

QUADAS-C: risk of bias in comparative diagnostic accuracy studies

Comparative review question

Patients:	
Index test A:	
Index test B:	
Reference standard and target condition:	

Add rows for additional index tests if necessary

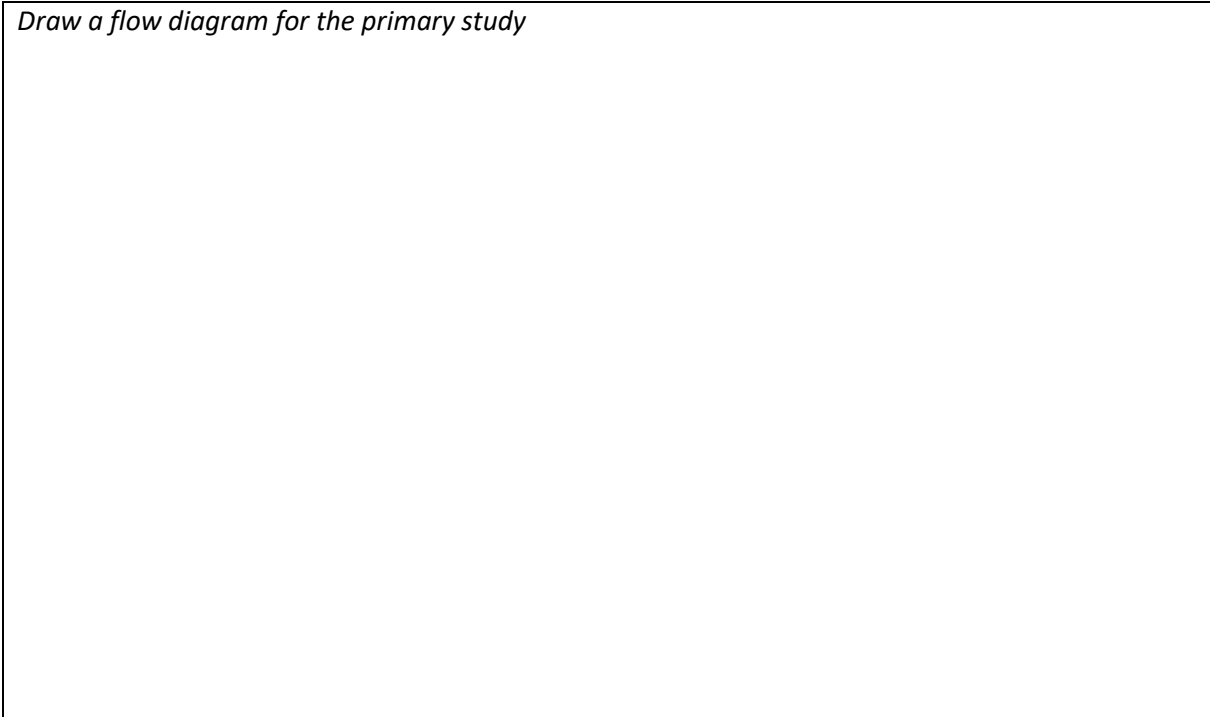
Comparative study design

Which of the following study designs does the primary study most strongly resemble?	<i>#1 Fully Paired #2 Randomized #3 Partially paired with random subset #4 Partially paired with nonrandom subset #5 Unpaired nonrandomized Other (please describe the study design):</i>
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The [QUADAS-C Guidance Document](#) contains example flow diagrams for each design

Flow diagram

Draw a flow diagram for the primary study



Domain 1: Patient Selection			
Information to support judgment	<i>Describe methods of patient selection. Describe included patients (previous testing, presentation, intended use of index test, and setting). Describe how patients were allocated to receive each of the index tests. If randomization was used to assign individual patients (or clusters of patients) to index tests, describe the randomization process.</i>		
Single test accuracy (QUADAS-2)		Answers for _____ (test A)*	Answers for _____ (test B)*
Signaling questions	1.1 Was a consecutive or random sample of patients enrolled?	Yes/No/Unclear	Yes/No/Unclear
	1.2 Was a case-control design avoided?	Yes/No/Unclear	Yes/No/Unclear
	1.3 Did the study avoid inappropriate exclusions?	Yes/No/Unclear	Yes/No/Unclear
Risk of bias	1.4 Could the selection of patients have introduced bias?	Low/High/Unclear	Low/High/Unclear
Concerns regarding applicability	1.5 Are there concerns that the included patients do not match the review question?	Low/High/Unclear	Low/High/Unclear
Comparative accuracy (QUADAS-C)		Answers for the test comparison	
Signaling questions	C1.1 Was the risk of bias for each index test judged 'low' for this domain?	Yes/No	
	C1.2 Was a fully paired or randomized design used?	Yes/No/Unclear	
	C1.3 Was the allocation sequence random?†	Yes/No/Unclear/ Not applicable	
	C1.4 Was the allocation sequence concealed until patients were enrolled and assigned to index tests?†	Yes/No/Unclear/ Not applicable	
Risk of bias	C1.5 Could the selection of patients have introduced bias in the comparison?	Low/High/Unclear	

* Example when the comparison is between two index tests. Additional columns can be added for each additional test in the comparison.

† Only applicable to randomized designs

See the [QUADAS-C Guidance Document](#) for more detailed explanations.

C1.1: Answer 'yes' if the risk of bias judgment for single test accuracy (question 1.4 in QUADAS-2) was 'low' for each index test.

C1.2: Answer 'yes' if one of the following methods was used for allocating patients to index tests: (1) each patient receiving all of the index tests (fully paired design) or (2) random allocation of patients to one of the index tests (randomized design).

C1.3: Answer 'yes' if the study generated a truly random allocation sequence, for example, computer-generated random numbers and random number tables.

C1.4: Answer 'yes' if the study used appropriate methods to conceal allocation, such as central randomization schemes and opaque sealed envelopes.

C1.5: Risk of bias can be judged 'low' if questions C1.1 to C1.4 were answered 'yes' (questions C1.3 and C1.4 are only applicable to randomized designs). If at least one question was answered 'no', users should consider a 'high risk of bias' judgment if the bias associated with the design feature is of such concern that the entire domain is deemed problematic. If C1.2 was answered 'no', strongly consider 'high risk of bias'.

Domain 2: Index Test			
Information to support judgment	<i>Describe the index tests and how they were conducted and interpreted. For paired comparative studies, describe the order in which the index tests were performed.</i>		
Single test accuracy (QUADAS-2)		Answers for _____ (test A)	Answers for _____ (test B)
Signaling questions	2.1 Were the index test results interpreted without knowledge of the results of the reference standard?	Yes/No/Unclear	Yes/No/Unclear
	2.2 If a threshold was used, was it prespecified?	Yes/No/Unclear	Yes/No/Unclear
Risk of bias	2.3 Could the conduct or interpretation of the index test have introduced bias?	Low/High/Unclear	Low/High/Unclear
Concerns regarding applicability	2.4 Are there concerns that the index test, its conduct or its interpretation differ from the review question?	Low/High/Unclear	Low/High/Unclear
Comparative accuracy (QUADAS-C)		Answers for the test comparison	
Signaling questions	C2.1 Was the risk of bias for each index test judged 'low' for this domain?	Yes/No	
	C2.2 Were the index test results interpreted without knowledge of the results of the other index test(s)?‡	Yes/No/Unclear/ Not applicable	
	C2.3 Is undergoing one index test <u>unlikely</u> to affect the performance of the other index test(s)?‡	Yes/No/Unclear/ Not applicable	
	C2.4 Were the index tests conducted and interpreted without advantaging one of the tests?	Yes/No/Unclear	
Risk of bias	C2.5 Could the conduct or interpretation of the index tests have introduced bias in the comparison?	Low/High/Unclear	

‡ Only applicable if patients received multiple index tests (fully or partially paired designs)

C2.1: Answer 'yes' if the risk of bias judgment for single test accuracy (question 2.3 in QUADAS-2) was 'low' for each index test.

C2.2: Answer 'yes' if index test A was interpreted blind to the results of index test B and vice versa. Blinding is not necessary if none of the index tests involve subjective interpretation.

C2.3: Answer 'yes' if one index test cannot influence or interfere with the results of subsequently performed index test(s). Examples of such influence or interference include distortion of sampling area (biopsies) and patient fatigue (questionnaires).

C2.4: Answer 'yes' if there were no differences between the index tests that may unfairly benefit one of the tests. An example of such a difference is when index test A was performed by an expert and index test B by a nonexpert. Differences between tests that reflect clinical practice are acceptable, in which case 'yes' is appropriate.

C2.5: Risk of bias can be judged 'low' if signaling questions C2.1 to C2.4 were answered 'yes' (C2.2 and C2.3 are only applicable to fully or partially paired designs). If at least one question was answered 'no', users should consider a 'high risk of bias' judgment if the bias associated with the design feature is of such concern that the entire domain is deemed problematic.

Domain 3: Reference Standard			
Information to support judgment	<i>Describe the reference standard, how it was conducted and interpreted, and whether any of the index tests were part of the reference standard.</i>		
Single test accuracy (QUADAS-2)		Answers for _____ (test A)	Answers for _____ (test B)
Signaling questions	3.1 Is the reference standard likely to correctly classify the target condition?	Yes/No/Unclear	Yes/No/Unclear
	3.2 Were the reference standard results interpreted without knowledge of the results of the index test?	Yes/No/Unclear	Yes/No/Unclear
Risk of bias	3.3 Could the reference standard, its conduct, or its interpretation have introduced bias?	Low/High/Unclear	Low/High/Unclear
Concerns regarding applicability	3.4 Are there concerns that the target condition as defined by the reference standard does not match the review question?	Low/High/Unclear	Low/High/Unclear
Comparative accuracy (QUADAS-C)		Answers for the test comparison	
Signaling questions	C3.1 Was the risk of bias for each index test judged 'low' for this domain?	Yes/No	
	C3.2 Did the reference standard avoid incorporating any of the index tests?	Yes/No/Unclear	
Risk of bias	C3.3 Could the reference standard, its conduct, or its interpretation have introduced bias in the comparison?	Low/High/Unclear	

C3.1: Answer 'yes' if the risk of bias judgment for single test accuracy (question 3.3 in QUADAS-2) was 'low' for each index test.

C3.2: Answer 'yes' if none of the index tests were part of the reference standard. Note that this issue is different from blinding (signaling question 3.2 in QUADAS-2).

C3.3: Risk of bias can be judged 'low' if signaling questions C3.1 and C3.2 were answered 'yes'. If at least one question was answered 'no', users should consider a 'high risk of bias' judgment if the bias associated with the design feature is of such concern that the entire domain is deemed problematic.

Domain 4: Flow and Timing			
Information to support judgment	<p><i>Describe any patients who did not receive the index tests or reference standard or who were excluded from the analysis.</i></p> <p><i>Describe the time interval and any interventions between the index tests and the reference standard.</i></p> <p><i>Describe the time interval and any interventions between the index tests being compared.</i></p>		
Single test accuracy (QUADAS-2)		Answers for _____ (test A)	Answers for _____ (test B)
Signaling questions	4.1 Was there an appropriate interval between index tests and reference standard?	Yes/No/Unclear	Yes/No/Unclear
	4.2 Did all patients receive a reference standard?	Yes/No/Unclear	Yes/No/Unclear
	4.3 Did all patients receive the same reference standard?	Yes/No/Unclear	Yes/No/Unclear
	4.4 Were all patients included in the analysis?	Yes/No/Unclear	Yes/No/Unclear
Risk of bias	4.5 Could the patient flow have introduced bias?	Low/High/Unclear	Low/High/Unclear
Comparative accuracy (QUADAS-C)		Answers for the test comparison	
Signaling questions	C4.1 Was the risk of bias for each index test judged 'low' for this domain?	Yes/No	
	C4.2 Was there an appropriate interval between the index tests?	Yes/No/Unclear	
	C4.3 Was the same reference standard used for all index tests?	Yes/No/Unclear	
	C4.4 Are the proportions and reasons for missing data similar across index tests?	Yes/No/Unclear	
Risk of bias	C4.5 Could the patient flow have introduced bias in the comparison?	Low/High/Unclear	

C4.1: Answer 'yes' if the risk of bias judgment for single test accuracy (question 4.5 in QUADAS-2) was 'low' for each index test.

C4.2: For many index tests, 'appropriate' would constitute performing the tests at the same time after patient enrolment. This excludes the possibility of disease progression or change in patient management. Some index tests have different 'diagnostic windows' and are ideally performed at different timepoints; subject-matter expertise is required to determine this.

C4.3: Answer 'yes' if either (1) a single reference standard was used in all patients or (2) multiple reference standards were used (e.g., either surgery or follow-up) and these reference standards were the same for patients receiving index test A and patients receiving index test B.

C4.4: Missing data occurs if test results are unavailable, invalid, inconclusive, or if patients are excluded from the analysis. Answer 'yes' if there is no missing data, or if the proportion and reasons for missing data are similar for index test A and index test B.

C4.5: Risk of bias can be judged 'low' if signaling questions C4.1 to C4.4 were answered 'yes'. If at least one question was answered 'no', users should consider a 'high risk of bias' judgment if the bias associated with the design feature is of such concern that the entire domain is deemed problematic.