Guidance on the use of IPD in systematic reviews

Establishing the state of the art to strengthen the role of evidence synthesis in clinical trials

Background

The conduct of individual participant data (IPD) meta-analyses has increased over time and their use has extended across a wide range of healthcare areas and to different study designs. Specific IPD meta-analyses have impacted on policy, practice, and research, and because they can provide a greater depth of understanding than standard systematic reviews, they have the potential to far better inform the design, conduct, analysis and interpretation of trials.

Current guidance on IPD meta-analyses doesn't adequately address the range of uses of IPD or the needs of stakeholders, other than the researchers who might do the systematic reviews. This can make it difficult for users, such as practitioners and patients, journals editors and referees, guideline developers and the public to identify the most robust evidence. It can also hinder attempts by those conducting PD meta-analyses to access funding, disseminate their reviews and influence clinical practice.

Aims

We aimed to provide improved guidance on IPD meta-analysis, through a series of papers in one or more high impact, open access journals, in order to provide a free and easily accessible resource for a range of audiences, in particular:

Clinical trialists:

1. To help them strengthen the design, conduct, analysis and interpretation of their trials
2. To help them understand the rationale, advantages, disadvantages and process of the IPD approach, should they be asked to contribute their data

Other stakeholders:

1. To help them appraise, interpret or conduct IPD meta-analyses
3. To raise awareness of recent methodological developments

Achievements to date

Workshop of IPD experts

In September 2012, we held a one-day workshop of IPD experts at the MRC Clinical Trials Unit in London. Drawing on members of the Cochrane IPD Meta-analysis Methods Group (4 of the applicants are the co-conveners of the Group), and individual Hubs, we used the workshop to discuss key IPD topics; start to define the content of the guidance papers and to establish writing committees. The writing committees have been developing five manuscripts, which will be published on behalf of the Cochrane IPD Meta-analysis Methods Group, with due acknowledgement of Hub Network funding.

Manuscript on the impact of IPD meta-analysis on trial design and conduct

With their higher quality data, more detailed analyses and collaborative approach, IPD meta-analyses have greater potential to influence the design, conduct, analysis and interpretation of trials than standard systematic reviews. We used the workshop to start to gather potential examples of impact, checking and adding to these via a small writing committee. The manuscript describes how IPD meta-analyses have impacted on trial design and conduct, highlighting where IPD is particularly advantageous, and also where potential opportunities are being missed. The penultimate draft will be circulated to the writing committee in February 2014.

Manuscript on the appraisal of IPD meta-analyses of randomised controlled trial (RCTs)

Despite being coined the 'gold standard' method for systematic reviews, not all IPD meta-analyses are done to the same standard, and because the process of collecting, checking and analysing IPD is generally more complex than for aggregate data, judging their quality is not straightforward. This manuscript provides step-by-step guidance on appraising the design and conduct of IPD meta-analyses. This should help trialists who are considering participating in an IPD meta-analysis to understand the sort of standards to expect, and ensure that users can recognise the most robust evidence about the effects of interventions. This manuscript was submitted to Plos Medicine in December 2013.

Manuscript on the appraisal of IPD meta-analyses of study designs other than RCTS

IPD are now being collected for systematic reviews of prognostic/diagnostic studies, as well as randomised trials, and offer particular advantages in this context, but the methodology is still developing. This manuscript will offer guidance on the different or additional issues that need to be considered when appraising such IPD meta-analyses, compared to those based on trials. The manuscript is currently being drafted.

Manuscript on the impact of IPD reviews on guidelines

As they often provide better quality evidence than standard reviews (for example, by including data on unpublished trials or outcomes and analyses of the effects in particular subgroups of participants), IPD meta-analyses would be expected to have a substantial influence on clinical practice guidelines. The manuscript describes an empirical study on the uptake of a cohort of IPD meta-analyses in related practice guidelines and suggests that IPD meta-analyses are sometimes under-utilised, and not necessarily preferred over standard systematic reviews. The manuscript also provides guidance on how this situation could be improved. The penultimate draft was circulated to the writing committee in December 2013.

Manuscript on the ethical considerations and issues for IPD reviews

Sharing data for IPD meta-analyses raises ethical uses for both trialists and those conducting IPD-meta-analyses. The writing committee has surveyed the Cochrane IPD Meta-analysis Methods Group to identify key ethical questions. These form the basis of the manuscript, which is currently being drafted currently and might include information on examples of data sharing agreements that have been used in IPD meta-analyses.

Dissemination of guidance

Although not all of the manuscripts have been completed and published, Plos Medicine has recently expressed increased interest in all the topics, and is considering their suitability for a special collection (pending peer review and acceptance of each article). They have suggested that a group of IPD papers in a single open access location would have greater impact than a series of apparently independent papers published in isolation, and we are actively exploring the possibility of such a special collection. However, any manuscripts not accepted for publication in Plos Medicine would be submitted to other general medical journals to ensure wide readership. We have also used some of the funds to begin dissemination of the guidance in 2013, through:

- Impact of IPD meta-analyses on trials: Oral presentations at the Hub Network Annual Meeting in Oxford (April 2013) and the 2nd Clinical Trials Methodology Conference in Edinburgh (November 2013)
- Impact of IPD meta-analysis on guidelines: Oral presentation at the 21st Cochrane Colloquium in Quebec City (September 2013) and Poster Presentation at the 2nd Clinical Trials Methodology Conference in Edinburgh (November 2013)
- Appraisal of IPD meta-analysis: Workshop at the 21st Cochrane Colloquium in Quebec City (September 2013)

Future plans

A related paper providing an extension to the PRISMA reporting guidelines for systematic reviews (PRISMA-IPD) will be submitted to Plos Medicine in February 2014, as part of the collection. Furthermore, all the papers will add considerably to the revised IPD chapter for the new version of the Cochrane Handbook for Systematic Reviews of Interventions.