

Interactive Web-based App for Intention-to-Diagnose (ITD)

Quick User Instructions

(Recommended browsers: Firefox, Google Chrome)

1. Data Input

The ITD App requires

- The label for the investigational test (A)
- Selection of method for confidence interval and the confidence level (B), and
- The investigational test × the reference results contingency table (C)

Intention to Diagnose
Data Input
Robustness analysis of test accuracy
Range Analysis
Predictive Values

Pre-specified Settings

Default

A

Investigational test label

B

Confidence level for two-sided CI

0.5 0.95

Method for confidence interval

☒ Agresti-Coull
☐ Wilson score
☐ Wilson score with continuity correction

Data Input Table

Result	Reference Result		Total
	Positive	Negative	
Valid	Positive		
Valid	Equivocal		
Valid	Negative		
Invalid	INVATA		
Invalid	INVATS		
	Total		

Note:
INVATA = invalid associated with test application
INVATS = invalid associated with test science

C

1.1 Pre-specified settings

- The dropdown menu offers two options: Default and Example. Default allow users to manually enter their won data into all input fields; Example is using data from a study evaluating the performance of second-generation interferon- γ release assays (IGRAs) for diagnosing tuberculosis (TB).

Pre-specified Settings
 Default

Investigational test label

Confidence level for two-sided CI
 0.5 0.95

Method for confidence interval
☒ Agresti-Coull
☐ Wilson score
☐ Wilson score with continuity correction

Data Input Table

Result		Reference Result		Total
		Positive	Negative	
Valid	Positive			
Valid	Equivocal			
Valid	Negative			
Invalid	INVATA			
Invalid	INVATS			
Total				

Note:

INVATA = invalid associated with test application

INVATS = invalid associated with test science

➤ Once the example is selected, all the data inputs will be filled out automatically.

Pre-specified Settings
 Tuberculosis-IGRAs
 Default
 EXAMPLES
 Tuberculosis-IGRAs

Confidence level for two-sided CI
 0.5 0.95

Method for confidence interval
☒ Agresti-Coull
☐ Wilson score
☐ Wilson score with continuity correction

Data Input Table

IGRAs Result		Reference Result		Total
		Positive	Negative	
Valid	Positive	273	74	347
Valid	Equivocal	22	17	39
Valid	Negative	33	296	329
Invalid	INVATA	17	36	53
Invalid	INVATS	18	16	34
Total		363	439	802

Note:

INVATA = invalid associated with test application

INVATS = invalid associated with test science

1.2 Label for the investigational test

- Input the label for the investigational test

Pre-specified Settings

Default

Investigational test label

Confidence level for two-sided CI

0.5 0.95

Method for confidence interval

☒ Agresti-Coull

☐ Wilson score

☐ Wilson score with continuity correction

Data Input Table

Result		Reference Result		Total
		Positive	Negative	
Valid	Positive			
Valid	Equivocal			
Valid	Negative			
Invalid	INVATA			
Invalid	INVATS			
Total				

Note:

INVATA = invalid associated with test application

INVATS = invalid associated with test science

1.3 Confidence Level for Confidence Interval and Method Options for the Confidence Interval

- Specify confidence level for two-sided confidence interval for the measurements of different type of accuracy as well as for the range analysis
 - The default value for confidence level is 95% and the default method for estimating the confidence interval is Agresti-Coull

Pre-specified Settings

Default

Investigational test label

Confidence level for two-sided CI

0.5 0.95

Method for confidence interval

☒ Agresti-Coull

☐ Wilson score

☐ Wilson score with continuity correction

Data Input Table

Result		Reference Result		Total
		Positive	Negative	
Valid	Positive			
Valid	Equivocal			
Valid	Negative			
Invalid	INVATA			
Invalid	INVATS			
Total				

Note:

INVATA = invalid associated with test application

INVATS = invalid associated with test science

1.4 Data Input Table

- Double-clicking a cell allow for inputting data

Data Input Table

IGRAs Result		Reference Result		Total
		Positive	Negative	
Valid	Positive			
Valid	Equivocal			
Valid	Negative			
Invalid	INVATA			
Invalid	INVATS			
Total				

Double click

Note:

INVATA = invalid associated with test application

INVATS = invalid associated with test science

2. App Implementation

2.1 Example

Whitworth HS, Badhan A, Boakye AA, et al. Clinical Utility of Existing and Second-Generation Interferon- γ Release Assays for Diagnostic Evaluation of Tuberculosis: An Observational Cohort Study. *Lancet Infect Dis* 2019; 19(2): 193-202.

Table: Summary Table for a Diagnostic Test Accuracy Study of Interferon- γ Release Assays (IGRAs) for Diagnosis of Tuberculosis

			Reference Test		Total
			Positive	Negative	
Second-generation IGRAs	Valid	Positive	273	74	347
		Equivocal	22	17	39
		Negative	33	296	329
	Invalid	INVATA	17	36	53
		INVATS	18	16	34

INVATS = invalid associated with test science; INVATS = invalid associated with test science.

2.2 Data Input

Intention to Diagnose
Data Input
Robustness analysis of test accuracy
Range Analysis
Predictive Values
Support

Pre-specified Settings

Tuberculosis-IGRAs

Investigational test label

IGRAs

Confidence level for two-sided CI

0.5

0.95

Method for confidence interval

☒ Agresti-Coull
☐ Wilson score
☐ Wilson score with continuity correction

Data Input Table

IGRAs Result		Reference Result		Total
		Positive	Negative	
Valid	Positive	273	74	347
Valid	Equivocal	22	17	39
Valid	Negative	33	296	329
Invalid	INVATA	17	36	53
Invalid	INVATS	18	16	34
Total		363	439	802

Note:
INVATA = invalid associated with test application
INVATS = invalid associated with test science

2.3 Intention-to-Diagnose Analysis Result

- All the results can be saved in cvs for tables or png for figures (click on “Save” icon).
 - Robustness analysis of test accuracy

Intention to Diagnose

Data Input

Robustness analysis of test accuracy

Range Analysis

Predictive Values

Select x-axis range

☒ Default
 ☐ Customize

☐ Perform hypothesis tests

Note: Set up null threshold for each measurement

Pragmatic Application Accuracy ?

Confidence interval (CI) estimates of pragmatic application accuracy

	Estimate (%)	CI (%)
Sensitivity	75.2 (273/363)	(70.5, 79.4)
Cumulative sensitivity	81.3 (295/363)	(76.9, 85.0)
Specificity	67.4 (296/439)	(62.9, 71.6)
Cumulative specificity	71.3 (313/439)	(66.9, 75.3)

Save +

Select x-axis range

☒ Default
 ☐ Customize

☐ Perform hypothesis tests

Note: Set up null threshold for each measurement

Pragmatic scientific accuracy ?

Confidence interval (CI) estimates of pragmatic scientific accuracy

	Estimate (%)	CI (%)
Sensitivity	78.9 (273/346)	(74.3, 82.9)
Cumulative sensitivity	85.3 (295/346)	(81.1, 88.6)
Specificity	73.4 (296/403)	(68.9, 77.5)
Cumulative specificity	77.7 (313/403)	(73.3, 81.5)

Save +

Select x-axis range

☒ Default
 ☐ Customize

☐ Perform hypothesis tests

Note: Set up null threshold for each measurement

Explanatory scientific accuracy -- Non-informative (NI) imputation ?

Confidence interval (CI) estimates of explanatory scientific accuracy -- NI imputation

	Estimate (%)	CI (%)
Sensitivity	81.4 (282/346)	(77.0, 85.2)
Cumulative sensitivity	88.1 (305/346)	(84.2, 91.1)
Specificity	75.3 (303/403)	(70.8, 79.2)
Cumulative specificity	79.7 (321/403)	(75.5, 83.4)

Save +

Do you want to combine all the three forest plots into one?

☐ YES
 ☒ NO

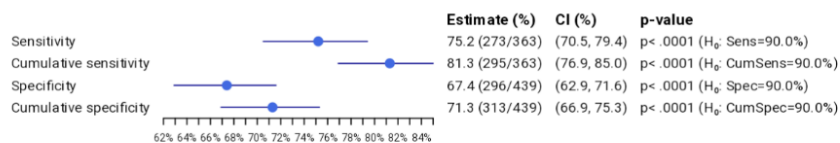
- X-axis is adjustable. Select “customize” to adjust.
- Option to perform hypothesis tests based on score test. Select the box “Perform hypothesis tests”.
- Option to combine all the three forest plots into one.

Select x-axis range
☒ Default
☐ Customize

☒ Perform hypothesis tests
 Note: Set up null threshold for each measurement
 Sensitivity null(%)
 90
 Cumulative sensitivity null(%)
 90
 Specificity null(%)
 90
 Cumulative specificity null(%)
 90

Pragmatic Application Accuracy ?

Confidence interval (CI) estimates of pragmatic application accuracy



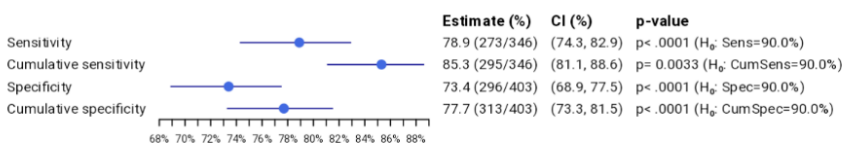
Save +

Select x-axis range
☒ Default
☐ Customize

☒ Perform hypothesis tests
 Note: Set up null threshold for each measurement
 Sensitivity null(%)
 90
 Cumulative sensitivity null(%)
 90
 Specificity null(%)
 90
 Cumulative specificity null(%)
 90

Pragmatic scientific accuracy ?

Confidence interval (CI) estimates of pragmatic scientific accuracy



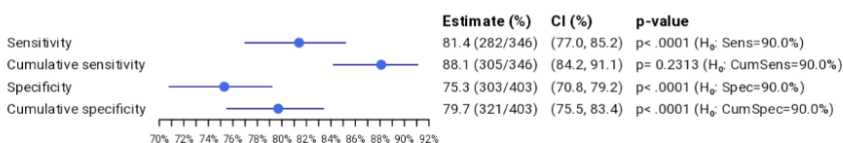
Save +

Select x-axis range
☒ Default
☐ Customize

☒ Perform hypothesis tests
 Note: Set up null threshold for each measurement
 Sensitivity null(%)
 90
 Cumulative sensitivity null(%)
 90
 Specificity null(%)
 90
 Cumulative specificity null(%)
 90

Explanatory scientific accuracy -- Non-informative (NI) imputation ?

Confidence interval (CI) estimates of explanatory scientific accuracy -- NI imputation



Save +

Do you want to combine all the three forest plots into one?

☐ YES ☒ NO

- When the box of “Perform hypothesis tests” is selected, null thresholds for sensitivity, cumulative sensitivity, specificity, and cumulative specificity can be specified. The default null thresholds are 90%.
- The corresponding p-value would be displayed in the forest plots.

Do you want to combine all the three forest plots into one?

☒ YES ☐ NO

Do you want to perform hypothesis tests for each measurement?

☐ YES ☒ NO

Generate

Do you want to combine all the three forest plots into one?

☒ YES ☐ NO

Do you want to perform hypothesis tests for each measurement?

☒ YES ☐ NO

Please check the three "Perform hypothesis test" boxes on the left panels above and set up null thresholds.

Generate

- To combine all the three forest plots into one, select "YES". Option to perform hypothesis tests for each measurement. Click on "Generate" to generate the combined forest plot.
- If the option to perform hypothesis tests for each measurement is selected, make sure to check the three "Perform hypothesis test" boxes on the left panels above and set up null thresholds.

Do you want to combine all the three forest plots into one?

☒ YES ☐ NO

Do you want to perform hypothesis tests for each measurement?

☐ YES ☒ NO

Generate

Select x-axis range

☒ Default
☐ Customize

Confidende interval (CI) estimates of robustness analysis

Pragmatic application accuracy

		Estimate (%)	CI (%)
Sensitivity		75.2 (273/363)	(70.5, 79.4)
Cumulative sensitivity		81.3 (295/363)	(76.9, 85.0)
Specificity		67.4 (296/439)	(62.9, 71.6)
Cumulative specificity		71.3 (313/439)	(66.9, 75.3)

Pragmatic scientific accuracy

Sensitivity		78.9 (273/346)	(74.3, 82.9)
Cumulative sensitivity		85.3 (295/346)	(81.1, 88.6)
Specificity		73.4 (296/403)	(68.9, 77.5)
Cumulative specificity		77.7 (313/403)	(73.3, 81.5)

Explanatory scientific accuracy - NI imputation

Sensitivity		81.4 (282/346)	(77.0, 85.2)
Cumulative sensitivity		88.1 (305/346)	(84.2, 91.1)
Specificity		75.3 (303/403)	(70.8, 79.2)
Cumulative specificity		79.7 (321/403)	(75.5, 83.4)

62% 65% 68% 71% 74% 77% 80% 83% 86% 89% 92%

Save

Do you want to combine all the three forest plots into one?

☒ YES ☐ NO

Do you want to perform hypothesis tests for each measurement?

☒ YES ☐ NO

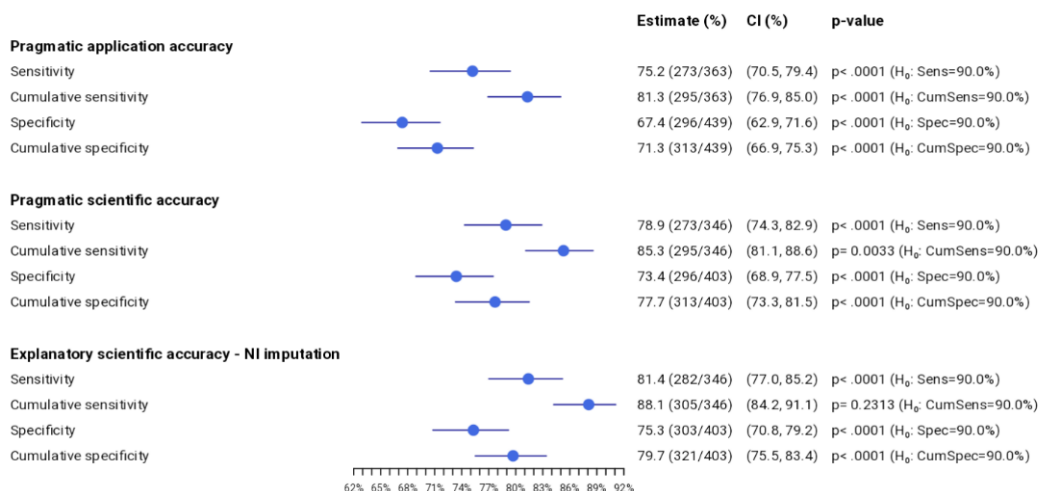
The null thresholds will be the same as you set on the left panels above.

Generate

Select x-axis range

☒ Default
☐ Customize

Confidence interval (CI) estimates of robustness analysis



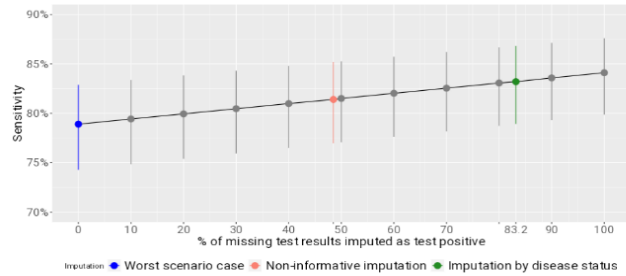
Save

- X axis is adjustable. Select “customize” to adjust.
- If the option to perform hypothesis tests for each measurement is selected, the null thresholds would be the same as above. The corresponding p-value would be displayed in the forest plots.

➤ Range Analysis

Intention to Diagnose Data Input Robustness analysis of test accuracy **Range Analysis** Predictive Values

Single imputation for explanatory scientific accuracy -- range analysis for sensitivity

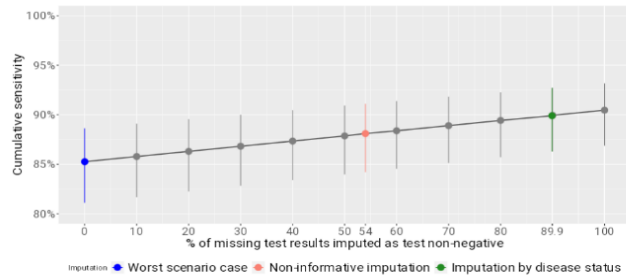


Save

% of missing imputed to positive	Sensitivity (%)	Confidence Interval (%)	Imputation
0.0	78.9	(74.2, 82.8)	Worst scenario case
10.0	79.4	(74.8, 83.3)	Worst scenario case
20.0	79.9	(75.3, 83.8)	Worst scenario case
30.0	80.5	(75.9, 84.3)	Worst scenario case
40.0	81.0	(76.5, 84.7)	Worst scenario case
48.3	81.4	(76.9, 85.1)	Non-informative imputation
50.0	81.5	(77.0, 85.2)	Non-informative imputation
60.0	82.0	(77.6, 85.7)	Non-informative imputation
70.0	82.5	(78.1, 86.1)	Non-informative imputation
80.0	83.1	(78.7, 86.6)	Non-informative imputation
83.2	83.2	(78.9, 86.8)	Imputation by disease status
90.0	83.6	(79.2, 87.1)	Imputation by disease status
100.0	84.1	(79.8, 87.5)	Imputation by disease status

Save

Single imputation for explanatory scientific accuracy -- range analysis for cumulative sensitivity

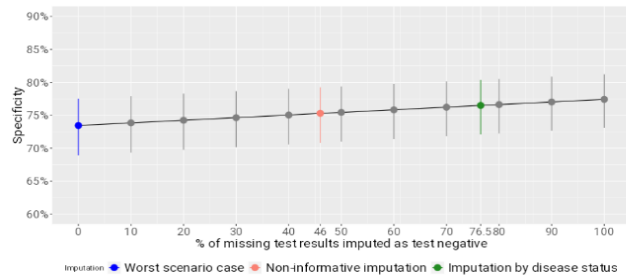


Save

% of missing imputed to non-negative	Cumulative sensitivity (%)	Confidence Interval (%)	Imputation
0.0	85.3	(81.1, 88.6)	Worst scenario case
10.0	85.8	(81.6, 89.0)	Worst scenario case
20.0	86.3	(82.2, 89.5)	Worst scenario case
30.0	86.8	(82.8, 90.0)	Worst scenario case
40.0	87.3	(83.3, 90.4)	Worst scenario case
50.0	87.9	(83.9, 90.9)	Worst scenario case
54.0	88.1	(84.2, 91.0)	Non-informative imputation
60.0	88.4	(84.5, 91.3)	Non-informative imputation
70.0	88.9	(85.1, 91.8)	Non-informative imputation
80.0	89.4	(85.7, 92.2)	Non-informative imputation
89.9	89.9	(86.2, 92.7)	Imputation by disease status
90.0	89.9	(86.2, 92.7)	Imputation by disease status
100.0	90.5	(86.8, 93.1)	Imputation by disease status

Save

Single imputation for explanatory scientific accuracy -- range analysis for specificity

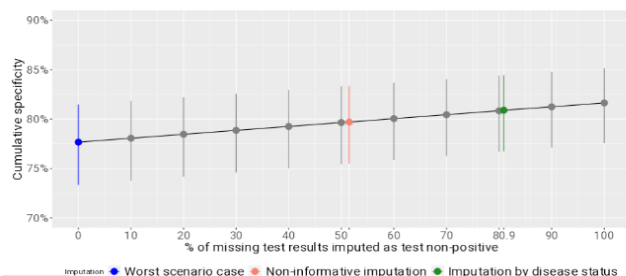


Save

% of missing imputed to negative	Specificity (%)	Confidence Interval (%)	Imputation
0.0	73.4	(68.9, 77.5)	Worst scenario case
10.0	73.8	(69.3, 77.9)	Worst scenario case
20.0	74.2	(69.7, 78.2)	Worst scenario case
30.0	74.6	(70.1, 78.6)	Worst scenario case
40.0	75.0	(70.5, 79.0)	Worst scenario case
46.0	75.3	(70.8, 79.2)	Non-informative imputation
50.0	75.4	(70.9, 79.3)	Non-informative imputation
60.0	75.8	(71.4, 79.7)	Non-informative imputation
70.0	76.2	(71.8, 80.1)	Non-informative imputation
76.5	76.5	(72.1, 80.3)	Imputation by disease status
80.0	76.6	(72.2, 80.5)	Imputation by disease status
90.0	77.0	(72.6, 80.8)	Imputation by disease status
100.0	77.4	(73.0, 81.2)	Imputation by disease status

Save

Single imputation for explanatory scientific accuracy -- range analysis for cumulative specificity



Save

% of missing imputed to non-positive	Cumulative specificity (%)	Confidence Interval (%)	Imputation
0.0	77.7	(73.3, 81.4)	Worst scenario case
10.0	78.1	(73.7, 81.8)	Worst scenario case
20.0	78.5	(74.1, 82.2)	Worst scenario case
30.0	78.9	(74.5, 82.5)	Worst scenario case
40.0	79.3	(75.0, 82.9)	Worst scenario case
50.0	79.7	(75.4, 83.3)	Worst scenario case
51.5	79.7	(75.5, 83.3)	Non-informative imputation
60.0	80.0	(75.8, 83.6)	Non-informative imputation
70.0	80.4	(76.2, 84.0)	Non-informative imputation
80.0	80.8	(76.7, 84.3)	Non-informative imputation
80.9	80.9	(76.7, 84.4)	Imputation by disease status
90.0	81.2	(77.1, 84.7)	Imputation by disease status
100.0	81.6	(77.5, 85.1)	Imputation by disease status

Save

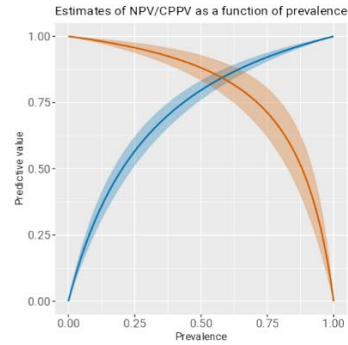
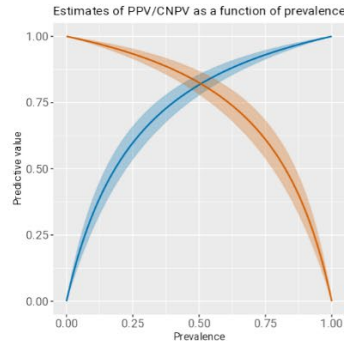
- Three imputation methods are considered: worst scenario case, non-informative imputation, and imputation by disease status. The confidence intervals of % of missing imputed are calculated using method selected under 'Data Input' tag.

➤ Predictive values

Intention to Diagnose Data Input Robustness analysis of test accuracy Range Analysis **Predictive Values**

☐ Specify the prevalence

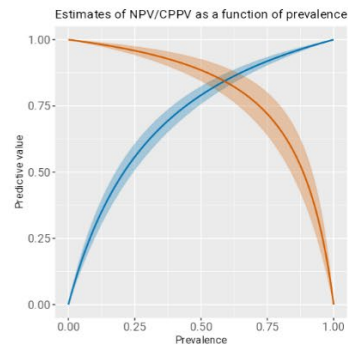
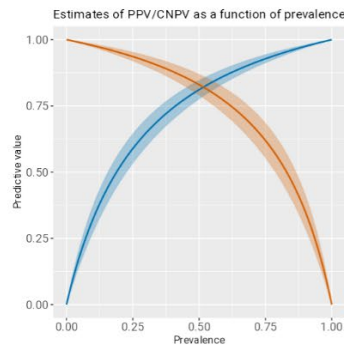
Pragmatic Application Accuracy



Positive predictive value Cumulative negative predictive Cumulative positive predictive value Negative predictive

Save

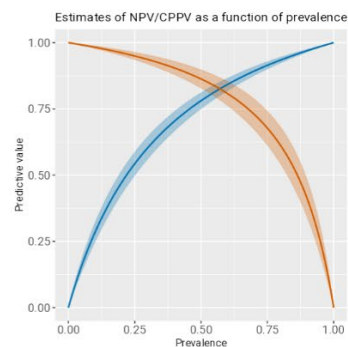
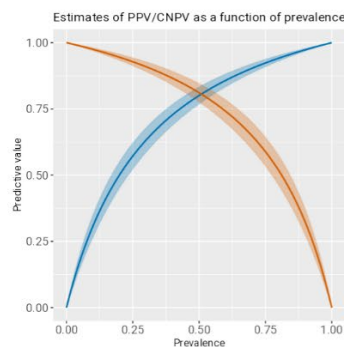
Pragmatic Scientific Accuracy



Positive predictive value Cumulative negative predictive Cumulative positive predictive value Negative predictive

Save

Explanatory Scientific Accuracy -- NI Imputation



Positive predictive value Cumulative negative predictive Cumulative positive predictive value Negative predictive

Save

- Prevalence (range 0 – 1) can be specified. The vertical lines would then be added to the plots to reflect the specified prevalence. A summary table of predictive values with confidence intervals (based on selected CI method and confidence level) would be generated.

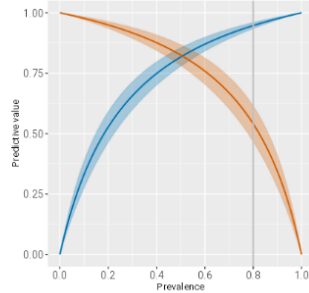
☒ Specify the prevalence

Prevalence (range 0 ~ 1)

0.8

Pragmatic Application Accuracy

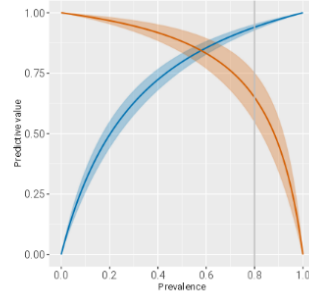
Estimates of PPV/CNPV as a function of prevalence



Positive predictive value Cumulative negative predictive value

Save

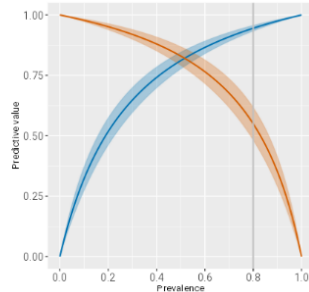
Estimates of NPV/CPPV as a function of prevalence



Cumulative positive predictive value Negative predictive value

Pragmatic Scientific Accuracy

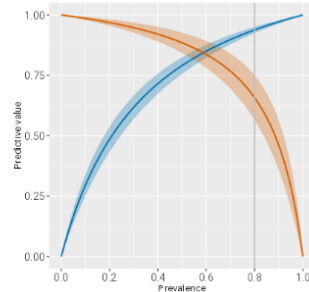
Estimates of PPV/CNPV as a function of prevalence



Positive predictive value Cumulative negative predictive value

Save

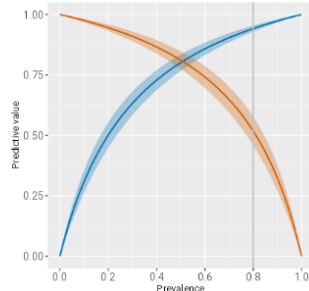
Estimates of NPV/CPPV as a function of prevalence



Cumulative positive predictive value Negative predictive value

Explanatory Scientific Accuracy -- NI Imputation

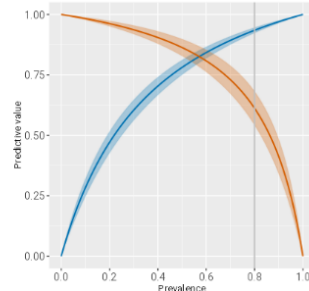
Estimates of PPV/CNPV as a function of prevalence



Positive predictive value Cumulative negative predictive value

Save

Estimates of NPV/CPPV as a function of prevalence



Cumulative positive predictive value Negative predictive value

Table: Predictive values with confidence intervals

	PPV (%)	CNPV (%)	NPV (%)	CPPV (%)	Prevalence
Pragmatic application accuracy	94.7 (93.4, 96.0)	54.0 (46.6, 61.5)	94.0 (92.8, 95.2)	65.0 (54.8, 75.1)	0.8
Pragmatic scientific accuracy	94.5 (93.3, 95.7)	55.0 (48.2, 61.8)	93.8 (92.7, 94.9)	65.8 (56.9, 74.7)	0.8
Explanatory scientific accuracy	94.1 (93.0, 95.2)	51.8 (46.1, 57.4)	93.4 (92.4, 94.5)	61.2 (54.3, 68.1)	0.8

Save