



Structure of a DTA Review



THE COCHRANE
COLLABORATION®

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Dutch Cochrane Centre

Copenhagen
26 February 2009



Diagnostic Test Accuracy Reviews

- Question formulation
- Identification of studies
- Selection of relevant studies
- Quality assessment
- Data-extraction
- Data analysis
- Presentation and interpretation of results



- Diagnostic test accuracy review
 - Title
 - Review information
 - Main text
 - Tables
 - Studies and references
 - Data and analyses
 - Figures
 - Sources of support
 - Feedback
 - Appendices

Laboratory tests for caffeine addiction in PhD students

Review information

Authors

John Brown¹, Peter Smith¹, Sarah Jones¹

¹[Empty affiliation]

Citation example: Brown J, Smith P, Jones S. Laboratory tests for caffeine addiction in PhD students. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Add Author

Contact person

[Empty name]

Dates

Assessed as Up-to-date:

Date of Search:

Next Stage Expected:

Protocol First Published: Not specified

Review First Published: Not specified

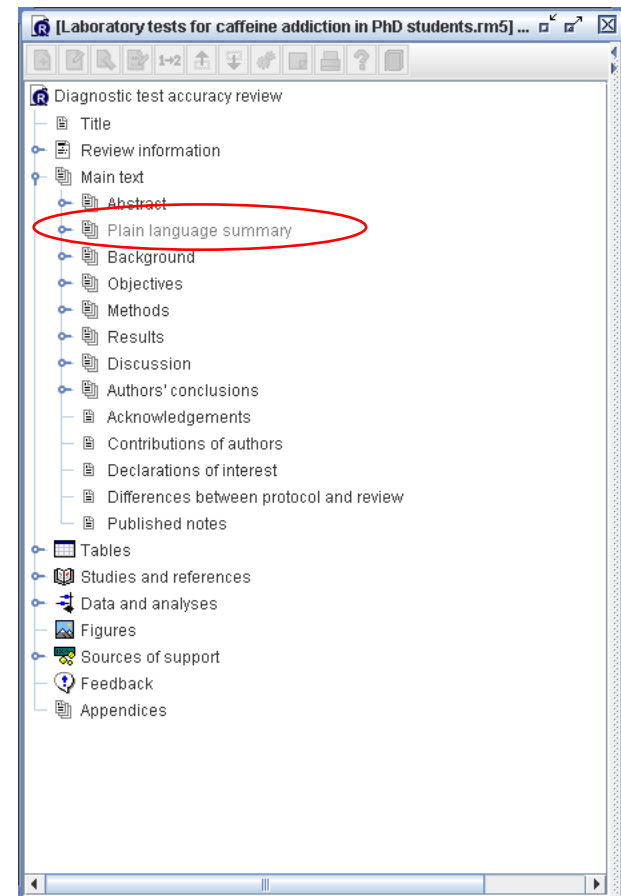
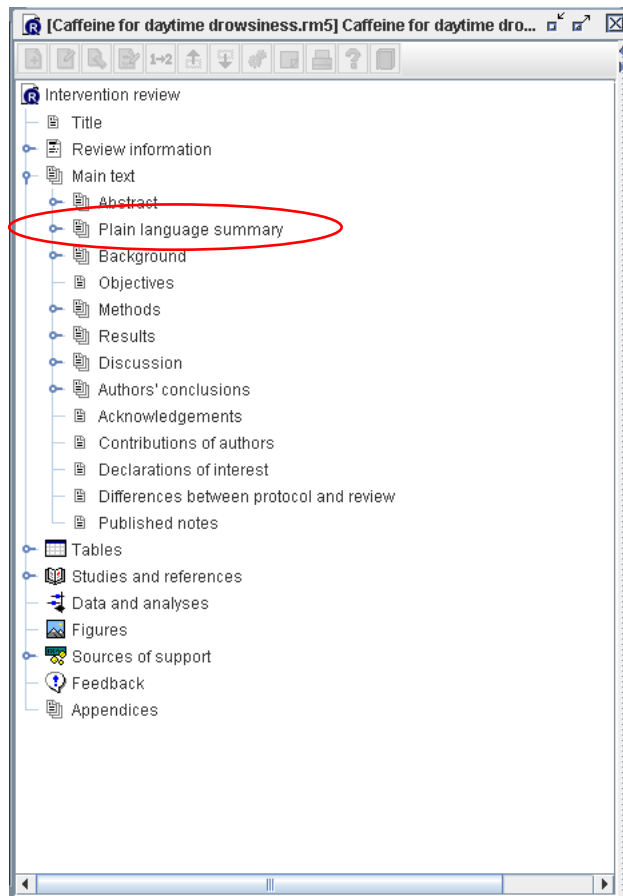
Last Citation Issue: Not specified

Intervention vs. Diagnostic

The screenshot shows the 'Text of Review' window for an intervention review. The title is 'Caffeine for daytime drowsiness'. The left sidebar lists sections: Intervention review, Title, Review information, Main text, Tables, Studies and references, Data and analyses, Figures, Sources of support, Feedback, and Appendices. The main content area shows the 'Review information' section, which includes an 'Authors' field with '[Empty name]¹' and '[Empty affiliation]', a 'Citation example' field with '[Empty name] daytime drowsiness. Cochrane Database of Systematic Reviews [Year]', an 'Add Author' button, and a 'Contact person' field with '[Empty name]'.

The screenshot shows the 'Text of Review' window for a diagnostic test accuracy review. The title is 'Laboratory tests for caffeine addiction in PhD students'. The left sidebar lists sections: Diagnostic test accuracy review, Title, Review information, Main text, Tables, Studies and references, Data and analyses, Figures, Sources of support, Feedback, and Appendices. The main content area shows the 'Review information' section, which includes an 'Authors' field with 'John Brown¹, Peter Smith¹, S...', '[Empty affiliation]', a 'Citation example' field with 'Brown J, Smith P. Laboratory tests for caffeine addiction in PhD students. Cochrane Database of Systematic Reviews [Year], Issue [Issue]', an 'Add Author' button, and a 'Contact person' field.

Intervention vs. Diagnostic



Titles intervention reviews

New Review Wizard

What is the title of the review?

Title:

- [Intervention] for [health problem]
- [Intervention A] versus [intervention B] for [health problem]
- [Intervention] for [health problem] in [participant group/location]
- [Use if title does not fit any of the formats above]

Cancel < Back Next > Finish

Titles DTA Reviews

New Review Wizard

What is the title of the review?

Title:

- [Index test(s)] versus [comparator(s)] for [target condition(s)] in [participant description]
- [Index test(s)] versus [comparator(s)] for [target condition(s)]
- [Index test(s)] for [target condition(s)] in [participant description]
- [Index test(s)] for [target condition(s)]

Cancel **< Back** **Next >** **Finish**

Example of title

New Review Wizard [Close]

New Review Wizard [Help] [Mobile]

What is the title of the review?

Title:

[Index test(s)] versus [comparator(s)] for [target condition(s)] in [participant description]

[Index test(s)] versus [comparator(s)] for [target condition(s)]

Clinical assessment for diagnosing congenital heart disease in new born infants with Down syndrome

[Index test(s)] for [target condition(s)]



Exercise: the right title format?

- Diagnostic accuracy of image-guided biopsy in indeterminate renal masses.
- Physical examination for lumbar radiculopathy due to disc herniation in patients with low-back pain.
- Cell-free fetal DNA for non-invasive prenatal diagnosis of sex.

Text of Review - Background

[Caffeine for daytime drowsiness.rm5] Caffeine for daytime drow...

- Intervention review
 - Title
 - Review information
 - Main text
 - Abstract
 - Plain language summary
 - Background
 - Description of the condition
 - Description of the intervention
 - How the intervention might work
 - Why it is important to do this review
 - Objectives
 - Methods
 - Results
 - Discussion
 - Authors' conclusions
 - Acknowledgements
 - Contributions of authors
 - Declarations of interest
 - Differences between protocol and review
 - Published notes
 - Tables
 - Studies and references
 - Data and analyses
 - Figures
 - Sources of support
 - Feedback
 - Appendices

[Laboratory tests for caffeine addiction in PhD students.rm5] ...

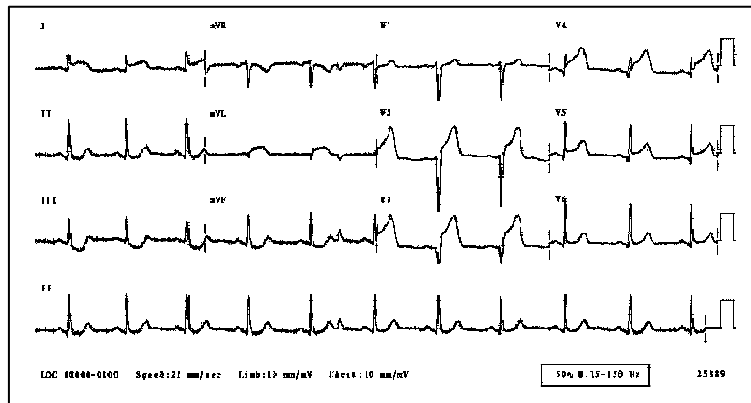
- Diagnostic test accuracy review
 - Title
 - Review information
 - Main text
 - Abstract
 - Plain language summary
 - Background
 - Target condition being diagnosed
 - Index test(s)
 - Alternative test(s)
 - Rationale
 - Objectives
 - Methods
 - Results
 - Discussion
 - Authors' conclusions
 - Acknowledgements
 - Contributions of authors
 - Declarations of interest
 - Differences between protocol and review
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Background

- Target condition being diagnosed
 - A description of the target condition of interest (frequency, severity, prognosis and possible treatments).
- Index test
 - A description of the index tests that are being evaluated in this review, including current use and intended roles
- Alternative test
 - Possible tests and strategies that are used in clinical practice, irrespective of whether they are evaluated in this review.
- Rationale

Example?



Text of Review

The screenshot displays the Review Manager 5 interface. The title bar reads "Review Manager 5". The menu bar includes "File", "Edit", "Format", "View", "Tools", "Table", "Window", and "Help". The toolbar contains various icons for file operations and editing. The main window title is "FDG PET versus CT for non-small cell lung cancer".

The left pane shows a tree view of the review structure. The "Main text" section is expanded, showing a list of sections: Abstract, Plain language summary, Background, Objectives, Methods, Results, Discussion, Authors' conclusions, Acknowledgements, Contributions of authors, Declarations of interest, Differences between protocol and review, and Published notes.

The right pane, titled "Text of Review", displays a list of sections with expandable icons. The sections are: Abstract, Plain language summary, Background, Target condition being diagnosed, Index test(s), Alternative test(s), Rationale, Objectives, Secondary objectives, Investigation of sources of heterogeneity, Methods, Criteria for considering studies for this review, and Types of studies. A red rectangular box highlights the "Objectives" section and its sub-items: "Secondary objectives", "Investigation of sources of heterogeneity", "Methods", "Criteria for considering studies for this review", and "Types of studies".

Objectives (example)

Clinical assessment for diagnosing congenital heart disease in newborn infants with Down syndrome

- Protocol for Cochrane Review of Diagnostic Test Accuracy -

William McGuire, Peter W Fowlie, and Johannes B Reitsma

OBJECTIVES

Primary objectives

The objective of this review is to assess the accuracy of clinical assessment in diagnosing congenital heart disease in newborn infants with Down syndrome and specifically to determine how well the absence of abnormal findings on clinical assessment rules out a diagnosis in newborn infants with Down syndrome.





Question formulation

Objective of a DTA SR can be

- To make comparisons between tests concerning their global accuracy
- To estimate the accuracy of a test operating at a particular threshold
- To understand why results of studies vary



Components of a question

- For intervention reviews
 - **P**atients
 - **I**ntervention
 - (**C**omparative intervention)
 - **O**utcome



Components of a question

- For diagnostic test accuracy reviews
 - **P**atients

 - **I**ndex test
 - (**C**omparator test)

 - **T**arget disorder



Components of a question

- For diagnostic test accuracy reviews
 - **P**atients
 - **P**resentation
 - **P**rior tests

 - **I**ndex test
 - (**C**omparator test)
 - **P**urpose

 - **T**arget disorder
 - **R**eference standard

Index and comparator tests

- The **index test** is the “new” test we wish to evaluate. A review may consider and compare several index tests.
- The **comparator test** is the alternative diagnostic management strategy which is standard practice and with which we would like to make comparisons





Target condition and reference standard

- Target disease is the condition we are trying to diagnose
- Reference standard is the best way available of identifying target condition
 - May comprise several pieces of information
 - May only be available subsequently

Methods

No RCTs!

- Methods
 - Criteria for considering studies for this review
 - Types of studies
 - Participants
 - Index tests
 - ✓ Comparator tests
 - Target conditions
 - Reference standards
 - Search methods for identification of studies
 - Electronic searches
 - ✓ Searching other resources
 - Data collection and analysis
 - Selection of studies
 - Data extraction and management
 - Assessment of methodological quality
 - Statistical analysis and data synthesis
 - ✓ Investigations of heterogeneity
 - ✓ Sensitivity analyses
 - ✓ Assessment of reporting bias

Intervention Reviews vs DTA Reviews

- Methods
 - Criteria for considering studies for this review
 - Search methods for identification of studies
 - Data collection and analysis
 - Selection of studies
 - Data extraction and management
 - Assessment of risk of bias in included studies
 - Measures of treatment effect
 - Unit of analysis issues
 - Dealing with missing data
 - Assessment of heterogeneity
 - Assessment of reporting biases
 - Data synthesis
 - Subgroup analysis and investigation of heterogeneity
 - Sensitivity analysis



Identification of studies

Problems in indexing of DTA studies

- No study design terms (MeSH: sensitivity-and-specificity)
- Diagnostic search filters based on terms used to report results
- Filters don't work (loss of relevant articles and not reducing NNR)

Search Strategy: include elements for

- target condition AND index test
- (more titles to screen)

Database of DTA studies is being developed in Sydney



Diagnostic Test Accuracy Reviews

- Question formulation
- Identification of studies
- Selection of relevant studies
- Quality assessment (later)
- Data-extraction
- Data analysis (later)
- Presentation and interpretation of results



[Caffeine for daytime drowsiness.rm5] Caffeine for day...

- Intervention review
 - Title
 - Review information
 - Main text
 - Abstract
 - Plain language summary
 - Background
 - Objectives
 - Methods
 - Results
 - Description of studies
 - Results of the search
 - Included studies
 - Excluded studies
 - Risk of bias in included studies
 - Allocation
 - Blinding
 - Incomplete outcome data
 - Selective reporting
 - Other potential sources of bias
 - Effects of interventions
 - Discussion
 - Authors' conclusions
 - Acknowledgements
 - Contributions of authors
 - Declarations of interest









[Galactomannan detection for invasive aspergillosis...] Galactomannan detection for invasive aspergillosis...

- Diagnostic test accuracy review
 - Title
 - Review information
 - Main text
 - Abstract
 - Plain language summary
 - Background
 - Objectives
 - Methods
 - Results
 - Results of the search
 - Methodological quality of included studies
 - Findings
 - Discussion
 - Authors' conclusions
 - Acknowledgements
 - Contributions of authors
 - Declarations of interest
 - Differences between protocol and review
 - Published notes
 - Tables
 - Studies and references
 - Data and analyses
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Tables





-  Tables
 -  Characteristics of studies
 -  Characteristics of included studies
 -  Characteristics of excluded studies
 -  Characteristics of studies awaiting classification
 -  Characteristics of ongoing studies
 -  Summary of results tables
 -  Additional tables

- Diagnostic test accuracy review
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Text of Review

Characteristics of studies
 Characteristics of included studies

Dorlas 2006

Clinical features and settings	Primary care; sleep deprivation, loss of concentration, hyperactivity.
Participants	405 Dutch PhD students; no further information provided
Study design	Cross-sectional design; single group with equal suspicion of caffeine addiction; consecutive enrollments; every student underwent all tests.
Target condition and reference standard(s)	Caffeine addiction, measured by coffee consumption in liters per day
Index and comparator tests	Index test is spectrometry; comparator is questionnaire.
Follow-up	Two weeks follow up
Notes	Three students withdrew; reasons not explained.

Assessment of methodological quality table

Item	Judgement	Description
Representative spectrum?	Unclear	No information provided
Acceptable reference standard?	Yes	Coffee consumption
Acceptable delay between tests?	Yes	During two weeks, coffee consumption is daily measured; after one week



- Diagnostic test accuracy review
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Assessment of methodological quality table

Item	Judgement	Description
Representative spectrum?	Unclear	No information provided
Acceptable reference standard?	Yes	Coffee consumption
Acceptable delay between tests?	Yes	During two weeks, coffee consumption is daily measured; after one week and after two weeks, serum is measured; after two weeks questionnaire .
Partial verification avoided?	Unclear	
Differential verification avoided?	Yes	
Incorporation avoided?	Yes	
Reference standard results blinded?	Unclear	
Index test results blinded?	Unclear	
Relevant clinical information?	No	
Uninterpretable results reported?	Yes	
Withdrawals explained?	No	

Egberts 2001

Clinical features and settings



Quality assessment: diagnosis

- Relation between quality items and bias is not as straightforward as it is for interventions
- Many more items: 11 mandatory and >10 facultative (QUADAS)
- Methodological Quality Table
 - “Risk of Bias Table”

Assessment of methodological quality

The screenshot shows a software dialog box titled "Characteristics of Included Studies Properties". It has two tabs: "General" and "Assessment of methodological quality tables". The "Assessment of methodological quality tables" tab is active. On the left, a list of 11 items is shown, all with checked boxes: "Representative spectrum?", "Acceptable reference standard?", "Acceptable delay between tests?", "Partial verification avoided?", "Differential verification avoided?", "Incorporation avoided?", "Reference standard results blinded?", "Index test results blinded?", "Relevant clinical information?", "Uninterpretable results reported?", and "Withdrawals explained?". The main area on the right is for editing a specific item. It is checked as "Activated". The "Item:" field contains "Representative spectrum?". The "Full Question:" field contains "Was the spectrum of patients representative of the patients who will receive the test in practice?". The "Level:" dropdown menu is set to "Test level". Below this, there are two tables. The first table, titled "Groups", has a header "Test Group" and one row with the text "All tests". To the right of this table are "Add" and "Delete" buttons. The second table, titled "Test", has a header "Test" and two rows: "1 Spectrometry" and "2 Short Questionnaire". Each row in this table has a checkbox on the left. At the bottom of the dialog, there are "Add" and "Delete" buttons on the left, and "OK" and "Cancel" buttons on the right. A help icon (?) and a folder icon are also visible in the bottom-left corner.

Characteristics of Included Studies Properties

Assessment of methodological quality tables

- Representative spectrum?
- Acceptable reference standard?
- Acceptable delay between tests?
- Partial verification avoided?
- Differential verification avoided?
- Incorporation avoided?
- Reference standard results blinded?
- Index test results blinded?
- Relevant clinical information?
- Uninterpretable results reported?
- Withdrawals explained?

Activated

Item: Representative spectrum?

Full Question: Was the spectrum of patients representative of the patients who will receive the test in practice?

Level: Test level

Groups	
Test Group	
All tests	

Add **Delete**

Test	
<input type="checkbox"/>	1 Spectrometry
<input type="checkbox"/>	2 Short Questionnaire

Add **Delete** **OK** **Cancel**

- Plain language summary
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Text of Review

Differential verification avoided?	No	
Incorporation avoided?	No	
Reference standard results blinded?	No	

Footnotes

New Figure Wizard

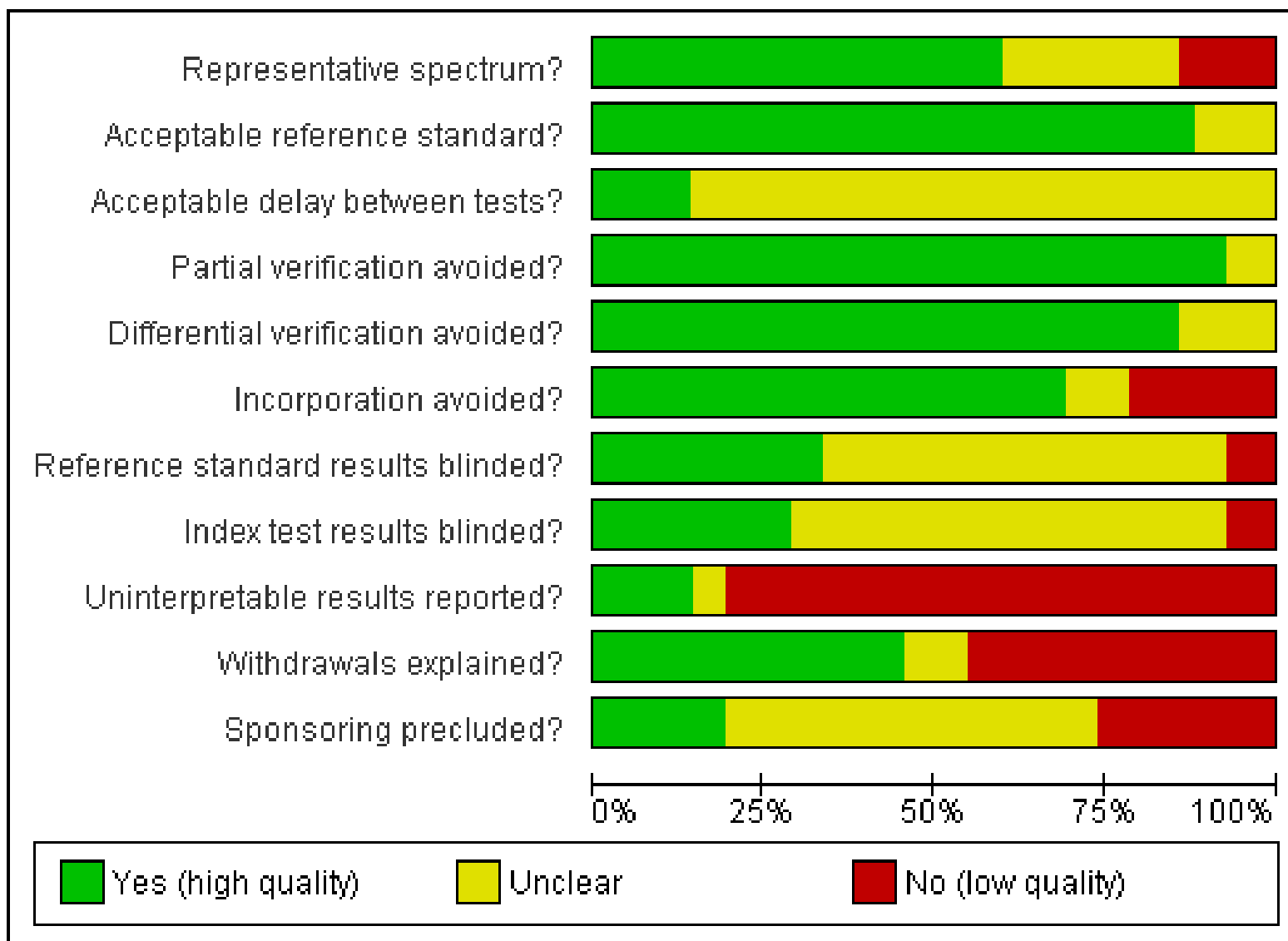
Which type of figure do you want to create?

Figure Type:

- Forest plot
- SROC plot
- Methodological quality graph**
- Methodological quality summary
- Other figure

A cumulative barplot of methodological quality items across all studies.

Cancel < Back Next > Finish



- Contributions of authors
- Declarations of interest
- Differences between protocol and published notes
- Published notes
- Tables
 - Characteristics of studies
 - Characteristics of included studies
 - Characteristics of excluded studies
 - Characteristics of studies awaiting evaluation
 - Characteristics of ongoing studies
 - Summary of results tables
 - Additional tables
- Studies and references
- Data and analyses
- Figures
 - Figure 1
 - Figure 2
 - Figure 3
 - Figure 4 (Analysis 1)
 - Figure 5 (Analysis 1)
 - Figure 6 (Analysis 6)
 - Figure 7 (Analysis 3)
 - Figure 8 (Analysis 4)
 - Figure 9 (Analysis 5)
 - Figure 10
 - Figure 11 (Analysis 8)

Text of Review **Figure 3**

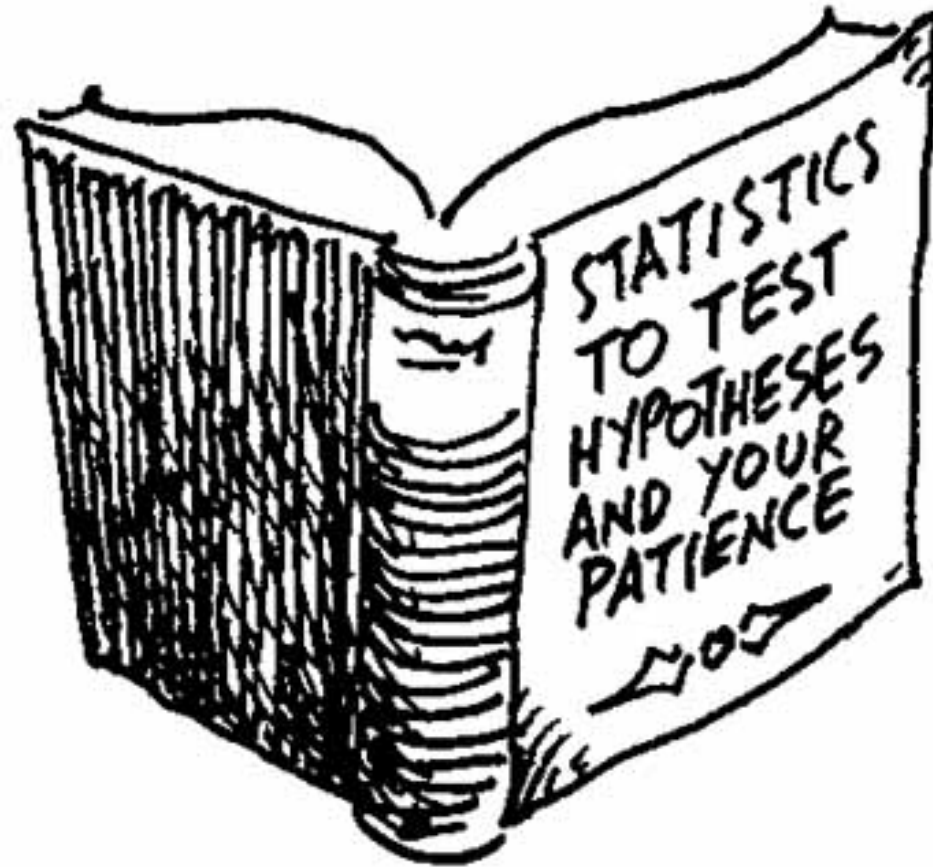
This figure is updated dynamically when the data change.

	Representative spectrum?	Acceptable reference standard?	Acceptable delay between tests?	Partial verification avoided?	Differential verification avoided?	Incorporation avoided?	Reference standard results blinded?	Index test results blinded?	Uninterpretable results reported?	Withdrawals explained?	Sponsoring precluded?
Adam 2004	+	+	?	+	+	?	?	?	-	+	?
Allan 2005	+	+	?	+	+	+	+	?	-	-	-
Becker 2003	+	+	?	+	+	+	+	+	+	+	?
Bialek 2002	?	+	?	+	?	+	+	+	?	-	+
Bretagne 1997	+	+	?	+	+	+	?	?	-	-	-
Bretagne 1998	?	+	?	+	?	+	?	?	-	-	?
Buchheidt 2004	?	+	?	+	+	-	?	?	-	-	+
Busca 2006	+	+	?	+	+	+	?	?	-	+	?
Challier 2004	-	+	?	+	+	-	?	?	-	-	?

Caption: Figure 3

Methodological quality summary: Review authors' judgments about each methodological quality item for each included study.

Data and analyses





[Caffeine for daytime drowsiness.rm5] Caffeine for daytime drow...

- Intervention review
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[Laboratory tests for caffeine addiction in PhD students.rm5] ...

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Data and Analysis

In diagnostics, less straightforward than RCT:

- Additional challenges are:
 - Pairs of sensitivity and specificity
 - Cut-off problems
 - Heterogeneity is rule rather than exception

NB: Apart from sources of heterogeneity known from the therapeutic field, we have to deal with the many different research designs used



- Diagnostic test accuracy review
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 - Data tables by test
 - 1 Spectrometry
 - 2 Short Questionnaire
 - Data tables by study
 - Dorlas 2006
 - Egberts 2001
 - Gunnink 2003
 - Havelaar 2005
 - Kanis 2007
 - Levelt 2007
 - Smit 2006
 - Van Nelle 1999
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Data and analyses

Data tables by test

Test	Studies	Participants
1 Spectrometry	5	1618
2 Short Questionnaire	5	1141

Figures

Sources of support

- Internal sources
 - No sources of support provided
- External sources
 - No sources of support provided

Feedback



- Abstract
- Plain language summary
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- Published notes
- Tables
- Studies and references
 - References to studies
 - Included studies
 - Excluded studies
 - Studies awaiting classification
 - Ongoing studies
 - Other references
- Data and analyses
 - Data tables
 - 1 Spectrometry
 - Covariates
 - Analyses
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- Sources of funding
- Feedback

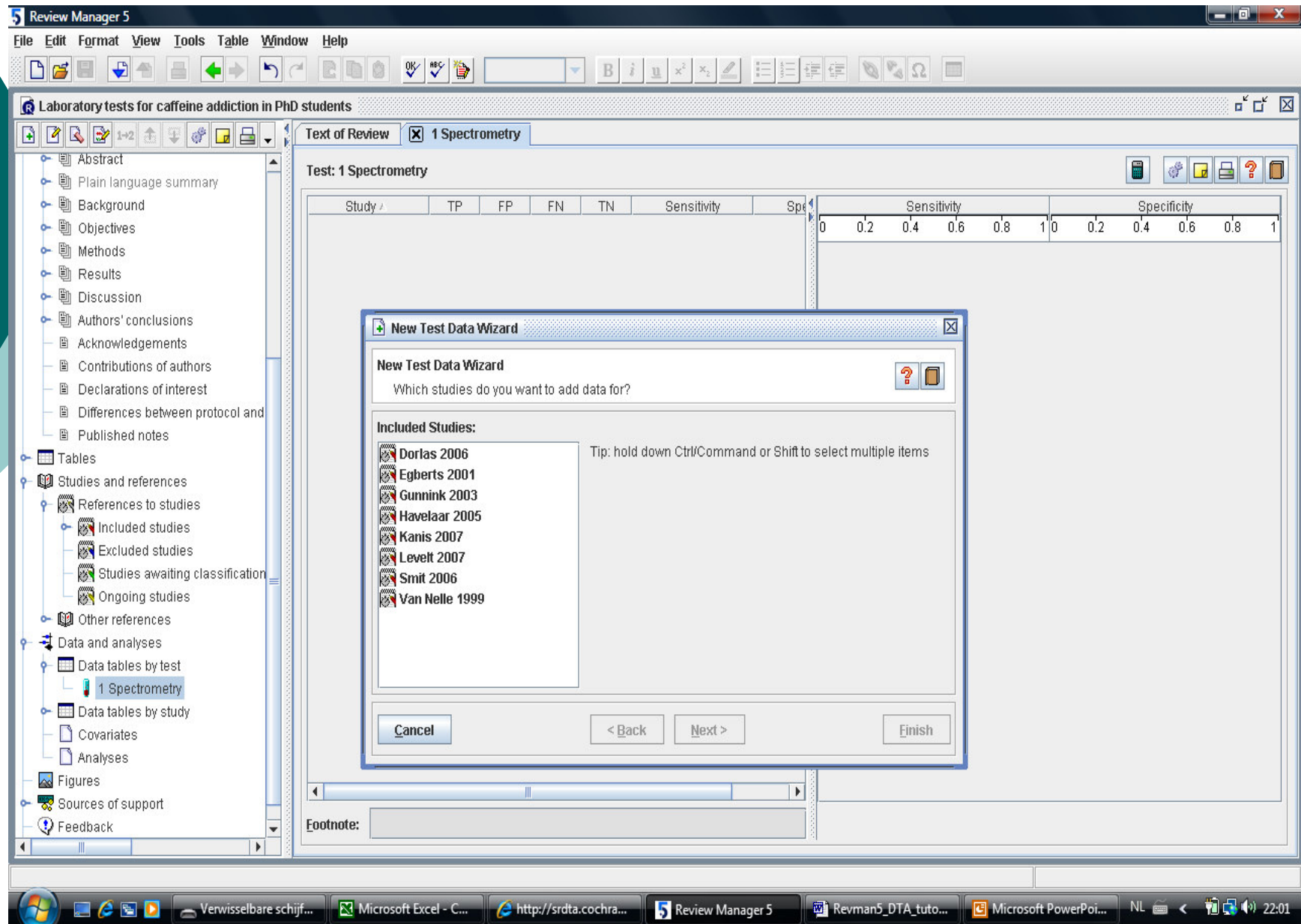
Text of Review 1 Spectrometry

Test: 1 Spectrometry

Study	TP	FP	FN	TN	Sensitivity	Sp	Sensitivity	Specificity
							0 0.2 0.4 0.6 0.8 1.0	0 0.2 0.4 0.6 0.8 1.0

Footnote:

- Add Test Data
- Edit Test
- Delete Test
- Rename Test
- Move Up
- Move Down
- Properties...
- Notes...
- Print...
- Help
- Handbook



Review Manager 5

File Edit Format View Tools Table Window Help

Laboratory tests for caffeine addiction in PhD students

Text of Review 1 Spectrometry

Test: 1 Spectrometry

Study	TP	FP	FN	TN	Sensitivity	Sp
Egberts 2001	0	0	0	0	Not estimable	N
Gunnink 2003	0	0	0	0	Not estimable	N
Havelaar 2005	0	0	0	0	Not estimable	N
Kanis 2007	0	0	0	0	Not estimable	N
Van Nelle 1999	0	0	0	0	Not estimable	N

Sensitivity

Specificity

Footnote:

Verwisselbare schijf... Microsoft Excel - C... http://srda.cochra... Review Manager 5 Revman5_DTA_tuto... Microsoft PowerPoi... NL 22:02

Review Manager 5

File Edit Format View Tools Table Window Help

Laboratory tests for caffeine addiction in PhD students

Text of Review 1 Spectrometry

Test: 1 Spectrometry

Study	TP	FP	FN	TN	Sensitivity	Sp
Egberts 2001	0	0	0	0	Not estimable	N
Gunnink 2003	0	0	0	0	Not estimable	N
Havelaar 2005	0	0	0	0	Not estimable	N
Kanis 2007	0	0	0	0	Not estimable	N
Van Nelle 1999	0	0	0	0	Not estimable	N

Calculator

Reference standard						
	+	-	Total			
Index test	+	TP 18	FP	Test+	Sensitivity 0.36	Specificity 0.92
	-	FN 32	TN	Test-	PPV	NPV
Total	D+	50	D-	N	LR+	LR-
					4.5000	0.6957

Reset OK Cancel

Footnote:

Verwisselbare schijf... Microsoft Excel - C... http://srda.cochra... Review Manager 5 Revman5_DTA_tuto... Microsoft PowerPoi... NL 22:05

Review Manager 5

File Edit Format View Tools Table Window Help

Laboratory tests for caffeine addiction in PhD students

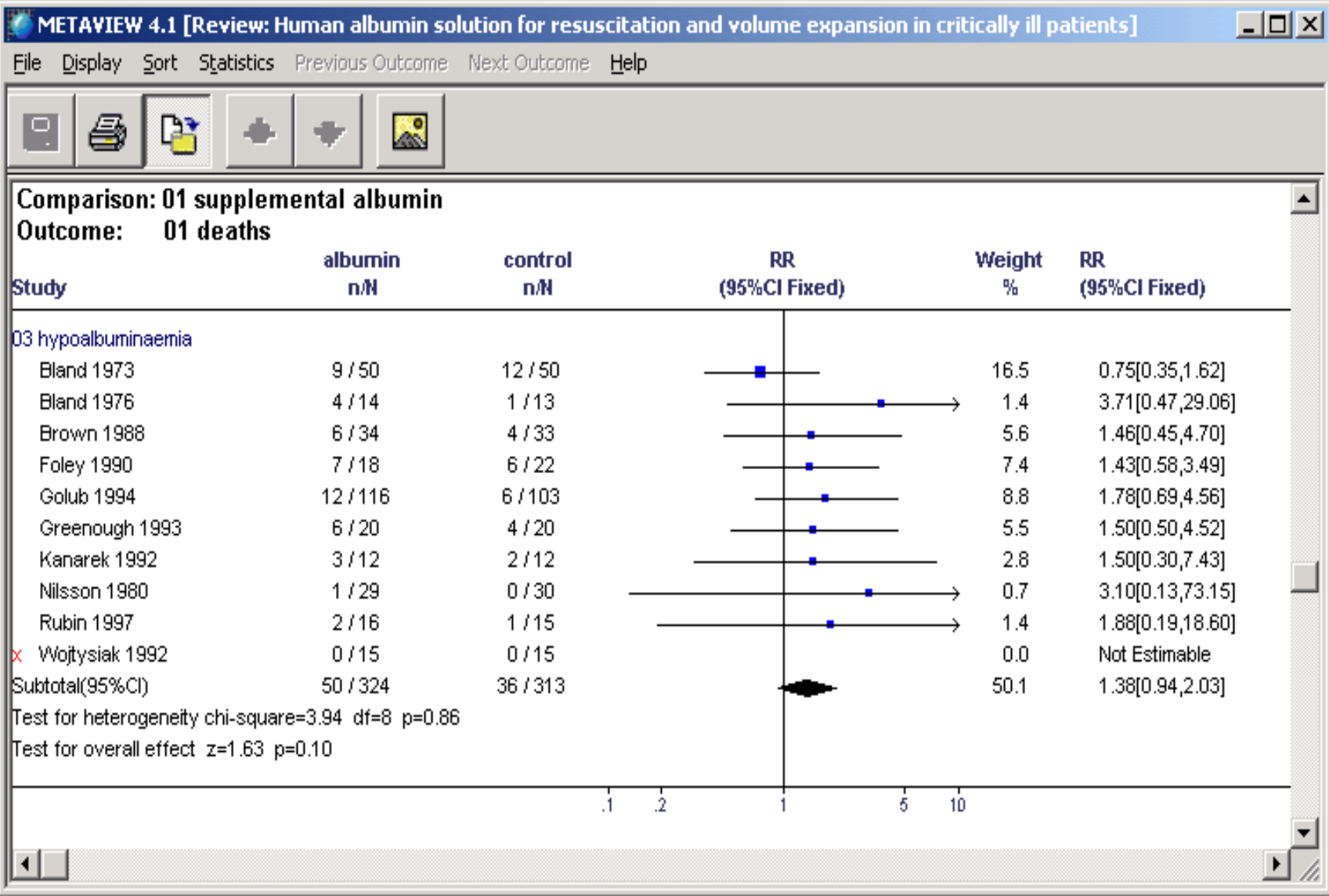
Text of Review 1 Spectrometry

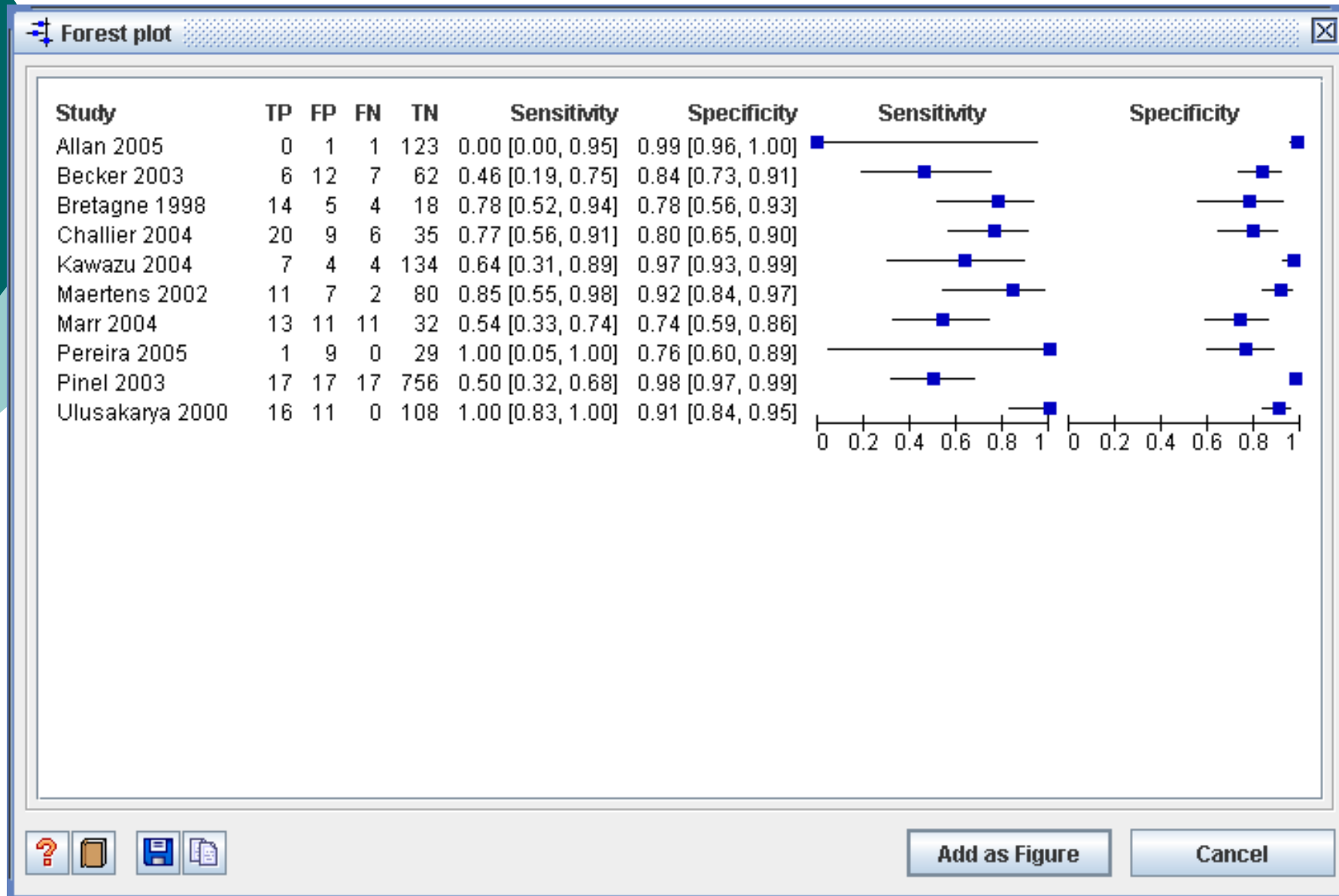
Test: 1 Spectrometry

Study	TP	FP	FN	TN	Sensitivity	Specificity
Egberts 2001	189	15	66	67	0.74 [0.68, 0.79]	0.82 [0.72, 0.89]
Gunnink 2003	23	4	1	9	0.96 [0.79, 1.00]	0.69 [0.39, 0.91]
Havelaar 2005	0	0	0	0	Not estimable	Not estimable
Kanis 2007	0	0	0	0	Not estimable	Not estimable
Van Nelle 1999	18	8	32	92	0.36 [0.23, 0.51]	0.92 [0.85, 0.96]

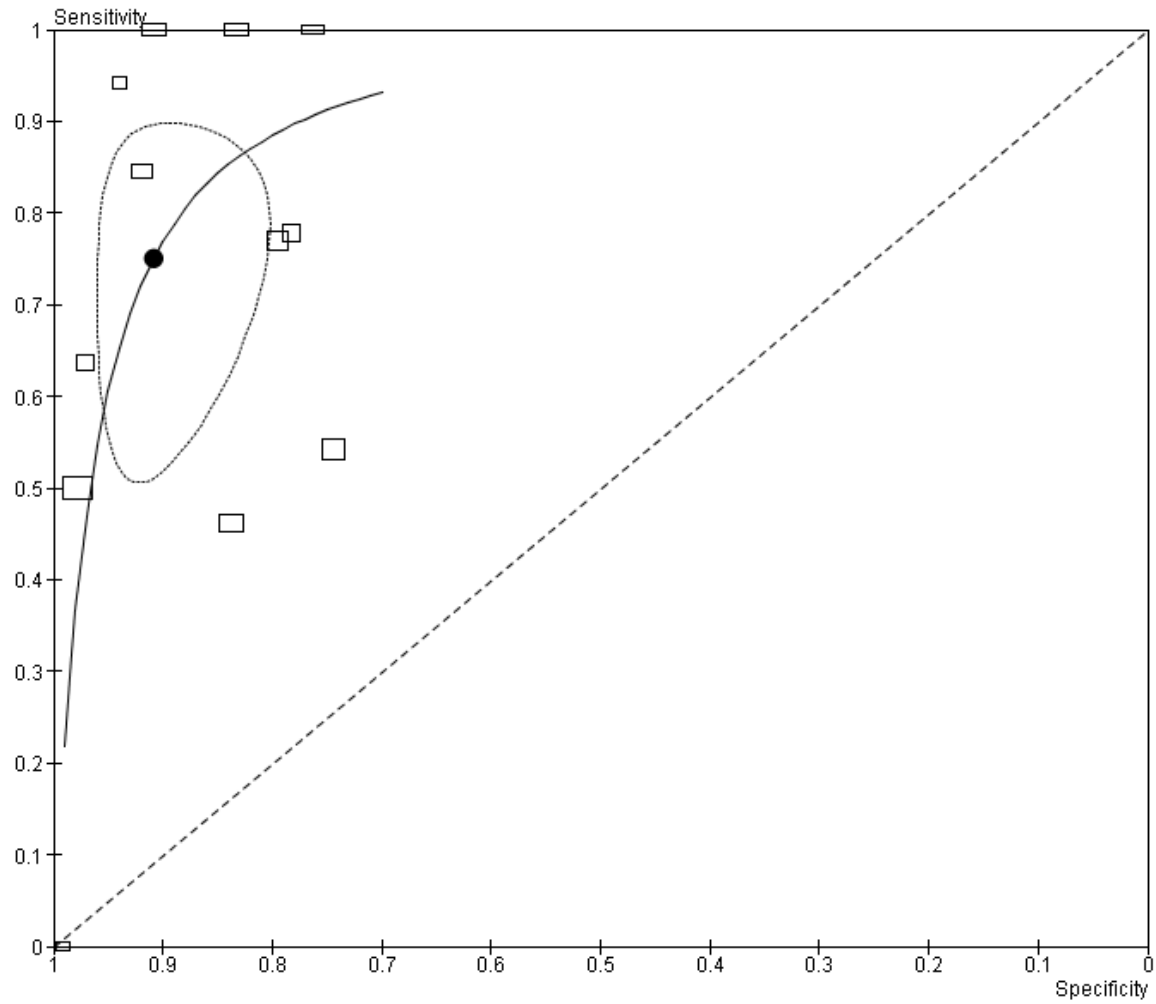
Footnote:

Verwisselbare schijf... Microsoft Excel - C... http://srda.cochra... Review Manager 5 Revman5_DTA_tuto... Microsoft PowerPoi... NL 22:10





ROC Plot



Parameters from external software

Externally Calculated Parameters

HSROC model parameters

Parameter	Estimate
Lambda	
Theta	
beta	
Var(accuracy)	
Var(threshold)	

Bivariate model parameters

Parameter	Estimate
E(logitSe)	1.1005
E(logitSp)	2.2949
Var(logitSe)	0.9851
Var(logitSp)	0.9203
Cov(logits)	0.2679

Confidence and prediction regions

Parameter	Estimate
SE(E(logitSe))	0.3758
SE(E(logitSp))	0.3133
Cov(Es)	-0.02231
Studies	12

Display summary curve

Display summary point

Display 95% confidence region

Display 95% prediction region

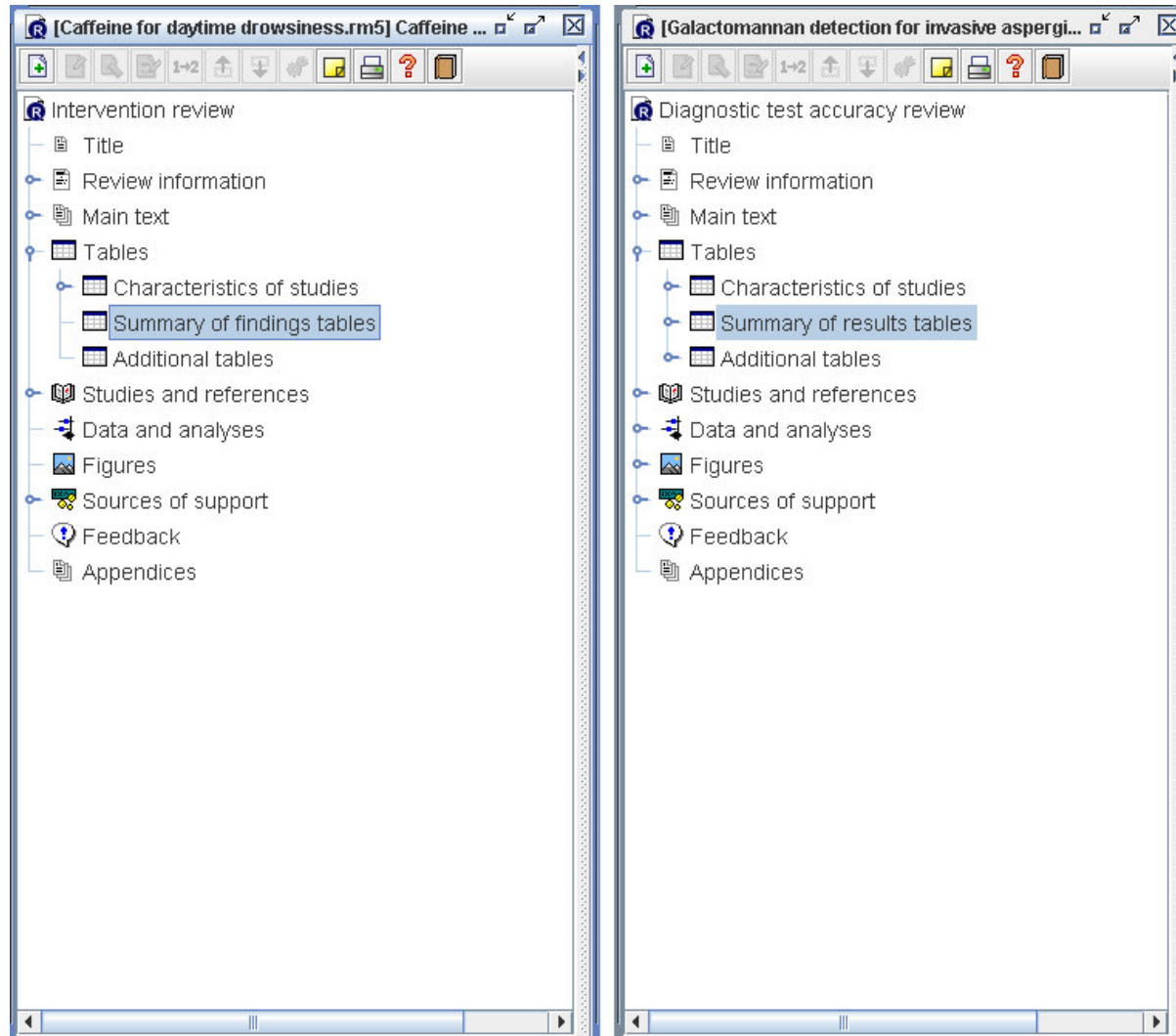


When all the results are analyzed...

... then we can build the Summary of Results Table

- What are the results of our search, inclusion and quality assessment?
- What are the results of our meta-analysis?
- How sure are we about these results?

SoF versus SoR





SoF versus SoR

Intervention reviews

- Format for SoF table is clear and predefined
- You can use GRADE software to build SoF table

DTA reviews

- There is no predefined format
- Authors are explicitly invited to be creative
- There is no existing software to help you



[Caffeine for daytime drowsiness.rm5] Caffeine for daytime drow...

- Intervention review
 - Title
 - Review information
 - Main text
 - Abstract
 - Plain language summary
 - Background
 - Objectives
 - Methods
 - Results
 - Discussion
 - Summary of main results
 - Overall completeness and applicability of evidence
 - Quality of the evidence
 - Potential biases in the review process
 - Agreements and disagreements with other studies or reviews
 - Authors' conclusions
 - Acknowledgements
 - Contributions of authors
 - Declarations of interest
 - Differences between protocol and review
 - Published notes
 - Tables
 - Studies and references
 - Data and analyses
 - Figures
 - Sources of support
 - Feedback
 - Appendices

[Laboratory tests for caffeine addiction in PhD students.rm5] ...

- Diagnostic test accuracy review
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 - Methods
 - Results
 - Discussion
 - Summary of main results
 - Strengths and weaknesses of the review
 - Applicability of findings to clinical practice and policy
 - Authors' conclusions
 - Acknowledgements
 - Contributions of authors
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Summary

- No Plain Language Summary
- Methodological Quality (not RoB)
- Summary of Results (not SoF)
- Differences in background
- Differences in methods: see upcoming presentations