Quality assessment of diagnostic test accuracy studies

Montreal, Monday May 25th, 2009

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Steps in a systematic review

1. Formulating the question
   (and defining criteria for inclusion of studies)
2. Searching for studies
3. Selecting studies
4. Collecting data
5. Assessing methodological quality
6. Analysing and presenting results
7. Interpreting results
Quality assessment

Why assess quality?

- Problem 1: Bias in primary studies can lead to misleading summary estimates of accuracy
- Problem 2: Results of primary studies may vary
- Quality assessment to guide the interpretation of results in terms of potential for bias and sources of heterogeneity
Echocardiography in Coronary Heart Disease

![Graph showing sensitivity vs. 1-specificity](image-url)
GLAL in Gram Negative Sepsis
F/T PSA in the Detection of Prostate cancer

![Graph showing sensitivity vs. 1-specificity]
Dip-stick Testing for Urinary Tract Infection

![Graph showing sensitivity vs. 1-specificity for dip-stick testing.]
Cochrane definition of quality

“the methodological quality of a study; the degree to which the design and conduct of a study fit to the study objectives”
How to assess quality?

- Quality assessment tools:
  - Large number of different tools
  - Styles: Quality scores/levels of evidence/component approach
  - Cochrane handbook recommends modified version of the QUADAS tool
QUADAS

- General tool
- Systematically developed based on empirical evidence and a formal consensus method
- Set of 11 required (strongly suggested) items, and a list of additional items to consider
## QUADAS items

<table>
<thead>
<tr>
<th>Item</th>
<th>Question</th>
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<tbody>
<tr>
<td>1</td>
<td>Was the spectrum of patients representative of the patients who will receive the test in practice?</td>
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<td>10</td>
<td>Were uninterpretable/ intermediate test results reported?</td>
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<td>11</td>
<td>Were withdrawals from the study explained?</td>
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Sources of bias and variation

  - overview of sources of bias and variation

  - development of QUADAS

Cochrane Handbook for Reviews of Diagnostic Test Accuracy
Basic Test Accuracy Study

1. Series of patients
2. Index test
3. Reference standard
4. Blinded cross-verification
Problems with spectrum

Measures of accuracy vary across patient groups:
- Patient characteristics e.g. age
- Patient selection/Study design
- Setting
Diagnostic case-control design

Healthy controls

Index test

Specificity

Known cases

Index test

Sensitivity
Reference standard bias

Consecutive series of patients

Index test

Non optimal reference standard

Blinded cross-verification
Time between index test and reference standard

Series of patients

Index test

Reference standard

Blinded cross-verification

Therapy
Disease progression etc
Partial verification bias

Consecutive series of patients

Index test

Reference standard

Blinded cross-verification
Differential verification bias

Consecutive series of patients

Index test


Blinded cross-verification
Incorporation bias

Consecutive series of patients

Index test

Index test + other test(s)

Blinded cross-verification
Blinding

1. Series of patients
2. Index test
3. Reference standard
4. Blinded cross-verification

Blinded cross-verification is applied to the reference standard before comparing it with the index test results.
Blinding

1. Series of patients
2. Index test
3. Reference standard
4. Blinded cross-verification

Clinical Information
Two important reporting items

- Reporting of uninterpretable/intermediate test results
- Explanation of withdrawals

<table>
<thead>
<tr>
<th>biopsy</th>
<th>+</th>
<th>-</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV+</td>
<td>45</td>
<td>68</td>
<td>113</td>
</tr>
<tr>
<td>+/-</td>
<td>20</td>
<td>25</td>
<td>45</td>
</tr>
<tr>
<td>HPV-</td>
<td>7</td>
<td>161</td>
<td>198</td>
</tr>
<tr>
<td></td>
<td>72</td>
<td>254</td>
<td>356</td>
</tr>
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</table>
Study characteristics*

Severe cases and healthy controls
Other case-control designs

Selection: referral for index test
Selection: other test results

Limited challenge
Increased challenge

Nonconsecutive sample
Random sample
Sampling not reported

Retrospective data collection
Data collection not reported

Post hoc definition of cutoff
Cutoff definition not reported

RDOR (95% CI)
4.9 (0.6-37.3)
1.1 (0.4-3.4)
0.5 (0.3-0.9)
0.9 (0.6-1.3)
0.9 (0.6-1.3)
1.0 (0.6-1.7)
1.5 (1.0-2.1)
1.7 (0.9-3.2)
0.9 (0.6-1.3)
1.6 (1.1-2.2)
1.0 (0.7-1.5)
1.3 (0.8-1.9)
0.9 (0.7-1.3)
Assessment of items

- All items scored as yes/no/unclear
- Items phrased so that yes indicates absence of bias
- Background document describes how items should be scored
Practical Issues

- Number of assessors
- Background of assessors
- Resolving disagreement
- Piloting the assessment process
- Develop your quality assessment tool
Your quality assessment tool

- Items to include
  - Core items
  - Additional items
    - select from suggested items
    - add your own if other items are important for your review topic

- Produce scoring guidelines specific to your review
## Additional items

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<tr>
<td>12.</td>
<td>If a cut-off value has been used, was it established before the study was started (pre-specified cut-off value)?</td>
</tr>
<tr>
<td>13.</td>
<td>Is the technology of the index test likely to have changed since the study was carried out?</td>
</tr>
<tr>
<td>14.</td>
<td>Did the study provide a clear definition of what was considered to be a “positive” result?</td>
</tr>
<tr>
<td>15.</td>
<td>Was treatment started after the index test was carried out but before the reference standard was performed?</td>
</tr>
<tr>
<td>16.</td>
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</tr>
<tr>
<td>17.</td>
<td>Were data on observer variation reported?</td>
</tr>
<tr>
<td>18.</td>
<td>Were data on instrument variation reported?</td>
</tr>
<tr>
<td>19.</td>
<td>Were data presented for appropriate patient sub-groups?</td>
</tr>
<tr>
<td>20.</td>
<td>Was an appropriate sample size included?</td>
</tr>
<tr>
<td>21.</td>
<td>Were objectives pre-specified?</td>
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Presenting study quality

- Present the results of the quality assessment:
  - Graphically
Methodological Quality Graph

Review authors' judgments about each methodological quality item presented as percentages across all included studies.
Incorporating study quality

- Present the results of the quality assessment:
  - In a table
  - Graphically
Methodological quality summary.

Review authors' judgments about each methodological quality item for each included study.
Using study quality

- Present the results of the quality assessment:
  - In a table
  - Graphically
- Investigate individual quality items as potential sources of heterogeneity
- Basis for recommendations for future research
Formal incorporation of study quality

- Restricting the analysis to high quality studies
- Stratified analysis according to presence/absence of specific quality criteria
- Sensitivity analyses to investigate robustness of results
- Investigate several features simultaneously using meta-regression analysis

Always: define methodological criteria a priori
Problems with quality assessment

- Not as straightforward as it might sound!
- Hampered by poor reporting
- Quality assessment is subjective
- Quality scores are not recommended
- Statistical incorporation of quality problematic with limited studies
Now it’s your turn!
Example: BNP for heart failure

- **Aim:** To assess the accuracy of BNP for the diagnosis of heart failure

- In small groups:
  1. Produce a flow diagram for the study
  2. Discuss (attention to what has been done, what is missing and possible consequences):
     - QUADAS item 1 (spectrum)
     - QUADAS items 2, 4 and 5 (verification)
  3. Discuss the conclusion of the authors
| QUADAS items |  
|----------------|-------------------------------------------------|
| 1 | Was the spectrum of patients representative of the patients who will receive the test in practice? |
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Biochemical diagnosis of ventricular dysfunction in elderly patients in general practice: observational study. BMJ 2000;320:9906-8

Eligible Elderly in General Practice, n=1056

Not included n=299

echocardiography n=817

Heart Failure n=?
Randomly excluded n=?
Unavailable n=?

No Heart Failure n=?
Randomly excluded n=?
Unavailable n=?

B type natriuretic peptide n=12
≥ 18.7 pmol/l n=11
<18.7 pmol/l n=1

≥ 18.7 pmol/l n=50
<18.7 pmol/l n=93

B type natriuretic peptide n=143

Conclusions

- Quality assessment is essential, but exact effects not (yet) known
- The QUADAS tool should be used as a starting point
- Study quality should be incorporated into all reviews
- The quality items and scoring guidelines should be tailored to your review question
- The results of the quality assessment should be presented
- No quality scores and cut-offs for ‘good’ quality