

## **SOLUTION: Diagnostic Test Accuracy Meta-Analysis Worksheet**

(Suzanne Freeman, Nicola Cooper and Alex Sutton)

Diagnostic tests generally comprise of a measure which splits individuals into healthy or diseased. To assess accuracy, a diagnostic test is compared to the “gold standard” test which is assumed to provide the true diagnosis of individuals. There are two parameters which are often used to assess the accuracy of diagnostic tests. Sensitivity is the proportion of patients with the disease correctly diagnosed by the test. Specificity is the proportion of patients without the disease correctly diagnosed by the test. For those new to this topic, an interactive primer on the evaluation of diagnostic test accuracy can be found here: <https://crsu.shinyapps.io/diagprimer/>.

A meta-analysis of diagnostic test accuracy (DTA) studies synthesises both sensitivity and specificity from multiple studies to evaluate the performance of a diagnostic test. The results are often presented either around a mean point or as a summary receiver operating curve (ROC). *Diagnostic Test Accuracy Meta-Analysis (DTA MA)* is a web-based App for conducting meta-analysis of diagnostic test accuracy studies. The App produces summary ROC plots, and pooled estimates for sensitivity and specificity together with uncertainty in their estimation. The App can also be used to aid sensitivity analyses by excluding studies.

After completing this worksheet, you should be able to:

- Use the *DTA MA* app to perform a meta-analysis of diagnostic test accuracy studies, obtain pooled estimates of sensitivity and specificity and interpret the results
- Use the *DTA MA* app to produce and download a summary ROC plot
- Use the *DTA MA* app to examine the influence of studies when they are included and excluded in a sensitivity analysis

The app can be accessed from: [https://crsu.shinyapps.io/dta\\_ma/](https://crsu.shinyapps.io/dta_ma/)

The default dataset is a subset of data from a study on unhealthy alcohol use and alcohol use disorders (Kriston et al. *Ann Intern Med.* 2008; 149: 879). The dataset consists of fourteen studies assessing the use of the AUDIT-C (Alcohol Use Disorders Identification Test-Consumption) questionnaire for identifying patients with an unhealthy alcohol use problem.

Start by viewing the data in the ‘Load Data’ tab and then use the AUDIT-C dataset to complete the following questions:

1. Click on the ‘Load Data’ page and select the ‘Data for Analysis’ tab. Check you understand the data that is loaded and ready for analysis. (Optional: Calculate sensitivity by hand for Aalto and check your result using the ‘Study-level Outcomes’ tab on the ‘Meta-Analysis’ page).

*The dataset consists of fourteen trials. In the third column TP represents the number of patients with a true positive test result. In the fourth column FN represents the number of patients with a false negative test result. In the fifth column FP represents the number of patients with a false positive test result. In the sixth column TN represents the number of patients with a true negative test result.*

*Optional: Sensitivity = Number of true positives / Total number of patients with the disease*

*Aalto: Sensitivity = 47 / (47+9) = 0.83*

2. a) Use the 'Study-level Outcomes' tab on the 'Meta-Analysis' page to complete the following table:

Author	Year	Sensitivity	Specificity
Aertgeerts02	2002	0.650	0.939
Bradley03	2003	0.912	0.779
Bush	1998	0.971	0.566
Gordon	2001	0.999	0.480
Rumpf	2002	0.738	0.830
Tuunanen	2007	0.748	0.742

b) Across all studies:

- i) Which studies have the largest and smallest values for sensitivity?

*Largest sensitivity = Gordon*

*Smallest sensitivity = Aertgeerts02*

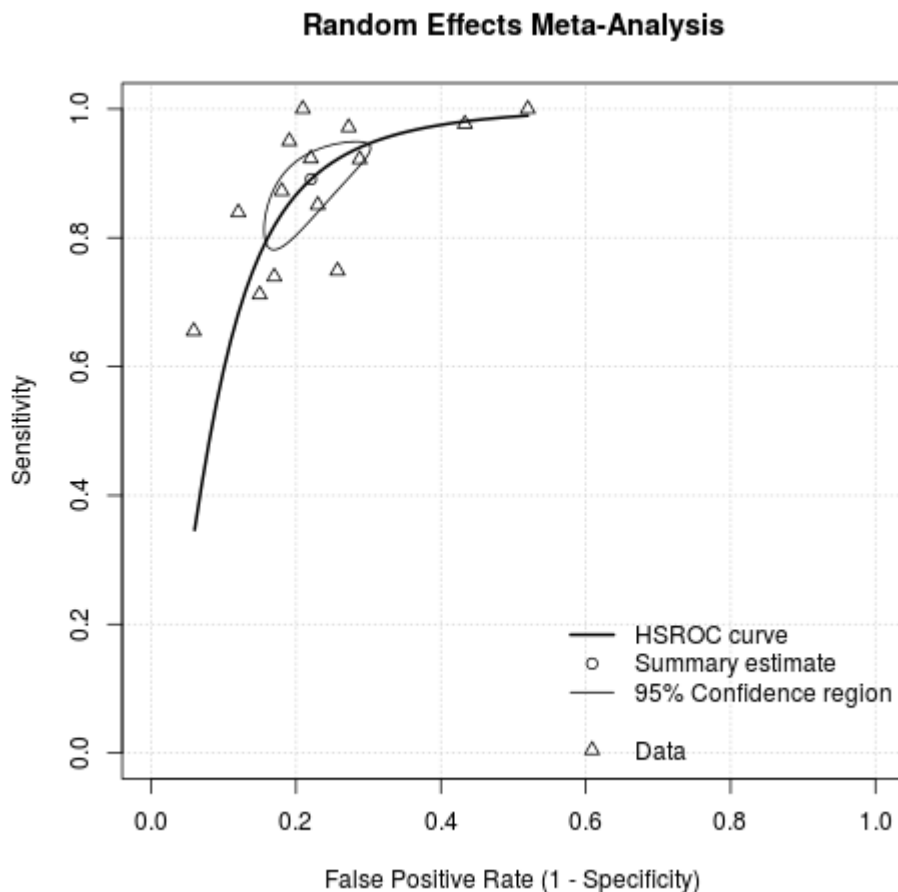
- ii) Which studies have the largest and smallest values for specificity?

*Largest specificity = Aertgeerts02*

*Smallest specificity = Gordon*

*The largest and smallest values of sensitivity and specificity can be obtained in two ways:*

- *On the 'study-level outcomes' tab the triangles to the right of the column headings can be used to sort the data in the table by ascending or descending order.*
  - *Using the 'ROC curve' tab on the 'sensitivity analysis' page. When you hover over a data point on the ROC plot the sensitivity and false-positive rate corresponding to that study are displayed below the plot.*
3. Use the 'ROC Curve' tab on the 'Meta-Analysis' page to produce a plot which shows the HSROC curve (this stands for hierarchical summary receiver operating characteristics curve and is a pooled curve taking all the data points into account and including random effects to allow for between study heterogeneity), summary estimate, 95% confidence region and individual study estimates. Change the title to "AUDIT-C Meta-Analysis". (Optional: Download the plot and place into a Word document).



4. a) Use the 'Statistics' tab on the 'Meta-Analysis' page to complete the following table:

Parameter	Estimate	2.5%	97.5%
Sensitivity	0.891	0.808	0.941
Specificity	0.779	0.715	0.833
False Positive Rate	0.221	0.167	0.285
Diagnostic Odds Ratio	29.7	18.3	45.5

b) Interpret the sensitivity, specificity and false-positive rate

*Sensitivity of 0.891 (95% confidence interval (CI): 0.808, 0.941) indicates that 89% of people with an unhealthy alcohol use problem would be correctly identified by the AUDIT-C screening test. Specificity of 0.779 (95% CI: 0.715, 0.833) indicates that 78% of patients without an unhealthy alcohol use problem would be correctly identified by the AUDIT-C screening test. The false positive rate is equal to 1-specificity. Therefore the false positive rate indicates that 22% of people without an unhealthy alcohol use problem would be incorrectly identified as having an unhealthy alcohol use problem.*

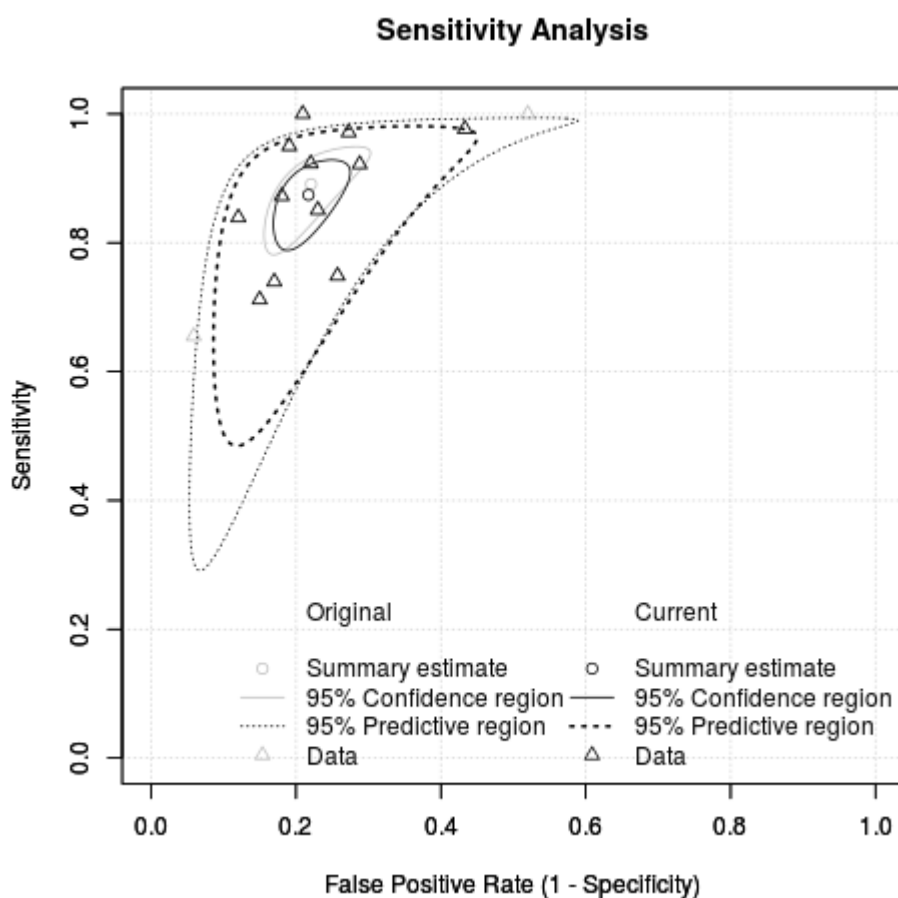
c) Interpret the diagnostic odds ratio

*The diagnostic odds ratio represents how many times more likely a patient is to have the disease given that they have a positive test result compared to a patient with a negative test result. The diagnostic odds ratio of 29.7 (95% CI: 18.3, 45.4) indicates that patients with a positive test result are almost 30 times more likely to have an unhealthy alcohol use problem than patients with a negative test result.*

- Use the 'Sensitivity Analysis' page to exclude the trials with the largest values of sensitivity and specificity:

*Exclude Aertgeerts02 and Gordon*

- Use the 'ROC Curve' tab to produce a plot which shows the data points, summary estimate, 95% confidence region and 95% predictive region. Change the title to "Sensitivity Analysis". (Optional: Download the plot and place in a Word document)



- How do the estimates of sensitivity and specificity change compared to the analysis with all studies?

*When Aertgeerts02 and Gordon are excluded sensitivity is reduced to 0.874 (95% CI: 0.808, 0.920) and specificity is increased to 0.783 (95% CI: 0.737, 0.822).*

- Use the 'Sensitivity Analysis' page to compare the earliest seven studies with the most recent seven studies:

*On the 'Study-level Outcomes' tab the triangle to the right of the column heading for 'Year' can be used to sort the data in the table by ascending or descending order according to 'Year'.*

*Seven earliest studies: Aertgeerts01, Aertgeerts02, Bradley03, Bush, Gordon, Gual, Rumpf*

*Seven later studies: Aalto, Bradley07, Gomez, Seale, Selin, Tsai, Tuunanen*

- a) Is there a difference between the estimates of sensitivity?

*In the seven earliest studies sensitivity is 0.891 (95% CI: 0.719, 0.963). In the seven later studies sensitivity is 0.876 (95% CI: 0.802, 0.925). There is little difference between the two estimates of sensitivity.*

- b) Is there a difference between the estimates of specificity?

*In the seven earliest studies specificity is 0.754 (95% CI: 0.628, 0.847). In the seven later studies specificity is 0.799 (95% CI: 0.757, 0.835). ). There is little difference between the two estimates of specificity.*