Publication writing and real world evidence

Annick Moon
Publication mix

Based on 72 publications from 2004 to 2018
Publication writing

• How does publication writing differ for interventional trials and observational studies?
How to write a publication

1. Write the methods
2. Write the results
3. Write the introduction and the discussion
Interventional trial: clinical study report
# CONSORT methods

<table>
<thead>
<tr>
<th>Methods</th>
<th>3a</th>
<th>3b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial design</td>
<td>Description of trial design (such as parallel, factorial) including allocation ratio</td>
<td>Import changes to methods after trial commencement (such as eligibility criteria), with reasons</td>
</tr>
<tr>
<td>Participants</td>
<td>4a</td>
<td>4b</td>
</tr>
<tr>
<td>Setting and locations where the data were collected</td>
<td>Eligibility criteria for participants</td>
<td></td>
</tr>
<tr>
<td>Interventions</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>The interventions for each group with sufficient details to allow replication, including how and when they were actually administered</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outcomes</td>
<td>6a</td>
<td>6b</td>
</tr>
<tr>
<td>Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed</td>
<td>Any changes to trial outcomes after the trial commenced, with reasons</td>
<td></td>
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Trial design
3a
3b

Participants
4a
4b

Interventions
5

Outcomes
6a
6b
Methods
Design and participants
This was a randomized, double-blind, placebo-controlled study of the efficacy of TIV in prevention of vaccine-matched, culture-confirmed influenza (VMCCI) conducted in the 2005-2006 and 2006-2007 influenza seasons in the US.

The original primary outcome measure defined by the study protocol was the average vaccine efficacy over two consecutive seasons in the prevention of culture-confirmed influenza. In correspondence following the 2005-2006 season, the FDA Center for Biologics Evaluation and Research noted that the season was marked by a significant frequency of circulation of influenza virus strains that were antigenically-drifted from those in the vaccine, and required that the protocol be modified to assess the average efficacy against VMCCI across both seasons as the primary measure of vaccine efficacy.

Male and female volunteers aged 18 to 49 years inclusive were eligible to participate if they were clinically healthy, understood the study procedures, had access to telephone contact throughout study, and provided informed written consent. In Season 1, eligible participants were enrolled at 37 centers, and in Season 2, eligible participants were enrolled at 44 centers.

Exclusion criteria included: a significant acute or chronic, or medical or psychiatric illness requiring institution of new medical or surgical treatment, or a significant alteration of usual medication within the past 30 days. These criteria were as follows:

• Significant acute or chronic, or medical or psychiatric illness requiring institution of new medical or surgical treatment, or a significant alteration of usual medication within the past 30 days.

• Presence of any condition that might place the participant at risk of treatment-related complications during the conduct of the clinical study.

• Presence of any condition that would make it difficult to evaluate the participant for the outcome measures of the study.

• Presence of any condition that would make it difficult to obtain informed consent from the participant or legal guardian.

• Presence of any condition that would make it difficult to administer the correct doses of the investigative or placebo product.

• Presence of any condition that would make it difficult to adhere to the specific protocol requirements of the study.
# CONSORT methods

<table>
<thead>
<tr>
<th>Methods</th>
<th>8a</th>
<th>8b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomisation Sequence generation</td>
<td></td>
<td>Method used to generate the random allocation sequence</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Type of randomisation; details of any restriction (such as blocking and block size)</td>
</tr>
<tr>
<td>Allocation concealment mechanism</td>
<td>9</td>
<td>Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned</td>
</tr>
<tr>
<td>Implementation</td>
<td>10</td>
<td>Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions</td>
</tr>
<tr>
<td>Blinding</td>
<td>11a</td>
<td>If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how</td>
</tr>
<tr>
<td></td>
<td>11b</td>
<td></td>
</tr>
<tr>
<td>Statistical methods</td>
<td>12a</td>
<td>Statistical methods used to compare groups for primary and secondary outcomes</td>
</tr>
<tr>
<td></td>
<td>12b</td>
<td>Methods for additional analyses, such as subgroup analyses and adjusted analyses</td>
</tr>
</tbody>
</table>
Inferential analysis

- Determines if there is a relationship between an intervention and an outcome
- Determines the strength of the relationship

The analysis of the primary end point was done using the closed-test principle. As a first step, a 2-sided Cochran-Mantel-Haenszel test adjusted for the variable pooled center was used for the micafungin dose groups on a significance level of $\alpha = 0.05$ to assess the difference between the dose groups. If the results allowed rejection of the null hypothesis of equality of the proportion $p_x$ of patients with response (for $H_0$, $p_{50\ mg} = p_{100\ mg} = p_{150\ mg}$), then the groups were tested further with pairwise comparisons ($p_{50\ mg} = p_{100\ mg}$, $p_{50\ mg} = p_{150\ mg}$, $p_{100\ mg} = p_{150\ mg}$), each at a significance level of $\alpha = 0.05$, using a 2-sided Cochran-Mantel-Haenszel test adjusted for the variable pooled center.
Descriptive analysis

- Describes the data: mean, median, standard deviation, confidence interval
  - Demographic data
  - Secondary outcomes
  - Safety data
- Occasionally primary outcome analysed descriptively
Observational studies

Registry studies
National disease databases
Surveillance network studies
Medical records
Medical claims databases
Surveys

- Rare genetic disorders
- Surgery
- Transplantation
- Infectious disease
Observational studies

- Varied/new concepts
- Mass of information
## Starting the publication

<table>
<thead>
<tr>
<th>STROBE: Introduction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Background/rationale</strong></td>
</tr>
<tr>
<td><strong>Objective</strong></td>
</tr>
</tbody>
</table>
Don’t be a squid

Clear thoughts = clear writing
Behind the ink

- Researchers/modellers/statisticians have written the methods/report/publication
They see

A clear description of the study using all the special scientific words

You see
What was measured, how was it measured, and how was bias minimised?

1. Outcomes
2. Data sources
3. Statistics: confounders and adjusters
How was bias minimised?

<table>
<thead>
<tr>
<th>STROBE: Methods</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Variables</td>
<td>7</td>
</tr>
<tr>
<td>Clearly define all outcomes, exposures, predictors, <strong>potential confounders, and effect modifiers</strong>. Give diagnostic criteria if applicable.</td>
<td></td>
</tr>
<tr>
<td>Data sources/measurement</td>
<td>8</td>
</tr>
<tr>
<td>For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group.</td>
<td></td>
</tr>
<tr>
<td>Bias</td>
<td>9</td>
</tr>
<tr>
<td>Describe any <strong>efforts to address potential sources of bias</strong></td>
<td></td>
</tr>
<tr>
<td>Study size</td>
<td>10</td>
</tr>
<tr>
<td>Explain how the study size was arrived at.</td>
<td></td>
</tr>
<tr>
<td>Quantitative variables</td>
<td>11</td>
</tr>
<tr>
<td>Explain how quantitative variables were handled in the analyses. If applicable, describe which grouping were chosen and why.</td>
<td></td>
</tr>
<tr>
<td>Statistical methods</td>
<td>12</td>
</tr>
<tr>
<td>(a) Describe all statistical methods, including those <strong>used to control for confounding</strong></td>
<td></td>
</tr>
<tr>
<td>(b) Describe any methods used to examine subgroups and interactions</td>
<td></td>
</tr>
<tr>
<td>(c) Explain how missing data were addressed</td>
<td></td>
</tr>
</tbody>
</table>
| (d) Cohort study  
If applicable, explain how loss to follow-up was addressed  |
| Case-control study — if applicable, explain how matching of cases and controls was addressed  |
| Cross-sectional study – If applicable, describe analytical methods taking into account of sampling strategy  |
| (e) **Describe any sensitivity analyses**  |
Research the statistical methods

- Time series
- Immortal time bias
- Case-negative control
- Case-matched control
Publication development

Draft 1
Methods
Results

Draft 2

Stat

Draft 3
Discussion
Writing the discussion

• Interventional trial
  • Presents the results in context of the literature
  • A paragraph on limitations describes the weaknesses of the study design

• Observational trial
  • Presents the results in context of potential confounders and how bias was addressed
  • Puts results in context of the literature
Thank you