

Reporting Discrepancies Between the ClinicalTrials.gov Results Database and Peer-Reviewed Publications

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Background: ClinicalTrials.gov requires reporting of result summaries for many drug and device trials.

Purpose: To evaluate the consistency of reporting of trials that are registered in the ClinicalTrials.gov results database and published in the literature.

Data Sources: ClinicalTrials.gov results database and matched publications identified through ClinicalTrials.gov and a manual search of 2 electronic databases.

Study Selection: 10% random sample of phase 3 or 4 trials with results in the ClinicalTrials.gov results database, completed before 1 January 2009, with 2 or more groups.

Data Extraction: One reviewer extracted data about trial design and results from the results database and matching publications. A subsample was independently verified.

Data Synthesis: Of 110 trials with results, most were industry-sponsored, parallel-design drug studies. The most common inconsistency was the number of secondary outcome measures reported (80%). Sixteen trials (15%) reported the primary outcome description inconsistently, and 22 (20%) reported the primary outcome

value inconsistently. Thirty-eight trials inconsistently reported the number of individuals with a serious adverse event (SAE); of these, 33 (87%) reported more SAEs in ClinicalTrials.gov. Among the 84 trials that reported SAEs in ClinicalTrials.gov, 11 publications did not mention SAEs, 5 reported them as zero or not occurring, and 21 reported a different number of SAEs. Among 29 trials that reported deaths in ClinicalTrials.gov, 28% differed from the matched publication.

Limitation: Small sample that included earliest results posted to the database.

Conclusion: Reporting discrepancies between the ClinicalTrials.gov results database and matching publications are common. Which source contains the more accurate account of results is unclear, although ClinicalTrials.gov may provide a more comprehensive description of adverse events than the publication.

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Medical decision makers who use clinical trial evidence most often rely on findings that are published in peer-reviewed journals. Selective reporting of clinical trial results is a well-documented problem that raises concerns about using journal publications (1). Clinical trial registration is one mechanism aimed at reducing the effect of dissemination biases. Although many clinical trial registries exist, the single largest publicly accessible trial registry, and the only one with a results database, is ClinicalTrials.gov (2). Administered through the National Library of Medicine, ClinicalTrials.gov was developed to provide the public with a Web-based, searchable source of information about trials conducted within the United States. In September 2007, the Food and Drug Administration Amendments Act (FDAAA) was passed, greatly expanding the legal requirements for trial registration and mandating the creation of a publicly accessible clinical trial results database (3). According to FDAAA section 801, as of September 2008, basic summary results must be submitted for certain trials (called “applicable clinical trials” in the statute). Applicable clinical trials include most phase 2 through 4 trials of drugs, devices, or biologics regulated by the FDA having at least 1 site in the United States or conducted under an investigational new drug application or investigational device exemption (4). Several elements are required to be reported, including number of participants entering and completing the study; number of par-

ticipants analyzed; demographic data, such as age and sex; summary results for all prespecified primary and secondary outcome measures; and anticipated and unanticipated adverse events by organ system. Results are generally required to be reported within 1 year of study completion, although submission may be delayed if the drug or device is not yet approved or if an application for a new use is to be submitted.

The ClinicalTrials.gov results database has the potential to be a great asset for clinicians, patients, and researchers, but the ultimate validity of posted results is unclear. In contrast to the scientific scrutiny trials undergo during peer review for journals, results posted to ClinicalTrials.gov go through a quality assurance process focusing on internal consistency and logic. Although a gold standard repository of clinical trial results does not exist, inconsistencies between the ClinicalTrials.gov results database and other sources of clinical trial data suggest validity problems in 1 or both sources. The goal of this study was to assess the consistency of results reported in the ClinicalTrials.gov re-

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sults database compared with those summarized in peer-reviewed journal publications.

METHODS

Trial Selection

Studies were eligible for inclusion if they posted results to ClinicalTrials.gov, were interventional, and were phase 3 or 4. To allow sufficient time for publication, we limited our search to trials with a primary completion date before 1 January 2009 or a start date before 1 July 2008 if the primary completion date field was not populated. Completed trials with results were sequenced in random order using Excel 2010 (Microsoft, Redmond, Washington) and were screened for the presence of a matching publication until a 10% random sample of trials with results was obtained. Trials were excluded if they did not assign participants to 2 or more interventional groups.

We identified matching publications in a sequential process, first examining citations provided within ClinicalTrials.gov and then using a manual search of 2 electronic bibliographic databases. PubMed citations embedded within ClinicalTrials.gov can be provided by the investigator or the National Library of Medicine on the basis of matching National Clinical Trial (NCT) identifiers (5). We considered a publication to be a match if the intervention was the same and 1 or more groups in the trial had an identical number of participants. If relevant studies were not identified using citations provided within ClinicalTrials.gov, an electronic search of MEDLINE and the Cochrane Central Register of Controlled Trials was conducted using the study interventions, condition, principal investigator (if supplied), and date of trial completion as search criteria.

Data Abstraction and Comparisons

The following elements were abstracted and compared between the ClinicalTrials.gov results record and its corresponding publications: trial design, number of groups, primary outcome measure (POM) descriptions, secondary outcome measure (SOM) descriptions, total enrollment, and primary outcome results. We also abstracted the number of individuals affected by at least 1 adverse event (AE) and the number of individuals at risk, as reported to ClinicalTrials.gov. Comparisons of counts (such as enrollment, participants analyzed for the primary outcome, and number with an AE) were considered discrepant if they were not an exact match. The primary outcome result was required to be consistent to 1 decimal place. In cases of multiple publications, inconsistencies between the ClinicalTrials.gov results record and descriptions in any of the associated publications were considered a discrepancy.

We classified POM description inconsistencies by using an existing framework describing the specificity of outcome reporting in ClinicalTrials.gov (6). The POM could deviate entirely in the domain measured or the number reported, the measurement tool used (for example, change

in low-density lipoprotein cholesterol level vs. change in total cholesterol level), how the measure was used (for example, percentage change from baseline vs. absolute value), or the method of aggregation (for example, hemoglobin A_{1c} level <7% vs. <8%). We considered SOMs to be consistent if they were mentioned in the results or methods section of the publication and were listed in the ClinicalTrials.gov results record. For trials with multiple publications, we considered the aggregate number of SOMs across all associated publications. When evaluating POM reporting consistency, we first determined whether the descriptions were consistent in both sources. When they were, we looked for discrepancies in the reported value (for example, mean response or count with outcome) or the number of individuals analyzed for the outcome (for example, denominator or number analyzed). For trials with more than 1 POM specified in both sources, any inconsistency in the result numerator or denominator was considered a discrepancy. If discrepancies in trial features resulted in downstream inconsistencies, we compared only the highest-order feature to avoid double counting.

Adverse events did not become a mandatory reporting element until September 2009 and are summarized in the ClinicalTrials.gov results record in 2 tables: serious AEs (SAEs) and other (nonserious) AEs (OAEs). The FDA defines an SAE as any event that results in death, is life-threatening, requires or extends hospitalization, results in significant incapacity or interferes with normal life functions, or causes a congenital anomaly or birth defect (7). We compared the total number of SAEs reported in ClinicalTrials.gov with the total reported in the corresponding publications. In cases where the SAE counts differed, we compared the risk difference (experimental group risk minus control group risk) reported in ClinicalTrials.gov with the published estimate. For trials with multiple experimental groups, we selected the group of primary interest stated in the paper; if multiple FDA-approved dosing groups were assessed, we combined these for comparison with the control group. For OAEs, we restricted our comparison to specific AEs that could be matched to the publication without ambiguity and that were not also reported as an SAE in order to eliminate the possibility of double counting participants who may have had both a serious and nonserious AE. We distinguished publications reporting only treatment-related (attributable) AEs because ClinicalTrials.gov requires reporting of AEs regardless of attribution. Finally, we compared the number of deaths reported in each source. In ClinicalTrials.gov, deaths can be reported as an outcome, in the participant flow section, or as an SAE. If death was not a primary or secondary outcome, we compared the number of deaths reported in the participant flow or SAE section of ClinicalTrials.gov with the number reported in the publication. We classified the sources as discrepant only if counts of death differed between them.

A second reviewer independently assessed reporting discrepancies between the ClinicalTrials.gov results record and the matched publication in a 20% random sample (22 trials) for all comparisons. Agreement between the primary and secondary abstractors was high, with an average κ of 0.98 across categories and no single category with a κ less than 0.91.

Role of the Funding Source

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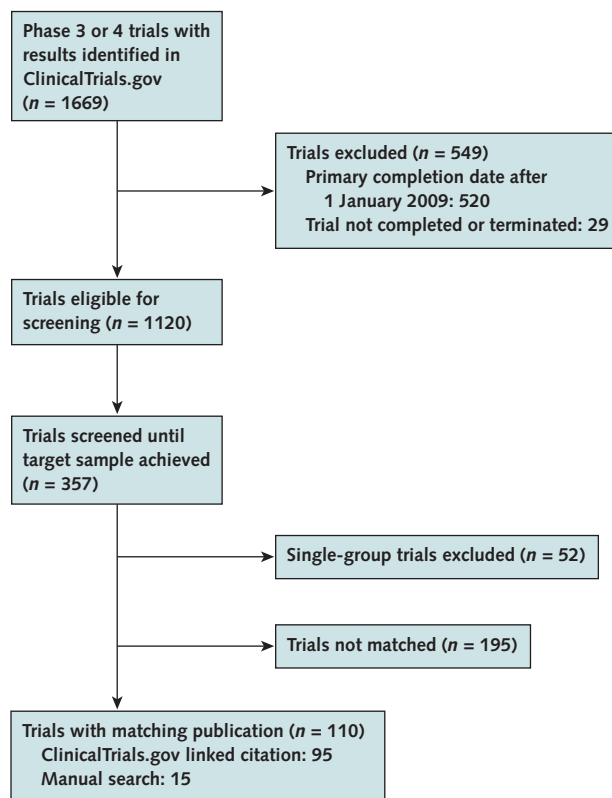
RESULTS

The **Figure** describes the flow of trials from the initial ClinicalTrials.gov candidate pool to the final study sample. A total of 1669 phase 3 and 4 trials with posted results were initially identified through a query of ClinicalTrials.gov on 15 February 2011. After exclusion of trials with a primary completion date after 1 January 2009 and those not completed or terminated, 1120 trials remained. We randomly screened 357 potentially includable trials until a 10% sample ($n = 110$) was achieved. Three trials reported results in multiple publications. **Table 1** describes the characteristics of the 110 matched trials and the 195 unmatched trials. Most studies were industry-funded, parallel-design trials of drugs. Unmatched trials were more likely to investigate something other than a drug or device and less likely to be cardiovascular trials. Twenty-nine trials (26%) described more than 1 POM in ClinicalTrials.gov.

Table 2 summarizes reporting discrepancies between the ClinicalTrials.gov results database and the matching publications. Sixteen trials (15%) had discrepant POM descriptions. In 9 of these trials (56%), POM descriptions reported in ClinicalTrials.gov were not reported as POMs in the publication. Primary outcome measure descriptions in all but 1 of these studies were reported as SOMs in the publication. The only publication not reporting POM descriptions reported in ClinicalTrials.gov omitted 3 POMs related to pharmacokinetic outcomes (NCT00158600). Publications listed an average of 2.4 more SOMs than the ClinicalTrials.gov results database. Three trials (3%) reported enrollment results inconsistently. The inconsistencies in enrollment reflected differences in up to 14% of the total enrollment.

Twenty-two trials (20%) inconsistently reported the primary outcome result (**Supplement 1**, available at www.annals.org). Seven of these (32%) reported larger treatment effects in the publication than in ClinicalTrials.gov, and 2 (9%) reported larger treatment effects in ClinicalTrials.gov. For the 7 trials with larger treatment effects reported in the publication, the median relative increase in treatment effect was 10% (range, 1% to 270%). On an

Figure. Summary of evidence search and selection.



absolute scale, most discrepancies were small and did not affect the statistical significance of the reported results.

Of the 104 ClinicalTrials.gov entries reporting information about SAEs, 84 trials reported at least 1 SAE. Among these, 11 publications did not mention SAEs and 5 reported them as zero or not occurring (**Table 2**). In total, 38 trials had SAE reporting discrepancies (**Supplement 2**, available at www.annals.org). For 33 of these (87%), more SAEs were reported in the ClinicalTrials.gov registry than in the publications. Four publications reported only treatment-related SAEs. When the risk for SAEs was higher for the experimental group in ClinicalTrials.gov, 17 of 20 (85%) publications reported SAE risks more favorable to the experimental group. For 3 of these trials, the publication reported that the risk for an SAE was lower in the experimental group than in the control group. Two publications reported attenuated SAE risk differences that implied that 10 and 500 more patients needed to receive the intervention in order to cause 1 SAE. For the remainder of the publications ($n = 12$), SAEs were reported as zero ($n = 3$) or were not reported ($n = 9$). For these 12 trials, the number needed to harm for the intervention ranged from 5 to 125 (median, 37). When the SAE rate was higher for the control group in ClinicalTrials.gov, 7 of 15 publications (47%) reported differences even more favor-

Table 1. Description of Matched and Unmatched Trial Characteristics as Reported in ClinicalTrials.gov*

| Characteristic† | Matched Sample (n = 110) | Unmatched Sample (n = 195) |
|-----------------------------------|-----------------------------|-------------------------------|
| Median enrollment (IQR), n | 352 (537) | 263 (486) |
| Study condition | | |
| Cancer | 8 (7) | 5 (3) |
| Cardiovascular | 28 (26) | 17 (9) |
| Endocrine and metabolic | 13 (12) | 19 (10) |
| Mental health | 15 (14) | 14 (7) |
| Respiratory | 6 (6) | 29 (15) |
| Other | 40 (36) | 111 (57) |
| Sponsor‡ | | |
| Government | 1 (1) | 0 (0) |
| Industry | 98 (89) | 183 (94) |
| Other | 11 (10) | 12 (6) |
| Intervention type§ | | |
| Device | 3 (3) | 10 (5) |
| Drug | 104 (95) | 158 (81) |
| Other | 3 (3) | 27 (14) |
| Design | | |
| Parallel | 104 (95) | 179 (92) |
| Cross-over | 6 (6) | 13 (7) |
| Factorial | 0 (0) | 3 (2) |
| Allocation groups | | |
| 2 | 73 (66) | 138 (71) |
| 3 | 22 (20) | 34 (17) |
| >3 | 15 (14) | 23 (12) |
| >1 primary outcome | 29 (26) | 52 (27) |

IQR = interquartile range.

* Data are numbers (percentages) unless otherwise indicated.

† All characteristics were abstracted from the ClinicalTrials.gov registry.

‡ If >1 sponsor was listed, the information provider was considered the primary sponsor. "Other" sponsors included foundations, health systems, and universities.

§ Based on hierarchy of interventions: device, drug, or other (e.g., any trial with a group with a device was categorized as a device trial, whereas "other" trials had no devices or drugs).

able toward the intervention. In 3 trials, the SAE risks could not be compared clearly between groups.

Thirty-five of 95 trials that reported 1 or more OAEs in their ClinicalTrials.gov entry had at least 1 reporting discrepancy. In 19 of these trials (54%), the publication reported fewer OAEs than the ClinicalTrials.gov record. Eleven of the 35 trials (31%) had more individuals with an OAE in the publication than in ClinicalTrials.gov, and 5 of them (14%) had reporting differences in both directions. Nine trials reported zero OAEs in ClinicalTrials.gov, and 5 of these (56%) reported 1 or more OAEs in the publication.

Eighty-one trials did not report on deaths in ClinicalTrials.gov. Of these, 14 (17%) had deaths reported in the matched publication. In 16 of 29 trials that reported deaths in ClinicalTrials.gov, the publication reported the same number of deaths (Supplement 3, available at www.annals.org). In 5 others, deaths were reported as counts in 1 source and as a survival analysis (without counts) in the

other. Counts of death were discrepant in the remaining 8 trials. Death was a primary outcome or part of a composite primary outcome in 2 of these trials. One of them had a relatively small discrepancy (NCT00379769); the other, a large trial of irbesartan (NCT00095238), had a large discrepancy (1003 deaths in ClinicalTrials.gov vs. 881 in the publication) that may have been due to different lengths of follow-up. There were 6 discrepancies among trials that reported deaths in the participant flow or SAE section of ClinicalTrials.gov. In 3 of 5 trials that reported deaths in the SAE section, more deaths were reported in the publication than in the results database.

DISCUSSION

Reporting discrepancies between the ClinicalTrials.gov results database and matching publications were common for several key trial attributes and results. Overall, 20% of trials inconsistently reported the primary outcome result, although only a few could be considered to have potentially meaningful discrepancies. Descriptions of POMs were different between the ClinicalTrials.gov results database and publications 15% of the time, most often when 1 or more primary outcomes were dropped from primacy. This estimate is lower than in other studies that have explored inconsistencies between clinical trial protocols and published results (62%) (8) or trial registry entries and journal publications (31%) (9, 10). The lower proportion of discrepant POMs found in our sample may reflect improved reporting when summary results, rather than simply a description of outcomes (as a requirement for registration), are recorded. As in previous studies, we found that 80% of trials contained an SOM reporting discrepancy (10, 11). Huić and colleagues compared 9 World Health Organization Minimum Data Set trial registration elements from ClinicalTrials.gov with corresponding publications and found that 65% differed in reporting of SOMs (11). Similar to our finding, the most common SOM differences they noted were outcomes listed in the publication but missing from ClinicalTrials.gov. Although this may reflect incomplete reporting in the ClinicalTrials.gov database, it could also indicate the misrepresentation of post hoc analyses as prespecified SOMs in the publication.

Adverse events were reported inconsistently in more than one third of trials. Omission or underreporting in the publication was the predominant inconsistency, with most discrepant trials reporting fewer SAEs in the publication than in ClinicalTrials.gov. Underreporting of AEs, even when not differential between groups, is of great concern because it can minimize impressions of the overall safety of an intervention (12). Most inconsistencies were either complete SAE nonreporting or differences in 10 or fewer individuals that did not alter the direction of risk. However, when discrepant trials reported an increased SAE risk with the intervention relative to the control group in

ClinicalTrials.gov, the published account of this risk was almost universally less pronounced (that is, was more favorable to the intervention). In 3 trials, the discrepancies reversed the direction of risk. For example, in 1 trial (NCT00323492), the publication reported a 4.5% decrease in the risk for an SAE with the intervention (emtricitabine and tenofovir), whereas ClinicalTrials.gov reported an 8.2% increase in SAE risk. Publications infrequently provided detailed SAE descriptions, and whether AEs classified as serious in ClinicalTrials.gov were reclassified in the publication was unclear. Although there is some inherent subjectivity in the FDA's standard criteria for an SAE, determination of AEs as serious should not change on the basis of reporting sources (7). We identified 2 trial publications in type 2 diabetes with ambiguous and potentially misleading reporting of serious hypoglycemic episodes. In 1 trial (NCT00313313), the publication described no cases of hypoglycemia judged to be an SAE; however, the ClinicalTrials.gov entry recorded 2 patients having an SAE of hypoglycemia (1 in each group receiving the study drug). Another publication (NCT00494013) mentioned "two of seven patient-reported severe hypoglycemia episodes as serious AEs" but did not attribute these to a specific study group. The ClinicalTrials.gov record for this trial indicated that these events occurred in the active treatment group (long-acting insulin). A similar pattern was also observed in the reporting of OAEs, although a more focused examination of specific AEs by disease state is needed.

In our sample, only a quarter of trials reported on deaths in ClinicalTrials.gov. In most cases, omission of death data from ClinicalTrials.gov probably occurred because there were no deaths in the trial. However, in 17% of trials that did not report deaths in ClinicalTrials.gov, deaths were documented in the publication. When ClinicalTrials.gov reported deaths, the number was inconsistent with the publication in about one quarter of trials. Reporting of deaths was more consistent when they were included in the outcomes section of ClinicalTrials.gov. We found only 1 discrepancy that could be considered meaningful among 14 trials in which death was a prespecified outcome. Although our sample was small, our results suggest that reporting of deaths in the SAE section of ClinicalTrials.gov was often inconsistent. Earley and colleagues noted that ClinicalTrials.gov does not have a uniform template for reporting deaths and that internal consistency is sometimes problematic (13).

Underreporting of AEs is a major concern because it can distort how decision makers balance the benefits and harms of medical interventions. Even when the inconsistencies are minor in individual studies, as was the case for several of the trials analyzed, these distortions can be amplified when results are combined within systematic reviews (12, 14). Suboptimum reporting of AEs may relate

Table 2. Summary of Reporting Discrepancies Between ClinicalTrials.gov Records (*n* = 110) and Matched Publications (*n* = 113)*

| Characteristic | Value |
|---|---------------|
| Design (<i>n</i> = 110) | |
| Trial design | 0 (0) |
| Number of groups | 1 (1) |
| POM description | |
| Number of POMs not consistent | 9 (8) |
| Different measurement tools used | 1 (1) |
| Measurement tool used differently | 6 (6) |
| SOM descriptions | |
| Trials with discrepant number of SOMs | 88 (80) |
| Mean (SD) secondary outcomes in publication, <i>n</i> | 9.6 (7.9) |
| Mean (SD) secondary outcomes in ClinicalTrials.gov results record, <i>n</i> | 7.2 (8.1) |
| Difference (95% CI) | 2.4 (1.1–3.8) |
| Results (<i>n</i> = 110) | |
| Total enrollment | 3 (3) |
| Smallest and largest discrepancy as proportion of total enrollment | 1–14 |
| Primary outcome results | |
| Larger treatment effect in publication | 7 (32)† |
| Larger treatment effect in ClinicalTrials.gov | 2 (9)† |
| Other discrepancies‡ | 13 (59)‡ |
| AEs (<i>n</i> = 104)§ | |
| SAEs | |
| Trials with ≥1 SAE reported in ClinicalTrials.gov (<i>n</i> = 84) | |
| Discrepant: not reported in publication | 11 (11) |
| Discrepant: reported as zero or not occurring in publication | 5 (5) |
| Discrepant: different number reported in publication | 21 (20) |
| Trials with no SAEs reported in ClinicalTrials.gov (<i>n</i> = 20) | |
| Discrepant: ≥1 SAE reported in publication | 1 (1) |
| OAEs | |
| Trials with ≥1 OAE reported in ClinicalTrials.gov (<i>n</i> = 95) | |
| Discrepant: comparable categories with differential reporting | 35 (34) |
| Discrepant: AE not reported in publication | 1 (1) |
| Trials with no OAEs reported in ClinicalTrials.gov (<i>n</i> = 9) | |
| Discrepant: ≥1 OAE reported in publication | 5 (5) |
| Deaths (<i>n</i> = 110) | |
| Trials reporting deaths in ClinicalTrials.gov (<i>n</i> = 29) | |
| Discrepant: different from number reported in publication | 7 (24)¶ |
| Discrepant: not reported in publication | 1 (3)¶ |
| Trials not reporting deaths in ClinicalTrials.gov (<i>n</i> = 81) | |
| ≥1 deaths reported in publication | 14 (17)** |
| Zero deaths reported in publication | 28 (35)** |
| Deaths not reported in publication | 39 (48)** |

AE = adverse event; OAE = other adverse event; POM = primary outcome measure; SAE = serious adverse event; SOM = secondary outcome measure.

* Data are numbers (percentages) unless otherwise indicated.

† Denominator is 22 trials with primary outcome result discrepancy.

‡ Seven trials (NCT00886600, NCT00308711, NCT01218958, NCT00432237, NCT00313820, NCT00452426, and NCT00337727) had inconsistent analysis denominators that did not affect reported outcomes, 2 trials (NCT00852917 and NCT00422734) had multiple primary outcomes where direction of discrepancy differed between outcomes, 2 trials (NCT00287053 and NCT00806403) had transposition errors where values or denominators were reversed between groups, 1 trial (NCT00029172) did not report the outcome by treatment group in ClinicalTrials.gov, and 1 trial (NCT00494013) had a discrepancy in reported outcome values for each group but the between-group differences were consistent.

§ Six trials were posted before the AE reporting requirement.

|| Denominator is 104 trials reporting SAEs.

¶ Denominator is 29 trials.

** Denominator is 81 trials.

to space restriction imposed by journals, the use of study designs that poorly measure harms, or purposeful concealing of unfavorable data (15–17). It is unclear from our study why some trials reported AE data more consistently

than others. In general, however, ClinicalTrials.gov seems to provide a more comprehensive summary of AEs.

This study has several limitations. First, the study sample consisted of trials that were completed by 1 January 2009. These trials were probably among the first posted to the ClinicalTrials.gov results database and may contain inconsistencies that reflect investigators' inexperience in entering results into the system. Reporting consistency may be improving as investigators become more familiar with the data submission process. The ClinicalTrials.gov registry allows investigators to change their registered protocol by using a track change function that is archived in a companion Web site (<http://clinicaltrials.gov/archive>). We did not evaluate changes in POMs or SOMs archived over time, only what was reported in the final results record. Modification of registered clinical trial protocols, specifically POM and SOM additions or deletions, is common before publication and may partially explain why POM discrepancies were lower in our study compared with what others have observed (11). Although we attempted to find matching publications through citations within ClinicalTrials.gov and a search of 2 electronic bibliographic databases, some matches may have been overlooked. Finally, many discrepancies were observed in only a small number of trials, and estimates should be regarded as preliminary.

This analysis documents that different instances of reporting results from a given trial frequently lead to discrepant data. Although there are many possible explanations for such discrepancies, these findings contribute to the growing sense that the process of taking the initially collected "raw" participant-level data and deriving the ultimately reported aggregate or "summary" data involves a series of decisions that are not entirely prespecified or objective; different iterations of the process thus produce different results. It is uncertain whether the discrepancies that we observed represent deliberate misrepresentation, reporting carelessness, the influence of journal editors, or simply an evolution of investigators' thinking or analytic approach over time. For example, the process of peer review may introduce modifications in how results are analyzed or reported that may contrast with data submitted to the ClinicalTrials.gov results registry. Many of the primary outcome result discrepancies seem to be small inconsistencies that may be errors in data entry or the result of additional or modified analyses requested by the specific journal. However, it is important to note that our analysis examined the summary metric (for example, mean response rate) and not the associated statistical analysis. We believe that it is uncommon for peer review to lead to actual changes in the data as opposed to changes in the types of statistical analyses and resulting inferences that are considered appropriate, although future research might examine this issue further. If investigators do not (or cannot) provide consistent quantitative summaries of the fundamental features of their trials, one must question how ac-

curate either reporting source could be. Because there is no gold standard source for clinical trial reporting, for now the only possible path to resolving discrepancies is to seek clarifications from the investigator. Although the FDA commonly uses independent analysis of participant-level data for product reviews, clinicians, patients, and other decision makers generally rely on summary data from journal articles and other sources to inform their decisions. Although there is great interest in making participant-level clinical trial data publicly available for independent analysis and dissemination, models that balance public and private data use concerns are just beginning to emerge (18, 19). It remains unclear whether greater reporting transparency, up to and including access to participant-level data, will improve the reliability and ultimately the validity of clinical trial research for decision makers.

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References

1. Song F, Parekh S, Hooper L, Loke YK, Ryder J, Sutton AJ, et al. Dissemination and publication of research findings: an updated review of related biases. *Health Technol Assess*. 2010;14:iii, ix-xi, 1-193. [PMID: 20181324]
2. Zarin DA, Ide NC, Tse T, Harlan WR, West JC, Lindberg DA. Issues in the registration of clinical trials. *JAMA*. 2007;297:2112-20. [PMID: 17507347]
3. Zarin DA, Tse T. Medicine. Moving toward transparency of clinical trials. *Science*. 2008;319:1340-2. [PMID: 18323436]
4. Tse T, Williams RJ, Zarin DA. Reporting "basic results" in ClinicalTrials.gov. *Chest*. 2009;136:295-303. [PMID: 19584212]
5. U.S. National Library of Medicine. Clinical Trial Registry Numbers in MEDLINE/PubMed Records. Bethesda, MD: U.S. National Library of Medicine; 2011. Accessed at www.nlm.nih.gov/bsd/policy/clin_trials.html on 21 January 2014.

6. Zarin DA, Tse T, Williams RJ, Califf RM, Ide NC. The ClinicalTrials.gov results database—update and key issues. *N Engl J Med.* 2011;364:852-60. [PMID: 21366476]
7. U.S. Food and Drug Administration. IND safety reporting. 21 CFR §312.32(a). Accessed at www.gpo.gov/fdsys/pkg/CFR-2013-title21-vol5/pdf/CFR-2013-title21-vol5-part312.pdf on 28 October 2013.
8. Chan AW, Hróbjartsson A, Haahr MT, Gøtzsche PC, Altman DG. Empirical evidence for selective reporting of outcomes in randomized trials: comparison of protocols to published articles. *JAMA.* 2004;291:2457-65. [PMID: 15161896]
9. Mathieu S, Boutron I, Moher D, Altman DG, Ravaud P. Comparison of registered and published primary outcomes in randomized controlled trials. *JAMA.* 2009;302:977-84. [PMID: 19724045]
10. Ewart R, Lausen H, Millian N. Undisclosed changes in outcomes in randomized controlled trials: an observational study. *Ann Fam Med.* 2009;7:542-6. [PMID: 19901314]
11. Huić M, Marušić M, Marušić A. Completeness and changes in registered data and reporting bias of randomized controlled trials in ICMJE journals after trial registration policy. *PLoS One.* 2011;6:e25258. [PMID: 21957485]
12. Fu R, Selph S, McDonagh M, Peterson K, Tiwari A, Chou R, et al. Effectiveness and harms of recombinant human bone morphogenetic protein-2 in spine fusion: a systematic review and meta-analysis. *Ann Intern Med.* 2013; 158:890-902. [PMID: 23778906]
13. Earley A, Lau J, Uhlig K. Haphazard reporting of deaths in clinical trials: a review of cases of ClinicalTrials.gov records and matched publications—a cross-sectional study. *BMJ Open.* 2013;3. [PMID: 23335556]
14. Carragee EJ, Hurwitz EL, Weiner BK. A critical review of recombinant human bone morphogenetic protein-2 trials in spinal surgery: emerging safety concerns and lessons learned. *Spine J.* 2011;11:471-91. [PMID: 21729796]
15. Pitrou I, Boutron I, Ahmad N, Ravaud P. Reporting of safety results in published reports of randomized controlled trials. *Arch Intern Med.* 2009;169: 1756-61. [PMID: 19858432]
16. Ioannidis JP, Lau J. Completeness of safety reporting in randomized trials: an evaluation of 7 medical areas. *JAMA.* 2001;285:437-43. [PMID: 11242428]
17. Ioannidis JP. Adverse events in randomized trials: neglected, restricted, distorted, and silenced [Editorial]. *Arch Intern Med.* 2009;169:1737-9. [PMID: 19858427]
18. Krumholz HM, Ross JS. A model for dissemination and independent analysis of industry data. *JAMA.* 2011;306:1593-4. [PMID: 21990302]
19. Ross JS, Krumholz HM. Ushering in a new era of open science through data sharing: the wall must come down. *JAMA.* 2013;309:1355-6. [PMID: 23508736]

2013 ANNALS POETRY PRIZE

Congratulations to Bonnie Salomon, MD, winner of the 2013 *Annals* Poetry Prize. Her poem "DLROW" was published in the 2 July 2013 issue (vol. 159, no. 121, page 69).

Dr. Salomon's poem was selected from poetry published in *Annals* in 2013 by our two judges: Daniel Bosch, poet, teacher, editor; and Abigail Zuger, who writes for *The New York Times*.

Daniel Bosch's book *Crucible* was published by Other Press in 2002. His poems have been published in such journals as *Poetry*, *Slate*, *The Times Literary Supplement*, *Agni*, *Berfrois*, *The New Republic*, *The Huffington Post*, and *The Paris Review*. In 1998, he was awarded the *Boston Review* Poetry Prize.

Dr. Zuger is Associate Professor of Clinical Medicine at Columbia University College of Physicians and Surgeons and Senior Attending Physician at St. Luke's-Roosevelt Hospital Center. She is a board-certified internist and infectious disease specialist with particular interest and expertise in HIV. Dr. Zuger writes frequently on medical topics for the *New York Times* and national publications. Her book, *Strong Shadows: Scenes from an Inner City AIDS Clinic*, was published by WH Freeman in 1995.

For information on the Poetry Prize contest, visit www.annals.org/public/poetryprize.aspx.

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