MODERNIZING RESEARCH AND EVIDENCE (MoRE) CONSENSUS DEFINITIONS: AN FDA-NIH COLLABORATION

Prepared by the FDA and NIH

June 2025

Introduction to the FDA-NIH MoRE Consensus Definitions:

The U.S. Food and Drug Administration (FDA) and the National Institutes of Health (NIH), as Federal Agencies with roles in the clinical research enterprise, share a mutual interest in facilitating efficient, well-designed clinical studies of drugs, devices, and biological products. Because clinical research plays a crucial role in advancing science and supporting the development of new medical products, effective collaboration among the clinical research community is key.

As novel approaches in clinical research have expanded, so has the terminology used to describe these approaches. However, shared understanding of terms has not always kept pace. Challenges to understanding the intended meaning and impact of terms can arise from varied use among the research community. Recognizing the importance of clear communication and scientific understanding, the FDA and NIH worked collaboratively, with input from the public to develop consensus definitions for commonly used terminology.

This document is intended to facilitate communication within the clinical research community by helping establish a common vocabulary to more uniformly characterize clinical research. This includes innovative trial designs and studies using real-world data, that support scientific, clinical, and/or regulatory decision-making. By referencing this consensus terminology, the research community may be better situated to evaluate potential strengths and limitations of individual studies, and to convey clinical research findings in a meaningful way to funders, reviewers, and the public.

Format of the list of Consensus Definitions:

Terms are grouped into two categories:

1. FDA-NIH Modernizing Research and Evidence Glossary Working Group defined terms: These terms describe design, methods, analysis, and interpretation of innovative clinical study designs. Where an existing definition is used or adapted, the source(s) is listed.
2. Terms for Reference: * Denotes 20 terms with an existing definition. These terms are included to add context but were not defined by the FDA-NIH Working Group.

This list of consensus definitions does not constitute FDA or NIH policy, guidance, recommendations, or requirements.

For information about the development of these consensus definitions please see the Modernizing Research and Evidence (MoRE) Consensus Definitions: An FDA-NIH Collaboration published in JAMA Network Open.

Modernizing Research and Evidence (MoRE) Glossary

A

***Adaptive Design**
A clinical trial design that allows for prospectively planned modifications to one or more aspects of the design based on accumulating data from subjects in the trial.
Source: U.S. Food and Drug Administration Adaptive Design Clinical Trials for Drugs and Biologics Guidance for Industry. Published December 2019.

Administrative Claims Data
The information obtained from health care claims submitted to payers for reimbursement of treatments and other interventions. Claims data use standardized medical coding systems (nomenclatures), such as the World Health Organization International Classification of Diseases to identify diagnoses, National Drug Code to identify drugs, and Current Procedural Terminology to identify procedures.

B

***Basket Trial**
Trial designed to evaluate a medical product for different diseases, conditions, or disease subtypes.
Source: U.S. Food and Drug Administration. Master Protocols for Drug and Biological Product Development. Draft Guidance for Industry. Published December 2023.

C

Causal Effect
A difference in outcome between groups that is attributable to the difference in the exposure of interest and not to any other differences between comparator groups. For example, a difference in outcome that would be expected in individuals subjected to an exposure of interest compared to the expected outcome if those same individuals were subjected to a specified alternative exposure (including no exposure).

Source: Adapted from Musci RJ, Stuart E. Ensuring causal, not casual, inference. *Prev Sci*. 2019;20(3):452-456. doi:10.1007/s11121-018-0971-9.

Causal Inference
The process of evaluation, estimation, and attribution of an effect.

Cluster Randomized Trial (or Group Randomized Trial)
A trial in which randomization is at a group level (for instance, by community, health care facility or medical provider) rather than an individual level.

Source: Adapted from the U.S. Department of Health and Human Services, Secretary's Advisory Committee on Human Research Protections. Attachment C: recommendations on regulatory issues in cluster studies. Accessed October 27, 2024. https://www.hhs.gov/ohrp/sachrp-committee/recommendations/2014-july-3-letter-attachment-c/index.html.

Collider

A variable on the causal pathway that is a common effect of both the exposure and outcome. Adjusting for a collider can result in distorted estimation of the causal effect between the exposure and outcome.

Source: Adapted from VanderWeele TJ. Explanation in Causal Inference: Methods for Mediation and Interaction. Oxford University Press; 2015:1-706. Cited in https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9204564/#:~:text=Mediator-,A%20mediator%20is%20an%20intermediate%20variable%20between%20an%20exposure%20and,is%20independent%20of%20this%20pathway.

Common Data Element
A standardized, precisely defined variable or question that is paired with a set of specific allowable values or responses, that are used systematically across different sites, studies, or clinical trials to ensure consistent data collection and/or analysis.

Source: Adapted from the National Institutes of Health. Common Data Elements repository. Accessed October 27, 2024. https://cde.nlm.nih.gov/home

Common Data Model (CDM)
Comprehensive framework, including definitions, specifications, and operational rules, that allows for data to be presented and used in a common manner to enable interoperability.

Source: Adapted from Daniel G, Silcox C, Bryan J, McClellan M, Romine M, Frank K. Characterizing RWD quality and relevancy for regulatory purposes. Accessed October 27, 2024. https://healthpolicy.duke.edu/sites/default/files/2020-03/characterizing_rwd.pdf.

Completeness of Capture
The extent to which a data source includes a complete representation of the exposures, outcomes, and covariates needed for the proposed analysis. Incomplete capture may be due to variables that were not recorded or variables that include missing values.

Computable Phenotype
A clinical condition or characteristic that can be ascertained using a computerized query to data sources (e.g., electronic health record data, clinical data repository, or administrative claims database) using a defined set of data elements and logical expressions. Computable phenotype definitions provide the specifications for identifying populations likely to have the conditions or characteristics of interest.

Source: Adapted from U.S. Food and Drug Administration. Real-world data: assessing electronic health records and medical claims data to support regulatory decision-making for drug and biological products: guidance for industry. Updated July 2024. Accessed October 27, 2024. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/real-world-data-assessing-electronic-health-records-and-medical-claims-data-support-regulatory.

***Conceptual Definition**
Explains a study construct (e.g., exposure, outcomes, covariates) or feature in general or qualitative terms.
Source: International Conference on Harmonisation. M14 General Principles on Plan, Design, and Analysis of Pharmacoepidemiologic Studies that Utilize Real-World Data for Safety Assessment of Medicines. Published July 2024.

Confounding
Systematic error in estimation of the measure of the effect of a medical product on an outcome due to another factor that is associated with both the exposure and the outcome and not along the causal pathway between exposure and outcome.

Source: Adapted from Porta M, ed. *A Dictionary of Epidemiology*. Oxford University Press; 2014. doi:10.1093/acref/9780199976720.001.0001.

Continuity of Coverage
The period of time over which an individual is enrolled or included in a health care system (e.g., provider, pharmacy, insurer, or other) and for which data on provided or reimbursed health care services and treatments are captured in that system.

Source: Adapted from U.S. Food and Drug Administration. Real-world data: assessing electronic health records and medical claims data to support regulatory decision-making for drug and biological products: guidance for industry. Updated July 2024. Accessed October 27, 2024. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/real-world-data-assessing-electronic-health-records-and-medical-claims-data-support-regulatory.

D

Data Curation
Processing of source data (unstructured and/or structured data) into a dataset suitable for analyses. The cu ration process involves the application of standards for the exchange, integration, sharing, and retrieval of source data, often from various sources. For example, the application of standard medical diagnostic codes to adverse events, disease staging, the progression of disease, and other medical and clinical concepts.

Source: Adapted from U.S. Food and Drug Administration. CVM GFI: #266: Use of real-world data and real-world evidence to support effectiveness of new animal drugs. Updated October 2021. Accessed October 27, 2024. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/cvm-gfi-266-use-real-world-data-and-real-world-evidence-support-effectiveness-new-animal-drugs.

Data Harmonization
The process of combining data from different sources and reorganizing it according to a single unified schema so that data are compatible, comparable, and analyzable. Data are combined by either identifying equivalent data elements between the sources or by applying specific transformations between the elements to derive a common data element.

Source: Adapted from the National Institute of Environmental Health Sciences. Common language glossary from the Environmental Health Language Collaborative. Accessed October 27, 2024. https://www.niehs.nih.gov/research/programs/ehlc/resources/glossary.

Data Imputation
A process using statistical techniques to estimate missing data values, facilitating subsequent analyses.

Source: Adapted from Food and Agricultural Organization of the United Nations. Statistical standard series imputation version 2.0. Accessed October 27, 2024. https://www.fao.org/3/cb9339en/cb9339en.pdf.

Data Lake
A controlled, centralized environment that stores structured and unstructured data in its native form and provides infrastructure for organizing large volumes of diverse data from multiple sources.

Source: Adapted from Amazon Web Services. *Cloud computing concepts hub*. Accessed May 19, 2025. https://aws.amazon.com/what-is/?faq-hub-cards.sort-by=item.additionalFields.sortDate&faq-hub-cards.sort-order=desc&awsf.tech-category=*all.

***Data Relevance**
Includes consideration of availability, timeliness, and generalizability of the real world data.
Source: U.S. Food and Drug Administration. Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices. Draft Guidance for Industry and Food and Drug Administration Staff. December 2023.

Includes the availability of data for key study variables (exposures, outcomes, covariates) and sufficient numbers of representative patients for the study.
Source: U.S. Food and Drug Administration. Real-World Data: Assessing Electronic Health Records and Medical Claims Data To Support Regulatory Decision-Making for Drug and Biological Products. Draft Guidance for Industry. July 2024.

***Data Reliability**
Includes consideration of accrual, quality, and integrity of real world data.
Source: U.S. Food and Drug Administration. Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices. Draft Guidance for Industry and Food and Drug Administration Staff. December 2023.

Includes accuracy, completeness, and traceability.
Source: U.S. Food and Drug Administration. Real-World Data: Assessing Electronic Health Records and Medical Claims Data To Support Regulatory Decision-Making for Drug and Biological Products. Draft Guidance for Industry. July 2024.

***Data Standard**
Defined rules, conventions, guidelines, characteristics, methods, formats, and terminologies that provide structure and consistency for exchange and utilization of data.
Source: Clinical Data Interchange Standards Consortium. Glossary v. 19.0. September 2024.

Data Transformation
The process of converting data from one format or structure into another format or structure. It is a process of data extraction and conversion or normalization in construction of analytic datasets.

Source: Adapted from U.S. Food and Drug Administration. CVM GFI: #266: Use of real-world data and real-world evidence to support effectiveness of new animal drugs. Updated October 2021. Accessed October 27, 2024. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/cvm-gfi-266-use-real-world-data-and-real-world-evidence-support-effectiveness-new-animal-drugs.

Data Warehouse
A controlled, centralized environment that stores structured data (can be from multiple sources) in a processed form for analysis and provide infrastructure for data access by multiple applications.

Source: Adapted from U.S. Food and Drug Administration. Real-world data: assessing electronic health records and medical claims data to support regulatory decision-making for drug and biological products: guidance for industry. Updated September 2021. Accessed October 27, 2024. https://www.regulations.gov/document/FDA-2020-D-2307-0002.

***Decentralized Clinical Trial**
A clinical trial that includes decentralized elements where trial-related activities occur at locations other than traditional clinical trial sites.
Source: U.S. Food and Drug Administration. Conducting Clinical Trials with Decentralized Elements. Guidance for Industry, Investigators, and Other Interested Parties. September 2024.

Distributed Data Network
A network in which data from multiple sites are generally transformed into a single common data model with the ability to execute a query without substantial modifications on multiple datasets.

Source: Adapted from U.S. Food and Drug Administration. Real-world data: assessing electronic health records and medical claims data to support regulatory decision-making for drug and biological products: guidance for industry. Updated July 2024. Accessed October 27, 2024. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/real-world-data-assessing-electronic-health-records-and-medical-claims-data-support-regulatory.

E

Electronic Health Record
An individual patient record contained within an electronic system. A typical individual record may include the patient's medical history, allergies, diagnoses, medications, immunizations, procedures, images and imaging reports, and laboratory and other test results.

Source: Adapted from U.S. Food and Drug Administration. Use of electronic health record data in clinical investigations: guidance for industry. Updated July 2018. Accessed October 27, 2024. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-electronic-health-record-data-clinical-investigations-guidance-industry

***Estimand (in the context of healthcare interventions)**
A precise description of the treatment effect reflecting the clinical question posed by the trial objective. It summarizes at a population-level what the outcomes would be in the same patients under different treatment conditions being compared.
Source: International Conference on Harmonisation. E9(R1) Statistical Principles for Clinical Trials: Addendum: Estimands and Sensitivity Analysis in Clinical Trials. Guidance for Industry. May 2021.

***Externally Controlled Trial**
In an externally controlled trial, outcomes in participants receiving the test treatment according to a protocol are compared to outcomes in a group of people external to the trial who had not received the same treatment. The external control arm can be a group of people, treated or untreated, from an earlier time (historical control), or it can be a group of people, treated or untreated, during the same time period (concurrent control) but in another setting.
Source: U.S. Food and Drug Administration. Considerations for the Design and Conduct of Externally Controlled Trials for Drug and Biological Products. Draft Guidance for Industry. February 2023.

F

***Fit-for-use (may also be referred to as fit-for-purpose)**
See **Data Relevance** and **Data Reliability**

G

***Generalizability**
(1) Representative of the population in the RWD source eligible for use of the device* within the specified indication and (2) generalizable to the target population with the condition of interest.

*may be applied to medical products
Source: U.S. Food and Drug Administration. Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices. Draft Guidance for Industry and Food and Drug Administration Staff. December 2023.

I

Immortal Time
A span of time in the observation or follow-up period of a cohort during which the outcome under study could not have occurred, due to the cohort design and/or exposure definition.

Source: Adapted from Suissa S. Immortal time bias in pharmaco-epidemiology. *Am J Epidemiol*. 2008;167(4):492-499. doi:10.1093/aje/kwm324.

***Individually Randomized Group Treatment (IRGT) Trial**
In an individually randomized group-treatment (IRGT) trial, also called a partially clustered or partially nested design, individuals are randomized to study conditions but receive at least some of their intervention with other participants or through an interventionist or facilitator shared with other participants.
Source: National Institutes of Health Research Methods Resources. Individually Randomized Group-Treatment Trials | Research Methods Resources. Accessed September 19, 2024.

Information Bias
Systematic error in estimation of an association or other parameter of interest arising from measurement error in the data (e.g., exposure, outcome, and covariates). Measurement error may sometimes be referred to as classification error or misclassification.

Source: Adapted from Daniel G, Silcox C, Bryan J, McClellan M, Romine M, Frank K. Characterizing RWD quality and relevancy for regulatory purposes. Accessed October 27, 2024. https://healthpolicy.duke.edu/sites/default/files/2020-03/characterizing_rwd.pdf and Rothman KJ, Greenland S, Lash TL. *Modern Epidemiology*. Wolters Kluwer and Lippincott Williams & Wilkins; 2008.

Interventional Study
A study involving participants (e.g., healthy individuals or individuals with a disease or condition of interest) whose exposure or interaction with a medical product is assigned according to a study protocol to evaluate the effect on health outcomes or product performance.

Source: Adapted from U.S. Food and Drug Administration. Considerations for the use of real-world data and real-world evidence to support regulatory decision-making for drug and biological products: guidance for industry. Updated August 2023. Accessed October 27, 2024. https://www.fda.gov/media/171667/download.

M

***Master Protocol**
A protocol designed with multiple sub-studies, which may have different objectives and involve coordinated efforts to evaluate one or more medical products in one or more diseases or conditions within the overall study structure.
Source: U.S. Food and Drug Administration. Master Protocols for Drug and Biological Product Development. Draft Guidance for Industry. Published December 2023.

Mediator (also referred to as Modifier)
An intermediate variable between an exposure and the outcome that is influenced by the exposure on the causal pathway to the outcome.

Source: Adapted from VanderWeele TJ. Explanation in Causal Inference: Methods for Mediation and Interaction. Oxford University Press; 2015:1-706. Cited in https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9204564/#:~:text=Mediator-,A%20mediator%20is%20an%20intermediate%20variable%20between%20an%20exposure%20and,is%20independent%20of%20this%20pathway.

Moderator
A variable that alters the direction or magnitude of the effect of an exposure on an outcome.

Source: Lee H, Cashin AG, Lamb SE, et al; AGReMA group. A Guideline for Reporting Mediation Analyses of Randomized Trials and Observational Studies: The AGREMA Statement. *JAMA*. 2021;326(11):1045-1056. doi:10.1001/jama.2021.14075.

Missing Data
Data that would have been used in the study analysis but were not observed, collected, or accessible. These refer to information that was intended to be collected but is absent and information that was not intended to be collected and is therefore absent.

Source: Adapted from U.S. Food and Drug Administration. Real-world data: assessing electronic health records and medical claims data to support regulatory decision-making for drug and biological products: guidance for industry. Updated July 2024. Accessed October 27, 2024. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/real-world-data-assessing-electronic-health-records-and-medical-claims-data-support-regulatory.

Note: In a clinical trial, these are data that would be meaningful for the analysis of a given estimand but were not collected. They should be distinguished from data that do not exist or data that are not considered meaningful because of an intercurrent event. In real-world data sources (e.g., electronic health records or claims), there may be special considerations; for example, such data are generally not collected for primary research purposes and therefore may not have systematic data capture to answer a research question.

Source: U.S. Food and Drug Administration. E9(R1) statistical principles for clinical trials: addendum: estimands and sensitivity analysis in clinical trials: guidance for industry. Updated May 2021. Accessed May 13, 2025. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/e9r1-statistical-principles-clinical-trials-addendum-estimands-and-sensitivity-analysis-clinical.

N

N of 1 Trial
A clinical trial evaluating an intervention or multiple interventions in a single participant according to a protocol in which there is either switching between intervention(s) and control or a planned comparison between an intervention and a natural history.

Non-interventional (observational) study
A type of study in which exposure or interaction with the medical product generally occurs in routine clinical care and individuals are not assigned according to a study protocol.

Source: Adapted from U.S. Food and Drug Administration. Considerations for the use of real-world data and real-world evidence to support regulatory decision-making for drug and biological products: guidance for industry. Updated August 2023. Accessed October 27, 2024. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/considerations-use-real-world-data-and-real-world-evidence-support-regulatory-decision-making-drug and U.S. Food and Drug Administration. Use of real-world evidence to support regulatory decision-making for medical devices. Updated August 2017. Accessed May 13, 2025. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-real-world-evidence-support-regulatory-decision-making-medical-devices.

O

***Observational Study, Prospective**
A study in which the population of interest is identified at the start of the study, and exposure/treatment and outcome data are collected from that point forward. The start of the study is defined as the time the research protocol for the specific study question was initiated.
Source: U.S. Food and Drug Administration. Framework for FDA's Real-World Evidence Program. December 2018.

Observational Study, Retrospective
A study that identifies the population and determines the exposure or treatment from data collected before the initiation of the study. The variables and outcomes of interest are determined at the time the study is designed.

Source: Adapted from U.S. Food and Drug Administration. Use of real-world evidence to support regulatory decision-making for medical devices. Updated August 2017. Accessed May 13, 2025. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-real-world-evidence-support-regulatory-decision-making-medical-devices and U.S. Food and Drug Administration. Framework for FDA's real-world evidence program. Updated December 2018. Accessed May 13, 2025. https://www.fda.gov/media/120060/download.

***Operational Definition**
The data-specific operation or procedure a researcher followed to measure constructs in a particular study.
Source: International Conference on Harmonisation. M14 General Principles on Plan, Design, and Analysis of Pharmacoepidemiologic Studies that Utilize Real-World Data for Safety Assessment of Medicines. Published July 2024.

P

***Patient Generated Health Data**

Health-related data created, recorded, or gathered by or from patients, family members, or other caregivers to help address a health concern.

Source: Definition adapted from U.S. Food and Drug Administration. Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices. Draft Guidance for Industry and Food and Drug Administration Staff. December 2023 and Assistant Secretary for Technology Policy. Patient-Generated Health Data. Accessed September 19, 2024.

***Platform Trial**

Trial designed to evaluate multiple medical products for a disease or condition in an ongoing manner, with medical products entering or leaving the platform.

Source: U.S. Food and Drug Administration. Master Protocols for Drug and Biological Product Development. Draft Guidance for Industry. Published December 2023.

Pragmatic Clinical Trial

A clinical trial designed to efficiently inform decision-making on the benefits, burdens, and risks of health interventions in representative populations by including pragmatic elements that (1) are partially or fully integrated into routine clinical practice and/or (2) streamline trial design and conduct.

Source: Adapted from Califf RM, Sugarman J. Exploring the ethical and regulatory issues in pragmatic clinical trials. *Clin Trials*. 2015;12(5):436-441. doi:10.1177/1740774515598334.

Pragmatic Elements

Design features that can be integrated into a clinical trial, including but not limited to, ~l of the following elements: broad eligibility criteria, simplified recruitment and follow-up, flexibility in delivery of the intervention (e.g., community settings), flexibility in assessment frequency, streamlined data collection, and measurement of outcomes relevant to the population.

Source: Informed by Suissa S, Dell'Aniello S. Time-related biases in pharmacoepidemiology. *Pharmacoepidemiol Drug Saf*. 2020;29(9):1101-1110. doi:10.1002/pds.5083.

Propensity Score

The estimated conditional probability of assignment to a particular treatment given a set (e.g., vector) of observed covariates.

Source: Adapted from Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. *Biometrika*. 1983;70(1):41-55. doi:10.1093/biomet/70.1.41.

R

***Real-World Data**

Data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources.
Source: U.S. Food and Drug Administration. Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices. Draft Guidance for Industry and Food and Drug Administration Staff. December 2023.
U.S. Food and Drug Administration. Framework for FDA's Real-World Evidence Program. December 2018.
U.S. Food and Drug Administration. Considerations for the Use of Real-World Data and Real-World Evidence To Support Regulatory Decision-Making for Drug and Biological Products. Guidance for Industry. August 2023.

***Real-World Evidence**

The clinical evidence about the usage and potential benefits or risks of a medical product derived from analysis of real-world data.
Source: U.S. Food and Drug Administration. Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices. Draft Guidance for Industry and Food and Drug Administration Staff. December 2023.
U.S. Food and Drug Administration. Framework for FDA's Real-World Evidence Program. December 2018.
U.S. Food and Drug Administration. Considerations for the Use of Real-World Data and Real-World Evidence To Support Regulatory Decision-Making for Drug and Biological Products. Guidance for Industry. August 2023.

Registry

An organized system that collects clinical and other data in a standardized format for a population defined by a particular disease, condition, or exposure.

Source: Adapted from U.S. Food and Drug Administration. Use of real-world evidence to support regulatory decision-making for medical devices. Updated August 2017. Accessed May 13, 2025. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-real-world-evidence-support-regulatory-decision-making-medical-devices and U.S. Food and Drug Administration. Real-world data: assessing registries to support regulatory decision-making for drug and biological products. Updated December 2023. Accessed May 13, 2025. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/real-world-data-assessing-registries-support-regulatory-decision-making-drug-and-biological-products.

Residual Confounding

Confounding that remains after adjusting for measured confounders.

Source: Adapted from Porta M, ed. *A Dictionary of Epidemiology*. Oxford University Press; 2014. doi:10.1093/acref/9780199976720.001.0001.

S

Selection Bias
Systematic error in estimation of an association or other parameter that results from factors that influence study participation or eligibility for analyses.

Source: Adapted from Rothman KJ, Greenland S, Lash TL. *Modern Epidemiology*. Wolters Kluwer and Lippincott Williams & Wilkins; 2008.

Sequential, Multiple Assignment, Randomized Trial (SMART)
A trial designed to evaluate a collection of interventions guided by a sequence of decision rules that specifies when and how the type and/or intensity of an intervention should be modified, depending on the patient's past or present characteristics and/or ongoing clinical state or performance (e.g., response, adherence), to optimize clinically important outcomes. In such a trial, patients move along multiple stages and are randomly assigned to one of several suitable intervention options at each stage.

Source: Adapted from U.S. Food and Drug Administration. Interacting with the FDA on complex innovative trial designs for drugs and biological products: guidance for industry. Updated December 2020. Accessed May 13, 2025. https://www.fda.gov/media/130897/download.

Stepped Wedge Cluster Randomized Trial (or Stepped Wedge Group Randomized Trial)
A trial in which groups or clusters are randomized to sequences that direct them to switch from a control to the intervention at predetermined time points in a sequential, staggered fashion until all groups or clusters receive the intervention.

Source: Adapted from National Institutes of Health. Research methods resources. Updated 2024. Accessed May 13, 2025. https://researchmethodsresources.nih.gov/.

Synthetic Data
Data that have been created artificially (e.g., through statistical modeling, computer simulation) so that new values and/or data elements are generated. Generally, synthetic data are intended to represent the structure, properties, and relationships seen in actual patient data, except that they do not contain any real or specific information about individuals.

T

Target Trial Emulation
A framework for designing and analyzing an observational study based on conceptualizing a target randomized trial to answer a scientific question and designing the observational study to mimic the trial estimand(s) (including specification of population eligibility criteria, treatment strategies and assignment procedures, outcomes, handling of intercurrent events, and follow-up period).

Source: Adapted from Hernán MA, Wang W, Leaf DE. Target trial emulation: a framework for causal inference from observational data. *JAMA*. 2022;328(24):2446-2447. doi:10.1001/jama.2022.21383.

Time-Related Bias
Systematic error in estimation of an association or other parameter of interest due to misclassification or exclusion of person-time attributed to the treatment, intervention, or exposure. Examples include protopathic bias, latency time bias, immortal time bias, time-window bias, depletion of susceptibles, immeasurable time bias, and other such biases.

Source: Adapted from Suissa S, Dell'Aniello S. Time-related biases in pharmacoepidemiology. *Pharmacoepidemiol Drug Saf*. 2020;29(9):1101-1110. doi:10.1002/pds.5083.

***Traceability**
Permits an understanding of the relationships between the analysis results (tables, listings and figures in the study report), analysis datasets, tabulation datasets, and source data.
Source*:* U.S. Food and Drug Administration. Study Data Technical Conformance Guide. Technical Specifications Document. Incorporated by reference into U.S. Food and Drug Administration. Guidance. Providing Regulatory Submissions in Electronic Format Standardized Study Data. March 2025.

U

Umbrella Trial
Trial designed to evaluate multiple medical products in separate substudies concurrently for a single disease or condition. An umbrella trial generally uses a master protocol.

Source: Adapted from U.S. Food and Drug Administration. Guidance document: master protocols for drug and biological product development. Updated December 2023. Accessed May 13, 2025. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/master-protocols-drug-and-biological-product-development.