

Availability and Use of Shared Data From Cardiometabolic Clinical Trials

BACKGROUND: Sharing of patient-level clinical trial data has been widely endorsed. Little is known about how extensively these data have been used for cardiometabolic diseases. We sought to evaluate the availability and use of shared data from cardiometabolic clinical trials.

METHODS: We extracted data from ClinicalStudyDataRequest.com, a large, multisponsor data-sharing platform hosting individual patient-level data from completed studies sponsored by 13 pharmaceutical companies.

RESULTS: From January 2013 to May 2017, the platform had data from 3374 clinical trials, of which 537 (16%) evaluated cardiometabolic therapeutics (phase 1, 36%; phase 2, 17%; phase 2/3, 1%; phase 3, 42%; phase 4, 4%). They covered 74 therapies and 398 925 patients. Diabetes mellitus (60%) and hypertension (15%) were the most common study topics. Median time from study completion to data availability was 79 months. As of May 2017, ClinicalStudyDataRequest.com had received 318 submitted proposals, of which 163 had signed data-sharing agreements. Thirty of these proposals were related to cardiometabolic therapies and requested data from 79 unique studies (15% of all trials, 29% of phase 3/4 trials). Most (96%) data requesters of cardiometabolic clinical trial data were from academic centers in North America and Western Europe, and half the proposals were unfunded. Most proposals were for secondary hypothesis-generating questions, with only 1 proposed reanalysis of the original study primary hypothesis. To date, 3 peer-reviewed articles have been published after a median of 19 months (9–32 months) from the data-sharing agreement.

CONCLUSIONS: Despite availability of data from >500 cardiometabolic trials in a multisponsor data-sharing platform, only 15% of these trials and 29% of phase 3/4 trials have been accessed by investigators thus far, and a negligible minority of analyses have reached publication.

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Clinical Perspective

What Is New?

- Data from >500 cardiometabolic trials have been made available on a large, multisponsor data-sharing platform.
- Median time from study completion to data availability was >6 years.
- Most data requesters of cardiometabolic clinical trial data were from academic centers in North America and Western Europe, and half the proposals were unfunded.
- Only 15% of these trials have been accessed by investigators thus far, and few findings have reached publication.
- Most requests for shared data access focus on new hypothesis-generating questions rather than validation of original study findings.

What Are the Clinical Implications?

- As we prepare for more widespread data sharing in cardiology, this interim look at an existing data-sharing initiative may allow anticipation of barriers to effective system implementation and shared data consumption.

Clinical trials represent the gold standard to test emerging cardiometabolic therapeutics and form the basis of most regulatory approvals.¹ These studies are increasingly becoming larger, costlier, and more complex to conduct.² Sharing participant-level data after trial completion is proposed as a mechanism to broaden their scientific impact and to maximize return on investment. Responsible data sharing promises to enhance the individual contributions of research participants and may confirm study reproducibility and validity. Efforts to advance data sharing have accrued a broad base of support from governmental officials,³ journal editors,^{4,5} charitable foundations,^{6,7} regulatory bodies,⁸ the pharmaceutical industry,⁹ and clinical trialists.¹⁰ ACCESS CV (Academic Research Organization Consortium for Continuing Evaluation of Scientific Studies–Cardiovascular),¹¹ a 31-member panel of cardiovascular clinical trialists, was recently formed to operationalize these calls for data sharing in cardiology.

Despite this progress to improve data transparency and access, effective implementation and the mechanics of data sharing require further attention. Several existing data-sharing initiatives have provided early insights into patterns of use of aggregate data across medical disciplines (Table 1)^{8,12–16} and suggest that these data are underused. Specialty-specific use, including the use of data from cardiometabolic trials, is less clear. Of the pioneering industry-based

data-sharing platforms, ClinicalStudyDataRequest.com (CSDR)¹⁷ is one of the oldest and largest and hosts the greatest number of cardiometabolic trials from various industry sponsors. We provide an assessment of the availability and use of shared data from cardiometabolic clinical trials hosted by the CSDR multisponsor data repository. We hypothesized that similar to the experience with general medical clinical trials, demand for access to cardiometabolic trials would be limited.

METHODS

ClinicalStudyDataRequest.com

We extracted data from CSDR,¹⁷ a publicly available, online, multisponsor data-sharing platform that is hosted by ideaPoint, Inc (Boston, MA) and has been available since January 2013. Thirteen pharmaceutical companies, including Astellas, Bayer, Boehringer Ingelheim, Daiichi Sankyo, Eisai, GlaxoSmithKline, Lilly, Novartis, Roche, Sanofi, Takeda, UCB, and ViiV Healthcare, deposit deidentified, individual patient-level data into CSDR. Key eligibility criteria for listing, exempted or unshared studies, conditions for data access, and details about data sets and meta-data are summarized in Table 2 and expanded online.¹⁷

Procedures for Data Requests

The procedures for data requests have been described previously¹⁸ and are summarized in Figure 1. In brief, data requesters first submit a proposal related to 1 or more hosted studies via a secure, web-based portal. Specific enquiries can also be submitted to sponsors concerning the availability of data from studies not hosted by CSDR.

Next, an independent review panel managed by the Wellcome Trust (as of March 2015) reviews each proposal for completeness, scientific merit, the ability of the research plan to achieve the stated aims, and the qualifications and conflicts of interest of the research team. The panel then reaches a decision, and the data requesters sign a data use agreement.

Access to deidentified data and meta-data is then granted through a secure enclave with in-built SAS (SAS Institute, Cary, NC) and R (R Foundation) statistical software for 12 to 24 months. Up to 5 statistical software licenses to analyze shared data are supported by the involved study sponsors. The private user interface is password protected and accessible only to data requesters. Data elements are fully anonymized with technical safeguards in place to prevent researchers from downloading original patient-level data. The analysis system further allows data requesters to combine study data from multiple sponsors.

The entire data-sharing process via CSDR is tracked and transparently displayed online. The number of requests for data access of listed and unlisted studies and final decisions from the independent review panel are presented. A lay summary and the key study details of each approved proposal are made publicly available after data use agreements are signed. Data requesters are expected to post a summary of their research plan on a registry or website within 1 year and to

Table 1. Select Published Experiences of Existing Clinical Trial Data-Sharing Platforms Across Medical Disciplines

Platform	Reference	Time Frame of Access	Type of Data Shared	Total Trials Hosted, n	Total Requests, n	Total Granted or Approved, n
Data reports submitted for regulatory approval						
EMA	Bonini et al ⁸	2010–2013	Any data submitted for marketing authorization of any medicinal product	...	750	480
Federally funded clinical studies						
NHLBI Data Repository	Coady et al ¹²	2000–2016	Patient-level data from large NHLBI-supported trials and observational studies	100	800–850	...
Industry-sponsored clinical studies						
CSDR, SOAR initiative, and YODA project	Navar et al ¹⁴	2013–2015	Patient-level data from select clinical studies sponsored by 14 companies	3255	234	154
CSDR	Strom et al ¹⁶	2013–2015	Patient-level data from select clinical studies sponsored by 13 companies	3049	177	144
	Strom et al ¹⁵	2013–2014	Patient-level data from select clinical studies sponsored by 10 companies	>1200	58	36
YODA project	Krumholz and Waldstreicher ¹³	2014–2015	Patient-level data from select trials sponsored by Johnson & Johnson	123	29	29

CSDR indicates ClinicalStudyDataRequest.com; EMA, European Medicines Agency; NHLBI, National Heart, Lung, and Blood Institute; SOAR, Supporting Open Access to Researchers; and YODA, Yale Open Data Access.

submit their findings for peer-reviewed publication. Protocols and expectations for reviewing manuscripts before submission are sponsor specific. After publication, the citation and statistical analysis plan are also posted on CSDR.

Data Extraction, Linked Sources, and Statistical Methods

We queried ClinicalTrials.gov to obtain a crude estimate of total trial portfolio per sponsor, including the number of unshared trials. We identified studies registered with ClinicalTrials.gov that are supported by each sponsor by using the following limits: updated through May 2017, interventional study design, closed enrollment, and trial phase (2–4).

We detailed category of study identified by each sponsor. We identified cardiometabolic trials as those evaluating therapies targeting established cardiovascular disease (atrial fibrillation/atrial flutter, coronary artery disease, heart failure, peripheral vascular disease, stroke, venous thromboembolism) or cardiometabolic risk factors (diabetes mellitus, dyslipidemia, hypertension, metabolic syndrome, obesity). Trial size, phase, drug or drug combination, and date of data availability were also documented. We then linked each cardiometabolic study with its corresponding ClinicalTrials.gov and sponsor entry to estimate time from study completion to data availability.

We reviewed all approved proposals from the inception of the platform through May 2017. Key characteristics of lead data requesters were detailed by reviewing their CSDR affiliation information and online faculty profile. For each cardiometabolic proposal, we applied the search terms of the first and last names of the submitting investigator and key words from the title of the proposal in PubMed/MEDLINE to determine publication status. All queries were performed through May 2017. Only publicly available trial-level data were accessed; thus, this study was not submitted for institutional review board approval, and individual trial participants were not contacted for informed consent.

RESULTS

Shared Data Availability on CSDR

From January 2013 to May 2017, the platform had data from 3374 clinical trials, of which 537 (16%) evaluated cardiometabolic therapeutics (phase 1, 36%; phase 2, 17%; phase 2/3, 1%; phase 3, 42%; phase 4, 4%). They covered 74 therapies and 398 925 patients (Figure 2). Diabetes mellitus (60%) and hypertension (15%) were the most common study topics (Figure 3).

Median time from study completion to data availability was 79 months (interquartile range, 52–108 months) with a range of 5 to 211 months (Figure 4). When only trials made available in 2016 and 2017 were examined, time to data availability was slightly shorter (median, 65 months; interquartile range, 40–86 months; range, 5–187 months).

Sponsor-Specific Data Sharing

Most industry sponsors required the original study to be accepted or published at the time of data sharing, and sponsors variably required study drugs to have been approved by the US Food and Drug Administration, the European Medicines Agency, or both (Table 2). Common reasons for study exemption include any factors that posed challenges to fully anonymizing data (small, single-center experiences, studies of rare diseases, genomic data), non-English studies, practical constraints related to trial size, certain legal provisions, or threats to commercial/intellectual property. Sponsors shared between 1% and 95% of their total estimated portfolio from ClinicalTrials.gov on the CSDR platform. Glax-

Table 2. Inclusion Criteria, Number of Trials With Available Individual Patient–Level Data, and Estimated Total Trial Portfolio by Industry Sponsor

Sponsor	Inclusion Criteria for Data Sharing	Shared Cardiometabolic Trials, n	Other Shared Trials, n	Total Trials With Available Data, n	Crude Estimate of Trial Portfolio per Sponsor, n*	Estimated Trial Portfolio With Shared Data on CSDR, %
Astellas	Phase 1–4 interventional studies for approved products completed after January 2010	12	26	38	624	6
	Phase 1–4 interventional studies for compounds terminated after June 2015					
Bayer	Approved products (by both FDA and EMA) after January 2014	0	8	8	763	1
	Approved products (by only 1 agency) after January 2014 if no plan for ongoing review or submission					
Boehringer Ingelheim	—	75	262	337	1303	26
Daiichi-Sankyo	Phase 2–4 interventional studies for approved products after January 2014 (by FDA and EMA)	16	0	16	165	10
Eisai	Phase 2 and 3 studies for approved products after January 2014 (by FDA and EMA) accepted for publication	0	7	7	251	3
	Phase 4 published interventional studies for approved products after January 2014 (by FDA and EMA)					
GSK	Global interventional studies ongoing or started after December 2000	234	1793	2027	2633	77
	All interventional studies started after January 2013					
Lilly	Phase 2–4 interventional studies for FDA-approved products on/after 1999	13	253	266	953	28
	Phase 2–4 global interventional studies for FDA- and EMA-approved products started after January 2007					
	Phase 2–4 regional/local interventional studies for FDA- and EMA-approved products started after January 2014					
Novartis	Phase 2–3 studies for previously approved products (by FDA and EMA) being submitted for new indication as of January 2014 with decision on original study publication	3	65	68	1455	5
	Phase 2–3 studies for approved products before January 2014 (case-by-case review) with decision on original study publication					
Roche	Phase 2 and 3 studies started after January 1999	11	176	187	858	22
	Phase 4 studies for approved or terminated products started after January 1999					
Sanofi	Phase 2–4 interventional clinical studies for approved products after January 2014 with accepted manuscript of original study	27	7	34	1379	2
Takeda	Phase 1–4 intervention trials for approved products after January 2005	146	165	311	430	72
	Phase 1–4 interventional trials for products terminated on or after January 2014					
UCB	Pivotal studies for regulatory approval of certolizumab, lacosamide, rotigotine, and levetiracetam	0	34	34	324	10
ViiV	Phase 2–4 global interventional studies of HIV drugs	0	41	41	43	95
All sponsors		537	2837	3374	11 181	30

CSDR indicates ClinicalStudyDataRequest.com; EMA, European Medicines Agency; FDA, US Food and Drug Administration; GSK, GlaxoSmithKline; and HIV, human immunodeficiency virus.

*ClinicalTrials.gov was queried for completed interventional trials sponsored by the company without limits on study completion/initiation dates, global or regional enrollment, drug approval status, or publication status.

oSmithKline shared data from the highest number of cardiometabolic trials (n=234) and total trials (n=2027, 77% of the total estimated trial portfolio).

Cardiometabolic Proposals and Data Use

As of May 2017, CSDR had received 318 submitted proposals, of which 235 met initial processing requirements.

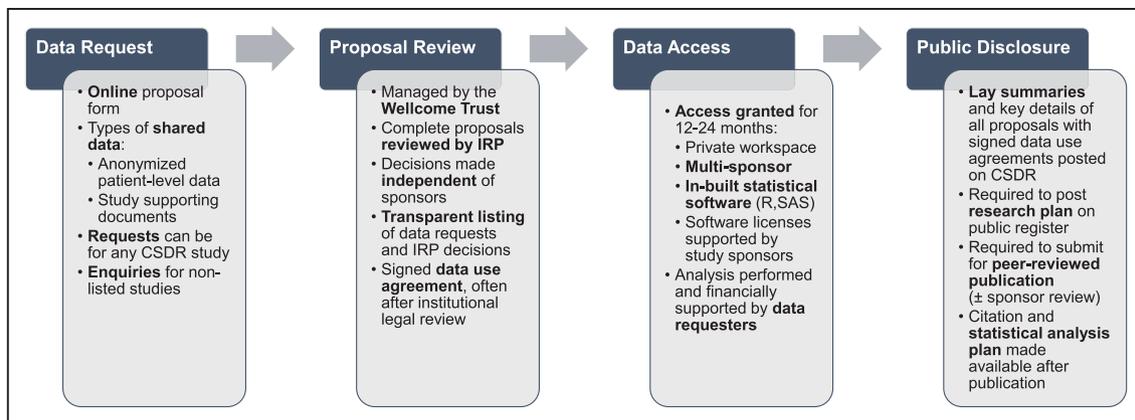


Figure 1. Mechanics of data sharing via the ClinicalStudyDataRequest.com (CSDR) platform.

This flow diagram highlights the 4 major steps of this data-sharing model, including the initial request for access to clinical trial data, review by an independent review panel (IRP), access to a multisponsor analysis system, and public dissemination of secondary research findings.

Of these, 5 remain in process, 6 were withdrawn by the requester, and 26 were rejected or required revision. Therefore, 198 were approved (with or without conditions) and 163 (51%) had signed data use agreements.

Thirty of these proposals were related to cardiometabolic therapies and requested data from 79 unique studies (representing 15% of available cardiometabolic trials; Figure 2). These studies were primarily phase 3 ($n=57$ trials, 25% of available phase 3 cardiometabolic studies) and phase 4 ($n=14$ trials, 61% of available phase 4 cardiometabolic studies). The median number of trials requested by each proposal was 1 (range, 1–45). Most proposals requested data from a single sponsor, whereas 5 requested data from >1

sponsor. Five studies were requested more than once (range, 2–6 times requested). The most common topics of requested studies were diabetes mellitus (72%), venous thromboembolism (8%), and atrial fibrillation/atrial flutter (8%). Half of the proposals did not specify a funding source for the analysis.

Most proposals focused on statistical or research methodology ($n=6$), risk prediction ($n=6$), or meta-analyses/systematic reviews ($n=4$). Other proposal objectives, including translation of clinical trial findings to real-world settings ($n=3$), subgroup analyses ($n=3$), predictors of response ($n=2$), or disease characterization ($n=2$), were less common. Only 1 proposal intended to reanalyze the original study primary hypothesis.

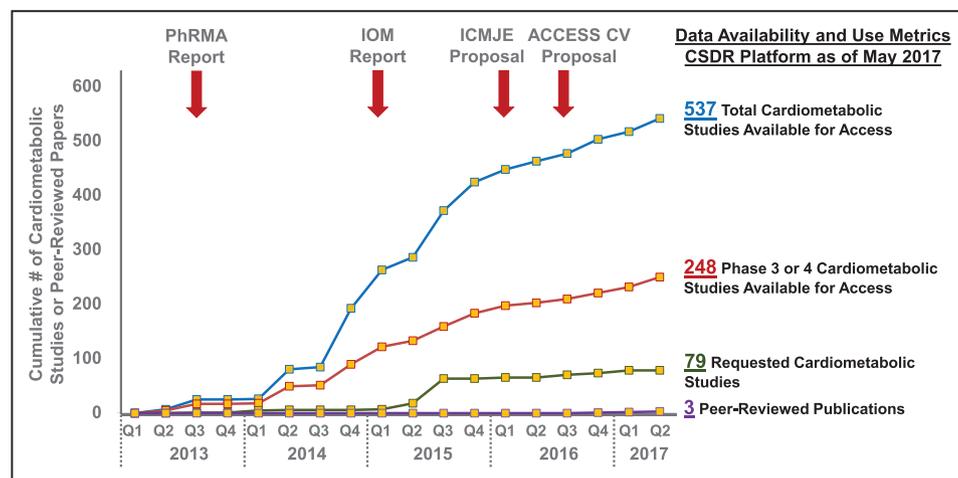


Figure 2. Availability and metrics of the use of cardiometabolic clinical trial data hosted on the multisponsor data-sharing platform, ClinicalStudyDataRequest.com.

Landmark working group reports and proposals endorsing access to individual patient-level data are highlighted (red arrows). Blue and red lines reflect the availability of data from completed cardiometabolic clinical trials. Green line reflects dates that each cardiometabolic study was first requested through this platform with signed data-sharing agreements. Purple line reflects peer-reviewed publications based on these shared data identified through PubMed/MEDLINE. ACCESS CV indicates Academic Research Organization Consortium for Continuing Evaluation of Scientific Studies–Cardiovascular; CSDR, ClinicalStudyDataRequest.com; ICMJE, International Committee of Medical Journal Editors; IOM, Institute of Medicine; PhRMA, Pharmaceutical Research and Manufacturers of America; and Q, quarter.

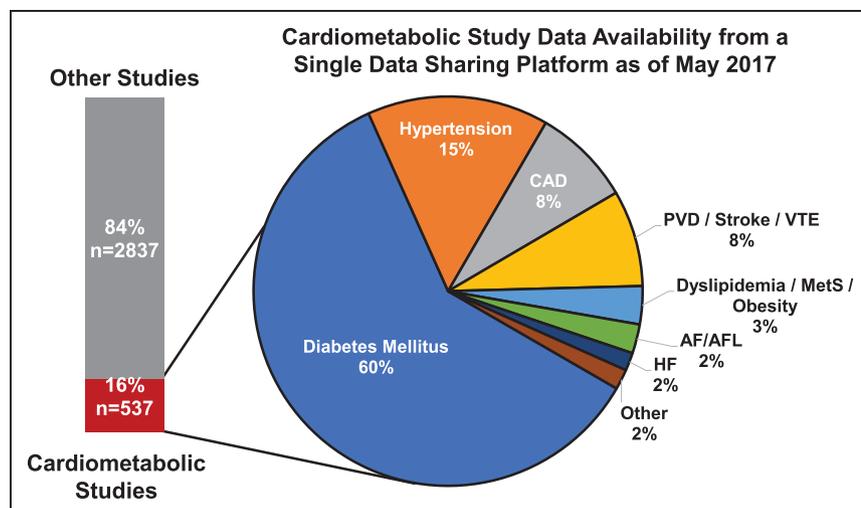


Figure 3. Breakdown by study area of cardiometabolic trials available for data requests.

Diabetes mellitus (60%) and hypertension (15%) were the most common study topics. AF/AFL indicates atrial fibrillation/atrial flutter; CAD, coronary artery disease; HF, heart failure; MetS, metabolic syndrome; PVD, peripheral vascular disease; and VTE, venous thromboembolism.

Characteristics of Data Requesters

Four investigators were the lead researchers on >1 proposal, such that there were 26 unique data requesters of cardiometabolic studies. The majority (85%) were men. Data access requests spanned 6 countries. Twenty-five of the 26 investigators were based in North America or Western Europe and were affiliated primarily with an academic medical center. A single data requester worked for a pharmaceutical company. Thirty-eight percent of data requesters were specialists in cardiology, hypertension, or diabetes mellitus; the remaining worked in areas outside cardiometabolic health, including epidemiology, statistics, health services, and public health.

Publication Status

To date, 3 of the 30 proposals (10%) had accompanying peer-reviewed publications^{19–21} at a median of 19 months (9–32 months) from completion of the data

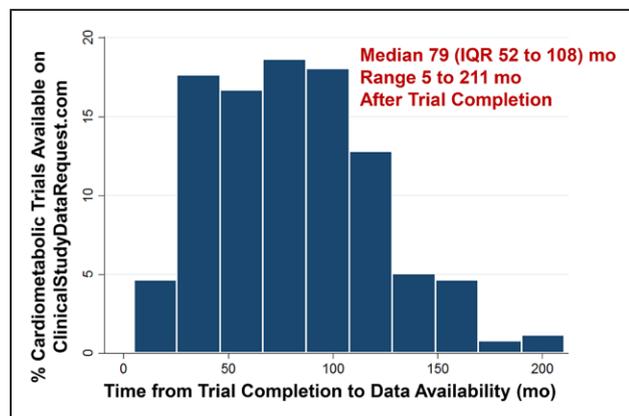


Figure 4. How long does it take for data to become accessible?

Time from trial completion (extracted from ClinicalTrials.gov) to individual patient-level data availability on the ClinicalStudyDataRequest.com platform. IQR indicates interquartile range.

use agreement. Kent et al²⁰ assessed the relationship between baseline risk and absolute treatment effects across 32 large trials (only 1 of which was requested through CSDR). Hilkens et al¹⁹ performed an exploratory analysis defining risk of intracerebral hemorrhage with varying systemic blood pressures in patients with recent ischemic stroke. Walker et al²¹ conducted a systematic review of 12 studies (only 1 of which was requested through CSDR) on the efficacy and safety of dipeptidyl peptidase-4 inhibitors in patients with diabetes mellitus and chronic kidney disease.

DISCUSSION

This interim analysis of cardiometabolic clinical trials hosted on a large, multisponsor data-sharing platform highlights several important findings. First, although individual patient-level data from >500 cardiometabolic trials are already available, only 15% have been accessed to date (≈ 4.5 years after the inception of the platform). Second, requests for data access were commonly unfunded and come from a small number of investigators of restricted demographics (the vast majority from North America/Western Europe and academic medical centers). Third, data access requests often focus on new hypothesis-generating questions and rarely attempt to validate or refute original study findings. Finally, few publications have resulted a median of >18 months after data access.

Data Sharing in Cardiology

The pharmaceutical industry has already pioneered efforts to expand data access and transparency. Although CSDR represents the most comprehensive data-sharing platform of industry-supported clinical trials, we estimate that only a fraction ($\approx 30\%$), varying significantly by sponsor, of total trial portfolios are available for access and become accessible >5 years after trial comple-

tion, even for studies added in the last 2 years. A previous analysis consistently reported that 25% of large, industry-sponsored, advanced-phase cardiovascular trials had available individual patient-level data.²² Indeed, a recent systematic audit demonstrated that commitments and policies to individual-level patient data access are highly variable across major pharmaceutical companies.²³

As we prepare for more widespread and routine data sharing on shorter timelines in cardiology,¹¹ examining these existing initiatives may allow anticipation of barriers to effective system implementation and shared data consumption. This analysis embedded within CSDR demonstrated relatively sparse use of these cardiometabolic clinical trial data, consistent with prior published reports of earlier analyses of shared general medical clinical trial data hosted on multiple industry-supported open-access platforms.^{13–16} A previous report provided an overview of 3 data-sharing platforms of industry-sponsored trials through the end of 2015 and demonstrated that only ≈15% of studies had been requested.¹⁴ In the present analysis, we specifically looked at availability and use of cardiometabolic trials through mid-2017 on the largest of these platforms, CSDR, and found similar overall demand for access. We further linked each hosted cardiometabolic study with its corresponding ClinicalTrials.gov and sponsor entry (for key trial characteristics) and linked each approved proposal with a PubMed/MEDLINE query (to determine publication status).

The National Heart, Lung, and Blood Institute (NHLBI) data repository,¹² which is coordinated by Biological Specimen and Data Repository Information Coordinating Center, has shown greater demand for data reuse of its large clinical trials and observational studies. Although the data repository hosts data from only 100 clinical trials, >800 data requests were received from 2000 to 2016, especially for larger, more recent cardiovascular treatment and prevention trials.¹²

Reasons for Data Requests

Consistent with prior experiences,^{13–16} most requests for cardiometabolic trial data focused on new hypothesis-generating questions or exploratory analyses. Only 1 cardiometabolic proposal in CSDR requested data for reanalysis (of the COPERNICUS trial [Carvedilol Prospective Randomized Cumulative Survival]),²⁴ perhaps because of low perceived publication value of analyses confirming previously published clinical trial findings. Reanalysis of the original study hypotheses, which was infrequent in this CSDR experience, may theoretically validate²⁵ or refute the findings of the original trial.²⁶ In a systematic review of 37 reanalyses of published studies, more than one third led to data interpretations that diverged from the conclusions of the original stud-

ies.²⁷ In addition, platforms such as CSDR enable data requests from >1 sponsor, but multisponsor proposals were infrequent in our experience.

Barriers to Data Sharing and Usability

Although the collective goals of data sharing are to advance science, to maximize the return of patient participation, and ultimately to improve public health, several practical considerations need to be addressed before this promise and potential are realized. Many hurdles remain in transforming existing platforms of data access into integrated systems that promote data usability, utility, and productivity.^{7,28}

Building and maintaining high-quality data repositories is cost and resource intensive. Costs incurred may depend on the specific data-sharing model, the size and complexity of shared data, and the structure of the user interface. However, the following 4 elements that contribute to cost are likely common to any viable data-sharing platform: infrastructure and maintenance, data standardization and quality control, human resources for technical expertise and administration, and opportunity costs and potential loss in investment to other research activities.²⁹ Upfront resource investment in building sustainable and comprehensive data-sharing platforms with standardized data elements and user-friendly interfaces may enhance the quality, accessibility, and usability of shared data but may be costly and financially untenable.

The actual costs of data sharing are difficult to estimate. Costs to support data-sharing models that provide limited or open access to data stored on digital repositories such as Dryad³⁰ depend on the size of shared data and may still be high for larger data sets such as genomic data³¹ because of overage fees incurred after a certain size limit. Costs and resources required for models facilitating extensive and comprehensive data sharing may be more substantial. Efforts to prepare data and meta-data for broad sharing in the NHLBI data repository were estimated as ranging from 85 to 350 full-time equivalent hours per study.¹² The initial cost required to establish an online data-sharing system for 2 large cancer screening trials supported by the National Cancer Institute was estimated at ≈\$300 000, with an additional ≈\$26 000 needed for monthly support and maintenance.³² The Alzheimer's Disease Neuroimaging Initiative, a disease-specific data-sharing platform that maintains secure, standardized, and comprehensive data, also provided early estimates of the practical costs of data sharing. Data-sharing efforts were estimated to account for 10% to 15% of the \$130 million total project costs and occupy 15% of the time of the primary project investigators.²⁹ Whether the clinical trial data-sharing enterprise should be financed by sponsors or data requesters remains to be determined.³³

Secondary data analyses also necessitate funding and analytical resources, which may explain the demographic predilection of data requesters. Data requesters of cardiometabolic studies in CSDR were primarily from academic medical centers in North America or Western Europe. Consistently, 88% of data requests from the NHLBI data repository originated from the United States or Canada.¹² This initial data use pattern supports general concerns about the preferential shared data use in high- compared with low-income countries.⁷ We found that half the proposals disclosed no specific external funding, which may preclude timely completion of data analyses and hinder ultimate publication. Limited funding and support were commonly cited factors in a cross-sectional, web-based survey of Biological Specimen and Data Repository Information Coordinating Center users as reasons delaying completion of analyses and publication.³⁴

The limited requests of industry-sponsored trials may be related to lack of knowledge of data availability by the general cardiovascular research community. Indeed, when data-sharing efforts are actively advertised and promoted, interest in data access appears to be high. For instance, in the SPRINT (Systolic Blood Pressure Intervention Trial) Data Analysis Challenge,³⁵ which represented a collaboration between the *New England Journal of Medicine*, the NHLBI, and the SPRINT Data Coordinating Center, 143 complete entries were received from 26 countries over a short duration. It is encouraging that data requesters in our CSDR-based experience had diverse backgrounds, with nearly two thirds in fields outside cardiometabolic health. These shared data sources represent important opportunities in the development of research careers across disciplines.

Although CSDR uses a “learned-intermediary”³⁶ or “gatekeeper”³⁷ model for data sharing, which leverages an independent review board that handles and transparently documents data access decisions, the optimal models for data sharing are yet to be determined. Ongoing efforts to merge isolated shared data silos into an integrated, secure,³⁸ global clinical trial platform³⁹ with standardized data elements⁴⁰ are currently underway. Consortia such as ACCESS CV will need to tackle other unresolved issues, including appropriate incentives and credit for data generators,⁴¹ a reasonable timeline for proprietary data use before public release, and mechanisms and structures to ensure compliance.

Study Limitations

This data-sharing report is subject to certain limitations. There are a number of existing industry-based data-sharing mechanisms, including CSDR, the Supporting Open Access to Researchers initiative, the Yale Open Data Access project, and direct-to-sponsor models. We

restricted our analysis to CSDR because other industry-sponsored platforms hosted few cardiometabolic trials. Only proposals with active data use agreements were accessible via CSDR; thus, we were not able to analyze all data requests before screening and review. We did not have access to the timeline of the approval process within CSDR to better understand the efficiency of the system. Although we applied inclusive search criteria in PubMed/MEDLINE, it is possible that we missed publications generated from these analyses. Our estimate of total trial portfolio using ClinicalTrials.gov was crude and may overestimate eligible trials because the query was not limited to specific time windows or drug approval status and did not account for unregistered trials or those registered elsewhere.

Conclusions

Although data from >500 cardiometabolic trials have been made available on a large, multisponsor data-sharing platform, only 15% of these trials have been accessed by investigators thus far, and few analyses have reached publication. Most proposals evaluated hypothesis-generating or exploratory aims; validation studies were rarely conducted. Barriers to use, optimal time frame to availability, and funding mechanisms for shared data of cardiometabolic clinical trials need clarification.

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None.

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associate editor), Population Health Research Institute (clinical trial steering committee), Slack Publications (chief medical editor, *Cardiology Today's Intervention*), Society of Cardiovascular Patient Care (secretary/treasurer), and WebMD (CME steering committees); other: *Clinical Cardiology* (deputy editor), NCDR-ACTION Registry Steering Committee (chair), and VA CART Research and Publications Committee (chair); research funding: Amgen, Amgen, AstraZeneca, Bristol-Myers Squibb, Chiesi, Eisai, Ethicon, Forest Laboratories, Ironwood, Ischemix, Lilly, Medtronic, Pfizer, Roche, Sanofi Aventis, and The Medicines Company; royalties: Elsevier (editor, *Cardiovascular Intervention: A Companion to Braunwald's Heart Disease*); site co-investigator: Biotronik, Boston Scientific, and St. Jude Medical (now Abbott); trustee: American College of Cardiology; and unfunded research: FlowCo, Merck, Plx Pharma, and Takeda. Dr Fonarow reports consulting for Novartis, Amgen, Janssen, Medtronic, and St. Jude Medical. Dr Butler has received research support from the National Institutes of Health and European Union and has been a consultant for Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, CVRx, Janssen, Luitpold Pharmaceuticals, Medtronic, Merck, Novartis, Relypsa, Vifor Pharma, and ZS Pharma. Drs Nagarur, Patel, and Yancy report no conflicts.

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FOOTNOTES

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