Trial Corresponding Author Country, Year, and Journal Impact Factor Associated with Data Contribution to IPDMAs

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ABSTRACT

**Background:** Objectives were to determine the proportion of eligible randomized controlled trials (RCTs) that contributed data to individual participant data meta-analyses (IPDMAs) and explore associated factors.

**Study Design and Setting:** IPDMAs with ≥10 eligible RCTs were identified by searching MEDLINE, EMBASE, CINAHL and Cochrane May 1, 2015 to February 13, 2017. Mixed effect logistic regression was used to identify factors associated with data contribution.

**Results:** Of 774 eligible RCTs from 35 included IPDMAs, 517 (67%, 95% confidence interval [CI] 63-70%) contributed data. Compared to RCTs from journals with low impact factors (0-2.4), RCTs from journals with higher impact factors were more likely to contribute data: impact factor 5.0-9.9, odds ratio [OR] 2.6, 95% CI 1.37-4.86; impact factor 10.0-19.9, OR 5.7, 95% CI 3.0-10.8; impact factor >20.0, OR 4.6, 95% CI 1.9-11.4. RCTs from the United Kingdom were more likely to contribute data than those from the United States (reference; OR 2.4, 95% CI 1.3-4.6). There was an increase in OR per publication year (OR 1.05, 95% CI 1.02-1.09).

**Conclusion:** Country where RCTs are conducted, impact factor of the journal where RCTs are published, and RCT publication year were associated with data contribution in IPDMAs with ≥10 eligible RCTs.

**Key Words:** meta-analysis, individual participant data meta-analysis, randomized controlled trial, data contribution, data sharing
BACKGROUND

Increasingly, members of the scientific community and stakeholders expect transparency in the conduct and reporting of randomized controlled trials (RCTs), and measures have been implemented to attempt to increase the accessibility and availability of trial data.\textsuperscript{1,2} Data sharing promotes transparent verification and replication of trial results, ensures that important trial findings are reported, reduces waste in research by avoiding unnecessary repetition of efforts, guides the planning of future trials, and may serve to reduce the frequency and impact of non-publication and selective reporting of trial results.\textsuperscript{3-7}

Whereas aggregate-data meta-analyses synthesize summary results from study reports, individual participant data meta-analyses (IPDMAs) synthesize raw data from participants.\textsuperscript{8} Advantages of IPDMAs include the ability to analyze outcomes not included in some primary study reports, to address subgroup analyses not explored in primary studies, and to increase standardization by combining data using consistent inclusion and exclusion criteria and analysis methods.\textsuperscript{8-13}

Despite expectations for data sharing articulated by government agencies, journal editors, journals, and not-for-profit organizations,\textsuperscript{14-25} in practice, data sharing is largely left at the discretion of study authors. Several studies have documented difficulty obtaining primary data for IPDMAs or examined factors associated with data contribution in single projects.\textsuperscript{26-28} One study examined IPDMA characteristics associated with data contribution in over 760 IPDMAs but did not examine characteristics of included primary studies.\textsuperscript{29} No studies have examined characteristics of IPDMAs and included studies associated with data contribution in more than 1-2 IPDMAs. Our objectives were to: (1) determine the proportion of eligible primary studies that contributed data in published IPDMAs of randomized controlled trials (RCTs) with \(\geq 10\) eligible
RCTs and (2) identify IPDMAs and included RCT characteristics associated with data
contribution.

METHODS

Eligibility of IPDMAs

Eligible IPDMAs compared the effects of a healthcare intervention between two or more
groups using data from RCTs, documented a systematic review of the literature, published
references for all eligible RCTs, and indicated which provided data, and if there were $\geq 10$
eligible RCTs. IPDMA that included non-RCTs were included only if RCT results were reported
separately. We included only IPDMAs with $\geq 10$ eligible trials, because it is possible that
potential IPDMAs with a few eligible trials would only be conducted if data authors ascertained
that data would be available.

Search Strategy

We identified potentially eligible IPDMAs by searching the MEDLINE, Embase,
CINAHL and Cochrane databases (see Appendix 1). We estimated the length of the search
period that would be needed to obtain the total number of IPDMAs sought based on our power
analysis ($N = 34$ IPDMAs; see statistical analyses section). Our initial search included IPDMAs
published from January 1, 2016 to November 1, 2016. We subsequently extended the search
backward to May 1, 2015 and forward to February 13, 2017, until we obtained the pre-specified
number of included IPDMAs.

References were uploaded into RefWorks (RefWorks, RefWorks-COS, Bethesda, MD,
USA), then into the systematic review program DistillerSR (Evidence Partners, Ottawa, Canada).
DistillerSR was used for all coding procedures and to track results of the review process.
**Selection of Eligible IPDMAs**

We used a liberal accelerated method. Three investigators independently assessed article titles and abstracts for possible eligibility in random order. Articles that were deemed potentially eligible by a single reviewer were moved forward to full-text review, whereas two reviewers were needed to exclude. In full-text review, all citations were reviewed independently by two investigators with any disagreements resolved by consensus, involving a third investigator, as necessary.

**Data Extraction**

A single reviewer extracted data, and all extracted data were validated by a second reviewer using the DistillerSR Quality Control function. Any discrepancies were resolved by consensus. Data were extracted from included IPDMAs and each eligible trial referenced in the IPDMA, including trials that contributed data and trials that did not. Variables extracted were chosen a priori by members of the research team, and all data were extracted into a pre-specified data extraction form. Categories for analyses were defined in some cases after extracting data based on frequencies and conceptual reasons, including to ensure enough data per category for meaningful analysis. This was done in all cases prior to examining associations with data contribution.

From each IPDMA, we ascertained if there was a published protocol or a PROSPERO registration (yes/no), country of the corresponding author (United Kingdom; United States; other [Belgium, Brazil, Canada, Denmark, France, Germany, Ghana, Japan, Netherlands and Sweden]), participant population medical condition (cancer; cardiovascular disease; other [chronic pain; diabetes; infectious disease; kidney disease; mental health; mixed conditions; mixed surgery; musculoskeletal; obesity; pregnancy; respiratory disease; seizures]), and type of
intervention assessed (drug or biologic; device; non-regulated intervention). To determine whether an IPDMA had a published protocol or registration, we verified whether either was referenced in the publication. If not, we searched in any related protocols or meta-analysis reports. Then, we searched the PROSPERO website (https://www.crd.york.ac.uk/PROSPERO/) using first and corresponding author names, study keywords, funding source, intervention, non-intervention comparator group, and design. If these steps did not identify a protocol or registration, the IPDMA was considered as having neither for our study purposes.

We emailed corresponding authors of included IPDMAs to determine whether contributing trialists were invited to become co-authors in the IPDMA publication at the time data were sought. Authorship was categorized as: authorship offered, group authorship offered; no authorship offered; not applicable; undetermined. If no response was received after three emails, IPDMA co-authors were contacted by email once. If no response was received, we verified whether trialists were included in the IPDMA publication author list and classified authorship accordingly to the extent possible (e.g., if IPDMA included authors from all included RCTs, we coded authorship offered). Three meta-analyses of drugs for epilepsy were coded as not applicable since most of the data were contributed to a collaboration in the 1990s, and few datasets were newly sought based on updated reviews.

For all eligible RCTs within each IPDMA, we ascertained if the RCT had contributed data, 2015 Thomson Reuters impact factor of the journal where the RCT was published (as a rough proxy for trial quality), RCT publication year, RCT funding source (national, state, or provincial government agency; not-for-profit agency; university or hospital; industry; not reported), corresponding author country (Australia or New Zealand; Canada; United Kingdom; United State; European Union or Western Europe; other), and presence of author financial
conflict of interest (yes – study funding, author-industry financial ties, author employment)/no), and the number of participants from the RCT included in the IPDMA, We considered a trial to have industry funding if it was funded directly by industry, funded by an industry-funded foundation, if some authors were industry employees, or if industry provided supplies. RCTs with multiple funding sources were classified as having each source of funding. The number of participants from each trial included in the IPDMA was extracted from the IPDMA publication, or, if not available, from the primary trial publication.

We classified the results of primary RCT outcomes as significant and favorable, significant and unfavorable, non-significant, and indeterminate, as previously done by Tricco et al. We used the result published in the RCT if the RCT reported the same outcome as the IPDMA primary outcome, even if different analysis methods were used. If the RCT publication did not report the primary outcome of the IPDMA, but the IPDMA publication provided results on the primary outcome for included primary studies, we used results reported in the IPDMA. For primary studies with continuous outcomes, if multiple outcomes were presented in primary trial reports, we prioritized ANCOVA analyses that controlled for baseline values, followed by analyses of change scores, then analyses that considered endpoint data only. If the primary study reported on a trial with multiple intervention arms, results of the primary study associated with the same comparison reported in the IPDMA report were extracted. If the primary outcome of the IPDMA was a composite outcome, and the primary study reported a similar primary outcome that was also a composite outcome, but with minor differences in definition, the IPDMA and the primary study outcome were considered as matching. If the IDPMA evaluated an outcome that was not reported in the primary RCT, this outcome was coded indeterminate for the RCT.
Statistical Analyses

For our power calculation, we assumed that a 15% difference (e.g., \( p_0 = 0.70, p_1 = 0.85 \)) in the proportion of data contributors for dichotomous predictor variables would be important and an intraclass correlation coefficient of 0.1. We initially calculated that we would need approximately 45 IPDMAs with 10 RCTs per IPDMA. After our first search and identification of eligible IPDMAs, we re-evaluated the number of RCTs per IPDMA. With an average cluster size of 22 RCTs per IPDMA, we estimated that 34 IPDMAs and a total of 732 primary studies were necessary to have 80% power with alpha = 0.05. Thus, we sought 35 IPDMAs.

To evaluate RCT and IPDMA factors associated with data contribution from eligible RCTs, we fit a marginal model estimated via Generalized Estimating Equations with a logit link function. We used an exchangeable correlation structure with robust standard errors to account for correlation between primary studies within the same IPDMA. All of the aforementioned variables extracted at the IPDMA and the RCT level were included in the model except for authorship because almost all IPDMA author groups offered data contributors authorship (28 of 35 IPDMAs (80%). Analyses were run using the geepack package in R version 3.4.1.

All data extracted and analyzed for the present study are available at https://osf.io/e3zf6/ (Filename = DataFile_2019-07-14.xlsx).

RESULTS

Selection of Eligible IPDMAs

The combined searches retrieved 2,959 citations, of which 1,786 were excluded after title and abstract review and 1,138 after full-text review. Hence, a total of 35 IPDMAs with 774 eligible RCTs were included (Figure 1). The average number of eligible RCTs per IPDMA was 22.1 (standard deviation [SD] = 16.6; range 10 to 75). Mean impact factor of the journal
publishing the IPDMAs was 11.1 (SD = 10.1; range 1.7 to 44.0). More than half of the IPDMAs were either registered in PROSPERO or published a protocol (N = 19, 54.3%) and were from the United Kingdom (N = 18, 51.4%). The most common conditions studied were cardiovascular disease (N = 9, 26%) and cancer (N = 6, 17%) with the remaining 20 (57%) in other conditions. Characteristics of the 35 included IPDMAs are presented in Appendix 2, and summary statistics are presented in Table 1.

**Objective 1: Proportion of Studies that Contributed Data**

Of the 774 eligible RCTs, 517 (67%, 95% CI, 63% to 70%) contributed data. The proportion that contributed data within individual IPDMAs varied from 16% to 100%: < 20% = 1 IPDMA (3%); 20% to 39% = 2 IPDMAs (6%); 40% to 59% = 5 IPDMAs (20%); 60% to 79% = 13 IPDMAs (37%), ≥ 80% = 14 IPDMAs (40%).

**Objective 2: IPDMA and RCT Characteristics Associated with Data Contribution**

When bivariate associations were considered, greater odds of data contribution were associated with national, state or provincial funding of RCTs compared to other sources of funding, interventions on cancer compared to non-cancer and non-cardiovascular interventions, journal impact factor greater than 2.5 compared to journal impact factor of less than 2.5, and RCTs from the United Kingdom (reference = United States). Characteristics associated with lower odds of data contribution included not reporting conflicts of interest compared to reporting no conflict of interest; and RCTs from China and “other non-European countries” (reference = United States. A post-hoc analysis that evaluated impact factor as a continuous variable showed that each one-point increase in impact factor was associated with a 4% higher odds of data contribution (OR 1.04, 95% CI 1.02-1.07). See Table 1. Characteristics of individual RCTs included in IPDMAs are available at https://osf.io/e3zf6/.
Of the 774 RCTs, 748 (97%) had complete data for all included variables and were included in the multivariate analysis. As shown in Table 1, characteristics associated with contributing data included: trials from the United Kingdom (reference = United States); publication of RCTs in higher impact journals, and year of RCT publication.

**DISCUSSION**

Among the 35 IPDMAs with at least 10 eligible RCTs that were included in the study, 67% of 774 eligible RCTs contributed data. Data contribution was independently associated with higher impact factor of the journals that published the RCTs, the RCT being conducted in the United Kingdom (compared to the United States), and a more recent publication year of the RCT.

We are aware of two previous studies that have attempted to identify factors associated with contribution of trial data to IPDMAs. In one,27 the authors obtained data from 8 of 29 trials on exercise in adults with rheumatic diseases, but did not find any trial characteristics that were associated with data contribution. In the other study,28 a randomized trial was conducted to examine whether a small financial incentive would encourage authors of 137 studies to contribute data to two systematic reviews, one on the safety and effectiveness of cognitive enhancers for Alzheimer's dementia, and the other on the safety and effectiveness of long-acting versus intermediate-acting insulin for patients with type 1 diabetes. The authors, however, only obtained data from 2 of 137 trials (107 with industry sponsors). Thus, the authors could only analyze factors associated with responding to certain requests, but not related to providing data. In our study, 67% of RCTs tested drugs or biologics, but only 30% had any industry funding, and some of this constituted relatively minor support, rather than full sponsorship. Since we analyzed
results from only published IPDMAs, we were not able to identify factors, such as barriers related to industry sponsorship, that may derail efforts to conduct IPDMAs altogether.

We found that impact factor of journals where trials were published was associated with data contribution. Many top medical journals are ICMJE member journals or abide by ICMJE data sharing policies, which might be one explanation. It could also be the case that impact factor was a rough proxy for quality and that trials published in higher impact journals may be conducted by more conscientious and skilled investigators who would be more willing and able to provide data, regardless of journal policy.

Specific barriers to data sharing expressed by primary study authors have been discussed by others.\textsuperscript{32-35} One set of barriers involves the lack of standardized structures, easily available repositories, and funding for the cost of data preparation.\textsuperscript{32} One solution could be the establishment of centralized repositories for storing clinical trial data. Such a platform has been recommended by the Clinical Data Interchange Standards Consortium.\textsuperscript{33} Other proposed solutions involve incentives, such as the inclusion of data sharing as a criterion for promotions and career advancement, similar to publishing in reputable peer-reviewed journals.\textsuperscript{34,35} For instance, a sharing index (s-index) analogous to the h-index for measuring citations of an author’s publications, could be implement as a means to evaluate data sharing with other research groups.\textsuperscript{35}

A strength of the present study is that it is the first study to describe characteristics of individual studies associated with data contribution to IPDMAs and to evaluate characteristics of both IPDMAs and eligible studies associated with data contribution. There are a number of limitations to consider in evaluating results from the present study. First, it is certainly the case that many IPDMA investigators who are unsuccessful in obtaining individual participant data do
not go forward with an IPDMA and do not publish that information, especially if there were only a few eligible studies. Hence, the proportion of contributing studies that we found (67%) can only be interpreted as a characterization of the proportion of RCTs that contributed data in published IPDMAs with at least 10 eligible trials and not as the proportion of RCT authors who contribute data to IPDMAs. Furthermore, we were not able to identify factors associated with the ability to obtain enough data to conduct and IPDMA, but rather could only characterize IPDMA and RCT characteristics among successfully published IPDMAs. Second, we excluded 43 IPDMAs with fewer than 10 eligible RCTs and 17 that did not provide a list of all eligible RCTs. We did not attempt to contact authors of the 17 IPDMAs that did not provide a reference list of all eligible RCTs. It is not known to what degree this may have influenced our findings. Third, we removed 26 trials with missing observations from the multivariate analysis. Given that this was only 3% of included RCTs, we do not believe that this influenced the results. Fourth, the results of this study can only be generalized to successfully published IPDMAs with at least 10 eligible RCTs. Fifth, we used impact factor of journals where trials were published as a rough proxy for quality. This is because risk of bias assessments were not consistently provided for individual trials in IPDMAs, and coding risk of bias for all included trials was beyond the scope and resources of the study. Sixth, our analysis identified trial characteristics, such as country, associated with data contribution, but that are not explanatory in themselves.

Future studies should evaluate data contribution in other types of studies including observational and diagnostic test accuracy studies. Even more importantly, studies are needed that examine large numbers of IPDMAs that are planned or attempted, rather than successfully published. One possibility would be to use systematic review registrations, although reviewers
may only develop protocols and register IPDMAs if they have already ascertained that they will be able to obtain the necessary data.

CONCLUSIONS

We found that among successfully published IPDMAs with at least 10 eligible RCTs, data from 67% of identified RCTs were included. Statistically significantly higher odds of data contribution was associated with trials from the United Kingdom (reference United States), publication of RCTs in higher impact journals, and year of RCT publication. A limitation is that we only examined successfully published IPDMAs and could not identify factors associated with non-completion of planned or attempted IPDMAs. Nonetheless, this study provides insight into potential factors associated with data sharing that may guide future interventions and practices to increase open data sharing.
DECLARATIONS

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Availability of data and materials
All data and materials are available in the present updated report and supplementary materials.

Competing interests
The authors declare that they have no competing interests.

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AUTHORS’ CONTRIBUTIONS
MA, AB, IS and BDT contributed to the conception and design of the study. MC designed and conducted the database searches. MA, KER, MI, AK, MC, TS and BDT were involved in acquisition of data. MA, AB, IS and BDT were involved in the interpretation of results. MA and BDT drafted this manuscript. All authors provided critical revisions of the manuscript and approved submission of the final manuscript.

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Table 1. Results of Bivariate Analysis (N = 774) and Multivariate Analysis Using a Generalized Estimating Equation (N = 748)\(^a\) of Factors Associated with Data Contribution

<table>
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<tr>
<th>Coefficient</th>
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<th>Multivariate OR (95% CI)</th>
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<td>Reference</td>
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<td>Reference (0.48, 2.04)</td>
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</tr>
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<td>0.82 (0.31, 2.15)</td>
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<td>Device</td>
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<td>0.82 (0.40, 1.68)</td>
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<td>University or hospital funding of RCT</td>
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<td>5.71 (3.03, 10.77)</td>
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<td>1.48 (0.47, 4.61)</td>
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<td>Reference</td>
<td>Reference</td>
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<td>0.81 (0.33, 2.01)</td>
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<td>0.71 (0.31, 1.66)</td>
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<td>0.35 (0.09, 1.29)</td>
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<td>34</td>
<td>1.63 (0.77, 3.45)</td>
<td>2.76 (0.78, 9.82)</td>
</tr>
<tr>
<td>Germany</td>
<td>49</td>
<td>0.96 (0.43, 2.19)</td>
<td>1.09 (0.43, 2.75)</td>
</tr>
<tr>
<td>Italy</td>
<td>30</td>
<td>0.90 (0.41, 1.99)</td>
<td>1.11 (0.42, 2.95)</td>
</tr>
<tr>
<td>Japan</td>
<td>44</td>
<td>0.93 (0.38, 2.25)</td>
<td>1.29 (0.49, 3.43)</td>
</tr>
<tr>
<td>Netherlands</td>
<td>37</td>
<td>4.40 (0.41, 47.15)</td>
<td>3.45 (0.42, 28.52)</td>
</tr>
<tr>
<td>Sweden</td>
<td>33</td>
<td>1.16 (0.52, 2.57)</td>
<td>1.74 (0.74, 4.08)</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>85</td>
<td>2.50 (1.16, 5.39)</td>
<td>2.44 (1.28, 4.64)</td>
</tr>
<tr>
<td>Other European countries</td>
<td>82</td>
<td>1.18 (0.64, 2.16)</td>
<td>1.34 (0.63, 2.88)</td>
</tr>
<tr>
<td>Other non-European countries</td>
<td>105</td>
<td>0.42 (0.24, 0.73)</td>
<td>0.56 (0.27, 1.16)</td>
</tr>
</tbody>
</table>
Sample size of the RCT included in the IPDMA (rescaled)\textsuperscript{c,d}  
\begin{tabular}{lll}
749 & 2.93 (0.93, 9.17) & 1.55 (0.98, 2.44) \\
\end{tabular}

Publication year of the RCT (rescaled)\textsuperscript{c,d}  
\begin{tabular}{lll}
771 & 1.22 (0.96, 1.55) & 1.05 (1.02, 1.09) \\
\end{tabular}

\textsuperscript{a}Fewer trials included in multivariate analysis due to missing data; \textsuperscript{b}All 9 trials in this category contributed data; \textsuperscript{c}Missing values for these variable; \textsuperscript{d}Rescaled values were obtained by subtracting the mean from each value and dividing by the standard deviation.

Abbreviations: CI = confidence interval, IPDMA = Individual participant data meta-analysis, OR = odds ratio, RCT = randomized controlled trial
Figure 1. Flow Chart of Included Individual Participant Data Meta-Analyses

Articles included in title/abstract review (n = 2,959)

Full-text articles assessed for eligibility (n = 445)

Articles excluded after title/abstract review (n = 2,514)

Articles excluded at full-text review (n = 410)
- Not a meta-analysis: 309
- Not an individual patient data meta-analysis (IPDMA) of randomized controlled trials (RCTs): 36
- No reference list of all eligible RCTs provided: 17
- IPDMA of less than 10 eligible RCTs: 43
- Secondary report of an IPDMA that was already included in this study: 5

Articles included in analyses (n = 35, including n = 774 RCTs)
Appendix 1. Search Strategy

**MEDLINE and Embase**

1. (individual patient$ adj6 data).af.
2. (individual patient$ adj3 level$).af.
3. (individual patient$ and (meta analy$ or metaanaly$ or metanaly$ or subgroup analy$ or evidence synthesis or systematic review$ or pooled analys$)).af
4. (individual participant$ adj6 data).af.
5. (individual participant$ level$).af.
6. (individual participant$ and (meta analy$ or metaanaly$ or metanaly$ or subgroup analy$ or evidence synthesis or systematic review$ or pooled analys$)).af.
7. (individual level data and (meta analy$ or metaanaly$ or metanaly$ or subgroup analy$ or evidence synthesis or systematic review$ or pooled analys$)).af
8. participant level data.af.
9. (IPD not (immediate pigment darkening or invasive pneumococcal disease or idiopathic Parkinson$ disease or intermittent peritoneal dialysis or invasive pneumococcal disease or indirect photometric detection or interaural phase disparity or Invasive placental disease or Incremental peritoneal dialysis)).af.
10. IPDMA.af.
11. (individual subject$ data).af.
14. (individual data and (meta analy$ or metaanaly$ or metanaly$ or subgroup analy$ or evidence synthesis or systematic review$ or pooled analys$)).af.
15. (patient level and (meta analy$ or metaanaly$ or metanaly$ or subgroup analy$ or evidence synthesis or systematic review$ or pooled analys$)).af.
16. original patient$ data.af.
17. (patient based and (meta analy$ or metaanaly$ or metanaly$ or subgroup analy$ or evidence synthesis or systematic review$ or pooled analys$)).af.
18. (prospectively planned and (meta analy$ or metaanaly$ or metanaly$ or subgroup analy$ or evidence synthesis or systematic review$ or pooled analys$)).af.
19. collaborative re-analys$.af.
20. collaborative reanalys$.af.
21. OR/1-20

22. Limit 21 to yr="2016 -Current"

Notes
“af” (all fields) indicates that the search terms can appear anywhere in the record.
“$” is a truncation symbol that retrieves variations for word endings. E.g. patient$ will find ‘patient’ and ‘patients’
“adjn” is a proximity operator that specifies the distance between two terms. E.g. “individual patient$ adj6 data” indicates that ‘individual patient’ and ‘data’ need to be within six words of each other, in any order, for the article to be retrieved.

CINAHL
1. (individual patient*) N6 data
2. (individual patient*) N3 level
3. (individual patient*) AND ((meta analy*) or ( metaanaly*) or (metanaly*) or (subgroup analy*) or (evidence synthesis) or (systematic review*) or (pooled analys*))
4. (individual participant*) N6 data
5. (individual participant* level*)
6. (individual participant*) AND ((meta analy*) or ( metaanaly*) or (metanaly*) or (subgroup analy*) or (evidence synthesis) or (systematic review*) or (pooled analys*))
7. (individual level data) AND ((meta analy*) or ( metaanaly*) or (metanaly*) or (subgroup analy*) or (evidence synthesis) or (systematic review*) or (pooled analys*))
8. (patient level) AND ((meta analy*) or ( metaanaly*) or (metanaly*) or (subgroup analy*) or (evidence synthesis) or (systematic review*) or (pooled analys*))
9. participant level data
10. IPD NOT (invasive pneumococcal disease)
11. IPDMA
12. (individual subject* data)
13. (individual patient information)
14. (individual data) AND ((meta analy*) or ( metaanaly*) or (metanaly*) or (subgroup analy*) or (evidence synthesis) or (systematic review*) or (pooled analys*))
15. (original patient* data)
16. (patient based) AND ((meta analy*) or ( metaanaly*) or (metanaly*) or (subgroup analy*) or (evidence synthesis) or (systematic review*) or (pooled analys*))
17. (prospectively planned) AND ((meta analy*) or ( metaanaly*) or (metanaly*) or (subgroup analy*) or (evidence synthesis) or (systematic review*) or (pooled analys*))
18. (collaborative reanalys*)
19. 1-18/OR
Notes
“*” is truncation symbol that retrieves word ending variations.
“Na” is a proximity operator that specifies the maximum distance between two terms.

Search Strategy for Cochrane
1. (individual next patient*) near/6 data:ti,ab,kw
2. (individual next patient*) near/3 level:ti,ab,kw
3. individual next patient*:ti,ab,kw and (meta analy* or metaanaly* or metanaly* or (subgroup next analy*) or "evidence synthesis" or (systematic next review*) or (pooled next analy*)):ti,ab,kw
4. (individual next participant*) near/6 data:ti,ab,kw
5. (individual next participant*) near/3 level:ti,ab,kw
6. individual next participant*:ti,ab,kw and (meta analy* or metaanaly* or metanaly* or (subgroup next analy*) or "evidence synthesis" or (systematic next review*) or (pooled next analy*)):ti,ab,kw
7. "individual level data":ti,ab,kw and ((meta analy*) or (metaanaly*) or (metanaly*) or (subgroup next analy*) or "evidence synthesis" or (systematic next review*) or (pooled next analy*))
8. "patient level data":ti,ab,kw and (meta analy* or metaanaly* or metanaly* or (subgroup next analy*) or "evidence synthesis" or (systematic next review*) or (pooled next analy*))
9. "participant level data":ti,ab,kw
10. IPD:ti,ab,kw not "invasive pneumococcal disease":ti,ab,kw
11. IPDMA
12. individual next subject* next data:ti,ab,kw
13. "individual patient information":ti,ab,kw
14. "individual data":ti,ab,kw and (meta analy* or metaanaly* or metanaly* or (subgroup next analy*) or "evidence synthesis" or (systematic next review*) or (pooled next analy*)):ti,ab,kw
15. "patient level":ti,ab,kw and (meta analy* or metaanaly* or metanaly* or (subgroup next analy*) or "evidence synthesis" or (systematic next review*) or (pooled next analy*)):ti,ab,kw
16. "patient based":ti,ab,kw and (meta analy* or metaanaly* or metanaly* or (subgroup next analy*) or "evidence synthesis" or (systematic next review*) or (pooled next analy*)):ti,ab,kw

17. "original patient data"

18. "prospectively planned":ti,ab,kw and (meta analy* or metaanaly* or metanaly* or (subgroup next analy*) or "evidence synthesis" or (systematic next review*) or (pooled next analy*)):ti,ab,kw

19. "collaborative reanalysis":ti,ab,kw

20. [1-#19]

21. [1 -#19] Publication Year from 2016 to 2016

Notes
“ti,ab,kw” indicates that the search terms must be located in the title, abstract or keywords of the record.
“*” is a truncation symbol that retrieves word ending variations.
“Near/n” is a proximity operator that specifies the maximum distance between two terms.
## Appendix 2. Characteristics of Included Individual Participant Data Meta-Analyses (N = 35)

<table>
<thead>
<tr>
<th>Author</th>
<th>Title</th>
<th>Year of publication</th>
<th>Number of eligible RCTs</th>
<th>Number (%) of contributing RCTs</th>
<th>Published protocol</th>
<th>Journal name</th>
<th>2015 Impact factor</th>
<th>Authorship</th>
<th>Country of corresponding author</th>
<th>Medical condition of participant population</th>
<th>Type of intervention assessed</th>
<th>Primary outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol Treatment Trialists’ (CTT) Collaboration</td>
<td>Impact of renal function on the effects of LDL cholesterol lowering with statin-based regimens: a meta-analysis of individual participant data from 28 randomised trials.</td>
<td>2016</td>
<td>31</td>
<td>28 (90)</td>
<td>Yes</td>
<td>No</td>
<td>Lancet Diabetes &amp; Endocrinology</td>
<td>16.3</td>
<td>No authorship offered</td>
<td>United Kingdom</td>
<td>Kidney Disease</td>
<td>Drug/biologic</td>
</tr>
<tr>
<td>JR Brown et al.</td>
<td>Meta-Analysis of Individual Patient Data of Sodium Bicarbonate and Sodium Chloride for All-Cause Mortality After Coronary Angiography.</td>
<td>2016</td>
<td>10</td>
<td>7 (70)</td>
<td>No</td>
<td>Yes</td>
<td>American Journal of Cardiology</td>
<td>3.2</td>
<td>Authorship offered</td>
<td>United States</td>
<td>Cardiovascular disease</td>
<td>Drug/biologic</td>
</tr>
<tr>
<td>S Burdett et al.</td>
<td>Postoperative radiotherapy for non-small cell lung cancer.</td>
<td>2016</td>
<td>13</td>
<td>11 (85)</td>
<td>No</td>
<td>No</td>
<td>Cochrane Database of Systematic Reviews</td>
<td>6.1</td>
<td>Authorship offered</td>
<td>United Kingdom</td>
<td>Cancer</td>
<td>Device</td>
</tr>
<tr>
<td>DM Charytan et al.</td>
<td>Reduced risk of myocardial infarct and revascularization following coronary artery bypass grafting compared with percutaneous coronary intervention in patients with chronic kidney disease.</td>
<td>2016</td>
<td>20</td>
<td>10 (50)</td>
<td>No</td>
<td>No</td>
<td>Kidney International</td>
<td>7.7</td>
<td>Authorship offered</td>
<td>United States</td>
<td>Kidney Disease</td>
<td>Device, non-regulated</td>
</tr>
<tr>
<td>D. D. Ebert et al.</td>
<td>Does Internet-based guided-self-help for depression cause harm? An individual participant data meta-analysis on deterioration rates and its</td>
<td>2016</td>
<td>19</td>
<td>18 (95)</td>
<td>No</td>
<td>Yes</td>
<td>Psychological Medicine</td>
<td>5.5</td>
<td>Authorship offered</td>
<td>Germany</td>
<td>Mental health</td>
<td>Non-regulated</td>
</tr>
<tr>
<td>Study Authors</td>
<td>Study Title</td>
<td>Year</td>
<td>Sample Size</td>
<td>Randomized</td>
<td>Funded</td>
<td>Journal or Book</td>
<td>Impact Factor</td>
<td>Authorship Offered</td>
<td>United States</td>
<td>Disease</td>
<td>Drug/Biologic</td>
<td>Device</td>
</tr>
<tr>
<td>---------------------------------------</td>
<td>-----------------------------------------------------------------------------</td>
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</tr>
<tr>
<td>GG Saporito et al.</td>
<td>Safety and Efficacy of New-Generation Drug-Eluting Stents in Women Undergoing Complex Percutaneous Coronary Artery Revascularization: From the WIN-DES Collaborative Patient-Level Pooled Analysis</td>
<td>2016</td>
<td>26 (100)</td>
<td>No</td>
<td>No</td>
<td>JACC: Cardiovascular Interventions</td>
<td>7.6</td>
<td>Authorship offered</td>
<td>United States</td>
<td>Cardiovascular disease</td>
<td>Drug/biologic , device</td>
<td></td>
</tr>
<tr>
<td>NH Jonkman et al.</td>
<td>What are Effective Program Characteristics of Self-Management Interventions in Patients with Heart Failure? an Individual Patient Data Meta-Analysis</td>
<td>2016</td>
<td>32</td>
<td>Yes</td>
<td>Yes</td>
<td>Journal of Cardiac Failure</td>
<td>3.3</td>
<td>Authorship offered</td>
<td>Netherlands</td>
<td>Cardiovascular disease</td>
<td>Non-regulated</td>
<td></td>
</tr>
<tr>
<td>D Kotecha et al.</td>
<td>Effect of age and sex on efficacy and tolerability of beta blockers in patients with heart failure with reduced ejection fraction: individual patient data meta-analysis</td>
<td>2016</td>
<td>11</td>
<td>Yes</td>
<td>Yes</td>
<td>BMJ</td>
<td>19.7</td>
<td>Authorship offered</td>
<td>United Kingdom</td>
<td>Cardiovascular disease</td>
<td>Drug/biologic , non-regulated</td>
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<tr>
<td>KM Livingstone et al.</td>
<td>FTO genotype and weight loss: systematic review and meta-analysis of 9563 individual participant data from eight randomised controlled trials</td>
<td>2016</td>
<td>11</td>
<td>No</td>
<td>Yes</td>
<td>BMJ</td>
<td>19.7</td>
<td>Authorship offered</td>
<td>United Kingdom</td>
<td>Obesity</td>
<td>Drug/biologic , non-regulated</td>
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<tr>
<td>H. MacPherson et al.</td>
<td>The persistence of the effects of acupuncture after a course of treatment: A meta-analysis of patients with chronic pain.</td>
<td>2016</td>
<td>31</td>
<td>Yes</td>
<td>No</td>
<td>Pain</td>
<td>5.6</td>
<td>Group authorship offered</td>
<td>United Kingdom</td>
<td>Chronic pain</td>
<td>Non-regulated</td>
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<tr>
<td>AS Neto et al.</td>
<td>Association between driving pressure and development of postoperative pulmonary complications in patients undergoing mechanical ventilation</td>
<td>2016</td>
<td>25</td>
<td>Yes</td>
<td>No</td>
<td>The Lancet Respiratory Medicine</td>
<td>15.3</td>
<td>Authorship offered</td>
<td>Brazil</td>
<td>Mixed surgery</td>
<td>Device</td>
<td>Development of postoperative pulmonary complications</td>
</tr>
<tr>
<td>Study Title</td>
<td>Authors</td>
<td>Year</td>
<td>Sample Size (Allocation)</td>
<td>Allocation</td>
<td>Disease</td>
<td>Methodology</td>
<td>Country</td>
<td>Outcomes</td>
<td>Drug/Biologic</td>
<td>Type of Data</td>
<td>Research Organisation</td>
<td>Additional Information</td>
</tr>
<tr>
<td>-------------</td>
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<td>------------------------</td>
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<td>Ventilation for general anaesthesia: a meta-analysis of individual patient data.</td>
<td>SJ Nolan</td>
<td>2016</td>
<td>11</td>
<td>5 (46)</td>
<td>Yes</td>
<td>Yes</td>
<td>Cochrane Database of Systematic Reviews</td>
<td>United Kingdom</td>
<td>Seizures</td>
<td>Drug/biologic</td>
<td>Authors</td>
<td>Time to withdrawal of allocated treatment (retention time).</td>
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<tr>
<td>Phenytoin versus valproate monotherapy for partial onset seizures and generalised onset tonic-clonic seizures: an individual participant data review</td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>The efficacy of adjuvant immunochemotherapy with OK-432 after curative resection of gastric cancer: an individual patient data meta-analysis of randomized controlled trials.</td>
<td>MS Obas</td>
<td>2016</td>
<td>14</td>
<td>14 (100)</td>
<td>No</td>
<td>No</td>
<td>Gastric Cancer</td>
<td>Japan</td>
<td>Cancer</td>
<td>Drug/biologic</td>
<td>Overall survival at a median follow-up of 35 months.</td>
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<td>Association Between Chronic Physical Conditions and the Effectiveness of Collaborative Care for Depression: An Individual Participant Data Meta-analysis.</td>
<td>M Panagioti et al.</td>
<td>2016</td>
<td>76</td>
<td>32 (42)</td>
<td>Yes</td>
<td>No</td>
<td>JAMA Psychiatry</td>
<td>United Kingdom</td>
<td>Mental Health</td>
<td>Non-regulated</td>
<td>Continuous outcomes of depression severity symptoms between 4 and 6 months.</td>
<td></td>
</tr>
<tr>
<td>Effects of aspirin on risk and severity of early recurrent stroke after transient ischaemic attack and ischaemic stroke: time-course analysis of randomised trials.</td>
<td>PM Rothwell et al.</td>
<td>2016</td>
<td>12</td>
<td>12 (100)</td>
<td>No</td>
<td>No</td>
<td>Lancet</td>
<td>United Kingdom</td>
<td>Cardiovascular disease</td>
<td>Drug/biologic</td>
<td>6-week risk of recurrent ischemic stroke.</td>
<td></td>
</tr>
<tr>
<td>Admission avoidance hospital at home.</td>
<td>S Shepperd et al.</td>
<td>2016</td>
<td>10</td>
<td>6 (60)</td>
<td>No</td>
<td>No</td>
<td>Cochrane Database of Systematic Reviews</td>
<td>United Kingdom</td>
<td>Mixed conditions</td>
<td>Non-regulated</td>
<td>Mortality at 6 months.</td>
<td></td>
</tr>
<tr>
<td>Authors</td>
<td>Title</td>
<td>Year</td>
<td>Participants</td>
<td>Direction</td>
<td>Disease</td>
<td>Journal/Binding</td>
<td>Group Authorship Offered</td>
<td>Country</td>
<td>Disease Area</td>
<td>Drug/biologic</td>
<td>Additional Information</td>
<td></td>
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<tr>
<td>M. van Middelkoop et al.</td>
<td>The OA Trial Bank: meta-analysis of individual patient data from knee and hip osteoarthritis trials show that patients with severe pain exhibit greater benefit from intra-articular glucocorticoids.</td>
<td>2016</td>
<td>30 7 (23)</td>
<td>Yes</td>
<td>No</td>
<td>Osteoarthritis and Cartilage</td>
<td>Authorship offered</td>
<td>Netherlands</td>
<td>Musculoskeletal</td>
<td>Drug/biologic</td>
<td>Pain severity at short-term up to 4 weeks.</td>
<td></td>
</tr>
<tr>
<td>LA Beveridge et al.</td>
<td>Effect of Vitamin D Supplementation on Blood Pressure: A Systematic Review and Meta-analysis Incorporating Individual Patient Data</td>
<td>2015</td>
<td>46 20 (44)</td>
<td>No</td>
<td>Yes</td>
<td>JAMA Internal Medicine</td>
<td>Authorship offered*</td>
<td>United Kingdom</td>
<td>Mixed conditions</td>
<td>Drug/biologic</td>
<td>Change in systolic blood pressure readings</td>
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<tr>
<td>HP Brunner-La Rocca et al.</td>
<td>Which heart failure patients profit from natriuretic peptide guided therapy? A meta-analysis from individual patient data of randomized trials</td>
<td>2015</td>
<td>11 9 (82)</td>
<td>No</td>
<td>No</td>
<td>European Journal of Heart Failure</td>
<td>Authorship offered</td>
<td>Netherlands</td>
<td>Cardiovascular disease</td>
<td>Drug/biologic</td>
<td>All-cause mortality at last follow-up.</td>
<td></td>
</tr>
<tr>
<td>Author(s)</td>
<td>Title</td>
<td>Year</td>
<td>Sample Size</td>
<td>Randomization</td>
<td>Journal</td>
<td>Impact Factor</td>
<td>Country</td>
<td>Disease Area</td>
<td>Drug/biologic</td>
<td>Outcomes</td>
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<tr>
<td>G Patti et al.</td>
<td>Statin pretreatment and risk of in-hospital atrial fibrillation among patients undergoing cardiac surgery: a collaborative meta-analysis of 11 randomized controlled trials</td>
<td>2015</td>
<td>11 (100)</td>
<td>No</td>
<td>Europace</td>
<td>4.0</td>
<td>United Kingdom</td>
<td>Cardiovascular disease</td>
<td>Drug/biologic</td>
<td>Postoperative atrial fibrillation</td>
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<tr>
<td>K Benkhadra et al.</td>
<td>Real-time continuous glucose monitoring in type 1 diabetes: A systematic review and individual patient data meta-analysis.</td>
<td>2017</td>
<td>11 (91)</td>
<td>No</td>
<td>Clinical Endocrinology</td>
<td>3.5</td>
<td>United States</td>
<td>Diabetes</td>
<td>Device</td>
<td>Change in glycosylated haemoglobin (HbA1c) from baseline to follow-up.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S Burdett et al.</td>
<td>Adjuvant chemotherapy for resected early-stage non-small cell lung cancer</td>
<td>2015</td>
<td>43 (74)</td>
<td>No</td>
<td>Cochrane Database of Systematic Reviews</td>
<td>6.1</td>
<td>United Kingdom</td>
<td>Cancer</td>
<td>Drug/biologic</td>
<td>Overall survival with a median follow-up of 5.5 years.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TJ England et al.</td>
<td>Granulocyte-Colony Stimulating Factor (G-CSF) for stroke: an individual patient data meta-analysis.</td>
<td>2016</td>
<td>10 (60)</td>
<td>No</td>
<td>Scientific Reports</td>
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<td>End of trial Modified Rankin Scale score.</td>
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<td>D Mataix-Cols et al.</td>
<td>D-Cycloserine Augmentation of Exposure-Based Cognitive Behavior Therapy for Anxiety, Obsessive-Compulsive, and Posttraumatic Stress Disorders: A Systematic Review and Meta-analysis.</td>
<td>2017</td>
<td>22</td>
<td>21 (96)</td>
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<td>JAMA Psychiatry</td>
<td>Sweden</td>
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<td>Symptom improvement at follow-up as measured by the primary outcome measure stipulated by the authors in each individual study.</td>
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<td>SJ Nolan et al.</td>
<td>Carbamazepine versus phenobarbitone monotherapy for epilepsy: an individual participant data review</td>
<td>2015</td>
<td>11</td>
<td>7 (64)</td>
<td>No</td>
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<td>Time to withdrawal of allocated treatment.</td>
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*No author responses received, therefore categorized inferred by determining the proportion of trialists included in the IPDMA publication author list. All 4 meta-analyses included a named author for all included trials in the IPDMA author list and were therefore classified as offering authorship.*