Selective Reporting in epidemiology studies on phthalates
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Presentation Outline

• Background

• The project

• Results

• Interpretation
Background

- Recent studies reported new health effects from phased out chemicals (e.g. pesticides and endocrine disruptors)

- Studies typically reported weak associations, multiple associations per study, changing confounders, use existing databases and appear to lack a specific a priori hypothesis
(Outcome) Reporting Bias

• Evidence in clinical trials shows: positive results are overreported and positive secondary outcomes are presented as the primary effect

• How about observational studies?

• Conduct an “Outcome Reporting Bias” study (meta research)

• ECPI (European Council of Plasticizers and Intermediates) funded the project
The project

- Basic design: compare protocols with publications

- Retrospective study design: we started with a set of publications

- **Specific objectives:**
  1. assess completeness of reporting
  2. assess the quality of the underlying study protocols
  3. assess the concordance between the published articles and the underlying protocols
  4. assess the determinants of protocol provision
The project

- **Simple approach**: Compare the published results with the research questions and aims in the underlying study protocols

- **Study design**:
  1. Select a topic: ‘phthalate exposure and health’
  2. Contact the corresponding author, invite him/her for a short interview and ask a copy of the study protocol
  3. Compare the journal article with the protocol
  4. Investigate which factors influence participation in our study (determinants of transparency)
Project preparations

• First we prepared a detailed protocol ourselves, with input from three external experts and registered it with PROSPERO and on our website

• Recommendation: Follow the Systematic Review methodology
Project steps

1. Conduct a systematic literature search on phthalate epidemiology studies (N=158)

2. Score study characteristics and retrieve contact info of the corresponding author

3. Invite the corresponding authors for a short telephone interview and request a copy of the protocol

4. Conduct telephone interviews

5. Conduct quality checks on the protocols

6. Analyse the collected data

7. Prepare a report and publish it

8. Archive the project and its data via dataverse
Data collection

- **158 journal articles** on phthalates and health parameters found (PubMed, reference lists and consulting ECPI)
- Study characteristics were scored (design, outcome, n associations examined etc)

- All 158 corresponding authors contacted via e-mail + reminder, including 2 telephone attempts
- A copy of the **protocol was requested** and participating corresponding authors were **interviewed**
- Interviews recorded and transcribed
Characteristics of 158 phthalates papers

- Wide range of health outcomes, from sperm counts to breast cancer and ADHD

- On average 50 associations tested per article of which 8 statistically significantly positive

- 56% of the studies on already existing or partly existing data

- 46% cross-sectional research design

- 72% only 1 exposure measurement
### Response rates for interview invitation

<table>
<thead>
<tr>
<th>No response at all</th>
<th>45 (29%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refuses participation</td>
<td>66 (42%)</td>
</tr>
<tr>
<td>No reason given</td>
<td>9</td>
</tr>
<tr>
<td>Too busy</td>
<td>9</td>
</tr>
<tr>
<td>Objections to our methods</td>
<td>4</td>
</tr>
<tr>
<td>Sees Conflict of interest</td>
<td>2</td>
</tr>
<tr>
<td>Both the above</td>
<td>31</td>
</tr>
<tr>
<td>All information given in publication</td>
<td>4</td>
</tr>
<tr>
<td>Participated for other article</td>
<td>2</td>
</tr>
<tr>
<td>Other reason + protocol confidential</td>
<td>5</td>
</tr>
<tr>
<td>Intends to participate</td>
<td>47 (30%)</td>
</tr>
<tr>
<td>Total</td>
<td>158 (100%)</td>
</tr>
</tbody>
</table>
Response to protocol request after initial consent to participate

<table>
<thead>
<tr>
<th>Response Description</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admitted not having a protocol</td>
<td>16</td>
<td>(34%)</td>
</tr>
<tr>
<td>No further response</td>
<td>8</td>
<td>(17%)</td>
</tr>
<tr>
<td>Withdrawal after interview</td>
<td>1</td>
<td>(2%)</td>
</tr>
<tr>
<td>Complete participation</td>
<td>22</td>
<td>(47%)</td>
</tr>
<tr>
<td>Total</td>
<td>47</td>
<td>(100%)</td>
</tr>
</tbody>
</table>
Quality of the received protocols (N=22)

• Because of lacking details, quality cannot be evaluated

• 2 of the 22 protocols provided a reasonable description of the study reported in the subsequent article

• 2 “protocols” written after study was completed
Protocol provision?

Of the 43 journal articles for which it could be established whether a protocol was present, 16 had none and 3 were lost.
Determinants of protocol provision

• Authors reporting a positive study were three times less likely to participate (OR=0.31 95% CI:0.11-0.86)

• Authors using NHANES data were statistically significantly less likely to provide a study protocol (OR=0.83 95% CI:0.77-0.90)
Further observations

- Articles mention received grants, but these grants do not imply that a protocol existed

- Sample size and potential confounders not reported in protocol

- Some occasions with good internal control and review, when e.g. large cohort studies were requested to use their data

- Two occasions where authors’ refusals were surprisingly similar

- Some clear evidence of Outcome Reporting Bias. Eg started with POPs with null findings, then pesticides with null findings and then moved on to the phthalates
Summary by study objective:

1. Assess **completeness** of reporting: Not feasible, participation too low, but some interviews clearly indicated selective reporting

2. The **quality** of the study protocols: Disappointing. Only 2 of the 22 protocols were sufficiently detailed for an assessment

3. **Concordance** between the protocol and the published article: Not feasible because of lack of detail in the majority of the protocols

4. Determinants of **protocol provision**: Authors reporting a positive outcome were 3 times **less** likely to provide their protocol
Interpretation

- A substantial proportion of observational studies on phthalates is not protocolled

- When there is a protocol it often lacks detail

- This body of literature is unsuited for a Systematic Review: the quality cannot be guaranteed

- Structural improvements of the research process are needed: Responsible Epidemiologic Research Practice (RERP) demanding transparency and accountability
Thank You

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