HOW TO AVOID LOW QUALITY STUDIES

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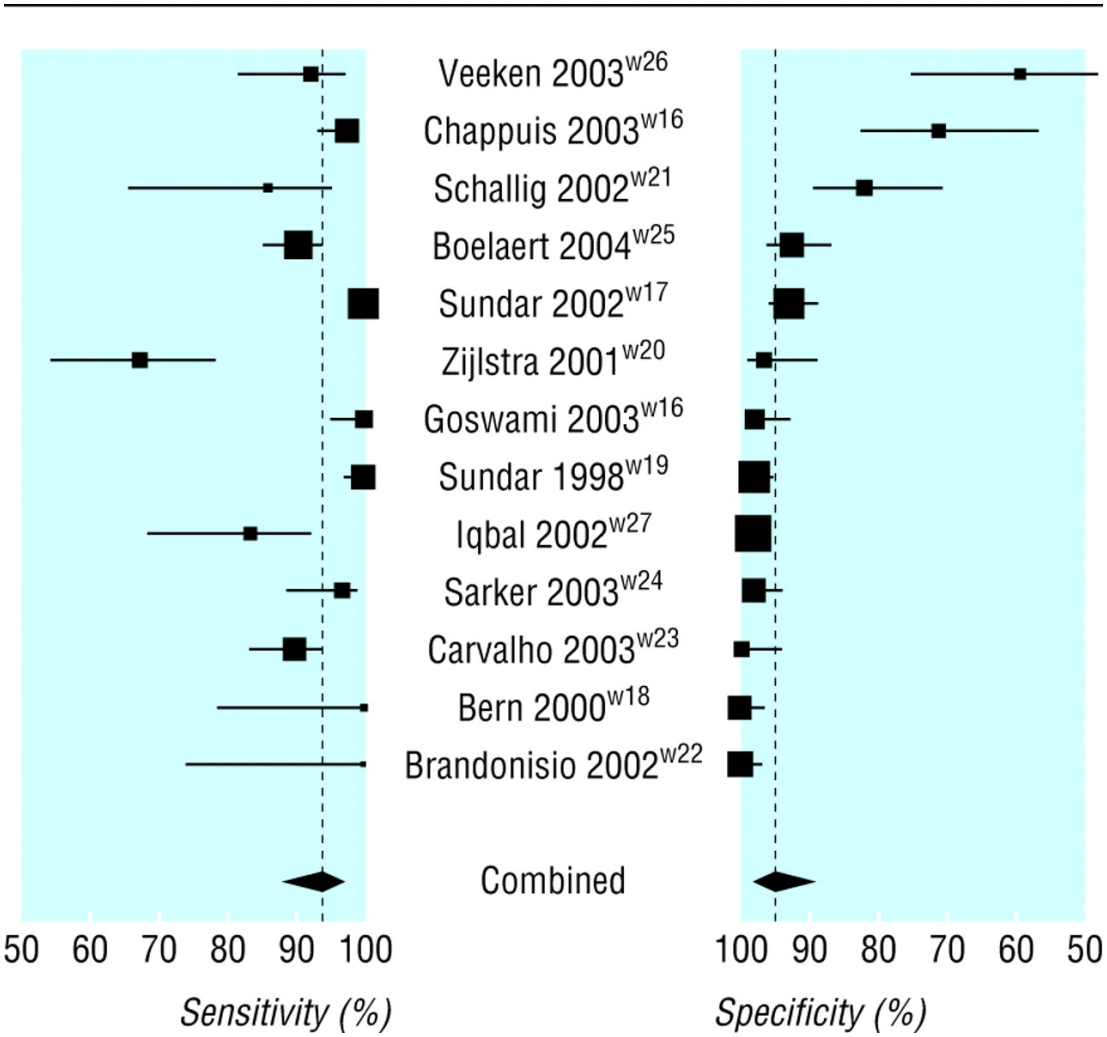
Outline

1. What is quality?
2. Finding your way
3. Tools
4. Practical application

What is quality?

- There's no such thing as the perfect study.
- As a user/buyer/patient/… I want to have confidence in the estimated value of a test.
- Problems in design, conduct and reporting
  - ➔ bias
  - ➔ differences between findings
- Support interpretation results systematic review

Estimates of sensitivity and specificity (95% confidence intervals) of rK39 dipstick.



Chappuis F et al. BMJ 2006;333:723

Bias

- Systematic error or deviation from the truth
  - Design or execution of the study
  - Recruiting wrong participants
  - Using wrong test
  - Using test wrongly

Design or execution of the study → Internal validity

Recruiting wrong participants, Using wrong test, Using test wrongly → External validity

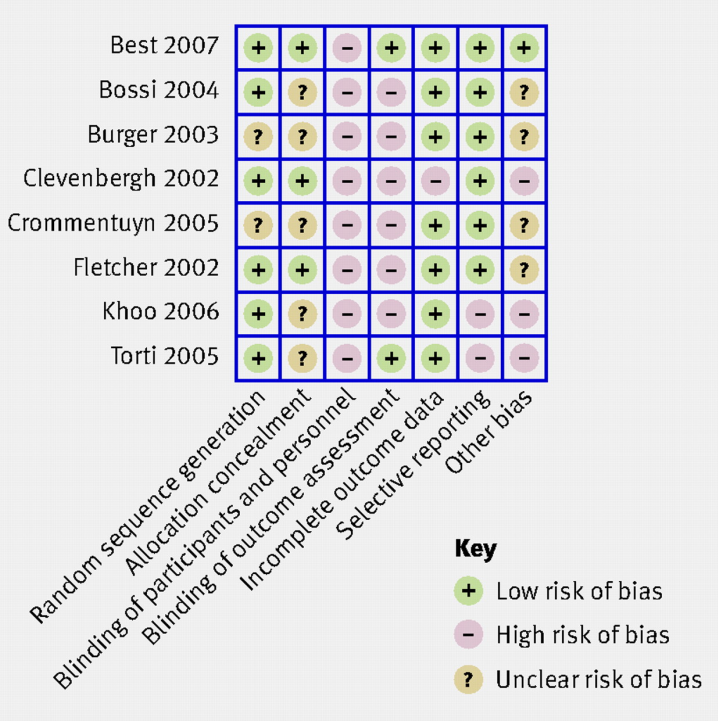
- Overestimates or underestimates of true accuracy
  - Certain?
  - Direction?
  - Magnitude?

RISK OF BIAS

Study design specific

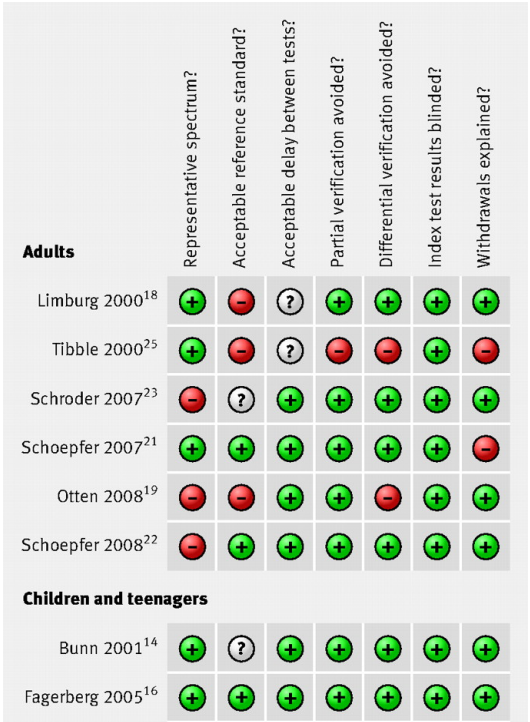
Randomised controlled trial

Risk of bias tool



Diagnostic accuracy study

QUADAS



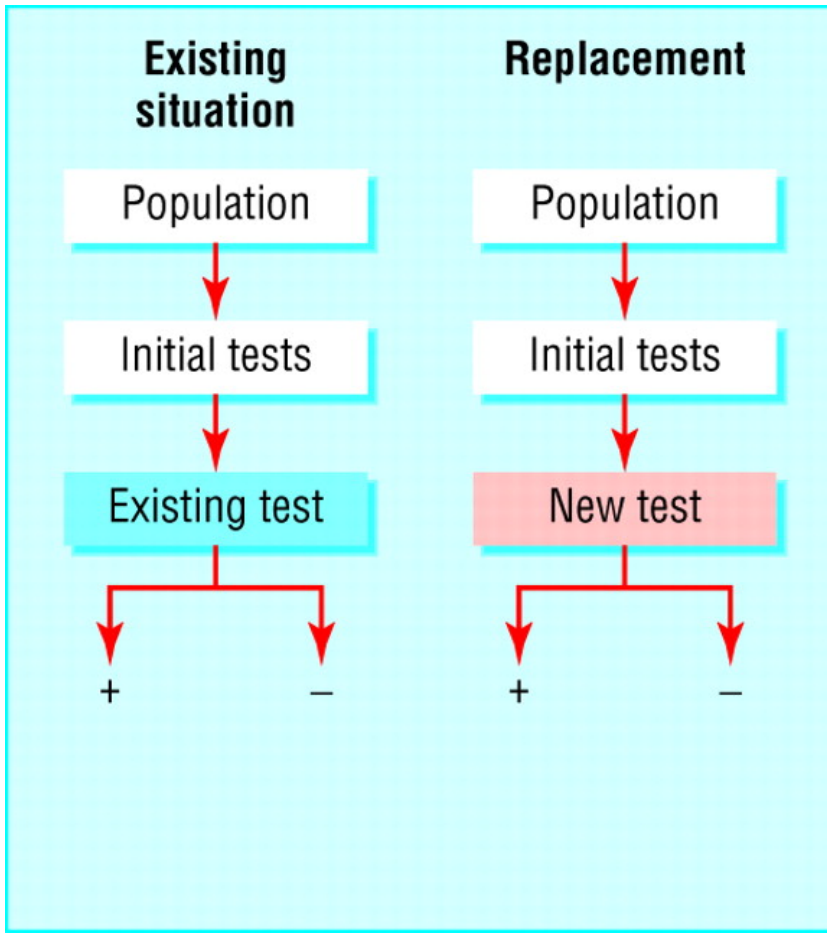
Cochrane handbook SRDTA

- Systematic reviews diagnostic test accuracy
- Assessment methodological quality
  - Bias
  - Relevance to review objective
  - Cause variation in findings

External validity

- Estimates may differ between populations
- Various applications of test
  - Intended role: triage – replacement – add-on

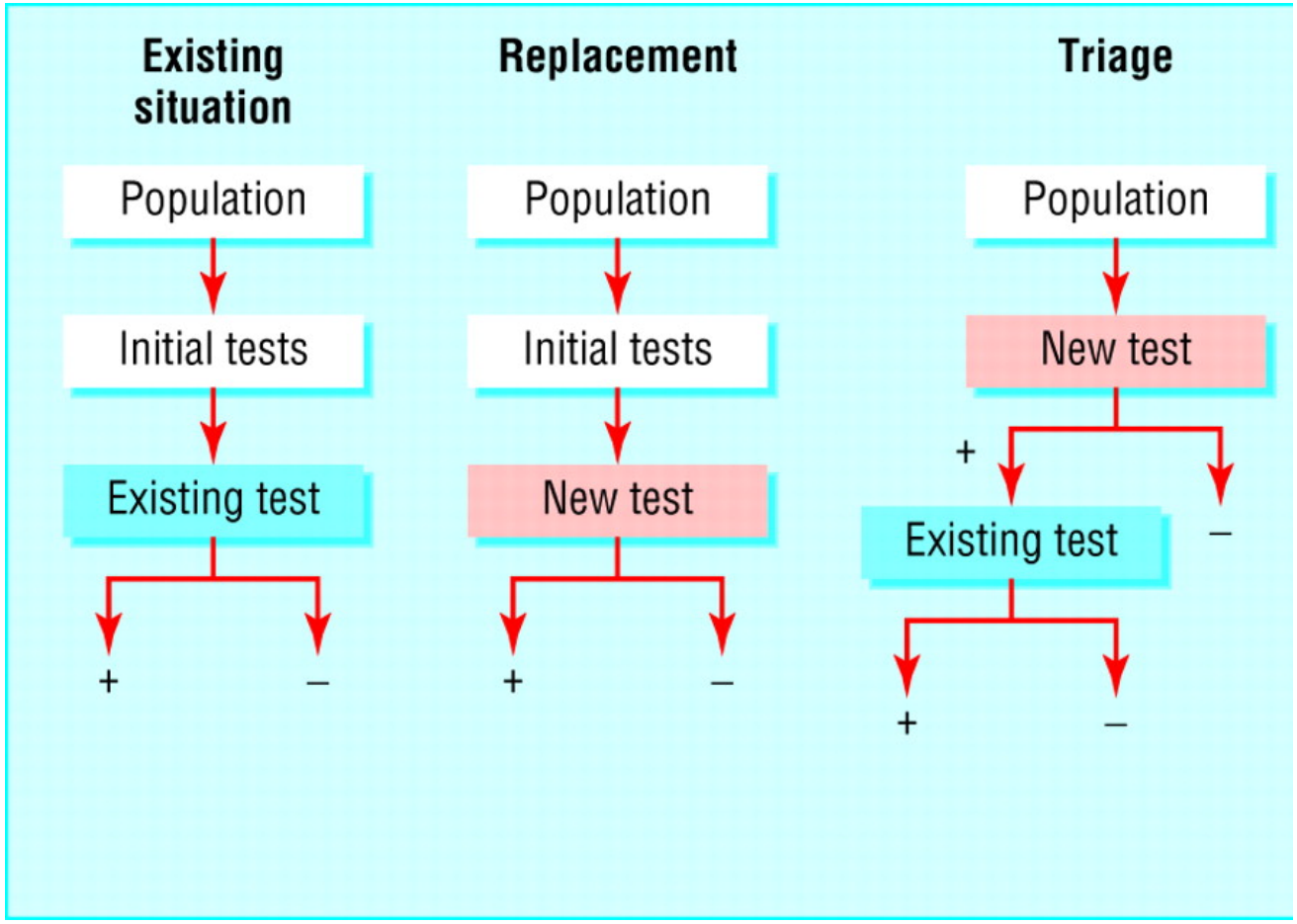
Intended role of tests



Bossuyt, P. M et al. BMJ 2006;332:1089-1092

BMJ

Intended role of tests



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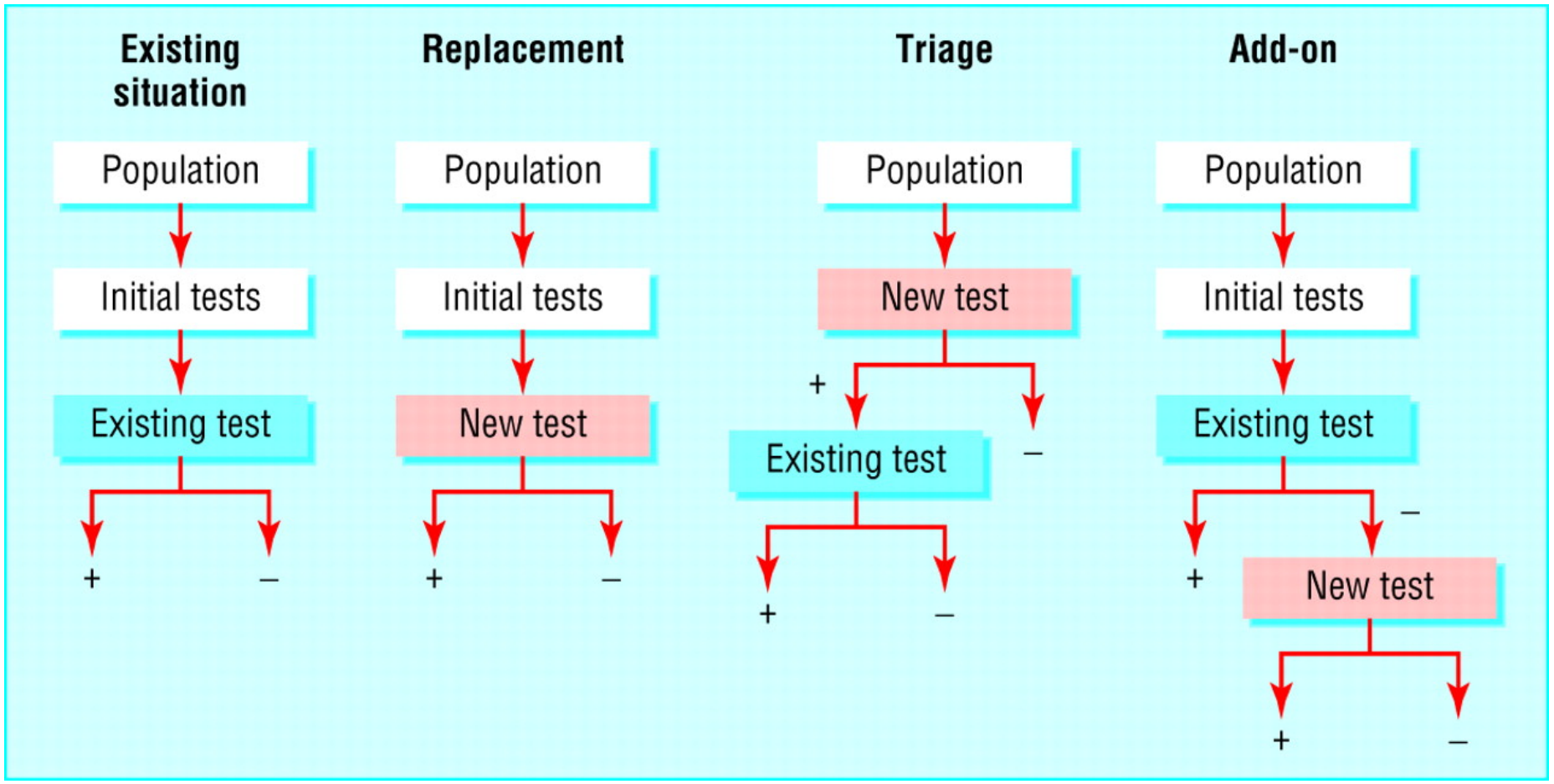
BMJ

Intended role of tests



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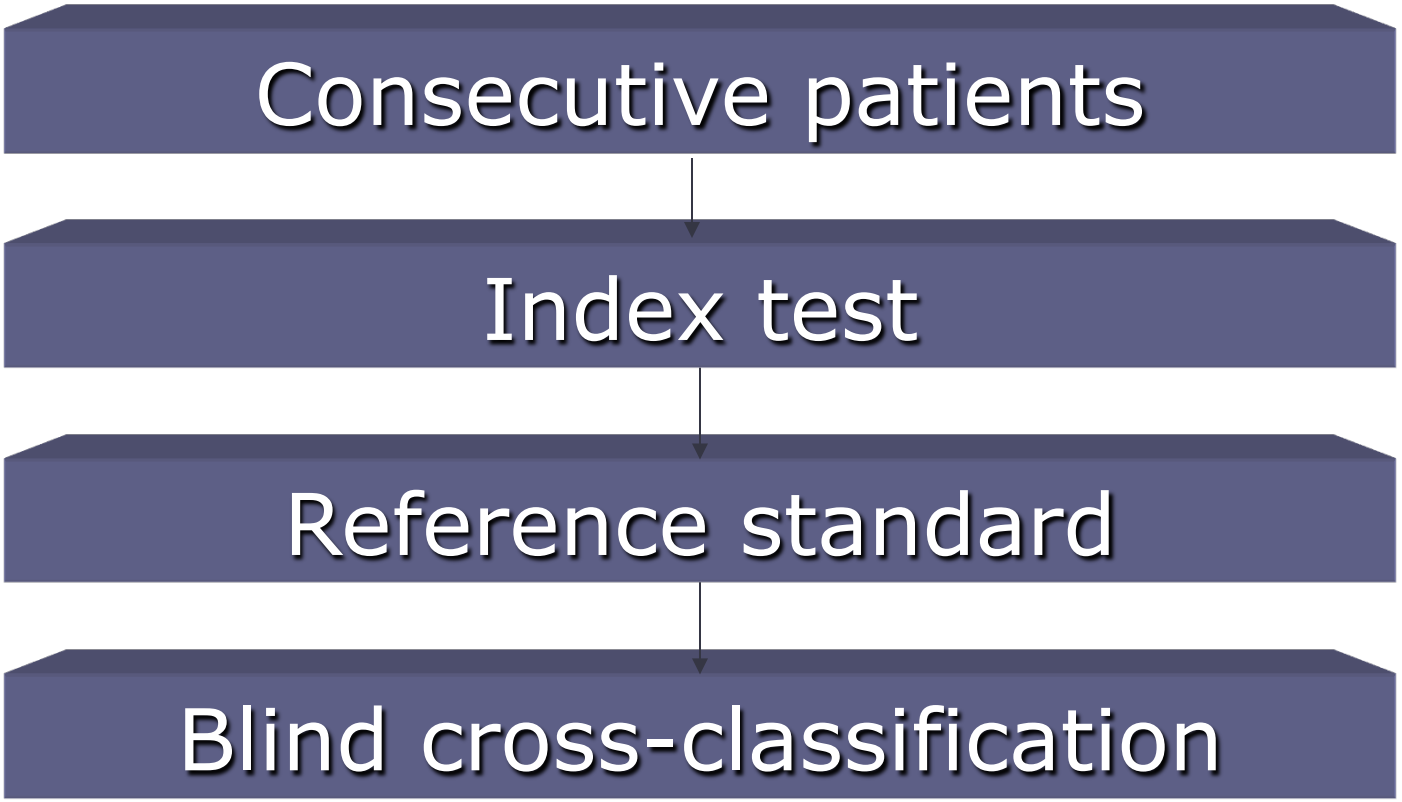
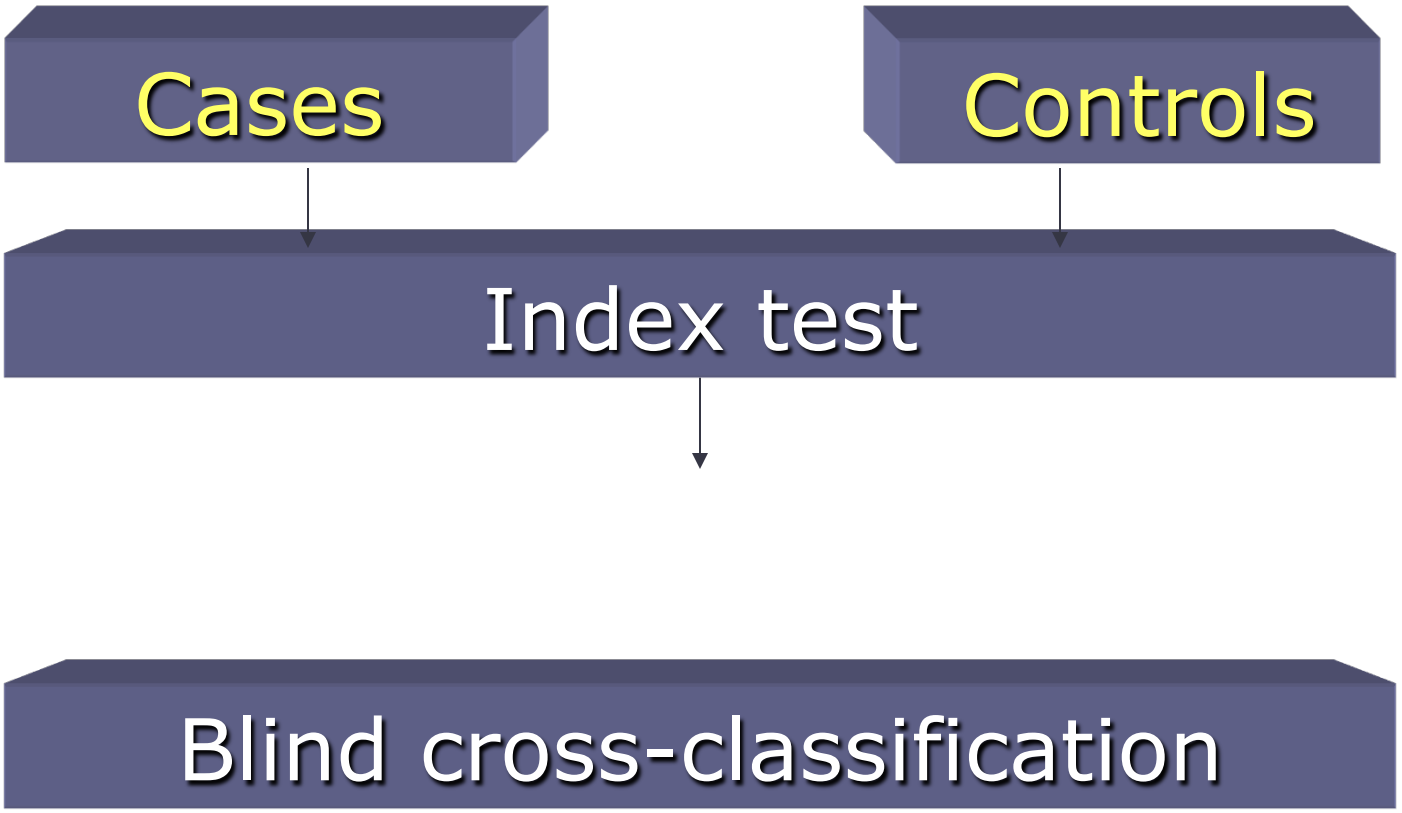
BMJ

Diagnostic Accuracy Study: Basic Design



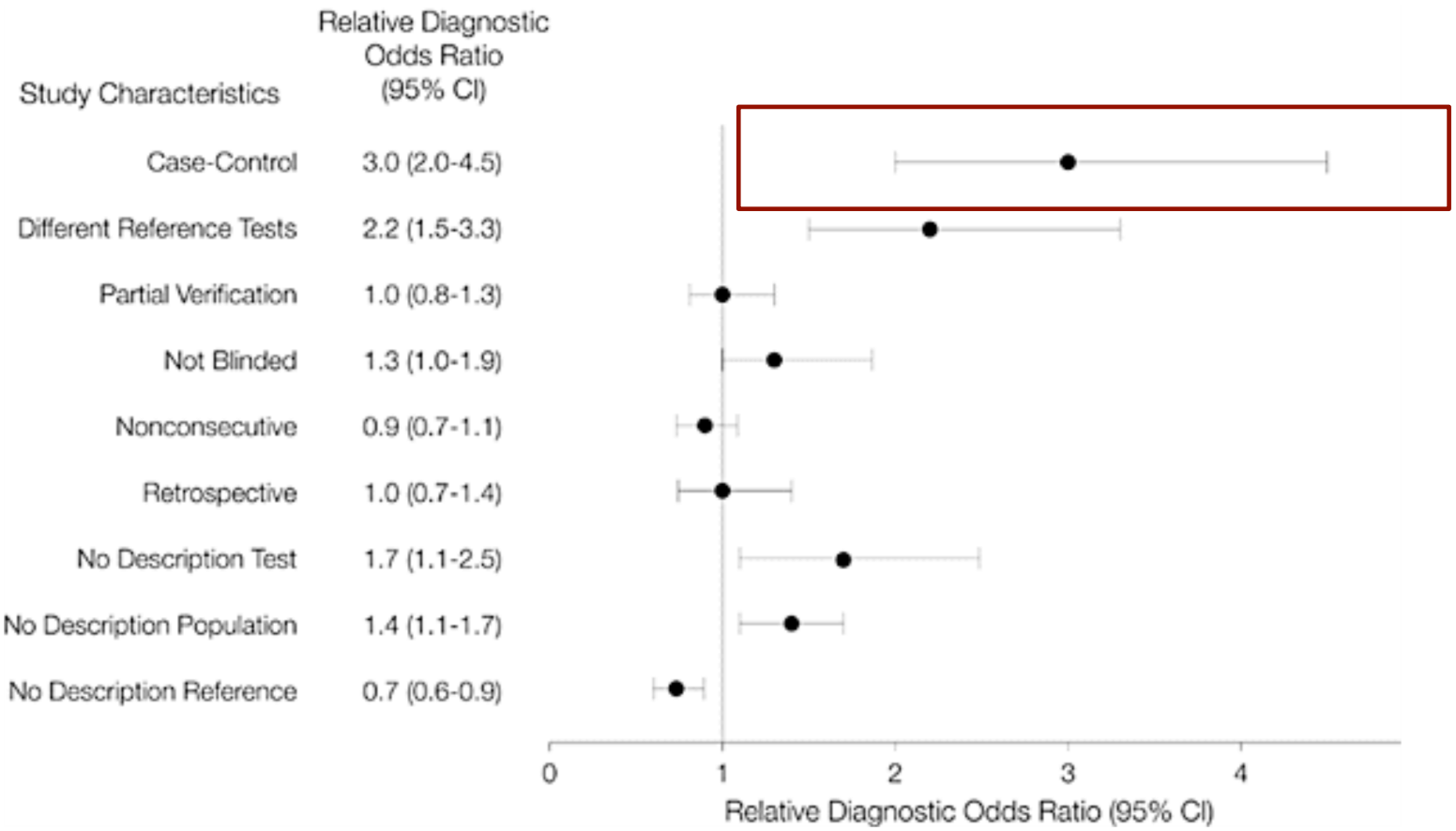
“Case-control” design



Case-control vs consecutive

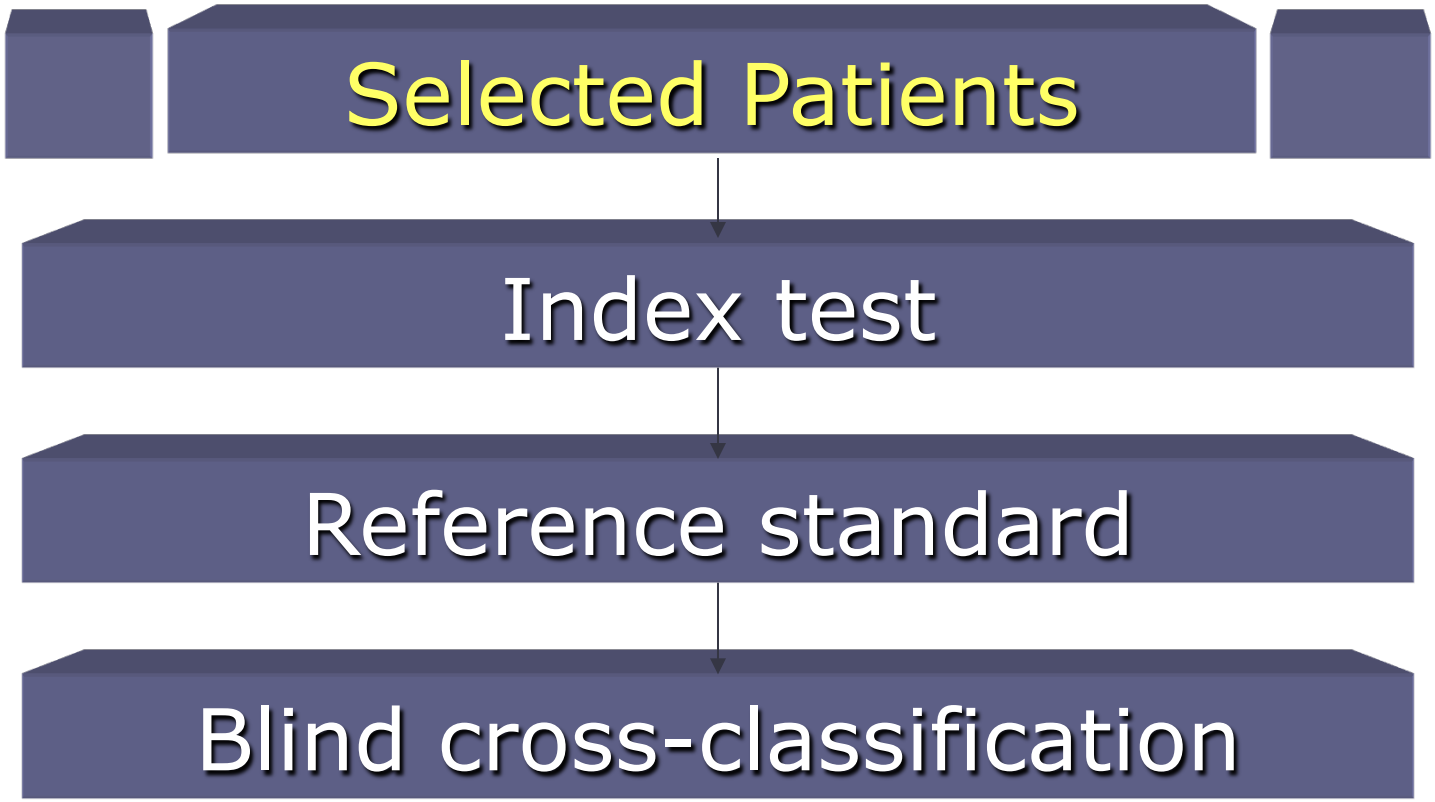
From: **Empirical Evidence of Design-Related Bias in Studies of Diagnostic Tests**

JAMA. 1999;282(11):1061-1066. doi:10.1001/jama.282.11.1061



Spectrum Bias

Can you think of a situation where spectrum bias would be likely?



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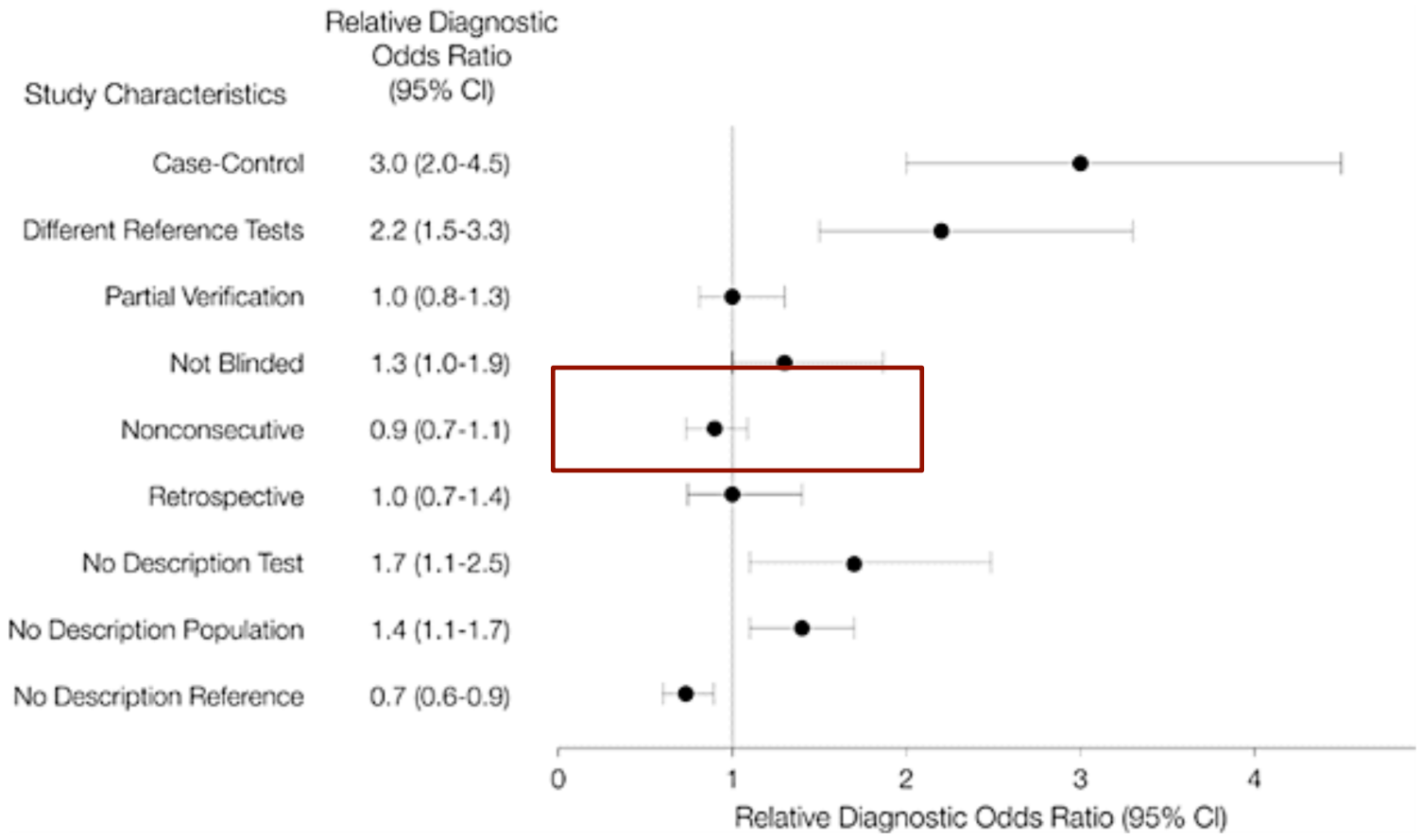
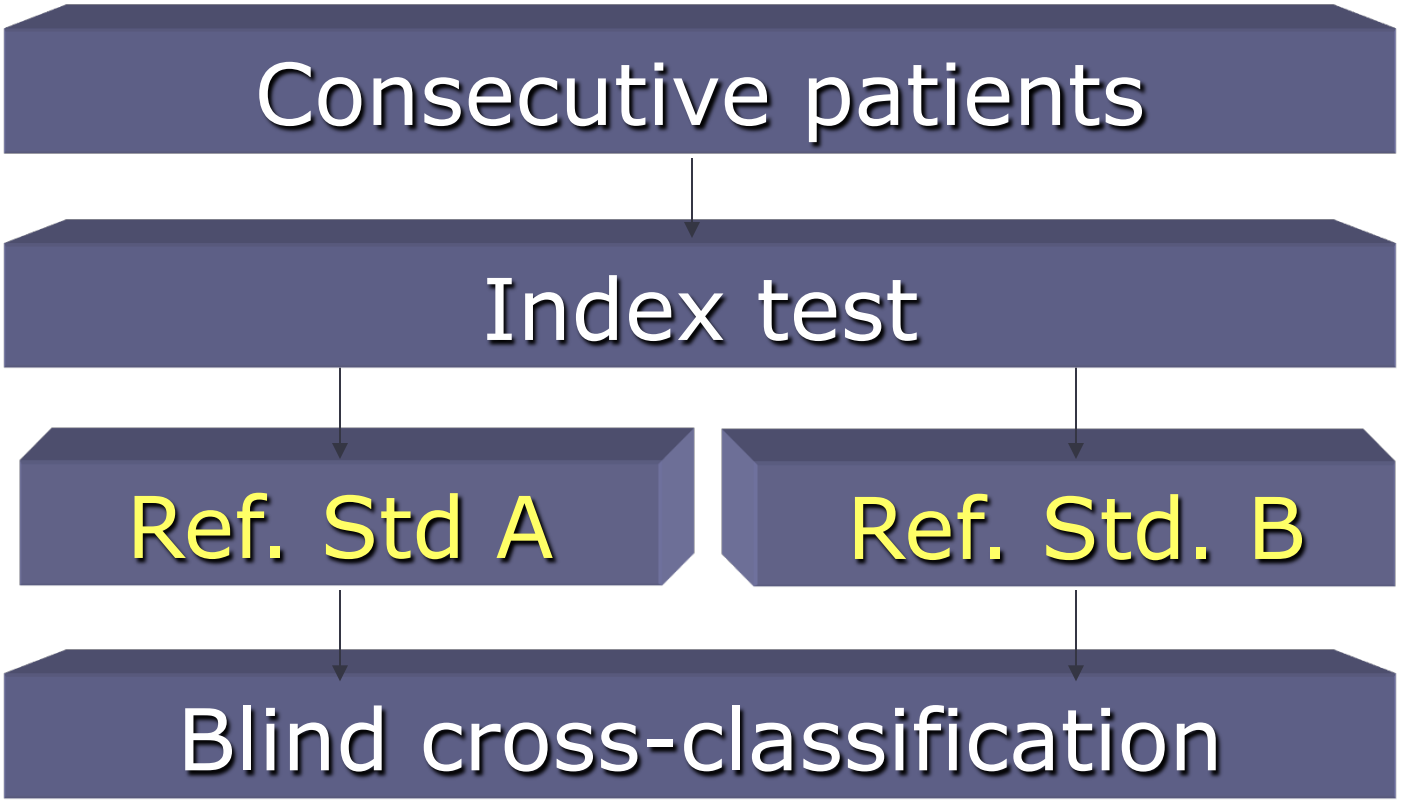


Differential Reference Bias



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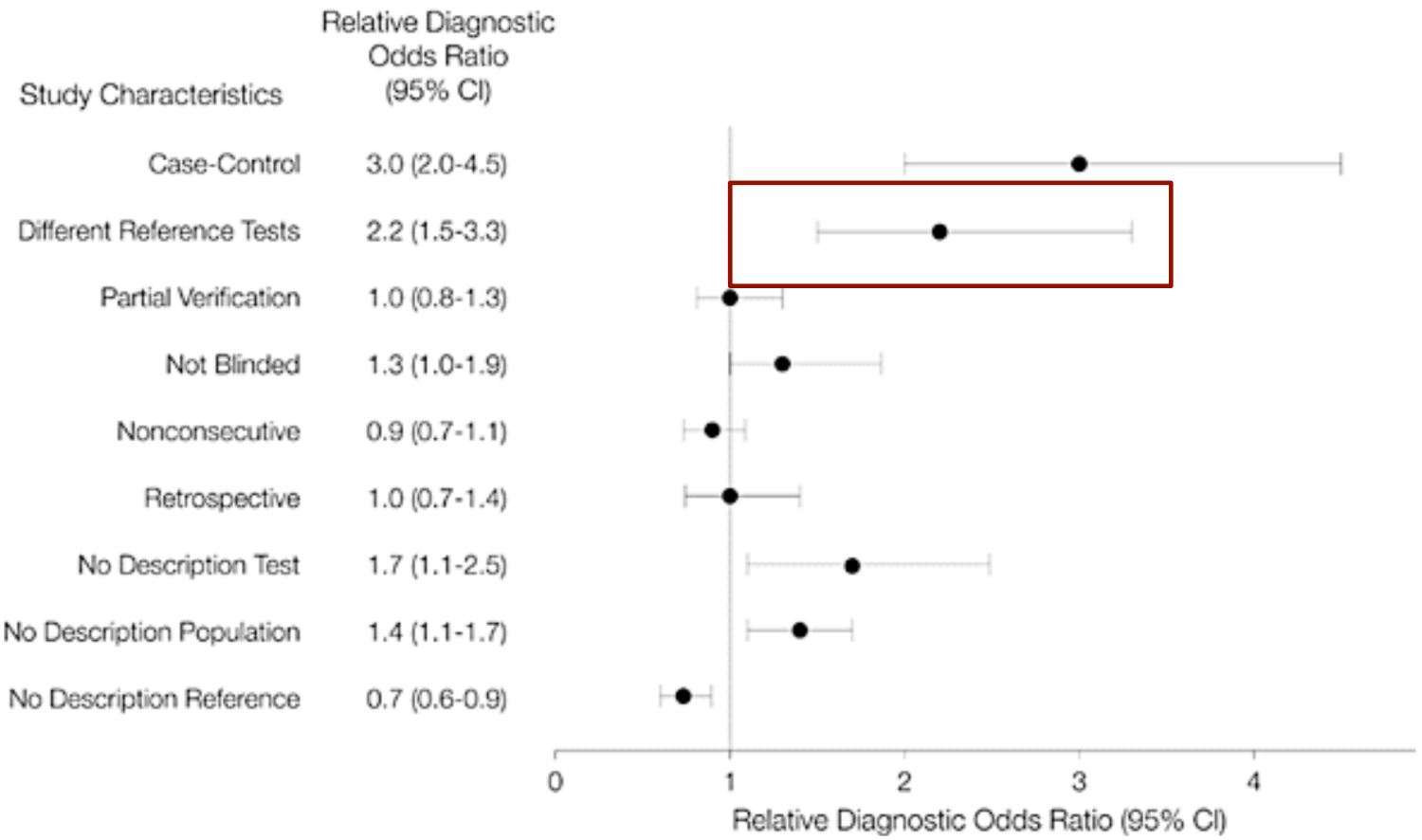
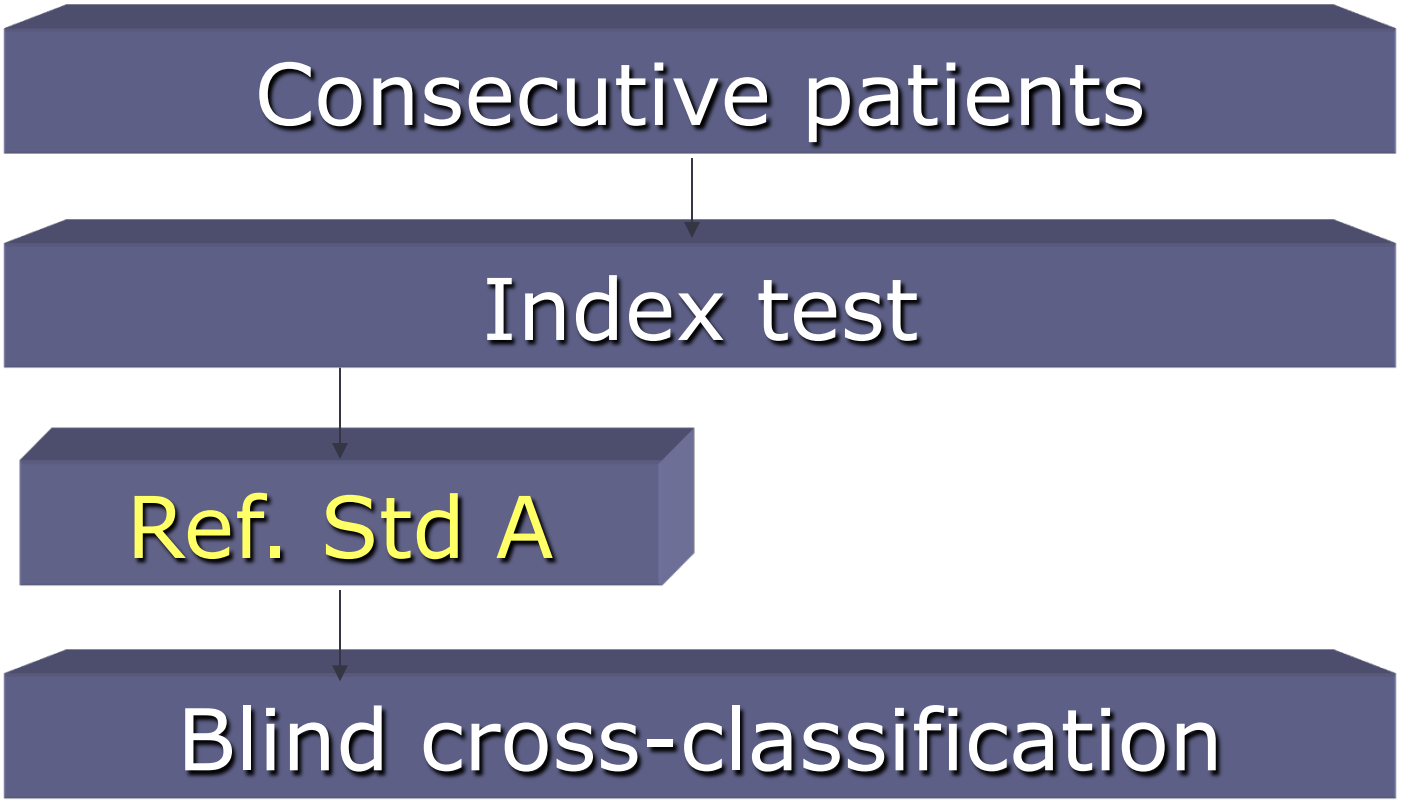


Partial Reference Bias



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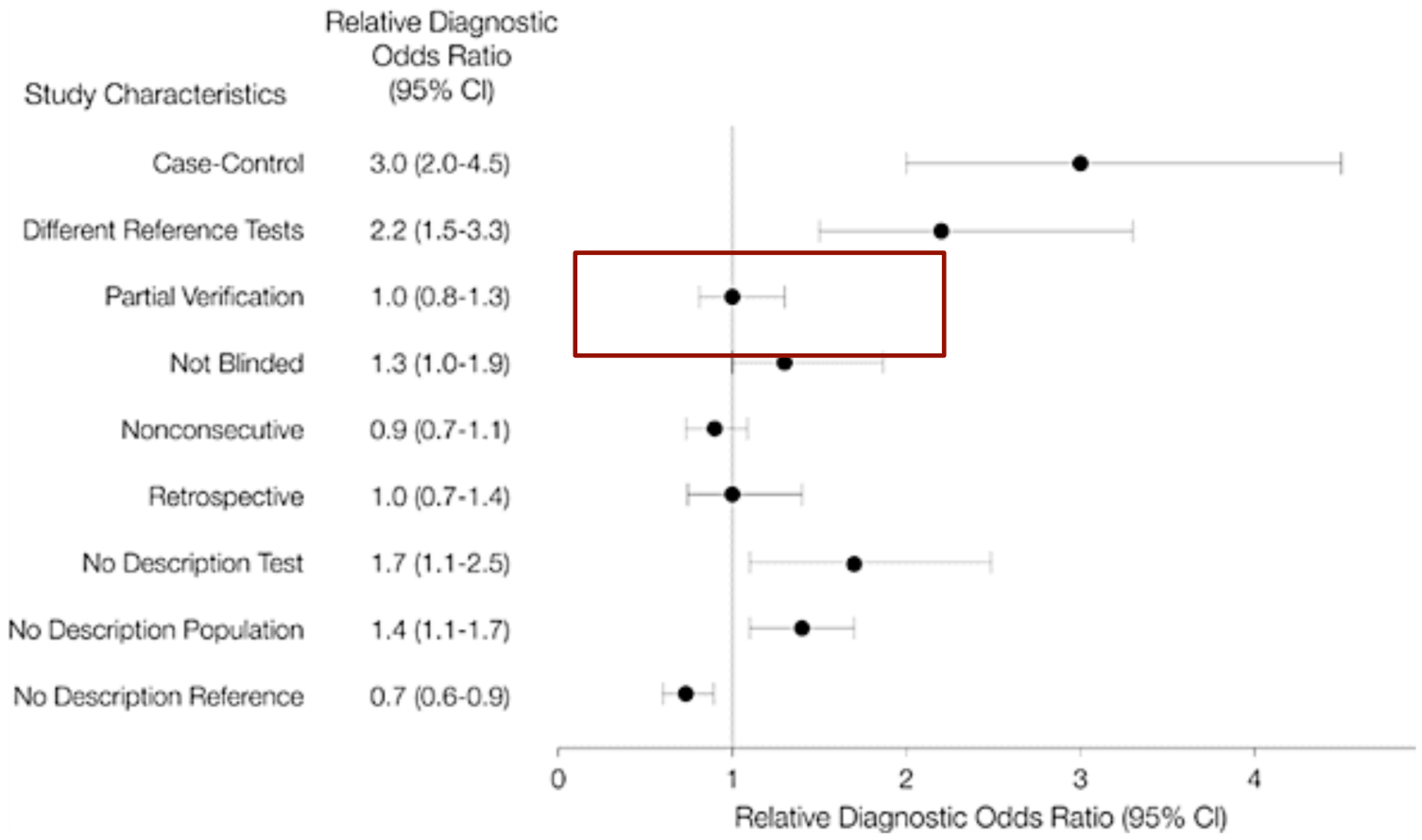
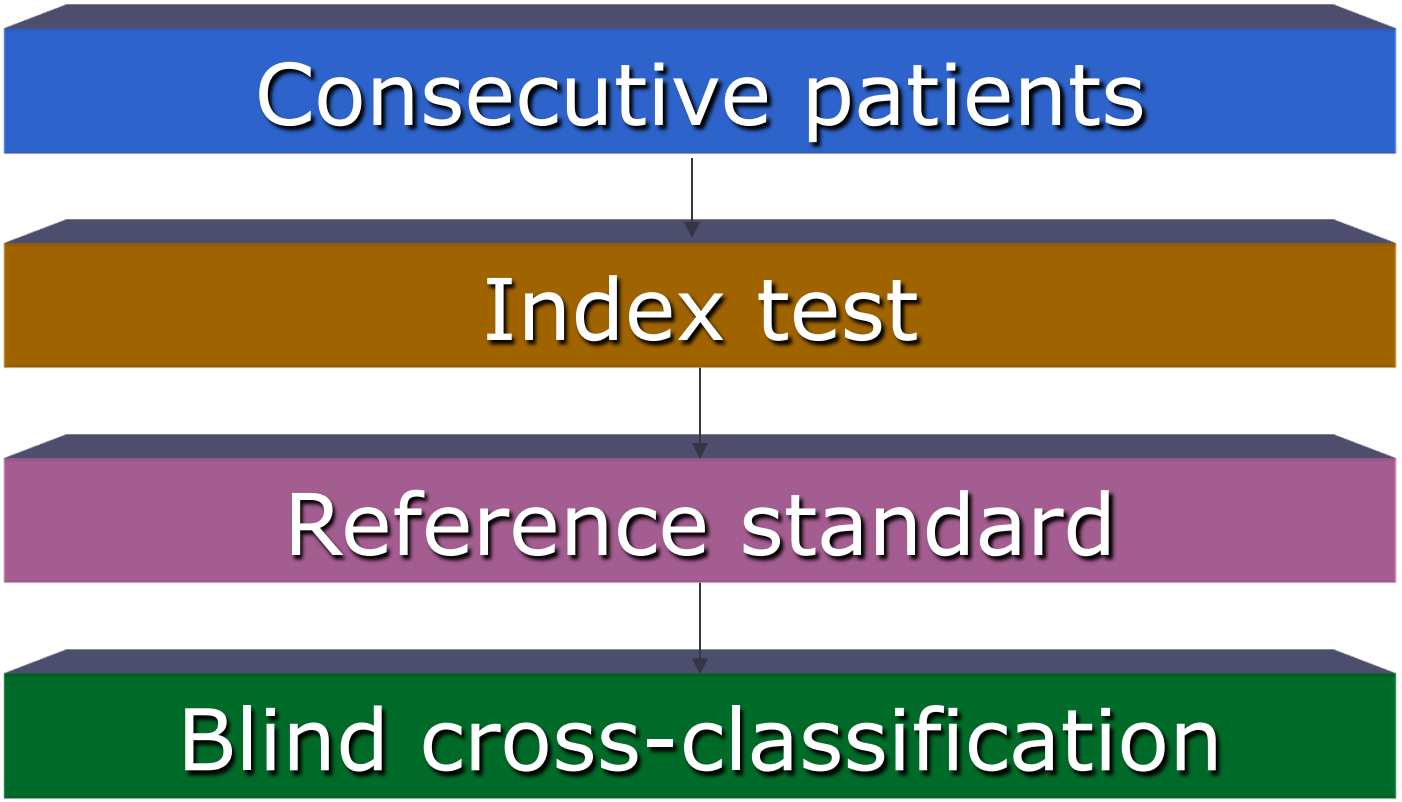
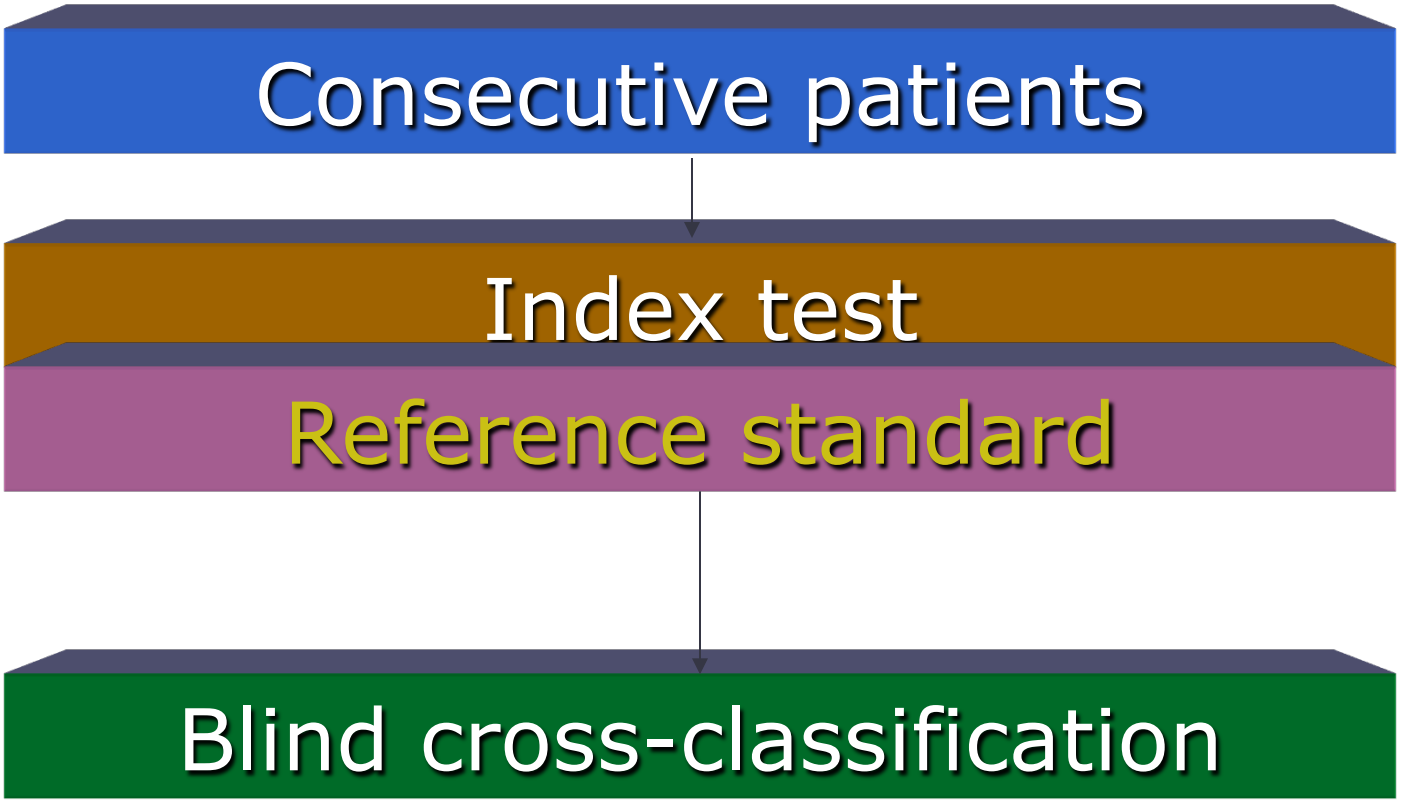


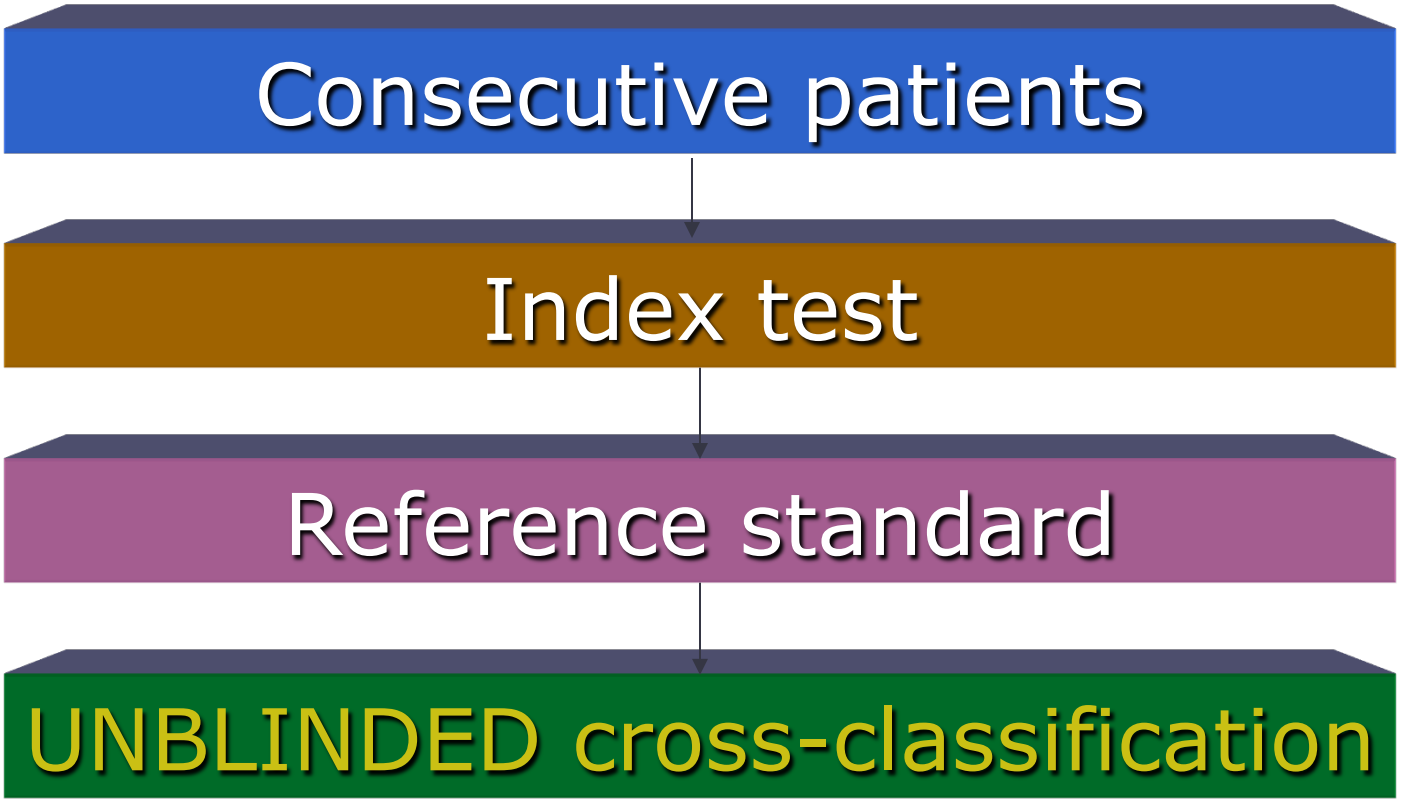
The ‘gold’ problem



Incorporation bias



Observer bias



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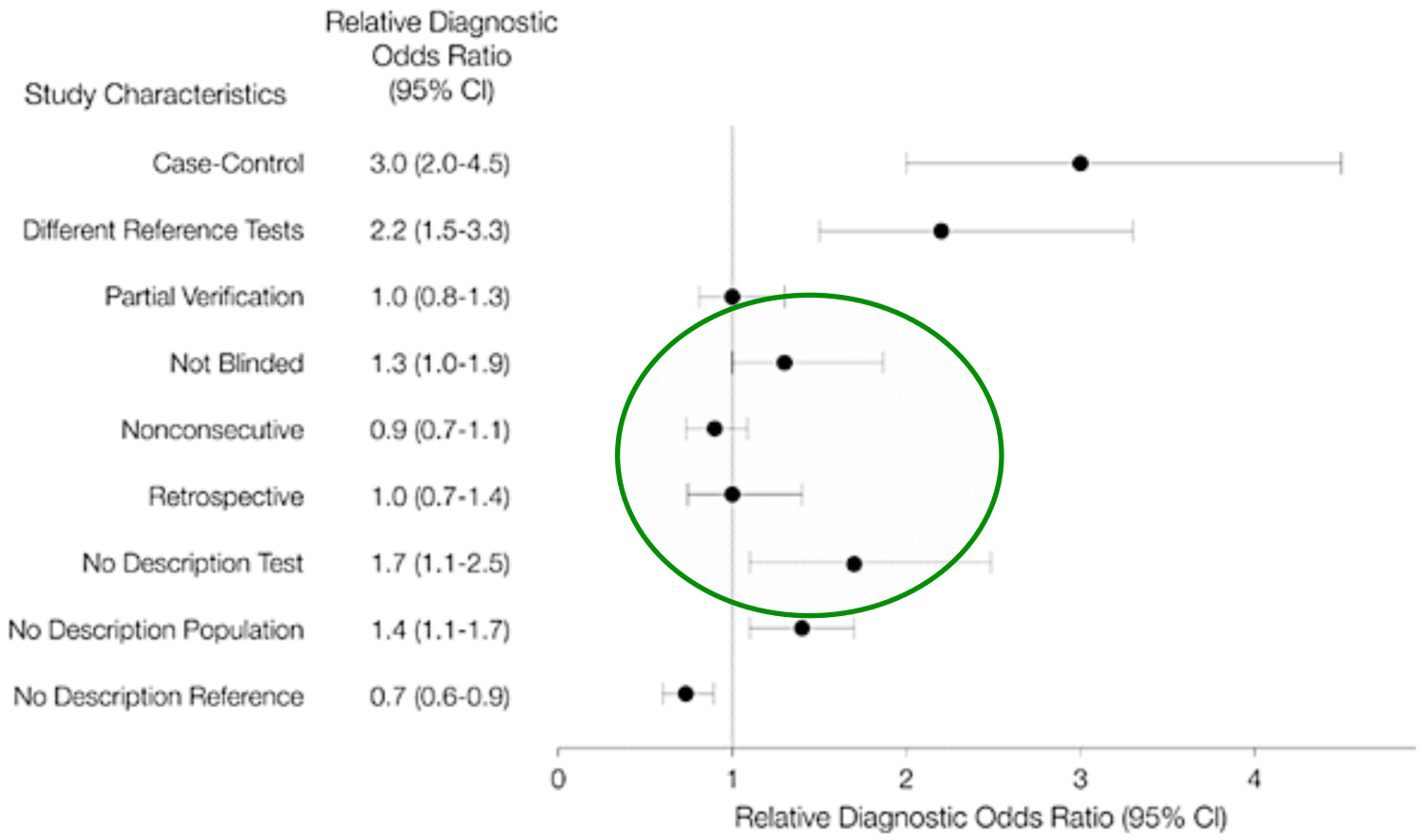
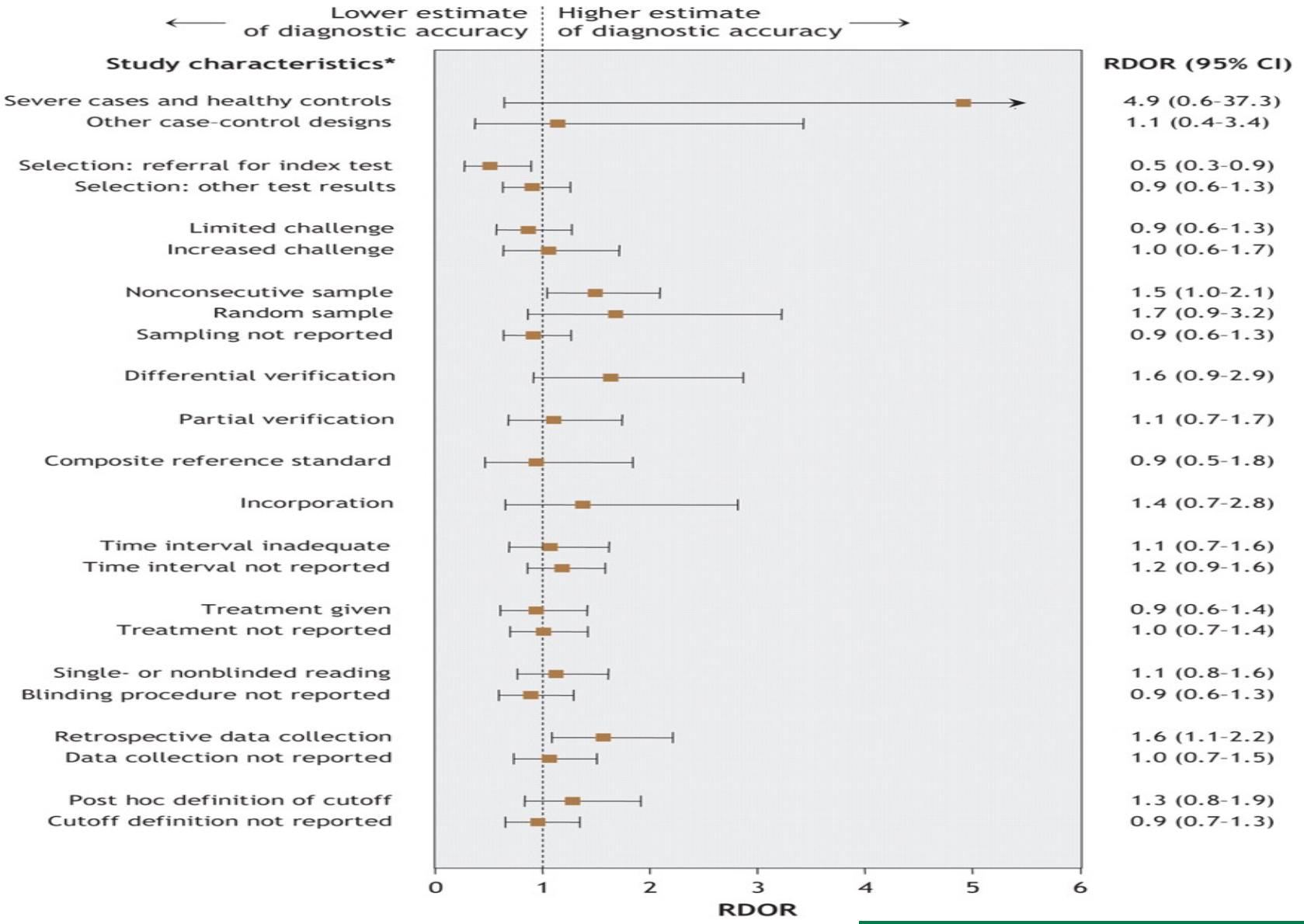


Let's talk

- Not blinded
- No description of test
- Retrospective

Relation between design features and odds ratio – the sequel



*See Appendix 2 for descriptions of the study characteristics.

Rutjes, A. W.S. et al. CMAJ 2006;174:469-476

Annals of Internal Medicine
Established in 1927 by the American College of Physicians

QUADAS-2: A Revised Tool for the Quality Assessment of Diagnostic Accuracy Studies

Table 1. **Risk of Bias and Applicability Judgments in QUADAS-2**

Domain	Patient Selection	Index Test	Reference Standard	Flow and Timing
Description	Describe methods of patient selection Describe included patients (previous testing, presentation, intended use of index test, and setting)	Describe the index test and how it was conducted and interpreted	Describe the reference standard and how it was conducted and interpreted	Describe any patients who did not receive the index tests or reference standard or who were excluded from the 2 × 2 table (refer to flow diagram) Describe the interval and any interventions between index tests and the reference standard
Signaling questions (yes, no, or unclear)	Was a consecutive or random sample of patients enrolled? Was a case–control design avoided? Did the study avoid inappropriate exclusions?	Were the index test results interpreted without knowledge of the results of the reference standard? If a threshold was used, was it prespecified?	Is the reference standard likely to correctly classify the target condition? Were the reference standard results interpreted without knowledge of the results of the index test?	Was there an appropriate interval between index tests and reference standard? Did all patients receive a reference standard? Did all patients receive the same reference standard? Were all patients included in the analysis?
Risk of bias (high, low, or unclear)	Could the selection of patients have introduced bias?	Could the conduct or interpretation of the index test have introduced bias?	Could the reference standard, its conduct, or its interpretation have introduced bias?	Could the patient flow have introduced bias?
Concerns about applicability (high, low, or unclear)	Are there concerns that the included patients do not match the review question?	Are there concerns that the index test, its conduct, or its interpretation differ from the review question?	Are there concerns that the target condition as defined by the reference standard does not match the review question?	

Ann Intern Med. 2011;155(8):529-536. doi: 10.7326/0003-4819-155-8-201110180-00009

QUADAS-2

- Phase 1: State the review question

- P
- I
- R
- T

QUADAS-2

- Phase 2: Tailor assessment tool to specific review questions

- Items that are obsolete?
- Items that are missing?

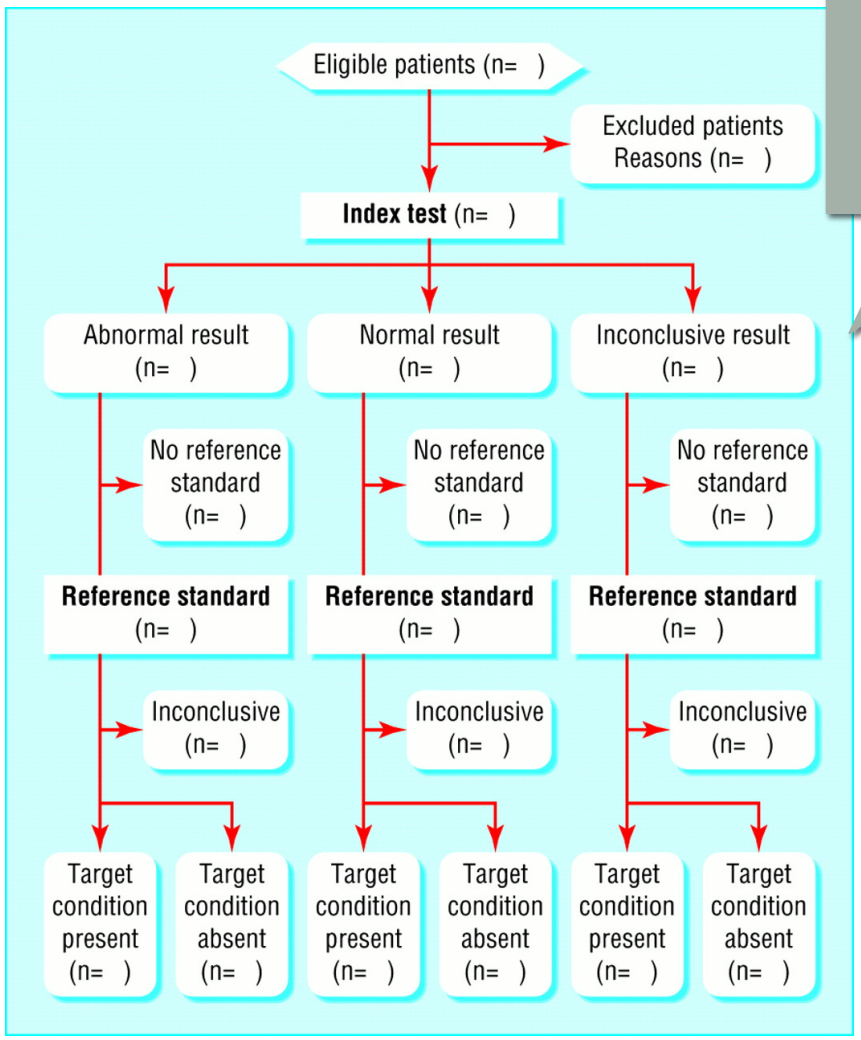
➔Consensus!

➔Pilot to check agreement between at least 2 authors

QUADAS-2

- Phase 3: Draw a flow diagram
  - How many patients had what and where?
  - Transparency on who was analysed

Prototype of a flow diagram for a study on diagnostic accuracy.



Now you try:
Harnden 2003

Bossuyt P M et al. BMJ 2003;326:41-44

BMJ

QUADAS-2

- Phase 4: Risk of bias and applicability

- 4 domains
  - Patient selection
  - Index test
  - Reference standard
  - Flow and timing

- Each with 1 or more signalling questions for bias and applicability assessment

QUADAS-2

- After the assessment, then what??
- No overall score!
- Narrative
  - Overall: ‘Low risk of bias’, ‘Concerns regarding applicability’
  - Summary per study or per item
- Tables

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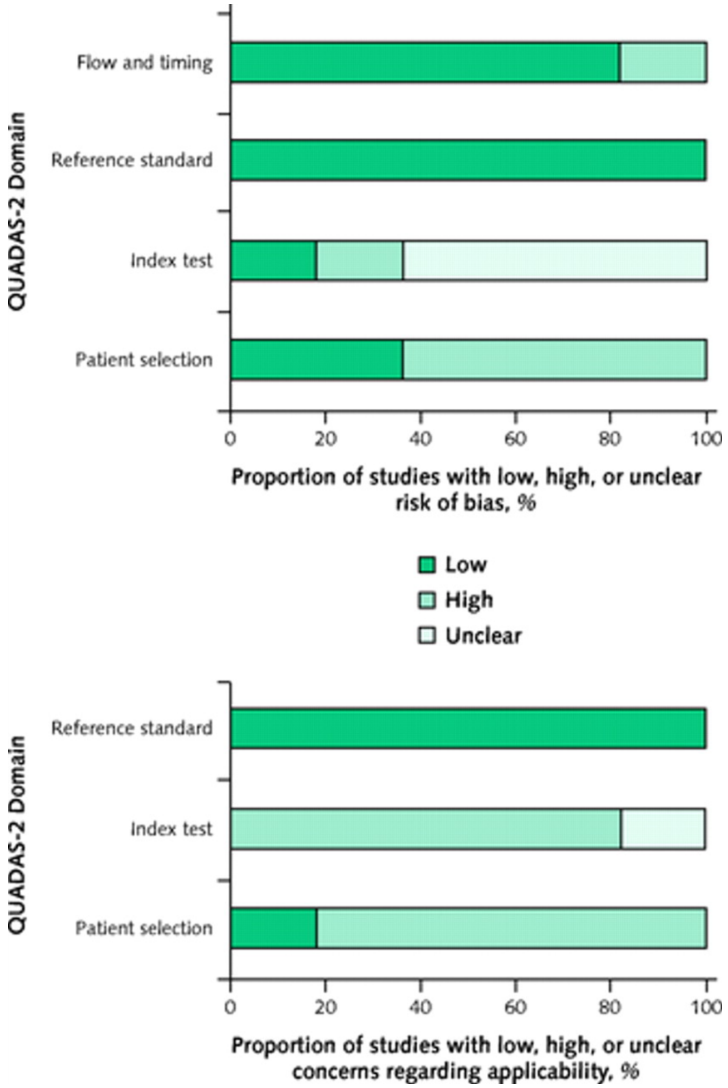
QUADAS-2: A Revised Tool for the Quality Assessment of Diagnostic Accuracy Studies



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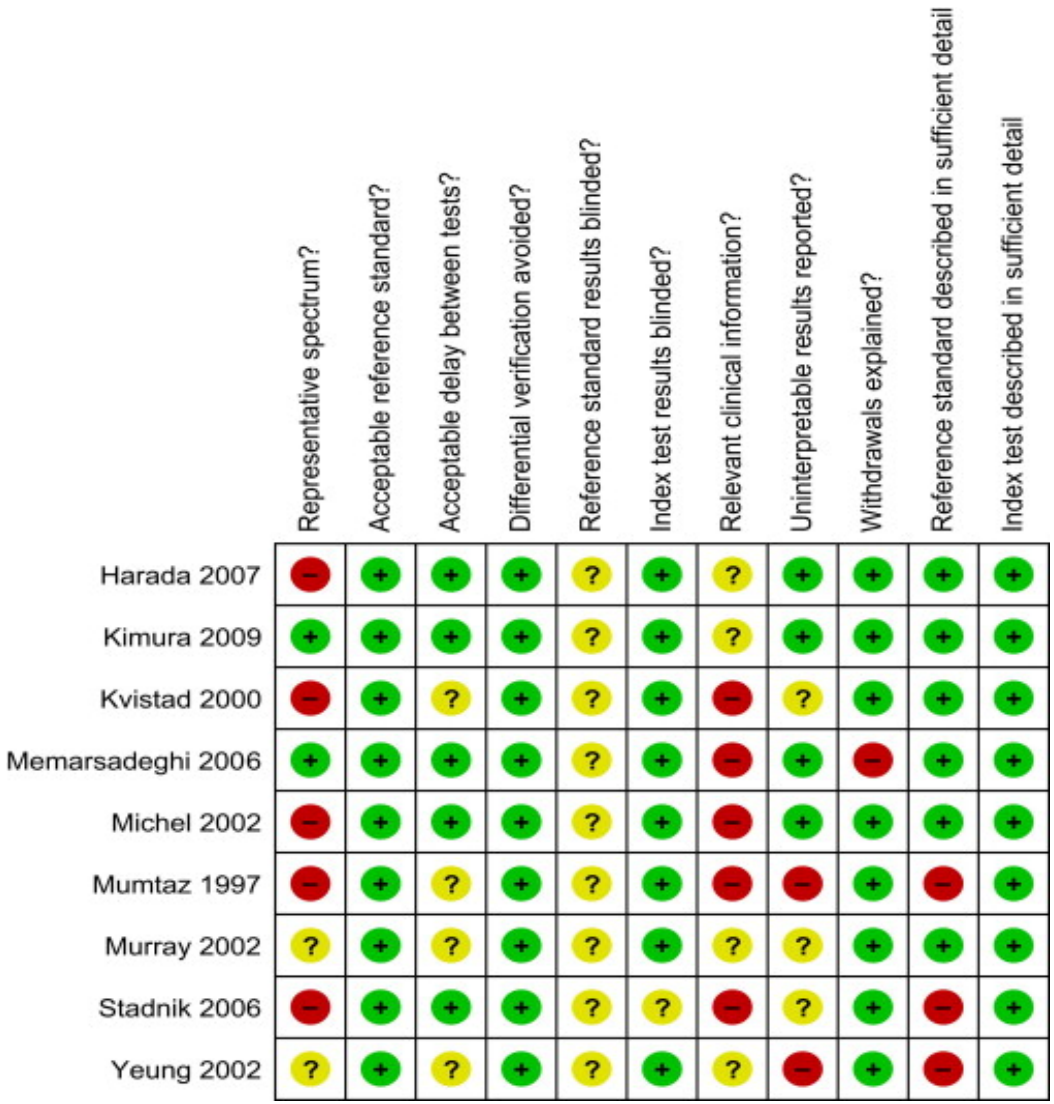


Magnetic resonance for assessment of axillary lymph node status in early breast cancer: A systematic review and meta-analysis

European Journal of Surgical Oncology (EJSO) Volume 37, Issue 11 2011 928 - 936

S.E. Harnan , K.L. Cooper , Y. Meng , S.E. Ward , P. Fitzgerald , D. Papaioannou , C. Ingram , E. Lorenz , I.D. ...

QUADAS-2

- How to incorporate results in analyses?

- Restrict inclusion
- Subgroup
- Sensitivity analysis
- Meta-regression
- Further research recommendations

Reporting

- Can’t judge what isn’t there
- Poor reporting
  - Fontela, PlosOne 2009
  - <25% studies reported on:
    - Withdrawals
    - Reference test execution
    - Index test review bias
    - Reference test review bias

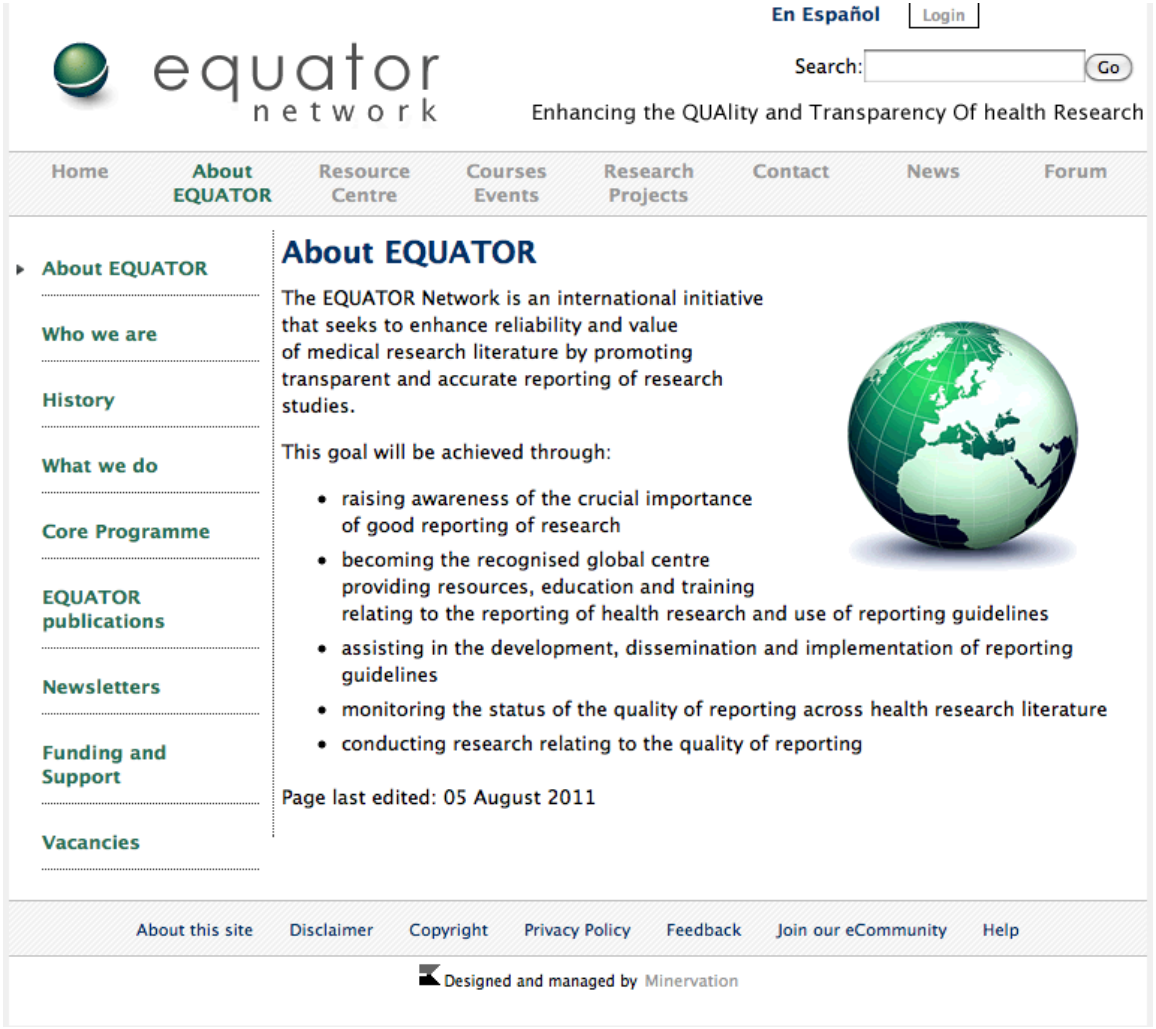
STARD statement

- 2003
- International collaborative group
- http://www.stard-statement.org
- Adopted by >200 journals

STARD checklist for the reporting of studies of diagnostic accuracy.
First official version, January 2003.

Section and Topic	Item #		On page #
TITLE/ABSTRACT/ KEYWORDS	1	Identify the article as a study of diagnostic accuracy (recommend MeSH heading 'sensitivity and specificity').	
INTRODUCTION	2	State the research questions or study aims, such as estimating diagnostic accuracy or comparing accuracy between tests or across participant groups.	
METHODS			
Participants	3	Describe the study population: The inclusion and exclusion criteria, setting and locations where the data were collected.	
	4	Describe participant recruitment: Was recruitment based on presenting symptoms, results from previous tests, or the fact that the participants had received the index tests or the reference standard?	
	5	Describe participant sampling: Was the study population a consecutive series of participants defined by the selection criteria in items 3 and 4? If not, specify how participants were further selected.	
	6	Describe data collection: Was data collection planned before the index test and reference standard were performed (prospective study) or after (retrospective study)?	
Test methods	7	Describe the reference standard and its rationale.	
	8	Describe technical specifications of material and methods involved including how and when measurements were taken, and/or cite references for index tests and reference standard.	
	9	Describe definition of and rationale for the units, cutoffs and/or categories of the results of the index tests and the reference standard.	
	10	Describe the number, training and expertise of the persons executing and reading the index tests and the reference standard.	
	11	Describe whether or not the readers of the index tests and reference standard were blind (masked) to the results of the other test and describe any other clinical information available to the readers.	
Statistical methods	12	Describe methods for calculating or comparing measures of diagnostic accuracy, and the statistical methods used to quantify uncertainty (e.g. 95% confidence intervals).	
	13	Describe methods for calculating test reproducibility, if done.	
RESULTS			
Participants	14	Report when study was done, including beginning and ending dates of recruitment.	
	15	Report clinical and demographic characteristics of the study population (e.g. age, sex, spectrum of presenting symptoms, comorbidity, current treatments, recruitment centers).	
	16	Report the number of participants satisfying the criteria for inclusion that did or did not undergo the index tests and/or the reference standard; describe why participants failed to receive either test (a flow diagram is strongly recommended).	
Test results	17	Report time interval from the index tests to the reference standard, and any treatment administered between.	
	18	Report distribution of severity of disease (define criteria) in those with the target condition; other diagnoses in participants without the target condition.	
	19	Report a cross tabulation of the results of the index tests (including indeterminate and missing results) by the results of the reference standard; for continuous results, the	

STARD statement



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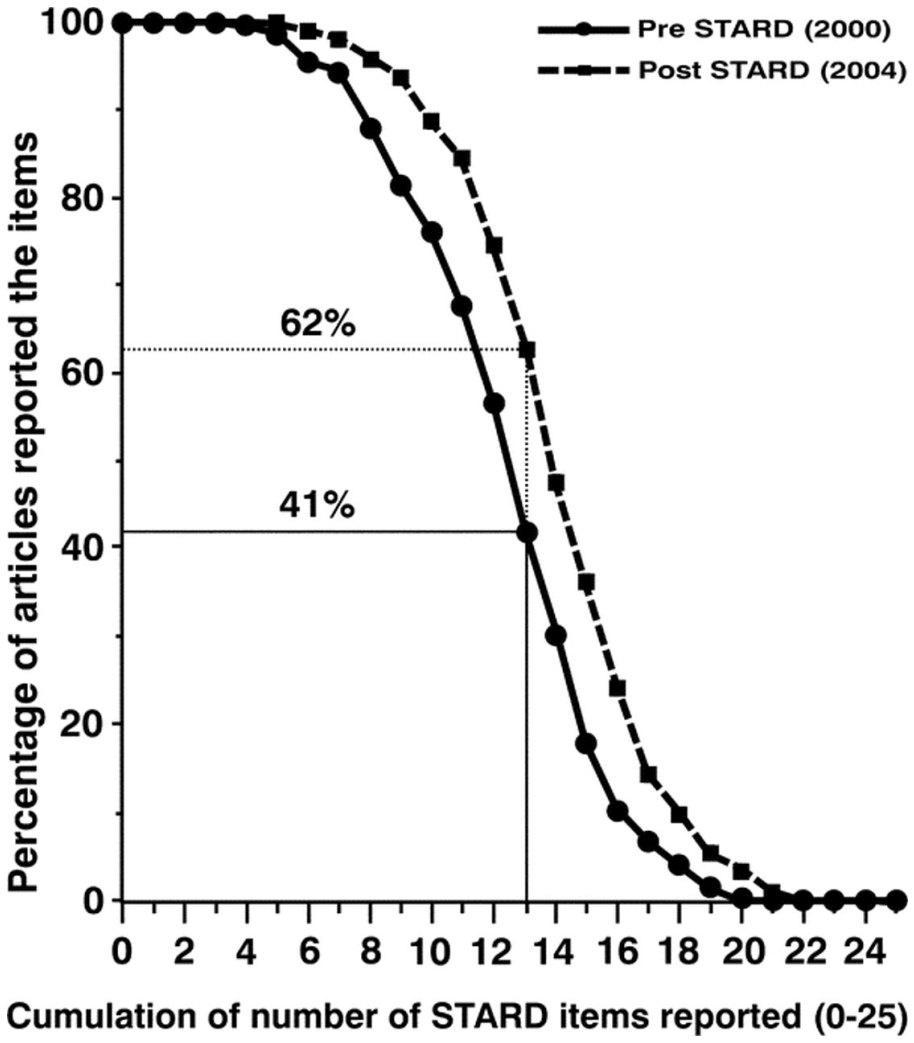

Smidt N et al. Neurology 2006;67:792-797

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- QUADAS-2: http://www.bris.ac.uk/quadas
- STARD statement: http://www.stard-statement.org

Questions?