Informational webinar

CRDSA Standard for Secondary Analysis of Clinical Study Data

Wednesday, April 10
10:00 to 11:00 a.m. EDT

Presented by:
Frank Rockhold (Duke Clinical Research Institute), Andrew Freeman (CRDSA), and Aaron Mann (CRDSA)

CRDSA
Clinical Research Data Sharing Alliance

Delivering Collaborative Solutions

CRDSA

Biopharma

Roche
NOVARTIS
Takeda
ucb
AstraZeneca
AMGEN

Data Platforms

CRITICAL PATH INSTITUTE
HDRUK Health Data Research UK
ClinicalStudy DataRequest.com
Project Data Sphere
Vivli CENTER FOR GLOBAL CLINICAL RESEARCH DATA
THE FORUM For Collaborative Research℠
Berkeley Public Health
CancerLinQ
COTA

Academic and Non-Profit

Duke Clinical Research Institute
THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH
Flinders University
THE UNIVERSITY OF CHICAGO PEDIATRIC CANCER DATA COMMONS

Service and Technology

parexel
Real Life Sciences
PRIVACY ANALYTICS an IQVIA company
d-wise An Instem Company
atorus Your Complete Data Solution

Partner Organizations

phuse

Presentation Outline

CRDSA

1. The need for standards
2. Scope, structure, and content overview
3. Principles
4. Adoption
5. How you can provide comments

Why are standards needed?

Why are standards needed?

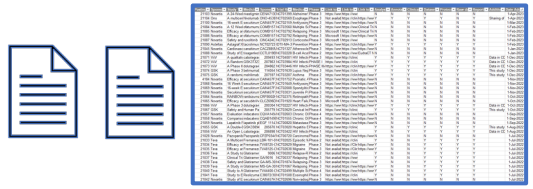
CRDSA

Researchers

- Need to be able to conduct accurate and reproducible analyses
- Need consistent and comprehensive data and meta-data

Data Contributors

- Want to ensure their data is used appropriately
- Benefit from a consistent approach and referenceable benchmarks



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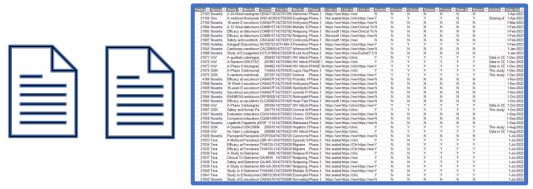
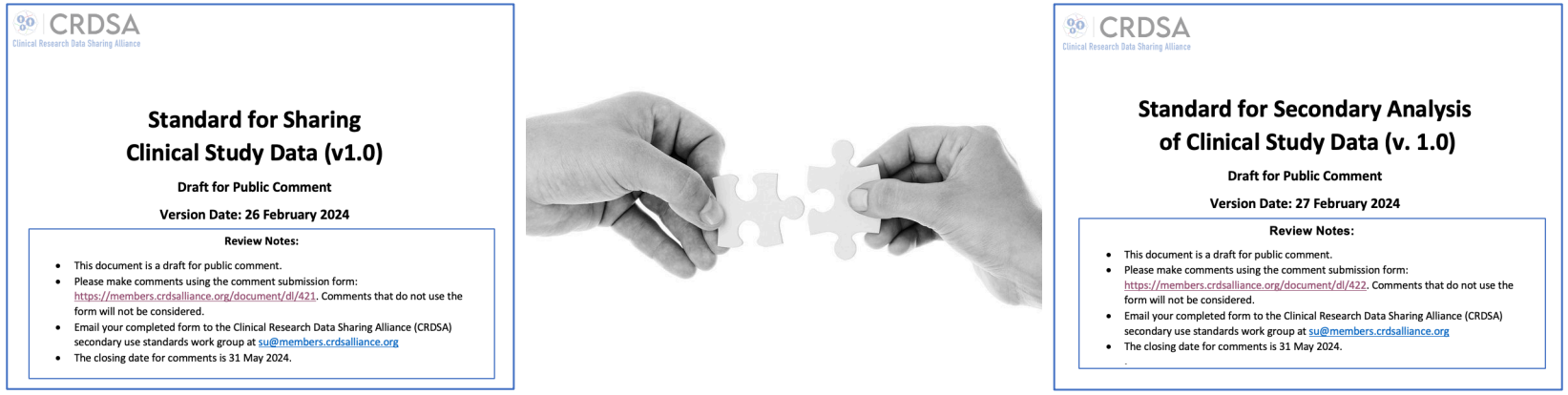


Current State

- Data sharing and research planning may be time-consuming
- Analyses may be found not to be feasible after data is provided
- Analysis errors can be made

Why are standards needed?

Data Sharing and Secondary Analysis Standards
work together to enable good science



How to share individual patient data (IPD) from clinical studies

How to use contributed IPD in secondary research

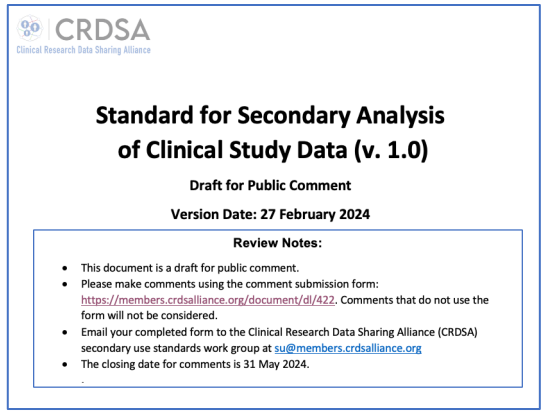
Addressing Key Research Challenges

CRDSA

1. The researcher is new to secondary data use and not aware of the necessary analysis steps
2. The researcher isn’t familiar with biopharma trial designs (crossover design, etc.)
3. The researcher isn’t conversant in the data formats, encoding, and structures used in biopharma studies

Scope, structure, and content overview

Secondary Analysis Standard - Scope


CRDSA
Clinical Research Data Sharing Alliance

Standard for Secondary Analysis of Clinical Study Data (v. 1.0)

Draft for Public Comment

Version Date: 27 February 2024

Review Notes:

- This document is a draft for public comment.
- Please make comments using the comment submission form: https://members.crdsalliance.org/document/dl/422. Comments that do not use the form will not be considered.
- Email your completed form to the Clinical Research Data Sharing Alliance (CRDSA) secondary use standards work group at su@members.crdsalliance.org
- The closing date for comments is 31 May 2024.

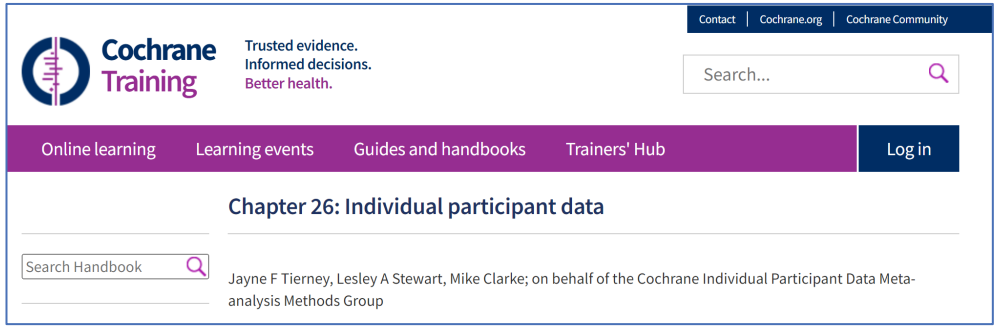
- Includes secondary analyses of interventional clinical trials conducted in patients and non-interventional clinical studies using patient data
- Includes planning, conducting and reporting secondary analyses
- Does not include details of statistical methods and analyses
- Based on CRDSA expertise and external publications – for example:


DOI: 10.1186/s12874-016-0171-x • Corpus ID: 35794000

EFSPI/PSI working group on data sharing: accessing and working with pharmaceutical clinical trial patient level datasets – a primer for academic researchers

R. Sudlow, J. Branson, T. Friede, D. Morgan, C. Whately-Smith less •

Published in BMC Medical Research... 8 July 2016 • Medicine, Business


Contact | Cochrane.org | Cochrane Community

Cochrane Training

Trusted evidence.
Informed decisions.
Better health.

Search...

Online learning | Learning events | Guides and handbooks | Trainers' Hub | Log in

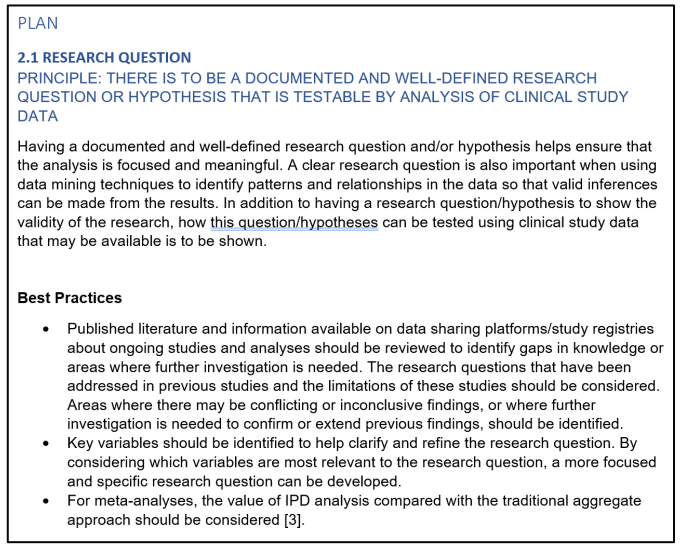
Chapter 26: Individual participant data

Search Handbook

Jayne F Tierney, Lesley A Stewart, Mike Clarke; on behalf of the Cochrane Individual Participant Data Meta-analysis Methods Group

Structure of the Standards

Principles (requirements)



PLAN

2.1 RESEARCH QUESTION

PRINCIPLE: THERE IS TO BE A DOCUMENTED AND WELL-DEFINED RESEARCH QUESTION OR HYPOTHESIS THAT IS TESTABLE BY ANALYSIS OF CLINICAL STUDY DATA

Having a documented and well-defined research question and/or hypothesis helps ensure that the analysis is focused and meaningful. A clear research question is also important when using data mining techniques to identify patterns and relationships in the data so that valid inferences can be made from the results. In addition to having a research question/hypothesis to show the validity of the research, how this question/hypotheses can be tested using clinical study data that may be available is to be shown.

Best Practices

- Published literature and information available on data sharing platforms/study registries about ongoing studies and analyses should be reviewed to identify gaps in knowledge or areas where further investigation is needed. The research questions that have been addressed in previous studies and the limitations of these studies should be considered. Areas where there may be conflicting or inconclusive findings, or where further investigation is needed to confirm or extend previous findings, should be identified.
- Key variables should be identified to help clarify and refine the research question. By considering which variables are most relevant to the research question, a more focused and specific research question can be developed.
- For meta-analyses, the value of IPD analysis compared with the traditional aggregate approach should be considered [3].

The Standards provide principles CRDSA considers to be mandatory. Principles may be supplemented with criteria to be followed to meet the principle

Non-mandatory recommendations are provided as best practices

Structure of the Standards

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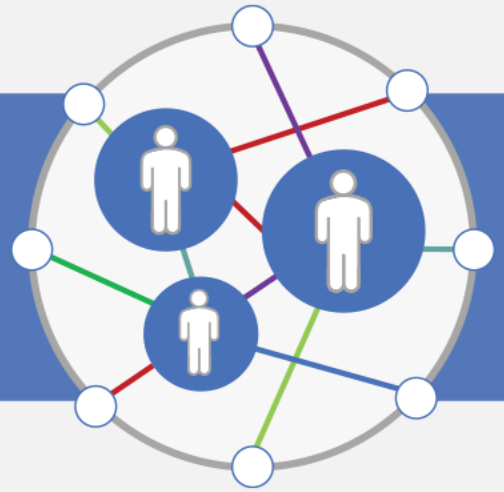
Checklist
(for case-by-case exceptions)

The principles and criteria may not be applicable for every study that is shared or every analysis that is conducted- a checklist is provided where any deviations or exceptions from the principles/criteria for a shared study or analysis can be explained

PLAN

		Yes/No/NA	NA Explanation
RESEARCH QUESTION	Is there a documented and well-defined research question and/or hypothesis that is testable using clinical trial data?		
STUDIES	Have studies that include the required data been objectively identified and assessed using predefined criteria?		
TEAM	Does the team have statistical expertise and experience in clinical trial data analysis as shown by statistical qualifications and previous analyses of clinical study data?		
	Does the team include the expertise and skill sets needed to navigate clinical study documents and fully understand the relationship of study designs to the intended analysis as shown by formal training and/or previous research?		
	Does the team include expertise to manage the types of datasets being accessed and use the relevant software as shown by formal training and/or previous research?		
	Does the team include specific expertise relevant for the analysis (e.g., MedDRA expertise for analysis of safety) as evidenced by formal training and/or previous research?		
SAP	Is there a prespecified statistical analysis plan (SAP) dated before the analysis was conducted?		
	Does the SAP include all of the following? - The questions and hypotheses being addressed - Effect measure of interest (e.g., for inferential studies: odds ratio, risk or rate ratio, risk or rate difference, absolute difference) - The populations and variables to be analyzed, including details of any subjects and data that will be included and excluded		



Content Overview

Contents

Data Sharing Standard

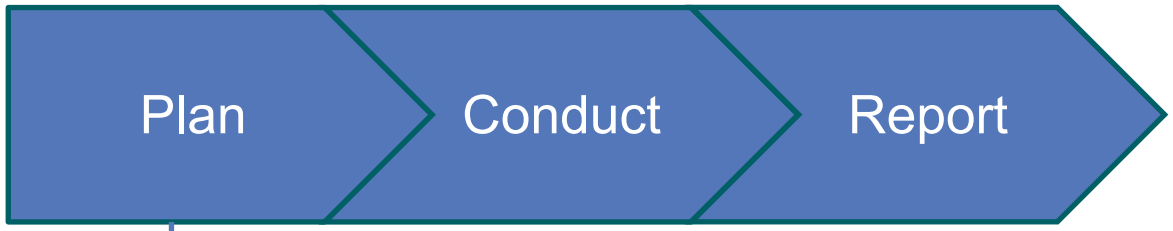
- Datasets to be shared
- Supporting documentation and meta-data to be shared
- Data transformation report
- When supporting documentation is to be shared

Secondary Analysis Standard

- Plan
- Conduct
- Report

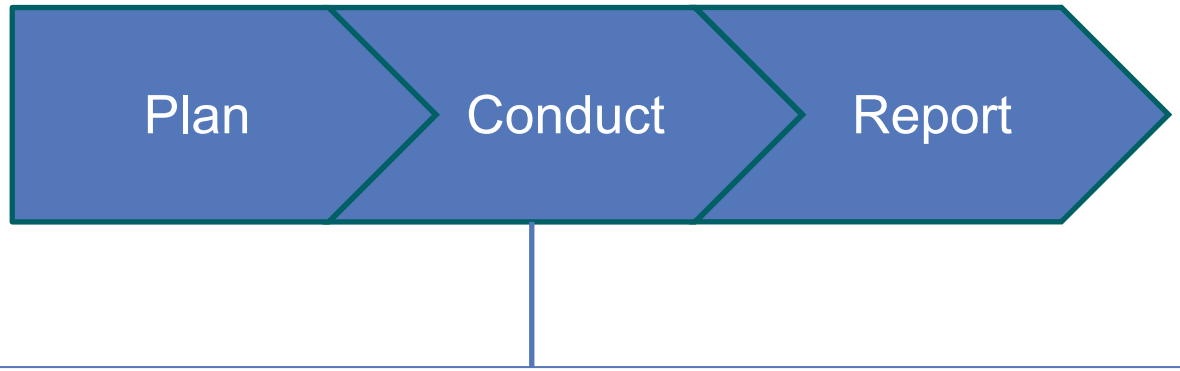
Principles

Plan



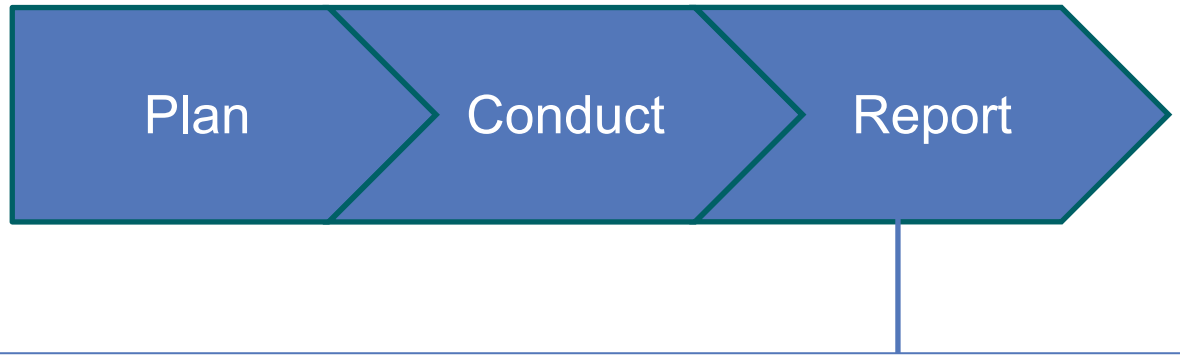
- Define the research question and hypothesis
- Identify the studies needed
- Assemble a team with the experience and expertise required
- Determine the appropriate statistical methods to be used
- Obtain required approvals
- Publicly disclose a summary of the planned analysis

Conduct

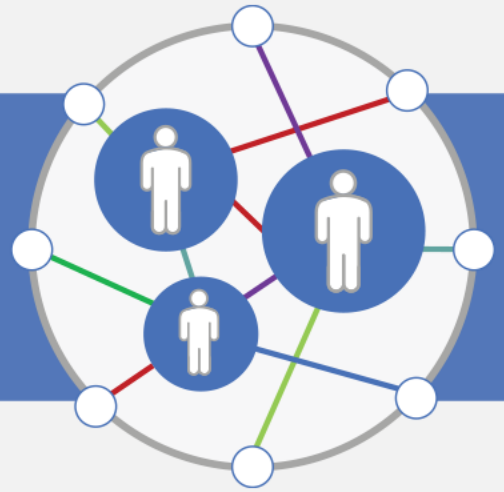


- Ensure that the IT system has controls and processes in place to protect the integrity and security of data
- Prepare to conduct the analysis by extracting data and transforming the data into a suitable format for analysis
- Test the code and reproduce selected analyses from the original study or studies
- Perform the statistical analysis according to the statistical analysis plan; justify and document any changes; and implement relevant quality control measures
- Interpret the results of the analysis, considering the research question and the study design
- Draw objective conclusions based on the findings and study limitations

Report



- Communicate findings through presentations and publications
- Share data, documents, and code used for the analysis for transparency and reproducibility



Notable Principles

Principles - Team

TEAM

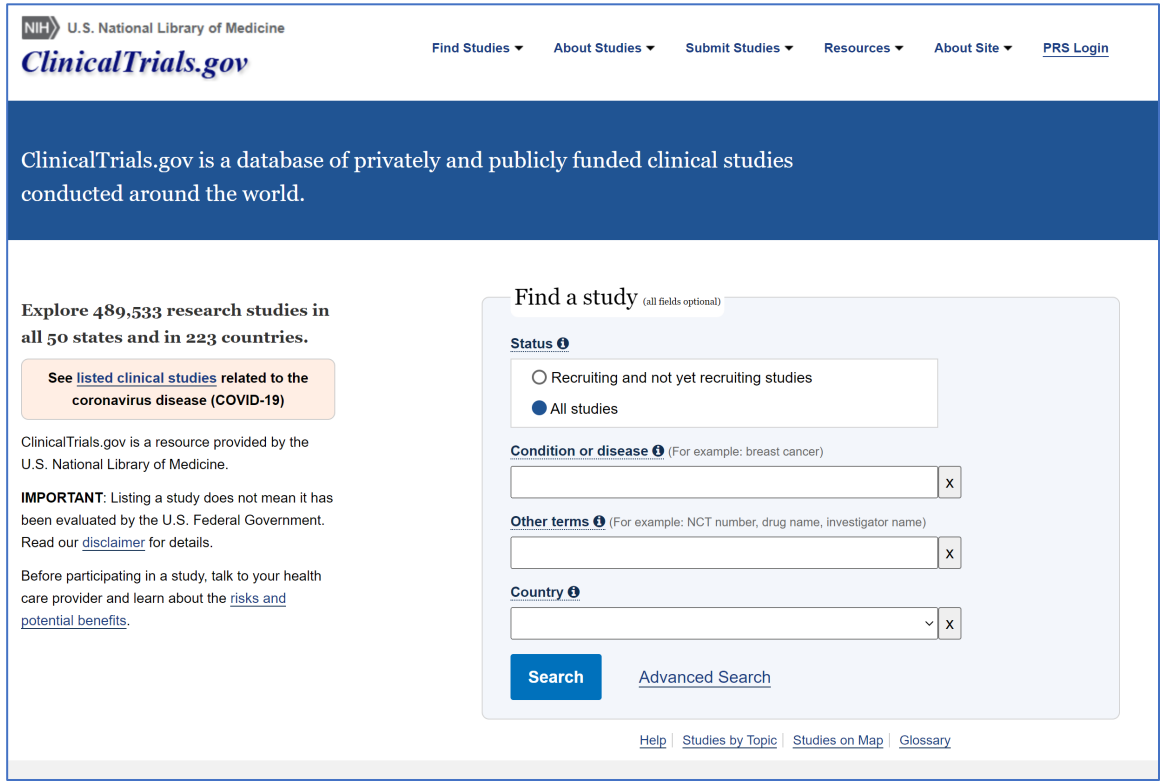
THE RESEARCH TEAM IS TO HAVE THE EXPERIENCE AND EXPERTISE TO CONDUCT THE ANALYSIS

- Statistical expertise and experience in clinical study data analysis
- Expertise and skill sets needed to navigate clinical study documents
- Expertise in managing the types of datasets being accessed and using the relevant software
- Specific expertise relevant for the analysis
  - Safety
  - Disease Area
  - AI

Principles – Study Selection

STUDIES

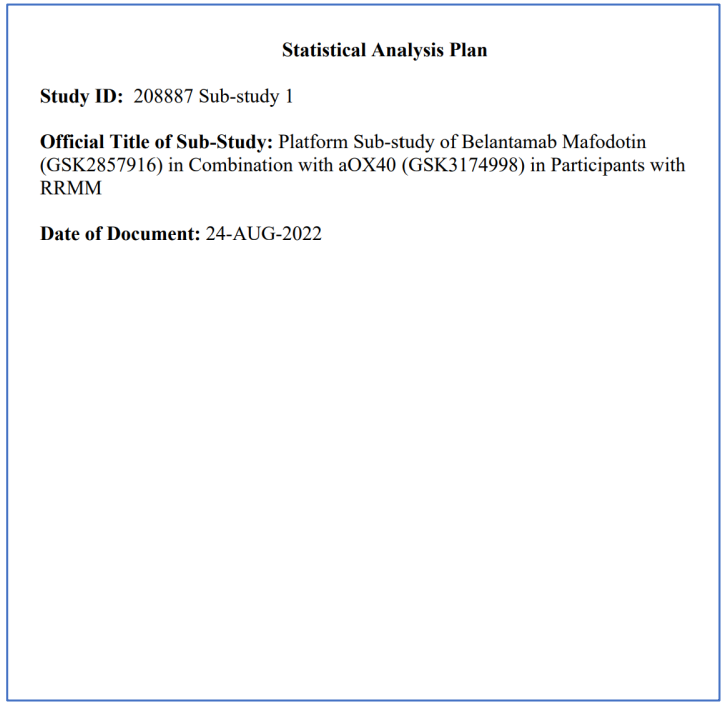
CLINICAL STUDIES THAT INCLUDE THE DATA FOR THE ANALYSIS ARE TO BE OBJECTIVELY IDENTIFIED AND ASSESSED USING PREDEFINED CRITERIA



- Ensures study selection is guided by the research question
- Minimizes bias in study selection
- Ensures selected studies meet the requisite criteria for analysis

Principles – Statistical Analysis Plan

STATISTICAL ANALYSIS PLAN
A PRESPECIFIED STATISTICAL ANALYSIS PLAN (SAP) IS TO BE IN PLACE



Statistical Analysis Plan

Study ID: 208887 Sub-study 1

Official Title of Sub-Study: Platform Sub-study of Belantamab Mafodotin (GSK2857916) in Combination with aOX40 (GSK3174998) in Participants with RRMM

Date of Document: 24-AUG-2022

- The questions and hypotheses
- Effect measure of interest
- The populations and variables to be analyzed
- Statistical analysis methods
- Any planned adjustment for covariates
- Meta-analysis methods, if applicable
- Power to detect a clinically important effect, or the precision of the effect estimate given the sample size available
- Any data transformations to be used, and how any missing data or outliers will be handled
- Any planned sensitivity analyses to explore the robustness of the results
- Any planned investigation of subgroups

Principles - Conduct

DATA MANAGEMENT

PREDETERMINED METHODS FOR DATA MANAGEMENT AND ANY READJUDICATION ARE TO BE FOLLOWED AND ANY DEVIATIONS ARE TO BE DOCUMENTED

Readjudication

- There is to be a documented justification for any analysis involving readjudication of a source study
- Multiple independent adjudicators are to be involved in the readjudication process
- The analyst or reviewers are to be blinded to the treatment group assignments and other relevant information to reduce bias
- MedDRA is to be used for the readjudication of adverse events
- For efficacy outcomes, the same standards as used in the original analysis or other standardized and referenceable criteria are to be used

Principles - Conduct

STUDY AND DATA UNDERSTANDING

TO DEMONSTRATE UNDERSTANDING OF THE STUDIES AND STUDY DATA, SELECTED ANALYSES IN THE ORIGINAL STUDIES ARE TO BE REPRODUCED AND ANY DIFFERENCES ARE TO BE EXPLAINED AND DOCUMENTED

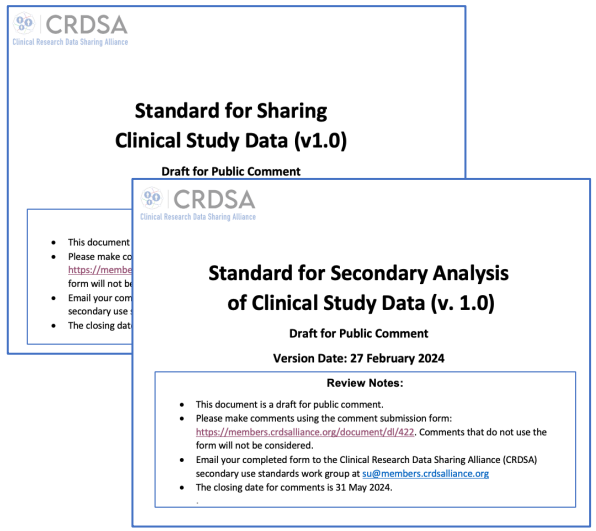
Principles - Report

RESULTS TRANSPARENCY

DATA, DOCUMENTS, AND CODE USED FOR THE ANALYSIS ARE TO BE SHARED OR MADE AVAILABLE ON REQUEST

Adoption

Adoption



The standards can be adopted by data sharing platforms, funders, research institutions, and scientific journals.

When adopting a CRDSA standard, the organization incorporates the principles into their policy (the organization governs compliance with the policy), for example:

"Organization X adopts the CRDSA Standard and requires data contributors/researchers to follow the principles and complete the checklist in the CRDSA Standard"

How to provide comments

How you can provide comments

- The draft standards are available for public comment at: https://crdsalliance.org/resources/#sus
- Please make comments using the comment submission form (linked in the draft documents)

CRDSA Secondary Analysis Standard: Comment Template
Submit to the CRDSA Standards Work Group at: su@members.crdsalliance.org

CRDSA
Clinical Research Data Sharing Alliance

Submitting Organization:

Contact Name/Email:

Comment #	Comment Type (General, Technical, Editorial)	Section #	Page #	Comment and Rationale (required)	Proposed Change
1					
2					
3					
4					
5					
6					

- Email your completed form to the CRDSA secondary use standards work group at su@members.crdsalliance.org
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Q&A

CRDSA

Clinical Research Data Sharing Alliance

Thank you!

For additional resources and information, please visit:

https://crdsalliance.org/resources