Diagnostic Test Accuracy Meta-Analysis Worksheet
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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). *MetaDTA* is a web-based App for conducting meta-analysis of diagnostic test accuracy studies. *MetaDTA* produces summary ROC plots, and pooled estimates for sensitivity and specificity together with uncertainty in their estimation and can also be used to aid sensitivity analyses by excluding studies.

After completing this worksheet, you should be able to:
- Use *MetaDTA* to perform a meta-analysis of diagnostic test accuracy studies, obtain pooled estimates of sensitivity and specificity and interpret the results
- Use *MetaDTA* to produce and download a summary ROC plot
- Use *MetaDTA* to examine the influence of studies when they are included and excluded in a sensitivity analysis

MetaDTA can be accessed from: https://crsu.shinyapps.io/dta_ma/. From here please follow the link to the Beta version of MetaDTA. A copy of the user guide can be downloaded from the home page.

MetaDTA has four inbuilt datasets which can be used to familiarise yourself with the features of MetaDTA. The four datasets are also available to download in csv format and can be used to help ensure that your own data is in the correct format for upload to MetaDTA. These datasets can be accessed from the grey box on the Load Data page. The example datasets come from a systematic review investigating the accuracy of an informant-based questionnaire, for detection of all cause dementia in adults. The datasets consist of thirteen studies assessing the use of the IQCODE (Informant Questionnaire on Cognitive Decline in the Elderly) tool for identifying adults with dementia within a secondary care setting.

The IQCODE tool contains a number of questions which are scored on a five point scale. The IQCODE tool has a number of different variants, depending on how many questions are asked. The questions are based on the performance of everyday tasks related to cognitive function. These are then rated on a scale of 1-5. The final score is an average score for each question. The threshold used in each study is included as a covariate (see below). The IQCODE tool is only a screening tool and does not offer a definitive diagnosis of dementia. A high value on the IQCODE tool is taken to indicate that a patient is at risk of dementia and further clinical investigations are needed for diagnosis.

Start by selecting the 'With Quality Assessment and Covariates' dataset from the grey box on the left hand side of the 'Load Data' page and then use this 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 Flicker and check your result using the 'Study-level Outcomes' tab on the 'Meta-Analysis' page).

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

Author	Year	Sensitivity	Specificity
Flicker	1997		
Garcia	2002		
Gonclaves	2011		
Hancock	2009		
Harwood	1997		
Jorm	1991		

b) Across all studies:
   i) Which studies have the largest and smallest values for sensitivity?

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

3. a) 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 operatic 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 of the plot. (Optional: Download the plot and place into a Word document).

b) Display the disease prevalence and percentage study weights for each study

c) Display the 95% study-level confidence levels for sensitivity and specificity

d) From the 'Display quality assessment scores' drop down menu in the grey box select the option 'Both risk of bias and applicability concerns'. Identify any studies where all seven QUADAS-2 domains are high or unclear risk of bias.

e) From the 'Display covariates' drop down menu in the grey box select the covariate IQCODE. Identify the one study which used the 32-item IQCODE variant.

f) Optional: Play around with the graphical options and see which options can be used in combination

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

Parameter	Estimate	2.5%	97.5%
Sensitivity			
Specificity			
False Positive Rate			
Diagnostic Odds Ratio			

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

c) Interpret the diagnostic odds ratio

5. Use the 'Sensitivity Analysis' page to exclude the two trials with high or unclear risk of bias for all seven QUADAS-2 domains:

a) 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)

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

6. The Prevalence page predicts how many patients in practice you would expect to have true positive, false positive, true negative and false negative results for a given disease prevalence based on the meta-analysis results and helps to give the results some clinical context. Use the 'Meta-analysis' tab on the 'Prevalence' page to identify the expected number of true positive, false positive, true negative and false negative results for a prevalence of 50% and how this would change if prevalence was increased to 70%.