Clinical trials reporting at Nordic medical universities and university hospitals

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Unreported trial results may cause bias.
Reporting of clinical trials

- Necessary for reliable and useful evidence for clinical practice
- An ethical obligation
  - Declaration of Helsinki
  - WHO
- A regulatory obligation
  - Reporting within 12 months for pharmaceutical trials in the EU
Many clinical trials are reported late, incompletely, or not at all

- IntoValue (Germany)
  - Fewer than half had reported results within 2 years
  - A quartered never reported results
  - Improvement over time

Riedel et al. 2022
Systematic follow-up of reporting of Nordic trials

- Eligible trials:
  → registered in EUCTR or clinicaltrials.gov and completed 2016–2019
  → where the sponsor is a university with a medical faculty or a university hospital
- Main outcomes are the proportion of studies reporting results and time to reporting
- Protocol preregistered on the Open Science Framework
Methods

- EUCTR data were retrieved from the EU Clinical Trials Tracker
- For ClinicalTrials.gov, we downloaded the complete Aggregate Analysis of ClinicalTrials.gov dataset (AACT)
- We searched manually for results publications
  → Checking the registry website for publications linked in the registration
  → Google search using the main trial ID
  → Google search using two combinations of terms from the registry, e.g., title, principal investigator name, intervention/treatment, disease/symptoms, or other
### Sample

<table>
<thead>
<tr>
<th>Trial characteristic</th>
<th>Trials</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td>2113</td>
<td>100</td>
</tr>
<tr>
<td><strong>Country</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Denmark</td>
<td>1019</td>
<td>48.2</td>
</tr>
<tr>
<td>Finland</td>
<td>231</td>
<td>10.9</td>
</tr>
<tr>
<td>Iceland</td>
<td>10</td>
<td>0.5</td>
</tr>
<tr>
<td>Norway</td>
<td>328</td>
<td>15.5</td>
</tr>
<tr>
<td>Sweden</td>
<td>525</td>
<td>24.8</td>
</tr>
<tr>
<td><strong>Intervention type</strong></td>
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<td></td>
</tr>
<tr>
<td>Medicinal product</td>
<td>675</td>
<td>31.9</td>
</tr>
<tr>
<td>Not medicinal product</td>
<td>1438</td>
<td>68.1</td>
</tr>
</tbody>
</table>
Studies were heterogeneous
WHO definition of clinical trials is broad

"[...] any research study that prospectively assigns human participants or groups of humans to health-related interventions to evaluate the effects on health outcomes"

https://www.who.int/news-room/questions-and-answers/item/clinical-trials
Time to publication of Nordic clinical trials
Time to publication of Nordic clinical trials

Updating bias
Time to publication of Nordic clinical trials

Never reported
Time to publication of Nordic clinical trials
Time to publication of Nordic clinical trials
Secondary outcomes

- Unreported trials \((n = 471)\) had a median planned sample size of 42 (IQR 75, range 1-15,030), for a total of 82,880 individuals
- 1257/2133 trials (59.5%) were prospectively registered
- Among trials registered at ClinicalTrials.gov likely falling under the requirement for registration in the EUCTR (non-phase-I medicinal product trials), less than two-thirds were found also in the EUCTR (195/333, 58.6%, 95%CI 53.2-63.7%)
Proportion reported by country

Summary results within 1 yr (%)

Published within 2 yrs (%)

Any results reported (%)

Number of trials:

- ○ 10
- ○ 100
- ○ 250
- ○ 500
- ○ 1000
Attrition and biases
Future perspectives

- Open comparisons between sponsors
- Extend follow-up (time, sponsors, registries, types of research)
- Investigate transparency, reproducibility, and accuracy of reporting
- Join efforts with others
IntoValue - Institutions’ contribution to increasing value and reducing waste

Clinical trial dissemination rates of all German university medical centers

The following Shiny app accompanies the two publications on the clinical trial dissemination rates of all German university medical centers and allows to further explore the results. The publications are Result dissemination from clinical trials conducted at German university medical centers was delayed and incomplete’ and ‘Result dissemination from completed clinical trials conducted at German university medical centers: results delayed and incomplete. The 2014-2017 cohort’. You can interactively choose different subsets of the data and different ways of defining timely publication. The results can be displayed both as diagram or in a table (see navigation bar at the top). Additionally, a Kaplan-Meier curve for the percentage of unpublished studies over time can be displayed for different subgroups of the data as well as different stratifying variables. The dataset, analysis code, as well as detailed methods can be found on the OSF project pages for the first and the second study and this Github repository. The combined dataset for both studies can be found here.

What counts as timely publication?
Count summary results
- Publications and Summary results

Count from which completion date
- Completion date

Published within how many month
- 24

Publication identified in which stage
- Full search (incl. Google Scholar)

There are different ways to define what a timely publication is. First, study results can either be posted as summary results on the registry or published in a peer-reviewed journal. Second, there are different dates on which a study could be considered completed: either the primary completion date (when all data for the primary endpoints were collected) or the completion date (last patient last visit). Third, there are different recommendations on how long it should take to make study results available. Note: when different periods are chosen in the “Published within how many month” box, only those trials are considered that were able to track for this period (e.g. 60 months since the completion date). Only exception is the category “Any duration/any follow-up period”, where all trials
Cooperation with institutional stakeholders

- Joint responsibility for improvement
- Important not to single out individual investigators
- Stronger institutional responsibility is needed
- We hope our data will help facilitate work by different stakeholders
Thank you


Cathrine Axfors