Is it getting easier to access individual participant data for secondary research? A systematic review of individual participant data meta-analyses

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Is it getting easier to access individual participant data for secondary research? A systematic review of individual participant data meta-analyses

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Abstract:

Objective: To investigate whether the success rate of retrieving individual participant data (IPD) for the purpose of IPD meta-analysis (IPDMA) has increased over time, and explore characteristics associated with IPD retrieval.

Design: Systematic review of published IPDMA, supplemented by a reflection of the Cochrane Epilepsy Group's 20 years of experience in requesting IPD

Data sources: Eligible IPDMA were identified from a systematic search of MEDLINE, Central, SCOPUS, Web of Science, CINAHL Plus and PsycINFO up to August 2015

Eligibility criteria for selecting studies: IPDMA of studies of all designs and all clinical areas published in English

Results: 760 IPDMA which identified studies via systematic methods published between 1987 and 2015 were included. Only a quarter of these IPDMA retrieved 100% of the eligible IPD for analysis

with a half of all IPDMA retrieving less than 80% of relevant IPD. There is insufficient evidence to suggest that IPD retrieval rates have improved over time. IPDMAs that included only randomised trials, had an authorship policy, included fewer eligible participants and were conducted outside of the Cochrane Database of Systematic reviews, were associated with a high or complete IPD retrieval rate. There was no association between the source of funding of the IPDMA and IPD retrieval rate. The IPD retrieval rate of the Cochrane Epilepsy Group has declined from 83% (up to 2005) to 65% (between 2012 and 2015) and reported reasons for lack of data availability have changed in recent years.

Conclusions: IPDMA are considered to be the 'gold-standard' approach to synthesise data from clinical research studies, however only one in four published IPDMA have had access to all IPD. It is hoped that the growing awareness of data sharing and transparency will improve this proportion in future years.

What is known on this subject?

- Individual participant data meta-analysis (IPDMA) is widely regarded as the gold standard approach to the synthesis of clinical research study data but are susceptible to bias if only a proportion of IPD is available for analysis
- IPDMA are often poorly reported in terms of proportion of IPD for retrieved and reasons for non-availability of IPD
- Recent years have seen a shift in attitudes and awareness towards data sharing. Improved access to IPD should therefore which could improve the proportion of IPD retrieved in an IPDMA

What this study adds:

- This systematic review of 760 IPDMA published between 1987 and 2015 showed that one in four IPDMA retrieved 100% of the eligible IPD for analysis, but half retrieved less than 80%.
- Despite the significant drive towards improving access to clinical research data, the IPD retrieval rate across 760 published IPDMAs has not improved over time.
- IPDMAs that included randomised trials only, contained fewer eligible participants, used an authorship policy and were conducted outside of a Cochrane Review, were associated with a higher IPD retrieval rate.

Introduction

Systematic reviews are considered to be the highest level of evidence in many contexts of medicine[1] and individual participant data (IPD) meta-analysis is widely regarded as the gold standard approach to the synthesis of clinical trial data with many documented advantages over traditional aggregate data (AD) meta-analysis.[2-7] Recent years have shown a sharp increase in the number of published IPD meta-analyses (IPDMA),[8-10] with an average of 49 published per year between 2005 and 2009[9] and an estimated increase of around 4 published IPDMA per year.[10] IPDMA have been shown recently to directly influence the design and conduct of clinical trials[11] and clinical practice guidelines.[12]

While an IPDMA may offer many advantages it is well recognised that greater resources are required to conduct them[5-7] and they are subject to a risk of selection bias and 'availability bias;' in that they may only include studies for which IPD is made available, which may not be representative of the whole evidence base. [13 14] Lack of transparent processes and barriers to accessing IPD may also substantially delay projects or even prevent the completion of planned IPD analyses.[15-18] Review articles have shown that around a quarter of IPDMA published up to 2001,[19] up to 2005[13] and even as recently as 2012[10] obtained IPD for less than 80% of eligible participants. These reviews also reveal poor reporting particularly in regard to the amount of included IPD, with between 10 and 20% of IPDMA not clearly stating how many studies and participants were eligible, requested and included in analysis.[8 10 13 19] The most recent of these reviews found that reasons for unavailability of IPD were reported in only 23% of a sample of 100 IPDMA.[8]

The culture of clinical trial data sharing has changed in recent years. Authors of published trials have reported an increased willingness to share data in surveys conducted in 2011[20 21] compared to an empirical study conducted in 2009.[17] The publication of data transparency strategies and policies by the Institute of Medicine[22] and the European Medicines Agency,[23] a proposed policy by the International Committee of Medical Journal Editors[24] and initiatives across the wider research community as a whole[21 25-27] may go some way to improving the sharing of IPD. Indeed, the launch of data sharing initiatives such as Clinical Study Data Request (CSDR),[28] a platform allowing researchers to request IPD from nearly 3000 clinical trials of thirteen pharmaceutical sponsors, should make access to IPD easier and faster. However, researchers have reported mixed experiences of using data sharing portals such as CSDR suggesting that the increased safeguards may have an unintended negative impact on the conduct of IPDMA.[29-32]

In this study we examine whether the shift in attitudes and awareness, and the increased number of options available for accessing IPD is reflected by a positive impact on IPDMA. We conduct a

systematic review of all published IPDMA to assess whether availability of IPD has improved over time, and explore characteristics associated with the retrieval of IPD. We also supplement this quantitative data by reflecting upon our research group's 20 years of experience in requesting IPD to undertake IPDMA in the field of epilepsy.

A systematic review of IPD meta-analyses (IPDMA)

The primary aim of this systematic review was to investigate whether the success rate of retrieving IPD for the purpose of IPDMA has increased over time. We also wanted to explore the characteristics associated with IPD retrieval.

Methodology: Search strategy and screening

We searched MEDLINE, Central, SCOPUS, Web of Science, CINAHL Plus and PsycINFO up to August 2015 using systematic search strategies adapted from the review of Riley *et al* 2010.[9 13] We also consulted the reference list of two reviews of individual participant data meta-analyses; Riley *et al* 2010[9 13] (provided by review author) and of Huang *et al* 2014[10] (available as an online appendix).

One author (SJN) performed title, abstract and full text screening of articles identified in electronic searches according to Inclusion and Exclusion Criteria described below and discussed any uncertainties with the senior author (CTS). We recorded principle reason for exclusion of all articles. For accuracy, two authors (BD and SR) screened a random sample of between 50 and 100 identified articles for eligibility; agreement between authors was good and any discrepancies were resolved by discussion.

Inclusion and Exclusion Criteria

IPDMA of studies of all types (randomised, observational, diagnostic etc.) and all clinical areas published in English were eligible for inclusion. Articles were included if IPD was requested from original study investigators, if IPD was already available to review authors or if review authors were able to extract IPD from published articles.

Methodological articles, conference abstracts, review protocols, non-clinical reviews (e.g. engineering articles etc.) were excluded. Articles including the analysis of IPD from a single study as a supplement to an AD meta-analysis or articles in which the primary analysis was not a synthesis (e.g. prognostic model validation studies, cost-effectiveness analysis) were excluded. Where duplicate publications relating to the same IPDMA were identified (e.g. identical publication across multiple journals) the most recently published article was retained.

Data extraction

Information was extracted from eligible IPDMA using a piloted data extraction form (Appendix 1). Information extracted included year of publication, authorship policy, source of funding, clinical area, type of studies, type of analysis, number of eligible studies providing IPD or AD, reasons for IPD not being provided and details of any sensitivity analyses performed to account for missing IPD.

One author (SJN) extracted information from all eligible IPDMA and three authors (BD, SR, LW) independently extracted from a subset of around 40% of the IPDMA. Agreement between authors was good and any discrepancies were resolved by discussion.

Data analysis and presentation of results

Multivariable logistic regression was performed in Stata version 14 to examine associations between the following IPDMA characteristics and a high IPD retrieval rate (at least 80% compared to less than 80% or unknown proportion of IPD provided) or complete IPD retrieval rate (100% compared to less than 100% or unknown proportion of IPD provided) (see Appendix 2 for further statistical details):

- Age of publication (calculated as years before 2016, log transformed due to skew)
- Number of participants eligible for inclusion in IPDMA (log transformed due to skew)
- Inclusion of randomised studies only in IPDMA compared to IPDMAs including non-randomised studies, diagnostic test accuracy studies or a combination of randomised and non-randomised studies
- IPDMA performed as a Cochrane Review compared to non-Cochrane IPDMAs
- IPDMAs with an authorship policy (individual authorship for those providing IPD or collaborative group) compared to no authorship policy
- IPDMAs with a commercial source of funding (pharmaceutical or manufacturer) compared to non-commercial sources of funding only, no funding or no information regarding funding provided.

Results of multivariable regression are presented as odds ratios and 95% confidence intervals. Other numerical results are presented as medians and ranges or numbers and percentages as appropriate.

Patient involvement

No patients were involved in setting the research question or the outcome measures, nor were they involved in the design and implementation of the study. There are no plans to involve patients in the dissemination of results.

Results

Characteristics of Individual Participant Data Meta-Analyses

We identified 1278 eligible articles describing 1280 IPDMA published to August 2015 (see Figure 1 for study flow diagram of our searching and screening process and Appendix 3 for reference list of eligible articles). A non-systematic method of identifying studies for inclusion, such as collaboration of a group of researchers with available IPD, had been used in 520 IPDMA. These analyses were mostly conducted with only the IPD which was already available to the analysts; therefore IPD retrieval rate is not relevant in these 520 IPDMA and we do not report any further results for this subgroup of reviews.

For the remaining 760 systematic IPDMA the number of eligible studies was reported in 746 (98%) IPDMA with a median number of eligible studies of 14 (range 2 to 923). The number of eligible participants within an IPDMA was only reported in 510 (67%) systematic IPDMAs with a median of 2369 (range 16 to 33369) patients.

IPD retrieval rate

IPD was provided from 100% of eligible studies in only 189 (25%) and from 100% of participants in only 188 (25%) out of 760 systematic IPDMA (Table 1); one IPDMA provided with IPD from 100% of studies received an incomplete dataset for one study. IPD from at least 80% of studies was retrieved in 375 systematic IPDMA (49%) and from 80% of participants in 324 systematic IPDMA (43%). IPD was retrieved for less than 50% of studies in 136 systematic IPDMA (18%) and for less than 50% of participants in 71 systematic IPDMA (9%). For 257 IPDMAs, the proportion of IPD retrieved could not be calculated where the number of eligible participants and/or the number of participants excluded from IPD analysis due to lack of IPD was not reported. Figure 2 shows the number of IPDMAs published by year and the proportion of IPD retrieved.

Table 1 shows the characteristics of the 760 systematic IPDMAs overall as well as separated according to IPD retrieval rate. Cochrane IPDMAs and IPDMAs with a higher number of eligible participants were less likely to retrieve a high proportion or all IPD. IPDMAs of Randomised trials were around 2.7 times more likely, and IPDMAs with an authorship policy were around 3.4 times more likely to retrieve at least 80% of IPD. There was no association between the IPD retrieval rate and source of funding or the date of publication of IPDMAs (Table 2).

Unavailability of IPD and the impact on analysis

Out of the 571 systematic IPDMA that failed to retrieve 100% of the IPD, 201 (34%) had supplemented IPD with aggregate data (AD) extracted from study publications. The additional AD had been included from a median of 5 (range 1 to 541) studies and a median of 683 (range 9 to 1,180,505) participants.

At least one study had been excluded from the meta-analysis due to lack of IPD or AD in 419 (55%) systematic IPDMA. Across these, a median of 4 (range 1 to 342) studies and a median of 478 (range 8 to 1,792,339) participants were excluded from IPDMAs but 241 systematic IPDMA (32%) failed to state how many participants were excluded from analysis.

Up to six reasons were reported for unavailability of IPD (Table 3); unspecific reasons, such as 'data was not available for analysis' were reported in 341 out of 571 systematic IPDMA (58%). The most common specific reasons for not obtaining IPD were that investigators could not be contacted, investigators had declined to share data or that data had been lost or destroyed. In 24 systematic IPDMA it was reported that data was not requested for all studies; mainly due to the size or quality of these studies.

In 143 (25%) out of the 571 systematic IPDMA there was no acknowledgement of potential bias resulting from missing IPD. In 199 (34%) of the systematic IPDMA additional analyses using AD had been performed and in a further 66 (11%) systematic IPDMA, a narrative description of the studies without IPD or a narrative comparison to an aggregate data meta-analysis had been provided. The remaining 183 (31%) systematic IPDMA make reference to the missing data; some acknowledging this may result in bias; without any further investigation of the implication on the conclusions of the review.

Changes in data sharing over time in epilepsy

The Cochrane Epilepsy Group have been making IPD requests to the authors of anti-epileptic drug (AED) monotherapy trials since the mid-1990s with eight reviews for IPDMA of pair-wise AED comparisons published to date since 2000.[33-40]

It is believed that with effective AED treatment, up to 70% of individuals with active epilepsy have the potential to become seizure-free and go into long-term remission shortly after starting therapy with a single AED. Over fifty AEDs are available worldwide for the treatment of epileptic seizures; therefore the correct choice of first-line AED for individuals with newly diagnosed epilepsy is of great

importance taking into account the highest quality evidence regarding the relative effectiveness and tolerability of AEDs appropriate to given seizure types are compared to one another.[41]

IPD is particularly desirable for meta-analysis of AED trials to allow complete re-analysis of important time-to-event outcomes such as time to withdrawal of randomised treatment due to poor seizure control or adverse effects, the recommended primary outcome of AED monotherapy trials[42] and to allow investigation of interaction between treatment and epilepsy type, as well as other potential prognostic factors of interest. [43] The group have also published an IPD network meta-analysis (NMA) including participants randomised to one of eight AEDs [44] in the earlier phase of reviews. This NMA is now currently being expanded and updated as a full Cochrane review of 10 AEDs.[41]

Supplementary Table 1 shows IPD retrieval rates and reasons given to us for unavailability of IPD (where applicable) categorised by the year in which requests for IPD were initiated and according to type of study sponsorship; pharmaceutical sponsored studies, government sponsored studies and academic studies defined as studies conducted within a university or hospital setting without clear pharmaceutical or government sponsorship or involvement.

Early data requesting and data sharing experiences

For the reviews and NMA published up to 2007,[33 44-50] we requested IPD for a total of 5887 participants from 29 randomised trials and we successfully received IPD for 4703 (80%) participants from 18 (62%) of these eligible trials. In addition, we had IPD available from our own 'SANAD' trial, [51 52] the largest ever in epilepsy at the time, which randomised 2437 participants. Over 90% of IPD requested from pharmaceutical and government sponsored studies was successfully received (data provided for 3695 out of 4084 participants from 12 out of 14 studies (86%)). However, only 56% of IPD (from 1008 out of 1803 participants) requested from 6 out of 15 academic sponsored studies (40% of studies) could be retrieved (Supplementary Table 1).

We failed to retrieve IPD from a total of 11 eligible trials recruiting 1184 participants (38% of all eligible trials); for the majority of these trials, data had been lost or was no longer available due to the time elapsed since the trial (Supplementary Table 1).

We emphasise that many of the data requests were initiated at a time when IPD meta-analysis was a relatively novel design and when e-mail was not commonly used. Exchanges were conducted by letter, fax, telephone and via face to face meetings with trial investigators. Some datasets supplied had never been computerised. Due to the informal nature of many of these requests, no data sharing agreements were exchanged and very little documentation was retained regarding the time

to complete data requests. Therefore, we are unable to make formal numerical comparisons between early and recent data requests; all comparisons are anecdotal.

Recent data requesting and data sharing experiences

Since our original NMA, additional AEDs have been used in clinical practice and additional clinical trials have been conducted which has prompted the need to update our original NMA. A new search for clinical trials was conducted[41] which identified 39 further eligible trials to be included with the previously received IPD. Data requesting for these eligible studies began in January 2012 and the database was closed at the end of 2015 to begin analysis (see Figure 3). In total IPD for 8261 participants from 39 additional trials were requested. Four of the requests for pharmaceutical studies were made via ClinicalStudyDataRequest.com (CSDR) (or original platform 'GSK Share' between May 2013 and January 2014). All other requests were made directly to the relevant sponsor.

For each trial meeting our inclusion criteria, a data request was sent to the first and/or corresponding author of the trial or to the trial sponsor where appropriate. Requests were sent by as many methods as possible (e-mail, postal mail, fax). In the event of no response to our IPD request, we sent a follow-up communication to the author / sponsor previously contacted. If we still received no response for a particular trial, we attempted to contact another trial author or sponsor where possible.

At the close of the database at the end of December 2015, IPD had been received for 5335 participants (65% of the total requested) from 15 (38%) clinical trials (Supplementary Table 1). For these trials, the median time from initial request to receiving data was similar between 24 academic studies (343 days (range 154 to 861 days)) and 14 pharmaceutical studies (363 days (range 280 to 725 days)). The time taken to receive IPD for a single trial via CSDR was 364 days. We note that the request was first submitted in June 2013 when the platform was newly initiated and processes still under development so this may not reflect current timelines to providing data in CSDR.

We failed to retrieve IPD from 24 trials conducted between 1989 and 2012. We were provided with a reason in 11 trials that had recruited 1537 participants; the median time from initial request to negative response from these 11 studies was 287 days (range 1 to 784 days).

Reasons for negative response were (i) country specific restrictions over anonymisation of data (one request submitted to CSDR for a pharmaceutical study conducted in 2005), (ii) cost of retrieving and preparing data prohibitive due to age of study (two requests submitted to CSDR for pharmaceutical

studies conducted in 2002 and 2007), (iii) data cannot be made available, no more specific details provided (three requests directly to pharmaceutical sponsors for studies conducted between 1997 and 2007), (iv) concerns regarding ethical approval for sharing data (one academic author, study conducted 2011), (v) the data we requested were not recorded (one academic author, study conducted 2005) and (vi) data were lost (three academic authors of studies conducted between 1992 and 2012; one of which provided additional unpublished summary data).

For the remaining 13 trials, two (one government and one academic) had indicated an initial positive response to our data requests but data was not provided by the close of database, whilst 11 studies (nine academic and two pharmaceutical) gave no response at all; these 13 data requests were closed at a median of 972 (range 640 to 1448 days) after initial request (Figure 3, Supplementary Table 1).

Therefore at the close of database, the total number of participants data provided for network meta-analysis was 10038 out of 14148 participants (71% of total eligible participants requested) from 33 out of 68 studies (49% of eligible studies requested).

Figure 4 shows the networks of studies with and without IPD, including the IPD available to us for 2437 participants from two trials conducted at our institution.[51 52] On visual inspection, there are no clear differences demonstrated between the networks. Furthermore, on examination of trial and participant characteristics and published results, there were no clear differences between studies providing IPD and those not providing IPD. Therefore, we deduce that the 29% of data not provided to us is likely to be missing 'at random' and unlikely to systematically impact on the resulting NMA.

Discussion

Statement of principle findings

To the best of our knowledge at the time of writing, our systematic review includes the largest cohort of published IPDMAs to date. Recent years have shown an increase in development of statistical methodology for the synthesis of IPD[53] as well as a rapid increase in the uptake of methods, with the number of systematic and non-systematic IPD meta-analyses published per year increasing to an average of 105 published per year between 2009 and 2015 compared to 49 per year published between 2005 and 2009.[9] However, these rapid increases do not seem to be mirrored by improved IPD retrieval rates.

The first Cochrane Epilepsy Group IPDMA was published in 2000 when such an approach was relatively novel and methodology limited.[33] This meta-analysis included IPD from 63% of total studies and 83% of total participants, a good retrieval rate in the wider context of all IPDMAs; however, of concern is that the success rate has declined from over 80% (up to 2005) to 65% (between 2012 and 2015). The findings of our systematic review showed that Cochrane reviews were less likely to retrieve all or a high proportion of IPD than non-Cochrane reviews. This may be explained by the inclusion of thorough search methods within Cochrane reviews leading to the identification of more eligible studies including more grey literature studies where IPD may be difficult to retrieve with resources available to Cochrane review authors.

Also of concern are changes in the reported reasons for lack of data availability. Our results demonstrate that loss of datasets is an issue for academic trials and has been for many years, highlighting a need for better methods of data curation and solutions for long-term storage and access. During our more recent requests the 'prohibitive costs' have prevented the sharing of pharmaceutical data. Additional costs and resources associated with IPDMA are generally considered to be incurred by the meta-analysts, [5-7] however in this new era of commercial data sharing platforms[28] and requirement of high level data de-identification, costs to data providers have certainly increased and should be taken under consideration when planning an IPDMA.[54] Collaboration, financial or otherwise, between meta-analysts and data providers may assist in sharing costs and resources, potentially maximising retrieval rates of IPD.

Despite our highlighted concerns, recent changes in methods of data sharing have resulted in several benefits to our analyses. Our most common reason for not retrieving data, an issue only for academic trials, was due to failing to make contact with data providers; data sharing platforms

provide a clear and transparent pathway of communication between data requestors and providers. In addition to improvements in Good Clinical Practice over time, resulting from regulations such as the European Union Clinical Trials Directive,[55] a greater focus on data privacy and additional preparation required to share a dataset has resulted in 'cleaner' datasets provided to us in recent requests compared to previous requests. While under the new framework of data sharing platforms, additional time and resources must allow for constructing a research proposal, independent scientific review, signing of data sharing agreements and de-identification of data; recent datasets provided to us have required much less data cleaning prior to analysis than in previous years; implying a shift in the time required to perform an IPDMA, rather than an increase.

Strengths and weaknesses of the study

We aimed to systematically identify all published IPD meta-analyses regardless of use of a systematic design to identify studies, resulting in a large cohort of nearly 1300 IPD meta-analyses. Our inclusion criteria were wide and reasons for exclusion were documented for all references identified in electronic searches. We were unable to include 90 abstracts which could not be matched to full text articles, despite our best efforts. Due to the size of the cohort of this study, double reference screening and data extraction was performed on only a subset of the articles. Agreement was good and all discrepancies were minor and easily resolved therefore we believe that any errors made in screening and extraction would be minimal and unlikely to influence the overall findings of the study.

We emphasise when interpreting the timelines of our requests between 2012 and 2015, that data sharing policies and platforms were under development, and that all of the pharmaceutical sponsors we contacted directly at the time of request have since committed to CSDR or an equivalent data sharing platform such as YODA.[56]

Relation to other studies and implications

Our results have shown that a quarter of systematic IPDMAs published since 1987 retrieved all IPD for analysis and only half retrieved at least 80% of relevant IPD. This latter finding is higher than previous results which reported that around 25% of IPD meta-analyses had included less than 80% of IPD,[8 10 13 19] however previous work has been based on smaller cohorts of IPDMAs, has mostly focused on IPDMAs of RCTs only and has been conducted over smaller time frames.

In line with previous work, [8 10 13 19] our results show that important inadequacies around conduct and reporting of IPDMA remain. Non-systematic methods, mostly based on the known availability of IPD,

had been used to select eligible studies for inclusion in 41% of the initial cohort of IPD meta-analyses we identified. It was outside the scope of this study to further examine the design of these analyses; however, we recommend that non-systematic pooling of IPD is conducted in the framework of a prospective meta-analysis[57] and that the conclusion of such analyses must be made taking the inevitable selection bias into account.

Our results also highlight the importance of clear reporting of study and participant numbers contributing to different stages of the IPD meta-analysis. The total number of eligible participants and the total number of participants' data requested was unclear in 34% of published IPD meta-analyses; hence it is unknown on how much of the relevant evidence the results are based and the implications on the conclusions of the meta-analysis. Furthermore, in 58% of the IPDMAs that failed to retrieve 100% of eligible IPD, there were no specific reasons provided for the unavailability of data, making interpretation of IPDMA results and conclusions in the presence of potential 'availability bias' difficult. Our own experiences of data requesting show that this issue is not restricted to the reporting of IPD reviews and meta-analysis and also exists at the study request level; IPD from three out of 35 studies was 'not available' to us with no further reason stated (Table 3).

We hope that uptake of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines for the conduct and reporting of IPD meta-analyses,[58] in addition to guidance on the use of IPD meta-analysis to synthesise the results of randomised controlled trials ,[59] will lead to improved conduct and reporting in IPDMAs, particularly regarding transparent reporting of the number of eligible studies and participants, how much data was requested and obtained with clear reasons for non-availability of IPD, preferably via a flow diagram. Discussion of limitations and impact on conclusions due to missing IPD is essential.

Conclusions

Individual participant data (IPD) meta-analyses are resource demanding, time consuming and methodologically challenging but when conducted well,[59] ideally following a registered protocol[60] and adhering to the PRISMA-IPD guidance,[58] can provide more detailed and potentially more reliable results than a meta-analysis of aggregate data. Meta-analysts must carefully consider the appropriateness of an IPD analysis and demonstrate awareness of potential biases induced by missing IPD. Only one in four published systematic IPD meta-analyses have had access to all IPD; we hope that this proportion will grow in future years with the growing awareness of data sharing and transparency in the pharmaceutical industry and beyond.[21-23 25-27] However, the research community

must ensure that procedures to access IPD do not become over-burdensome, over-costly and prohibitive, and that common sense and responsible risk proportionate approaches should be used.[22 26]

Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Details of contributors: SJN, AGM and CTS conceived and designed the research question. SJN, BD, SR and LW extracted data. SJN analysed data. SJN and CTS interpreted results. SJN wrote the manuscript under the supervision of AGM and CTS.

All authors had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

SJN acts as the guarantor of the study and affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Ethics approval: No ethics approval was required for the study

Data Sharing: Data underlying Tables and Figures is available on request from the corresponding author

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IPDMA Characteristic	All Systematic IPDMA (N)	IPDMA retrieving 100% of IPD (n and % of N)	IPDMA retrieving ≥80% of IPD (n and % of N)	IPDMA retrieving <80% or unknown proportion of IPD[1] (n and % of N)
Total	**760**	**188 (25%)**	**324 (43%)**	**436 (57%)**
Clinical area of meta-analysis				
Breast Cancer	40	8 (20%)	22 (55%)	18 (45%)
Cancer (other)	53	14 (26%)	27 (51%)	26(49%)
Cardiology	105	30 (29%)	53 (51%)	52 (49%)
Central Nervous System, Neurology and Brain Injury	50	13 (26%)	20 (40%)	30 (60%)
Cervical Cancer and Ovarian Cancer	16	1 (6%)	7 (44%)	9 (56%)
Gastroenterology, Colorectal and Gastric Cancer	49	11 (22%)	17 (35%)	32 (65%)
Diabetes and Endocrinology	30	8 (27%)	13 (43%)	17 (57%)
Gynaecology, Pregnancy and Neonatology	35	13 (37%)	18 (51%)	17 (49%)
Head and Neck Cancer	16	4 (25%)	8 (50%)	8 (50%)
Hepatitis and Liver Disease	19	7 (37%)	8 (42%)	11 (58%)
HIV	17	6 (35%)	8 (47%)	9 (53%)
Infection and Infectious Diseases	31	6 (19%)	9 (29%)	22 (71%)
Injuries and Wounds	21	2 (10%)	4 (19%)	17 (81%)
Haematology, Leukaemia and Blood Cancer	43	11 (26%)	20 (47%)	23 (53%)
Lung Cancer	32	9 (28%)	15 (47%)	17 (53%)
Mental and Psychiatric Disorders	32	7 (22%)	12 (38%)	20 (62%)
Musculoskeletal and Pain	34	9 (26%)	11 (32%)	23 (68%)
Otolaryngology, Opthamology and Periodontology	22	3 (14%)	5 (23%)	17 (67%)
Other[2]	26	5 (19%)	9 (34%)	15 (66%)
Renal and Urology	17	3 (18%)	6 (35%)	11 (65%)
Respiratory and Pulmonary	21	7 (33%)	11 (52%)	10 (48%)

Stroke, Thrombosis and Hypertension	51	12 (24%)	21 (41%)	30 (59%)
Design of included studies				
Randomised	405	117 (29%)	222 (55%)	183 (45%)
Non-Randomised	253	58 (23%)	81 (32%)	172 (68%)
Diagnostic Test Accuracy	34	5 (15%)	9 (26%)	25 (74%)
Both Randomised and Non-Randomised	68	8 (12%)	12 (18%)	56 (82%)
Type of included studies				
Diagnostic Test Accuracy	34	5 (15%)	9 (26%)	25 (74%)
Drug or device	348	102 (29%)	183 (53%)	165 (47%)
Epidemiological	185	38 (21%)	58 (31%)	127 (69%)
Non-drug (interventional)	193	43 (22%)	74 (38%)	119 (62%)
Type of IPDMA				
Cochrane Review	64	10 (16%)	25 (39%)	39 (61%)
Non Cochrane Review	696	178 (26%)	299 (43%)	397 (57%)
Authorship Policy				
Individual authorship	243	84 (35%)	116 (48%)	127 (52%)
Collaborative Group	264	40 (15%)	119 (45%)	145 (55%)
None[3]	253	64 (25%)	89 (35%)	164 (65%)
Source of Funding				
Non-commercial[4]	383	70 (18%)	155 (40%)	228 (60%)
Commercial[5]	72	26 (36%)	37 (51%)	35 (49%)
Mixed[6]	35	8 (23%)	20 (57%)	15 (43%)
No funding	77	25 (32%)	34 (44%)	43 (56%)
Not stated	193	59 (31%)	78 (40%)	115 (60%)
Number of eligible studies				
2 to 5	102	72 (71%)	83 (81%)	19 (19%)
6 to 10	174	67 (39%)	98 (56%)	76 (44%)
11 to 15	120	16 (13%)	47 (39%)	73 (61%)
16 to 20	87	12 (14%)	29 (33%)	58 (67%)
21 to 30	101	6 (6%)	30 (30%)	71 (70%)
31 to 40	50	3 (6%)	11 (22%)	39 (78%)
41 to 50	29	2 (7%)	5 (17%)	24 (83%)
over 50	83	10 (12%)	19 (23%)	64 (77%)
Not stated	14	0 (0%)	2 (14%)	12 (86%)
Number of eligible participants				
under 100	18	14 (78%)	16 (94%)	1 (6%)
101 to 200	20	13 (65%)	16 (80%)	4 (20%)

201 to 500	45	21 (47%)	25 (56%)	20 (44%)
501 to 1000	67	35 (52%)	45 (67%)	22 (33%)
1001 to 5000	198	70 (35%)	134 (68%)	64 (32%)
5001 to 10000	62	13 (21%)	37 (60%)	25 (40%)
10001 to 50000	100	22 (22%)	53 (53%)	47 (47%)
Not stated	250	0 (0%)	0 (0%)	250 (100%)

Table 1: Characteristics of all systematic IPD meta-analyses (IPDMA) according to proportion of IPD provided

1. Including 257 IPDMA where the proportion of IPD provided was unknown where the number of eligible participants and/or the number of participants excluded from IPD analysis due to lack of IPD was not reported.
2. Other defined as lifestyle, nutrition, emergency medicine, patient care, patient preference, Pharmacokinetics and Forensics
3. Including 83 IPDMA where IPD was extracted from published study reports (IPD not requested from original study authors)
4. Non-commercial sources included institutional, government, charity, research council or research foundation funding.
5. Commercial sources were defined as pharmaceutical or manufacturer funding.
6. Multiple commercial and non-commercial sources.

IPD MA Characteristic[1]	100% of IPD retrieved compared to less than 100% of IPD			At least 80% of IPD retrieved compared to less than 80% of IPD		
	Odds Ratio	95% Confidence Interval	P value	Odds Ratio	95% Confidence Interval	P value
Age of publication[2]	1.081	0.885 to 1.320	0.445	1.153	0.938 to 1.418	0.177
Number of eligible participants[2]	0.851	0.800 to 0.904	<0.001	0.889	0.837 to 0.943	<0.001
Includes randomised studies only	1.415	0.919 to 2.182	0.115	2.735	1.755 to 4.262	<0.001
Cochrane IPD-MA	0.402	0.189 to 0.859	0.019	0.427	0.218 to 0.835	0.013
Authorship Policy	1.667	1.074 to 2.585	0.022	3.366	2.183 to 5.190	<0.001
Commercial source of funding	1.291	0.762 to 2.187	0.341	1.043	0.568 to 1.914	0.892

Table 2: Multivariable logistic regression models: Characteristics associated with retrieving 100% of IPD or receiving more than 80% of IPD in 503 IPDMAs

1. See Appendix 2 for statistical details and definitions of characteristics
2. Log transformation applied due to skewed distribution of data

Reasons reported for not retrieving 100% of eligible IPD	Number of IPDMA[1,2,3]
Data not available[2]	341 (60%)
No contact could be made with study authors	104 (18%)
Investigators declined but no reason given	74 (13%)
Data lost or destroyed	65 (11%)
Data could not be extracted[3]	55 (10%)
Trial was still ongoing	42 (7%)
Data quality issues	29 (5%)
Failed to provide data in time for the IPDMA	26 (5%)
Data not requested	24 (4%)
Ethical / ownership restrictions	15 (3%)
Reason unclear	11 (2%)
Approach reported to account for missing IPD	**Number of IPDMA[1,2,3]**
None stated	143 (25%)
Separate meta-analyses are conducted including IPD only and IPD plus available AD	81 (14%)
Stated that missing IPD is a limitation of the meta-analysis and / or that availability bias may be present	76 (13%)
AD included in primary analysis	61 (11%)
Sensitivity analysis with AD performed	57 (10%)
Stated that the missing IPD is unlikely to change results	56 (10%)
Results from the studies without IPD summarised narratively	48 (8%)
Stated that the majority of data is included in analysis	47 (8%)
Narrative comparison to an AD meta-analysis	18 (3%)
Intend to include data in an update	14 (2%)

Table 3: Reasons reported for unavailability of IPD and approach to accounting for missing IPD in 571 systematic IPD meta-analyses (IPDMA) without 100% of IPD retrieved

IPD – individual participant data, AD – aggregate data, NA –not applicable

1. 189 IPDMA with 100% of IPD provided not included in the table.
2. IPDMAs reported up to six reasons for unavailability of IPD or described up to three approaches to account for missing IPD. Therefore total number of reasons / approaches is greater than 571.
3. Corresponds to the proportion of 571 IPDMAs; total percentages sum to greater than 100 as multiple reasons / approaches could be reported for an IPDMA.
4. The reason "data not available" corresponds to a statement in the review that IPD was not available for a proportion of studies without any specific reason given.
5. Reason applicable only in a small number of IPDMAs where IPD were extracted from publications rather than requested.

Figure titles and footnotes

Figure 1: Study Flow Diagram of identification of eligible Individual Participant Data Meta Analyses (IPDMA)

* two full text articles each reported two individual participant data meta-analyses

Figure 2: Number of distinct systematic individual participant data meta-analyses published to August 2015.

1. See Table 1 for proportion of systematic IPD meta-analyses providing 100%, 80-99% and less than 80% of IPD.

2. Six IPDMA were published from 1987 to 1993; three were provided with less than 80% of IPD and three were provided with 80 – 99% of IPD

Figure 3: Duration and outcome of data requests for 39 randomised controlled trials of anti-epileptic drugs

Figure 4: Plots of studies providing IPD and not providing IPD for a network meta-analysis of 10 anti-epileptic drugs (See Supplementary Table 1 for numbers of studies and participants providing and not providing IPD).

Abbreviations: Carbamazepine (CBZ), Phenobarbitone (PB), Oxcarbazepine (OXC) , Phenytoin (PHT), Valproate (VPA), Lamotrigine (LTG), Gabapentin (GBP), Topiramate (TPM), Levetiracatam (LEV), Zonisamide (ZNS)

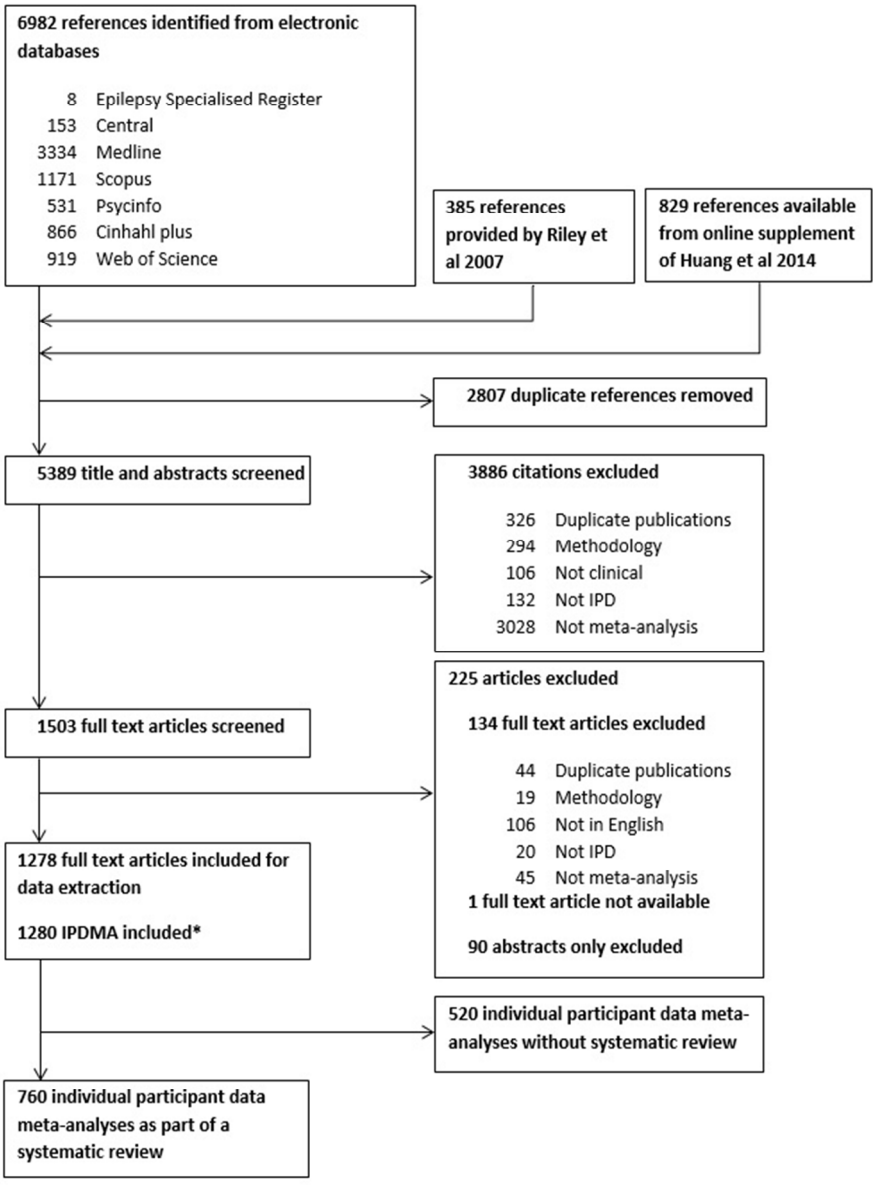

Figure 1: Study Flow Diagram of identification of eligible Individual Participant Data Meta Analyses (IPDMA)
* two full text articles each reported two individual participant data meta-analyses

Figure 1
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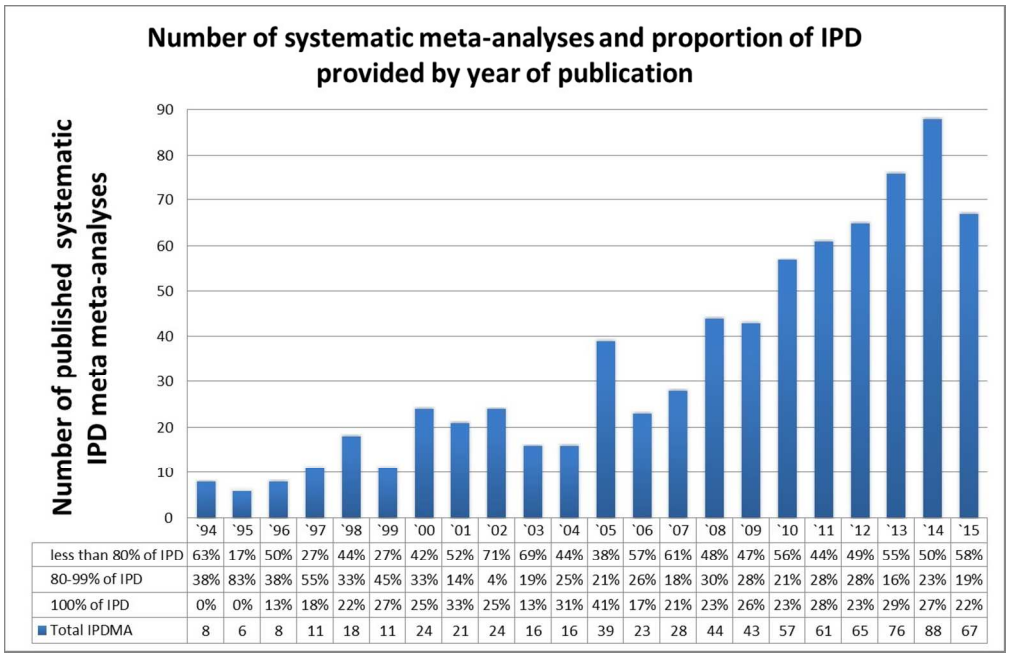

	`94	`95	`96	`97	`98	`99	`00	`01	`02	`03	`04	`05	`06	`07	`08	`09	`10	`11	`12	`13	`14	`15
less than 80% of IPD	63%	17%	50%	27%	44%	27%	42%	52%	71%	69%	44%	38%	57%	61%	48%	47%	56%	44%	49%	55%	50%	58%
80-99% of IPD	38%	83%	38%	55%	33%	45%	33%	14%	4%	19%	25%	21%	26%	18%	30%	28%	21%	28%	28%	16%	23%	19%
100% of IPD	0%	0%	13%	18%	22%	27%	25%	33%	25%	13%	31%	41%	17%	21%	23%	26%	23%	28%	23%	29%	27%	22%
Total IPDMA	8	6	8	11	18	11	24	21	24	16	16	39	23	28	44	43	57	61	65	76	88	67

Figure 2: Number of distinct systematic individual participant data meta-analyses published to August 2015.
1. See Table 1 for proportion of systematic IPD meta-analyses providing 100%, 80-99% and less than 80% of IPD.
2. Six IPDMA were published from 1987 to 1993; three were provided with less than 80% of IPD and three were provided with 80 – 99% of IPD

Figure 2
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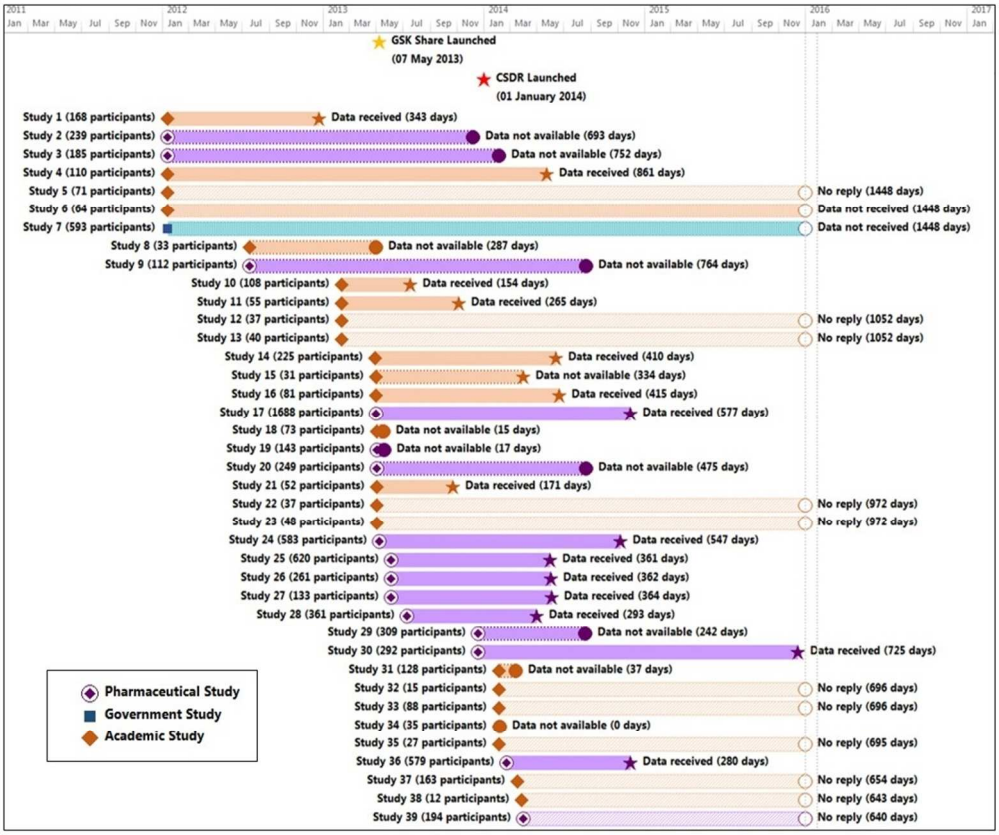

Figure 3: Duration and outcome of data requests for 39 randomised controlled trials of anti-epileptic drugs
Figure 3
368x307mm (72 x 72 DPI)

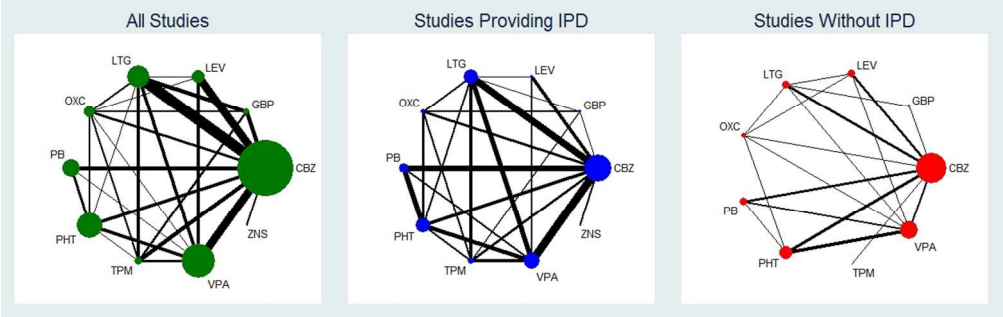

Figure 4: Plots of studies providing IPD and not providing IPD for a network meta-analysis of 10 anti-epileptic drugs (See Supplementary Table 1 for numbers of studies and participants providing and not providing IPD).
Abbreviations: Carbamazepine (CBZ), Phenobarbitone (PB), Oxcarbazepine (OXC) , Phenytoin (PHT), Valproate (VPA), Lamotrigine (LTG), Gabapentin (GBP), Topiramate (TPM), Levetiracatam (LEV), Zonisamide (ZNS)

Figure 4
442x139mm (72 x 72 DPI)

Number of studies and participants requested[1]	Original requests (approx. 1995 – 2005) by type of study				New requests (2012-2015) by type of study				All requests (approx. 1995-2015) by type of study			
	Ac	**Go**	**Ph**	**Total**	**Ac**	**Go**	**Ph**	**Total**	**Ac**	**Go**	**Ph**	**Total**
Eligible studies	15	4	10	**29**	24	1	14	**39**	39	5	24	**68**
Studies providing IPD (n (%))	6 (40%)	3 (75%)	9 (90%)	**18 (62%)**	7 (29%)	0 (0%)	8 (57%)	**15 (38%)**	13 (33%)	3 (60%)	17 (71%)	**33 (49%)**
Eligible participants	1803	1178	2906	**5887**	1897	593	5771	**8261**	3700	1771	8677	**14148**
Participants IPD is provided for (n (%))	1008 (56%)	1091 (93%)	2604 (90%)	**4703 (80%)**	801 (42%)	0 (0%)	4534 (79%)	**5335 (65%)**	1809 (49%)	1091 (62%)	7138 (82%)	**10038 (71%)**
Reason data was not available: Number of studies (n (%))												
Data lost	5 (33%)	1 (25%)	0 (0%)	**6 (21%)**	3 (13%)	0 (0%)	0 (0%)	**3 (8%)**	8 (21%)	1 (20%)	0 (0%)	**9 (13%)**
Relevant data not recorded	2 (13%)	0 (0%)	0 (0%)	**2 (7%)**	1 (4%)	0 (0%)	0 (0%)	**1 (3%)**	3 (8%)	0 (0%)	0 (0%)	**3 (4%)**
Unable to make contact with an author / sponsor	1 (7%)	0 (0%)	0 (0%)	**1 (3%)**	11 (46%)	0 (0%)	0 (0%)	**11 (28%)**	12 (31%)	0 (0%)	0 (0%)	**12 (18%)**
Positive response but no data received	1 (7%)	0 (0%)	0 (0%)	**1 (3%)**	1 (4%)	1 (100%)	0 (0%)	**2 (5%)**	2 (5%)	1 (20%)	0 (0%)	**3 (4%)**
Incomplete dataset provided which could not be used	0 (0%)	0 (0%)	1 (10%)	**1 (3%)**	0 (0%)	0 (0%)	0 (0%)	**0 (0%)**	0 (0%)	0 (0%)	1 (4%)	**1 (1%)**
Local authority / ethical restrictions	0 (0%)	0 (0%)	0 (0%)	**0 (0%)**	1 (4%)	0 (0%)	0 (0%)	**1 (3%)**	1 (3%)	0 (0%)	0 (0%)	**1 (1%)**
"Data not available"[2]	0 (0%)	0 (0%)	0 (0%)	**0 (0%)**	0 (0%)	0 (0%)	3 (21%)	**3 (8%)**	0 (0%)	0 (0%)	3 (13%)	**3 (4%)**
Costs of providing data are prohibitive	0 (0%)	0 (0%)	0 (0%)	**0 (0%)**	0 (0%)	0 (0%)	2 (14%)	**2 (5%)**	0 (0%)	0 (0%)	2 (8%)	**2 (3%)**
Country specific restrictions	0 (0%)	0 (0%)	0 (0%)	**0 (0%)**	0 (0%)	0 (0%)	1 (7%)	**1 (3%)**	0 (0%)	0 (0%)	1 (4%)	**1 (1%)**
Total	**9 (60%)**	**1 (25%)**	**1 (10%)**	**11 (38%)**	**17 (61%)**	**1 (100%)**	**6 (43%)**	**24 (62%)**	**26 (67%)**	**2 (40%)**	**7 (29%)**	**35 (51%)**

Supplementary Table 1: Outcome of individual participant data requests conducted between approx. 1995 to 2005 and 2012 to 2015.

Abbreviations: Ac: Academic studies, Go: Government Studies, Ph: Pharmaceutical Studies

Footnotes

1. In addition, we had IPD available from our own 'SANAD' trial, [50 51] the largest ever in epilepsy at the time, which randomised 2437 participants
2. Refers to a non-specific reason (data not available for secondary analysis with no further reason provided).

Individual Participant Data Meta-Analyses: Data Extraction Form

Date of Extraction:

Name of data extractor:

Meta-analysis First Author:

Meta-analysis Year:

Meta-analysis Title:

Journal or Source:

Authorship policy (individual authorship, collaborative group, none):

Source of funding:

Clinical area (lung cancer, breast cancer, epilepsy, diabetes etc.):

Design of studies included (Randomised / Non-randomised/ both / Other (diagnostic test accuracy etc.):

Type of studies included (Drug / Device / Observational / Other (diagnostic test accuracy etc.):

Type of pooled analysis: Systematic search performed or existing database of studies pooled/ collaboration?

Number of studies eligible for meta-analysis:

Number of participants in all eligible studies:

Year range of eligible studies:

Number of studies providing IPD:

Number of participants IPD is provided for:

Number of studies providing aggregate data (AD):

Number of participants AD is provided for:

Number of studies excluded due to no IPD or AD available:

Number of patients excluded due to no IPD or AD available:

Year range of studies IPD is not available for:

Any reported reasons that IPD was not provided (data no longer available, authors unwilling to collaborate)?

Were any adjustments/ sensitivity analyses performed to account for missing IPD? Or do meta-analysis authors note the limitation of missing IPD?

Additional notes:

Footnotes:

1. Reasons for IPD not being provided and sensitivity analyses recorded as free text and later classified into broad categories.
2. Source of funding recorded as free text and later classified as Commercial, Non-Commercial, Mixed (Commercial and Non-Commercial), No funding, Not stated.
3. Clinical area was also recorded as free text and later classified in broad categories based on the clinical areas covered by the review groups of the Cochrane Collaboration

Appendix 2: Statistical Analysis

1. Characteristics associated with a high success rate of IPD retrieval

Proportion of IPD retrieved (dependent variable of interest) was highly skewed, despite attempts at transformation, as few IPDMAs retrieved a very small proportion of data. It was therefore deemed most appropriate to dichotomise this variable to:

a) Complete IPD retrieval rate (100% compared to less than 100% or unknown proportion of IPD provided)

b) High IPD retrieval rate (at least 80% compared to less than 80% or unknown proportion of IPD provided)

Multivariable logistic regression was performed to examine associations between individual participant data meta-analyses (IPDMA) characteristics and a high or complete retrieval rate of IPD.

A total of 503 IPDMAs were included in this analysis for which we could calculate the proportion of IPD retrieved (i.e. the number of participant eligible for analysis and the number of participants data was provided for was reported).

The following variables were included in the model and results for all variables included in the model are presented regardless of statistical significance; no model selection techniques were used:

- Age of publication (calculated as years before 2016, log transformed due to skew)
- Number of participants eligible for inclusion in IPDMA (log transformed due to skew)
- Inclusion of randomised studies only in IPDMA compared to IPDMAs including non-randomised studies, diagnostic test accuracy studies or a combination of randomised and non-randomised studies
- IPDMA performed as a Cochrane Review compared to non-Cochrane IPDMAs
- IPDMAs with an authorship policy (individual authorship or collaborative group) compared to no authorship policy
- IPDMAs with a commercial source of funding (pharmaceutical or manufacturer) compared to non-commercial sources of funding only, no funding or no information regarding funding provided.

Sensitivity analyses (Results of the primary analysis presented in Table 2)

1. Type of study (drug or device (interventional), non-drug (interventional), diagnostic test accuracy or epidemiological study) was not included in the model due to correlation between this variable and type of study (interventional studies were significantly more likely to be randomised, chi-squared p<0.001) and source of funding (drug or device studies were significantly more likely to be commercially funded, chi- squared p<0.001).

   Sensitivity analysis was conducted adding an additional variable to this model of IPDMAs of drug or device studies compared to non-drug or device interventions, diagnostic test accuracy studies or epidemiological studies added to the model. Results showed that this

characteristic was not statistically significant, other numerical results were similar and conclusions were unchanged (results available on request from corresponding author).

2. A sensitivity analysis was conducted excluding 128 IPD-MAs with no information regarding funding. Numerical results were similar and conclusions were unchanged (results available on request from corresponding author).

3. A sensitivity analysis was conducted including all 760 IPDMAs, assuming the following scenarios for the 257 IPDMAs for which the proportion of IPD retrieved could not be calculated:
    a. Less than 80% of IPD was retrieved
    b. 80% or more IPD was retrieved
    c. 100% of IPD was retrieved

The multivariable regression was run under each scenario including the above variables except for number of eligible participants (not available for the 257 additional IPDMAs).

a) Assuming less than 80% of IPD was retrieved for 257 IPDMAs where proportion of IPD retrieved could not be calculated

IPD MA Characteristic	100% of IPD retrieved compared to less than 100% of IPD			At least 80% of IPD retrieved compared to less than 80% of IPD		
	Odds Ratio	95% Confidence Interval	P value	Odds Ratio	95% Confidence Interval	P value
Age of publication (log scale)	0.641	0.554 to 0.739	<0.001	0.713	0.624 to 0.816	<0.001
Includes randomised studies only	1.667	1.160 to 2.393	0.006	2.906	2.076 to 4.067	<0.001
Cochrane IPD-MA	0.334	0.161 to 0.701	0.004	0.489	0.278 to 0.861	0.013
Authorship Policy	0.505	0.372 to 0.685	<0.001	0.842	0.635 to 1.115	0.230
Commercial source of funding	1.102	0.687 to 1.767	0.687	0.994	0.642 to 1.541	0.980

b) Assuming 80% or more of IPD was retrieved for 257 IPDMAs where proportion of IPD retrieved could not be calculated

IPD MA Characteristic	100% of IPD retrieved compared to less than 100% of IPD			At least 80% of IPD retrieved compared to less than 80% of IPD		
	Odds Ratio	95% Confidence Interval	P value	Odds Ratio	95% Confidence Interval	P value
Age of publication (log scale)	0.641	0.554 to 0.739	<0.001	1.206	1.046 to 1.392	0.010
Includes randomised studies only	1.667	1.160 to 2.393	0.006	1.479	0.999 to 2.190	0.051
Cochrane IPD-MA	0.334	0.161 to 0.701	0.004	0.428	0.233 to 0.784	0.006
Authorship Policy	0.505	0.372 to 0.685	<0.001	3.222	2.340 to 4.439	<0.001
Commercial source of funding	1.102	0.687 to 1.767	0.687	1.002	0.577 to 1.743	0.993

c) Assuming 100% of IPD was retrieved for 257 IPDMAs where proportion of IPD retrieved could not be calculated

IPD MA Characteristic	100% of IPD retrieved compared to less than 100% of IPD			At least 80% of IPD retrieved compared to less than 80% of IPD		
	Odds Ratio	95% Confidence Interval	P value	Odds Ratio	95% Confidence Interval	P value
Age of publication (log scale)	1.109	0.975 to 1.392	0.114	1.206	1.046 to 1.392	0.010
Includes randomised studies only	0.682	0.492 to 0.947	0.022	1.479	0.999 to 2.190	0.051
Cochrane IPD-MA	0.477	0.269 to 0.846	0.011	0.428	0.233 to 0.784	0.006
Authorship Policy	1.762	1.331 to 2.332	<0.001	3.222	2.340 to 4.439	<0.001
Commercial source of funding	1.092	0.704 to 1.693	0.993	1.002	0.577 to 1.743	0.993

Results of these sensitivity analyses are varied compared to those reported in Table 2 – for example scenario a) and scenario b) contradict Table 2 and suggest that use of an authorship policy is negatively associated with a high or complete retrieval rate of IPD. These sensitivity analyses highlight the importance of a clear statement of the proportion of IPD retrieved in IPDMA.

4. Multivariable logistic regression was also performed to examine associations between the IPDMA characteristics defined above and the proportion of study data retrieved.

A total of 744 IPDMAs were included in this analysis for which we could calculate the proportion of study data retrieved (i.e. the number of studies eligible for analysis and the number of studies data was provided for was reported).

IPD MA Characteristic	100% of study data retrieved compared to less than 100% of study data			At least 80% of study data retrieved compared to less than 80% of study data		
	Odds Ratio	95% Confidence Interval	P value	Odds Ratio	95% Confidence Interval	P value
Age of publication (log scale)	1.172	0.961 to 1.431	0.116	1.235	1.050 to 1.454	0.011
Number of eligible studies (log scale)	0.498	0.428 to 0.576	<0.001	0.681	0.610 to 0.759	<0.001
Includes randomised studies only	1.555	1.050 to 2.304	0.028	1.301	0.936 to 1.807	0.117
Cochrane IPD-MA	0.441	0.207 to 0.937	0.033	0.664	0.373 to 1.181	0.163
Authorship Policy	1.078	0.739 to 1.573	0.695	1.851	1.355 to 2.529	<0.001
Commercial source of funding	1.339	0.819 to 2.187	0.244	1.227	0.781 to 1.927	0.375

Results of this sensitivity analysis are mostly similar to those reported in Table 2, however these results suggest that older publications may be more likely to retrieve a high proportion (at least 80%) of study data; suggesting that IPD retrieval rate on a study level has got worse over time.

2. Non-linear modelling of publication rates of IPDMA

From previous work conducted by Riley *et al,*[1] it was hypothesised that the number of IPDMAs published each year would be non-linear. This hypothesis was confirmed by visual inspection of Figure 2. Exponential (asymptotic), Logistic and Gompertz non-linear regression models built into the 'nl' command of Stata Version 14 were investigated to model the relationship. Modelling of this relationship was intended only for illustrative purposes, therefore development of user written non-linear models was deemed to be out of the scope of this analysis.

Model Type	Algebraic Model	Adjusted R^2	Residual Deviance
Linear	$y_i = b_0 + b_1 x_i$	0.839	192.95
Exponential (2 parameter)	$y_i = b_1(b_2)^{x_i}$	0.964	174.80
Exponential (3 parameter)	$y_i = b_0 + b_1(b_2)^{x_i}$	0.837	193.28
Logistic (4 parameter)	$y_i = b_0 + b_1/(1 + e^{-b_2(x_i - b_3)})$	0.924	171.01
Logistic (3 parameter)	$y_i = b_1/(1 + e^{-b_2(x_i - b_3)})$	0.968	171.06
Gompertz (4 parameter)	$y_i = b_0 + b_1\, e^{-e^{-b_2(x_i - b_3)}}$	0.922	171.88
Gompertz (3 parameter)	$y_i = b_1\, e^{-e^{-b_2(x_i - b_3)}}$	0.966	171.89

Where $i = 1$ to 26 corresponding to the number of years between 1987 and 2015 that at least one IPDMA was published

$y_i =$ Number of systematic IPD meta-analyses

$x_i =$ Years since first published IPD meta-analysis in 1987

According to Adjusted R^2 and Residual Deviance, it was deemed that the three parameter logistic model was the best fit to the publication rate of IPDMAs:

$$y_i = 142.69/(1 + e^{-0.165_2(x_i - 26.24)})$$

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