

**VALITEST webinar series and training activities**

# Practical sessions on the analysis of TPS results

30th – 31st March 2021

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# Performance criteria

## EXPECTED PERFORMANCES

Ability to detect at low-levels

Positive results with positive samples

Negative results with negative samples

Confidence in one result per sample

Confidence in results given in different conditions

Confidence in a positive test result

Confidence in a negative test result

## PERFORMANCE CRITERIA

→ Analytical sensitivity (Limit of detection)

→ Diagnostic sensitivity (DSE)

→ Diagnostic specificity (DSP)

→ Repeatability (accordance)

→ Reproducibility (concordance)

→ Positive likelihood ratio

→ Negative likelihood ratio

} calculated using DSE and DSP

# Analysing the data from a TPS

- Performance criteria
  - Analytical sensitivity (limit of detection)
  - *Analytical specificity*
  - Diagnostic sensitivity (true positive rate)
  - Diagnostic specificity (true negative rate)
  - Repeatability (accordance – within lab)
  - Reproducibility (concordance – between lab)
- For each performance criterion, alternative statistical methods were tested by project partners in a first round of TPS
  - Methods covered today are those found to be most suitable and applied in TPS2

# Data used in the exercises

- Zip file circulated
  - 3 folders of data,
  - 3 scripts written in R
- The pre-prepared data files were selected from TPS2 carried out in Valitest
  - Any exclusions have already been applied (relevant points removed)

# Technical Session 1 – Analytical sensitivity

- **Analytical sensitivity:** *“the smallest amount of target that can be detected reliably (this is sometimes referred to as the limit of detection)”* (EPPO PM 7/76, 2018).
- To quantify the limit of detection (LOD), first define ‘reliably’. Set a probability of detection for an infected sample, e.g.  $p = 0.95$

# Technical Session 1 – Analytical sensitivity

- Scenario: Contaminant is present in each set of measurements, but at different levels of dilution

$$\text{Dilution factor} = -\log_{10} \left( \frac{cfu}{\max(cf_u)} \right)$$

- This maps:
  - $\max(cf_u) \rightarrow 0$  (no dilution)
  - $\max(cf_u)/10 \rightarrow 1$
  - $\max(cf_u)/100 \rightarrow 2$
  - $\max(cf_u)/1000 \rightarrow 3$
  - $\max(cf_u)/10000 \rightarrow 4$

# Technical Session 1 – Analytical sensitivity

- Scenario: Contaminant is present in each set of measurements, but at different levels of dilution

	A	B
1	dilu	Results
2	0	1
3	0	1
4	0	1
5	0	1
6	0	1
7	1	1
8	1	1
9	1	1
10	2	1
11	2	1
12	2	0
13	2	1
14	3	1
15	3	0
16	3	0
17	3	1
18	4	0
19	4	0
20	4	0

Dilution	Measurement no.	Result
0	1, 2, 3, 4, 5	1,1,1,1,1
1	6,7,8	1,1,1
2	9,10,11,12	1,1,0,1
3	13,14,15,16	1,0,0,1
4	17,18,19	0,0,0

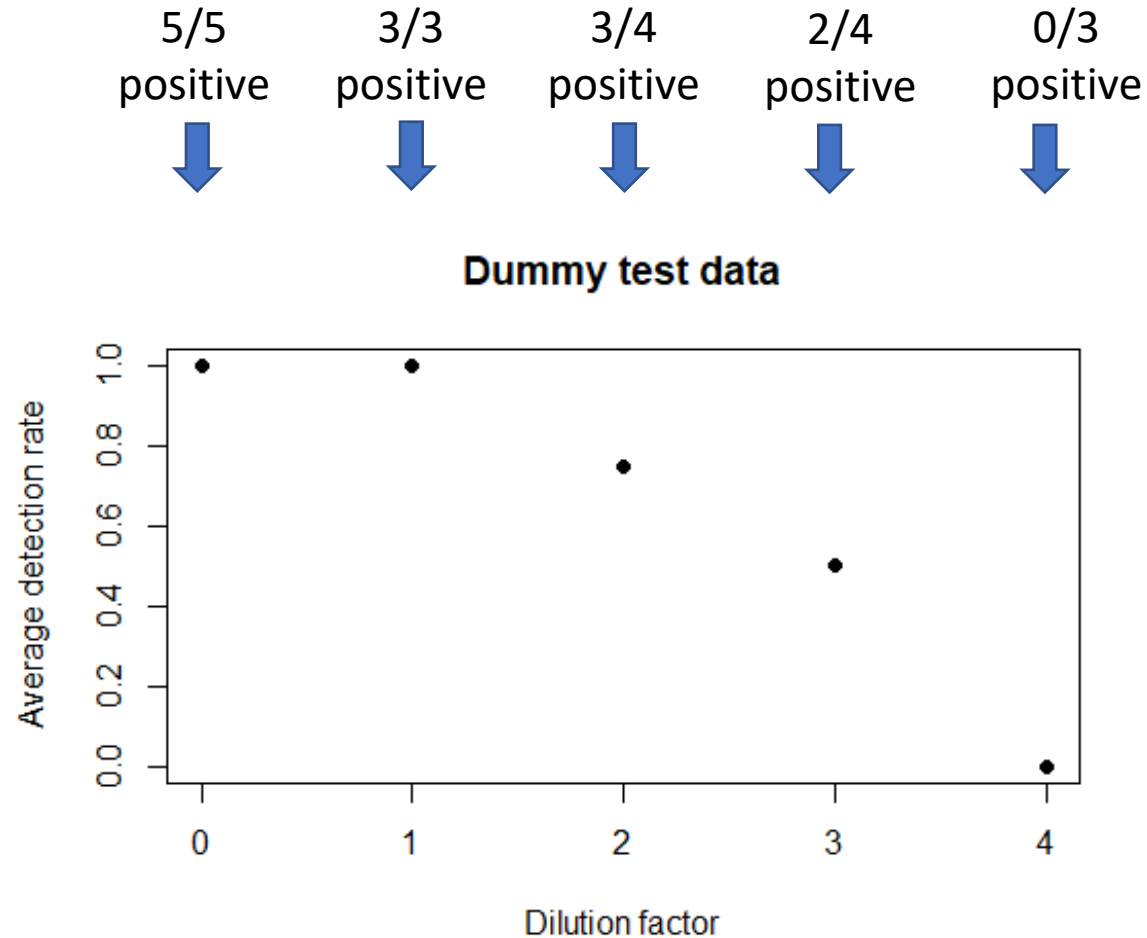
Highest concentration tested. All tests correct

With more dilution, increasing number of tests fail

Lowest concentration tested. High proportion of tests fail

How to use these data to estimate the analytical sensitivity (Limit of Detection) of this test?

# Technical Session 1 – Analytical sensitivity



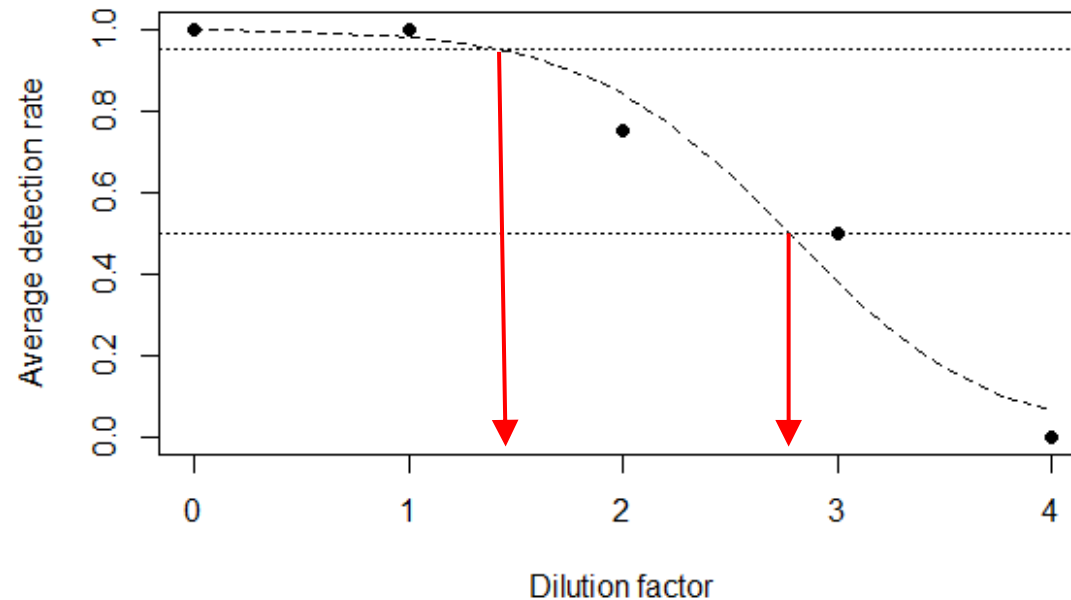


# Technical Session 1 – Analytical sensitivity

5/5 positive    3/3 positive    3/4 positive    2/4 positive    0/3 positive

↓                    ↓                    ↓                    ↓                    ↓

Dummy test data



# Technical Session 1 – Analytical sensitivity

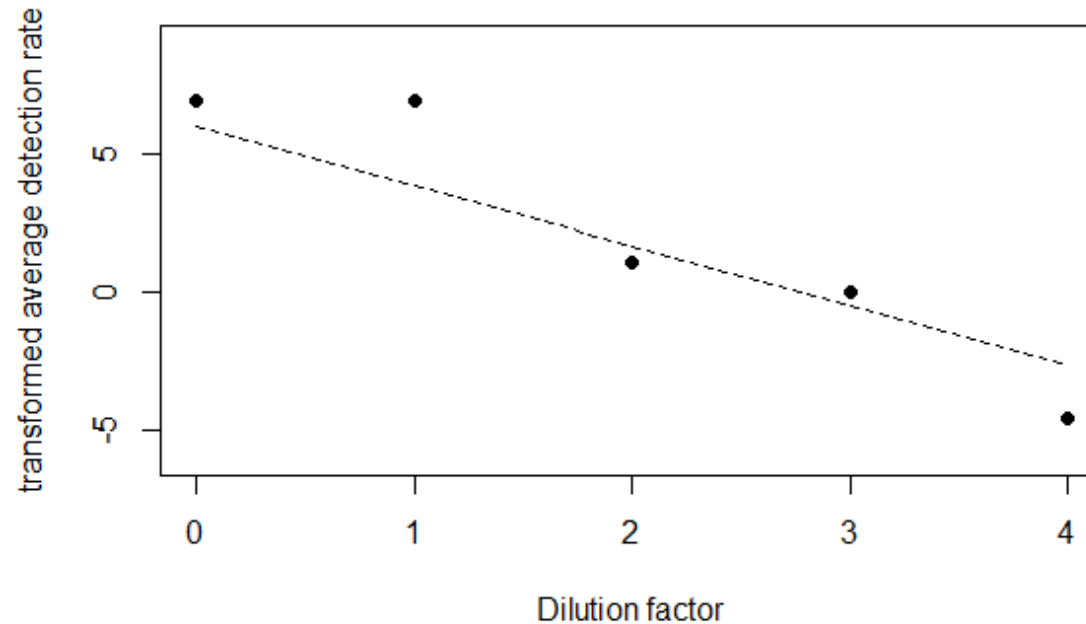
- **Generalized linear model with link function:** Link functions are used in generalized linear models to transform the linear predictor estimated by the model in the response space (here, a probability). The default link function for binomial models is the logit function, which is symmetrical and give equal weights to true or false responses (presence/absence, detection/non detection).

$$\text{logit}(p) = \log\left(\frac{p}{1-p}\right)$$

# Technical Session 1 – Analytical sensitivity

5/5 positive  
3/3 positive  
3/4 positive  
2/4 positive  
0/3 positive

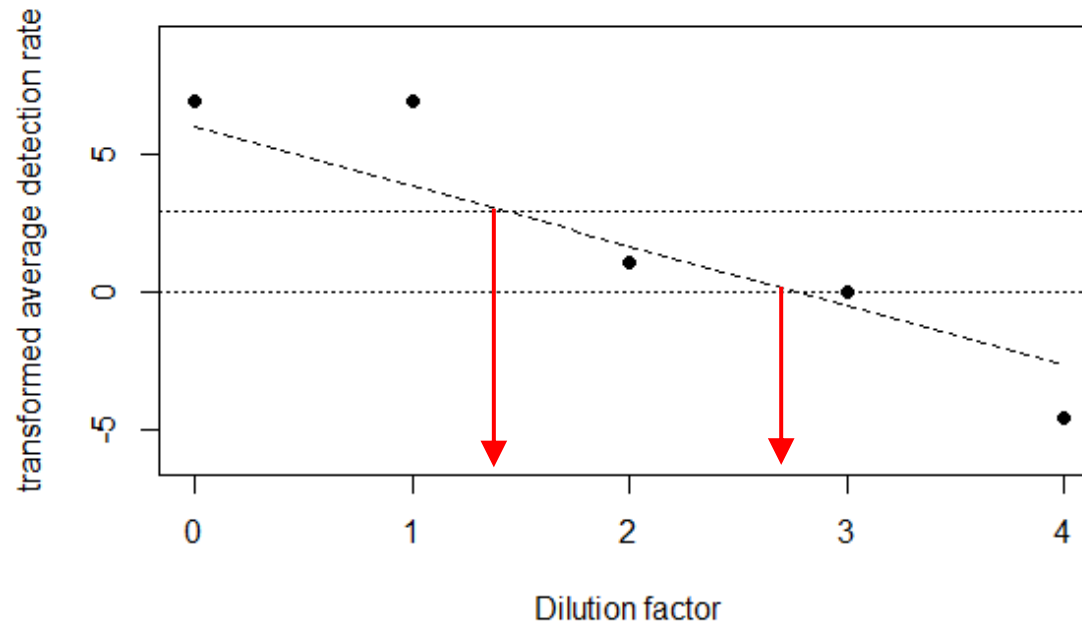
Dummy test data



# Technical Session 1 – Analytical sensitivity

5/5 positive  
3/3 positive  
3/4 positive  
2/4 positive  
0/3 positive

Dummy test data



Find dilution value (x)  
giving

$$y = \text{logit}(0.95) = 2.9444$$

$$y = \text{logit}(0.5) = 0$$

Fitting the model produces  
coefficients for a fitted line

$$y(x) = a + bx$$

On transformed scale

- Intercept a
- Slope  $b < 0$

# Technical Session 1 – Analytical sensitivity

- Generalised linear model with standard logit link
  - Also known as ‘logistic regression’
  - Widely available in statistical software, e.g. in R

```
glm_fit <- glm(Result ~ Dilution, data = dilution_data, family=binomial(link = "logit"))
```

In our regression line  $y = a + bx$  the results (a, b) are available as `coef(glm_fit)`

- For a given probability, e.g.  $p = 0.95$ , the required LOD is obtained as

```
LOD <- {log(p/(1-p)) - coef(glm_fit)[1]}/coef(glm_fit)[2]
```

Back-transform this ‘dilution factor’ to give concentration = max-cfu \*  $10^{-\text{LOD}}$

# Practical Session 1 – using example data

- Inconclusive results were excluded from the assessment of analytical sensitivity
- Instructions: Use the data provided to calculate the following:
  - Estimated model coefficients
  - LOD50
  - LOD95
  - Where does the method fail, and why?
  - Try modifying the script to generate LOD values for higher probabilities
- Save the results and record any questions or comments
- To be reviewed in next session

# Practical Session 1 – using example data

- ELISA1, ...

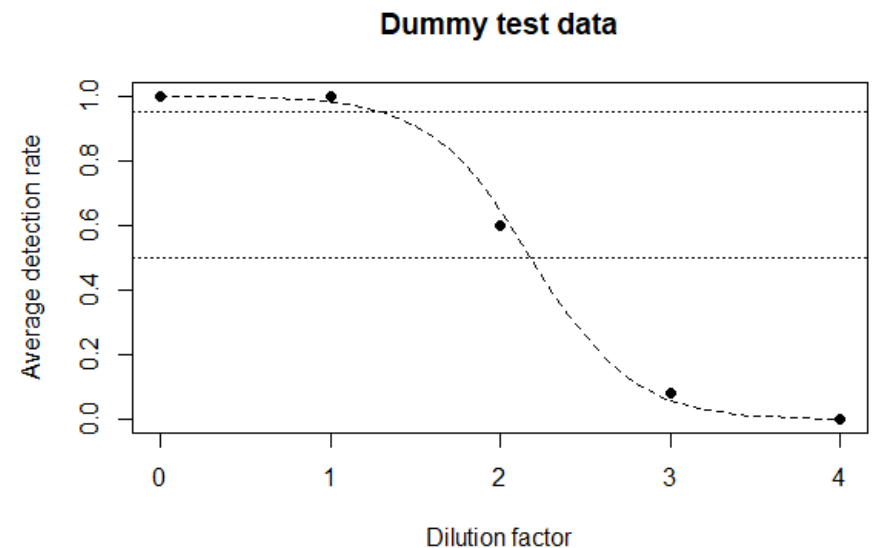
Call: `glm(formula = Results ~ dilu, family = binomial, data = dilution_data_test)`

Coefficients:

(Intercept)	dilu
7.346	-3.368

LOD50 = 2.18	→	concentration = max * 0.0066
LOD95 = 1.31	→	concentration = max * 0.049

Dilution	Positives/Total
0	8/8
1	12/12
2	6/10
3	1/12
4	0/12



# Practical Session 1 – using example data

- ELISA2, ...

Call: `glm(formula = Results ~ dilu, family = binomial, data = dilution_data_test)`

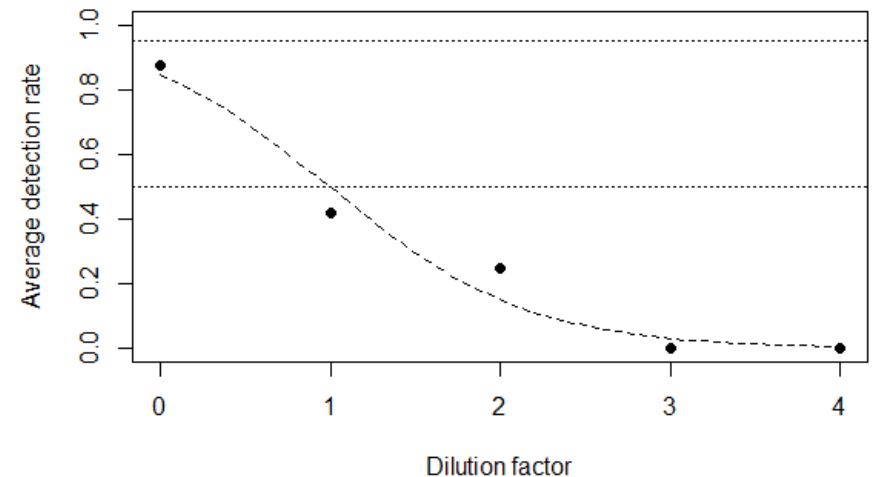
Coefficients:

(Intercept)	dilu
1.705	-1.715

LOD50 = 0.99	→	concentration = max * 0.102
LOD95 = -0.72	→	concentration = NA

Dilution	Positives/Total
0	7/8
1	5/12
2	3/12
3	0/12
4	0/12

Dummy test data





# Practical Session 1 – using example data

- IF1, ...

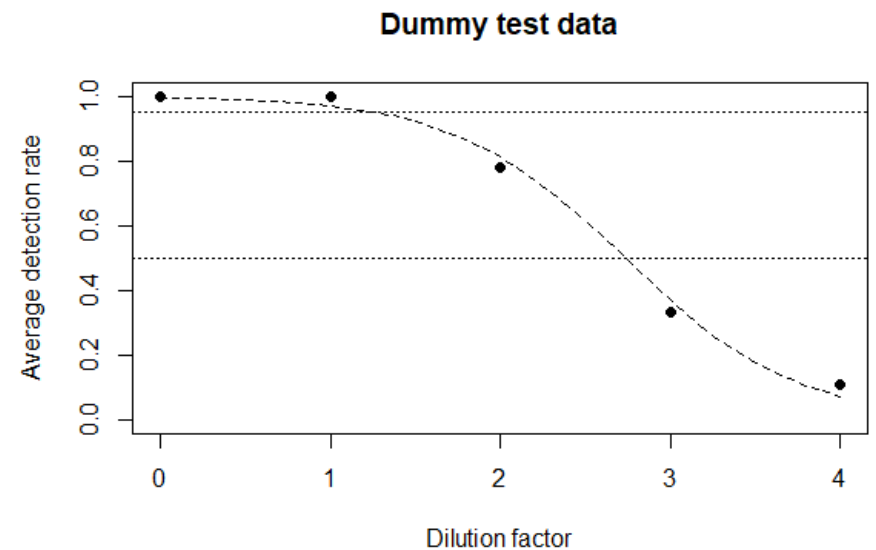
Call: `glm(formula = Results ~ dilu, family = binomial, data = dilution_data_test)`

Coefficients:

(Intercept)	dilu
5.439	-1.990

LOD50 = 2.73	→	concentration = max * 0.00186
LOD95 = 1.25	→	concentration = max * 0.0562

Dilution	Positives/Total
0	6/6
1	9/9
2	7/9
3	3/9
4	1/9



# Practical Session 1 – using example data

- IF2, ...

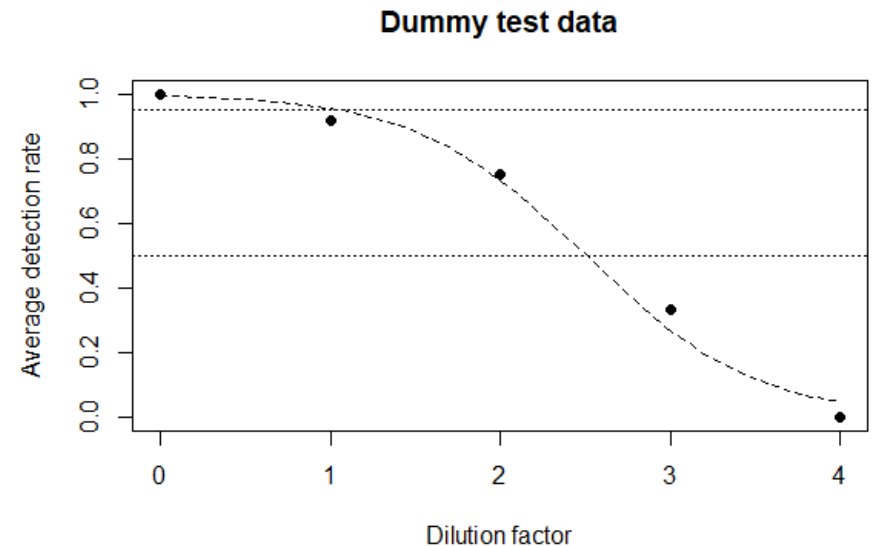
Call: `glm(formula = Results ~ dilu, family = binomial, data = dilution_data_test)`

Coefficients:

(Intercept)	dilu
5.052	-2.017

LOD50 = 2.50	→	concentration = max * 0.00316
LOD95 = 1.04	→	concentration = max * 0.0912

Dilution	Positives/Total
0	8/8
1	11/12
2	9/12
3	4/12
4	0/12



# Practical Session 1 – using example data

- PCR1, ...

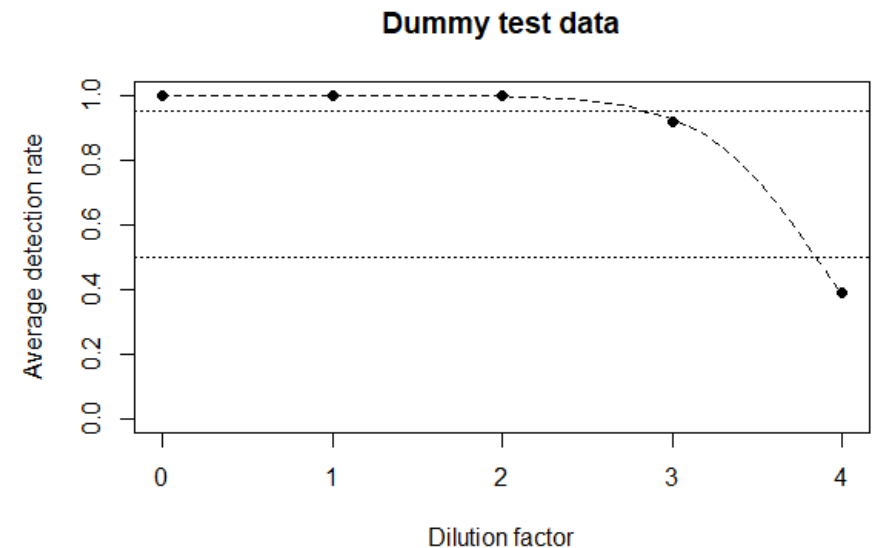
Call: `glm(formula = Results ~ dilu, family = binomial, data = dilution_data_test)`

Coefficients:

(Intercept)	dilu
11.461	-2.981

LOD50 = 3.85	→	concentration = max * 0.000141
LOD95 = 2.86	→	concentration = max * 0.00138

Dilution	Positives/Total
0	16/16
1	24/24
2	24/24
3	22/24
4	9/23



# Practical Session 1 – using example data

- PCR2, ...

Call: `glm(formula = Results ~ dilu, family = binomial, data = dilution_data_test)`

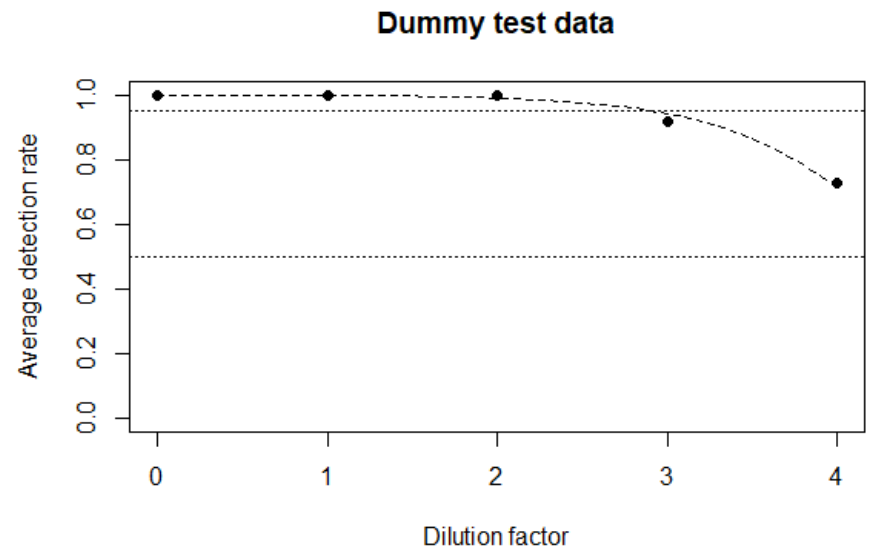
Coefficients:

(Intercept)	dilu
8.355	-1.861

LOD50 = 4.49	→	concentration = NA
LOD95 = 2.91	→	concentration = max * 0.00123

Solution for LOD50 is outside the data range

Dilution	Positives/Total
0	16/16
1	24/24
2	24/24
3	22/24
4	16/22



# Practical Session 1 – using example data

- PCR3, ...

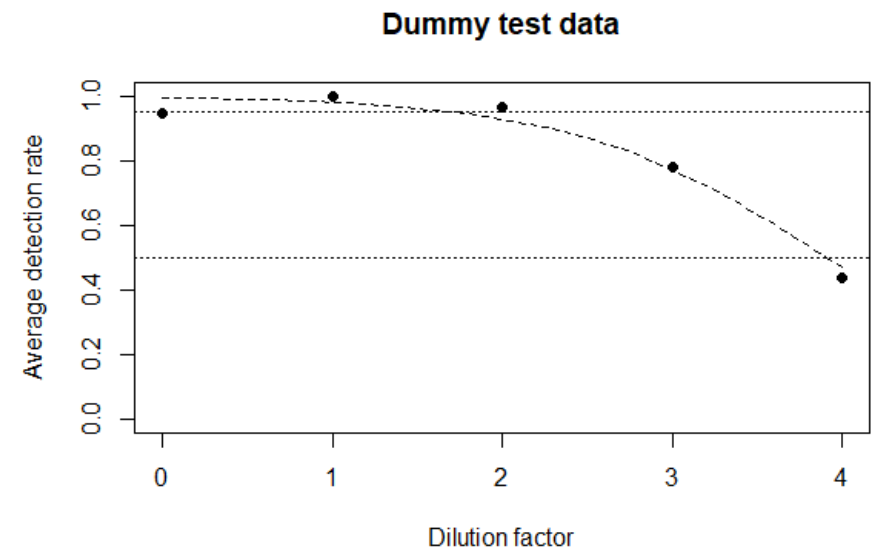
Call: `glm(formula = Results ~ dilu, family = binomial, data = dilution_data_test)`

Coefficients:

(Intercept)      dilu  
5.25      -1.344

LOD50 = 3.91	→	concentration = max * 0.000123
LOD95 = 1.72	→	concentration = max * 0.0191

Dilution	Positives/Total
0	17/18
1	27/27
2	26/27
3	21/27
4	11/25



# Practical Session 1 – using example data

- PCR4, ...

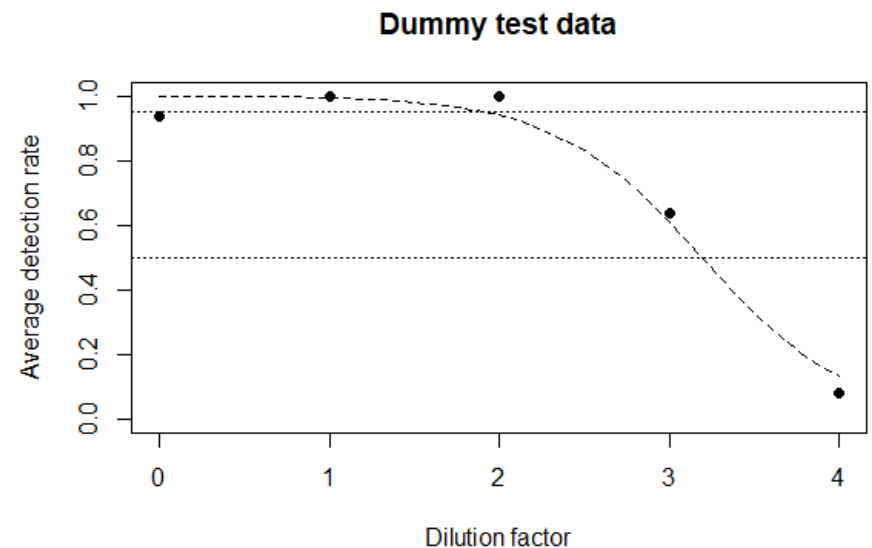
Call: `glm(formula = Results ~ dilu, family = binomial, data = dilution_data_test)`

Coefficients:

(Intercept)      dilu  
7.360      -2.306

LOD50 = 3.19	→	concentration = max * 0.00065
LOD95 = 1.91	→	concentration = max * 0.0123

Dilution	Positives/Total
0	15/16
1	24/24
2	24/24
3	14/22
4	2/24



# Practical Session 1 – using example data

- PCR5, ...

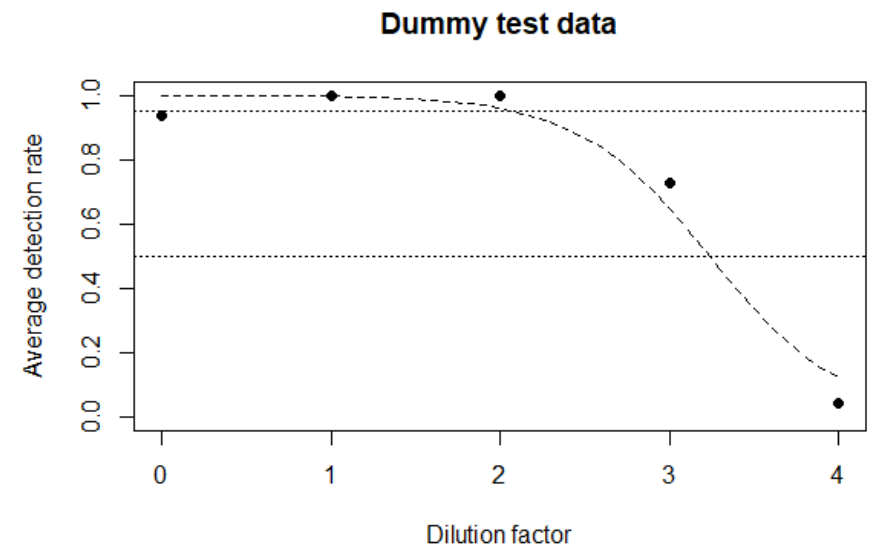
Call: `glm(formula = Results ~ dilu, family = binomial, data = dilution_data_test)`

Coefficients:

(Intercept)      dilu  
8.271      -2.557

LOD50 = 3.24	→	concentration = max * 0.000575
LOD95 = 2.08	→	concentration = max * 0.00832

Dilution	Positives/Total
0	15/16
1	24/24
2	24/24
3	16/22
4	1/23



# Technical Session 2 – diagnostic sensitivity and specificity

- **Diagnostic sensitivity:** “the proportion of infected/infested samples testing positive compared with results from an alternative test (or combination of tests). Diagnostic sensitivity =  $\text{true positives} / (\text{true positives} + \text{false negatives})$ ” (EPPO PM 7/76, 2018).
- **Diagnostic specificity:** “the proportion of uninfected/uninfested samples (true negatives) testing negative compared with results from an alternative test (or combination of tests). Diagnostic specificity =  $\text{true negatives} / (\text{true negatives} + \text{false positives})$ ” (EPPO PM 7/76, 2018).



# Technical Session 2 – diagnostic sensitivity and specificity

- Diagnostic sensitivity
  - $DSE = TP / (TP + FN)$
- Diagnostic specificity
  - $DSP = TN / (TN + FP)$
- TP: number of True Positive
- TN: number of True Negative
- FP: number of False Positive
- FN: number of False Negative

Diagnostic parameter	Test			
	qPCR Pirc ITS	qPCR Pirc Ams	qPCR Gotssberger	LAMP Shin
total data sets	28	25	28	8
total data points	560	500	560	160
% TP	69%	62%	60%	47%
% TN	18%	18%	19%	20%
% inconclusive	6%	8%	7%	8%
% FN	7%	11%	14%	25%
% FP	1%	1%	1%	0%
concordant	485	400	440	107
non-concordant	75	100	120	53
% concordant	87%	80%	79%	67%
% non-concordant	13%	20%	21%	33%
diagnostic sensitivity	91%	84%	81%	65%
diagnostic specificity	94%	97%	97%	98%
false positive rate	6%	3%	3%	2%
false negative rate	9%	16%	19%	35%
accuracy	92%	87%	85%	73%
power	152%	129%	148%	45%
positive predictive value	98%	99%	99%	99%
negative predictive value	73%	61%	58%	44%
diagnostic odds ratio	170.8	163.2	155.3	120.0

# Technical Session 2 – Diagnostic sensitivity and specificity

- Scenario: Single test assumed. Half of the measurements infected, half uninfected

High sensitivity if these are mostly positive results

Measurement no.	Test result	Status
1, 2, 3, 4, 5, 6, 7, 8, 9, 10	1,1,1,1,0, 0,0,1,1,1	1,1,1,1,1, 1,1,1,1,1
11,12,13,14,15, 16,17,18,19,20	0,0,1,0,1, 0,1,1,0,0	0,0,0,0,0 0,0,0,0,0

High specificity if these are mostly negative results

Infected and uninfected true status required to assess diagnostic sensitivity and specificity

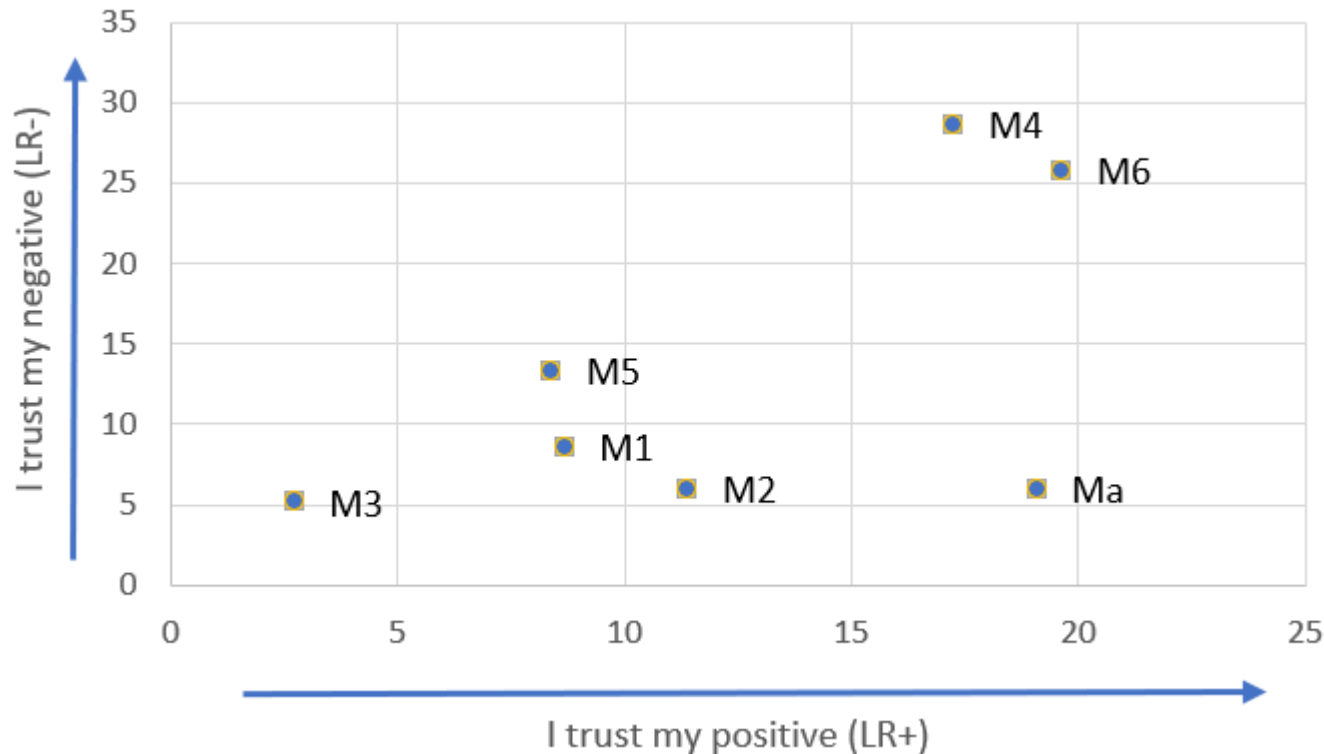
# Technical Session 2 – likelihood ratios

- Positive likelihood ratio: ratio of probability of positive test from an infected plant to the probability of a positive test from an uninfected plant
  - $LR+ = DSE/(1-DSP)$
  - The greater LR+ is (e.g. >20) the stronger indication that a **positive** test corresponds to a **true infected sample**
- Negative likelihood ratio: ratio of a probability of a negative test from an uninfected plant to the probability of negative test from an infected plant
  - $LR- = DSP/(1-DSE)$
  - The greater LR- is (e.g. >20) the stronger indication that a **negative** test corresponds to a **true uninfected sample**

Recommended presentation is a table, to show relative performance of different tests

# Technical Session 2 – likelihood ratios

- Interpreting LR+, LR- for selecting a test
- Example: 7 molecular tests Chabirand *et al.* (2017)



Positive and negative tests obtained with M4 and M6 most trusted, M3 least

# Technical Session 2 – likelihood ratios

- Based on the example data, simply by counting the number of cases we obtain

- TP = 7

- TN =

- FP =

- FN =

Measurement no.	Test result	Status
1, 2, 3, 4, 5, 6, 7, 8, 9, 10	1, 1, 1, 1, 0, 0, 0, 1, 1, 1	1,1,1,1,1, 1,1,1,1,1
11,12,13,14,15, 16,17,18,19,20	0, 0, 1, 0, 1, 0, 1, 1, 0, 0	0, 0, 0, 0, 0 0, 0, 0, 0, 0

# Technical Session 2 – likelihood ratios

- Based on the example data, simply by counting the number of cases we obtain

- TP = 7
- TN = 6
- FP =
- FN =

Measurement no.	Test result	Status
1, 2, 3, 4, 5, 6, 7, 8, 9, 10	1, 1, 1, 1, 0, 0, 0, 1, 1, 1	1,1,1,1,1, 1,1,1,1,1
11,12,13,14,15, 16,17,18,19,20	0, 0, 1, 0, 1, 0, 1, 1, 0, 0	0, 0, 0, 0, 0 0, 0, 0, 0, 0

# Technical Session 2 – likelihood ratios

- Based on the example data, simply by counting the number of cases we obtain

- TP = 7
- TN = 6
- FP = 4
- FN =

Measurement no.	Test result	Status
1, 2, 3, 4, 5, 6, 7, 8, 9, 10	1, 1, 1, 1, 0, 0, 0, 1, 1, 1	1,1,1,1,1, 1,1,1,1,1
11,12,13,14,15, 16,17,18,19,20	0, 0, 1, 0, 1, 0, 1, 1, 0, 0	0, 0, 0, 0, 0 0, 0, 0, 0, 0

# Technical Session 2 – likelihood ratios

- Based on the example data, simply by counting the number of cases we obtain

- TP = 7
- TN = 6
- FP = 4
- FN = 3

Measurement no.	Test result	Status
1, 2, 3, 4, 5, 6, 7, 8, 9, 10	1, 1, 1, 1, 0, 0, 0, 1, 1, 1	1,1,1,1,1, 1,1,1,1,1
11,12,13,14,15, 16,17,18,19,20	0,0,1,0,1, 0,1,1,0,0	0,0,0,0,0 0,0,0,0,0



# Technical Session 2 – likelihood ratios

- $DSE = TP / (TP + FN) = 7/10$  Proportion of infected plants giving a positive
- $DSP = TN / (TN + FP) = 6/10$  Proportion of uninfected plants giving a negative
  
- Positive likelihood ratio: **Given a positive test, increase in likelihood** that the sample is **infected**, compared to all plants
  - $LR+ = DSE / (1 - DSP) = 0.7 / 0.4 = 1.75$
  
- Negative likelihood ratio: **Given a negative test, increase in likelihood** that the sample is **uninfected**, compared to all plants
  - $LR- = DSP / (1 - DSE) = 0.6 / 0.3 = 2$

# Practical Session 2 – using example data

- Inconclusive results were treated as a false result (counting as false negative or false positive depending on the real status of the sample). Missing results were not included in this analysis.
- Instructions: Use the data provided to calculate the following:
  - DSE
  - DSP
  - LR+, LR-
- Save the results and record any questions or comments
- Results to be reviewed in next session

# Practical Session 2 – using example data

ELISA1		True status	
		Infected	Uninfected
Test result	Positive	28	1
	Negative	4	19

$$\text{DSE} = 28 / (28 + 4)$$

$$\text{DSP} = 19 / (1 + 19)$$

ELISA2		True status	
		Infected	Uninfected
Test result	Positive	19	0
	Negative	13	20

$$\text{DSE} = 19 / (19 + 13)$$

$$\text{DSP} = 20 / (0 + 20)$$

# Practical Session 2 – using example data

IF1		True status	
		Infected	Uninfected
Test result	Positive	23	3
	Negative	1	12

$$\text{DSE} = 23 / (23 + 1)$$

$$\text{DSP} = 12 / (3 + 12)$$

IF2		True status	
		Infected	Uninfected
Test result	Positive	30	4
	Negative	2	16

$$\text{DSE} = 30 / (30 + 2)$$

$$\text{DSP} = 16 / (4 + 16)$$

# Practical Session 2 – using example data

PCR1		True status	
		Infected	Uninfected
Test result	Positive	48	3
	Negative	0	37

$$\text{DSE} = 48 / (48 + 0)$$

$$\text{DSP} = 37 / (3 + 37)$$

PCR2		True status	
		Infected	Uninfected
Test result	Positive	48	5
	Negative	0	35

$$\text{DSE} = 48 / (48 + 0)$$

$$\text{DSP} = 35 / (5 + 35)$$

# Practical Session 2 – using example data

		PCR3	
		True status	
		Infected	Uninfected
Test result	Positive	53	2
	Negative	1	43

$$\text{DSE} = 53 / (53 + 1)$$

$$\text{DSP} = 43 / (2 + 43)$$

		PCR4	
		True status	
		Infected	Uninfected
Test result	Positive	46	1
	Negative	2	39

$$\text{DSE} = 46 / (46 + 2)$$

$$\text{DSP} = 39 / (1 + 39)$$

		PCR5	
		True status	
		Infected	Uninfected
Test result	Positive	47	1
	Negative	1	39

$$\text{DSE} = 47 / (47 + 1)$$

$$\text{DSP} = 39 / (1 + 39)$$

# Review of completed exercise 2

- Check individual results

	ELISA1	ELISA2	IF1	IF2	PCR1	PCR2	PCR3	PCR4	PCR5
DSE	0.875	0.594	0.958	0.938	1	1	0.981	0.958	0.979
DSP	0.95	1	0.8	0.8	0.925	0.875	0.956	0.975	0.975
LR+	17.5	Inf	4.79	4.69	13.3	8	22.1	38.3	39.2
LR-	7.6	2.46	19.2	12.8	Inf	Inf	51.6	23.4	46.8

# Review of completed exercise 2

- Check individual results
- These can easily be displayed as follows using Excel

	ELISA1	ELISA2	IF1	IF2	PCR1	PCR2	PCR3	PCR4	PCR5
DSE	0.875	0.594	0.958	0.938	1	1	0.981	0.958	0.979
DSP	0.95	1	0.8	0.8	0.925	0.875	0.956	0.975	0.975
LR+	17.5	Inf	4.79	4.69	13.3	8	22.1	38.3	39.2
LR-	7.6	2.46	19.2	12.8	Inf	Inf	51.6	23.4	46.8



# Technical session 3 – accordancy and concordance

- Accordancy = repeatability. Probability of finding the same result from replicates of identical samples analysed in the same lab and conditions
- Concordance = reproducibility. Probability of finding the same result from identical samples analysed in different laboratories

# Technical session 3 – accordancy (per lab)

- Accordancy = repeatability. Probability of finding the same result from replicates of identical samples analysed in the same lab and conditions

- For a **single laboratory and sample**,

$$p = \{k(k - 1) + (n - k)(n - k - 1)\} / \{n(n - 1)\}$$

where  $k$  is the number of positive results out of  $n$  test results

- Accordancy is the mean of these probabilities across all samples
  - Each method/laboratory has its own accordancy measure

# Accordance

LAB1			
Sample no. (reps)	Test result	n, k	p
1 (r1, r2, r3),	1, 1, 1	3,3	1
2 (r1, r2, r3),	0, 0, 1	3,1	0.33
3 (r1, r2, r3)	1, 0, 1	3,2	0.33

Using the formula, p is calculated for each sample using only n, k. Symmetry in the formula means that 'k = number of negative results' would give same p

3 reps per sample means that there are 3 pairs of test results. Manual checking can be done for each possible pair to confirm the results

Accordance:  
average p = **0.556**

LAB2			
Sample no. (reps)	Test result	n, k	p
4 (r1, r2, r3, r4),	1, 1, 1, 0	4,3	0.5
5 (r1, r2, r3, r4),	0, 0, 0, 0	4,0	1
6 (r1, r2, r3, r4)	1, 0, 1, 1	4,3	0.5

Accordance calculated for other labs and/or methods. Averaging of p across labs would lose information, as it would not account for any systematic laboratory effect

Accordance: average p =  $2/3$  = **0.667**

# Technical session 3 – accordancy (overall)

- Accordancy = repeatability. Probability of finding the same result from replicates of identical samples analysed in the same lab and conditions
- For a **single sample**, the overall accordancy of a method is the average accordancy across all laboratories

# Technical session 3 – concordance

- Concordance = reproducibility. Probability of finding the same result from identical samples analysed in different laboratories
  - Estimated as  $p = (\text{number of matching between-lab pairs}) / (\text{total number of between-lab pairs})$

Total number of matching between-lab pairs:

$$0.5\{K(K - 1) + (N - K)(N - K - 1) - \sum_i (k_i(k_i - 1) + (n_i - k_i)(n_i - k_i - 1))\}$$

Total number of between-lab pairs:

$$0.5\{N(N - 1) - \sum_i n_i(n_i - 1)\}$$

$N$  = total number of samples (all labs)       $K$  = total number of positives (all labs)

$n_i$  = total number of samples (lab  $i$ )       $k_i$  = total number of positives (lab  $i$ )

Finally, concordance is the average of these probabilities ( $p$ ) over all samples

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- Concordance = reproducibility. Probability of finding the same result from identical samples analysed in different laboratories
  - Estimated as  $p = \frac{\text{number of matching between-lab pairs}}{\text{total number of between-lab pairs}}$

Total number of matching between-lab pairs:

$$0.5\{K(K - 1) + (N - K)(N - K - 1) - \sum_i(k_i(k_i - 1) + (n_i - k_i)(n_i - k_i - 1))\}$$

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Finally, concordance is the average of these probabilities ( $p$ ) over all samples

# Concordance

$$N = 7, K = 6,$$

$$n = (3,4), k = (3,3)$$

Using the formula,  $p$  is calculated for each sample  $i$  using only  $N, K, n_j, k_j$  (across all labs testing sample  $i$ )

LAB1		
Sample no. $i$ (3 reps)	Test result	$n_{lab1}, k_{lab1}$
1 (r1, r2, r3),	1, 1, 1	3,3
2 (r1, r2, r3),	0, 0, 1	3,1
3 (r1, r2, r3)	1, 0, 1	3,2

LAB2		
Sample no. $i$ (3 reps)	Test result	$n_{lab2}, k_{lab2}$
1 (r1, r2, r3, r4),	1, 1, 1, 0	4,3
2 (r1, r2, r3, r4),	0, 0, 0, 0	4,0
3 (r1, r2, r3, r4)	1, 0, 1, 1	4,3

All labs
P per sample
0.75
0.667
0.583



# Concordance

$$N = 7, K = 1,$$
$$n = (3,4), k = (1,0)$$

Using the formula,  $p$  is calculated for each sample  $i$  using only  $N, K, n_j, k_j$  (across all labs testing sample  $i$ )

LAB1		
Sample no. $i$ (3 reps)	Test result	$n_{\text{lab1}}, k_{\text{lab1}}$
1 (r1, r2, r3),	1, 1, 1	3,3
2 (r1, r2, r3),	0, 0, 1	3,1
3 (r1, r2, r3)	1, 0, 1	3,2

LAB2		
Sample no. $i$ (3 reps)	Test result	$n_{\text{lab2}}, k_{\text{lab2}}$
1 (r1, r2, r3, r4),	1, 1, 1, 0	4,3
2 (r1, r2, r3, r4),	0, 0, 0, 0	4,0
3 (r1, r2, r3, r4)	1, 0, 1, 1	4,3

All labs
P per sample
0.75
0.667
0.583

# Concordance

$$N = 7, K = 5,$$

$$n = (3,4), k = (2,3)$$

Using the formula,  $p$  is calculated for each sample  $i$  using only  $N, K, n_j, k_j$  (across all labs testing sample  $i$ )

LAB1		
Sample no. $i$ (3 reps)	Test result	$n_{lab1}, k_{lab1}$
1 (r1, r2, r3),	1, 1, 1	3,3
2 (r1, r2, r3),	0, 0, 1	3,1
3 (r1, r2, r3)	1, 0, 1	3,2

LAB2		
Sample no. $i$ (3 reps)	Test result	$n_{lab2}, k_{lab2}$
1 (r1, r2, r3, r4),	1, 1, 1, 0	4,3
2 (r1, r2, r3, r4),	0, 0, 0, 0	4,0
3 (r1, r2, r3, r4)	1, 0, 1, 1	4,3

All labs
P per sample
0.75
0.667
0.583

Concordance:  
average  $p = 0.667$

In practice, the calculation should include many more labs (at least 10 recommended)



# Technical session 3 – concordance odds ratio

- Concordance odds ratio (COR) for a given method
- $$COR = \frac{Acc (1-Con)}{Con (1-Acc)}$$
- Acc = Accordance over all laboratories (again this estimate is computed **per sample** and an average is taken)
  - Estimated as [number of matching pairs] / [total number of pairs]
- COR is a convenient measure of variation between laboratories
  - Designed to remove bias that may be present in accordance & concordance separately (magnitude of Acc and Con strongly dependent on sensitivity)
  - High COR associated with high between-lab variability, ideally COR = 1

# Practical Session 3 – using example data

- Inconclusive results were excluded
- Instructions: Use the data provided to calculate the following:
  - Accordance (per laboratory and method)
  - Accordance (per method)
  - Concordance (per method)
  - Concordance odds ratio (COR)
- Save the spreadsheet/results and record any questions or comments
- Results to be reviewed in next session

# Practical Session 3 – Accordance

Mean = 0.741  
averaged across 9  
samples

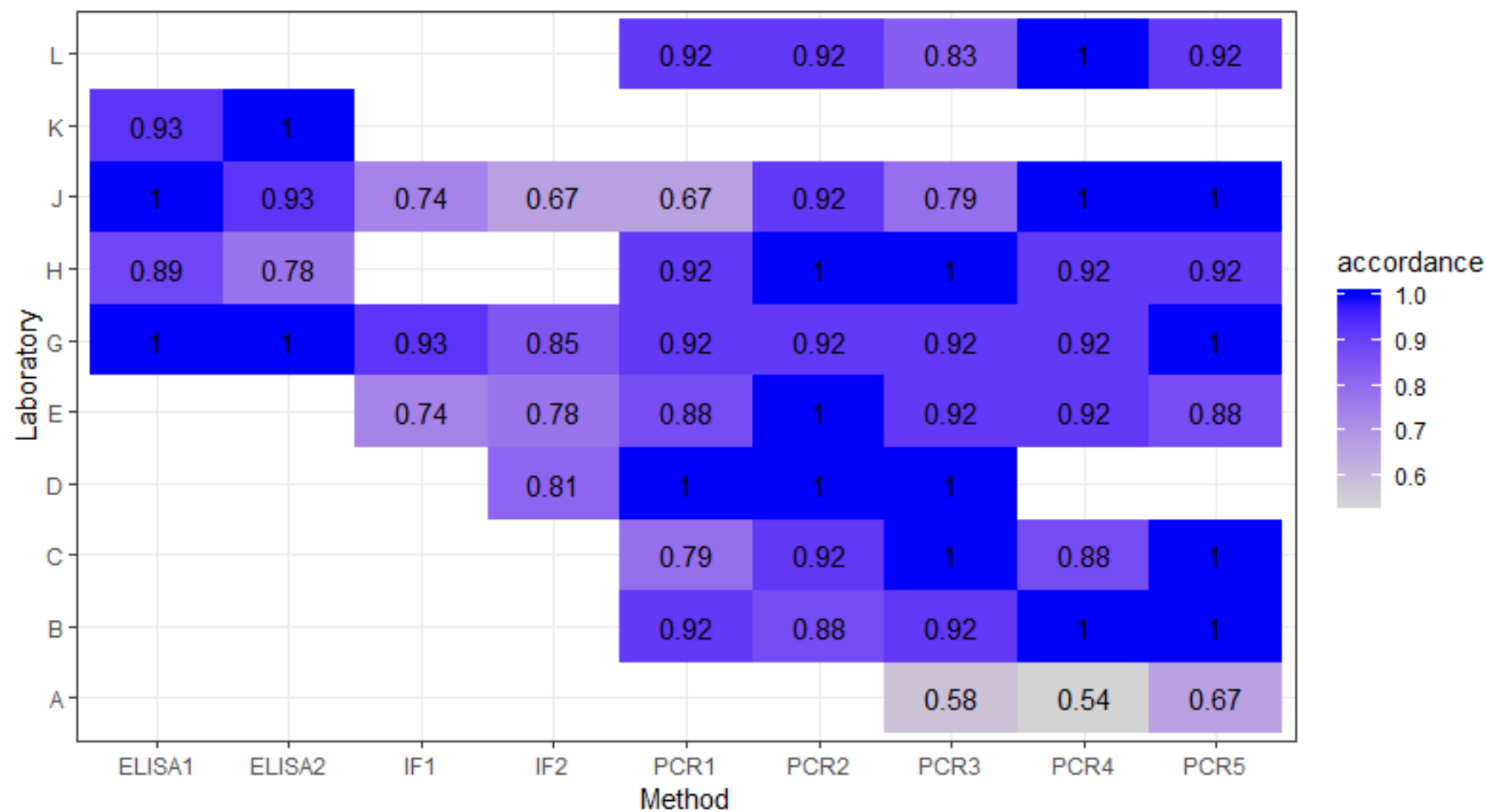
Sample	Laboratory	Method	Total_sample_pairs	Agreement_sample_pairs	Accordance
1	E	IF1	1	1	1
2	E	IF1	3	3	1
3	E	IF1	3	3	1
4	E	IF1	3	1	0.333
5	E	IF1	3	1	0.333
6	E	IF1	1	1	1
7	E	IF1	1	1	1
8	E	IF1	1	1	1
9	E	IF1	1	0	0
1	G	IF1	1	1	1
	Etc...	...	...	...	...

# Practical Session 3 – Accordance

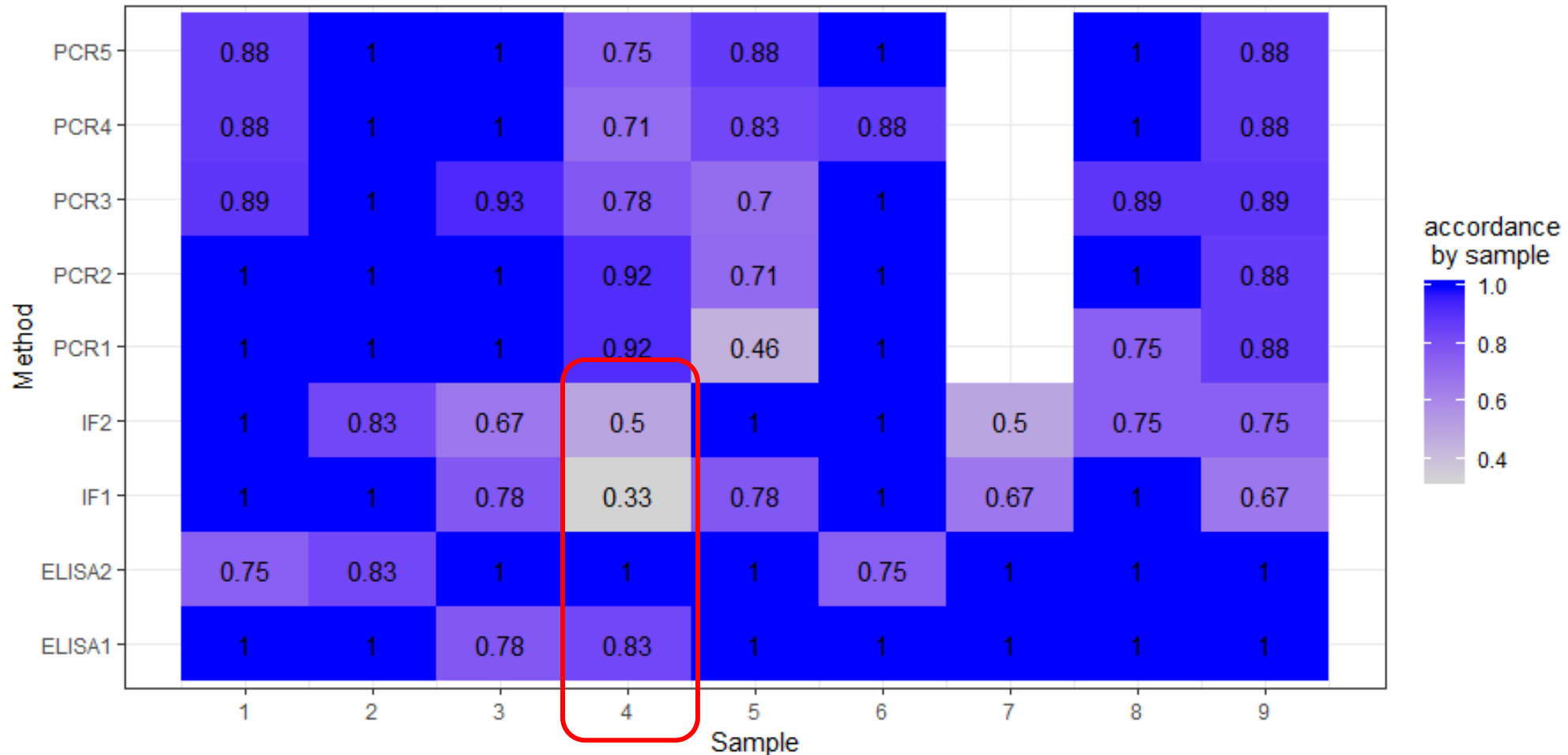
Laboratory	Method	Accordance
E	IF1	0.741
G	IF1	0.926
J	IF1	0.741
D	IF2	0.815
E	IF2	0.778
G	IF2	0.852
J	IF2	0.667
G	ELISA1	1
H	ELISA1	0.889
J	ELISA1	1
Etc...	...	...

Example data Session 3 accordance concordance/Valitest\_accordance\_examples\_averaged.csv

# TPS round 2 - *Xylophilus ampelinus*



# Practical Session 3 – Accordance (combined labs, per sample)





# Practical Session 3 – Accordance (combined labs, averaged over samples)

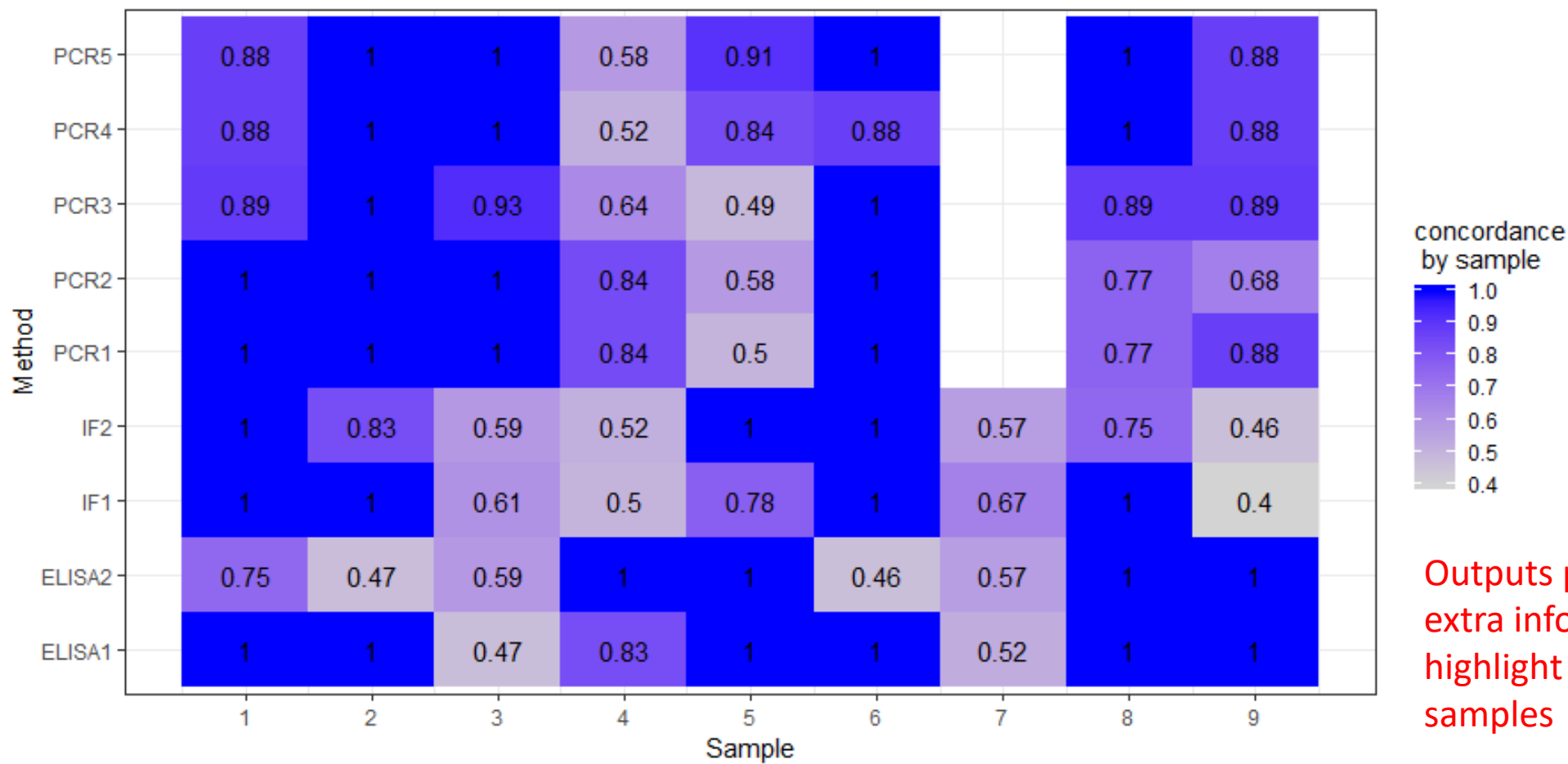
Method	Accordance
IF1	0.802
IF2	0.778
ELISA1	0.954
ELISA2	0.926
PCR1	0.875
PCR2	0.943
PCR3	0.884
PCR4	0.896
PCR5	0.922

These are the values used in calculating the Concordance Odds Ratio

# Practical Session 3 – Concordance (per sample and method)

Sample	Method	Total_sample_pairs	Agreement_sample_pairs	Concordance
1	IF1	15	15	1
2	IF1	36	36	1
3	IF1	36	22	0.611
4	IF1	36	18	0.5
5	IF1	36	28	0.778
6	IF1	15	15	1
7	IF1	15	10	0.667
8	IF1	15	15	1
9	IF1	15	6	0.4
Etc...	...	...	...	...

# TPS round 2 - *Xylophilus ampelinus*



Outputs per sample, provide extra information, e.g. could highlight issues with individual samples

# Practical Session 3 – Concordance (per method, averaged over samples)

Method	concordance
IF1	0.773
IF2	0.747
ELISA1	0.869
ELISA2	0.761
PCR1	0.873
PCR2	0.858
PCR3	0.84
PCR4	0.873
PCR5	0.906

# Practical Session 3 – Concordance odds ratio

Method	concordance	accordance	COR
IF1	0.773	0.802	1.194
IF2	0.747	0.778	1.184
ELISA1	0.869	0.954	3.097
ELISA2	0.761	0.926	3.932
PCR1	0.873	0.875	1.018
PCR2	0.858	0.943	2.716
PCR3	0.840	0.884	1.455
PCR4	0.873	0.896	1.256
PCR5	0.906	0.922	1.225

# Thank you for your attention!

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