S pe cial r ep or t

10-Year Update on Study Results Submitted to ClinicalTrials.gov

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In September 2008, the National Library of Medi- cine (NLM) of the National Institutes of Health (NIH) expanded the database at ClinicalTrials.gov to include the results of registered clinical trials in response to the Food and Drug Administra- tion Amendments Act (FDAAA).1 This database consists of structured tables of summary data regarding the results of trials without discussion or conclusions. The FDAAA, its implementing regulations (42 CFR Part 11),2,3 and several policies require the reporting of results to ClinicalTrials

.gov to address issues related to the nonpublica- tion of results of clinical trials and incomplete reporting of outcomes and adverse events.4 These issues have necessitated process changes for sponsors and investigators in both industry and academic medical centers.5

We previously estimated that the regulations and the trial-reporting policy of the NIH6 would affect more than half the registered trials con- ducted at academic medical centers in the United States.7 The scope and importance of these re- quirements demand that we monitor and evalu- ate the effect of this evolving results-reporting mechanism on the clinical trials enterprise. In 2011, we characterized early experiences with nearly 2200 posted results.4 A decade after launch, the results database contained more than 36,000 results as of May 2019. In this article, we de- scribe the current requirements, the state of re- sults reporting at ClinicalTrials.gov, and chal- lenges and opportunities for further advancement.

requirements for reporting results of u. s. Clinical trial s

**laws, regulations, and policies**

The FDAAA, its regulations, and several U.S. policies require or encourage the reporting of study results on ClinicalTrials.gov (Table 1). These regulations, which were an important milestone

in implementing the FDAAA, clarified key defi- nitions and information to be reported, includ- ing the additional requirement to submit full protocol documents with results information for trials completed on or after January 18, 2017.3 Under the regulations, the party responsible for reporting is generally the “sponsor,” which is defined as either the holder of the FDA investi- gational-product application or, if no holder has been designated, the initiator of the trial, such as a grantee institution. Sponsors may designate qualified principal investigators for meeting the requirements. We will refer to this entity or in- dividual as the “sponsor or investigator.”

Both the regulations and the trial-reporting policy of the NIH, which follow the regulatory reporting framework, require sponsors or inves- tigators to submit results data within 1 year after the primary completion date of the trial, which is generally defined as the final collection of data for the primary outcome measure; the de- layed submission of results is permitted in cer- tain situations. Registration and results informa- tion may also be submitted to ClinicalTrials.gov on an optional basis for clinical studies to which the law, regulations, or policies do not apply but must follow the established procedures for con- tent and quality-control review. Although this article focuses on the U.S. landscape, we note the international scope of requirements for report- ing results, including the Clinical Trial Regula- tions of the European Union.13

**content of required results Data**

Each record of a study that is posted on Clinical- Trials.gov represents one trial with information submitted by the sponsor or investigator. The registration section, which is generally provided at the time of trial initiation, summarizes key protocol details and other information to sup- port enrollment and tracking of the progress of

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| **Table 1. Summary of Key U.S. Laws, Regulations, and Policies Related to the Submission of Study Results to ClinicalTrials.gov.\*** | | | | |
| **Name** | **General Scope** | **Submission Type and Timeline** | **Relevant Dates** | **Possible Penalty for Noncompliance** |
| FDA Amendments Act (FDAAA)1  (U.S. federal law) and associated regulations, 42 CFR Part 112 (U.S.  federal regula- tions) | Clinical trials of FDA- regulated drug, biologic, or device products (“ap- plicable clinical trials”)  Excludes phase 1 trials and small feasibility studies | *Registration:* Within 21 days after enrollment of the first trial par- ticipant  *Summary results:* Within 12 mo after the primary completion date; sub- mission may be delayed with cer- tification, if specific conditions are met, for up to 2 additional yr or delayed for an approved period with extension request for “good cause” | FDAAA enacted on September 27, 2007  *Registration:* Applicable clinical trials initiated after September 27, 2007, or initiated on or before that date but still ongoing as of December 26, 2007  *Summary results:* Applicable clinical trials of FDA-approved, licensed, or cleared products that reached a “primary completion date” (i.e., data collection complete for the primary outcome) after December 26, 2007  Regulatory effective date: January 18, 2017  *Registration:* Applicable clinical trials initiated on or after January 18, 2017  *Summary results:* Applicable clinical trials that reached their primary completion date on or after January 18, 2017, regardless of product approval, licensing, or clearance by FDA | Civil monetary penalties of up to $10,000  per day Withholding of NIH  and other federal grant funds |
| Dissemination of NIH-funded clini- cal trial informa- tion6 (NIH policy) | NIH-funded clinical trials of any type of intervention Includes phase 1 trials and small feasibility studies | *Registration:* Same as for FDAAA and 42 CFR 11  *Summary results:* Same as for FDAAA and 42 CFR 11 | Effective date: January 18, 2017  Clinical trials supported by grants, other transactions, and contracts that submitted applications on or after January 18, 2017, for trials initiated on or after January 18, 2017  Clinical trials supported by NIH intramural program and initiated on or after January 18, 2017 | Suspension or termi- nation of NIH grant or contract funding and consideration in future funding decisions |
| Submission of results NIH-funded, phase 3 clini- *Registration:* Same as for FDAAA; out- Phase 3 applicable clinical trials (NIH-defined) under federal Consideration in future | | | | |
| of valid analyses | cal trials subject to | comes specified by sex and race | regulations supported by all new, competing grants and co- | funding decisions |
| by sex and race8,9 | FDAAA-associated | *Summary results:* Same as for FDAAA; | operative agreements awarded on or after December 13, 2017 |  |
| (U.S. federal law | regulations | “valid analyses” specified by sex |  |  |
| and NIH policy) |  | and race |  |  |
| International Com- | Clinical trials of any type | *Registration:* On or before enrollment | Effective dates: | Refusal by editor to |
| mittee of Medical | of intervention | of first trial participant | Clinically directive clinical trials initiated on or after July 1, 2005 | publish manuscript |
| Journal Editors Includes phase 1 trials and *Summary results:* If required, at time Ongoing clinically directive clinical trials initiated before Septem- | | | | |
| Clinical Trial | small feasibility studies | specified by funding and regulatory | ber 13, 2005 |  |
| Registration |  | agencies; otherwise encouraged | All clinical trials (expanded to include phase 1) initiated on or after |  |
| Policy10 |  |  | July 1, 2008 |  |
| Department of | Clinical trials funded by | *Registration:* Before enrollment of | Effective dates: | Condition of funding |
| Veterans Affairs | VA ORD | first participant | *Registration:* Any VA-sponsored clinical trial initiated on or after |  |
| Office of Re- |  | *Summary results:* Within 12 mo after | July 1, 2005 |  |
| search and |  | primary completion date | *Summary results:* All registered clinical trials starting in 2013 and |  |
| Development |  |  | retrospectively to include trials initiated or actively enrolling |  |
| (VA ORD)11 |  |  | since 2007 |  |
| Patient-Centered | Research studies (including | *Registration:* Before enrollment of first | Policy adoption: February 24, 2015 | Condition of funding |
| Outcomes Re- | observational studies) | trial participant |  |  |
| search Institute | funded by PCORI | *Summary results:* No less than 30 days |  |  |
| (PCORI)12 |  | before due date to PCORI |  |  |

\* CFR denotes Code of Federal Regulations, FDA Food and Drug Administration, and NIH National Institutes of Health.

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| **Table 2. Requirements for Submitting Results to ClinicalTrials.gov, According to Module, for Studies Completed since January 18, 2017.** | |
| **Module Name and Brief Description** | **Specific Items to Report** |
| **Participant flow**  A tabular summary of participants’ progress through the study by assignment group | Description of any important events (e.g., washout, run-in) after enrollment but before partici- pant assignment  Number of participants who started and completed the study; optional inclusion of additional study-specific milestones, periods, or phases, along with reasons and numbers of partici- pants who did not complete the study |
| **Demographic and baseline characteristics** Baseline measures, including age, sex or gender, race or ethnicity (if collected), and other mea-  A tabular summary of collected demo- sures assessed at baseline and used in the primary outcome analysis; optional inclusion of graphic and baseline data by analysis other baseline measures important for the study  group and overall For each measure, items that are required include a clear title and description, the number  of participants included in the analysis and description of the population, type of measure (e.g., mean) and measure of dispersion (e.g., standard deviation), and unit of measure | |
| **Outcomes and statistical analyses**  A tabular summary of aggregate results data for each outcome measure by analysis group and of statistical tests of significance or other measures estimated from the outcome data | All prespecified primary and secondary outcome measures and the results of any scientifically appropriate tests of statistical significance; optional inclusion of other prespecified or post hoc outcome measures and statistical analyses  For each measure, items that are required include a clear title and description, time frame, num- ber of participants included in the analysis and description of analysis population, type of measure (e.g., median), measure of dispersion or precision (e.g., interquartile range), and unit of measure  For each statistical analysis, items that are required include a description of the groups that are compared; statistical method, estimation measure, or both; calculated value; and related descriptive information |
| **Adverse events information**  A tabular summary of adverse events, independent of attribution and whether anticipated, by analysis group | Time frame, collection approach (systematic or nonsystematic), and any relevant definitional descriptions  Three tables, including data on all deaths during the study, all serious adverse events grouped according to organ system, and other adverse events that exceed a frequency of 5% in any analysis group, according to organ system; optional inclusion of a listing of standard terms for adverse events, if used, and a listing of other adverse events with a frequency of less than 5%  For each table, the number of participants who were affected and at risk (i.e., numerator and denominator) overall and for each event |
| **Study documents**  As submitted in archival portable document format | Protocol and statistical analysis plan (if not part of protocol); optional inclusion of a copy of the informed-consent form |
| **Other information**  Administrative and other relevant information about the study | A description of any agreements between sponsors and principal investigators that impose restrictions on disclosure of results and details regarding contact information; optional inclusion of limitations and caveats related to the study results |

the trial. After the completion of the trial, re- sults data can be added to the record with the use of required and optional data elements orga- nized into the following scientific modules: Participant Flow, Baseline Characteristics, Out- come Measures and Statistical Analyses, Adverse Events Information, and Study Documents (pro- tocol and statistical analysis plan)3 (Table 2).

**criteria and process for Quality-control review**

Information that is submitted to ClinicalTrials.gov undergoes quality-control review, which consists of automated validation followed by manual re- view by NLM staff members. The goal of quality- control review is to ensure that all required infor- mation is complete and meaningful by identifying

apparent errors, deficiencies, or inconsistencies.14 At the NLM, we developed review criteria that were based on established scientific-reporting principles15 and informed by our experience. Re- quirements for each data element are explained and reinforced by the tabular structure of the system — for example, any type of measure (e.g., mean) must have a unit of dispersion (e.g., standard deviation).16 The criteria for quality- control review are described in review-criteria documents,14 and when possible, automated mes- sages are provided before submission within the system.

As part of the process of quality-control re- view, NLM staff members apply the review crite- ria and provide data submitters with “major” comments noting issues that must be corrected

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or addressed and “advisory” comments that are provided as suggestions for improving clarity. This process ends when all noted major com- ments have been addressed in a subsequent sub- mission. Common types of issues include invalid or inconsistent units of measure (e.g., “time to myocardial infarction” as a measure, with “num- ber of participants” as the unit of measure), list- ing of a scale without the required information about the domain or the directionality (e.g., the minimum and maximum scores), and inconsisten- cies within the record (e.g., a number of patients who were included in an analysis of an outcome measure that is greater than the number who were enrolled in the study) (Table S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org).17

descrip tion of results in the database

In this review, we sought to characterize results that had been posted on ClinicalTrials.gov as of January 1, 2019, at which time more than 3300 sponsors or investigators had posted more than 34,000 records with results. As of May 2019, ap- proximately 120 new results were being posted to the site each week, with an additional 128 posted records with results updated each week. Most of the posted results were for clinical trials, whereas 1973 of the postings (6%) were for ob- servational studies.

Table S2 shows the characteristics of the posted trials with results. More than 1500 of the posted results were accompanied by documents that included a protocol and statistical analysis plan. The median interval between the primary completion date and the date of posting by the NLM was 2.0 years (interquartile range, 1.3 to 3.8), which includes the time from the final collec- tion of data until submission to the NLM, the time for the NLM quality-control review, and the time for sponsors or investigators to address quality-control issues.

After the regulations became effective in January 2017, there was an increase in the rate of posting of results for completed U.S. clinical trials, from an average of 50 new reports of results posted per week in 2016 to 86 new reports posted per week in 2017 (Fig. 1). Various research groups have estimated the adherence to compo- nents of FDAAA results-reporting requirements

using public data available on ClinicalTrials.gov. Such analyses are limited because accurate eval- uation sometimes requires study-specific consid- erations and nonpublic data (e.g., information not required or collected after the Final Rule effective date). Others have used various metrics to assess public dissemination of results generally (e.g., any results reported in published articles or on ClinicalTrials.gov within 2 years).18 According to these heterogeneous analyses, the percentage of completed trials that are listed on ClinicalTrials

.gov ranges from 22% of relevant trials com- pleted in 200919 to 66% completed as of May 2019.20 The efforts by various reviewers to high- light rates of reporting, including the naming of specific sponsors, correspond to improvements in reporting generally and by named sponsors. For example, an updated 2018 analysis by the health- oriented news website *STAT* documented the most improvement in overall rates of results reporting among sponsors that had been previously named in a 2016 analysis by the publication.21,22

key Issues in meeting

requirements for reporting results

To explore the degree to which sponsors and investigators are meeting the criteria for quality- control review, on October 31, 2018, we identi- fied all trial records (including both required and optional results) that had first been submit- ted on or after May 1, 2017, and that had under- gone quality-control review at least once by September 30, 2018. All the submissions (whether required or optional) were subject to the same review criteria and were considered to have met these criteria (“success”) for a review cycle if no major comments had been provided (see the Supplementary Appendix). The success rate dur- ing the first review cycle was 31% (862 of 2780 submissions) for industry records and 17% (582 of 3486 submissions) for nonindustry records. Cumulative success rates after the second review cycle increased to 77% (1653 of 2140 submis- sions) for industry records and 63% (1492 of 2359 submissions) for nonindustry records.

In our analysis of high-volume sponsors (i.e., those who submitted ≥20 results during the sample period), the success rates during cycle 1 were heterogeneous. For example, the success rate for high-volume industry sponsors during

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Average No. of Records/Wk** |  | | | | | | | | | | | |
| Trials completed | 58 | 79 | 89 | 92 | 99 | 103 | 104 | 111 | 112 | 122 | 120 | 135 |
| Results posted | 0 | 2 | 10 | 16 | 24 | 33 | 40 | 61 | 46 | 50 | 86 | 68 |

cycle 1 ranged from 16.4 to 77.1%, whereas the success rate for corresponding nonindustry sponsors ranged from 5.0 to 44.4% (Fig. S1). The fact that during cycle 1 some high-volume indus- try sponsors had a success rate of more than 70% indicated that the reporting requirements could be understood and followed appropriately. Although during cycle 1 the median success rate was relatively low, 62% had success after two review cycles. We believe that a goal of achieving success within two cycles is reasonable and is analogous to the need to make changes in re- sponse to editorial comments before journal publication (Fig. S2).

75,000

70,000

65,000

42 CFR part 11 regulatory effective date (Jan. 2017)

60,000

55,000

50,000

45,000

40,000

35,000

30,000

25,000

Notice of proposed rulemaking

issued for public comment (Nov. 2014)

Launch of ClinicalTrials.gov results database (Sept. 2008)

Registered U.S. clinical trials

20,000 FDAAA 801

15,000

10,000

5,000

0

statutory effective date

(Dec. 2007)

2007 2008 2009

Registered U.S. clinical trials with posted results

2010 2011 2012 2013 2014 2015 2016 2017 2018

**Year**

**Figure 1. Registered U.S. Clinical Trials and Trials with Posted Results on ClinicalTrials.gov.**

The blue line shows the cumulative number of clinical trials that were performed at one or more sites in the United States and that were registered on ClinicalTrials.gov with a primary completion date between 2007 and 2018, as of May 8, 2019. The orange line shows the cumulative number of registered U.S. clinical trials for which results were first posted on ClinicalTrials.gov between 2008 and 2018. CFR denotes Code of Federal Regulations, and FDAAA Food and Drug Administration Amendments Act.

**Cumulative No. of Trial Records**

We have observed that industry sponsors tend to be well staffed and have a centralized process for supporting the submission of results, whereas nonindustry sponsors tend to rely on individual investigators with minimal centralized support. A 2017 survey showed that academic medical centers had assigned the task of supervising registration and results submission to a median

of 0.08 full-time-equivalent staff members (work- ing 3.2 hours per week) with varying levels of education.5 In addition to limited support, some sponsors have described challenges with provid- ing structured information in a system that is unfamiliar in format and terminology.12 The NLM recognizes these challenges and has made im- provements to the system over time; we continue to invest in evaluating and improving the sys- tem, including providing more just-in-time auto- mated user support before submission. We also continue to conduct training workshops, add and improve resource materials (e.g., templates, checklists, and tutorials), and provide one-on-one assistance when needed.

effec t of results reporting on the evidence base

We reviewed the effect of the ClinicalTrials.gov registry in a previous article,23 and sample evi- dence for the effect of the results database is

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| **Table 3. Potential Benefits and Uses of Results Data Submitted to ClinicalTrials.gov.** |
| **Contribution to Clinical Trial Enterprise Sample Evidence** |
| Evaluate consistency of reporting Discrepancies have been identified in studies that compared results entries with  published data24-26 and that compared results entries with FDA review docu- ments.27 |
| Augment evidence base with results Half of sampled results entries have not been published4; in addition, results for unpublished trials entries are the only source of information for many terminated trials,28 and a  quarter of sampled drug trials with the same industry sponsor for the same drug and condition have results entries that had not been published.29 |
| Provide more complete results for There is evidence that many results entries provide more complete information published trials than that provided in published articles, especially regarding serious adverse  events.30 Some published articles refer readers to results entries containing information on prespecified secondary outcome measures and adverse events information (e.g., in the FLAME [NCT01782326]31 and KIA [NCT01097694]32 trials). |
| Augment evidence base to mitigate Results entries that are uniquely available on ClinicalTrials.gov sometimes pro- publication bias vide unique evidence relevant to reviews, even though no study has shown  that such entries have an effect on conclusions of systematic reviews.33,34 |
| Monitor other effects of results- Among sampled trials of drugs with FDA review documents that supported new reporting requirements FDA approvals, implementation of the FDAAA has been associated with con-  cordance between results entries and the review documents for cardiovascu- lar and diabetes drugs35 and with a higher proportion of results reporting to ClinicalTrials.gov and lower publication bias among neuropsychiatric drugs.36 |
| Other uses Results entries can be used to compare trial discontinuation rates and reasons across trials for pain conditions.37 |

provided in Table 3. In addition, we conducted two analyses to evaluate the relationship between the results database and published literature (see the Supplementary Appendix).4

**relationship to published literature**

To investigate the broad effect of ClinicalTrials

.gov on public availability of trial results, we compared the timing of the availability of initial results between the results database and corre- sponding journal publications (when available). On March 1, 2018, we identified 1902 registered trials with required or optional results that had first been posted on ClinicalTrials.gov between April 1, 2017, and June 30, 2017. We then ex- tracted a 20% random set of 380 records with results, used methods that have been described previously to manually identify corresponding publications,38 and compared the date that re- sults were first posted on ClinicalTrials.gov with the publication date. We categorized as “simul- taneous” the posting date and publication date if they fell within a 1-month period, whereas other submissions were designated as having been published before or after posting.

Relative to the date of posting on Clinical-

Trials.gov, 31% (117 of 380) of the records had

an earlier publication date, 2% (7 of 380) were

published simultaneously, and 9% (36 of 380)

were published after posting; 58% (220 of 380) did not have a publication date by the end of the follow-up period on July 15, 2018. Twenty-four months after the primary completion date of the trial, 41% (156 of 380) had posted results on

ClinicalTrials.gov, and 27% (101 of 380) had been published (Table S2). These findings are consistent with those in previous analyses in which we found that the results of a substan- tial number of trials had not been published 2 to 4 years after trial completion.38 In the case of such trials, ClinicalTrials.gov provided the only public reporting of results.4,29

**completeness of results reporting** Researchers have previously shown inadequacies in the reporting of data on ClinicalTrials.gov and in the corresponding published articles. Included in these shortcomings is the lack of reporting

of all-cause mortality, which is critical, unam-

biguous information.24,39 To improve reporting on ClinicalTrials.gov, a table that includes data re- garding all-cause mortality is now required for

trials that were completed on or after January 18, 2017. Of the 160 trials in our sample for which the results had been published, we identi- fied 47 trials that included a table showing all- cause mortality on ClinicalTrials.gov. Of these trials, 26 reported the occurrence of no deaths, and 21 reported at least one death, for an overall total of 995 reported deaths. The associated published articles reported 964 deaths (Table S3). Among the trials for which no deaths were re- ported on ClinicalTrials.gov, 4% (1 of 26) of pub- lished articles stated that there were no deaths, and 96% (25 of 26) did not specifically mention deaths. Among the trials for which at least one death had been reported on ClinicalTrials.gov, 62% (13 of 21) were concordant with the pub-

lished data, 14% (3 of 21) reported fewer deaths in the published article, and 10% (2 of 21) re- ported the same overall number of deaths but in groups that were discordantly described; in 14% of the trials (3 of 21), the total number of deaths was ambiguous in the published article. In our sample, no published article reported more deaths than were reported on ClinicalTrials.gov. Although discrepancies between two or more sources generally raise questions about which is accurate, it is unlikely that sponsors or investiga- tors would report more deaths than actually oc- curred, especially because the focus on “all-cause mortality” should remove any subjectivity. Differ- ences in the timing of the disclosure of trial results may lead to some discrepancies, although we did not specifically evaluate that issue in our sample. For example, the publication of the re- sults of a trial before its completion would in- clude only deaths that had occurred to date, whereas the results reported on ClinicalTrials

.gov would include all the additional deaths that had been observed until trial completion and thereby serve as a key source of final results for such trials.

discussion

We have previously described the mandates to re- port results to ClinicalTrials.gov as an experiment for addressing the nonpublication and incom- plete reporting of clinical trial results.4 A decade after launch, the results database is the only publicly accessible source of results information for thousands of trials. As such, the database

supports the goal of complete reporting and serves as a tool for timely dissemination of trial results that complement existing published re- ports. The study records that have been posted on ClinicalTrials.gov provide an informational scaffold on which information about a trial can be discovered, including access to statements regarding the sharing of data for individual trial participants and, in some cases, links to sites where such data have been deposited.40,41 This scaffolding function is facilitated when docu- ments about a clinical trial (e.g., publications, data repositories, press releases, and news arti- cles) reference the ClinicalTrials.gov unique iden- tifier (NCT number) assigned to each registered study. The recent addition of protocol documents, statistical analysis plans, and informed-consent forms further informs users about a study’s de- sign — use that we encourage in meta-research and quality-improvement efforts.42

Efforts to improve the quality of reporting need to consider the full life cycle of a clinical trial. For example, the presumption of both trial registration and reporting of summary results had been that required information would flow directly from the trial protocol, the statistical analysis plan, and the data analysis itself. How- ever, based on the experience of operating ClinicalTrials.gov, we have seen heterogeneity in the degree to which the necessary information is specified or available. Thus, we support recent efforts aimed at strengthening this early stage of the clinical-research life cycle with structured, electronic protocol-development tools,43-45 as well as the use of standardized, well-specified outcome measures46 that are consistent with scientific prin- ciples and harmonized with ClinicalTrials.gov reporting. For such broad efforts and more tar- geted efforts to improve quality to take root, leadership in the clinical-research community is needed to champion the value of such efforts and provide resources and incentives. In parallel, as the database operators, we continue to evalu- ate users’ needs in order to ensure that reporting requirements are known and understood by those involved throughout the clinical-research life cy- cle and to improve the submission process and the quality of reporting.

We also think that the full value of the trial- reporting system will emerge when various par- ties recognize and leverage the substantial effort

that has been invested in the use of this curated, structured system for reporting of summary results. For example, providing appropriate academic credit for results that are posted on ClinicalTrials.gov (as a complement to credit for the publishing of articles) would incentivize more timely and careful entries by investigators. In ad- dition, the tables that are posted on the database can be reused in manuscripts and during the editorial or peer-review process to ensure consis- tency across sources. Publications can also refer to the full set of results on ClinicalTrials.gov while focusing on a subset of interest (e.g., pub- lishing data for 19 of 27 prespecified secondary outcome measures and providing a link to ac- cess results for remaining outcome measures on ClinicalTrials.gov31,32). Just as the results database supports systematic reviews, we see opportuni- ties for those who oversee research, including funders, ethics committees, and sponsoring or- ganizations, to conduct landscape analyses be- fore approving the initiation of new clinical trials and to monitor a field of research over time. In support of this goal, we aim to develop tools to further optimize search strategies and enhance the viewing and visualization of search results to support such activities. For instance, the NLM recently updated the way third-party software ac- cesses data on ClinicalTrials.gov by supporting better targeted queries and more expansive con- tent availability, as well as changes to the main search features on the website for other users.

Although the results database has evolved con- siderably in the past decade, efforts to strengthen the culture and practice of systematic reporting must continue. We have previously outlined steps that various stakeholders can take to enhance the trial-reporting system.23 These actions can be described in two broad themes: facilitating high-quality submissions while reducing the re- porting burden for data submitters and modify- ing incentives to encourage reporting and em- bracing its value as part of the scientific process. As such, we endeavor to support researchers and institutions in maximizing the value of their ef- forts and those of the research participants as well as the overall value of the ClinicalTrials.gov results database to the scientific enterprise.

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