- **Sensitivity**: Sensitivity of the test
- **Max\_FP**: False Positives (FP) are 1 - specificity.
- **Language**: "es" for Spanish or "en" for English

```
PPV_heatmap(Max_Prevalence = 1000,  
            Sensitivity = 100,  
            Max_FP = 2,  
            Language = "en")
```





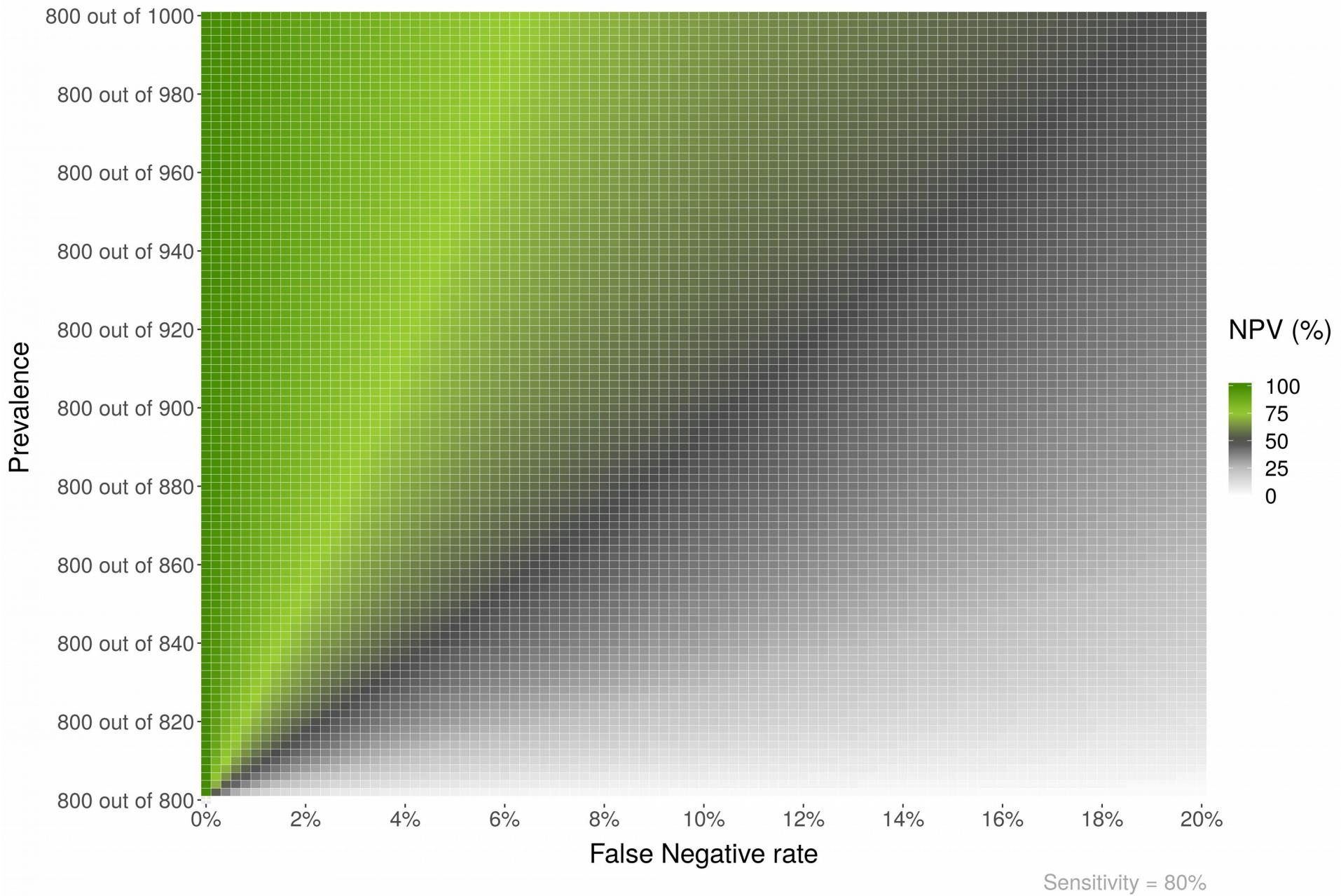
## PPV\_heatmap()

### NPV

You can also plot an NPV heatmap with the parameter:

- PPV\_NPV = "NPV".

```
PPV_heatmap(PPV_NPV = "NPV",
             Min_Prevalence = 800,
             Max_Prevalence = 1000,
             Sensitivity = 80,
             Max_FP = 5,
             Language = "en")
```



# PPV\_heatmap()

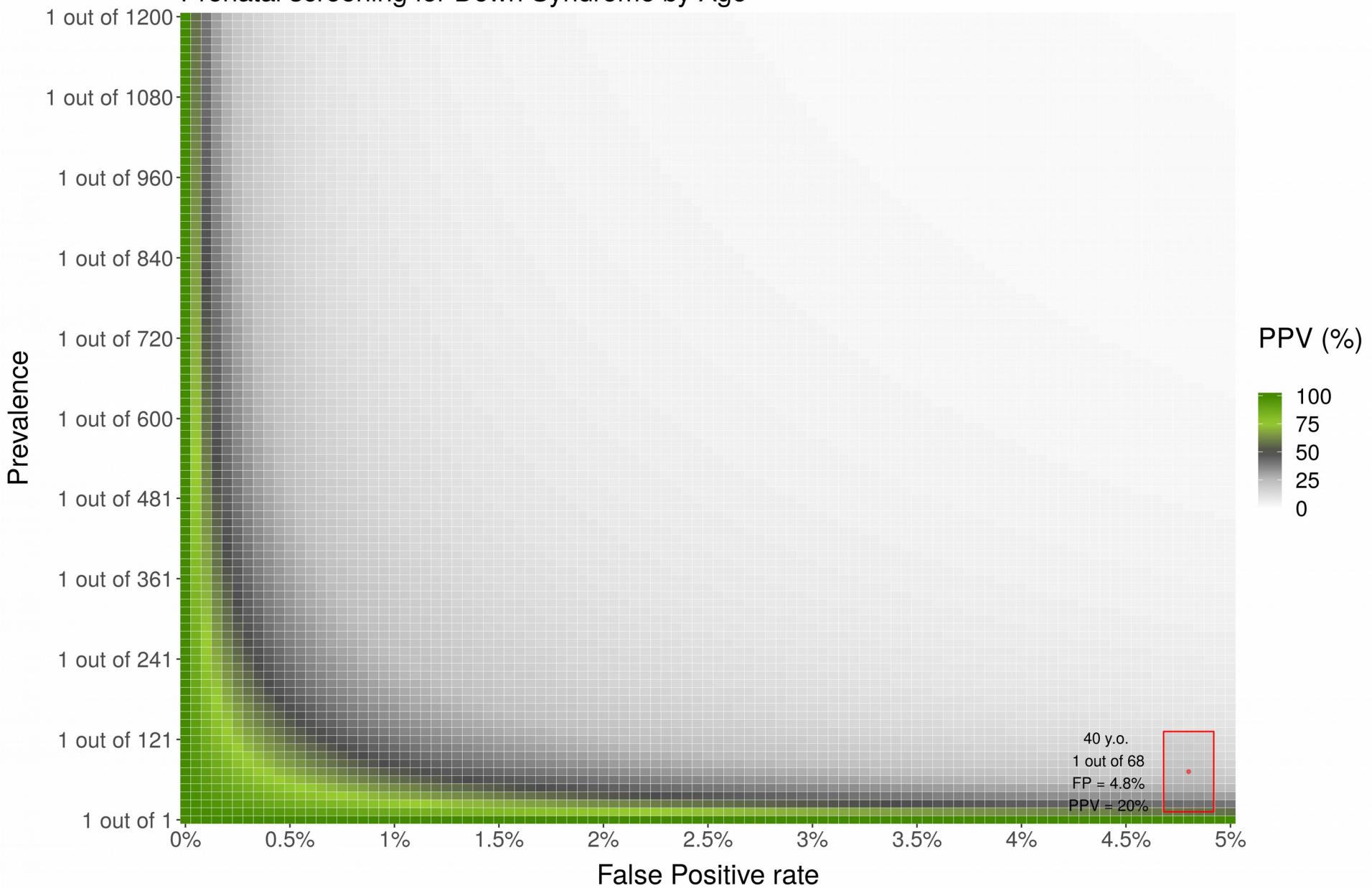
## Area overlay

You can add different types of overlay to the plots.

For example, an area overlay showing the point PPV for a given prevalence and FP or FN:

```
PPV_heatmap(Max_Prevalence = 1200, Sensitivity = 81, Max_FP = 5,  
            label_subtitle = "Prenatal screening for Down Syndrome by Age",  
            overlay = "area",  
            overlay_labels = "40 y.o.",  
            overlay_position_FP_FN = 4.8,  
            overlay_position_Prevalence = "1 out of 68")
```

## Prenatal screening for Down Syndrome by Age



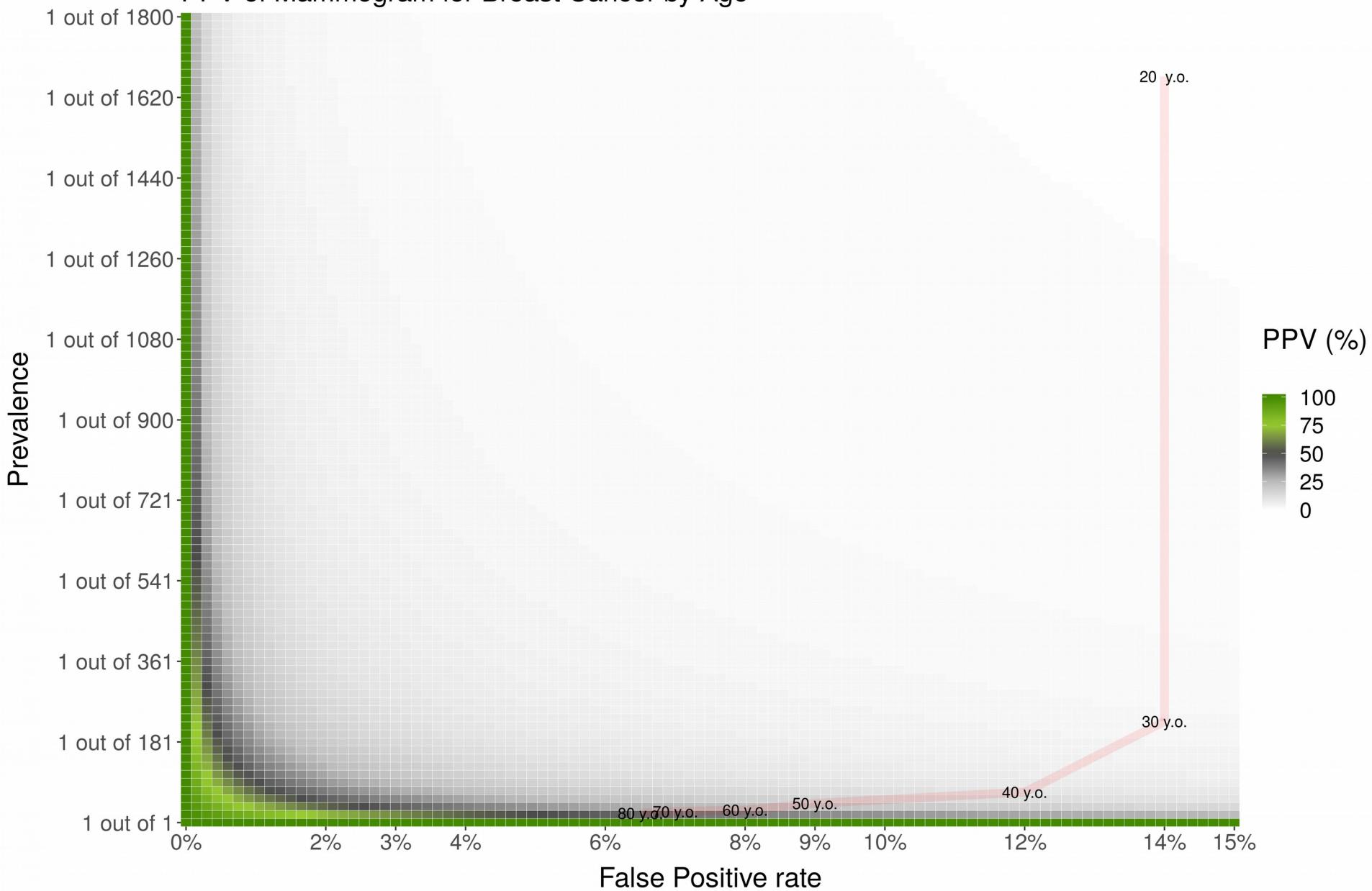
# PPV\_heatmap()

## Line overlay

Also, you can add a line overlay highlighting a range of prevalences and FP. This is useful, for example, to show how the PPV of a test changes with age:

```
PPV_heatmap(Max_Prevalence = 1800, Sensitivity = 90, Max_FP = 15,
             label_subtitle = "PPV of Mammogram for Breast Cancer by Age",
             overlay = "line",
             overlay_labels = c("80", "70", "60", "50", "40", "30", "20  y.o."),
             overlay_position_FP_FN = c(6.5, 7, 8, 9, 12, 14, 14),
             overlay_position_Prevalence = c(22, 26, 29, 44, 69, 227, 1667))
```

## PPV of Mammogram for Breast Cancer by Age



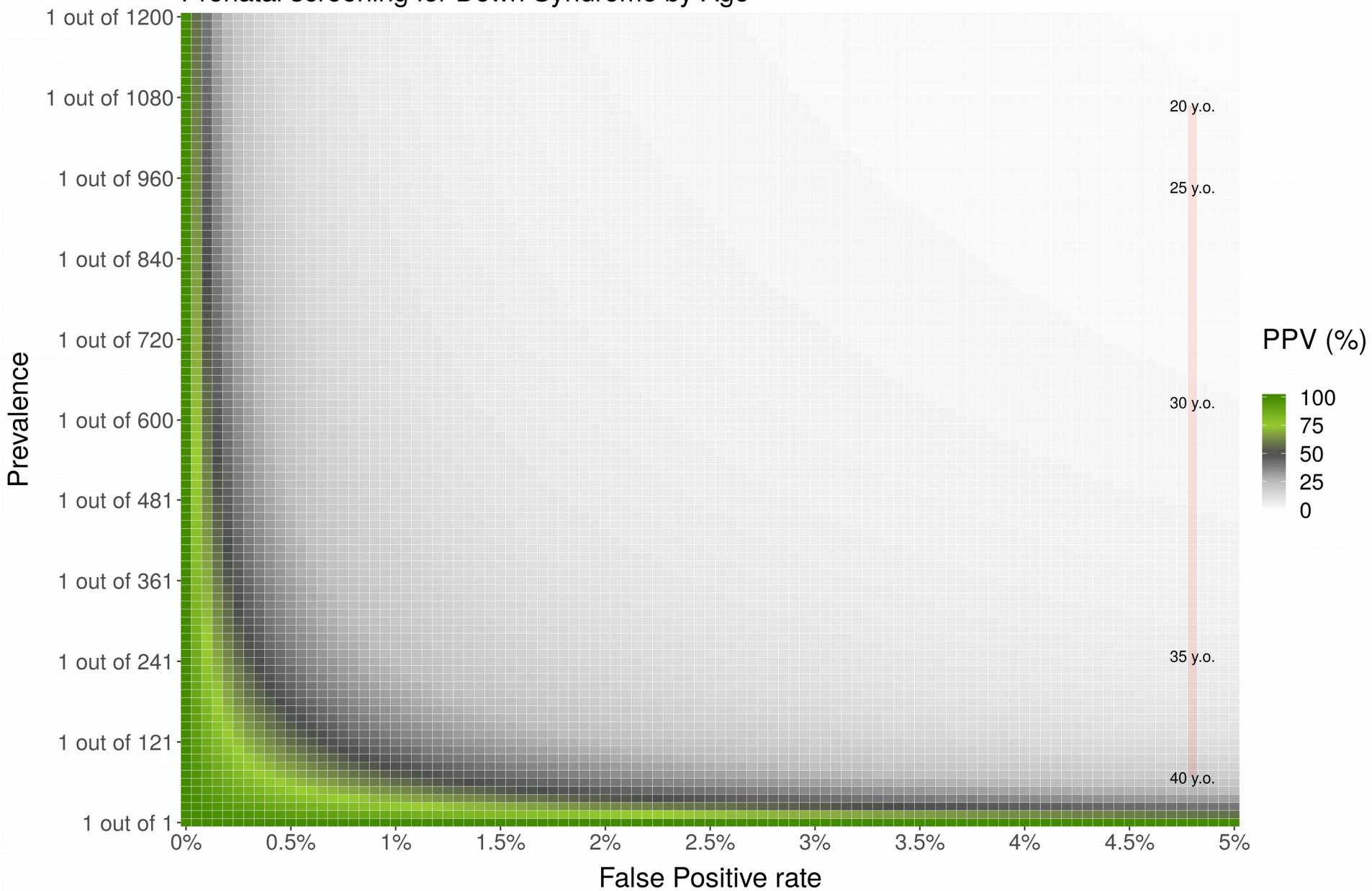
## PPV\_heatmap()

### Line overlay

Another example. In this case, the FP is constant across age:

```
PPV_heatmap(Max_Prevalence = 1200, Sensitivity = 81, Max_FP = 5,
             label_subtitle = "Prenatal screening for Down Syndrome by Age",
             overlay = "line",
             overlay_labels = c("40 y.o.", "35 y.o.", "30 y.o.", "25 y.o.", "20 y.o."),
             overlay_position_FP_FN = c(4.8, 4.8, 4.8, 4.8, 4.8),
             overlay_position_Prevalence = c(68, 249, 626, 946, 1068))
```

## Prenatal screening for Down Syndrome by Age





# BayesianReasoning

## **PPV\_diagnostic\_vs\_screening()**

Plots difference of PPV in diagnostic vs screening context

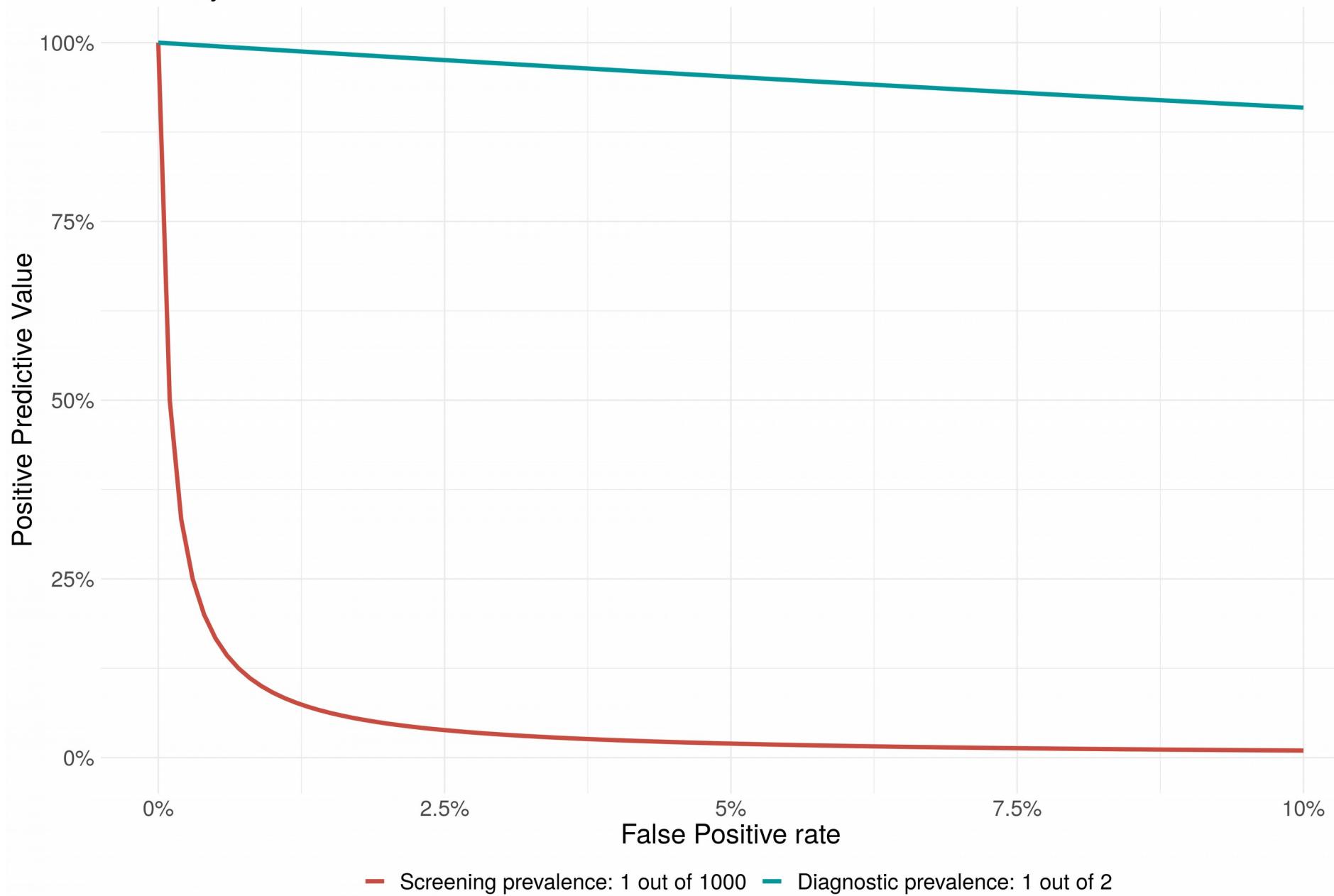
In scientific studies developing a new test for the early detection of a medical condition, it is quite common to use a sample where 50% of participants has a medical condition and the other 50% are normal controls.

**This has the unintended effect of maximizing the PPV of the test.**

## PPV\_diagnostic\_vs\_screening()

This function shows a plot with the difference between the PPV of a diagnostic context (very high prevalence; or a common study sample, e.g. ~50% prevalence) versus that of a screening context (lower prevalence).

Sensitivity = 100%





# BayesianReasoning

## **min\_possible\_prevalence()**

How high should the prevalence of a disease be to reach a desired PPV?

## min\_possible\_prevalence()

Imagine you would like to use a test in a population and want a 98% PPV. That is, IF a positive result comes out in the test, you would like a 98% chance that it is a true positive.

How high should the prevalence of the disease be in that group?

```
min_possible_prevalence(Sensitivity = 100,  
                         FP_test = 0.1,  
                         min_PPV_desired = 98)
```

> To reach a PPV of 98 when using a test with 100 % Sensitivity and 0.1 % False Positive Rate, you need a prevalence of at least 1 out of 21

## min\_possible\_prevalence()

Another example, with a very good test, and lower expectations:

```
min_possible_prevalence(Sensitivity = 99.9,
                        FP_test = .1,
                        min_PPV_desired = 70)
```

>To reach a PPV of 70 when using a test with 99.9 % Sensitivity and 0.1 % False Positive Rate, you need a prevalence of at least 1 out of 429





# BayesianReasoning

Improve medical risks communication

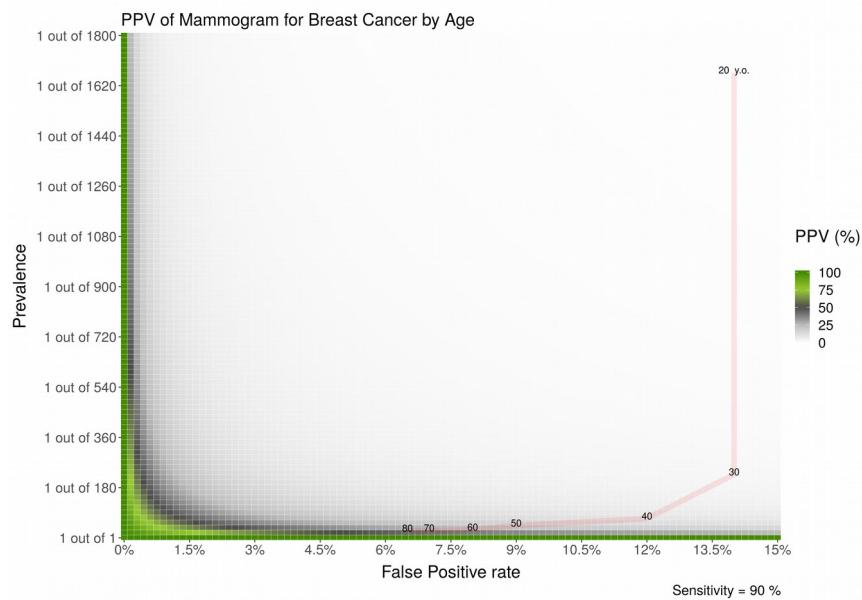


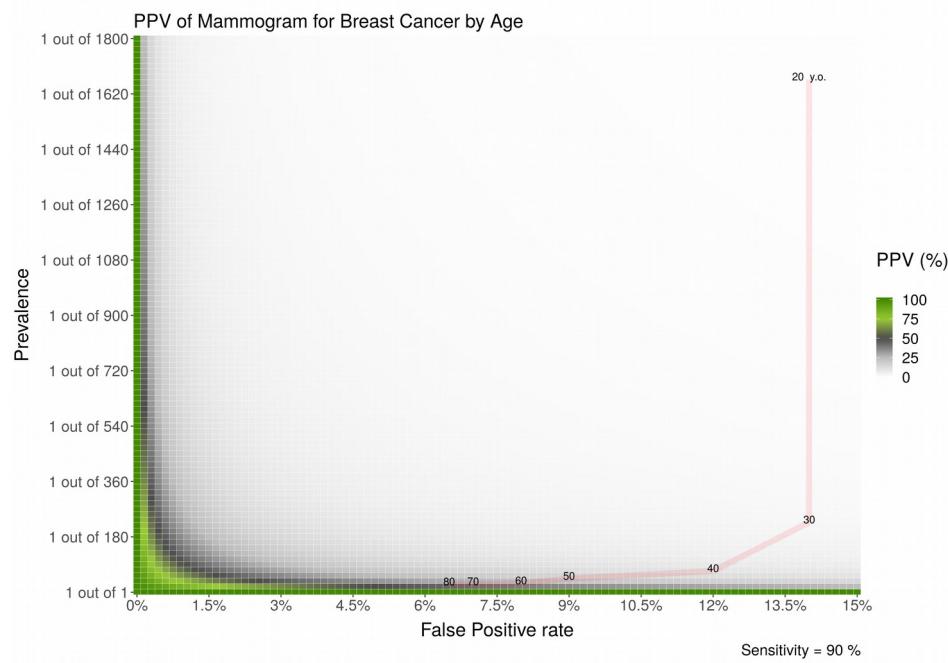
Decision making

$$p(Trisomy\ 21 \mid +\ test) =$$

$$(A) \frac{1\ out\ of\ 800 \times 99\%}{(1\ out\ of\ 800 \times 99\%) + (799\ out\ of\ 800 \times 0.1\%)} =$$

$$(B) \frac{0.123}{0.123 + 0.0998} = 0.55$$







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(2017-2019) Fondecyt Regular 1171035. Towards a more integrated model of Bayesian reasoning: calculation, understanding and decision making in medical contexts



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