Diagnostic Tests

Solymosi Norbert

Quantitative veterinary epidemiology

Department of Microbiology and Infectious Diseases
University of Veterinary Medicine Budapest

Lecture 3

Making a diagnosis

- assemble a list of differentials
- order the list as to which conditions are important, or more likely
- choose appropriate tests (and the order in which to do them)
- interpret the results

What is a test?

- any procedure that reduces uncertainty about the state of disease
- includes routine examination, questions posed during history taking, clinical signs, laboratory findings (haematology, serology, biochemistry, histopathology), post mortem findings

- Is a subject (individual, group, region, country)
  - diseased (abnormal, affected)
  - not diseased (normal, unaffected)?
- The testing process is imperfect
  - clarity of case definition (what is positive, what is negative)
  - quality of measurement tools
- Applications of testing
  - establish the presence of disease in an individual
  - establish the level of disease in a population
  - monitoring, screening and surveillance
- Test evaluation
  - The perfect diagnostic test allows us to differentiate between disease-positive and disease-negative individuals without error
  - Most tests that we use are imperfect
  - Imperfect tests should be compared with a 'gold standard' so we know how good they are

Stevenson 2012

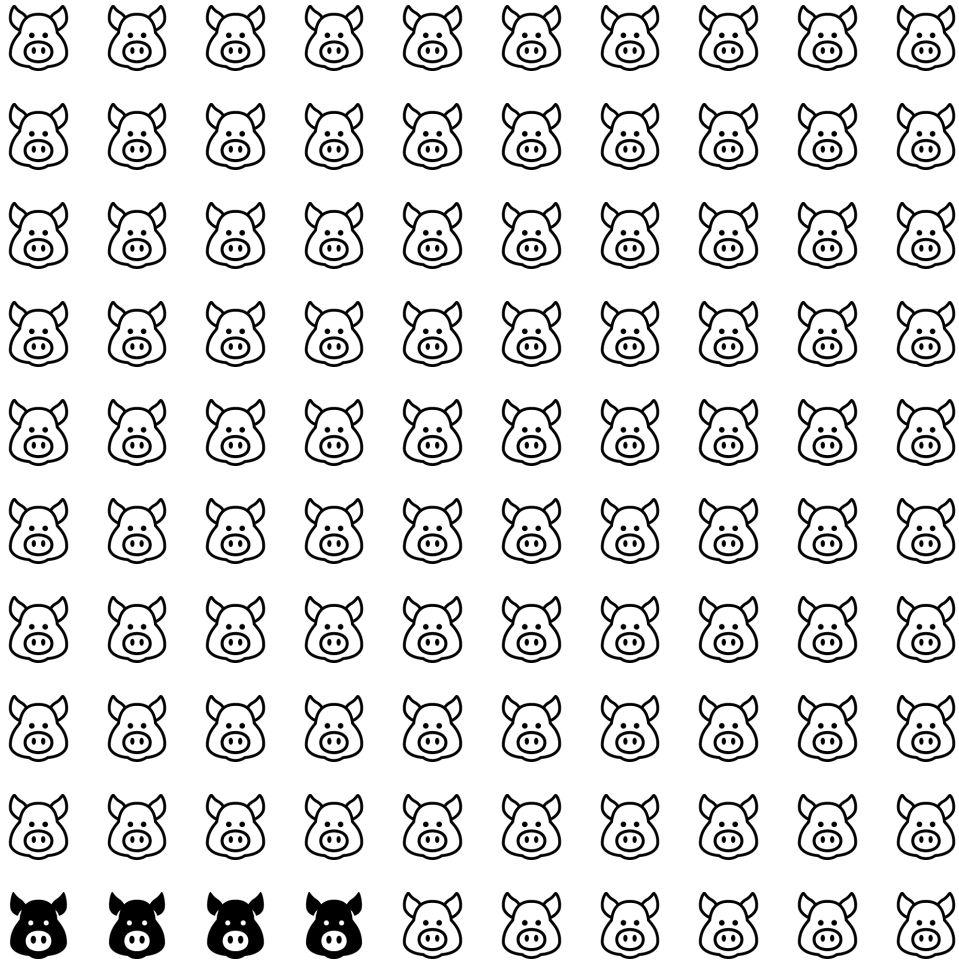
Contingency table

	Infection +	Infection −	Total
Test +	True positive a	False positive b	Test positive $a+b$
Test −	False negative c	True negative d	Test negative $c+d$
Total	$a+c$	$b+d$	$a+b+c+d$

infected pig

uninfected pig

let's say the prevalence of infection is 4% (4/100)

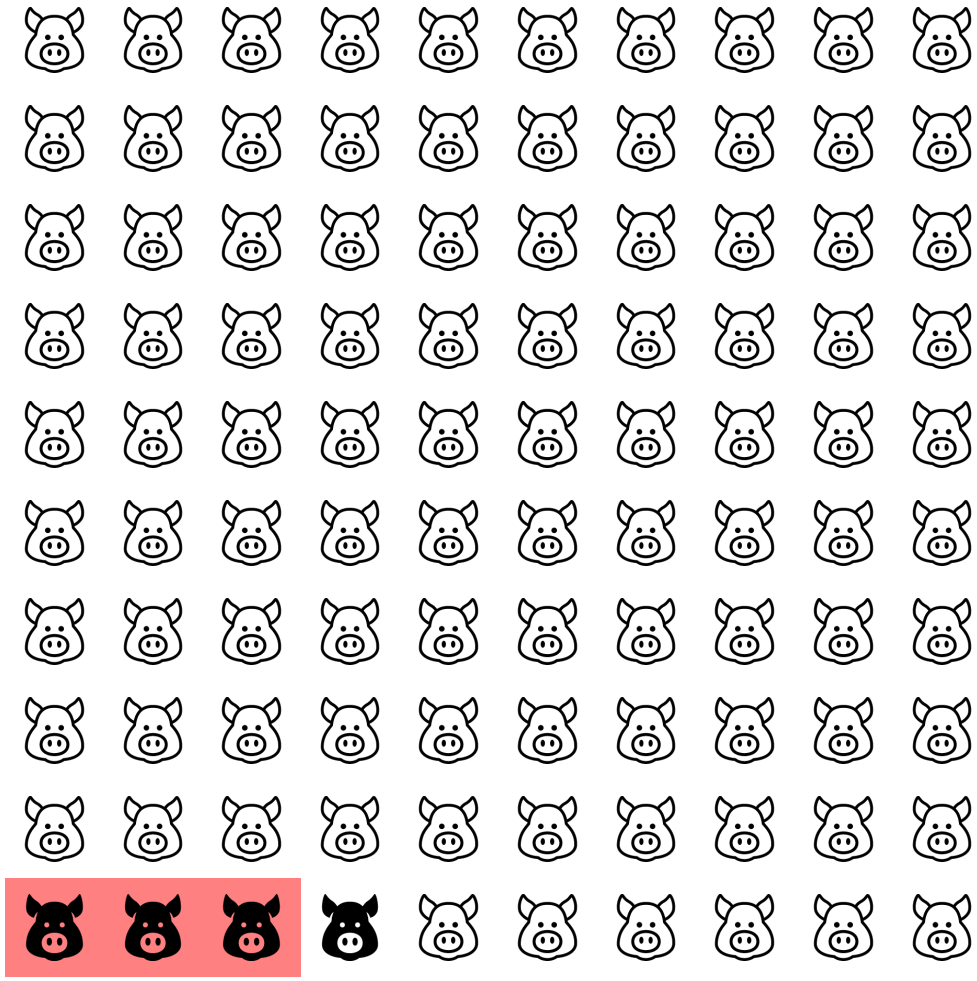


infected pig:

test positive

uninfected pig

with a diagnostic test 3 of 4 infected animals are positive



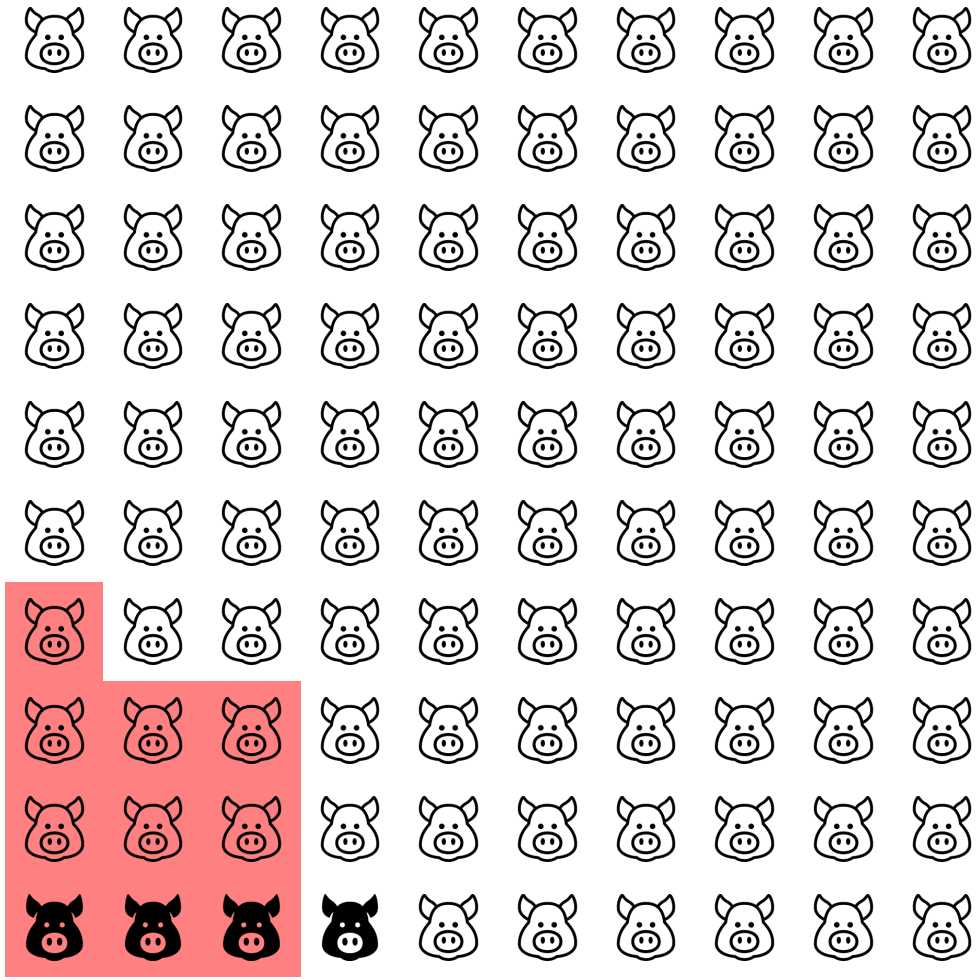
infected pig:

test positive

uninfected pig:

test positive

further 7 non infected animals were test positive



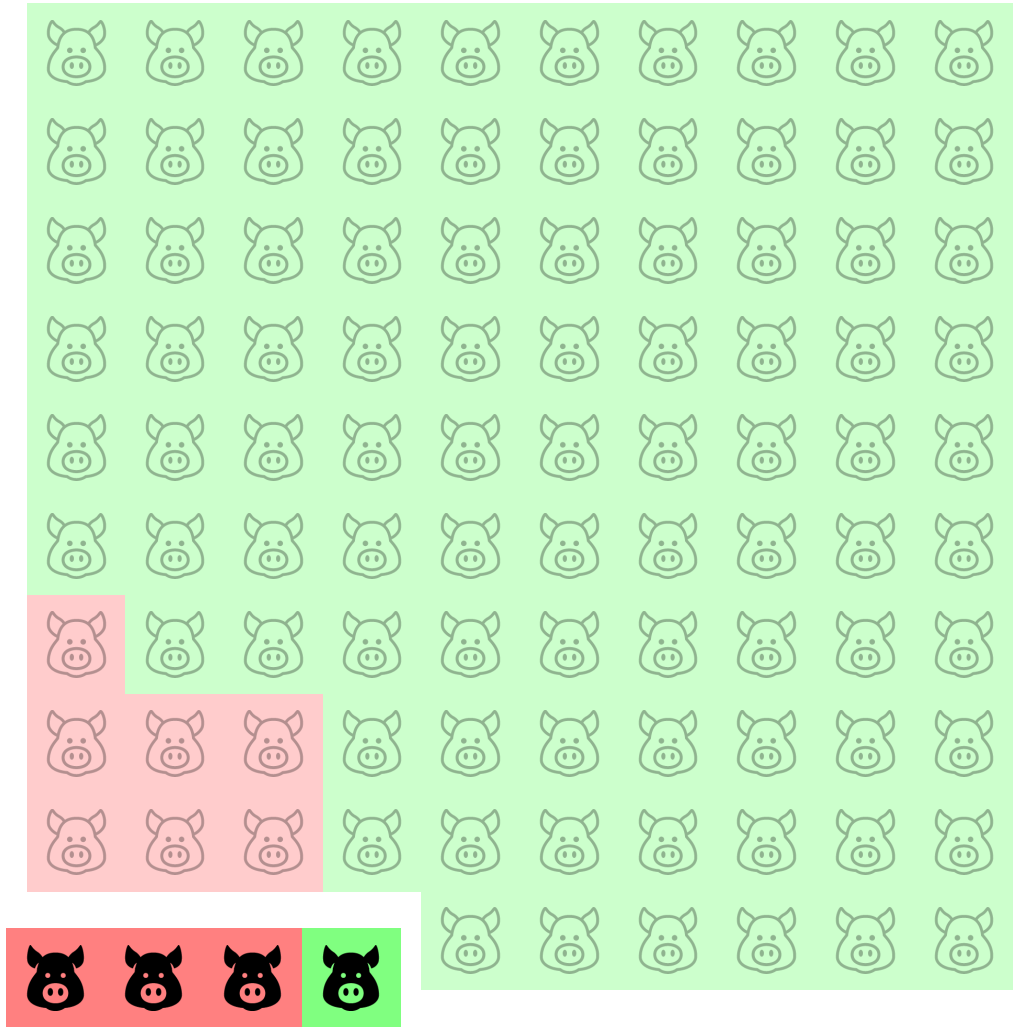
- uninfected pig:
  - test positive
  - test negative
- infected pig:
  - test positive
  - test negative

89 non infected and 1 infected animals were test negative

- uninfected pig:
  - test positive
  - test negative
- infected pig:
  - test positive
  - test negative

Sensitivity is the proportion of infected animals identified as positive by the test:

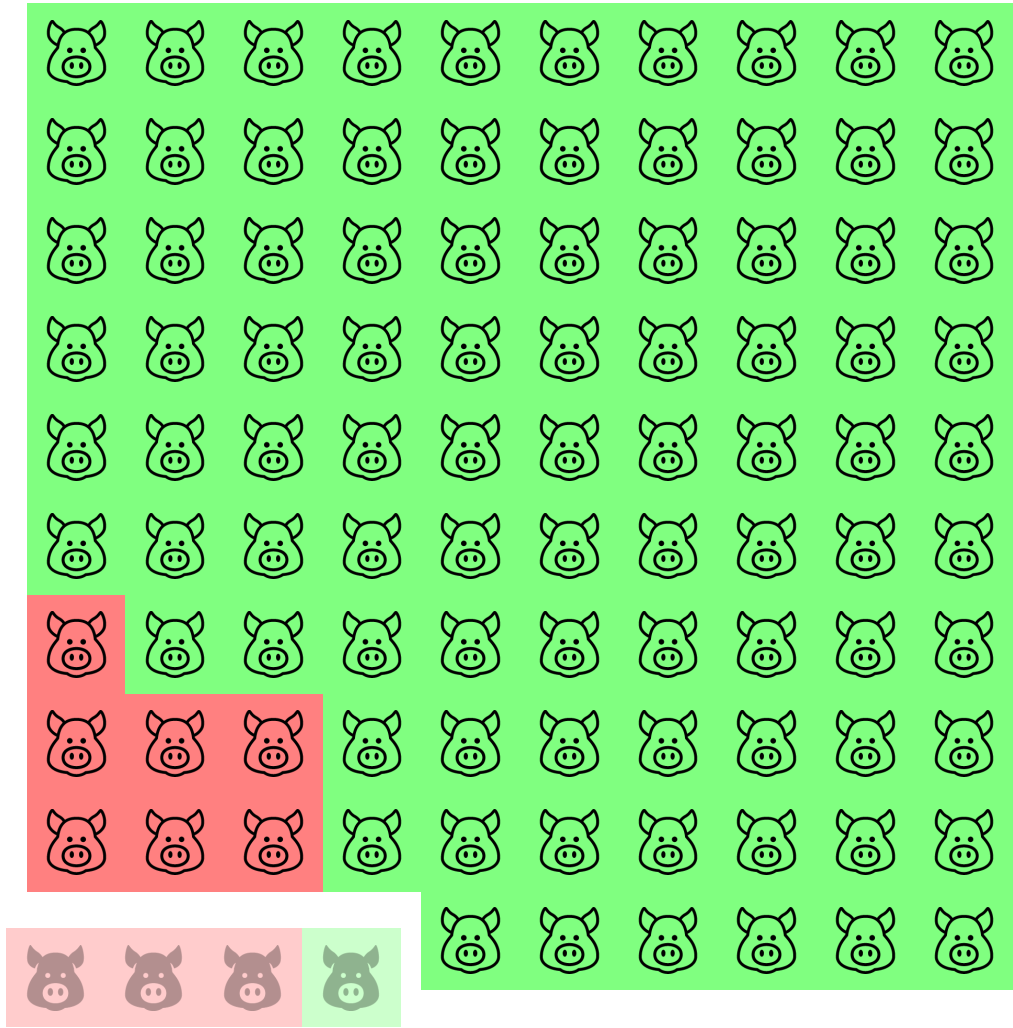
$$\frac{3}{4} = 0.75$$



- uninfected pig:
  - test positive
  - test negative
- infected pig:
  - test positive
  - test negative

Specificity is the proportion of uninfected animals identified as negative by the test:

$$\frac{89}{96} = 0.93$$



Contingency table

	Infection +	Infection −	Total
Test +	True positive a	False positive b	Test positive $a+b$
Test −	False negative c	True negative d	Test negative $c+d$
Total	$a+c$	$b+d$	$a+b+c+d$

	Infection +	Infection −	$\sum$
Test +	3	7	10
Test −	1	89	90
$\sum$	4	96	100

Sensitivity is the proportion of infected animals identified as positive by the test.
Or the probability that a truly diseased animal will be classified as diseased.

	Infection +	Infection −	Total
Test +	True positive a	False positive b	Test positive $a+b$
Test −	False negative c	True negative d	Test negative $c+d$
Total	$a+c$	$b+d$	$a+b+c+d$

Sensitivity is the proportion of infected animals identified as positive by the test.
Or the probability that a truly diseased animal will be classified as diseased.

	Infection +	Infection −	Total
Test +	True positive a	False positive b	Test positive $a+b$
Test −	False negative c	True negative d	Test negative $c+d$
Total	$a+c$	$b+d$	$a+b+c+d$

$$Se = \frac{a}{a+c} = \frac{3}{3+1} = 0.75$$

Specificity is the proportion of uninfected animals identified as negative by the test.
Or the probability that a truly non-diseased animal will be classified as non-diseased.

	Infection +	Infection −	Total
Test +	True positive a	False positive b	Test positive $a+b$
Test −	False negative c	True negative d	Test negative $c+d$
Total	$a+c$	$b+d$	$a+b+c+d$

Specificity is the proportion of uninfected animals identified as negative by the test.
Or the probability that a truly non-diseased animal will be classified as non-diseased.

	Infection +	Infection −	Total
Test +	True positive a	False positive b	Test positive $a+b$
Test −	False negative c	True negative d	Test negative $c+d$
Total	$a+c$	$b+d$	$a+b+c+d$

$$Sp = \frac{d}{b+d} = \frac{89}{7+89} = 0.93$$

- We've just considered two tests where differentiation between 'positive' and 'negative' is clear
- Some tests are measured on a continuous scale
  - blood pressure
  - blood chemistry
  - serum enzymes
  - serology
- So we need to set a cutpoint to distinguish between positives and negatives

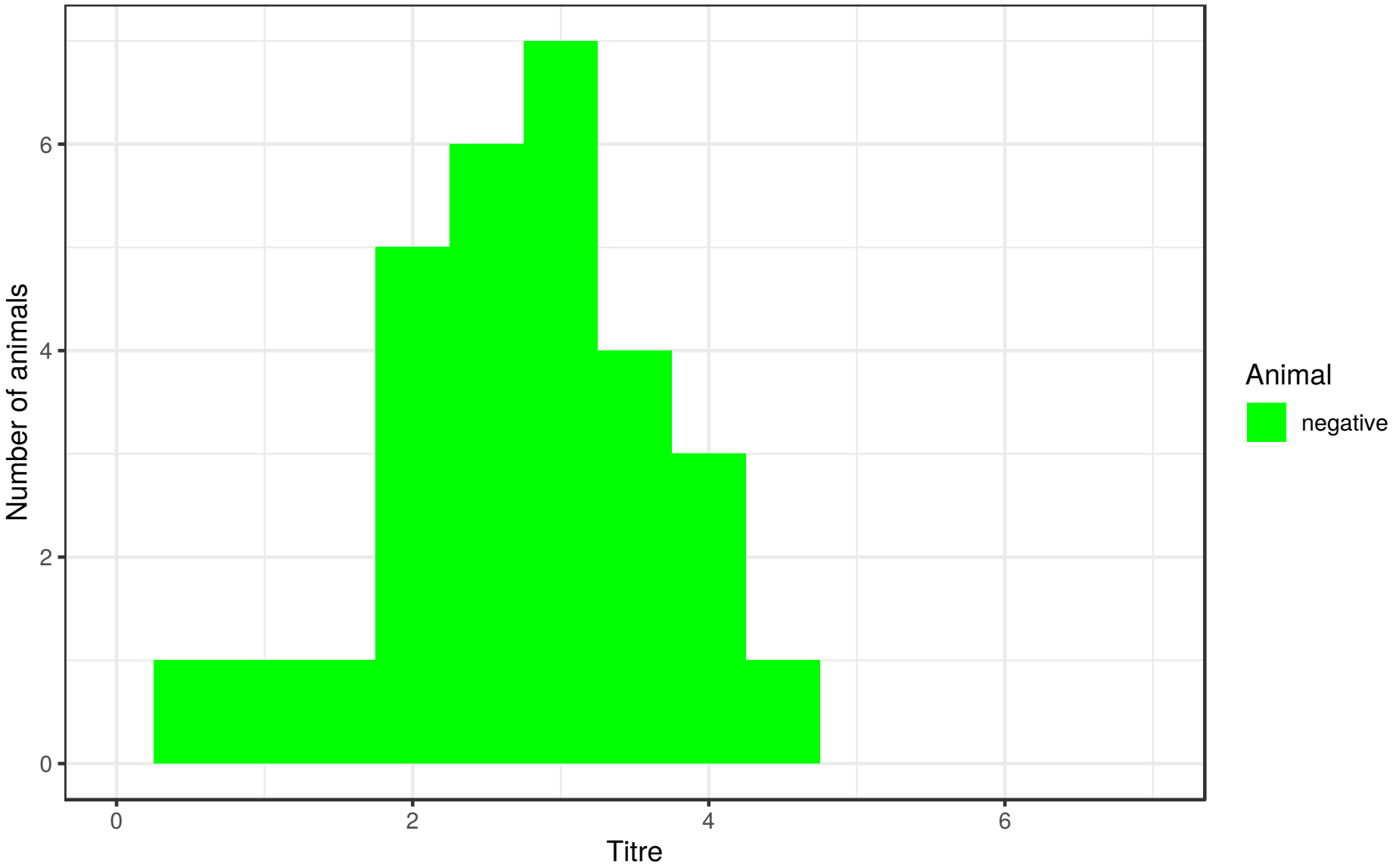
Stevenson 2012

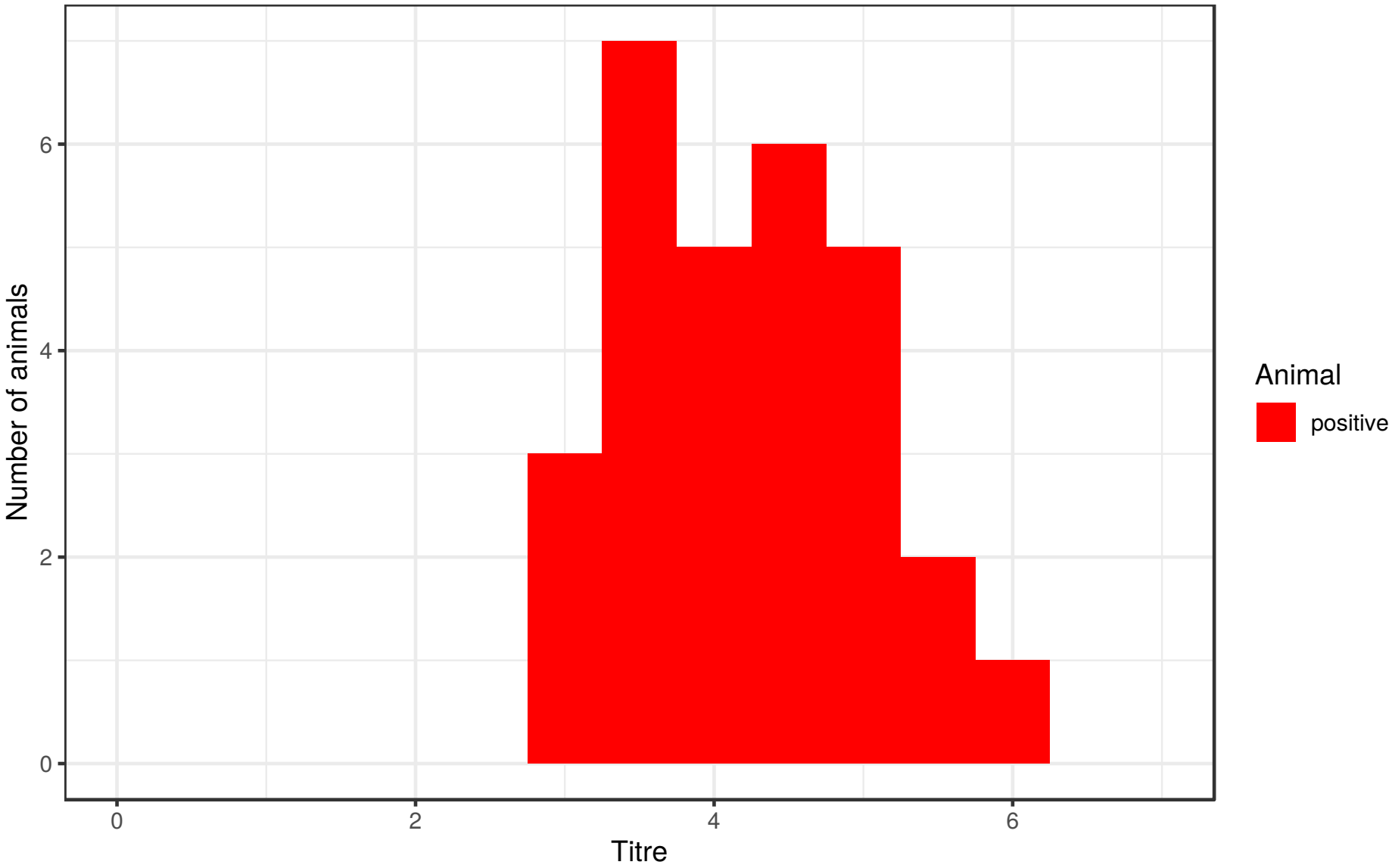
Titres of negative animals: 3, 2, 3.5, 3, 2, 2.5, 3, 1.5, 2.5, 3.5, 4, 2.5, 4, 2, 2, 3, 1, 2.5, 3.5, 0.5, 2.5, 4.5, 2.5, 3, 3, 3, 4, 2, 3.5

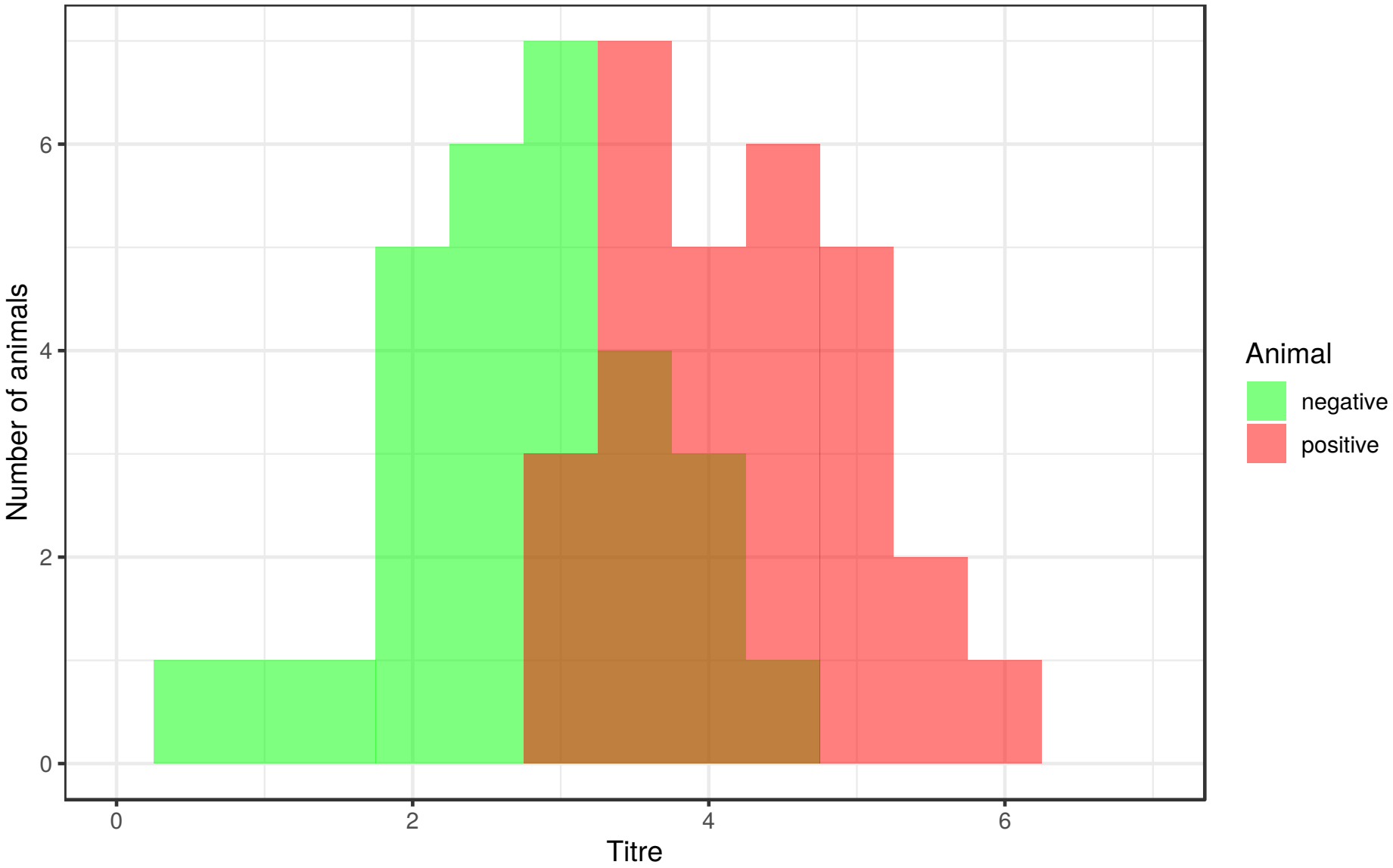
Titres of positive animals: 3.5, 3.5, 3.5, 4.5, 4, 5, 5.5, 4, 3.5, 4.5, 5, 3.5, 6, 4, 4.5, 3.5, 4, 3, 5, 5.5, 5, 3, 4.5, 4.5, 5, 3, 3.5, 4.5, 4

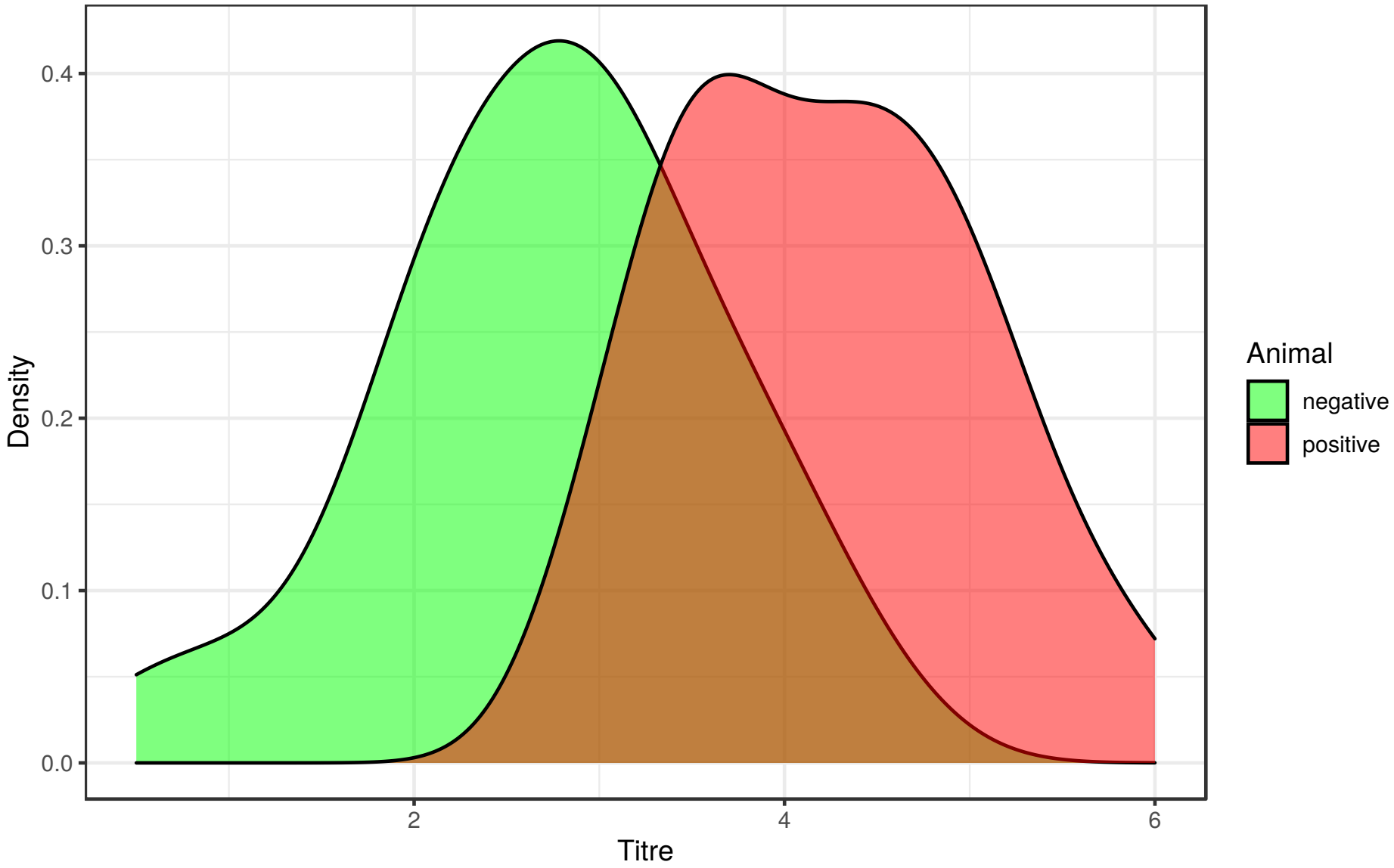
Titre	Number of animals negative	positive
0.5	1	
1.0	1	
1.5	1	
2.0	5	
2.5	6	
3.0	7	3
3.5	4	7
4.0	3	5
4.5	1	6
5.0		5
5.5		2
6.0		1

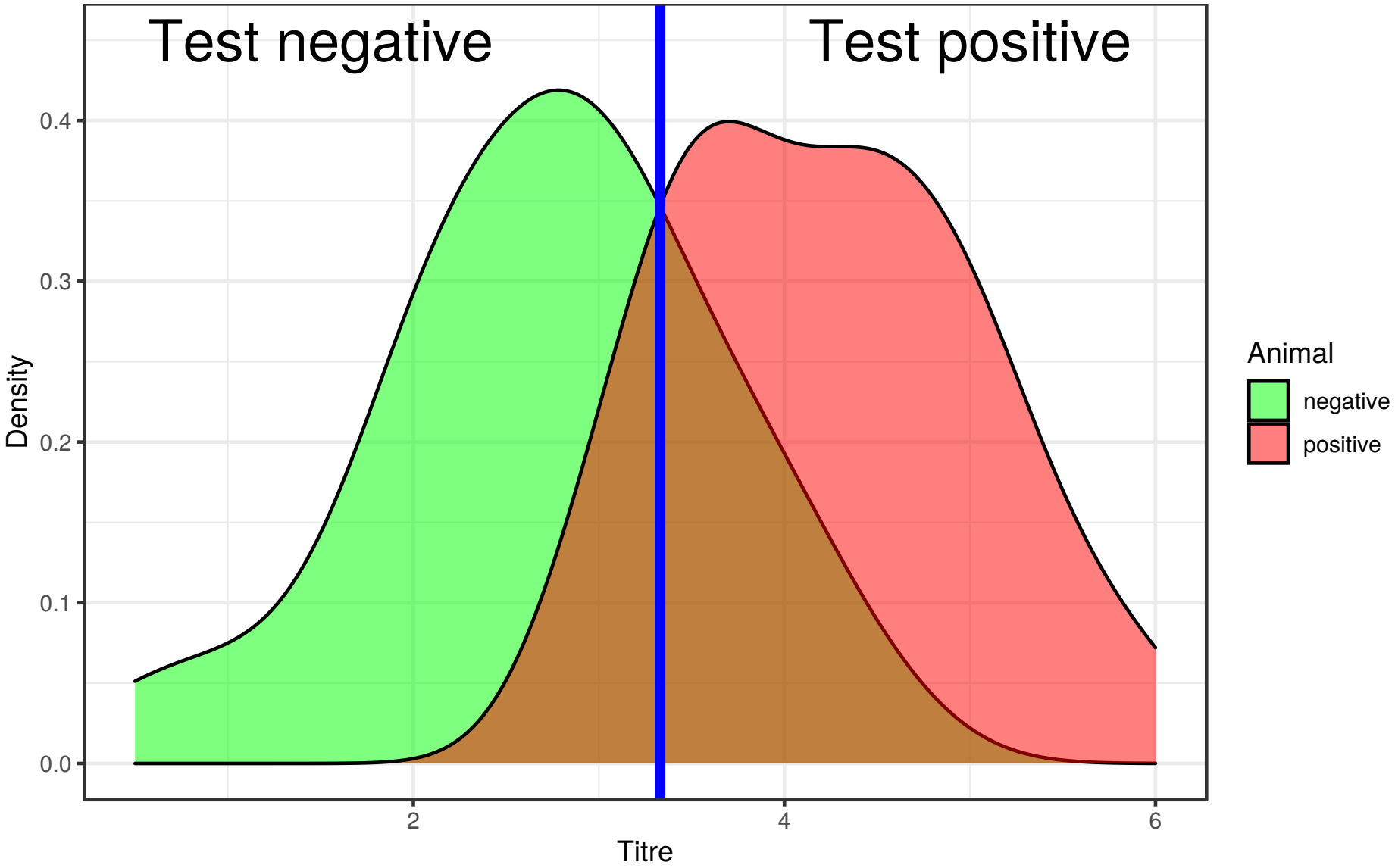
Noordhuizen et al. (2001)

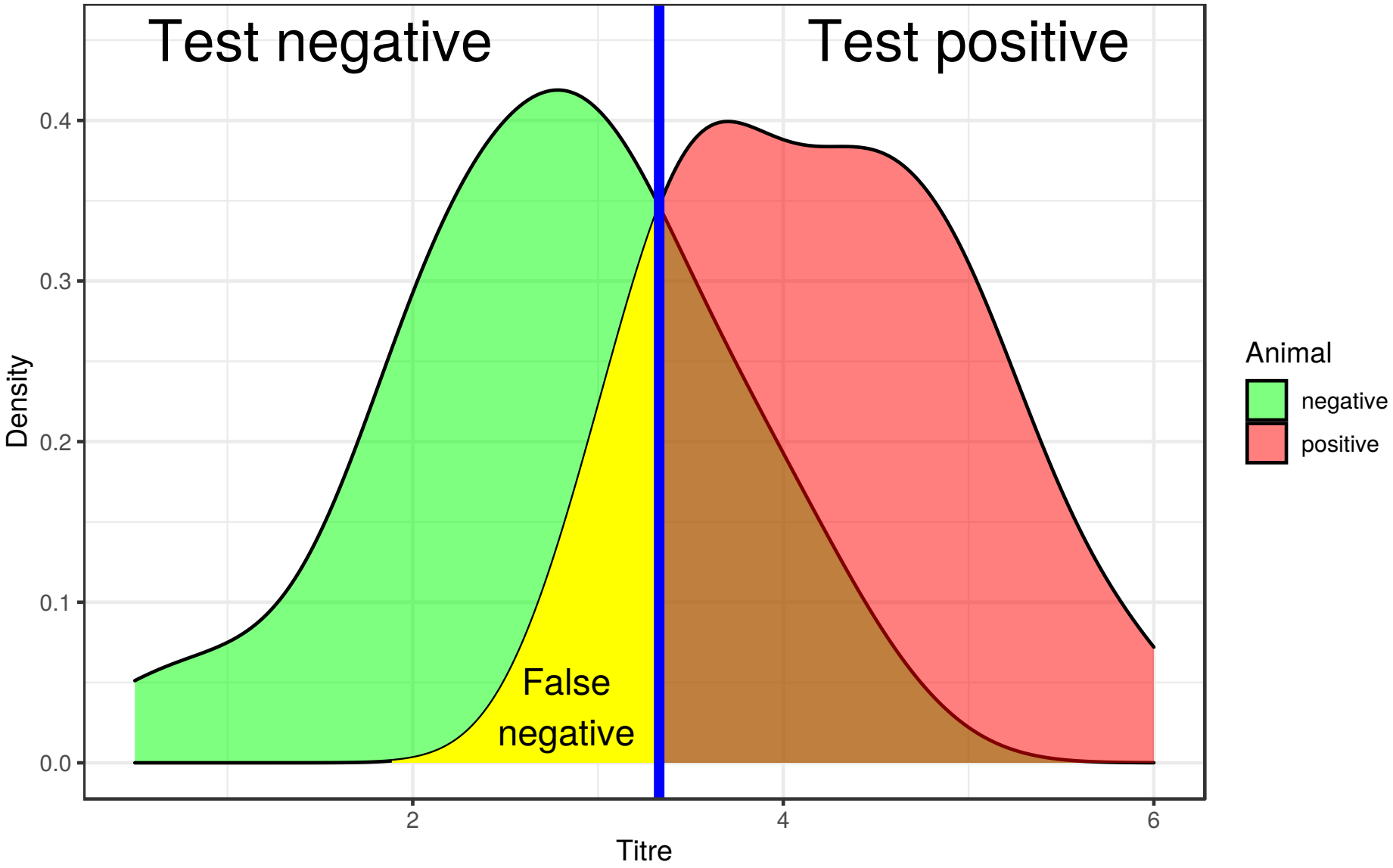

Number of animals
0
2
4
6
0
2
4
6
Titre
Animal
negative

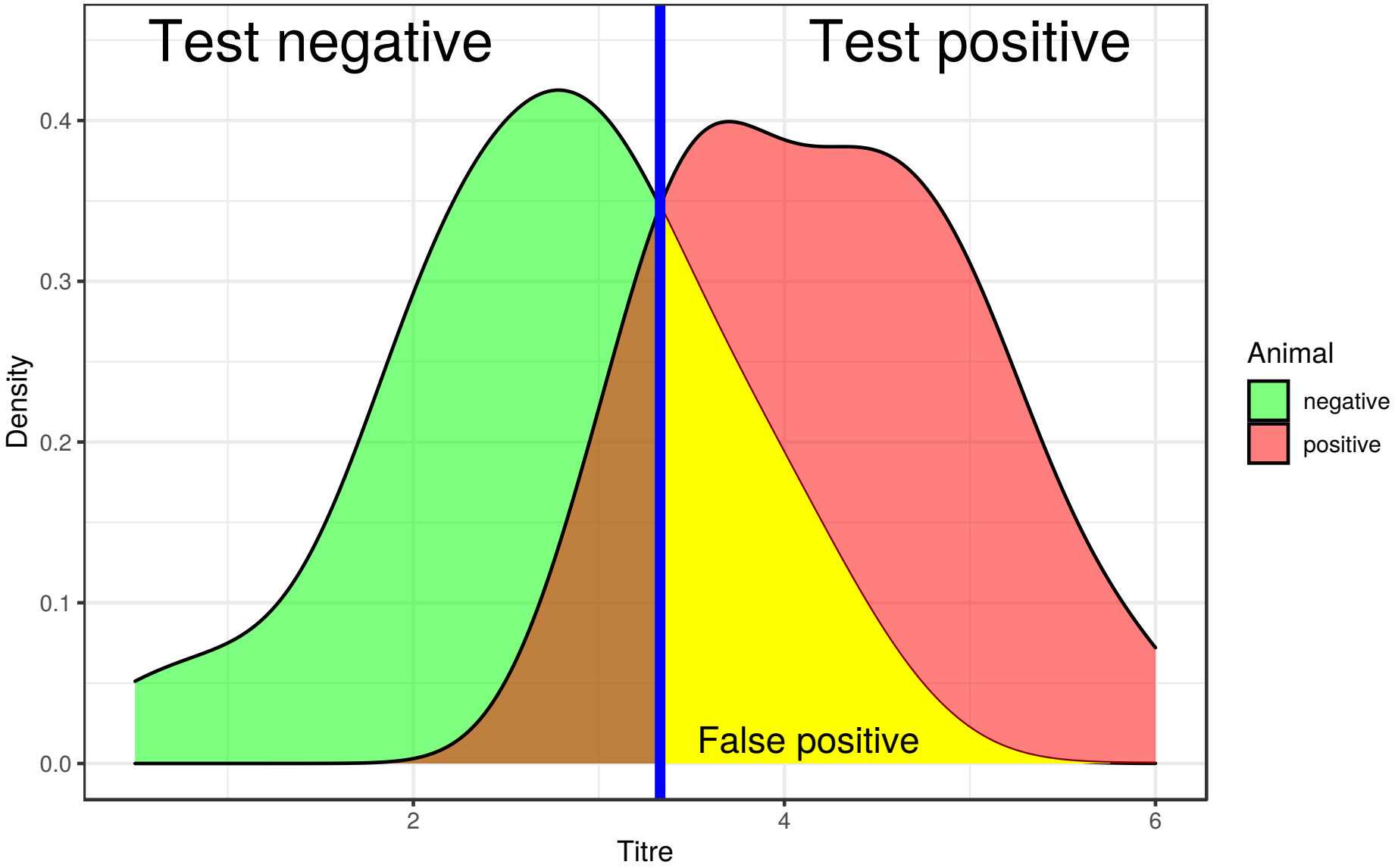

Number of animals
0
2
4
6
0
2
4
6
Titre
Animal
positive


Number of animals
0
2
4
6
0
2
4
6
Titre
Animal
negative
positive

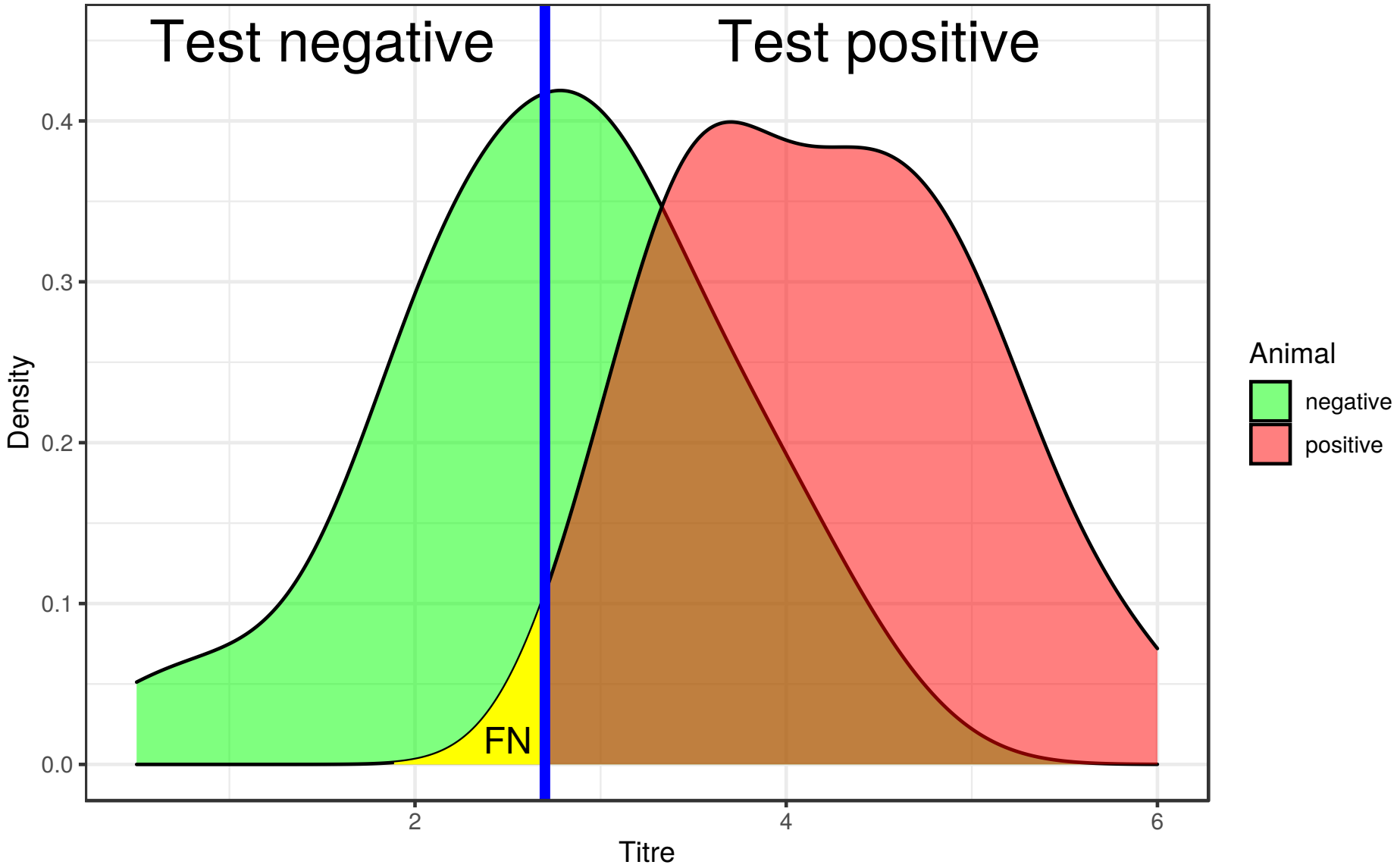

0.4
0.3
0.2
0.1
0.0
Density
2
4
6
Titre
Animal
negative
positive


Test negative
Test positive
Density
0.4
0.3
0.2
0.1
0.0
2
4
6
Titre
Animal
negative
positive

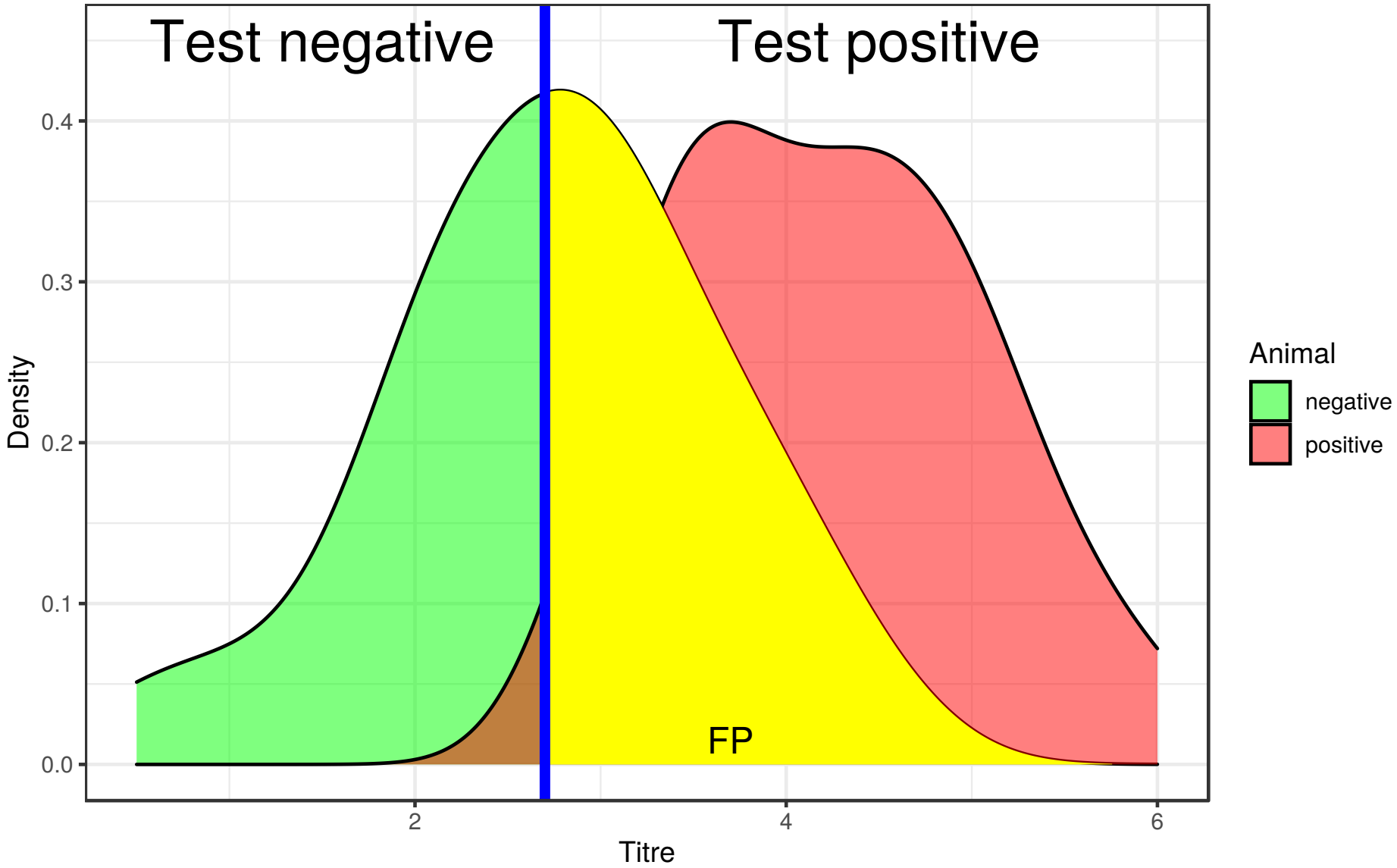

Test negative
Test positive
False
negative
Density
0.0
0.1
0.2
0.3
0.4
2
4
6
Titre
Animal
negative
positive


Test negative
Test positive
False positive
Density
0.0
0.1
0.2
0.3
0.4
2
4
6
Titre
Animal
negative
positive

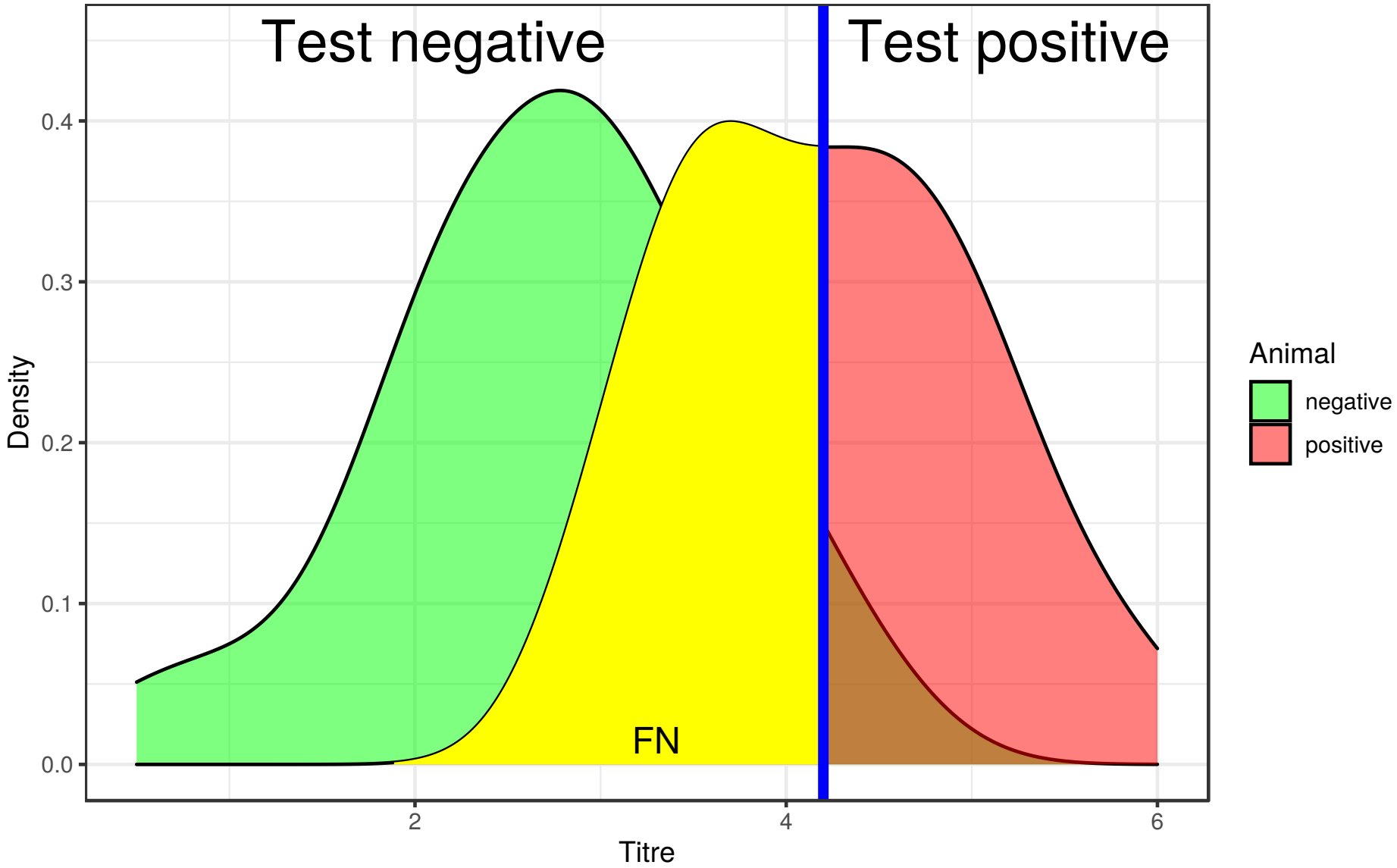
Se↑, Sp↓ → FN↓ (TN↓)


Test negative
Test positive
FN
Density
0.0
0.1
0.2
0.3
0.4
2
4
6
Titre
Animal
negative
positive

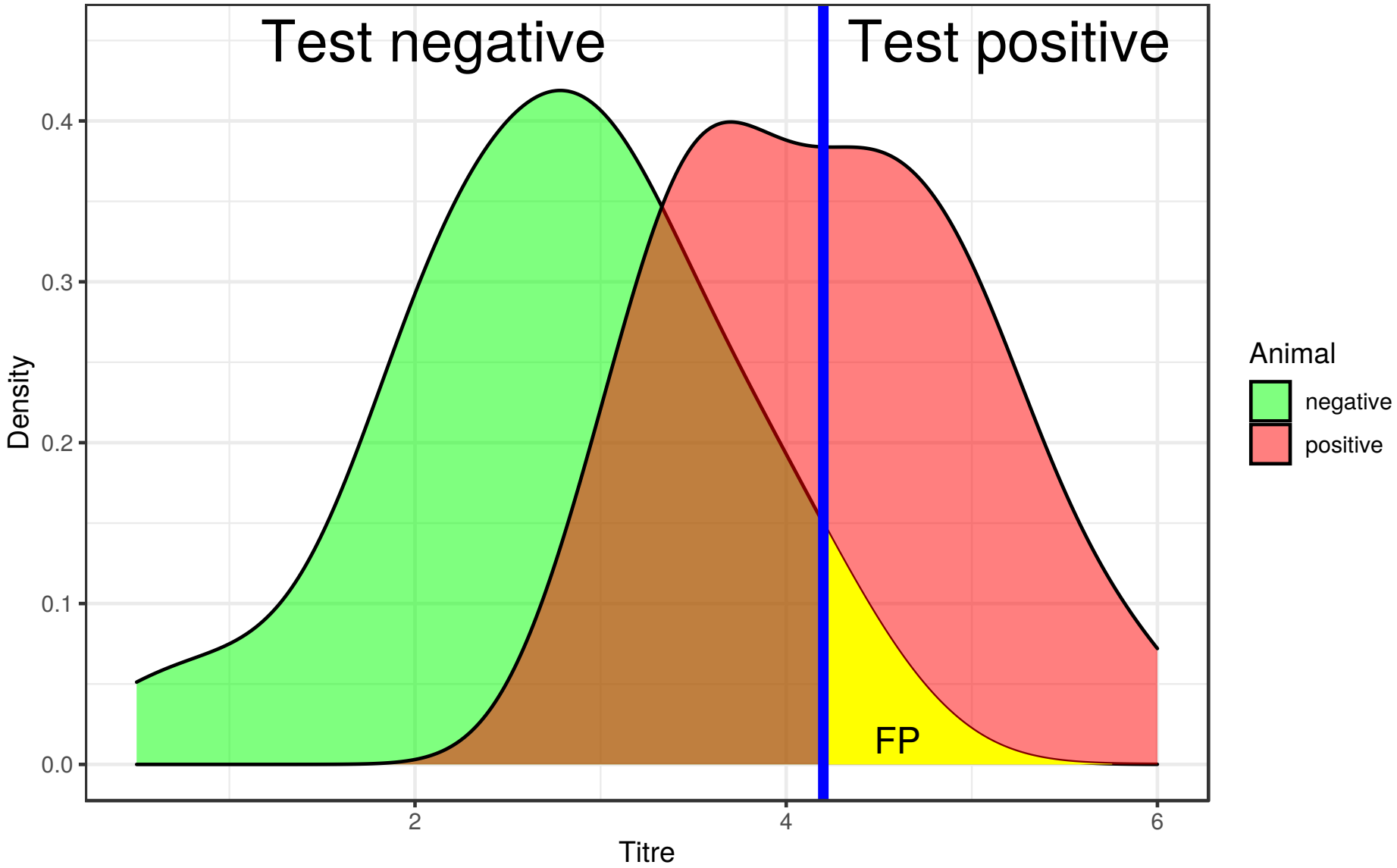
Se↑, Sp↓ → FP↑ (TP↑)


Test negative
Test positive
FP
Density
0.0
0.1
0.2
0.3
0.4
2
4
6
Titre
Animal
negative
positive

Se↓, Sp↑ → FN↑ (TN↑)


Test negative
Test positive
FN
Density
0.0
0.1
0.2
0.3
0.4
2
4
6
Titre
Animal
negative
positive

Se↓, Sp↑ → FP↓ (FP↓)


Test negative
Test positive
FP
Density
0.0
0.1
0.2
0.3
0.4
2
4
6
Titre
Animal
negative
positive

What threshold should be used?

- It depends on the purpose of testing.

Paolo Veronese (1582) Youth between Virtue and Vice

If the threshold is changed to increase the sensitivity, the specificity is decreased at the same time.

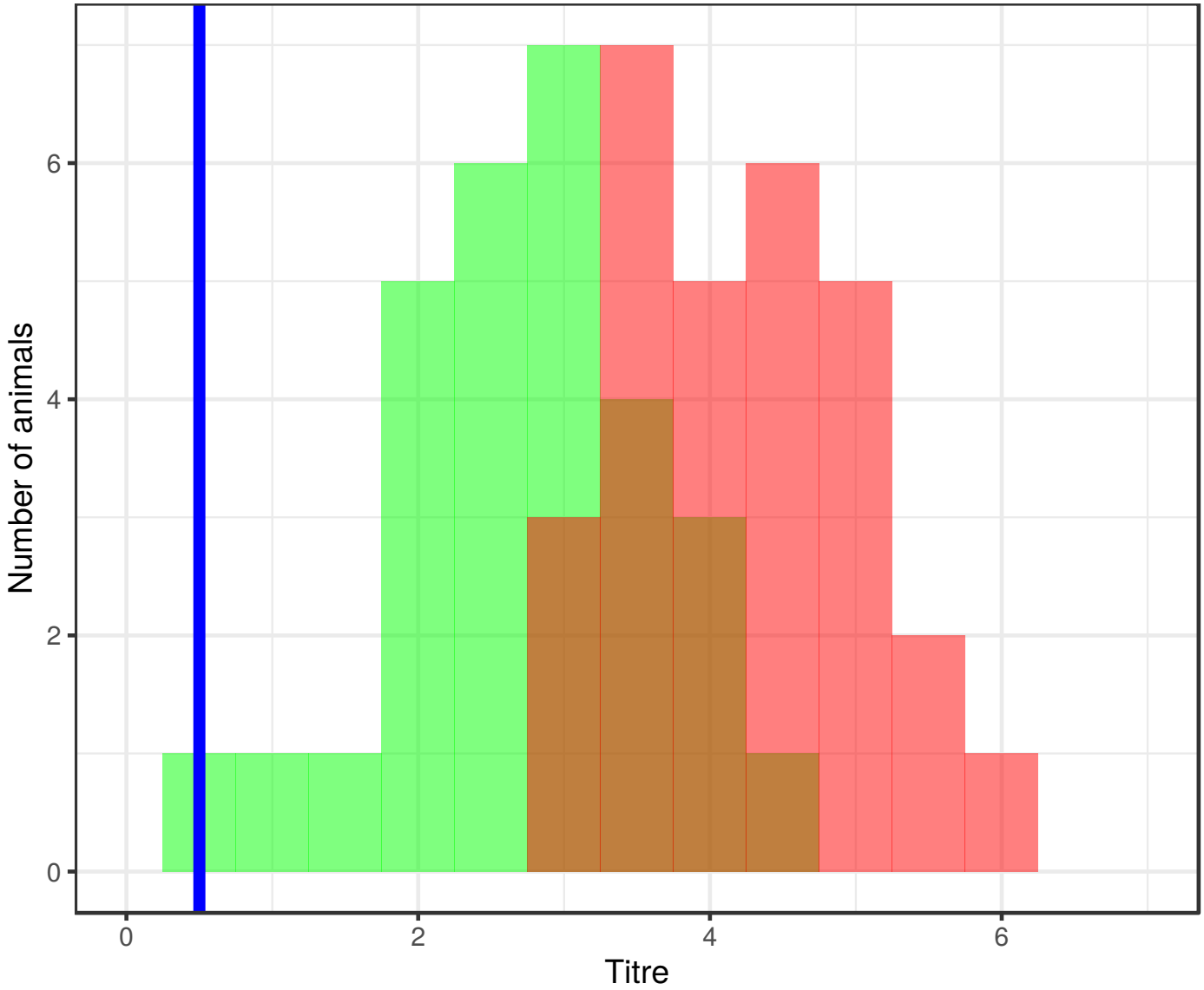
Se↑

- If we want to find all infected animals, we need to increase sensitivity.
- More infected animals will test positive and more uninfected animals will test positive.
- It increases the probability that test-negative animals are indeed not infected.
- When screening breeding pigs for purchase into a herd, a false-positive result would be much less harmful to a client than a false negative, which might allow infected pigs to enter a noninfected herd.

If the threshold is changed to increase the sensitivity, the specificity is decreased at the same time.

Sp↑

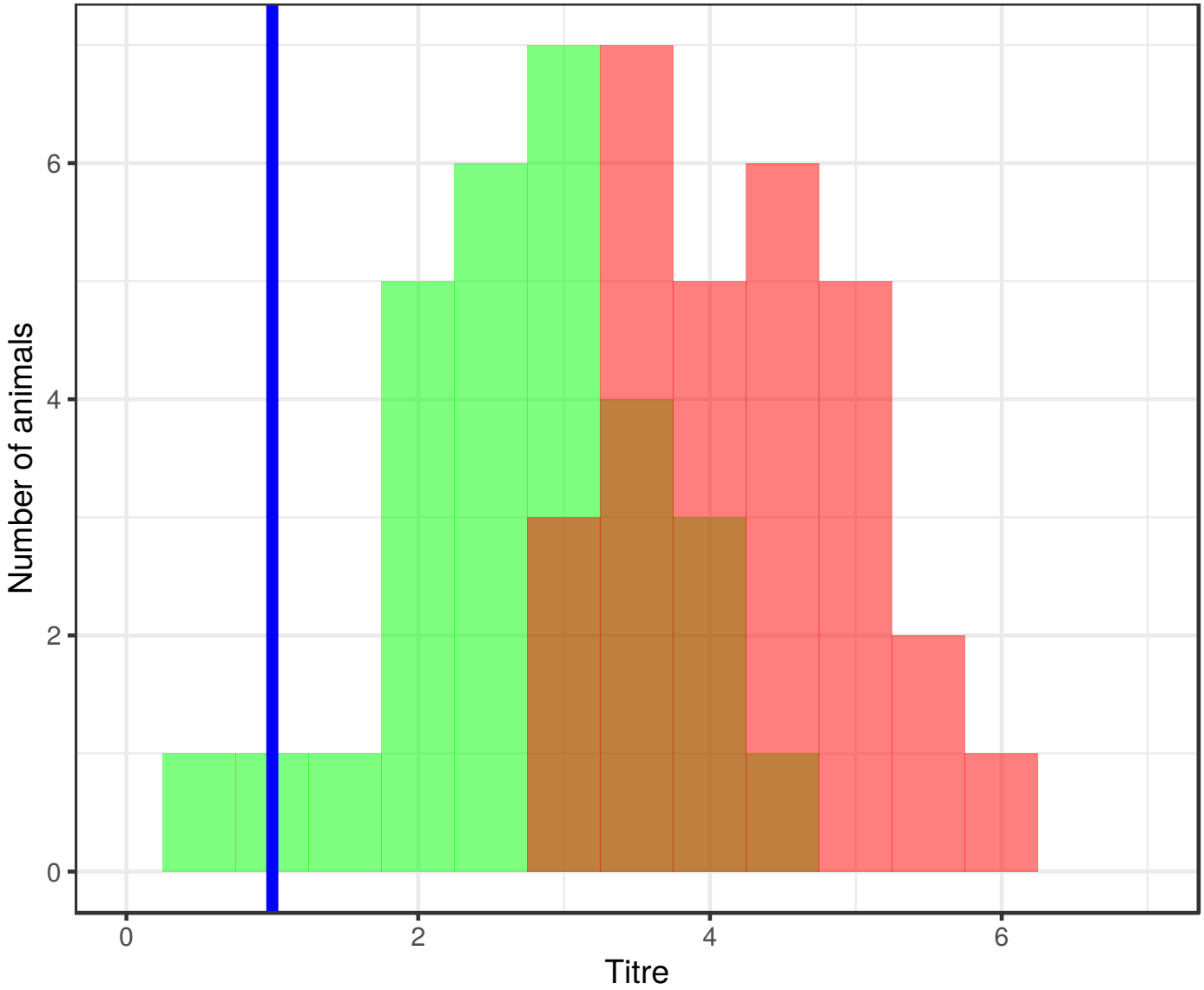
- If the goal is to make sure the test positives are truly infected, we need to increase the specificity.
- Fewer infected animals will be test positive, and parallel fewer uninfected animals will be test positive too.
- A veterinarian relying on the results of a test to decide to cull a sow probably wants to minimize the chance of a false-positive diagnosis by using a highly specific test, especially if the sow is asymptomatic and pregnant and there are no other reasons for culling.



Titre threshold:
T+: > 0.5
T−: ≤ 0.5

	I+	I−
T+	29	28
T−	0	1

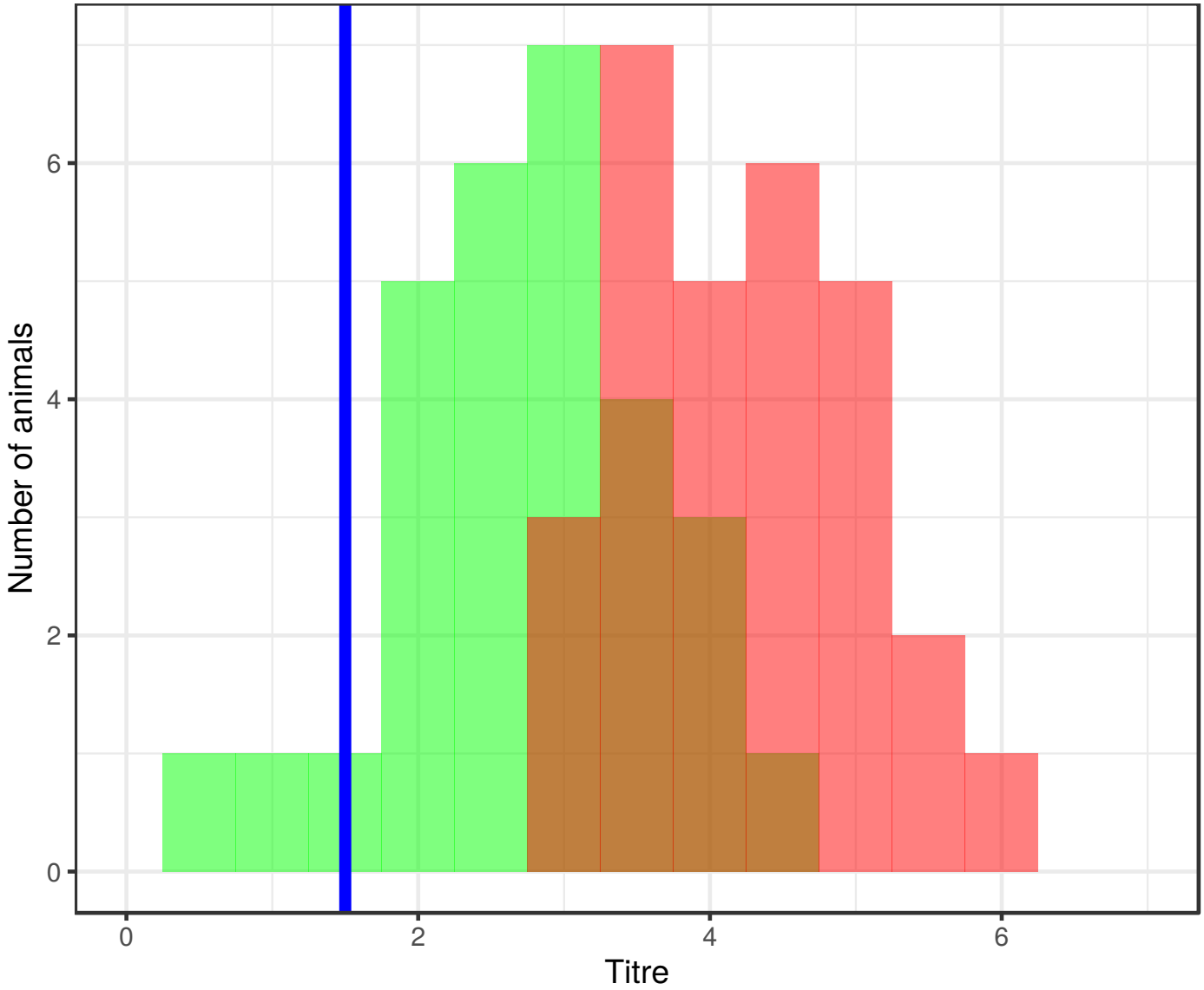
Se=1.00
Sp=0.03



Titre threshold:
T+: > 1.0
T−: ≤ 1.0

	I+	I−
T+	29	27
T−	0	2

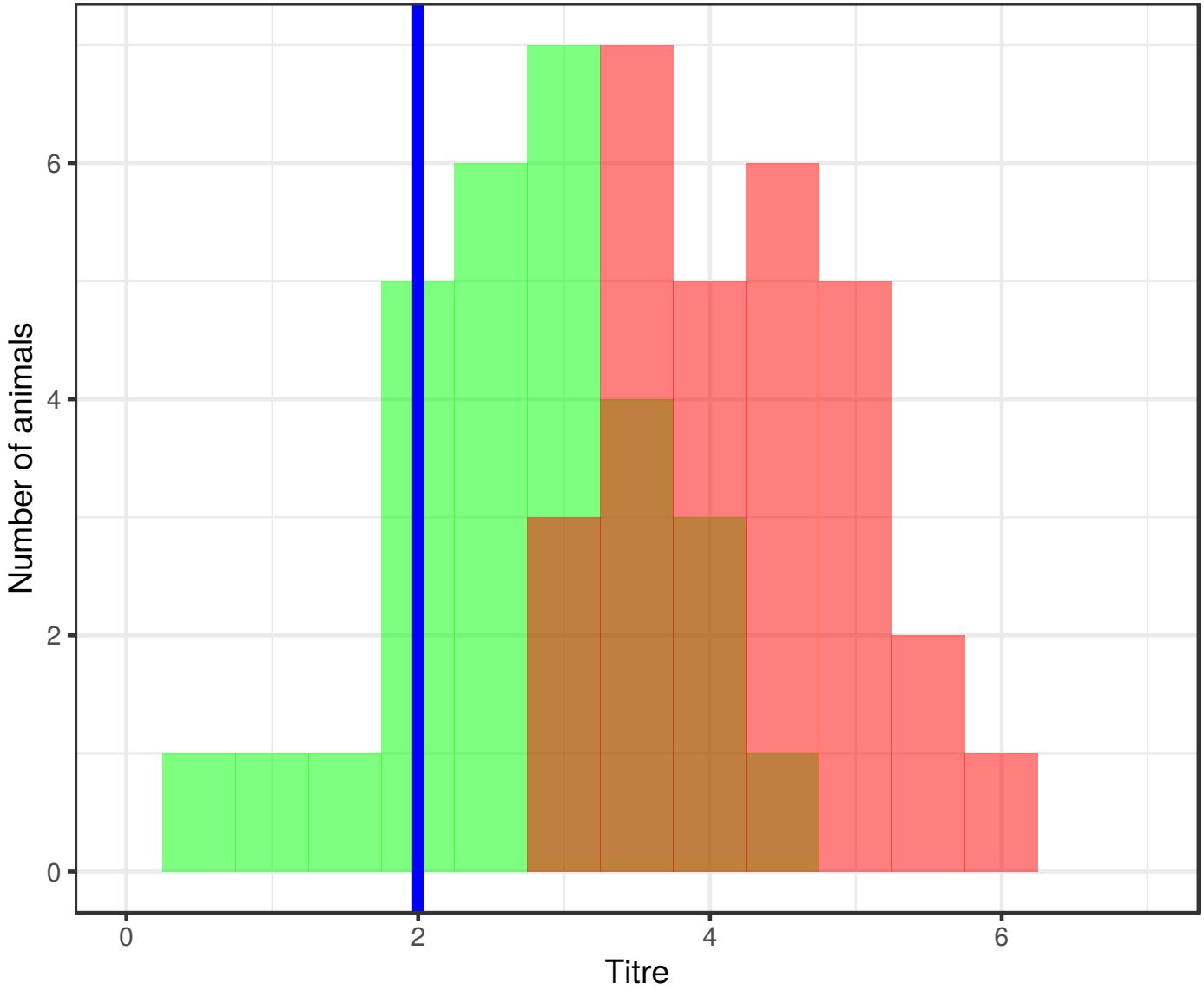
Se=1.00
Sp=0.07



Titre threshold:
T+: > 1.5
T−: ≤ 1.5

	I+	I−
T+	29	26
T−	0	3

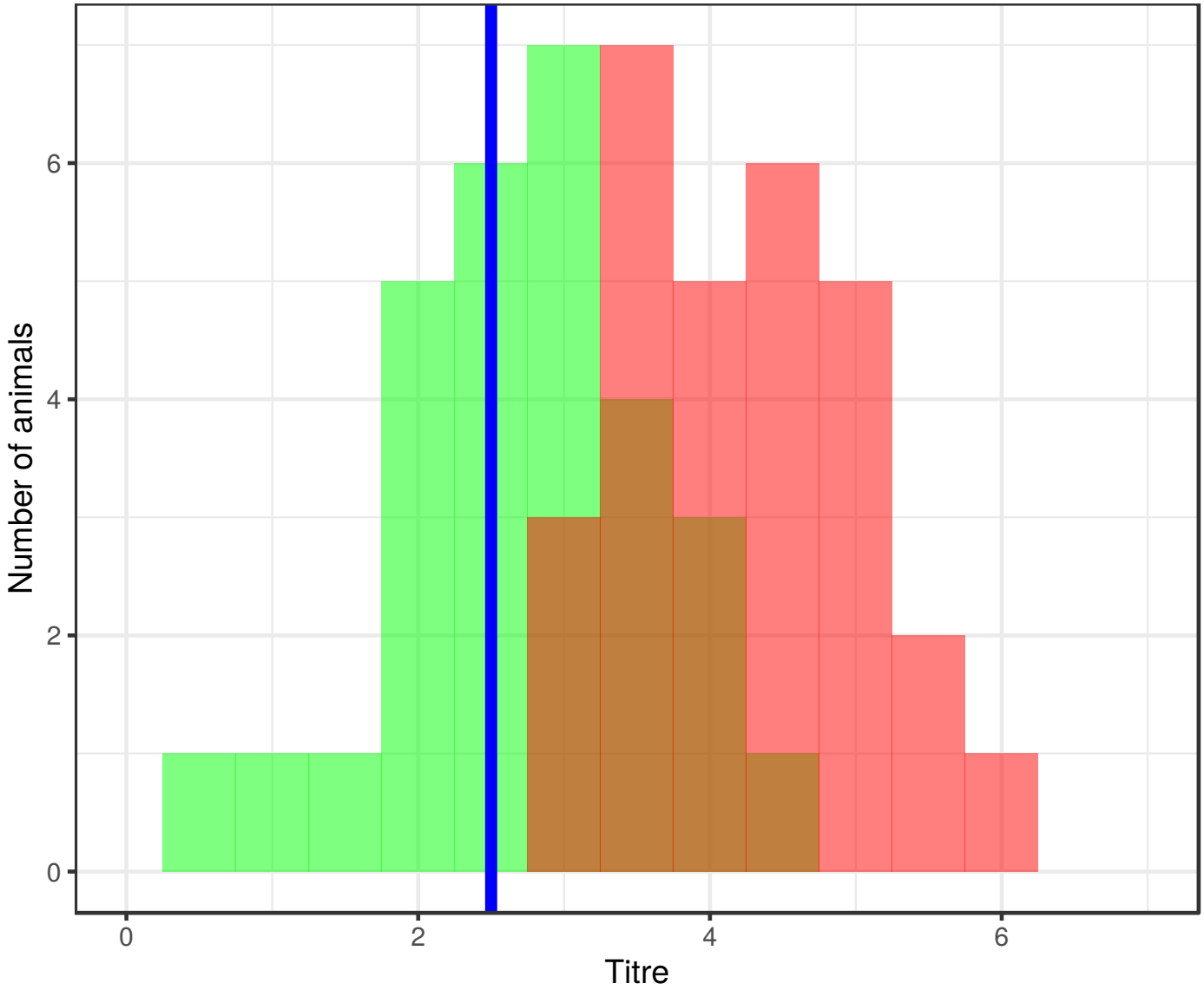
Se=1.00
Sp=0.10



Titre threshold:
T+: > 2.0
T−: ≤ 2.0

	I+	I−
T+	29	21
T−	0	8

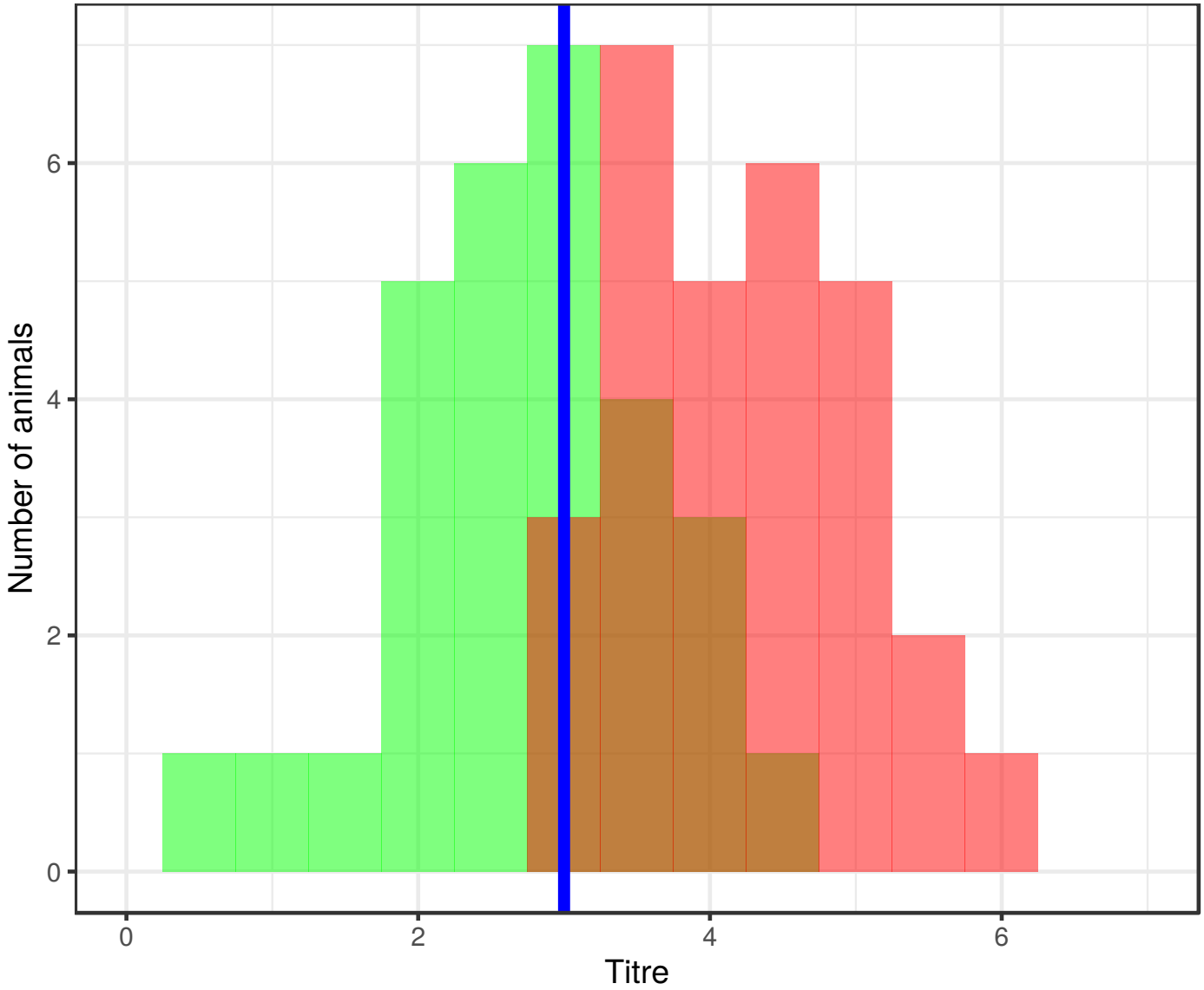
Se=1.00
Sp=0.28



Titre threshold:
T+: > 2.5
T−: ≤ 2.5

	I+	I−
T+	29	15
T−	0	14

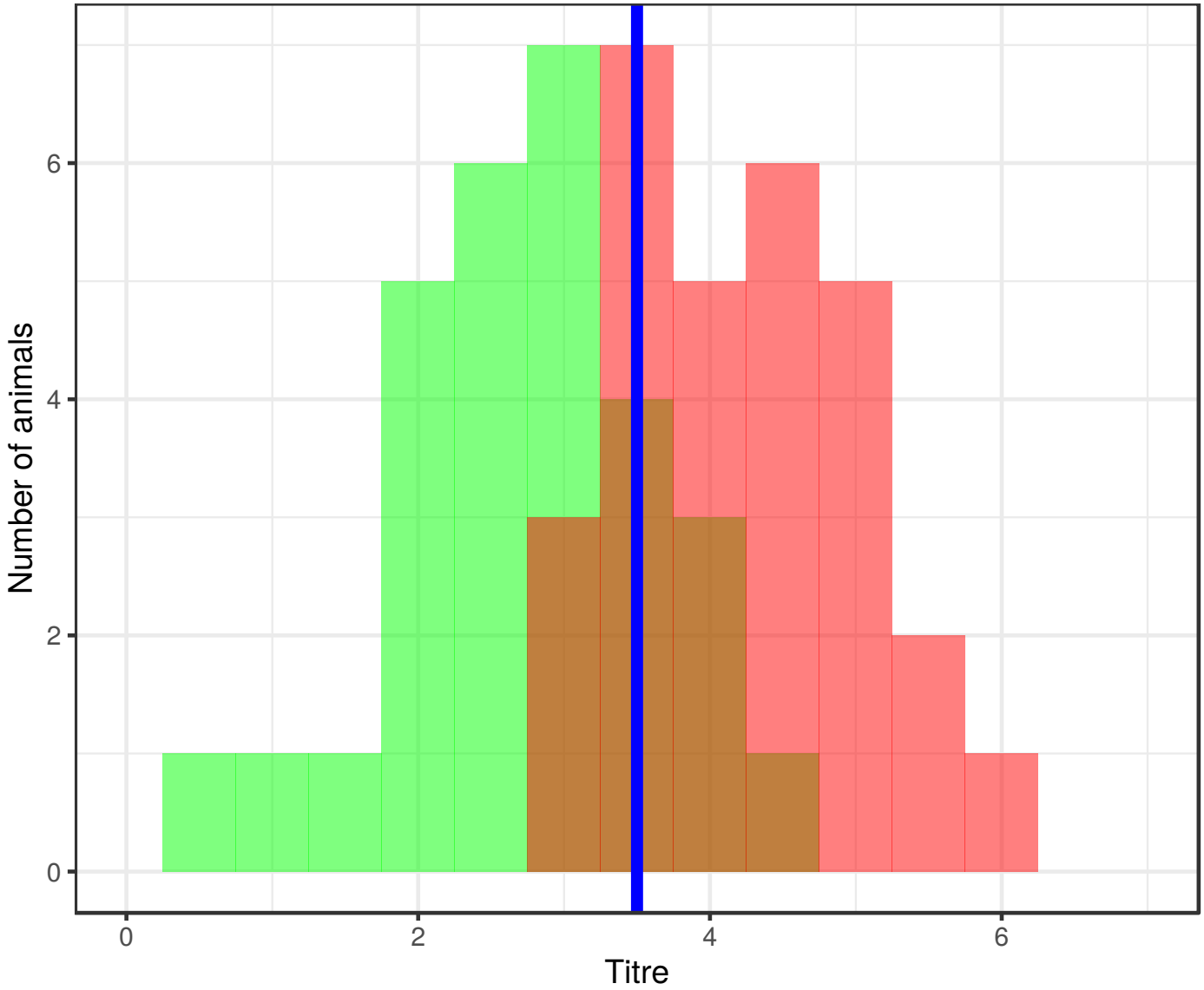
Se=1.00
Sp=0.48



Titre threshold:
T+: > 3.0
T−: ≤ 3.0

	I+	I−
T+	26	8
T−	3	21

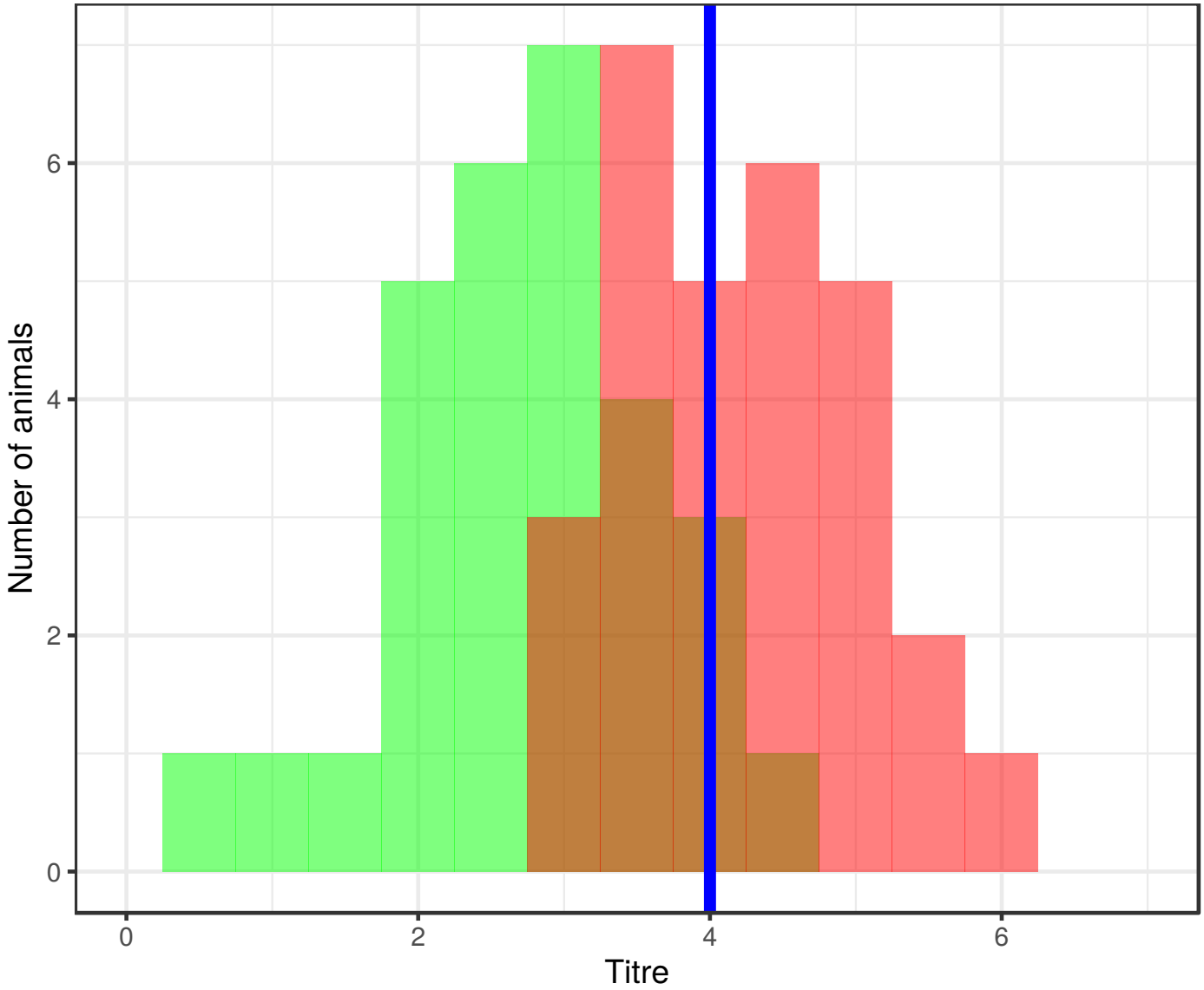
Se=0.90
Sp=0.72



Titre threshold:
T+: > 3.5
T−: ≤ 3.5

	I+	I−
T+	19	4
T−	10	25

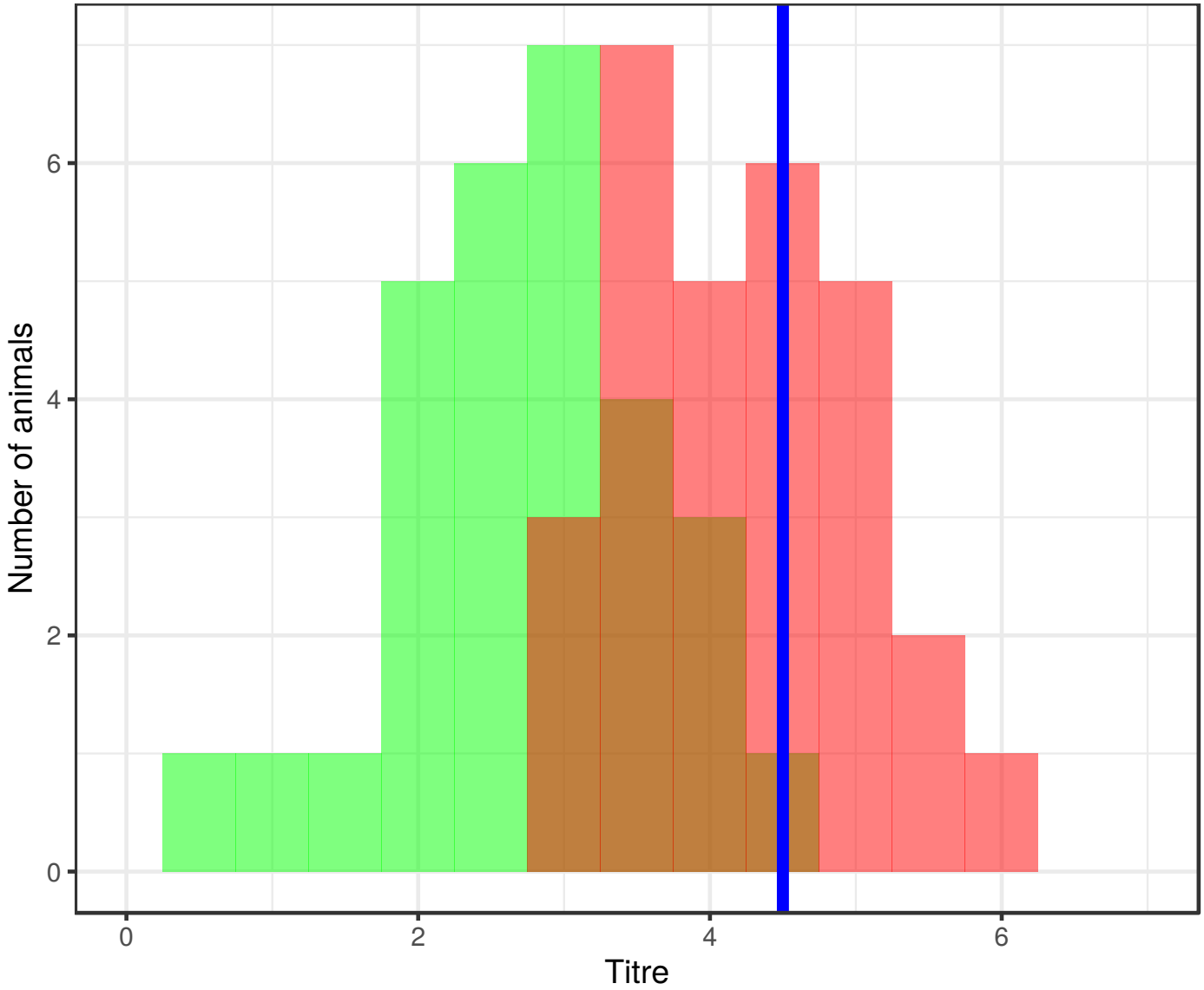
Se=0.66
Sp=0.86



Titre threshold:
T+: > 4.0
T−: ≤ 4.0

	I+	I−
T+	14	1
T−	15	28

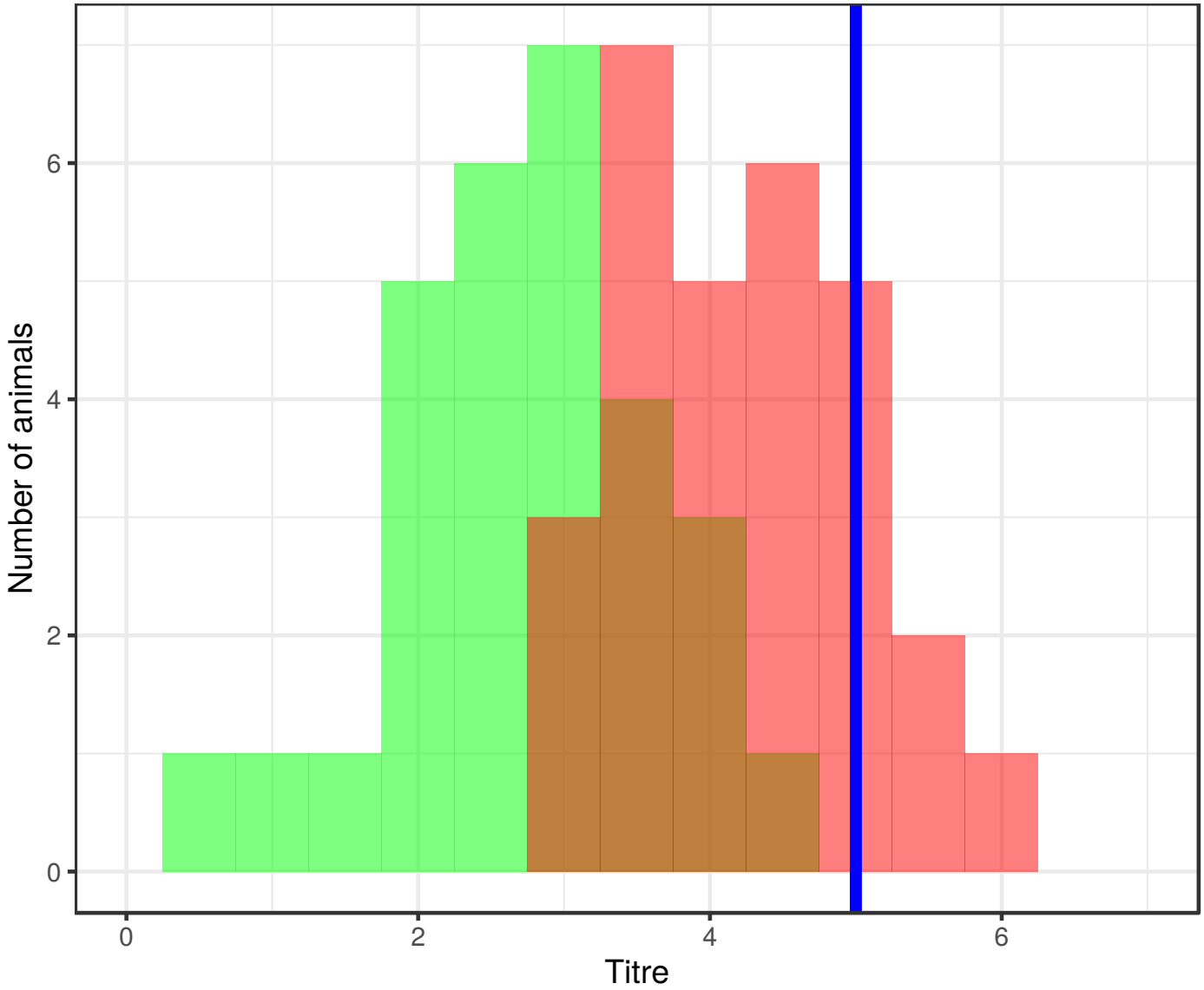
Se=0.48
Sp=0.97



Titre threshold:
T+: > 4.5
T−: ≤ 4.5

	I+	I−
T+	8	0
T−	21	29

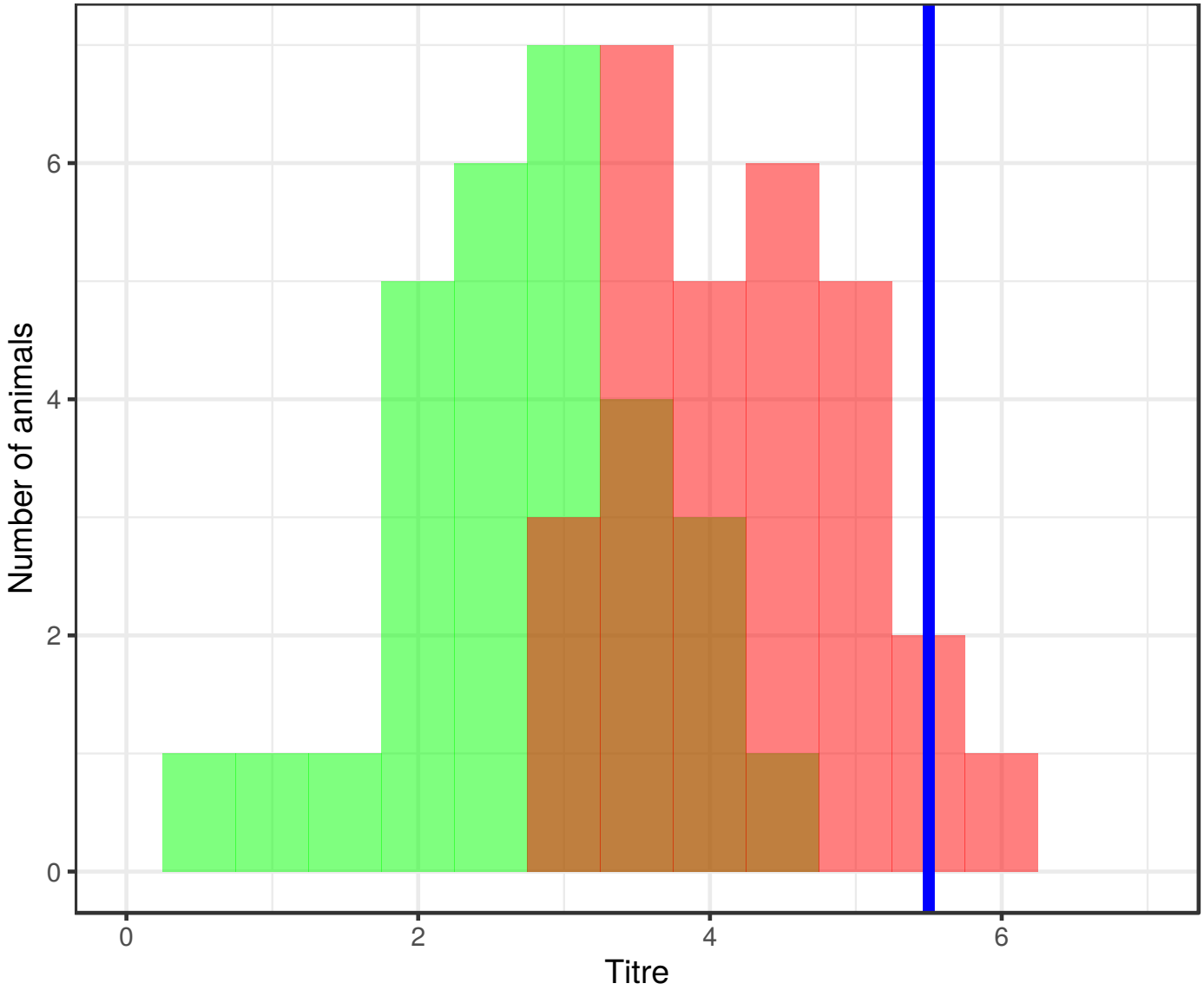
Se=0.28
Sp=1.00



Titre threshold:
T+: > 5.0
T−: ≤ 5.0

	I+	I−
T+	3	0
T−	26	29

Se=0.10
Sp=1.00



Titre threshold:
T+: > 5.5
T−: ≤ 5.5

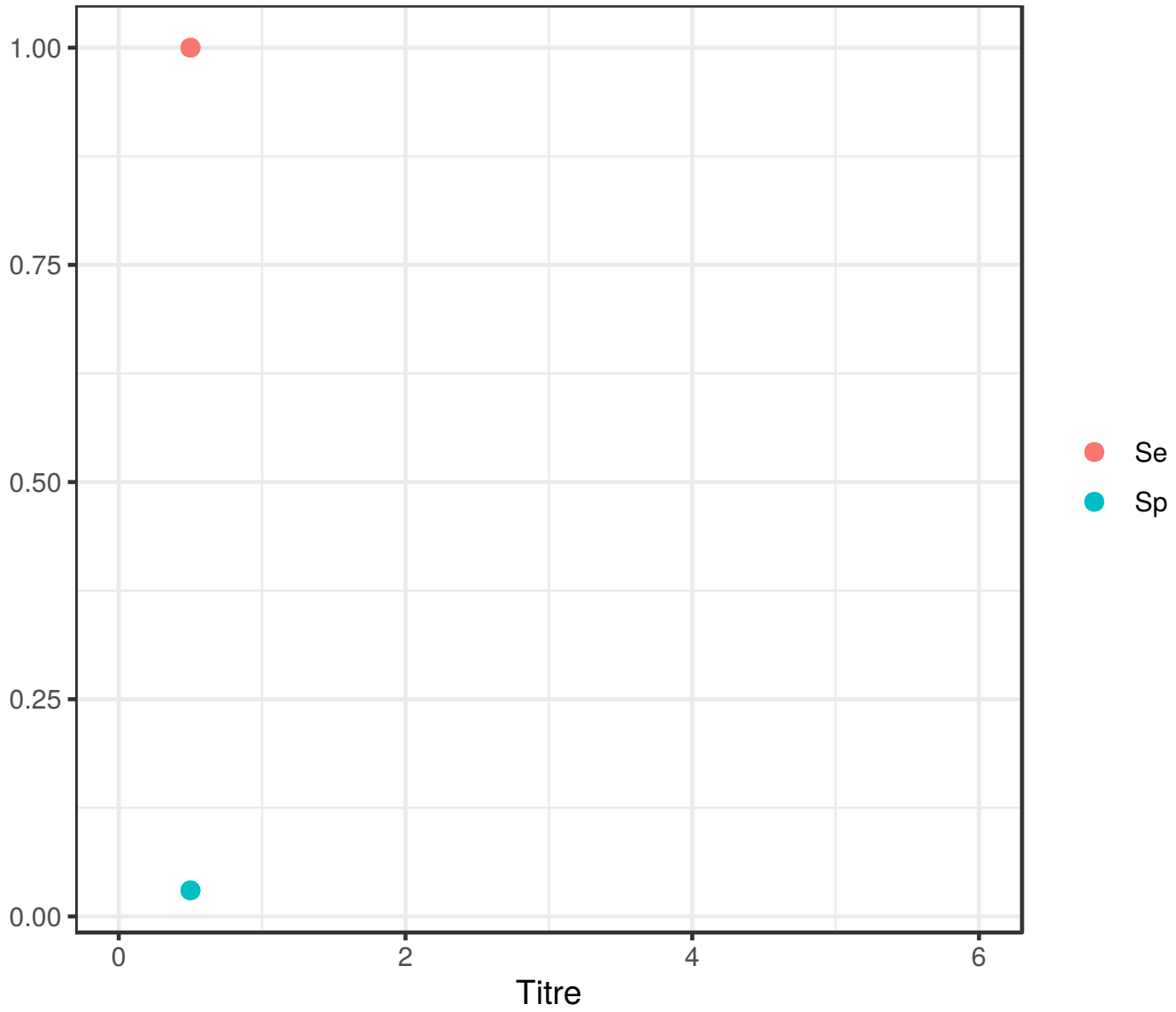
	I+	I−
T+	1	0
T−	28	29

Se=0.03
Sp=1.00

Titre threshold:
T+: > 0.5
T−: ≤ 0.5

	I+	I−
T+	29	28
T−	0	1

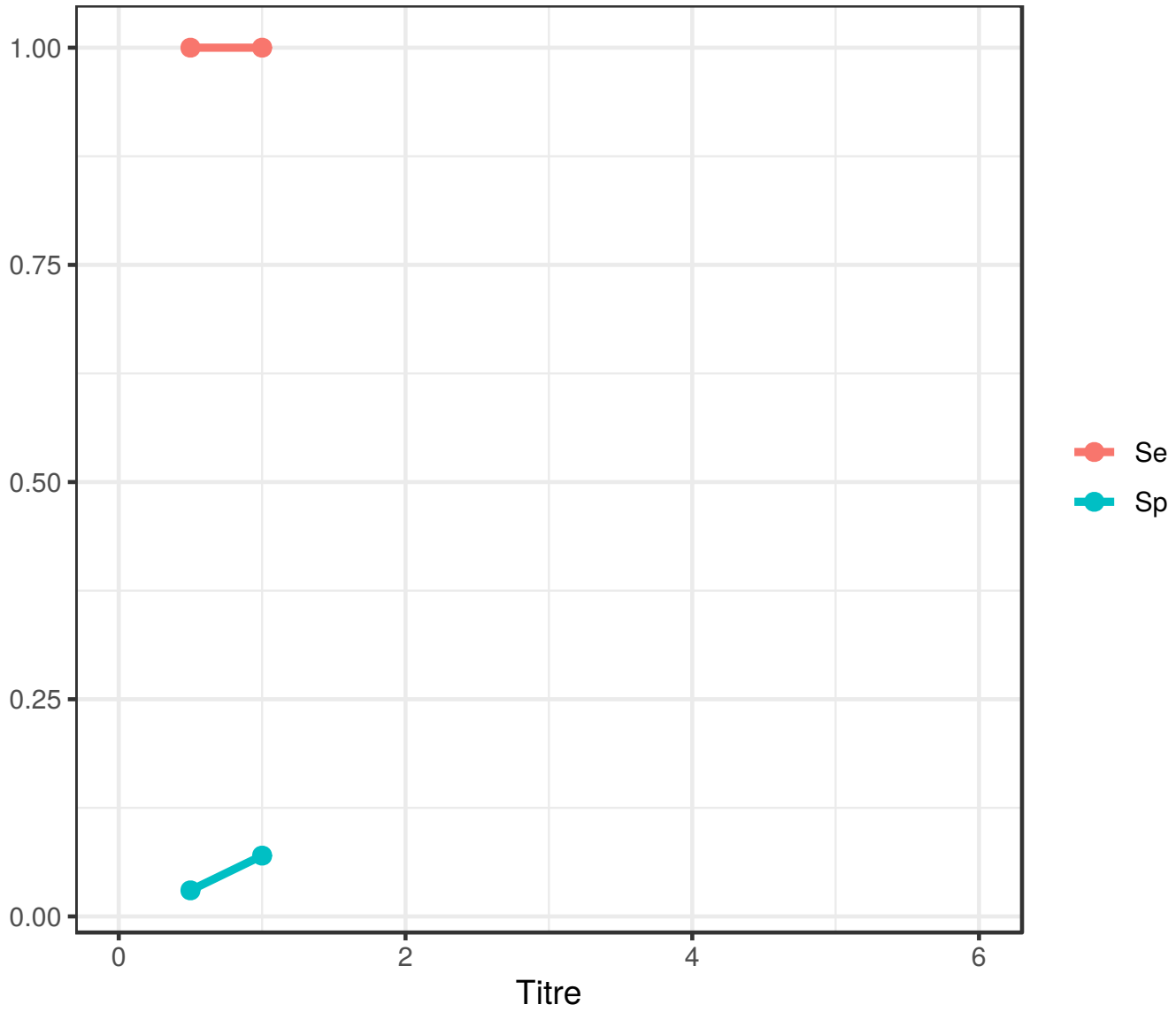
Se=1.00
Sp=0.03



Titre threshold:
T+: > 1.0
T−: ≤ 1.0

	I+	I−
T+	29	27
T−	0	2

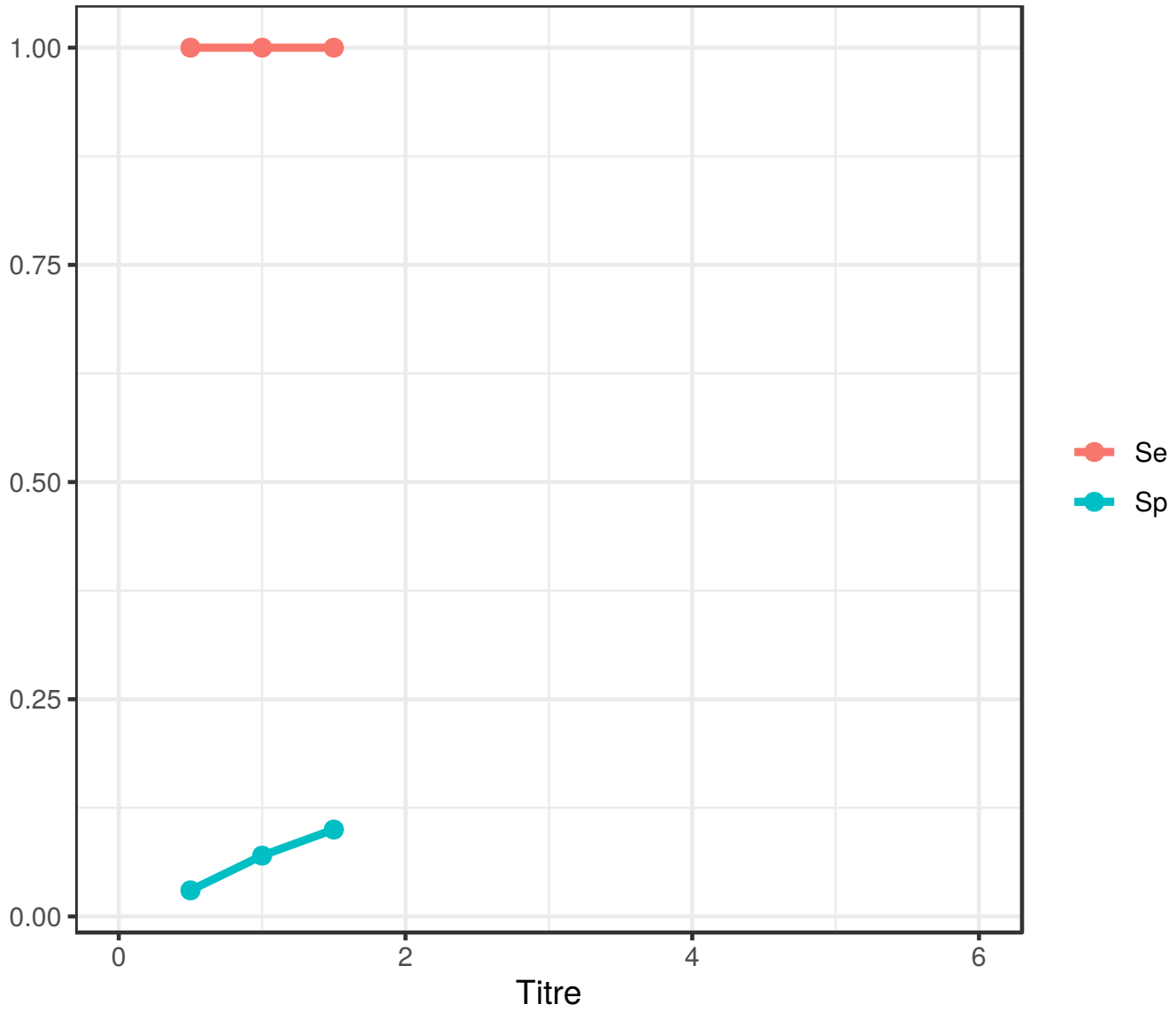
Se=1.00
Sp=0.07



Titre threshold:
T+: > 1.5
T−: ≤ 1.5

	I+	I−
T+	29	26
T−	0	3

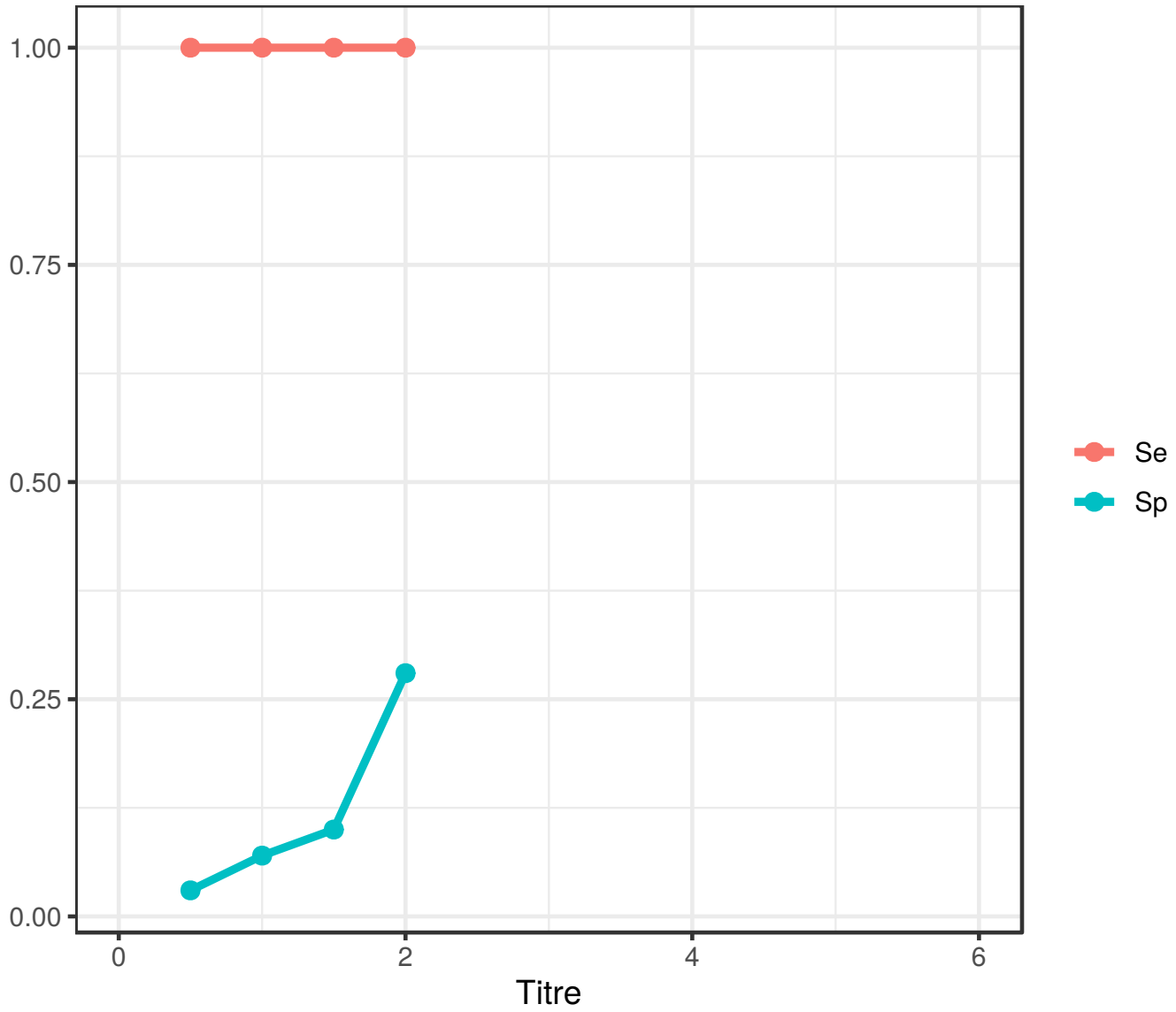
Se=1.00
Sp=0.10



Titre threshold:
T+: > 2.0
T−: ≤ 2.0

	I+	I−
T+	29	21
T−	0	8

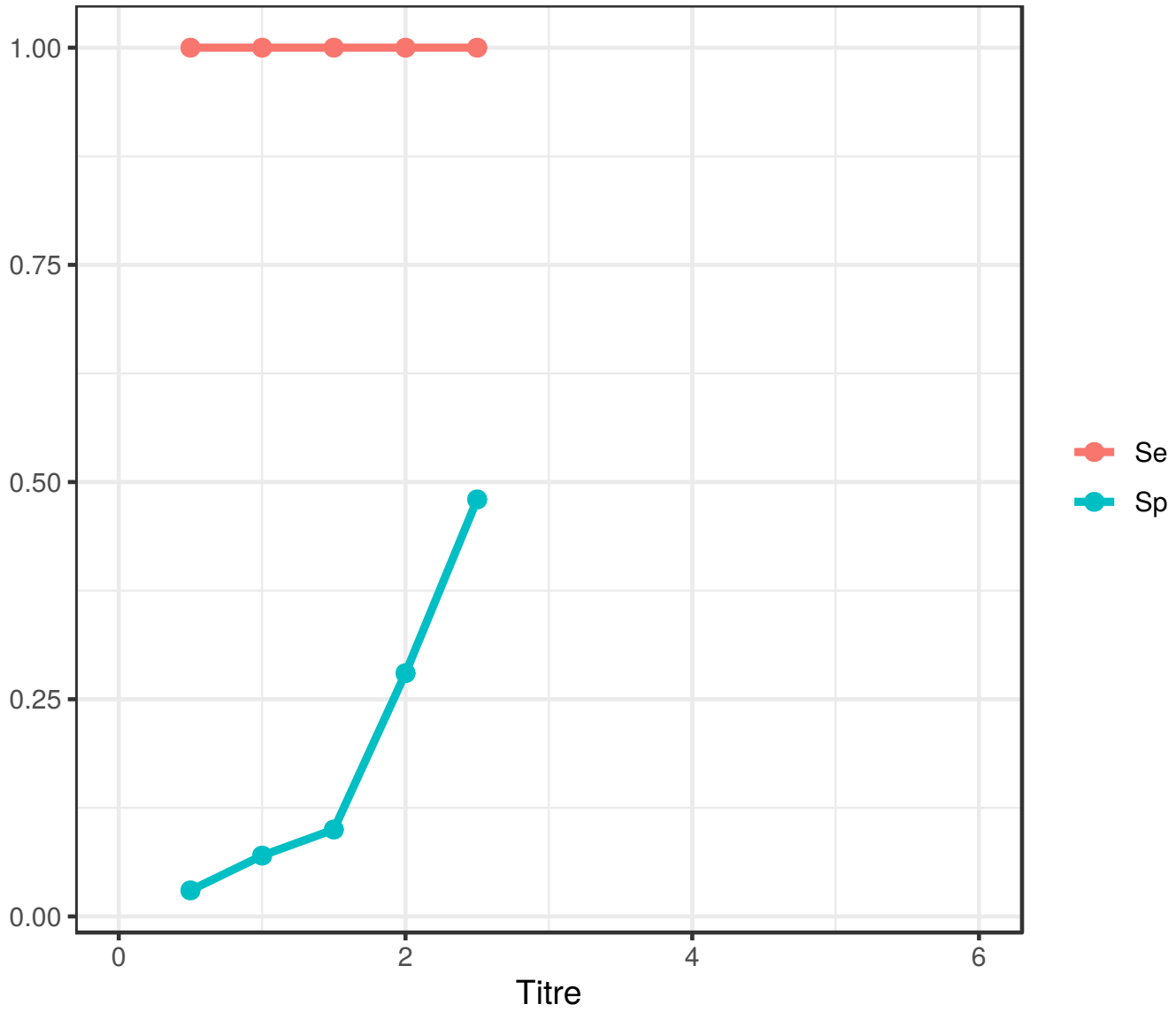
Se=1.00
Sp=0.28



Titre threshold:
T+: > 2.5
T−: ≤ 2.5

	I+	I−
T+	29	15
T−	0	14

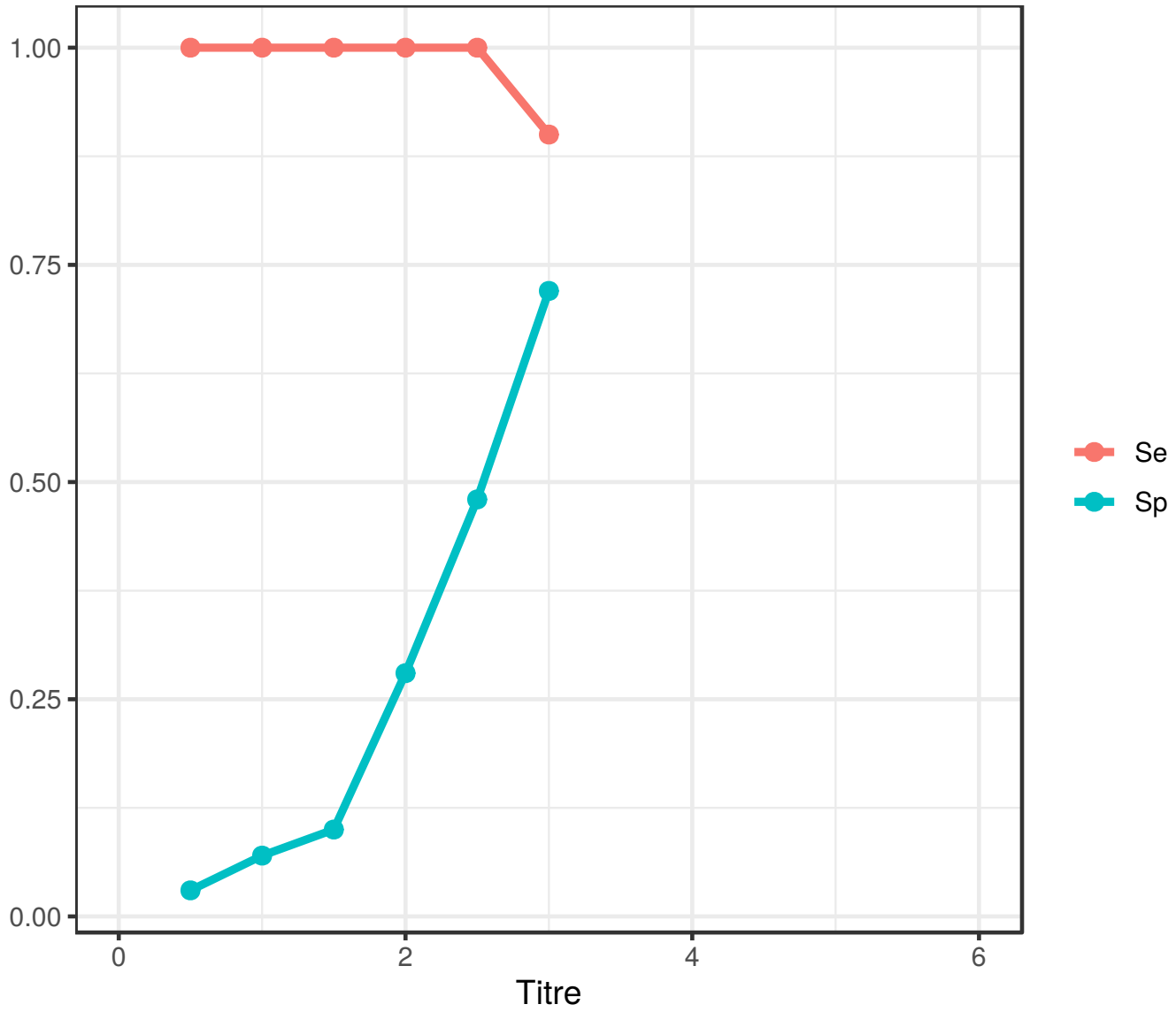
Se=1.00
Sp=0.48



Titre threshold:
T+: > 3.0
T−: ≤ 3.0

	I+	I−
T+	26	8
T−	3	21

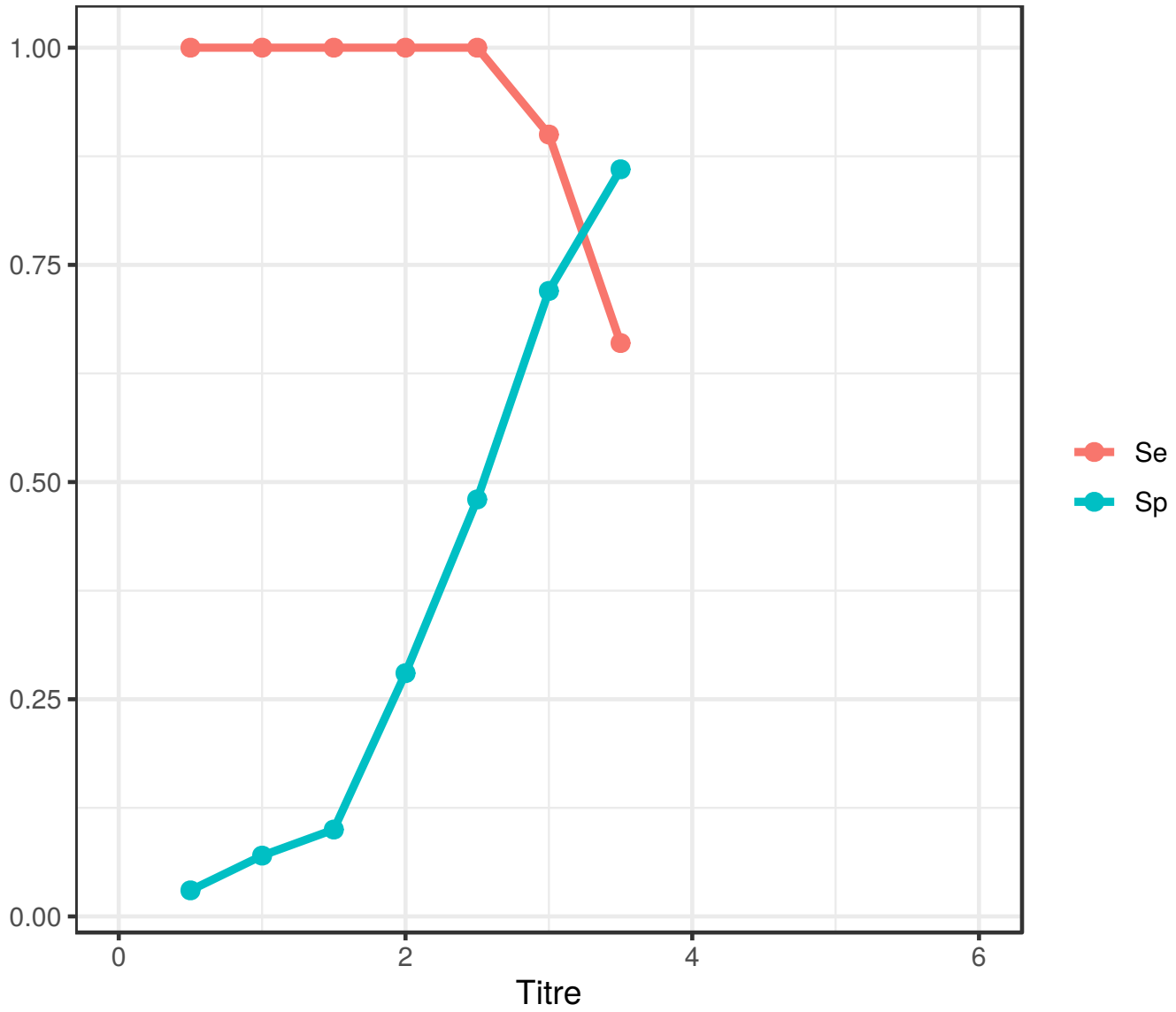
Se=0.90
Sp=0.72



Titre threshold:
T+: > 3.5
T−: ≤ 3.5

	I+	I−
T+	19	4
T−	10	25

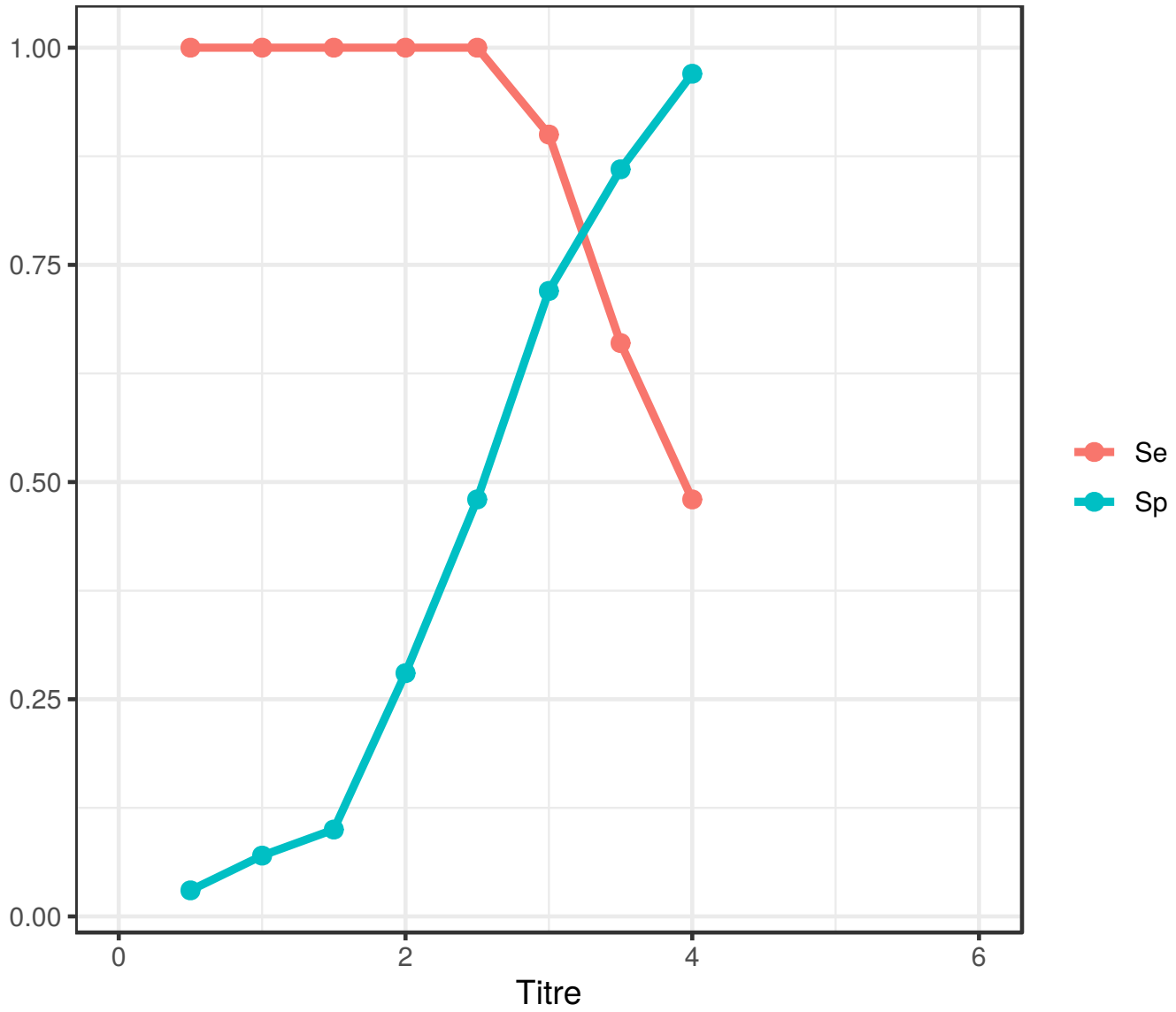
Se=0.66
Sp=0.86



Titre threshold:
T+: > 4.0
T−: ≤ 4.0

	I+	I−
T+	14	1
T−	15	28

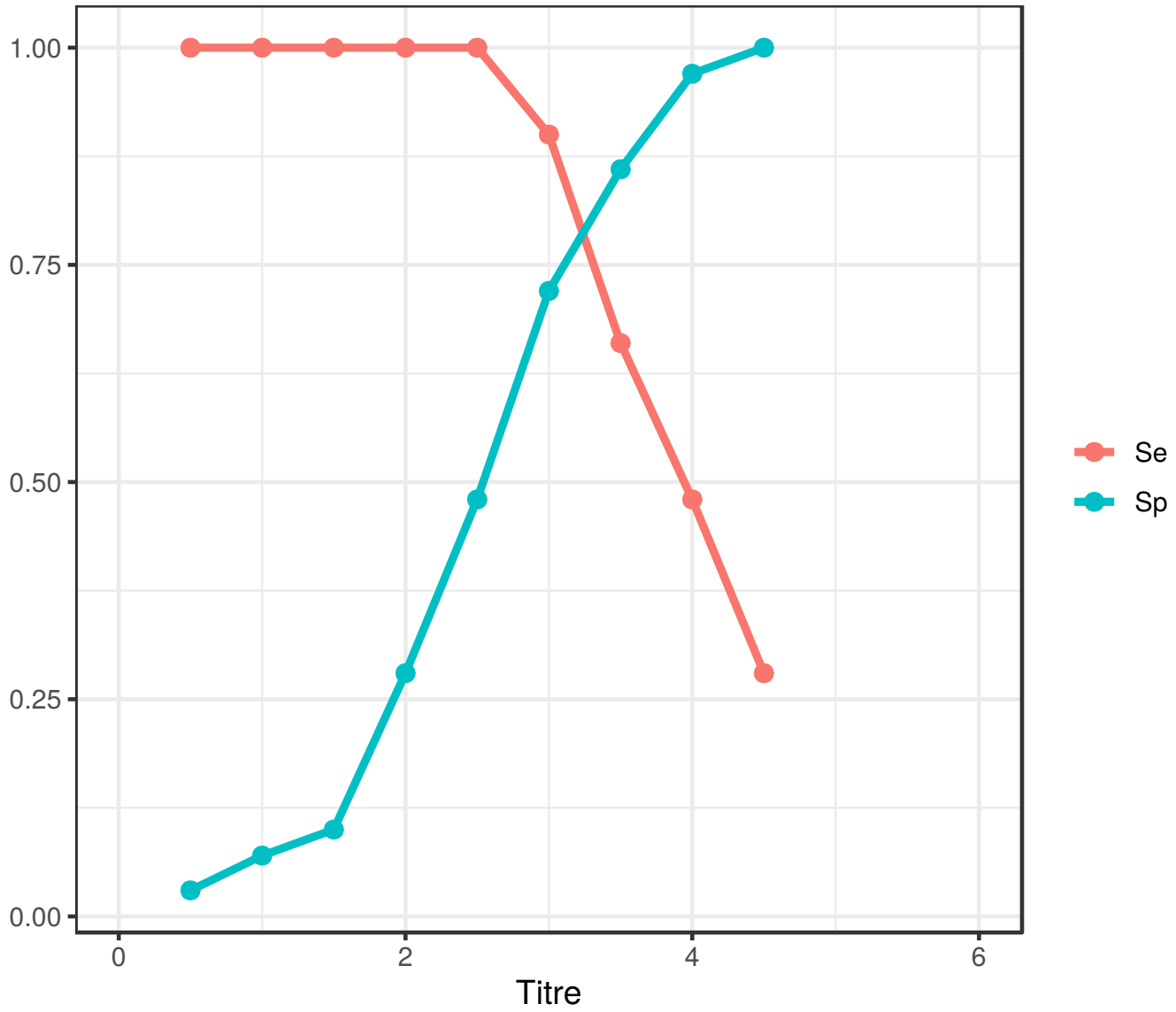
Se=0.48
Sp=0.97



Titre threshold:
T+: > 4.5
T−: ≤ 4.5

	I+	I−
T+	8	0
T−	21	29

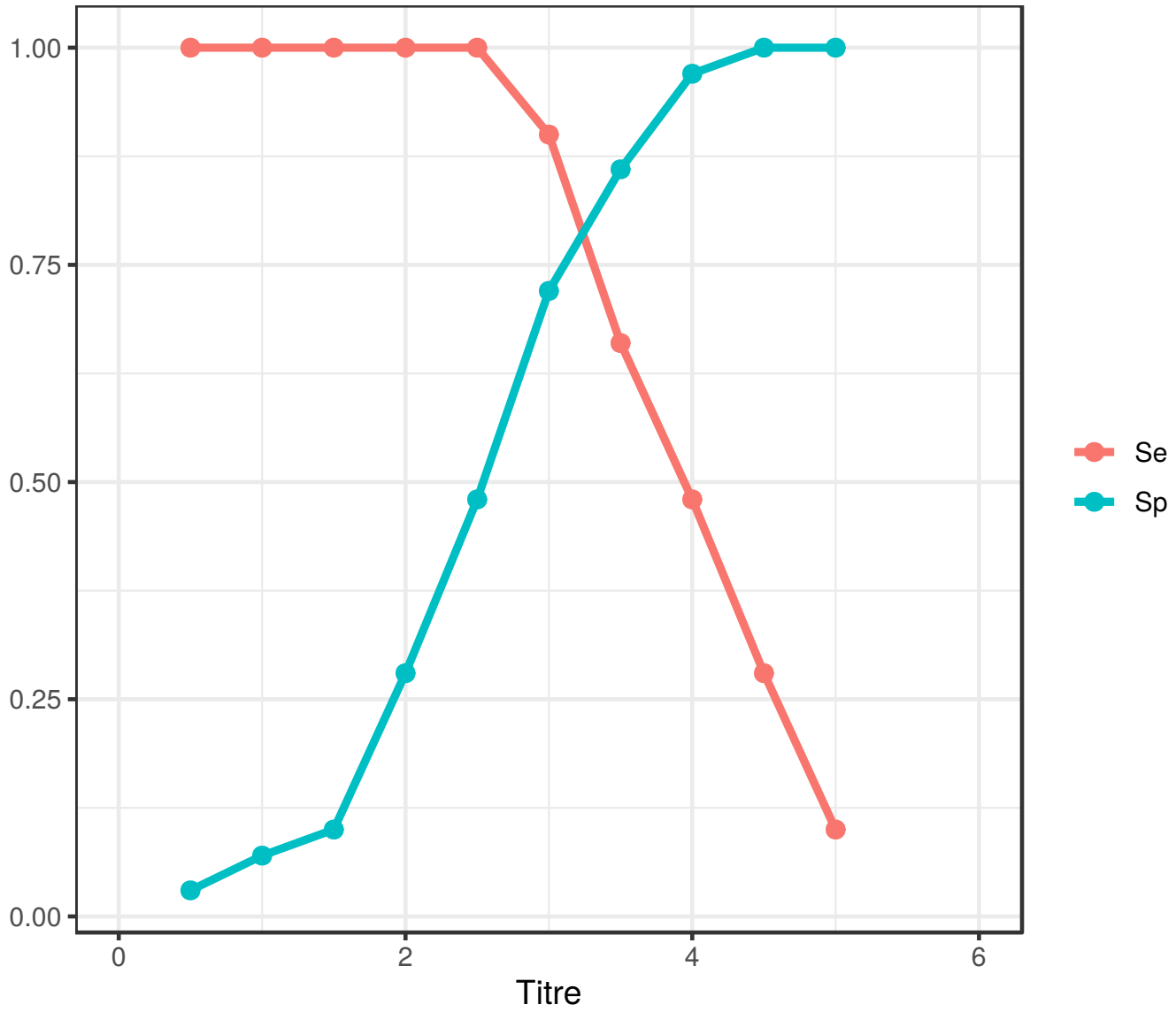
Se=0.28
Sp=1.00



Titre threshold:
T+: > 5.0
T−: ≤ 5.0

	I+	I−
T+	3	0
T−	26	29

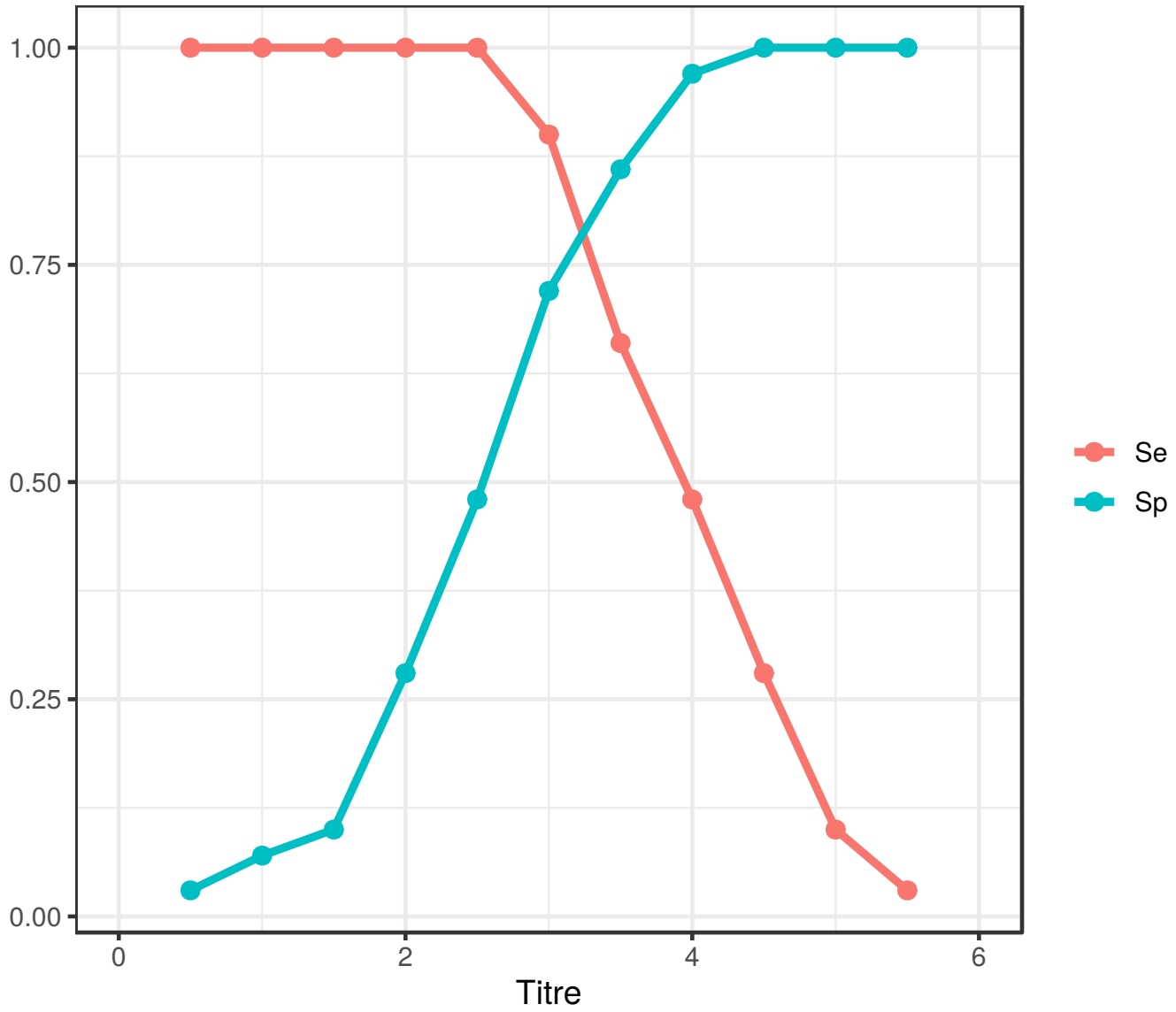
Se=0.10
Sp=1.00



Titre threshold:
T+: > 5.5
T−: ≤ 5.5

	I+	I−
T+	1	0
T−	28	29

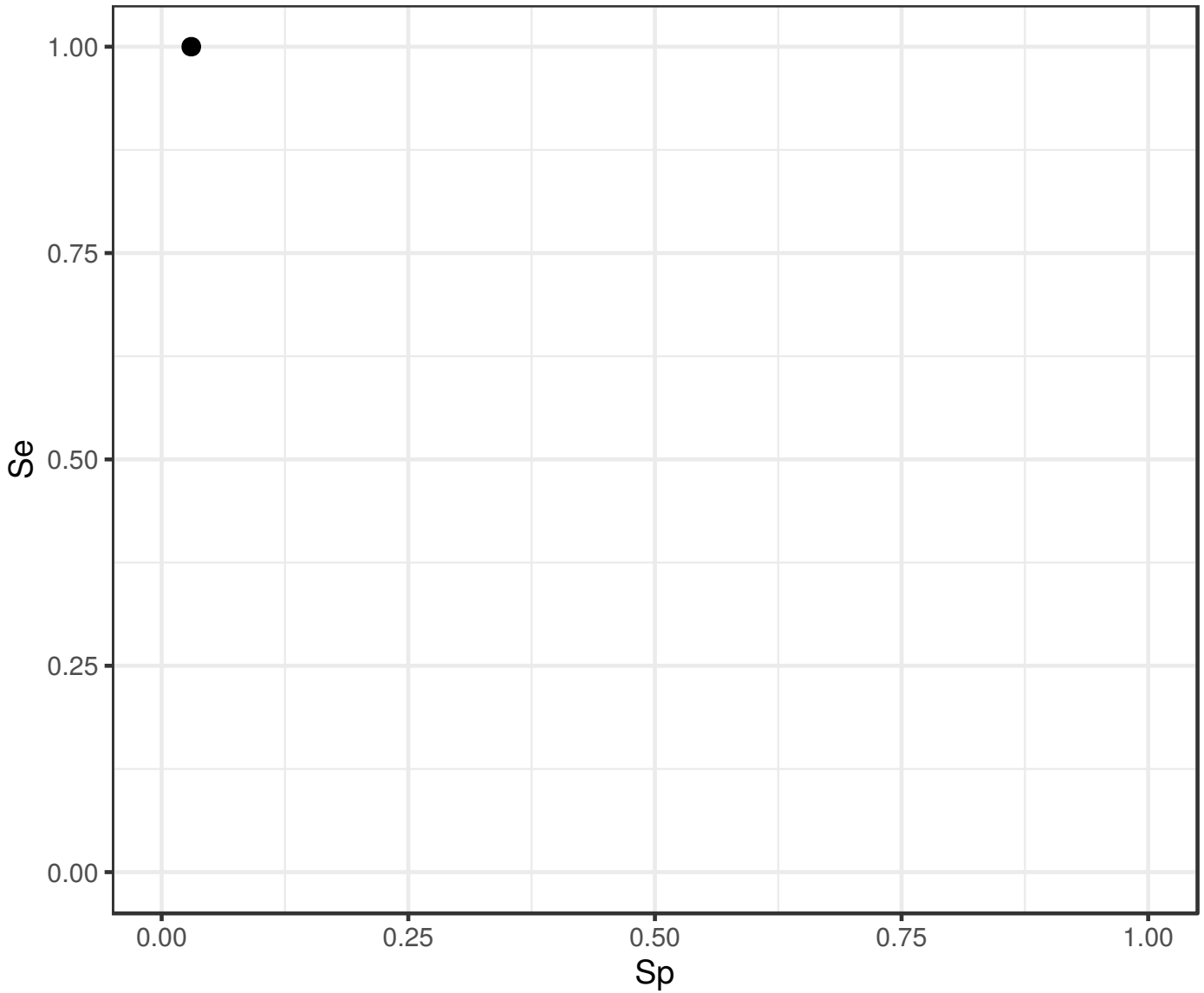
Se=0.03
Sp=1.00



Titre threshold:
T+: > 0.5
T−: ≤ 0.5

	I+	I−
T+	29	28
T−	0	1

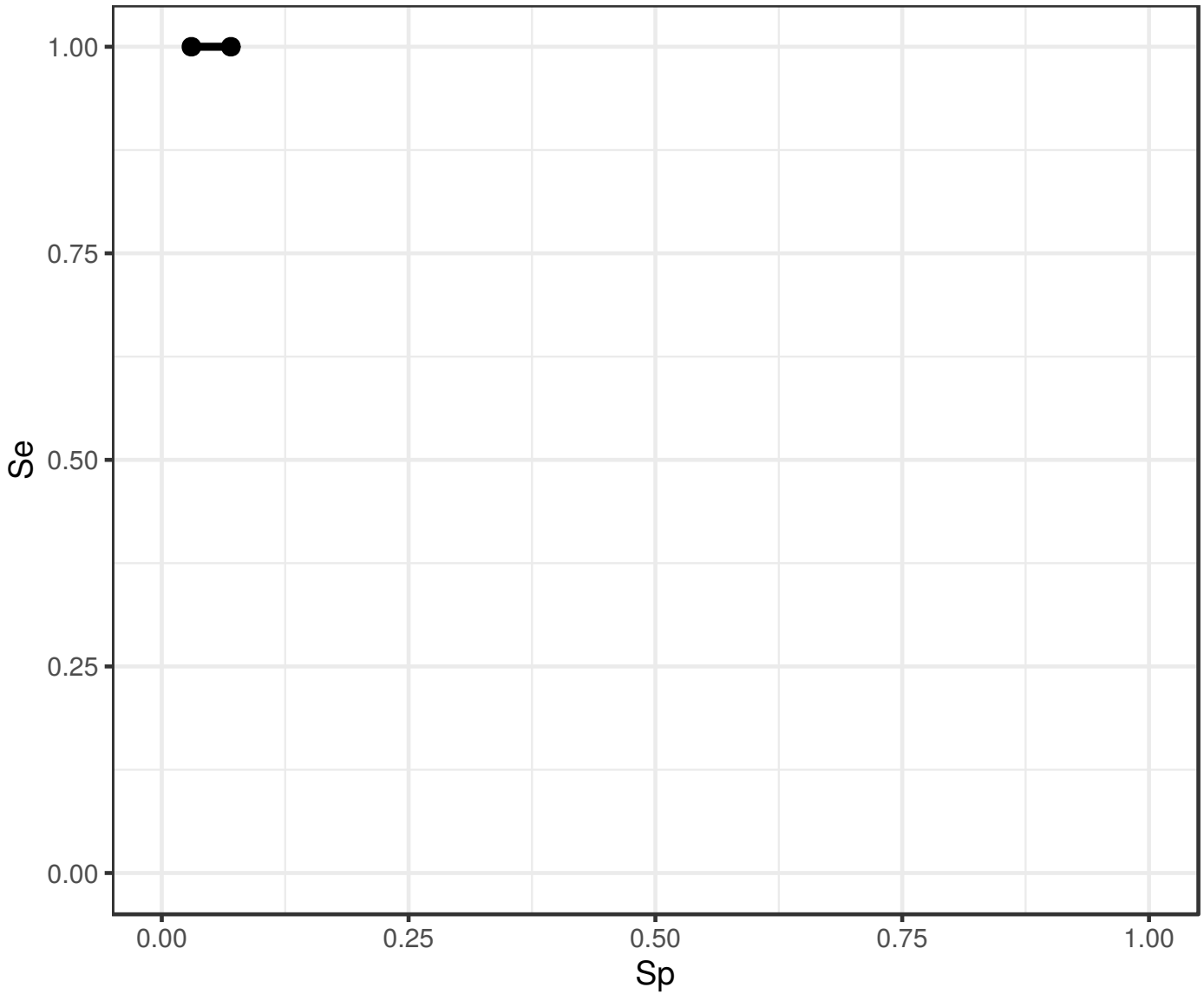
Se=1.00
Sp=0.03



Titre threshold:
T+: > 1.0
T−: ≤ 1.0

	I+	I−
T+	29	27
T−	0	2

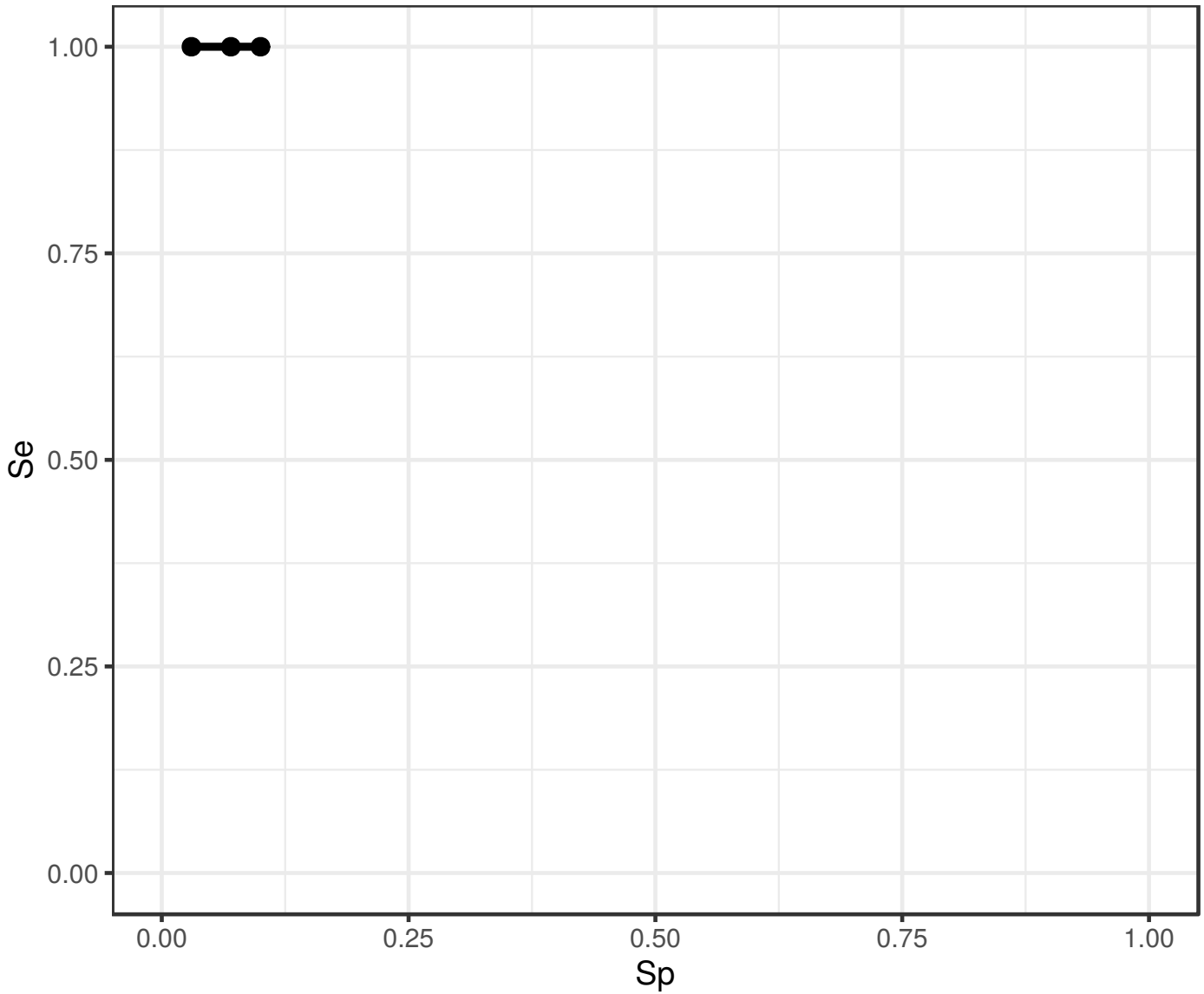
Se=1.00
Sp=0.07



Titre threshold:
T+: > 1.5
T−: ≤ 1.5

	I+	I−
T+	29	26
T−	0	3

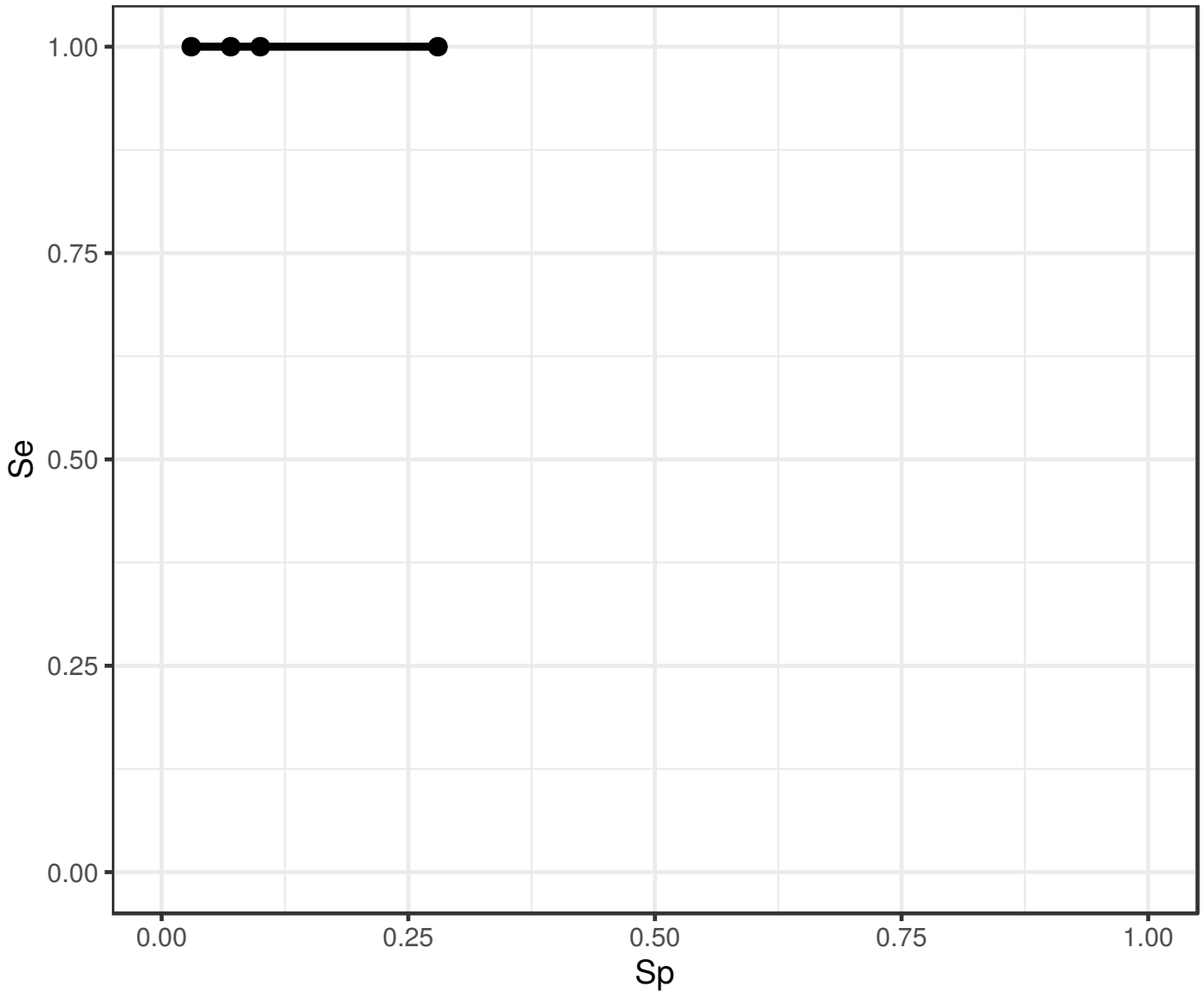
Se=1.00
Sp=0.10



Titre threshold:
T+: > 2.0
T−: ≤ 2.0

	I+	I−
T+	29	21
T−	0	8

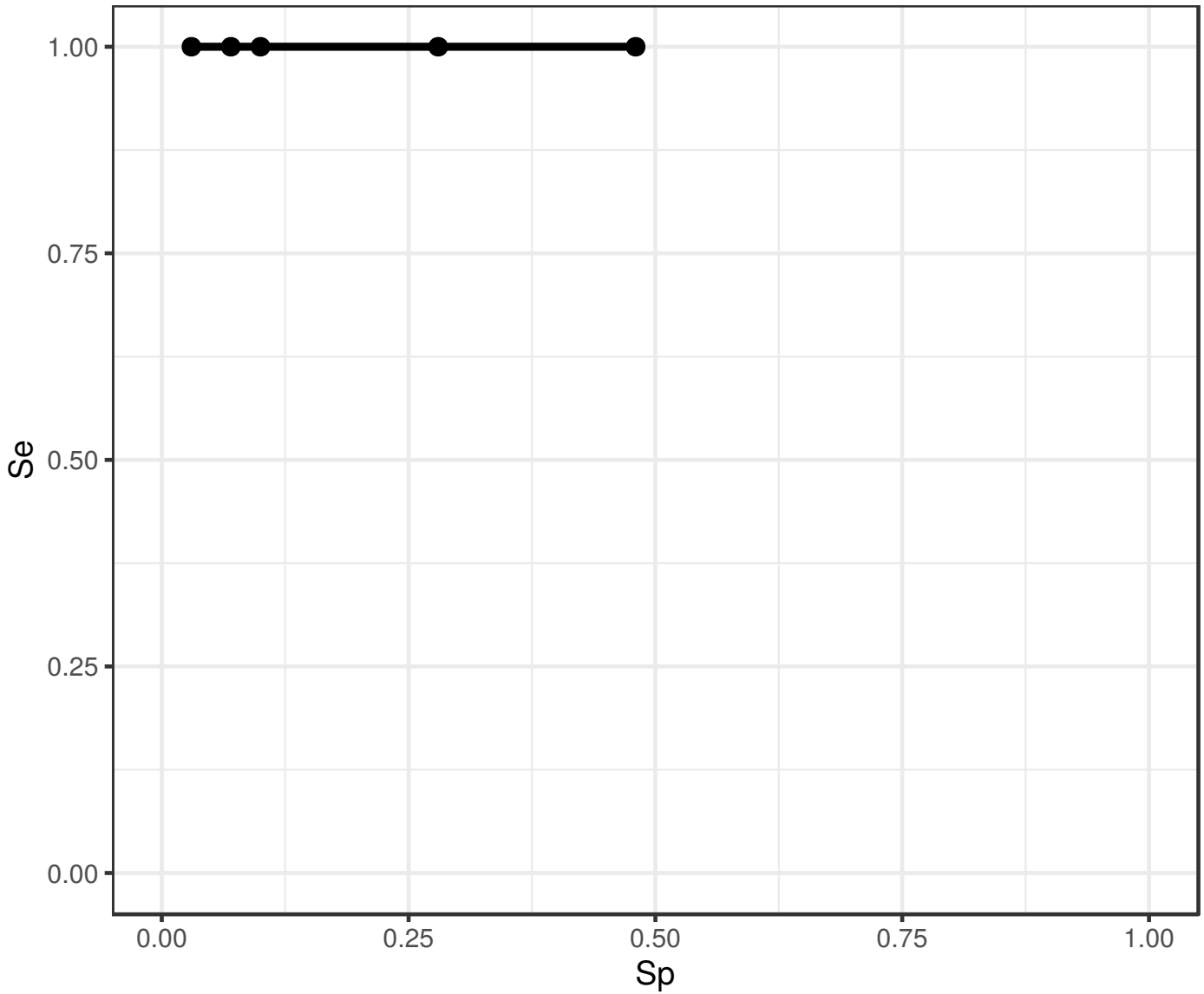
Se=1.00
Sp=0.28



Titre threshold:
T+: > 2.5
T−: ≤ 2.5

	I+	I−
T+	29	15
T−	0	14

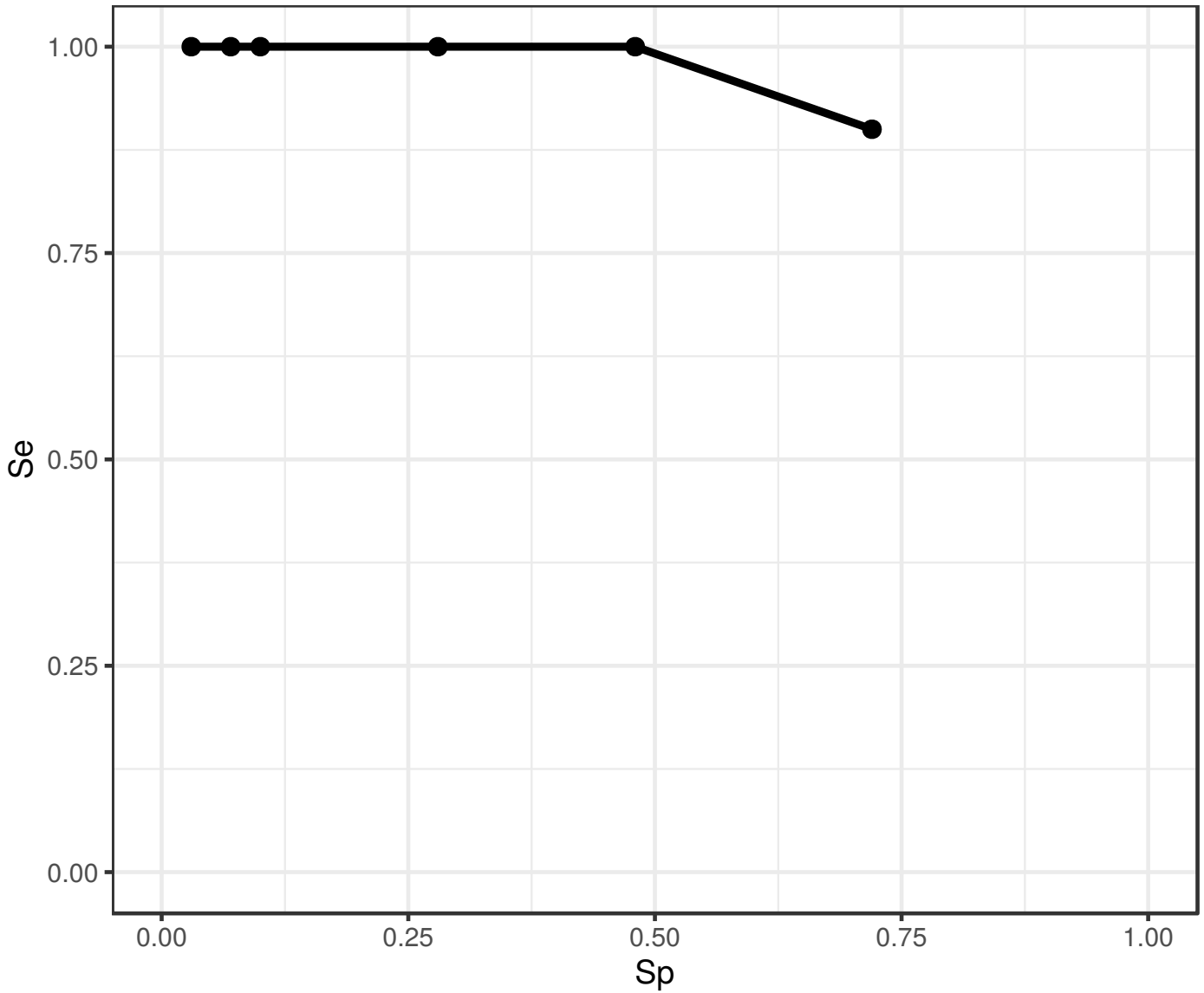
Se=1.00
Sp=0.48



Titre threshold:
T+: > 3.0
T−: ≤ 3.0

	I+	I−
T+	26	8
T−	3	21

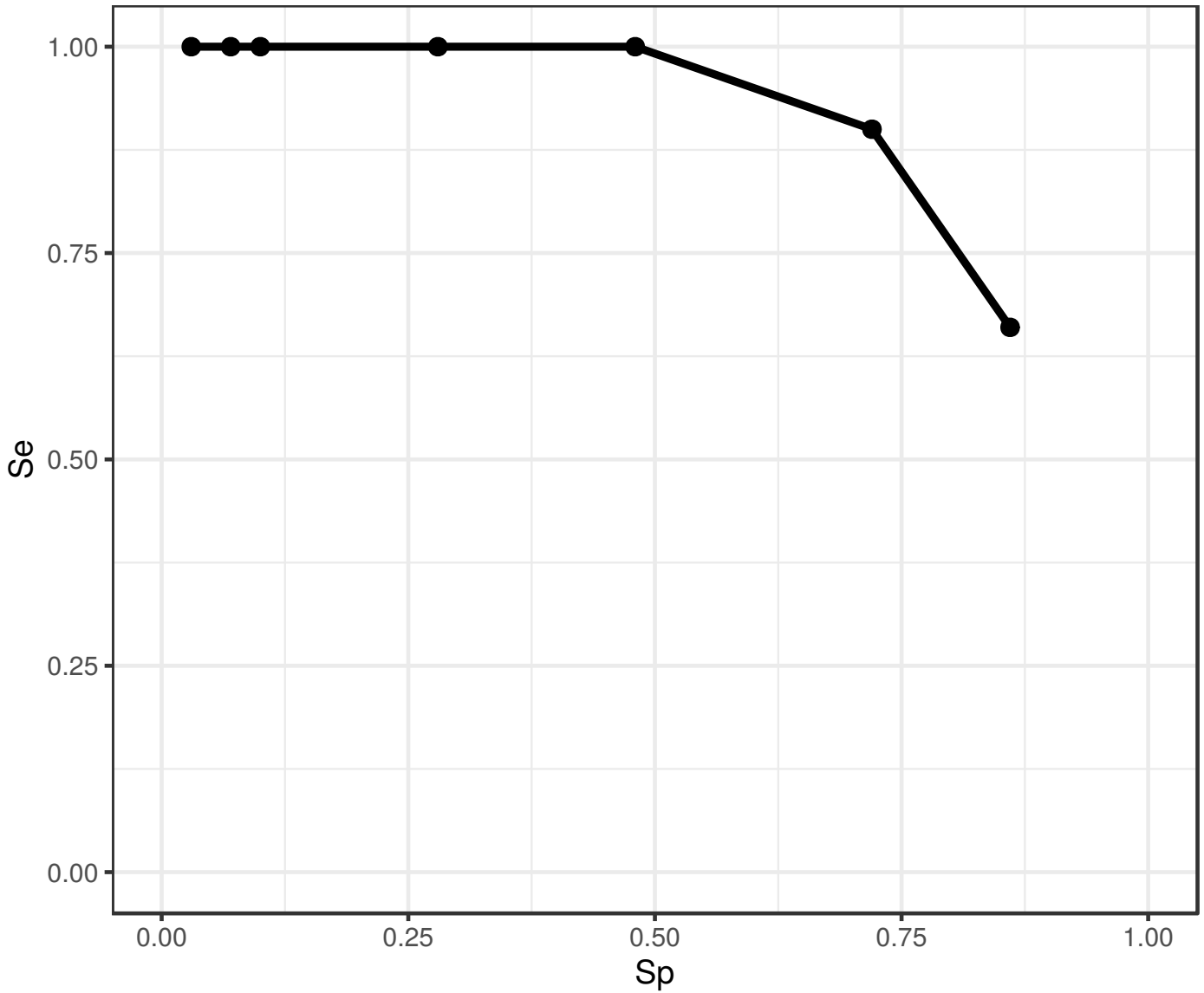
Se=0.90
Sp=0.72



Titre threshold:
T+: > 3.5
T−: ≤ 3.5

	I+	I−
T+	19	4
T−	10	25

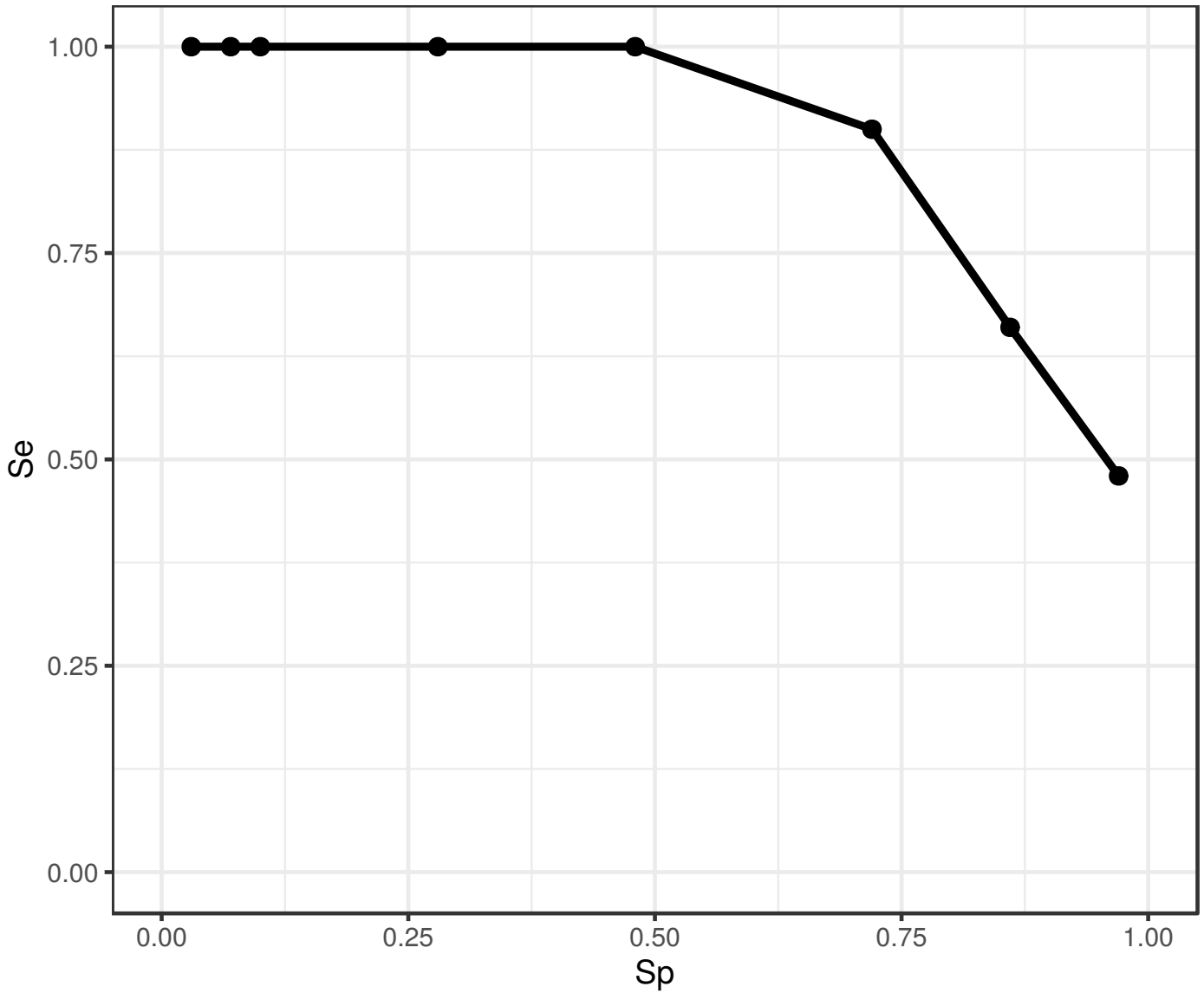
Se=0.66
Sp=0.86



Titre threshold:
T+: > 4.0
T−: ≤ 4.0

	I+	I−
T+	14	1
T−	15	28

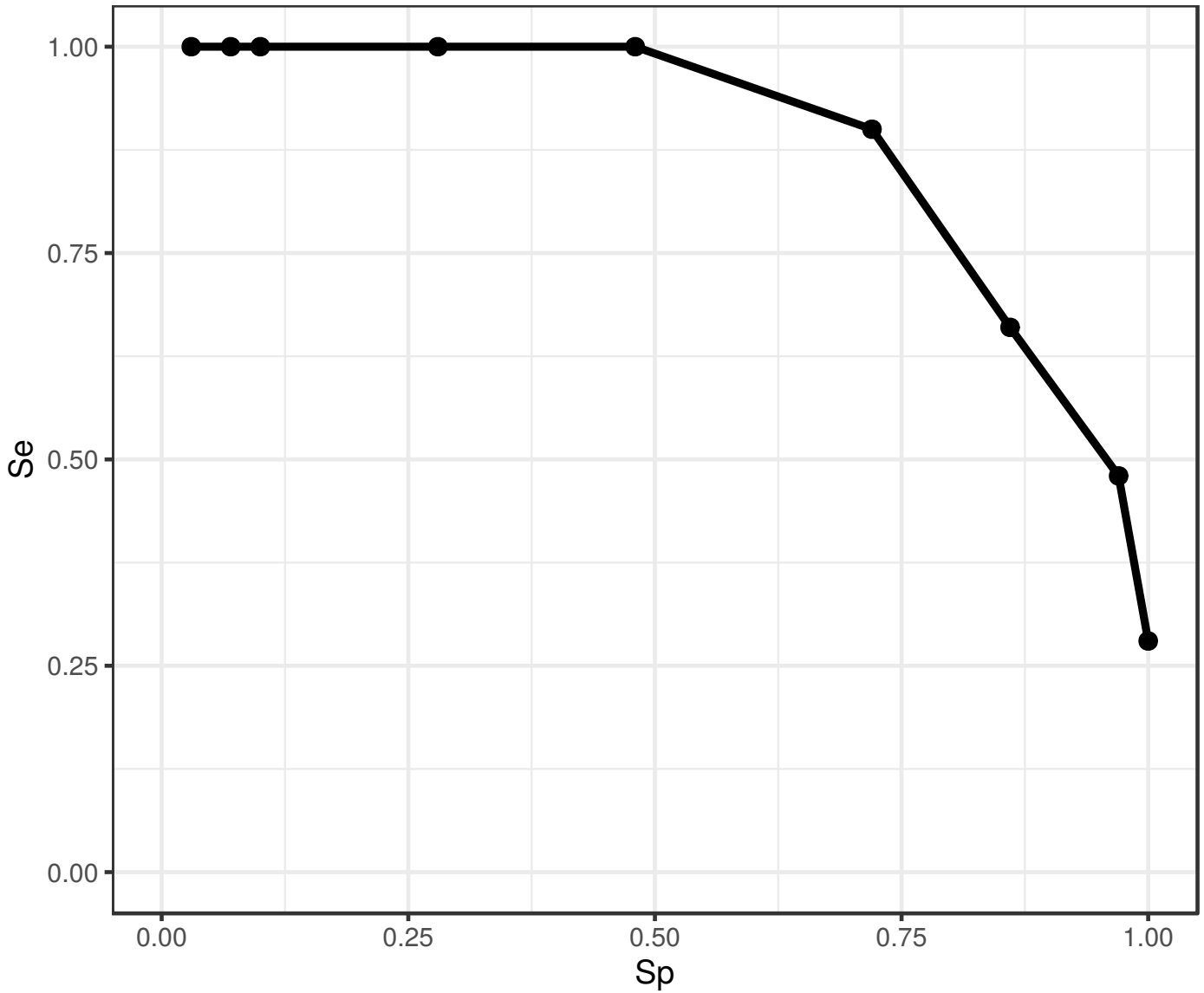
Se=0.48
Sp=0.97



Titre threshold:
T+: > 4.5
T−: ≤ 4.5

	I+	I−
T+	8	0
T−	21	29

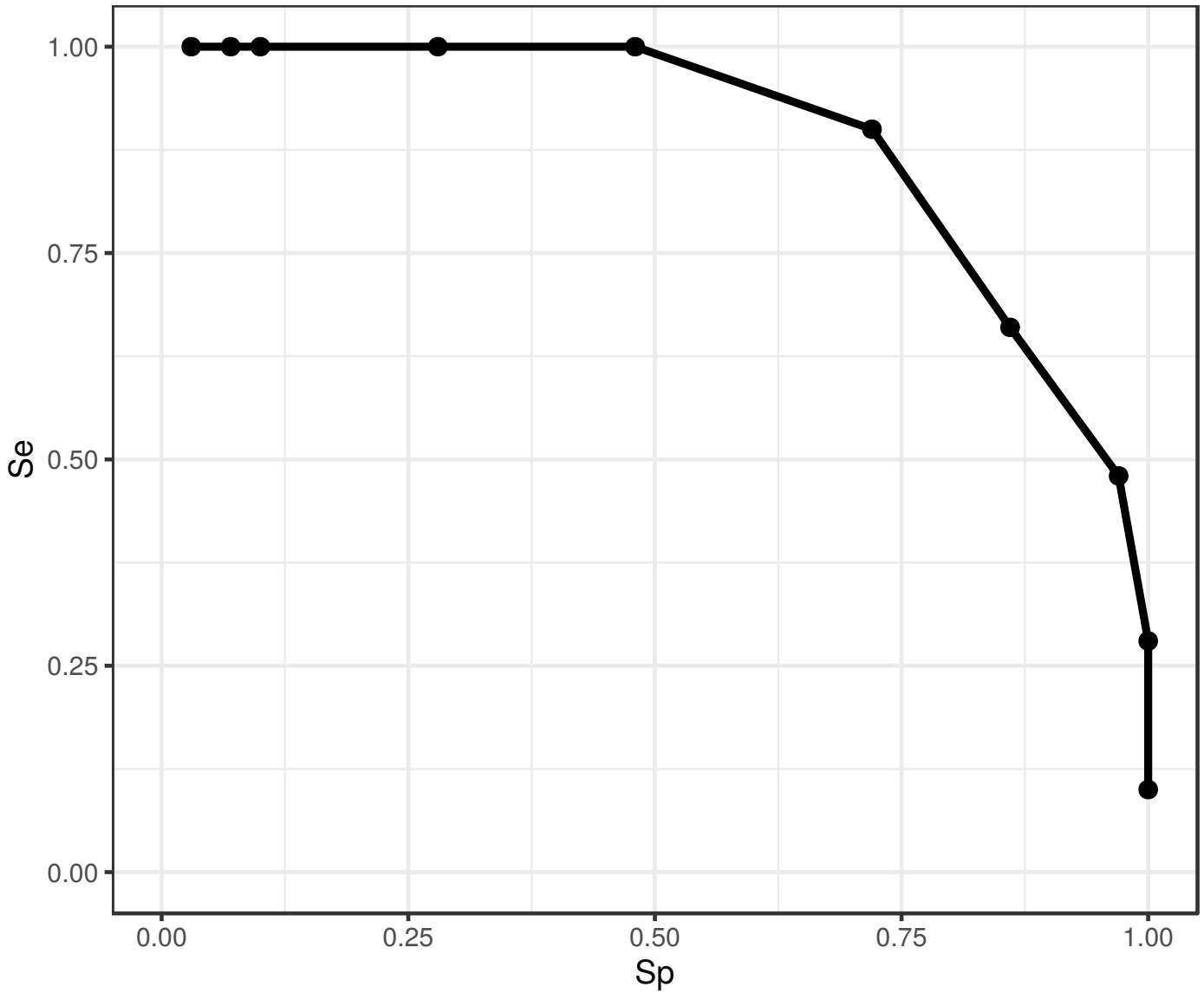
Se=0.28
Sp=1.00



Titre threshold:
T+: > 5.0
T−: ≤ 5.0

	I+	I−
T+	3	0
T−	26	29

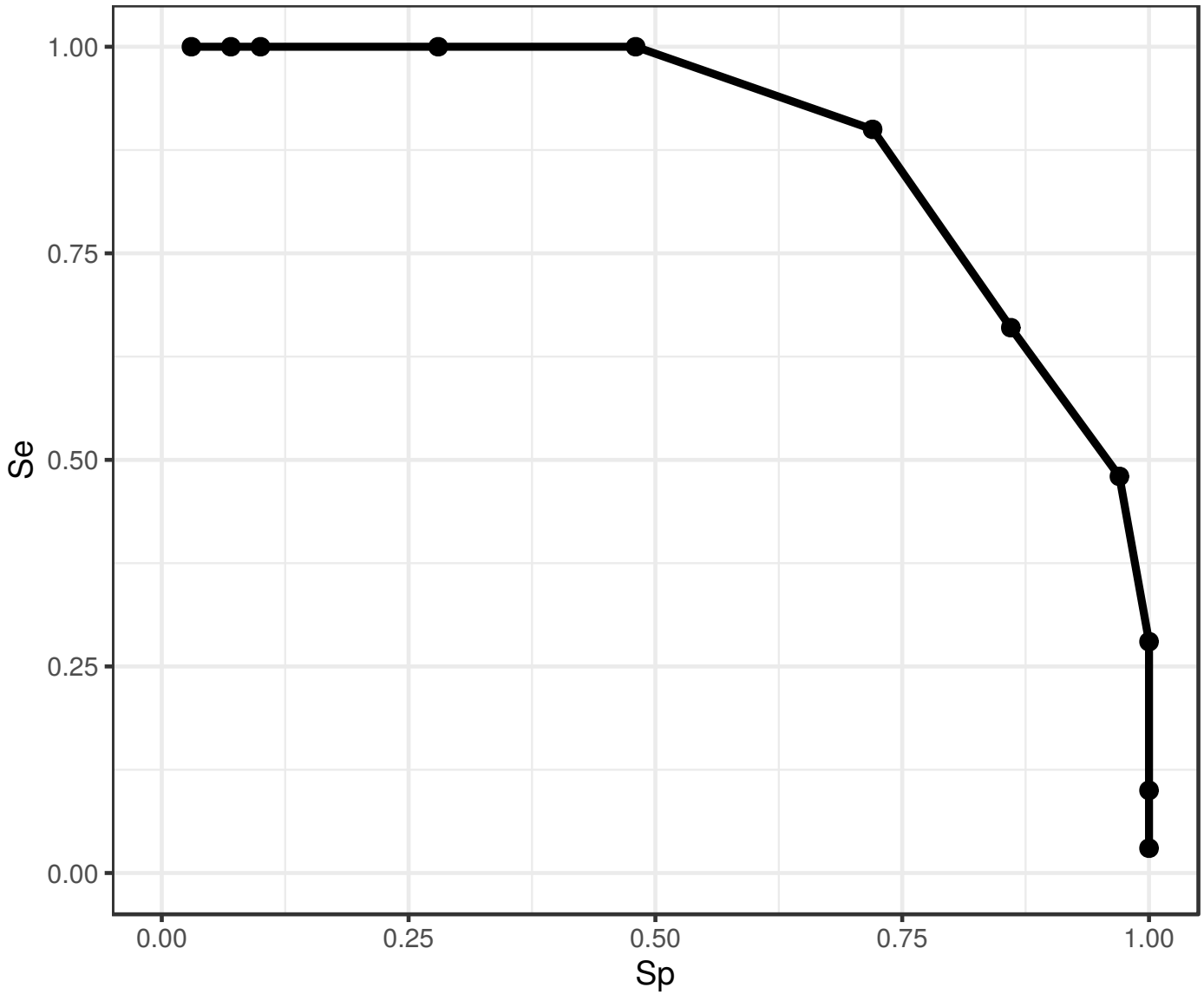
Se=0.10
Sp=1.00



Titre threshold:
T+: > 5.5
T−: ≤ 5.5

	I+	I−
T+	1	0
T−	28	29

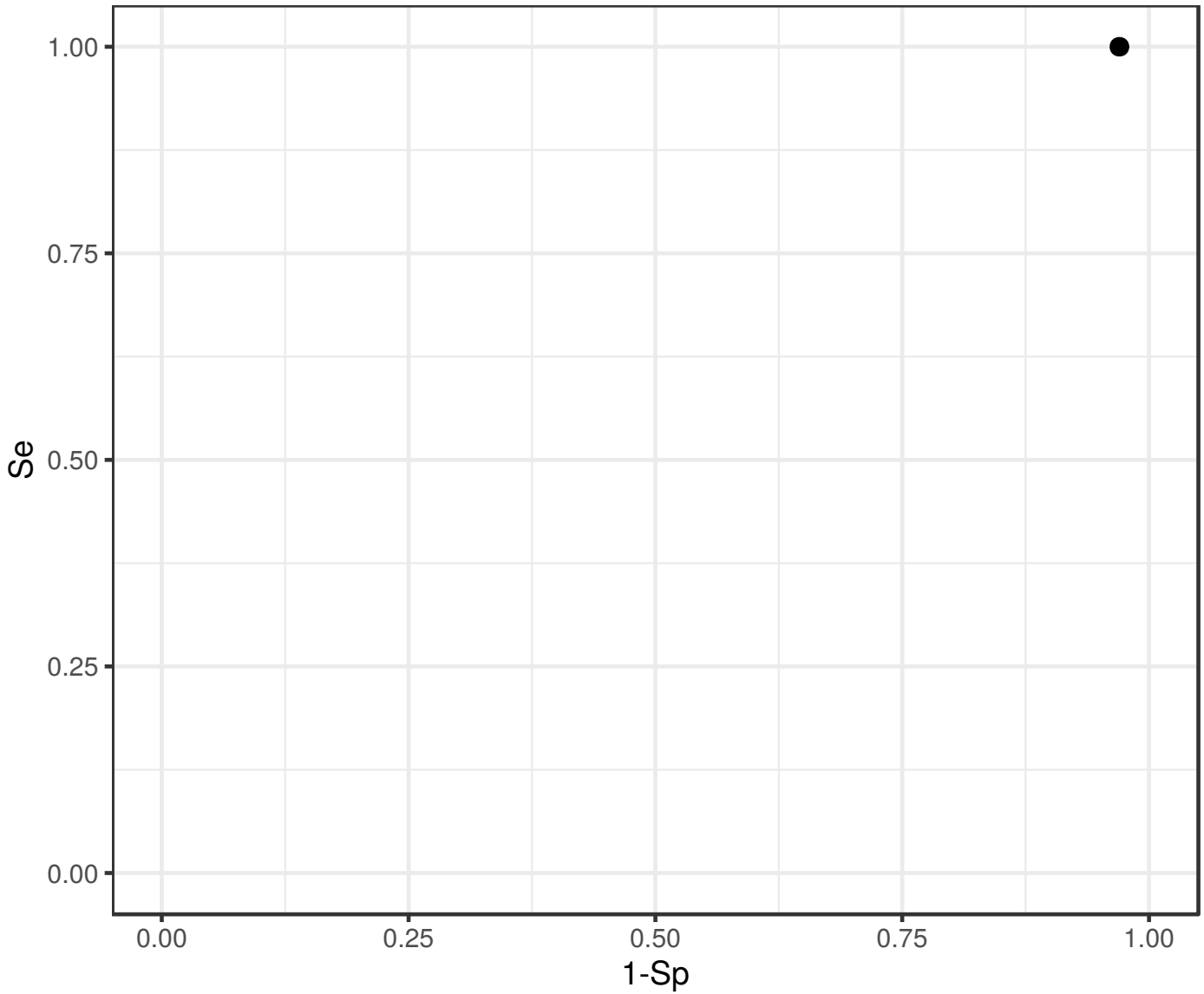
Se=0.03
Sp=1.00



Titre threshold:
T+: > 0.5
T−: ≤ 0.5

	I+	I−
T+	29	28
T−	0	1

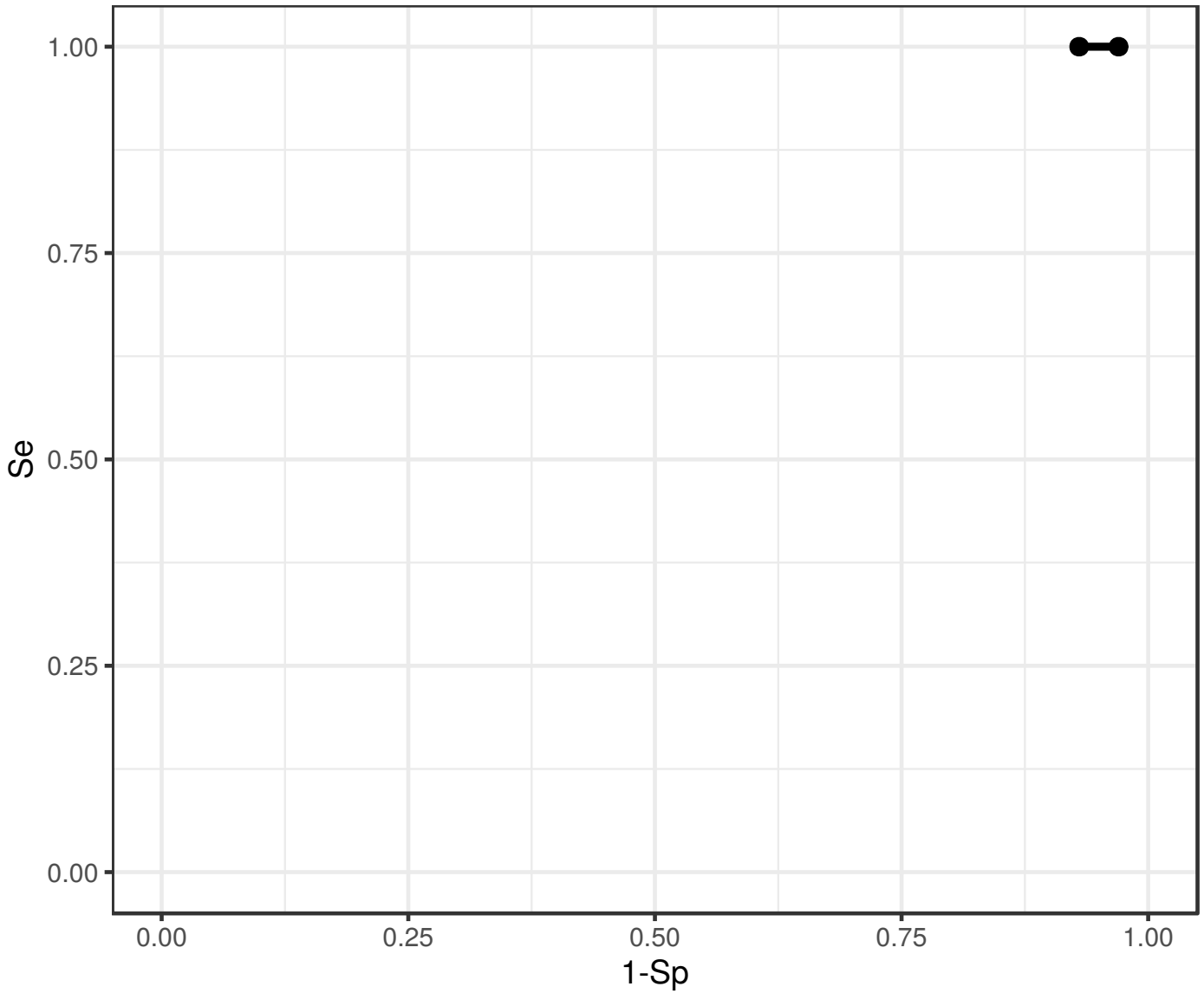
Se=1.00
Sp=0.03



Titre threshold:
T+: > 1.0
T−: ≤ 1.0

	I+	I−
T+	29	27
T−	0	2

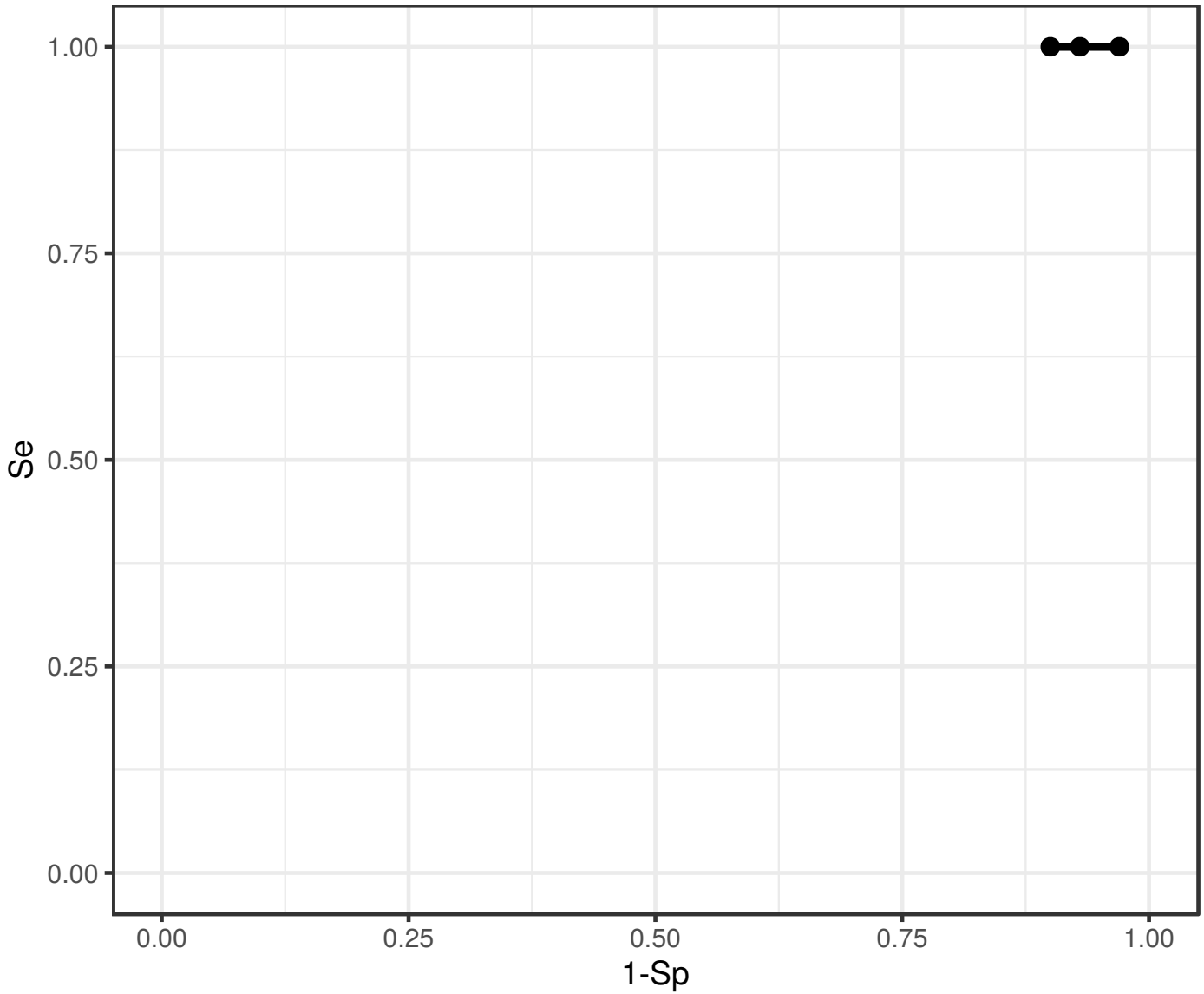
Se=1.00
Sp=0.07



Titre threshold:
T+: > 1.5
T−: ≤ 1.5

	I+	I−
T+	29	26
T−	0	3

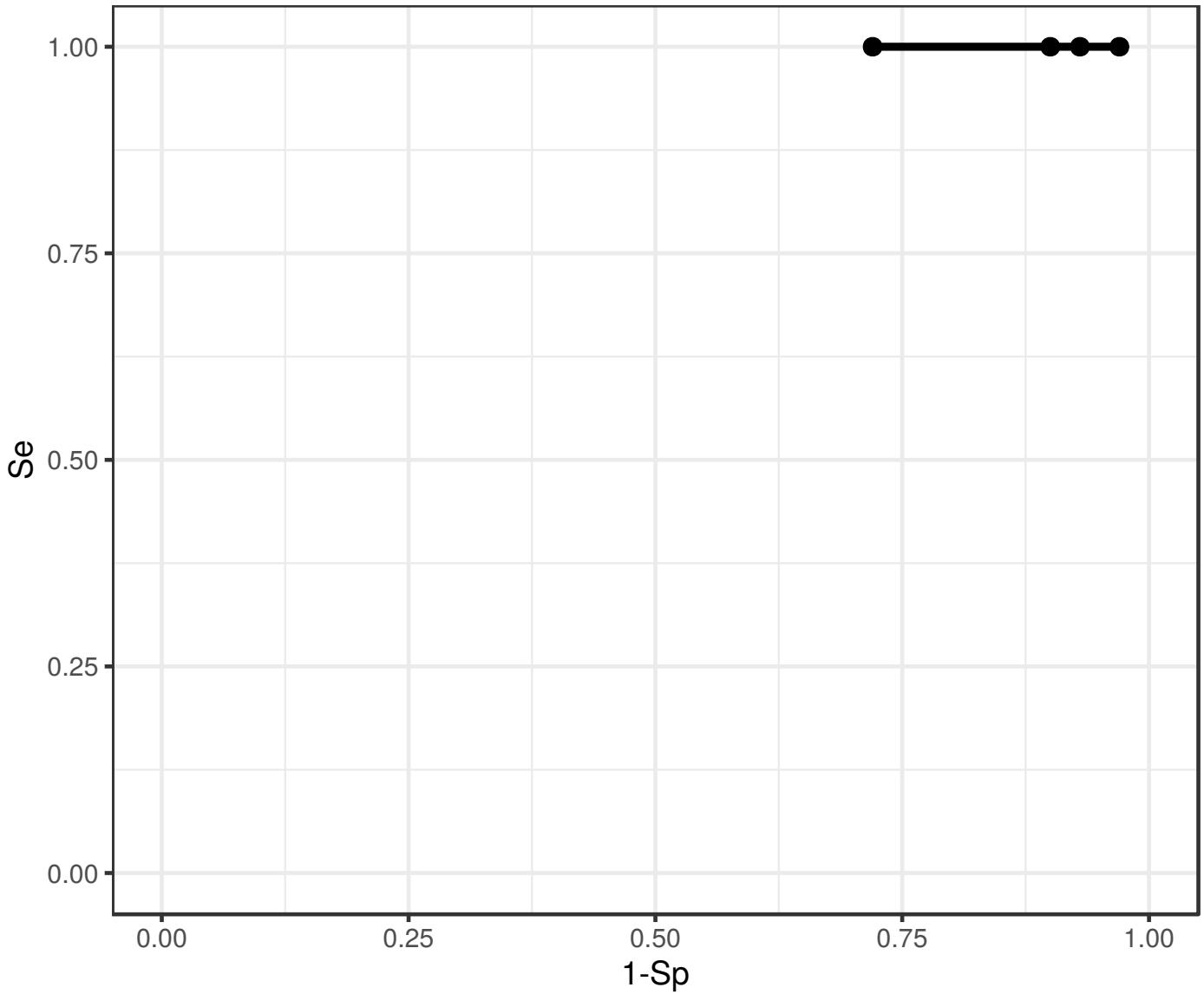
Se=1.00
Sp=0.10



Titre threshold:
T+: > 2.0
T−: ≤ 2.0

	I+	I−
T+	29	21
T−	0	8

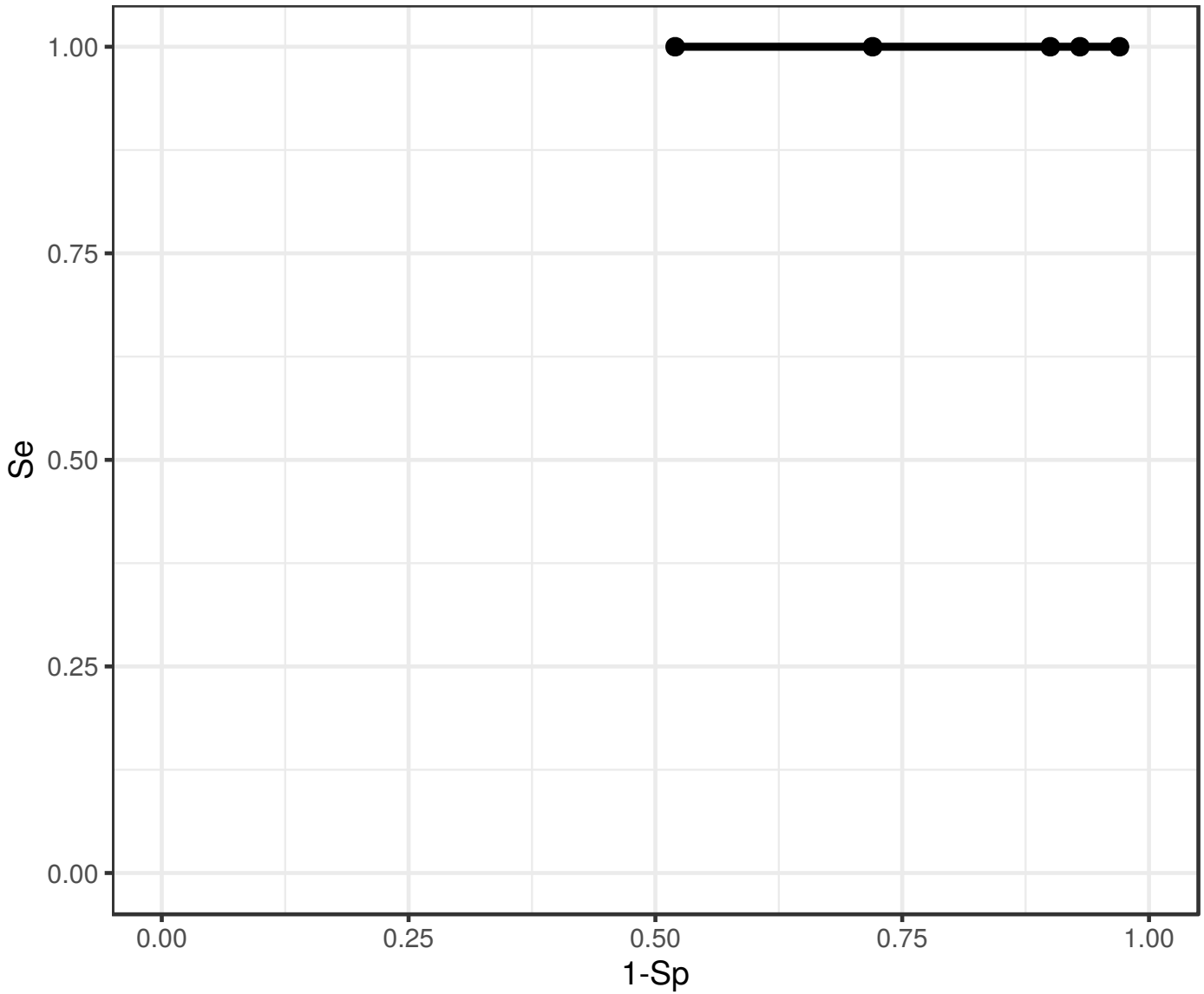
Se=1.00
Sp=0.28



Titre threshold:
T+: > 2.5
T−: ≤ 2.5

	I+	I−
T+	29	15
T−	0	14

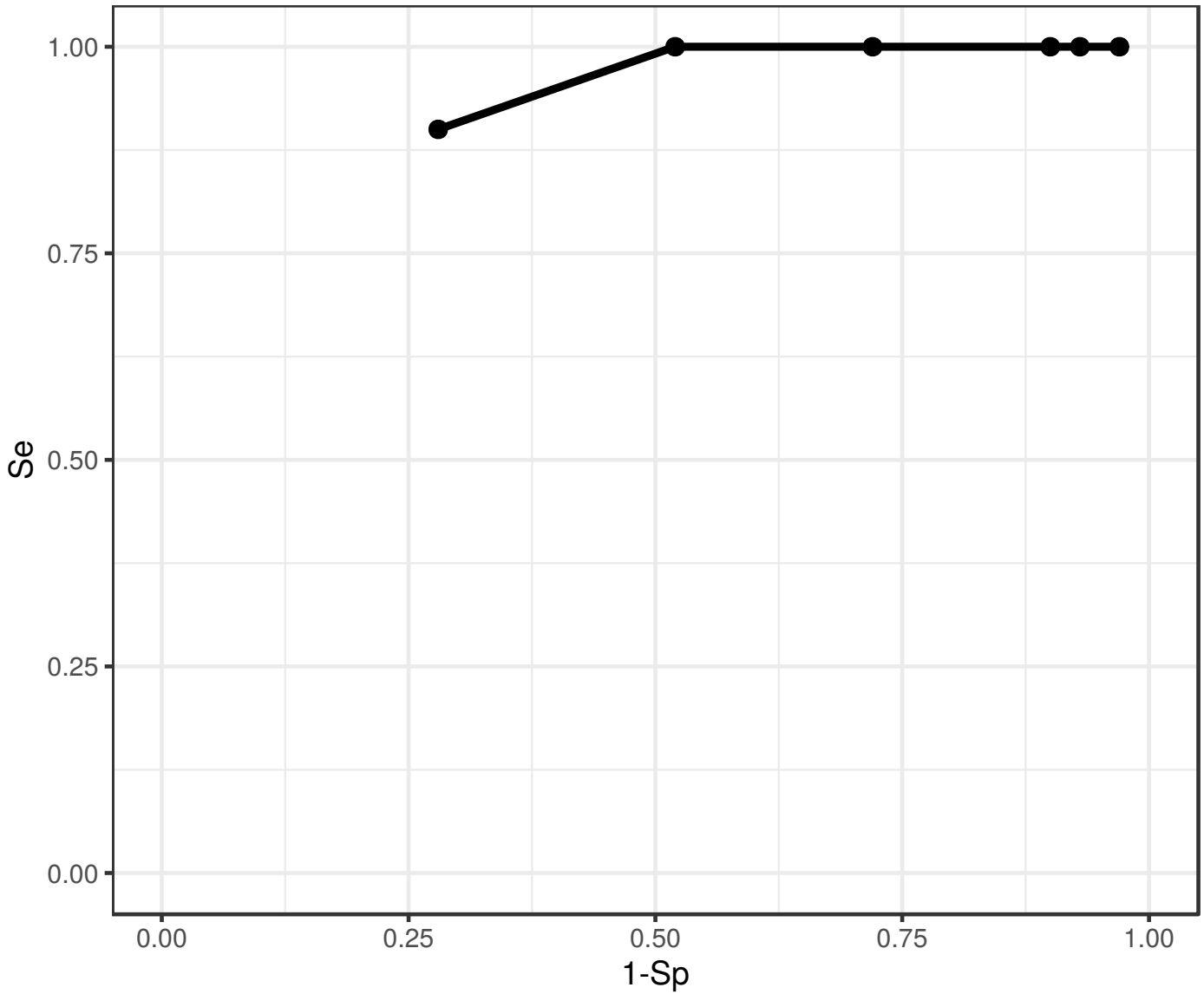
Se=1.00
Sp=0.48



Titre threshold:
T+: > 3.0
T−: ≤ 3.0

	I+	I−
T+	26	8
T−	3	21

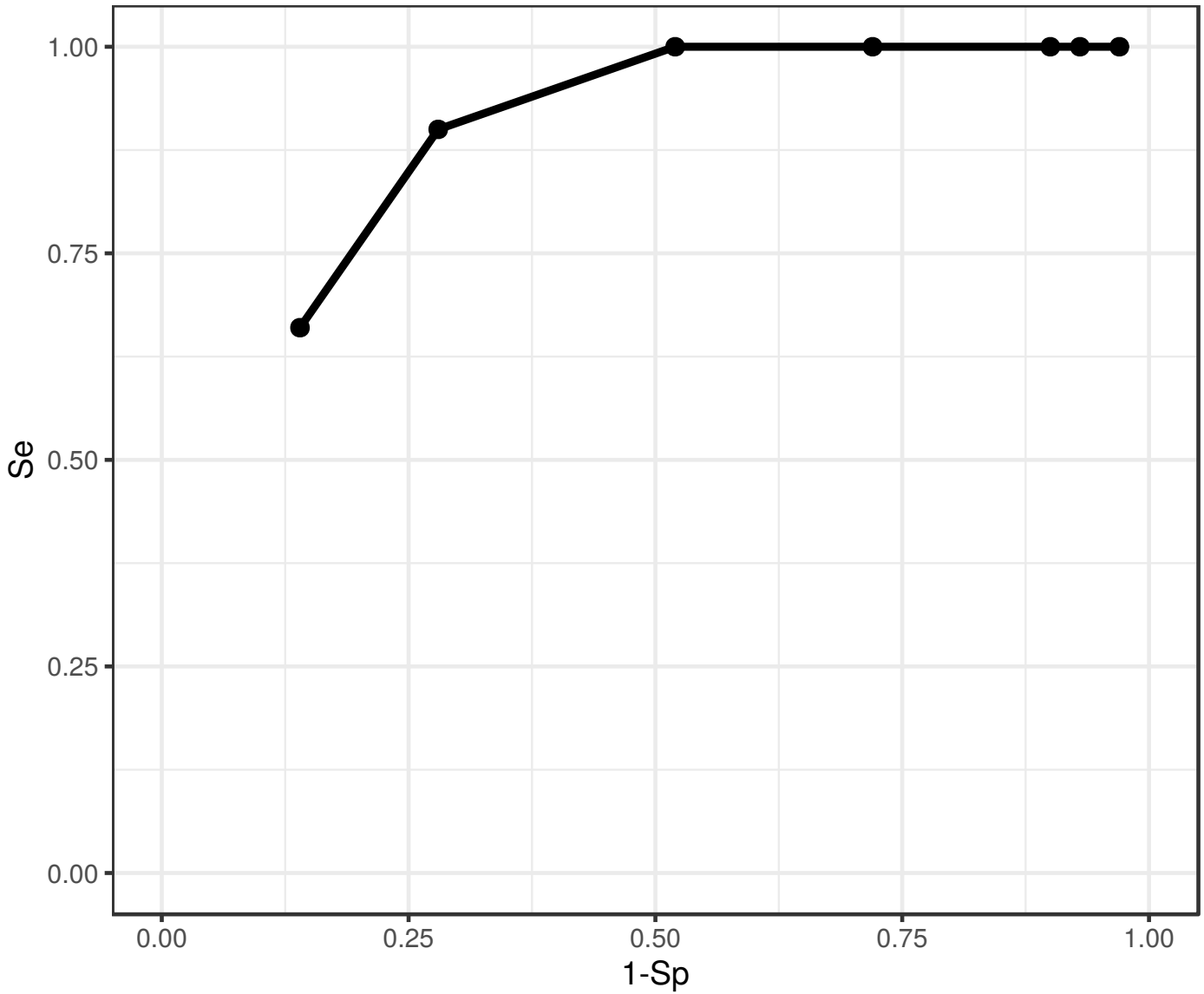
Se=0.90
Sp=0.72



Titre threshold:
T+: > 3.5
T−: ≤ 3.5

	I+	I−
T+	19	4
T−	10	25

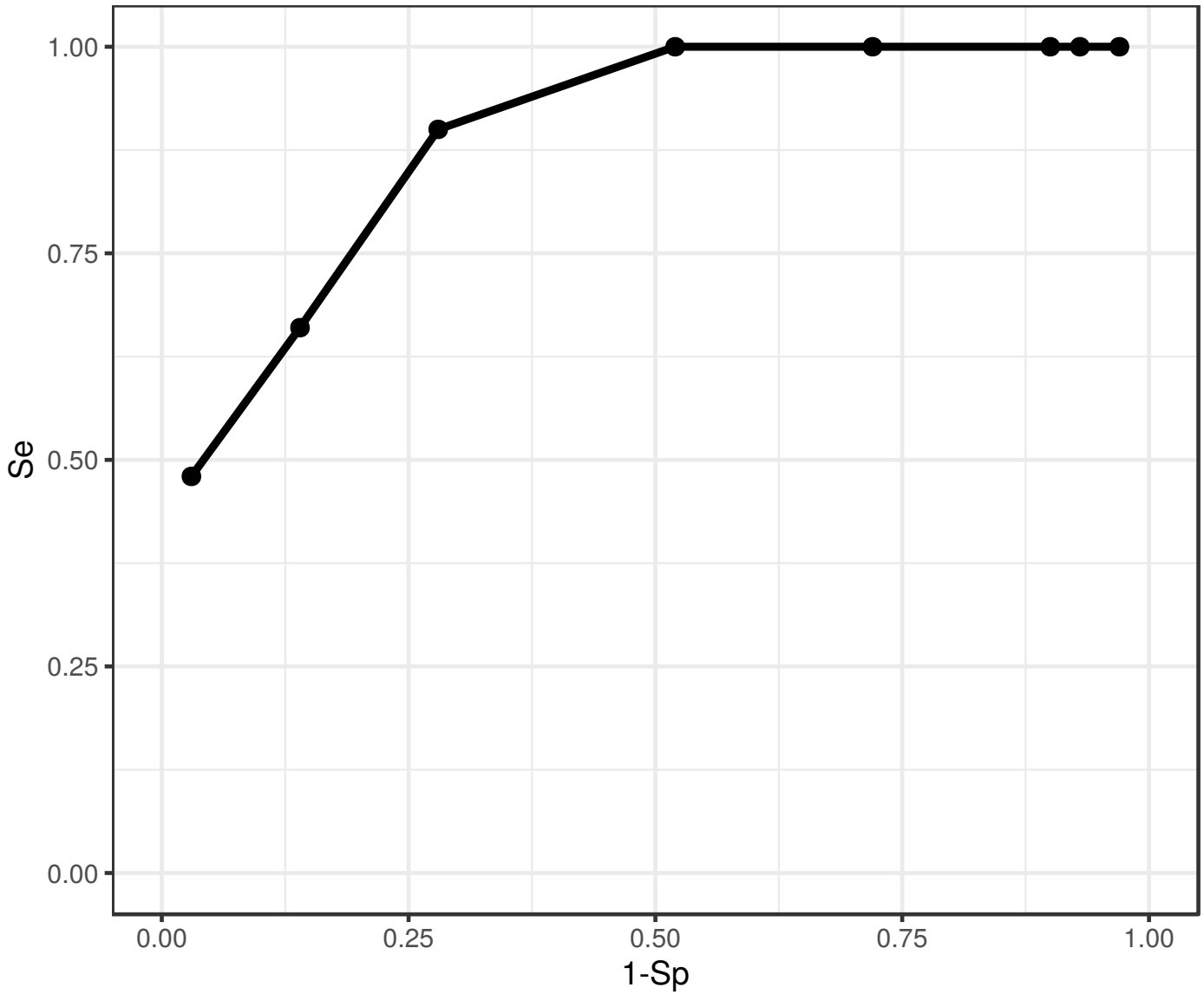
Se=0.66
Sp=0.86



Titre threshold:
T+: > 4.0
T−: ≤ 4.0

	I+	I−
T+	14	1
T−	15	28

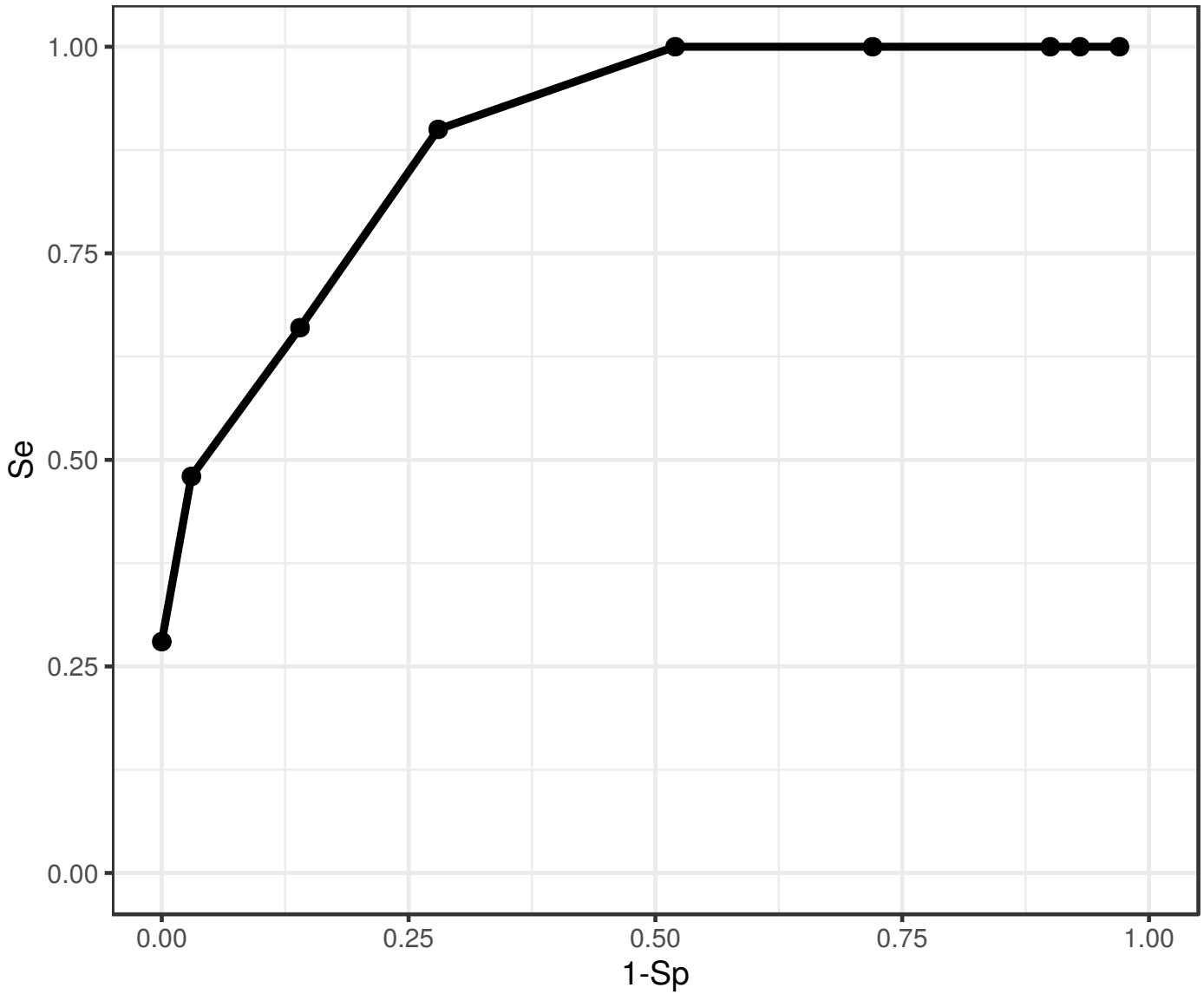
Se=0.48
Sp=0.97



Titre threshold:
T+: > 4.5
T−: ≤ 4.5

	I+	I−
T+	8	0
T−	21	29

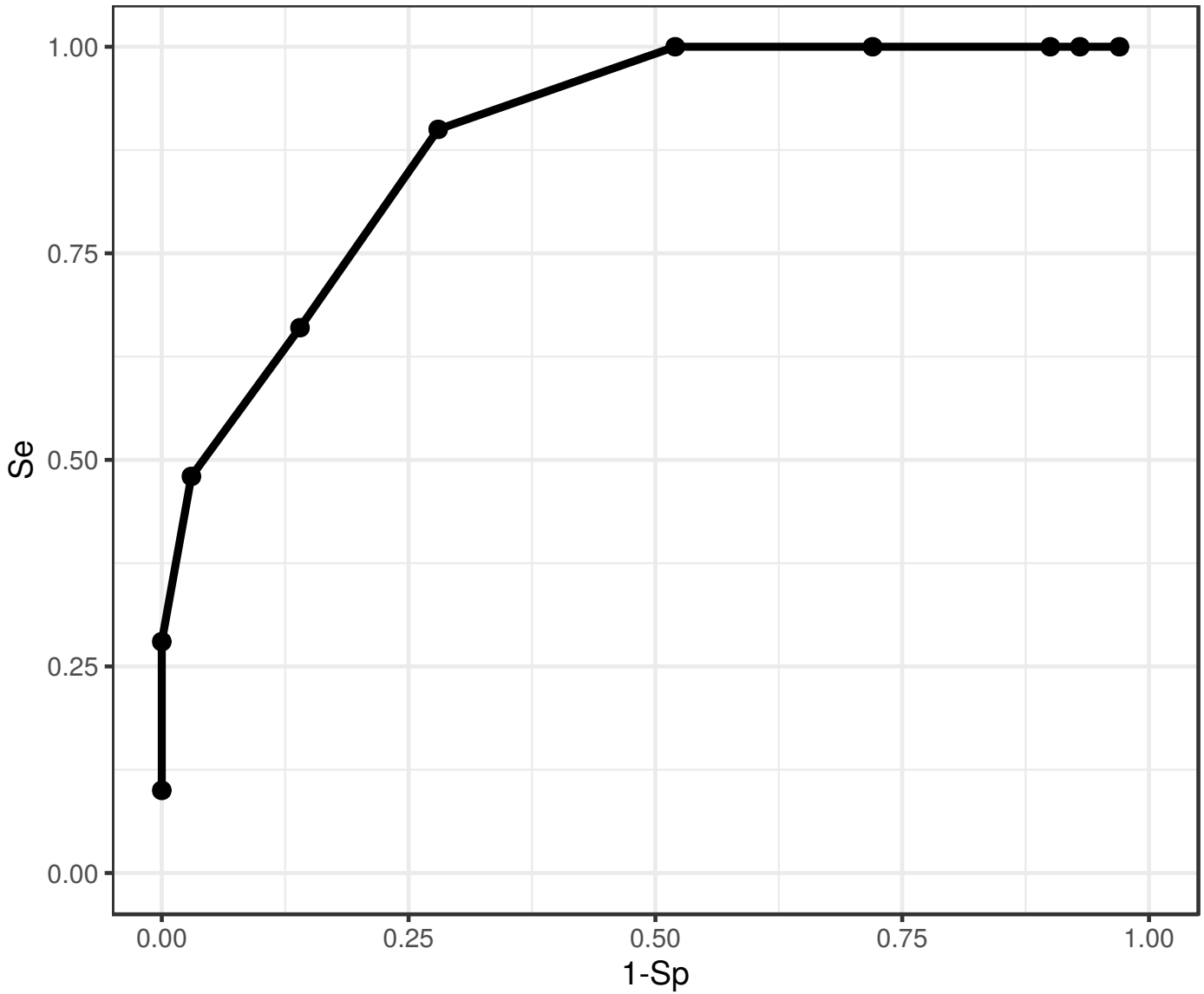
Se=0.28
Sp=1.00



Titre threshold:
T+: > 5.0
T−: ≤ 5.0

	I+	I−
T+	3	0
T−	26	29

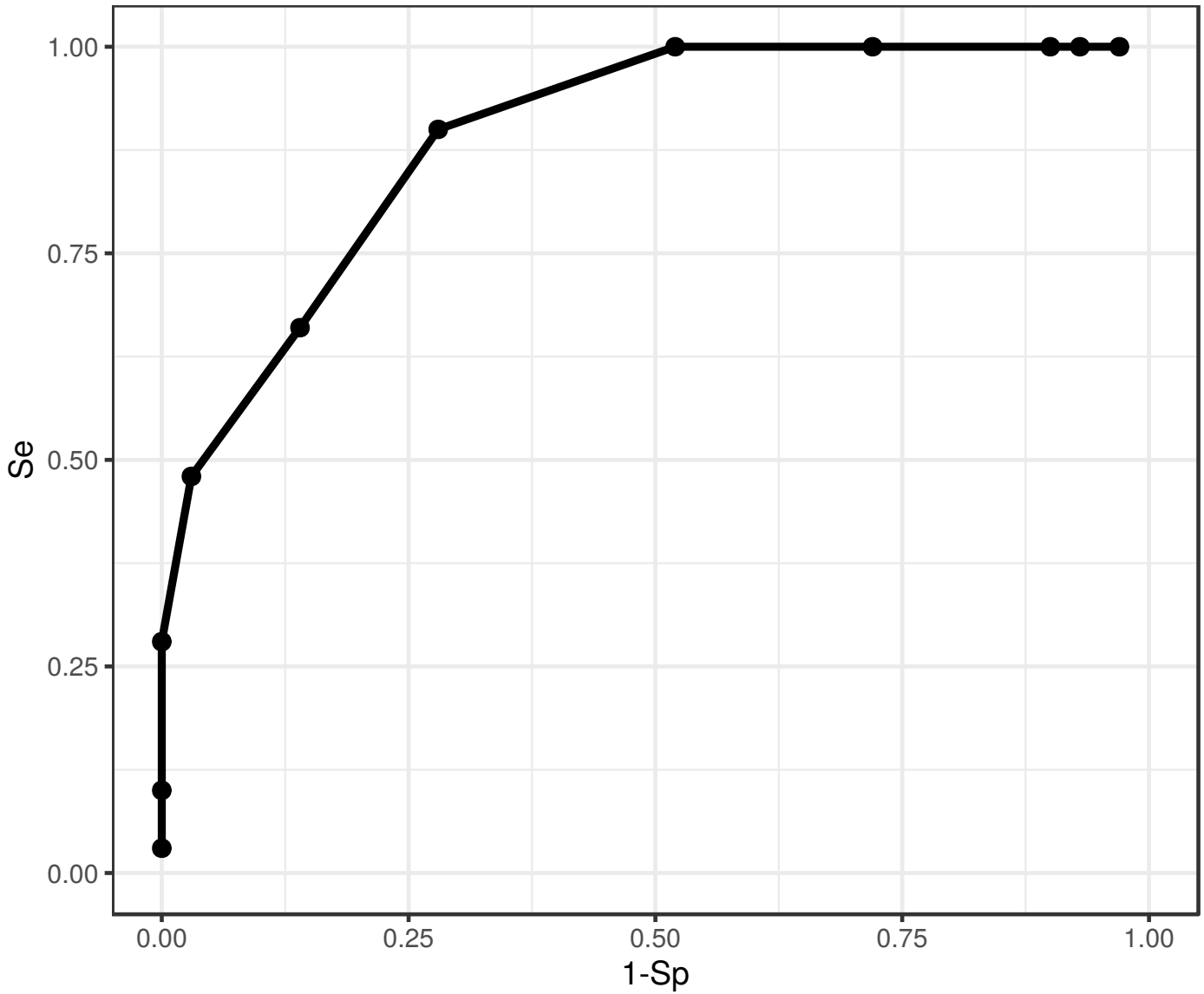
Se=0.10
Sp=1.00

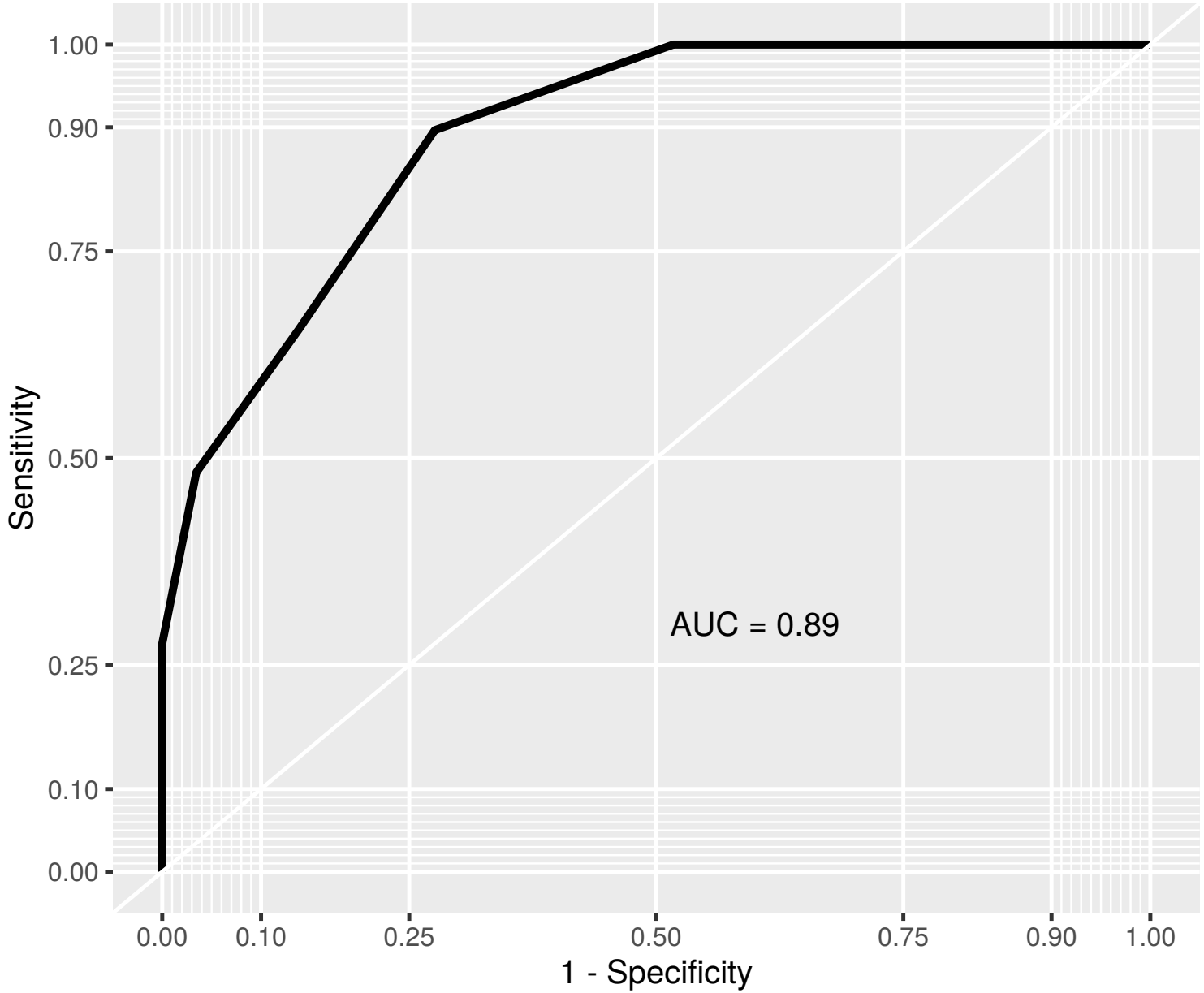


Titre threshold:
T+: > 5.5
T−: ≤ 5.5

	I+	I−
T+	1	0
T−	28	29

Se=0.03
Sp=1.00





Receiver operating characteristic (ROC) curve

Practical question: If the test result is positive or negative, what is the probability that the subject is affected or not, respectively?

Andrew got a tattoo. Two months later he was refused as a blood donor. The phlebotomist explained that he had to wait a year to make sure he didn't get hepatitis B from the tattoo. That got him worried, so he ordered a home test kit for hepatitis B virus (HBV) from a website. The website said that the sensitivity of the test was 0.99 and the specificity was 0.995.

Hepatitis B is rare among those who are not intravenous drug users – about 2 cases per 100,000 people. Studies suggest that getting a tattoo from an operator who follows accepted hygenie standards does not greatly increase the risk. Let's assume that Andrew believed that his risk was about 3 in 100,000.

If Andrew expect 10 million people as population at risk, then about 300 would have HBV, and the rest would not. As we know HBV test has 99% sensitivity, which means that it will catch 99% of the HBV cases (297 of the 300 cases) and miss the rest.

The test has 99.5% specificity, which means that 99.5% of the noninfected people will test negative, but 0.5% of them will be false positives.

	HBV +	HBV −	$\sum$
Test +	297	49,998	50,295
Test −	3	9,949,702	9,949,705
$\sum$	300	9,999,700	10,000,000

Suppose Andrew tests negative. There are 9,949,705 people like him – negative. Of these only 3 have HBV, so there are 3 chances in 9,949,705 (about 1 in 3.3 million) that a person who tests negative actually is infected.

On the other hand, suppose Andrew tests positive. There are 50,295 people like him – positive. Out of this group, only 297 really do have HBV (about 1 of 170). That means that even if Andrew tests positive, there is still only about 0.6% chance that he is actually infected.

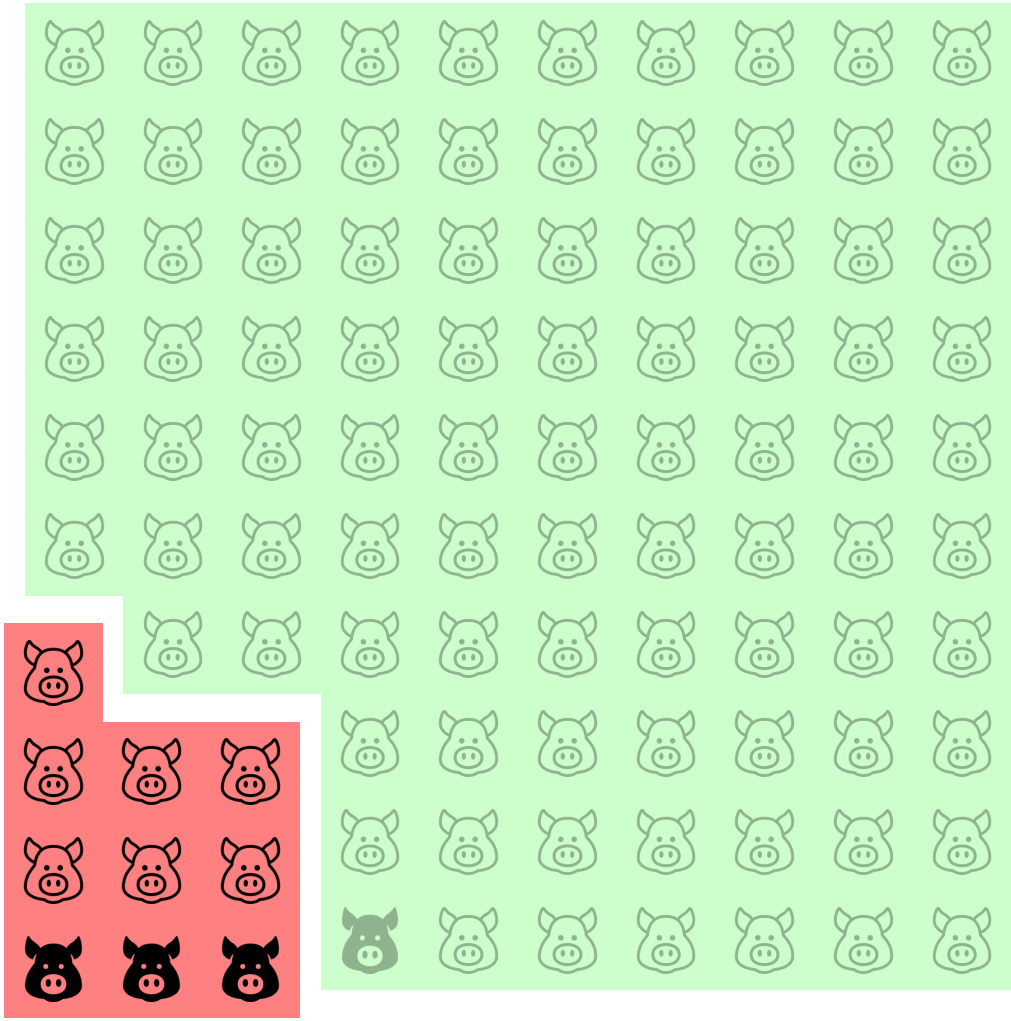
Another example: `http://yudkowsky.net/rational/bayes`

- uninfected pig:
  - test positive
  - test negative
- infected pig:
  - test positive
  - test negative

- uninfected pig:
  - test positive
  - test negative
- infected pig:
  - test positive
  - test negative

Positive predictive value is the proportion of test positives who actually infected:

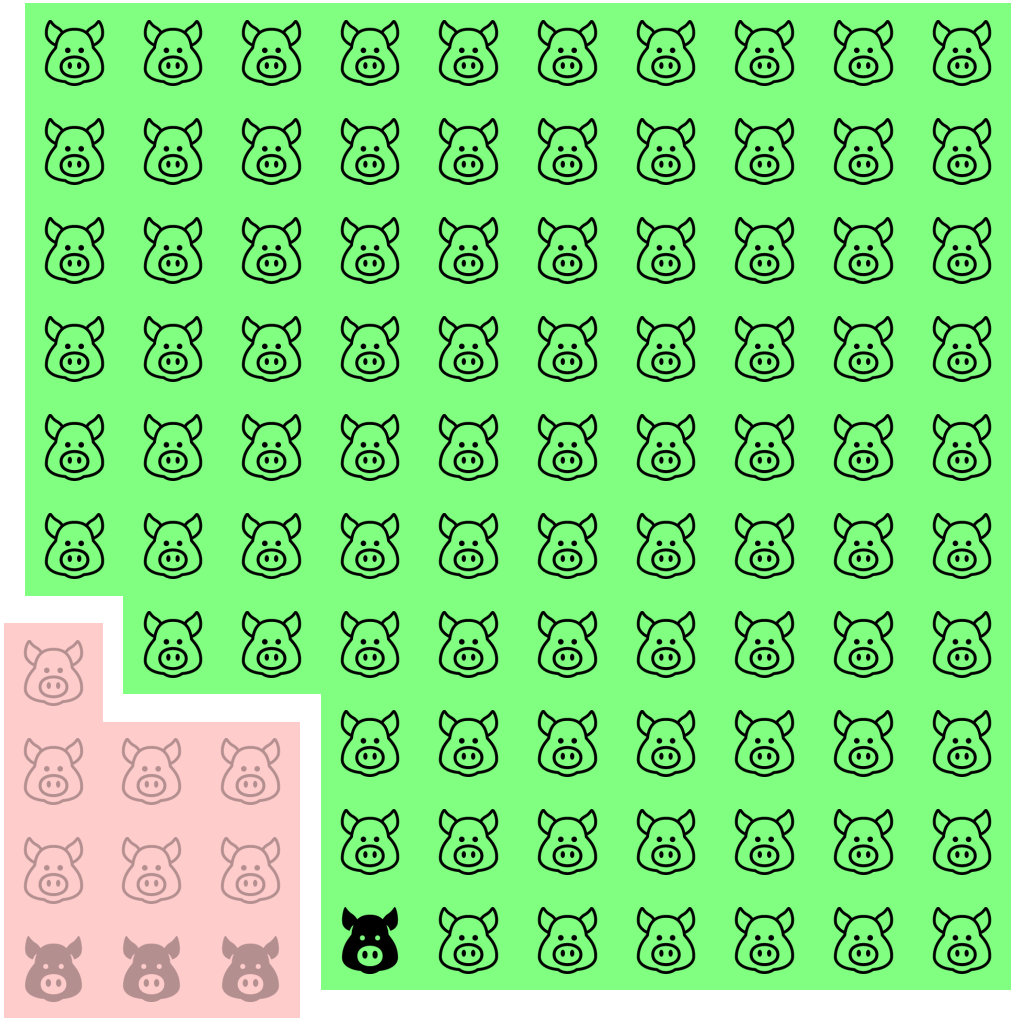
$$3/10 = 0.30$$



- uninfected pig:
  - test positive
  - test negative
- infected pig:
  - test positive
  - test negative

Negative predictive value is the proportion of test negatives who are noninfected:

$$89/90 = 0.99$$



Positive predictive value is the proportion of animals tested positive while they are truly infected.
Or the probability that animals with a positive test result truly infected.

	Infection +	Infection −	Total
Test +	True positive a	False positive b	Test positive $a+b$
Test −	False negative c	True negative d	Test negative $c+d$
Total	$a+c$	$b+d$	$a+b+c+d$

Positive predictive value is the proportion of animals tested positive while they are truly infected.
Or the probability that animals with a positive test result truly infected.

	Infection +	Infection −	Total
Test +	True positive a	False positive b	Test positive $a+b$
Test −	False negative c	True negative d	Test negative $c+d$
Total	$a+c$	$b+d$	$a+b+c+d$

$$PPV = \frac{a}{a+b} = \frac{3}{3+7} = 0.30$$

Negative predictive value is the proportion of animals tested negative while they are truly uninfected.
Or the probability that animals with a negative test result truly uninfected.

	Infection +	Infection −	Total
Test +	True positive a	False positive b	Test positive $a+b$
Test −	False negative c	True negative d	Test negative $c+d$
Total	$a+c$	$b+d$	$a+b+c+d$

Negative predictive value is the proportion of animals tested negative while they are truly uninfected.
Or the probability that animals with a negative test result truly uninfected.

	Infection +	Infection −	Total
Test +	True positive a	False positive b	Test positive $a+b$
Test −	False negative c	True negative d	Test negative $c+d$
Total	$a+c$	$b+d$	$a+b+c+d$

$$NPV = \frac{d}{c+d} = \frac{89}{1+89} = 0.99$$

Predictive values

- evaluate a test's ability to correctly identify the condition of interest: that is, is the test useful?
- depend on how much disease is in the population you're testing

Example

- bovine tuberculosis
- the caudal skin fold test has a sensitivity of 0.75 to 0.85 and a specificity of 0.99
- what is the positive predictive value in a herd with TB prevalence of 10%?

Stevenson 2012

Bovine tuberculosis

Farm size: 10000

	Infection +	Infection −	Total
Test +	a	b	$a+b$
Test −	c	d	$c+d$
Total	$a+c$	$b+d$	10000 $a+b+c+d$

Bovine tuberculosis

Farm size: 10000, Prevalence: 0.10

	Infection +	Infection −	Total
Test +	a	b	$a+b$
Test −	c	d	$c+d$
Total	1000 $a+c$	9000 $b+d$	10000 $a+b+c+d$

Bovine tuberculosis

Farm size: 10000, Prevalence: 0.10, Se: 0.80

	Infection +	Infection −	Total
Test +	800		
	a	b	$a+b$
Test −	200		
	c	d	$c+d$
Total	1000	9000	10000
	$a+c$	$b+d$	$a+b+c+d$

Bovine tuberculosis

Farm size: 10000, Prevalence: 0.10, Se: 0.80, Sp: 0.99

	Infection +	Infection −	Total
Test +	800	90	
	a	b	$a+b$
Test −	200	8910	
	c	d	$c+d$
Total	1000	9000	10000
	$a+c$	$b+d$	$a+b+c+d$

Bovine tuberculosis

Farm size: 10000, Prevalence: 0.10, Se: 0.80, Sp: 0.99

	Infection +	Infection −	Total
Test +	800	90	890
	a	b	$a+b$
Test −	200	8910	9110
	c	d	$c+d$
Total	1000	9000	10000
	$a+c$	$b+d$	$a+b+c+d$

Bovine tuberculosis

Farm size: 10000, Prevalence: 0.10, Se: 0.80, Sp: 0.99

	Infection +	Infection −	Total
Test +	800	90	890
	a	b	$a+b$
Test −	200	8910	9110
	c	d	$c+d$
Total	1000	9000	10000
	$a+c$	$b+d$	$a+b+c+d$

$$NPV = \frac{d}{c+d} = \frac{8910}{200+8910} = \frac{8910}{9110} = 97.8\%$$

$$PPV = \frac{a}{a+b} = \frac{800}{800+90} = \frac{800}{890} = 89.9\%$$

Bovine tuberculosis

Farm size: 10000, Prevalence: 0.01, Se: 0.80, Sp: 0.99

	Infection +	Infection −	Total
Test +	80	99	179
	a	b	$a+b$
Test −	20	9801	9821
	c	d	$c+d$
Total	100	9900	10000
	$a+c$	$b+d$	$a+b+c+d$

$$NPV = \frac{d}{c+d} = \frac{9801}{20+9801} = \frac{9801}{9821} = 99.8\%$$

$$PPV = \frac{a}{a+b} = \frac{80}{80+99} = \frac{80}{179} = 44.7\%$$

Bovine tuberculosis

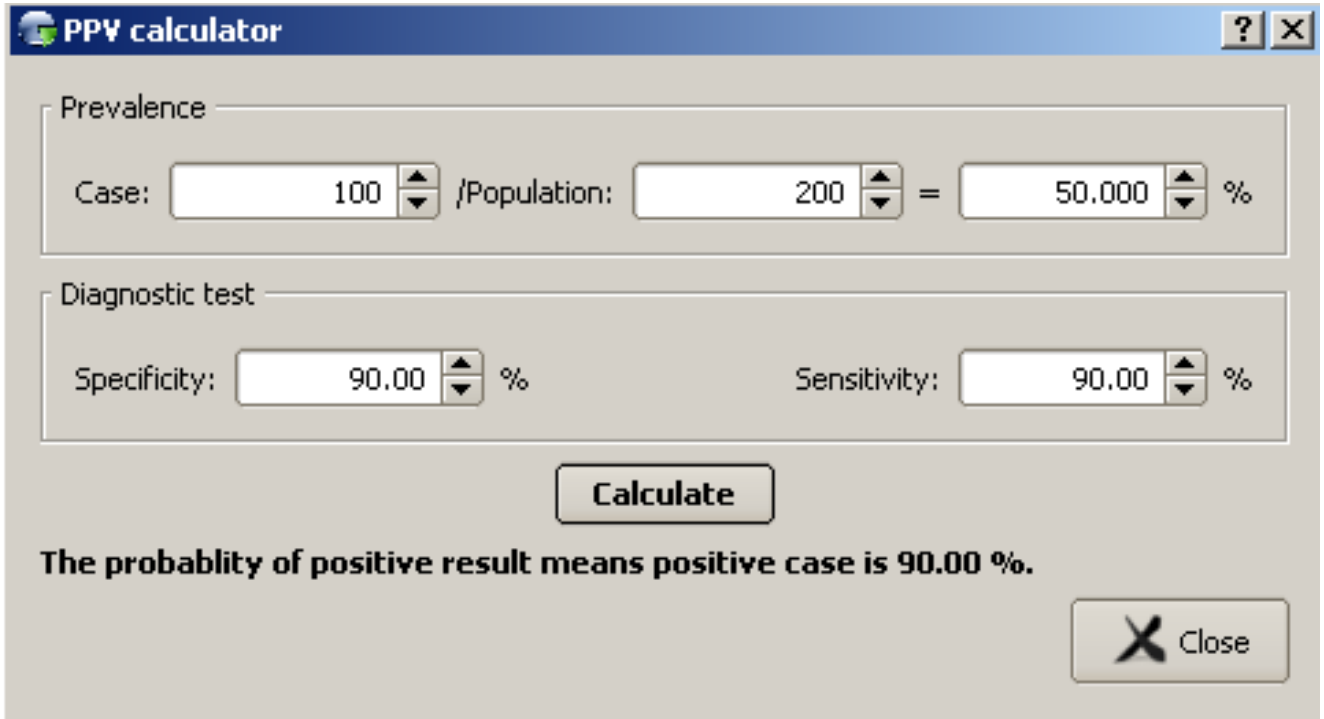
Prevalence: 0.10, Se: 0.80, Sp: 0.99

$$NPV = \frac{d}{c+d} = \frac{(1-P) \times Sp}{P \times (1-Se) + (1-P) \times Sp}$$
$$= \frac{(1-0.10) \times 0.99}{0.10 \times (1-0.80) + (1-0.10) \times 0.99} = 97.8$$

$$PPV = \frac{a}{a+b} = \frac{P \times Se}{P \times Se + (1-P) \times (1-Sp)}$$
$$= \frac{0.10 \times 0.80}{0.10 \times 0.80 + (1-0.10) \times (1-0.99)} = 89.9$$

- as prevalence falls
  - PPV decreases regardless of sensitivity and specificity of the test
  - even very good tests become very poor at predicting the presence of disease

"According to our calculation the positive predictive value of the best Lyme antibody tests if applied in this way is 9.1%."



`http://kullancs.hu/doc/PPVcalc_setup.exe`

Lakos et al. (2010)

How much the **odds of the disease increase** when a test is positive?

- likelihood ratio for positive test result

$$LR^{+} = \frac{Se}{1 - Sp}$$

How much the **odds of the disease decrease** when a test is negative?

- likelihood ratio for negative test result

$$LR^{-} = \frac{1 - Se}{Sp}$$

Bayes' Theorem:
Post-test probability = pre-test probability $\times$ likelihood

$$\text{Odds of event} = \frac{\text{Probability of event}}{\text{1-Probability of event}}$$

$$\text{Probability of event} = \frac{\text{Odds of event}}{\text{1+Odds of event}}$$

- California Mastitis Test Se: 68.8%, Sp: 71.5%
- $LR^+ = \dfrac{0.688}{1 - 0.715} = 2.414$
- $LR^- = \dfrac{1 - 0.688}{0.715} = 0.436$
- The pre-test probability of mastitis: $\dfrac{50}{1000} = 0.05$
- The pre-test odds of mastitis: $\dfrac{0.05}{1 - 0.05} = 0.053$
- The post-test odds of mastitis given a positive test result: pre-test odds $\times\, LR^+ = 0.053 \times 2.414 = 0.1279$
- The post-test probability of mastitis given a positive test result: $\dfrac{0.1279}{1 + 0.1279} = 0.11$

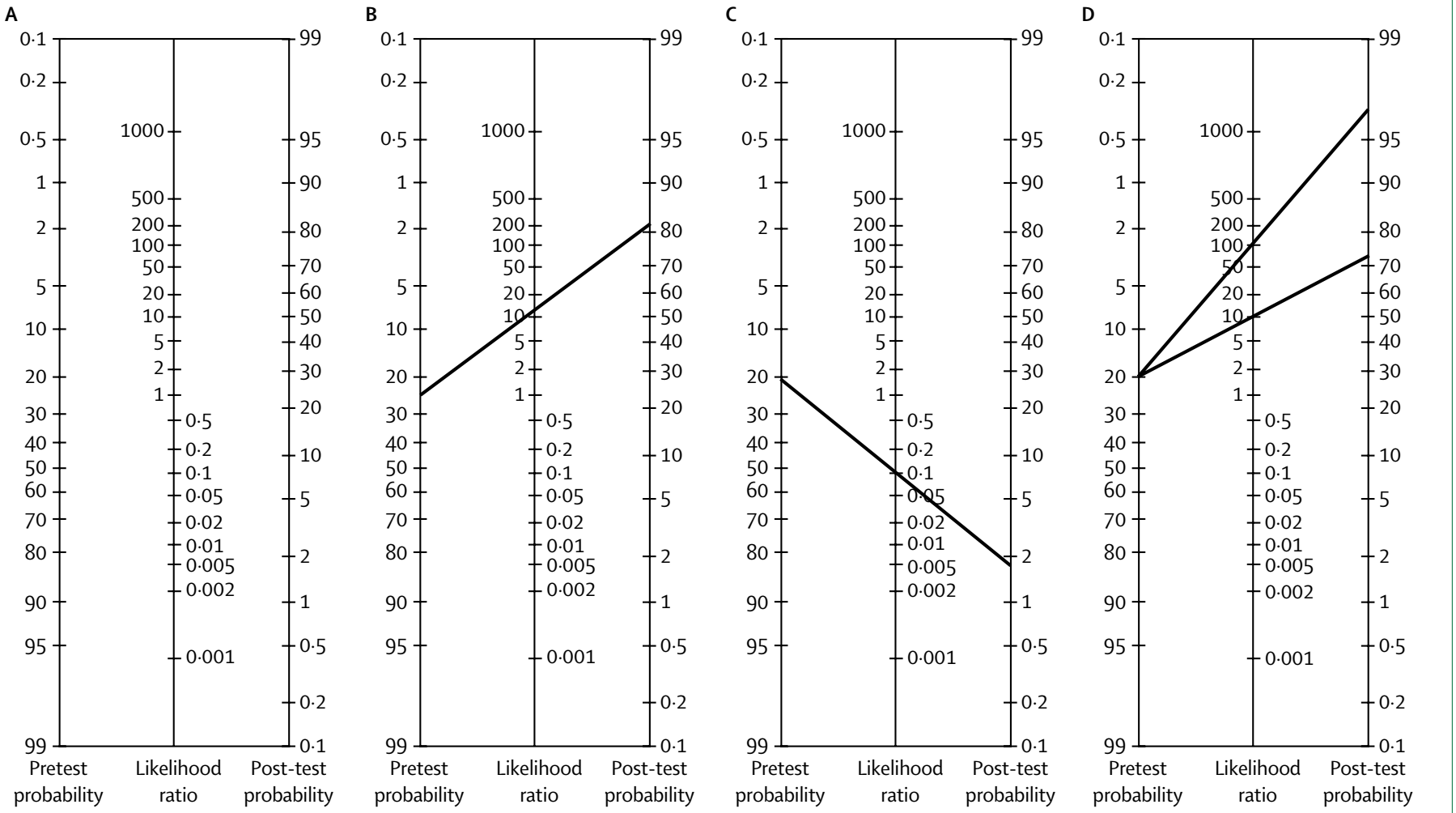


***Figure 2*: Nomograms for probabilities and likelihood ratios**[13]

(A) Nomogram reprinted from reference 13 with permission of the Massachusetts Medical Association. (B) Straight edge applied for pretest probability of 0·25 and likelihood ratio of 13. (C) Straight edge applied for pretest probability of 0·20 and likelihood ratio of 0·1. (D) Effect of likelihood ratios of 10 and 100 on pretest probability of 0·2.

Grimes and Schulz (2005)

Gardner, I. A. (2012). Analysis and use of diagnostic data. In *Diseases of Swine*, pp. 94–105. John Wiley & Sons, Ltd.

Grimes, D. A. and K. F. Schulz (2005). Refining clinical diagnosis with likelihood ratios. *The Lancet 365*(9469), 1500–1505.

Lakos, A., J. Reiczigel, and N. Solymosi (2010). The positive predictive value of borrelia burgdorferi serology in the light of symptoms of patients sent to an outpatient service for tick-borne diseases. *Inflammation research 59*(11), 959–964.

Noordhuizen, J. P. T. M., K. Frankena, M. Thrusfield, and E. A. M. Graat (2001). *Application of Quantitative Methods in Veterinary Epidemiology*. Wageningen, The Netherland: Wageningen Pers.

Stevenson, M. (2012). An introduction to veterinary epidemiology. EpiCentre, IVABS, Massey University, Palmerston North, New Zealand.

Woodworth, G. G. (2004). *Biostatistics: A Bayesian Introduction*. Probability and Statistics Series. Hoboken, New Jersey, USA: Wiley & Sons. ISBN 0471468428.