Do drug dossiers of pharmaceutical companies provide additional information on study methods compared to journal publications?

Background

- Since the latest health care reform in Germany (2011), pharmaceutical companies have to submit dossiers for early benefit assessments of drugs.

- These dossiers contain tabular descriptions of study methods for relevant RCTs.

- These descriptions of study methods have to adhere to CONSORT, including items 2b to 14b with a mandatory participant flow diagram.

- CONSORT is the standard of reporting in many medical journals.
Objective

- To evaluate to what extent tabular descriptions in drug dossiers contain additional CONSORT-relevant information on study methods compared to journal publications
- To investigate the effect of the CONSORT endorsement status of journals
- To examine the effect of journal publications’ supplementary study information (protocol / SAP)
Methods: selection criteria

- **Studies:**
  - The first 10 drug dossiers
  - RCTs with the new drug (i.e. tabular description available)
  - Clinical study report available

- **Journal publications:**
  - RCT-publications that were cited by the company
  - Primary publication, including supplementary materials (e.g. webappendix) and other journal publications cited by the primary publication for details on study methods.
Methods: assessment

- Two reviewers independently assessed additional relevant information in the tabular descriptions compared to publications, for individual CONSORT items 2b to 14b.

- Information in the tabular description was categorized on the basis of the CONSORT requirements as:
  1. **Fully new** information (*without* any information in the publication)
  2. **Partially new** information (*with* some information in the publication)
  3. **No new** information (independent of information in the publication)
Methods: analysis

- Analysis of all assessed CONSORT items (2b to 14b)
  - Introduction: objectives or hypotheses (2b)
  - Methods: trial design (3a, 3b), participants (4a, 4b), interventions (5), outcomes (6a, 6b), sample size (7a, 7b), randomisation (8a, 8b, 9, 10), blinding (11a, 11b), statistical methods (12a, 12b)
  - Results: participant flow (13a, 13b), recruitment (14a, 14b)

- Calculation of additional information per study:
  - Percentage of items with new information

- Characterization of individual CONSORT items:
  - Percentage of studies with new information
Results

10 drug dossiers

selection of RCTs:
- RCTs with the new drug
- RCTs the company included in the benefit assessment

27 studies
with dossier tabular description

selection of journal publications:
- publications the company cited in the dossier
- only the primary publication of the study

study without journal publication:
1218.50-study (Linagliptin)

26 studies with tabular description and journal publication
Journal Publications (1)

- New England Journal of Medicine 13 studies (50%)
- Journal of Hand Surgery (am. vol.) 4 studies (15%)
- Neurology 3 studies (11%)
- Lancet 2 studies (8%)
- Diabetic Medicine 1 study
- Diabetes, Obesity & Metabolism 1 study
- Gastroenterology 1 study
- Journal of Hepatology 1 study
Journal Publications (2)

- Endorsement of CONSORT: 20 publications (77%)
  - general medical journals: 15 publications (100%)
  - specific medical journals: 5 publications (46%)

- Supplementary webappendix: 18 publications (70%)
  - general medical journals: 13 publications (87%)
  - specific medical journals: 5 publications (46%)

- Supplementary protocol and SAP: 6 publications (23%)
  - general medical journals: 6 publications (40%)
  - specific medical journals: 0 publications (0%)

- 1 publication cited another paper for details on study methods.
Result (a): additional information per study

The tabular descriptions provided additional information in 40% of the items, of which 13% (~3 items) reported fully new information and 27% (~6 items) reported partially new information.
In 50 % of all assessed items (11/22), at least 50 % of the studies provided additional information in the tabular descriptions.
Result (b): Effect of CONSORT endorsement status

The tabular descriptions provided more fully new information (25% vs. 10%) for studies published in journals that do not endorse CONSORT.
studies published in journals that endorse CONSORT (n = 20)

studies published in journals that do not endorse CONSORT (n = 6)
Result (c): Effect of supplementary protocol / SAP

Percentage of items with no, partially or fully new information for studies published in the "New England Journal of Medicine" with or without a supplementary protocol / SAP

The tabular descriptions provided more additional information for studies published without a supplementary study protocol in the same journal (New England Journal of Medicine).
Studies published in the NEJM *with* supplementary study protocol / SAP (n = 6)

Studies published in the NEJM *without* supplementary study protocol / SAP (n = 7)
Summary & Conclusions

- The tabular descriptions in drug dossiers provide additional information on study methods compared to publications.
  - Additional information on study methods is publicly available soon after the introduction of new drugs into the German health care market.

- The effect is stronger for studies published in journals that do not endorse the CONSORT statement.
  - CONSORT-statement improves reporting quality of journal publications

- The effect is stronger for studies published without a supplementary study protocol / SAP in the NEJM
  - Journals should request the submission of study protocols as a compulsory prerequisite for accepting a manuscript for publication
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