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Review

A decade of individual participant data meta-analyses: A review of current practice

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ABSTRACT

Introduction: Individual participant data (IPD) systematic reviews and meta-analyses are often considered to be the gold standard for meta-analysis. In the ten years since the first review into the methodology and reporting practice of IPD reviews was published much has changed in the field. This paper investigates current reporting and statistical practice in IPD systematic reviews.
Methods: A systematic review was performed to identify systematic reviews that collected and analysed IPD. Data were extracted from each included publication on a variety of issues related to the reporting of IPD review process, and the statistical methods used.
Results: There has been considerable growth in the use of "one-stage" methods to perform IPD meta-analyses. The majority of reviews consider at least one covariate other than the primary intervention, either using subgroup analysis or including covariates in one-stage regression models. Random-effects analyses, however, are not often used.
Reporting of review methods was often limited, with few reviews presenting a risk-of-bias assessment. Details on issues specific to the use of IPD were little reported, including how IPD were obtained; how data was managed and checked for consistency and errors; and for how many studies and participants IPD were sought and obtained.
Conclusion: While the last ten years have seen substantial changes in how IPD meta-analyses are performed there remains considerable scope for improving the quality of reporting for both the process of IPD systematic reviews, and the statistical methods employed in them. It is to be hoped that the publication of the PRISMA-IPD guidelines specific to IPD reviews will improve reporting in this area.

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Contents

1. Introduction

The aim of individual participant data (IPD) systematic reviews and meta-analyses is to obtain all the original, raw participant data from all studies on a specified topic, in order to reanalyse the data and pool it across studies. While obtaining all the original data from all relevant

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studies may be time consuming and difficult, IPD meta-analysis is recognised as having many advantages over meta-analysis based on data reported in publications, and is considered the "gold standard" for meta-analysis [1–3].

Ten years ago the first review of the practice and reporting of individual participant data meta-analyses was published in Clinical Trials [4]. At that time IPD meta-analysis was still in its early stages with numbers of publications being limited before the late 1990s. The development of statistical methods in the area was also in its infancy, with key methods papers having been published only a few years before [5–7]. The review found that reporting of the processes of IPD meta-analyses was generally poor, particularly with regard to how much of the total IPD was obtained for analysis, and with poor reporting of statistical methods. Statistical analysis was also limited, with little investigation of heterogeneity, and most meta-analyses focussing on calculating overall treatment effects, with little consideration given to subgroup analyses, or how factors such as a participant's age might modify the effectiveness of a treatment. Another review performed in 2008 and published in 2010 [8] came to broadly similar conclusions.

In the ten years since that first review was published much has changed. The number of systematic reviews and meta-analyses published continues to grow, and consequently IPD meta-analysis has also grown in popularity. Advances in computing have also made meta-analyses easier to perform; most methods for IPD meta-analysis can now be implemented in all major statistical software packages. As the number of IPD meta-analyses grows there is an increased need to ensure high quality of conduct reporting of these analyses, to avoid some of the problems identified in the original review.

The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement [9] is widely used as guidance on how to report a systematic review and meta-analysis. Recently a new PRISMA-IPD statement has been released specifically to guide the conduct and reporting of IPD reviews and meta-analyses [10]. As part of the process of creating this statement, a review of current practice in reporting of IPD reviews was conducted to identify areas where reporting was poor to inform development of the guidance. This paper presents the results of this review, updated to 2014, and expanded to consider statistical methods used in IPD meta-analyses.

2. Methods

The aim of this review was to identify published systematic reviews of medical interventions that sought to obtain and meta-analyse IPD. It was intended to obtain a representative sample of recent reviews for analysis, rather than find all such reviews, so an exhaustive database search was not performed. A MEDLINE search was performed including terms "individual participant/patient data", "meta-analysis" and "systematic review". This search was originally performed in January 2013 and was updated in February 2015. Papers published from 2008 (when the previous review in this field by Riley et al. was performed (8)) up to the end of 2014 were sought.

Only systematic reviews of IPD were included, so we did not include "opportunistic" analyses (where the reviewers combined data to which they had access) or collaborative reviews (where data from several collaborators was combined without performing a formal systematic review). Other reasons for exclusion were: papers that did not consider a medical treatment (e.g. epidemiologic reviews of the causes of a disease, diagnostic test accuracy reviews and reviews of disease prognosis), and papers not published in English. One reviewer reviewed titles and abstracts. For those considered potentially eligible the full text was sought. Where full text could be obtained the paper was further checked for eligibility.

For all eligible papers one reviewer extracted a range of data covering the reporting of the review (such as reporting of medical field, numbers of included studies, whether quality assessment was performed); the statistical methods used (such as outcomes considered, whether one or two stage methods were used, descriptions of methods, and assessment of heterogeneity); reporting of results (how many outcomes reported, how many were statistically significant, reporting of subgroup analyses or meta-regression, use of forest plots). The data extracted from the publications was analysed by creating suitable summary tables and graphs.

3. Results

The original and updated search together identified 1371 potentially relevant records. After checking titles and abstracts 184 papers were considered for inclusion. After obtaining full texts (where readily available) and further checking, 100 systematic reviews of IPD were included in this review [11–110]. Because a specific rather than a sensitive search was used, and because we include only systematic reviews, these represent only a minority of all IPD meta-analyses performed. For comparison, in 2014 there were 68 references that matched "Individual participant/patient data meta-analysis" in MEDLINE, not all of which will be IPD meta-analyses. These remain a small minority of meta-analyses as a whole; 6020 papers were tagged as meta-analyses in MEDLINE in 2014.

In the sample considered here, the numbers of reviews per year varied from 10 to 22, but there was no evidence of a trend over time, suggesting that the use of IPD analysis has stabilised in recent years. Fig. 1 shows the medical field in which the reviews were conducted. As in the review published in 2005, cancer and cardiovascular disease predominate. IPD methods appear to be gaining popularity in other fields such as paediatrics and mental health, but numbers remain small. Fig. 2a shows the number of studies for which IPD was obtained, and Fig. 2b the total number of participants providing IPD, across the reviews. Sizes vary considerably from two studies to 78 (median 8), and from 64 to 70,528 participants (median 1879).

4. Quality of reporting

The included reviews varied considerably in how they reported aspects of the review process, such as the search strategy, and quality assessment process. The numbers of reviews reporting key aspects of the IPD review process are summarised in Table 1. In general, aspects of the review process common to all systematic reviews were well reported, with, for example, 80% of reviews reporting details of the search strategy and search process. Inclusion and exclusion criteria were also generally clearly described. One area that was not widely reported was risk-of-bias or study quality assessments, despite this being a component included in the PRISMA statement. Only 34% of reviews reported performing any risk-of-bias assessment, and only 65% (22 of 34) of those reported the findings of the assessment in any detail.

Aspects of reporting specific to IPD reviews were generally rather poorly reported. Only 48% of reviews explained why an IPD review was performed, rather than a review based on published data. Only 52% described how the IPD was obtained, and for most that did it was described simply as "by contacting the study authors" or with a similar phrase. Only 33% of reviews reported that any checking of the IPD was performed to ensure consistency or identify data errors. Just 23% of reviews described why IPD was unavailable where they could not obtain IPD from all relevant studies. The most common reasons given were inability to contact authors, non-cooperation of study authors, and loss of original data.

One aspect of IPD reviews identified as being particularly poorly reported in the 2005 paper was the numbers of studies and participants from which IPD was sought, but not necessarily obtained. As in 2005 this still appears to be poorly reported: 24% of reviews did not report how many studies were sought, and 56% did not report the total number of participants sought. Of those that did report these data, most reported that they obtained all the studies (45% of such reviews) and/or all participants (58%).

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