Barriers to Blinding: the feasibility of blinding in test-treatment RCTs

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Types and purpose of blinding

- B1 Blinding of study participants
  - performance bias – account for the placebo effect

- B2 Blinding of healthcare providers
  - performance bias – different co-intervention

- B3 Blinding of outcome assessors
  - ascertainment/detection bias
Treatment RCT

Test-Treat RCT
Can/should blinding be used in test-treat RCTs to control for performance and detection bias?

☐ How frequently do test-treat RCTs attempt blinding?
☐ How often was it possible to blind in these trials?
☐ What determines when blinding is feasible?
☐ What are there adverse effects of blinding?
Methods 1 - Cohort

- Cohort of 103 test-treat RCTs
  - Identified from validated search of CENTRAL 2004–7
  - Diagnosis or staging tests
  - Randomised patients to test-treat strategies
  - Patient outcome measured after treatment phase
Methods 2 – Assessment process

- All trials assessment for use of blinding by two individuals independently in duplicate

- Clinical/methodologist mixed teams assessed trials to develop criteria for feasibility of blinding, sampling until saturation

- Feasibility criteria were applied to cohort by a single reviewer
Methods 3 – Judgements of blinding feasibility

- What processes would need to happen to implement blinding in this trial?
- Would blinding have been feasible or impossible?
  - FEASIBLE: theoretically possible, given limitless resources and finances
  - IMPOSSIBLE: cannot apply methods to ensure masking without changing research question
- Method previously used for non-pharmacological intervention trials (Boutron J Clin Epi 2004;57:543)
Results 1: Blinding rarely attempted

- Patients: 5 RCTs (5%)
- Health care providers: 4 RCTs (4%)
- Outcome assessors: 22 RCTs (21%)

= High risk of performance and ascertainment bias
SPECT MPI vs Exercise ECG for suspected CAD
Adults with chest pain CAD suspected

Gated SPECT myocardial perfusion
- CA or medical Rx
- Discharge

Exercise ECG
- CA or medical Rx
- Discharge

Mortality

Suspected pulmonary embolism

V/Q Scan

7-Variable Clinical Model

<table>
<thead>
<tr>
<th>Predictor Variable</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Signs or Symptoms</td>
<td>3.0</td>
</tr>
<tr>
<td>Alternate Diagnosis Less Likely Than PE</td>
<td>1.5</td>
</tr>
<tr>
<td>Heart Rate &gt;100 Beats/min</td>
<td>1.5</td>
</tr>
<tr>
<td>Previous DVT or PE</td>
<td>1.5</td>
</tr>
<tr>
<td>Major Surgery and immobilization Within 4 wk</td>
<td>1.0</td>
</tr>
<tr>
<td>Major Trauma and immobilization Within 4 wk</td>
<td>1.0</td>
</tr>
</tbody>
</table>

BIOPED rule
Suspected Pulmonary Embolism

- **BIOPED**
  - **R**
    - **BIOPED**
      - **R**
        - **V/Q Scan**
          - **Anticoag**
        - **No Rx**
        - **Sham V/Q**
          - **No Rx**
        - **V/Q Scan**
          - **Anticoag**
          - **No Rx**

Recurrence of venous thromboembolism

Results 1: Blinding methods used

Patients
» receiving all tests randomising which result is revealed
» sham testing
» selection of *in vivo* test made in laboratory

Healthcare providers
» standardised reports of test results
» sham reports of test results
» 3rd party diagnostic decision–making

Outcome assessors
» independent expert panels
» clinicians not involved in patient care
» research staff
Results 2: Blinding often impossible

No blinding of any sort possible in 22–28% of trials
Results 3: Barriers to blinding patients

- Factors that prevent blinding -
  - Results interpreted in real-time
  - Tests undertaken at different time-points
  - Procedures with high or differing risks of harm
  - Patient response part of test
  - Tests given in different care settings
  - ‘Test’ and ‘Treat’ in same procedure
Barriers to blinding healthcare providers

- Multiple factors inhibit ability to standardise test results or disguise test identity
  - As above plus
  - Tests that measure different physiological processes
  - Tests that give additional information to comparator test
  - Triage test strategies
  - Test vs No Test comparisons
Barriers to blinding outcome assessors

- Depends on outcome
  - Patient reported outcomes can only be blind when the patient is blind
  - Clinical reported outcomes can only be blind with the healthcare providers are blind
  - Process of care outcomes may be assessed blind but are of dubious value when they have measured unblinded processes
4) Are there adverse effects of blinding?

- Processes used to create blinding may create unrepresentative effects
- e.g.
  - Patients may react unexpectedly to sham procedures
  - Clinical decision–making may differ from blinded decision–making
Isolating the “REAL EFFECT” does not answer the pragmatic question of importance to patients

- “Placebo effects” from testing may lead to real patient benefit – e.g. reassurance, increased compliance with treatment
- “Clinician confidence” in testing impacts on us of additional investigations and speed to commence treatment
Summary of Findings

- Blinding rarely undertaken in RCTs of tests
- Test-treatment RCTs susceptible to performance and ascertainment bias
- Theoretically feasible to blind patients and particularly outcome assessors more frequently
- Blinding healthcare providers often impossible
- Benefits of blinding may be outweighed by the blinding affecting generalisability and masking important impacts of tests on patients
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