Diagnostic accuracy studies: how to report and analyse inconclusive test results

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In diagnostic accuracy research, test results are typically presented as a dichotomy. However, in many cases, results do not exclusively fall into “positive” and “negative” categories. There is often a subset of results that are relatively uninformative and lead to an “inconclusive” diagnostic outcome. Inconclusive test results are often overlooked in diagnostic accuracy research. Require extra attention from clinicians e.g. repeating the test or using more costly (in terms of invasiveness, time, and expense) diagnostic tools.
Inconsistent Reporting

- STARD statement recommends: “report how indeterminate results, missing responses and outliers of the index tests are handled”
  - Advocates the reporting of “uninterpretable, indeterminate, and intermediate results”

- Explored whether inconclusive results are consistently reported in diagnostic accuracy research

- Searched the literature using the term “STARD” to identify systematic reviews assessing adherence to the STARD statement
Inconsistent Reporting

- Identified 22 systematic reviews comprising 1156 primary diagnostic accuracy studies

- 35% (400/1156) of diagnostic accuracy studies explicitly reported uninterpretable, indeterminate, intermediate, and missing results

- Wide variation in adherence across systematic reviews (range 0-66%), indicating that there was inconsistency in the quality of reporting in different clinical areas and/or the reviewers’ interpretation of the STARD statement
Types of Inconclusive Result

- Missing Results
- Uninterpretable Results
  - Negative Results
  - Valid Inconclusive Results
  - Positive Results
Valid Inconclusive Results

- Depends on the measurement scale of the test
- Report all valid inconclusive results on their original scale (before any grouping of results), broken down by the reference standard

<table>
<thead>
<tr>
<th>Test Result</th>
<th>Disease Status</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Disease Present</td>
</tr>
<tr>
<td>Positive</td>
<td>True Positive</td>
</tr>
<tr>
<td>Valid Inconclusive</td>
<td>Disease Present but Valid Inconclusive Result</td>
</tr>
<tr>
<td>Negative</td>
<td>False Negative</td>
</tr>
</tbody>
</table>
Invalid Inconclusive Results

- Recruitment
  - Missing Results
  - Uninterpretable Results
  - Valid Inconclusive Results
    - Negative Results
    - Positive Results
Invalid Inconclusive Results

- Often not directly related to test accuracy
  - Still an essential consideration in the evaluation of the overall clinical utility of the test
  - Report separately from the cross-tabulation of valid results by disease status

- Consideration of any known underlying causes need to be reported
  - Their presence may be informative
Analysing Inconclusive results

• No single ‘optimal’ approach
  • Diagnostic accuracy should always be analysed in line with how the test will be used in clinical practice

• Reviewed options:
  • Exclude
  • Exclude but report any additional summary statistic that accounts for them
  • Group with the positive or negative categories

• If valid inconclusive results are excluded from analyses (rarely justifiable), accuracy statistics should be reported when the inconclusive results are included as a secondary (sensitivity) analysis
Conclusion

• Reporting and analysis of inconclusive test results neglected in diagnostic accuracy studies

• Clearly report all inconclusive results, broken down by the reference standard when possible

• Complete transparency regarding the handling of inconclusive results in the analysis phase

• Readers should be able to recalculate key statistics if they disagree with the approach adopted by the author
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