Selective reporting in trials of high risk cardiovascular devices: cross sectional comparison between premarket approval summaries and published reports

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ABSTRACT

OBJECTIVE
To investigate characteristics of clinical trials and results on safety and effectiveness reported in US Food and Drug Administration (FDA) documents for recently approved high risk cardiovascular devices compared with the characteristics and results reported in peer reviewed publications.

DESIGN
A search of the publicly available FDA database was performed for all cardiovascular devices that received premarket approval from 1 January 2000 to 31 December 2010. For each study listed in the premarket approval documents, a Medline search was conducted to obtain the corresponding publication.

MAIN OUTCOME MEASURES
Clinical trial characteristics, primary endpoints, and safety and efficacy results in the FDA documents and corresponding publications.

RESULTS
106 cardiovascular devices received premarket approval from 1 January 2000 to 31 December 2010. FDA premarket approval documents for these devices contained 177 studies, of which 86 (49%) had been published by 1 January 2013. These 86 publications corresponded to 60 distinct devices. The mean time from FDA approval to publication in a peer reviewed journal was 6.5 months (range −4.8-7.5 years). In 22 (26%) of the 86 compared studies the number of participants enrolled in the study differed in the FDA summary and the corresponding publications. Of 152 primary endpoints identified in the FDA documents, in the corresponding publications three (2%) were labeled as secondary, 43 (28%) were unlabeled, and 15 (10%) were not found. Among the primary results, 69 (45%) were identical, 35 (23%) were similar, 17 (11%) were substantially different, and 31 (20%) could not be compared.

CONCLUSIONS
Many clinical trials for high risk cardiovascular devices approved by the FDA remain unpublished. Even when trials are published, the study population, primary endpoints, and results can differ substantially from data submitted to the FDA.

Introduction
As medical devices play an important role in healthcare, the quality of clinical trial evidence supporting their use is critical to patients’ health and safety. In the United States between 1990 and 2002, over 17 000 pacemakers and implantable cardioverter defibrillators were removed and over 60 deaths were attributed to confirmed device malfunctions.2 Manufacturers of new high risk devices, including many used to treat cardiovascular disease, are often required to submit clinical trial data to the US Food and Drug Administration (FDA) for evaluation of safety and effectiveness via the premarket approval process.2 A review of recently approved high risk cardiovascular devices showed that they are often approved on the basis of a single study, most of which are not randomized and lack prospective controls.3,4

FDA documents containing the evidence to support approval of devices are available but are not easy to access. For informed clinical decision making, the trial data that the FDA reviews should be accessible to clinicians in peer reviewed publications. Previous work has found that when clinical trial information in FDA new drug applications is compared with the corresponding publications, there was significant selective reporting. Results favoring the new drug over the comparator were significantly more likely to be reported in the literature than unfavorable results.5 The selective publication of favorable results for drugs includes several types of reporting bias, including failure to publish entire studies, failure to publish unfavorable outcomes, and publication of only selected prespecified outcome analyses.

The extent of selective reporting for medical devices has not been examined. To assess selective reporting for trials of high risk cardiovascular devices, we examined clinical trial data found in FDA summaries compared with corresponding peer reviewed publications. We compared characteristics of clinical trials and results on safety and effectiveness reported in FDA premarket approval documents for recently approved high risk cardiovascular devices (such as coronary stents and implantable cardioverter defibrillators) with the trial characteristics and results reported in journal publications.

WHAT IS ALREADY KNOW ON THIS TOPIC
There is reporting bias of clinical data in new drug applications when they are published
The extent of selective reporting for medical device clinical trials is unknown

WHAT THIS STUDY ADDS
Most clinical studies used to justify FDA approval of high risk cardiovascular devices are not published
When these studies are published, there are often clinically relevant discrepancies between FDA documents and corresponding publications, including changed primary endpoints
**Methods**

**Trials in FDA summaries of safety and effectiveness data for premarket approval process**

We searched the publicly available FDA premarket approval database (www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm) on 1 August 2012 for all devices meeting the following parameters: “Cardiovascular” under advisory committee and “Originals Only” under supplement type, with an FDA approval date between from 1 January 2000 to 31 December 2010. The end date was selected to allow at least two years from approval of the device to publication of the clinical trial. For each device’s premarket approval located using this approach, we examined the “summary of clinical studies” section to identify clinical studies. For all the identified studies, we abstracted study characteristics and data.

**Published trials**

For each FDA summary, we searched Medline on 15 January 2013 for a corresponding publication with a publication date from 1 January 1990 to 1 January 2013. As the summaries do not include study authors or names of principal investigators, we conducted the search primarily using clinical trial titles and product names. Publication matches were confirmed by comparing methods, number of study centers, enrollment number, primary endpoint, primary results, and study sponsor. There were no instances in which there was ambiguity between multiple publications.

If this process failed to identify a matching publication, we emailed the device manufacturer to inquire about publication status. If the manufacturer was unable to provide a reference for publication or did not respond after three separate contact attempts one month apart, we considered the clinical trial unpublished.

**Data coding and comparing summaries with publications**

Data were abstracted from FDA summaries and publications and compiled in a database to compare the study characteristics and results from each respective source. One author (SD) abstracted and coded the summary, which was verified by another author (LC). Two authors (LC and JC) coded the data from publications. Disagreements were resolved by consensus of all authors.

A study was classified as pivotal if it was the only one included in the summary, a multicenter randomized controlled trial, or explicitly noted in the summary as being a pivotal study. If there were multiple multicenter randomized controlled trials for a given device, we considered all of them as pivotal studies. Otherwise, the study was classified as feasibility, early, or supportive in accordance with what was stated in the summary.

For each publication, we recorded time to publication (defined as the earliest date of publication, either online or in print), journal of publication, source of funding (industry or public) disclosed in the publication, and any author disclosure of conflict of interest.

After abstraction of data from both sources, we compared the following study characteristics between the summary and publications: randomization (yes/no), blinding (single, double, or none as reported in the summary or publications), number of sites, number of patients enrolled, patient demographics (age, sex, race), and whether results from multiple studies were pooled into one publication.

**Primary endpoint analysis**

We identified all explicitly stated primary endpoints in FDA summaries and publications for each study. When not specified in the summary or publication, all endpoints were designated as primary if there were three or fewer endpoints. If there were more than three endpoints and none was designated as primary, the study was considered as having no primary endpoint. All summary primary endpoints were compared with matching endpoints in the corresponding publication (if one could be found), even if they were not designated as primary in the publication.

Primary endpoint features compared between summaries and publications were as follows: type of primary endpoint (equivalence, non-inferiority, objective performance criteria), type of controls, and number of patients analyzed for primary endpoint. An objective performance criterion is a surrogate benchmark for an outcome that serves as a control group for some studies.

We compared the results for each primary endpoint between the summaries and publications and classified them as identical, similar, different, or unknown. To be classified as identical, the results had to match in both numerical value and significance (same P value and confidence interval). Results were designated as similar if the publication value differed by less than 5% from the original summary values and significance was unchanged. Otherwise, the results were considered as different. They were classified as unknown if no corresponding primary endpoint result could be found in the publication.

**Data analysis**

We first compared characteristics of published and unpublished studies. We then further examined the characteristics of the publications. Finally, we examined discrepancies between study characteristics, primary endpoints, and results as reported in the summaries and publications. Summary statistics were calculated for each comparison outlined above and presented as numbers, percentages, means, standard deviations, and ranges when applicable. Significance was assessed with a generalized linear mixed effects model with a canonical logit link function for a binomial model and a random effect placed on the intercept to account for heterogeneity across devices. We then computed odds ratios, P values, and 95% confidence intervals. For the primary endpoint comparison of number analyzed, we used a general linear mixed effects model with random effect placed on the intercept to account for device clustering. All tests were two sided with P<0.05 as the criterion for significance. We performed a subgroup analysis on all pivotal studies.
### Results

From 2000 to 2010 there were summaries for 106 cardiovascular devices. We identified 177 studies (mean 1.7 per device) in these summaries, of which 86 (49%) were published. The 86 published studies corresponded to 60 distinct devices (mean 1.4 published studies per device). The pivotal studies also corresponded to the same 60 distinct devices (mean 1.1 published pivotal studies per device). We contacted 23 manufacturers to request publication references, and eight (35%) responded, confirming that the trials of interest had not been published. One manufacturer could not be contacted because of lack of any contact information. Subgroup analysis restricted to the pivotal studies showed that of 112 pivotal studies, there were 66 corresponding publications (59%).

#### Published versus unpublished trials

Published trials were more often randomized, blinded, and based exclusively in the US than unpublished trials. Of the 86 published trials, 34 (40%) were randomized, compared with 26 (29%) of the 91 unpublished trials (95% confidence interval for difference 3.7% to 25.1%). Similarly, 23/86 (27%) of published trials were blinded compared with 6/91 (7%) of unpublished trials (8.5% to 31.6%). Although nearly the same proportion of published and unpublished trials were conducted at multiple centers—85% and 87%, respectively—more published trials than unpublished trials (43% v 23%) were conducted exclusively in the US (5.3% to 33%).

#### Characteristics of published trials

The average time from FDA approval to publication was 6.5 months, with a range of −4.8 years to 7.5 years (table 1). For the 66 pivotal studies, the average time to publication was 7.9 months, and 22 (33%) were published before FDA approval. Of publications that specified a funding source, all were industry funded. Most publication authors disclosed additional conflicts of interest. Six studies, five of them pivotal, were presented as pooled data and not individual studies when published.

#### Comparison of demographics between summaries and publications

In 22 (26%) of the 86 published studies, the number of patients enrolled in study differed between the summary and the publication (table 2). When we used the summary data as the reference, the mean difference in the stated total number of patients enrolled was 12.8 (4% difference), with a maximum difference of 181 patients. Sixteen publications reported fewer patients enrolled and five reported more patients enrolled than the corresponding summary.

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#### Comparison of study characteristics between summaries and publications

Overall, 35 (41%) of the published studies reported a randomized design (table 3). Twenty three (27%) were blinded, 13 (57%) of which were double blinded. Characteristics of randomization and blinding were similar between the summaries and publications. Pivotal studies, compared with feasibility, early, and supportive studies, were similar in terms of likelihood of being randomized: 28/66 (42%) were randomized and 16/66 were blinded (24%), of which 10/16 (63%) were double blinded.

#### Comparison of primary endpoints characteristics between summaries and publications

For the 86 summary studies for which we found a corresponding publication, 139 total primary endpoints were characterized. Thirteen summary studies had no identifiable primary endpoint, but for purposes of analysis, as the summary data were considered the standard, these studies were considered to have one unknown primary endpoint and added to the 139 to comprise the denominator of 152 possible primary endpoints from the summaries. The primary endpoints were heterogeneous

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**Table 1 | Characteristics of published trials on high risk cardiovascular devices. Figures are numbers (percentage) unless stated otherwise**

| Characteristic                          | All studies (n=86) | Pivotal studies* (n=66) |
|-----------------------------------------|--------------------|------------------------|
| Mean (range) time to publication (months) | 6.5 (–58-90)       | 7.9 (–58-90)           |
| Industry funded                         | 62 (71)            | 50 (76)                |
| Source of funding not specified         | 24 (28)            | 16 (24)                |
| Author conflicts disclosed              | 156 (65)           | 43 (65)                |
| Multiple trials presented in pooled fashion | 6 (7)               | 5 (8)                  |

*Study was classified as pivotal if it was only one included in summary, multicenter randomized controlled trial, or explicitly noted in summary as being pivotal study.

**Table 2 | Comparison of enrollment and demographics reported in FDA premarket approval summaries with corresponding publications and those published studies. Figures are numbers (percentage) unless stated otherwise**

| Characteristic                          | All studies (n=86) | Pivotal studies* (n=66) |
|-----------------------------------------|--------------------|------------------------|
| Discrepancy in enrollment               | 22 (26)            | 18 (27)                |
| Discrepancy >5%                         | 14 (16)            | 11 (17)                |
| Discrepancy ≤5%                         | 8 (9)              | 7 (11)                 |
| Mean (range) difference in No of patients enrolled (range) | −1.4 (−104-181) | −1.1 (−104-181) |
| Mean (range) % difference in No of patients enrolled | −1.2 (−39-39) | −0.7 (−39-39) |
| Absolute difference in No of patients enrolled (range) | 12.8 (0-181) | 16.7 (0-181) |
| Absolute mean difference in % enrolled (range) | 4 (0-39) | 4 (0-39) |
| Discrepancy in mean age                 | 9 (1)              | 8 (12)                 |
| Discrepancy in % male                   | 14 (16)            | 12 (18)                |

*Study was classified as pivotal if it was only one included in summary, multicenter randomized controlled trial, or explicitly noted in summary as being pivotal study.
Comparison of study characteristics reported in FDA premarket approval summaries with corresponding publications and those published studies. Figures are numbers (percentage) unless stated otherwise.

Table 3

| Characteristic                        | All (n=86) | Pivotal (n=66)* |
|---------------------------------------|------------|-----------------|
|                                      | Summary    | Published       | Odds ratio (95% CI), P value† | Summary    | Published       | Odds ratio (95% CI), P value† |
| Randomized                           | 34 (40)    | 34 (40)         | 1.00 (0.43 to 2.33), 1.0       | 28 (42)    | 28 (42)         | 1.00 (0.38 to 2.62), 1.0       |
| Blinded studies                      | 23 (27)    | 23 (27)         | 1.00 (0.37 to 2.67), 1.0       | 16 (24)    | 16 (24)         | 1.00 (0.33 to 3.06), 1.0       |
| Double blind                         | 13 (15)    | 13 (15)         | 1.00 (0.35 to 2.85), 1.0       | 10 (15)    | 10 (15)         | 1.00 (0.32 to 3.11), 1.0       |
| Single blind                         | 10 (12)    | 10 (12)         | 1.00 (0.32 to 3.16), 1.0       | 6 (9)      | 6 (9)           | 1.00 (0.25 to 3.95), 1.0       |
| Multicenter                          | 73 (85)    | 76 (89)         | 1.45 (0.54 to 2.89), 0.46      | 64 (97)    | 65 (99)         | —‡                             |
| Single center                        | 8 (9)      | 7 (8)           | —‡                            | 1 (2)      | 1 (2)           | —‡                            |
| No of centers not specified          | 5 (6)      | 3 (4)           | 0.58 (0.11 to 2.53), 0.47      | 1 (2)      | 0 (0)           | —‡                            |
| Exclusively US sites                 | 37 (43)    | 43 (50)         | 1.42 (0.73 to 2.77), 0.31      | 35 (53)    | 36 (55)         | 1.09 (0.49 to 2.42), 0.84      |
| Location not specified               | 26 (28)    | 14 (16)         | 0.49 (0.23 to 1.04), 0.07      | 12 (18)    | 10 (15)         | 0.80 (0.31 to 2.03), 0.64      |

*Study was classified as pivotal if it was only one included in summary, multicenter randomized controlled trial, or explicitly noted in summary as being pivotal study.
†As calculated by generalized linear mixed effects model with canonical logit link and random effect placed on the intercept to account for heterogeneity across devices.
‡Too few events or counter-events for fitting of random effects model.

Primary not labeled in publication 43 (28%) were unlabeled, and 15 (10%) could not be compared with a control or with prospective control groups for both the summaries and publications. There were, however, 13 (9%) instances when the reported controls differed from the primary endpoints identified in the summaries in the corresponding publications, three (2%) were labeled as secondary endpoints, 43 (28%) were unlabeled, and 15 (10%) could not be found (table 4). Summary primary endpoints were compared with any matching endpoints in the corresponding publication even if they were not designated as primary. Of the summary primary endpoints, 110 (72%) were identical in definition and nine (6%) were similar to their corresponding publication endpoints. The findings were similar among the pivotal studies.

With regard to primary endpoint type, 47 (31%) in the summaries were measured against an objective performance criterion compared with 16 (11%) in the publications (odds ratio 0.35, 95% confidence interval 0.15 to 0.82) (table 5). Most primary endpoints in either the summary or publication did not specify the type: 77 (51%) versus 115 (76%), respectively (4.01, 2.30 to 6.99). Sixty three (41%) of the primary endpoints were compared with prospective control groups for both the summaries and publications. There were, however, 13 (9%) instances when the reported controls differed between summary and publication (table 4).

In 46 (30%) cases, the number of patients used for the primary endpoint analysis differed between the summaries and publications. Overall, however, the difference in number analyzed did not seem to be significant (table 5).

Comparison of primary endpoint results between summaries and publications

Analysis of the overall primary endpoint results showed that 69 (45%) were identical, 35 (23%) were similar, 17 (11%) were different, and 31 (20%) could not be compared (table 4). With regard to significance, 94 (62%) of the 152 summary primary results favored the device, eight (5%) favored the control (these eight included studies for which the objective performance criteria fell within the confidence interval or non-inferiority was not met), 12 (8%) favored neither device nor control, and 38 (25%) did not have a control or objective performance criteria by which to compare (table 5). In comparison, 65 (43%) of the published primary results significantly favored the device, three (2%) favored the control, 14 (9%) favored neither, and 70 (46%) could not be compared with a control or with
Discussion
Principal findings

About half (51%) of clinical studies of novel high risk cardiovascular devices remain unpublished over two years after FDA approval. Even when these studies are published, the results can differ substantially from FDA summaries in their presentation of primary endpoints. This finding remained true even when we restricted our analysis to pivotal studies. Reassuringly, a comparison of clinical design features including randomization, blinding, and number of centers as reported in summaries and publications showed that they were nearly identical. A quarter of trials, however, had discrepancies between summaries and publications in the numbers of enrolled patients, suggesting that the composition of the patient population had changed substantially and introducing a possible source of bias in reporting. This is further supported by the finding that sex and age demographics also differed between summary and publication in over 10% of the studies.

Clinicians might not be aware of the FDA device summaries and so might not critically examine these data. Thus for many high risk devices, clinical trial evidence might never be made readily available to the medical community or might be made available only after a long delay. While nearly all studies with disclosed funding were funded by industry, lengthy delays of publication have also been noted in NHLBI funded cardiovascular trials and in other NIH supported trials.5-11

Summaries and published studies differed in how their primary endpoints were presented: some endpoints labeled as primary in summaries were labeled as secondary in published studies and nearly 10% were entirely missing. These alterations mean that primary endpoints were rebranded to modify the emphasis of their findings in the literature. For instance, the summary for the “Xience V Rapid Exchange Everolimus-Eluting Stent System” (Abbott Vascular, IL, US) designates “co-primary endpoints” of “in-segment late loss at 240 days and target vessel failure at 270 days.”12 In the corresponding publication, however, the primary endpoint is “in-segment late loss at 240 days,” while the “secondary end point was ischemia-driven target vessel failure at 270 days.”13 In this case, the primary endpoint in the publication showed superiority of the tested device, whereas the rebranded secondary endpoint showed only non-inferiority. Others have reported similar findings.14 In a Cochrane review, 4-50% of randomized controlled trials exhibited discrepancies between primary outcomes registered and those published.15

Comparisons of results for primary endpoints between summaries and published studies showed that less than half of such results were identical, and 11% were substantially different. In addition, while many primary endpoints (31%) in the summaries were measured against objective performance criteria, far fewer endpoints (12%) were held to these criteria in the published literature. The significantly decreased number of objective performance criteria in the corresponding publications was the primary reason why devices seemed more favorable in the summaries than in the publication.7 8

Table 5 | Comparison of primary endpoints reported in FDA summaries with corresponding publications and those published studies. Figures are numbers (percentage) unless stated otherwise

| Type of endpoint analysis: | All studies (n=152) | Pivotal studies* (n=127) |
|--------------------------|--------------------|------------------------|
|                          | Summary            | Published              | Odds ratio (95% CI), P value† | Summary            | Published              | Odds ratio (95% CI), P value† |
|                          | Odds ratio (95% CI), P value† |                     |                          | Odds ratio (95% CI), P value† |                     |

Controls:

Prospective: 63 (41) 63 (41) 1.00 (0.50 to 1.99), 1.0 55 (33) 55 (33) 1.00 (0.43 to 2.30), 1.0
Retrospective: 20 (13) 15 (10) 0.64 (0.27 to 1.47), 0.29 19 (15) 13 (10) 0.54 (0.22 to 1.33), 0.18
None: 67 (44) 68 (45) 1.05 (0.57 to 1.94), 0.88 53 (42) 54 (43) 1.06 (0.54 to 2.11), 0.86
Unknown: 2 (1) 2 (1) 3.34 (0.63 to 17.66), 0.16 0 (0) 5 (4) —‡

Mean No of patients analyzed: 325.6 334.4 10.32 (<573.18 to 773.83), 0.77§ 338.1 348.6 12.22 (<236.64 to 68.08), 0.51§

Direction of favorability of endpoint results:

Device: 94 (62) 65 (43) 0.44 (0.27 to 0.70), <0.001 86 (68) 58 (46) 0.37 (0.22 to 0.63), <0.001
Control: 8 (5) 3 (2) 0.35 (0.09 to 1.37), 0.13 8 (6) 3 (2) 0.35 (0.09 to 1.37), 0.13
Neither: 12 (8) 14 (9) 1.33 (0.56 to 3.15), 0.51 10 (8) 11 (9) 1.26 (0.49 to 3.26), 0.63
Unknown: 38 (25) 70 (46) 2.77 (1.65 to 4.64), <0.001 23 (18) 55 (43) 3.84 (2.10 to 7.05), <0.001

*Study was classified as pivotal if it was only one included in summary, multicenter randomized controlled trial, or explicitly noted in summary as being pivotal study.
†Calculated by generalized linear mixed effects model with canonical logit link and random effect placed on intercept to account for heterogeneity across devices.
‡Too few events or counter-events for fitting of random effects model.
§Mean difference, (95% CI), P value calculated by general linear mixed effects model with random effect placed on intercept to account for device clustering.
catheter cryoablation is a safe and clinically effective major complication rate of 4.2%, and concludes that catheter cryoablation is a safe and clinically effective alternative to the standard of care. In rare cases, the endpoint reporting in the summary seemed more favorable than in the publication. For example, the summary for the “Talent Thoracic Stent Graft System” (Medtronic Vascular, MN, US) states a primary safety endpoint of all cause mortality at 12 months, to be compared with both an objective performance criterion of <29.8% and a retrospective control group. The summary reported 12 month all cause mortality of 16.1%, which both meets the objective performance criteria, but reports a non-significant P value of 0.29 for the comparison with the retrospective control.

Study limitations
A potential limitation of this study is that there is no systematic listing in the summaries of the trial principal investigators and clinical trial registries. In addition, we performed the Medline search on 15 January 2013, for publications up to 1 January 2013, and delays in indexing publications on Medline can exceed two weeks. To ensure that we did not inadvertently overlook a publication, we directly contacted the research divisions of device manufacturers and asked about any publications not found through our search algorithm. All of the manufacturers who responded confirmed that there was no publication for the respective study of interest. Another limitation is that our study focuses on selective outcome reporting and reporting of selected analyses such as follow-up intervals, and individual outcomes of composite endpoints were not explored.

Comparison with other studies
This study is the first to document selective reporting of device trials at both the study level and the outcome level, but it underscores a broader problem in the way clinical trial evidence is presented. Similar discrepancies have been identified for drug trials by comparing trial data reported in FDA New Drug Applications with the data in corresponding publications. A comparison of 128 drug trials as reported in FDA documents compared with the corresponding journal publications found differences in primary outcomes reported, types of data, results, P values, confidence intervals, and adverse event tables. Several types of selective outcome reporting for trials of off-label use of gabapentin have also been described, including discrepancies in numbers of patients randomized, definitions of primary outcomes, significance of reported outcomes, additions and deletions of outcomes, and differences in analyses. These discrepancies in the reporting led to more favorable efficacy data being presented in publications. These and our findings point to the importance of mandatory registration on a public clinical trials platform. Clinicaltrials.gov is an important step in this direction, but recent data show that published trials often have discrepant findings between clinicaltrials.gov and publications.

Conclusions and policy implications
Our findings have potential international implications. In the European Union, independent organizations called notified bodies authorize device marketing. The evidence reviewed by notified bodies is not mandated to be publicly available, which makes it challenging to directly compare published data with data reviewed by notified bodies. As devices generally receive CE mark before FDA approval, however, it is less likely that clinical studies have been published in the medical literature at the time of CE mark.

To protect the integrity of clinical trial research and, ultimately, safety of patients, the data from FDA reviews of devices should be readily accessible through peer reviewed publications. Although systematic reviews increasingly serve as a basis for evidence based clinical practice guidelines, documents from regulatory agencies are seldom included. Systematic reviewers might be unaware of the data that can be obtained from regulatory agencies. Thus, clinical practice guidelines might not be based on complete and accurate information about drugs or devices. Recent efforts, such as the intent of the European Medicines Agency (EMA) to make all clinical trial data for drug applications publicly available, would help enormously to fill these gaps by increasing the transparency and availability of important clinical trial data. In response to pushback, including from 33 drug companies or pharmaceutical industry associations, however, the EMA has imposed severe restrictions on the use of these data along with confidentiality agreements while making the data available only to registered users in a “view on screen only” mode. A recent study shows that FDA documents are more challenging to navigate than EMA reports, and the accessibility and user friendliness of FDA reports needs to be considerably improved. As clinicians can use devices immediately after FDA approval, it is in the public interest that all of the data be available to clinicians at that time.

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Ethical approval: Not required.

Transparency: The lead author (the manuscript’s guarantor) affirms that this 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 (and, if relevant, registered) have been explained.

Data sharing: Additional data from the study can be obtained for the corresponding author.

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