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Rapid report

Outcome reporting bias in observational epidemiology studies on phthalates

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Introduction

Phthalates are used in cosmetics, flooring adhesives, medical tubings, toys, food packaging materials, and so forth. A number of reviews of the epidemiology on phthalates have been published with conflicting results [1–10]. As also noted by previous reviewers, the phthalate epidemiology literature is very diverse [9]. It covers a wide range of health outcomes, and a range of research designs are used. In such instances, it is essential to know what the investigators had in mind when conducting the study, that is, what was stated in the research protocol. We therefore contacted all corresponding authors and invited them to participate in a short and confidential interview and asked for a copy of the protocol. Our study had the following specific aims: (1) assess the completeness of reporting, (2) assess the quality of the underlying study protocols, (3) assess the concordance between the published articles and the underlying protocols, and (4) assess the determinants of protocol provision. We registered our study protocol at the PROSPERO website (registration number CRD42015016017) at http://www.crd.york.ac.uk/PROSPERO, and our protocol was placed on the website of our department. The protocol describes the research methods that we applied, including how the corresponding authors were contacted interviewed and requested for a copy of the protocol. It also provided the scoring sheet and the criteria for assessing the received protocols.

Methods

The literature search yielded 158 journal articles on epidemiology studies on phthalates (see supplementary material). Study methodology characteristics and study outcome were independently scored by G.M.H.S. and M.J.E.U. individually and compared and finalized. Via an e-mail message and reminder, the corresponding authors were invited to participate in a telephone interview. The survey covered the study objective, study population, exposure measurement, health outcome parameter, the statistical analysis, and some items about the corresponding author's career and working environment. If no reply was received, they were contacted by telephone. If the author consented a copy of the project proposal, analytical description, grant submission, protocol, project description or ethical committee review submission, all designated here as "study protocol" was requested. The interviews were conducted by GS and MU was present. The telephone interview was pretested on five unrelated publications and their corresponding authors.

Results

With 45 (28.5%) of the 158 corresponding authors, it was not possible to establish any contact, despite multiple attempts via

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telephone and two e-mail invitations. With 113 corresponding authors, either a telephone conversation or a meaningful e-mail exchange was established (see Table 1).

Initially, 47 corresponding authors agreed to be interviewed. However, after having been requested a copy of the protocol, 16 corresponding authors indicated that they did not have a protocol or could not send a copy. Eight corresponding authors did not reply to our request for the protocol after having consented to participate. Twenty-three corresponding authors were interviewed and were willing to share their protocol. One corresponding author of the 23 withdrew from our project after having been interviewed. These data were excluded from our analysis.

For 43 publications, we received information whether a protocol was present. For 22 of these, a protocol was provided to us. Sixteen of the 43 stated that they did not have a protocol, of which three had been lost. Corresponding authors reporting positive associations ($n = 134$ of 158 positive studies according to the authors) between phthalates and health outcomes (based on the authors' own conclusions) were three times less likely to provide a copy of their protocol (odds ratio = 0.31; 95% CI, 0.11–0.86). Associations between other study characteristics and protocol provision, such as year of publication, affiliation, funding source, and number of associations tested, were not statistically significant. An explorative analysis not foreseen in our study protocol showed that corresponding authors of publications based on NHANES data were also less likely to provide their protocols (odds ratio = 0.83; 95% CI, 0.77–0.90, 23 of 158 studies were based on NHANES data).

Overall, we assessed 20 of 22 protocols as having insufficient detail to adequately describe the project. These lacked descriptions of the study population to be selected, how exposure would be measured (13 of 22), what type of statistical analysis would be done (11 of 22), and how confounding factors would be selected and treated (17 of 22), and in most instance combinations of these. Several protocols did not even mention phthalates as exposure variable, but only mentioned wide terms as environmental contaminant or exposure to environmental chemicals. Rule of thumb in the assessment was whether the protocol provided sufficient detail to get an understanding of how the study was conducted. Given this general lack of detail, we refrained from testing our third research aim: assessing concordance between the study protocol and publication.

Table 1
Participation of corresponding authors in the interview and protocol provision of the 158 included observational studies on phthalates

Participation status corresponding author	*N* (%)
No contact established	45 (28.5)
Refused all combined	66 (41.8)
without providing a reason	9 (5.6)
Too busy	9 (5.6)
Had methodological objections to our study	4 (2.5)
Saw conflict of interest in our study	2 (1.3)
Had both methodological objections and saw conflict of interest	31 (19.6)
Stated all information was in the publication	4 (2.5)
Had already been interviewed for earlier publication	2 (1.3)
Other reason including that the protocol was confidential	5 (3.2)
Agreed to participate in the interview	47 (29.7)
But had no protocol	16 (10.1)
First agreed to participate but no response after request for protocol	8 (5.1)
Full participation but later withdrawal because interviewed author did not feel comfortable	1 (0.6)
Full participation	22 (13.9)
Total	158 (100.0)

Discussion

We studied 158 observational epidemiology studies on phthalates with the four following research aims: (1) assess completeness of reporting, (2) assess the quality of the underlying protocols, (3) assess concordance between the published articles and the underlying protocols, and (4) assess the determinants of protocol provision.

Our study yielded insight in determinants of protocol provision. Corresponding authors of publications reporting a positive association study outcome were about three times less likely to participate in our study, which was statistically significant.

To our knowledge, this is the first study on observational epidemiology research in which corresponding authors were requested to provide their protocol and participate in a survey on how the research was conducted. In the field of clinical trials, some studies have been conducted with similar methodologies. Chan conducted two studies in which trialists were surveyed [11,12]. Both studies provided evidence of selective reporting in clinical trials. Similarly, Smyth et al. [13] contacted corresponding authors of 268 clinical trials and also found evidence of selective reporting. Recently, a series of articles were published on increasing the value and reducing waste in biomedical research [14]. In one of these articles, a strong recommendation was made to make publicly available full protocols, analysis plans, and raw data [15]. Our study underpins the need for these changes. After the field of clinical trials, we recommend observational epidemiology studies to be based on a detailed and publicly available. Increased transparency in observational epidemiology studies will contribute to the still high credibility of this type of research. It will also facilitate detecting outcome reporting bias provided protocols contain sufficient detail. Writing a study protocol and setting up a process of good project documentation and archiving are a part of responsible research conduct, and it is clear that this will require time and effort. Given the selective participation, the limited number of provided protocols, and the large portion of studies conducted without a protocol, we hesitate to use this literature as a reliable basis for a formal systematic review. Our study could enhance awareness for the need of responsible research conduct in observational epidemiology studies, similar to the clinical trials area and stimulate the discussion about the need of protocoled research in our field as well.

Role of sponsor

ECPI did not influence the development of our research protocol, neither did they influence its publication. ECPI periodically requested progress reports on the project. It had no influence on the article or its submission.

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