A

They lack glamor, they strain our resources and patience, and they protract the moment of truth to excruciating limits

Donald Fredrickson on clinical trials (1986)

a posteriori *adj* - Related to or derived by reasoning based on observed facts or data; inductive, empirical. **rt: a priori**

a posteriori treatment comparison *n* - post hoc treatment comparison

a priori *adj* - Relating to or derived by reasoning from presumptions or self-evident propositions; deductive. **rt: a posteriori**

a priori probability *n* - 1. A probability based on theory or belief. 2. A probability deduced or derived prior to the start of a study.

a priori treatment comparison *n* - [trials] A treatment comparison specified when the trial was designed. **ant: a posteriori treatment comparison, post hoc treatment comparison**

Abbreviated New Drug Application (ANDA) *n* - A New Drug Application submitted by the manufacturer or marketing agent of a proposed generic drug to the Food and Drug Administration for licensure; abbreviated because supporting data generally limited to those required to demonstrate bioequivalence of the proposed generic drug to its licensed counterpart proprietary drug. **rt: new drug, Investigational New Drug Application, Pre-Market Approval Application**

absolute risk reduction *n* - 1. [epidemiology] The amount by which risk of a disease is reduced by elimination of an exposure. 2. [trials] The fraction of people in the control-assigned group minus the fraction in the test-assigned group experiencing a specified bad outcome. **rt: relative risk reduction**

academic trial *n* - A trial designed and carried out by investigators located largely in academic institutions; such a trial involving use of existing therapeutic agents, funded by a governmental agency or nonproprietary firm or foundation, and done to determine or refine limits of use or to test utility in ameliorating or preventing disease or some adverse health condition. **rt: industry trial** *Usage note*: The label is often used in contradistinction to ''industry trials''. The distinction is unfortunate to the extent that it serves to imply the existence of different standards for the two classes of trials. The two kinds of trials differ in purpose and sponsorship, but the basic rules for design and conduct are the same. The label is also unfortunate to the extent that it serves to imply that ''academic trials'' are ivory tower abstractions not relevant to real world needs or uses.

acceptance region *n* - The set of values for a test statistic which leads to acceptance of the null hypothesis; regions defined by a single critical value for one-tailed tests and by an upper and lower critical value for two-tailed tests. **ant: rejection region**

accidental bias *n* - Bias due to chance, e.g., bias in the estimated treatment effect in a trial due to imbalance in the distribution of a baseline covariate.[71]

accuracy *n* - 1. Free of error or mistake; correctness. 2. Conformity to a truth, standard, or model; exactness. 3. The tendency of an estimator to be close to the true underlying value. **rt: precision, veracity**

achieved sample size *n* - The observed sample size at the completion of a study. **rt: expected sample size, observed sample size**

acknowledgment *n* - 1. An expression of appreciation or thanks. 2. A written expression of such appreciation or thanks, e.g., as appearing in a published manuscript. **rt: credit**

acronym *n* - A pronounceable word formed from the letters of words of a compound term or phrase, e.g., GRASE (generally recognized as safe and effective) or SOCA (Studies of Ocular Complications of AIDS). More broadly, such a formation even if not pronounceable, e.g., CDP (Coronary Drug Project).

active consent *n* - A consent process producing a documented consent. **ant: implied consent, passive consent**

active control treatment *n* - A negative or positive control treatment; a treatment capable of producing a treatment effect. **ant: inactive control treatment rt: negative control treatment, positive control treatment**

active followup *n* - Followup done by direct contact of persons of interest or via such contact with members of persons' family or persons' guardian; contact may be by letter, telephone, or face-to-face by home visits or clinic visits. **rt: passive followup**

active harm *n* - [trials] Harm of a study subject as a direct consequence of something done by study personnel. **ant: passive harm**

active substance *n* - 1. A substance that has biological activity. 2. In trials, a substance capable of producing a treatment effect in excess of a placebo. **ant: inactive substance**

active treatment *n* - A treatment capable of producing a treatment effect in excess of a placebo treatment. **ant: inactive treatment**

activities of daily living (AoDL, AODL, ADL) *n* - 1. The everyday activities of a normal person. 2. The activities necessary for independent living such as being able to sit, stand, walk, and talk and being able to dress and feed oneself. 3. A scale, such as devised by Katz et al.,[126] for assessing degree of disability by scoring responses to questions concerning one's ability to perform self-care tasks and functions.

ad hoc *adj* - Concerned with a specific end or purpose; formed or used for a specific purpose.

ad hoc meta-analysis *n* - A meta-analysis using data from two or more like studies selected post hoc. **ant: designed meta-analysis**

ad hoc subgroup *n* - A subgroup (defn 2) identified by data analysis. **ant: specified subgroup**

ad hoc subgroup comparison *n* - A comparison based on an ad hoc subgroup. **ant: designed subgroup comparison**

adaptive study design *n* - [trials] A study design constructed to accommodate change, e.g., a trial in which treatment assignment ratios change as a function of observed outcomes or as a function of baseline characteristics of people enrolled [Chow and Chang, 2008].[42] **ant: fixed study design** *Usage note*: Not to be confused with changes in trials with fixed study designs during conduct.

adaptive treatment assignment *n* - Any method of treatment assignment in which the treatment assignment ratio changes as a function of previous assignments, baseline data, or observed outcomes [Simon, 1977].[233] Types include: baseline adaptive treatment assignment, biased coin treatment assignment, minimum likelihood treatment assignment, minimization, number adaptive treatment assignment, outcome adaptive treatment assignment, play-the-winner treatment assignment, and urn model treatment assignment. **ant: fixed treatment assignment**

adequate and well-controlled *adj* - Vernacular of the Food and Drug Administration used to characterize trials considered suitable

for support of a New Drug Application; generally taken to imply designs involving a concurrently enrolled control group, though there may be circumstances in which historical controls suffice.

adequate and well-controlled trial *n* - In FDA parlance, as contained in CFR Title 21, Vol 5; revised 1 April 2011; http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=314.126; a trial having the following characteristics: (1) clear statement of objective; (2) design permitting valid comparison with a control (acceptable controls include placebo concurrent control, dose-comparison concurrent control, no treatment concurrent control, active treatment concurrent control, and historical control); (3) method of selection of subjects providing assurance they have the disease or condition of interest; (4) method of assignment of persons to treatment that minimizes risk of treatment-related assignment bias and designed to ensure baseline comparability of the treatment groups; (5) measures to minimize treatment-related bias on the part of study subjects, observers, and analysts; (6) methods of assessment of responses of study subjects well-defined and reliable; (7) analysis of results adequate to assess the effect of treatment. Note: The CFR refers to adequate and well-controlled studies but the characteristics are for trials.

adherence *n* - The act or quality of adhering to some scheme, procedure, or protocol. *Usage note*: Adherence and compliance have similar connotations and tend to be used interchangeably. Adherence is mildly preferred to compliance in uses having to do with the amount of medication taken by study subjects as measured against an ideal as specified in the study protocol, e.g., as in use of pill counts in a drug trial measured against the number taken if there was perfect adherence.

adjudicated reading *n* - 1. A reading provided by readers empaneled to review discrepant readings for the purpose of arriving at a final or official reading. 2. A reading by a person when readings provided from independent readings of a record are discrepant, especially such a reading used for making a final classification or determination. *Usage note*: Avoid in the sense of defn 2; limit to uses involving an active adjudication process as in defn 1.

adjudication *n* - In the context of trials and observational studies, a process involving a person or panel of persons to review events reported in a study to provide a coding and classification independent of study investigators. Typically, regarded as superior to counts of raw unadjudicated events because of variation in the way they are reported and because of the risk of bias in how events are codified or classified.

adjunctive treatment, adjunct treatment *n* - An additional treatment not essential to underlying treatment. *Usage note*: Not to be confused with adjuvant treatment. Adjuvant treatment is given in conjunction with another treatment with the expectation of synergism, adjunctive treatment is in addition to existing treatment without expectation of synergism. Placebo treatment is a form of adjunctive treatment when used in the presence of other underlying treatments for study participants.

adjust, adjusted, adjusting, adjusts *v* - To change or modify so as to fit, match, or make correspond.

adjusted *adj* - Modified or accommodated to a set of conditions or specifications; of or relating to adjustment. **ant: crude, unadjusted**

adjusted data *n* - Data subjected to adjustment. **ant: unadjusted data**

adjusted mortality rate *n* - A mortality rate that has been adjusted using some adjustment procedure. **ant: crude mortality rate**

adjustment *n* - [trials] Control of extraneous sources of variation affecting or believed to affect a treatment comparison by use of an adjustment procedure.

adjustment procedure *n* - Any of a variety of procedures intended to remove the effect of one or more extraneous sources of variation affecting a result; procedures include direct and indirect rate adjustment, subgroup analysis, analysis of covariance, and linear and nonlinear regression analysis.

adjustment variable *n* - A variable, such as age or gender, used for adjustment via some analysis procedure; in trials, usually a baseline variable or demographic characteristic such as gender, race, or age on entry.

adjuvant treatment *n* - A treatment given in conjunction with another with the expectation that the benefits will be greater than those expected with either treatment alone, e.g., immunotherapy as an adjuvant to chemotherapy for the treatment of a cancer. **rt: adjunctive treatment**

administered treatment *n* - The actual treatment administered to a person in a trial; not to be confused with assigned treatment.

administrative censoring ν - Censoring occurring because of the cessation of data collection in a study. **rt: interval censoring, left censoring, random censoring, right censoring**

administrative look *n* - [treatment effects monitoring] A look related simply to issues of performance to determine if the trial should continue unaltered; administrative review **rt: efficacy look, safety look**

administrative review *n* - [trials] 1. An ad hoc interim review of performance of some activity to determine whether it is practical to continue a trial unaltered; especially a review considering costs. 2. performance review 3. performance monitoring. *Usage note*: Note that defn 1 has a different operational meaning than defn 3; defn 3 refers to an ad hoc evaluation, whereas defn 3 refers to an ongoing process; not to be used interchangeably. Not to be confused with reviews involving evaluations of treatment results as in safety review, efficacy review, or in treatment effects monitoring. Do not use in contexts where the review includes a review of treatment results. Use is ordinarily limited to review of performance where there is a desire or need to distinguish such a review from one involving an interim look at results, as in relation to treatment effects monitoring, efficacy monitoring, or safety monitoring.

admissible data *n* - 1. Data specified for collection in a study protocol; data collected according to specified procedures; required data collected within indicated time windows. 2. Data judged suitable for inclusion in an analysis database. **ant: inadmissible data**

adult *n* - In respect to research on human beings and regulations underlying IRBs: Typically a person who has reached the age of majority; sometimes, under special circumstances, an emancipated minor; legal age of adulthood in the United States is a matter of state and local laws; hence definitions vary from state to state. **rt: child, minor**

adverse drug experience (ADE) *n* - As defined in the Code of Federal Regulations for the Food and Drug Administration: *Any adverse event associated with the use of a drug in humans, whether or not considered drug related, including the following: An adverse event occurring in the course of the use of a drug product in professional practice; an adverse event occurring from drug overdose, whether accidental or intentional; an adverse event occurring from drug abuse; an adverse event occurring from drug withdrawal; and any failure of expected pharmacological action.*[82] (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=314.80; CFR Title 21, Vol. 5, revised 1 April 2011) **rt: safety report, serious**

adverse drug experience, unexpected **adverse drug experience**

adverse drug reaction (ADR) *n* - A drug reaction that results in hospitalization, prolongation of hospitalization, or one having negative health implications. **rt: serious adverse drug experience, toxic drug reaction**

adverse event (AE) *n* - [trials] 1. Any unfavorable sign, symptom, state, condition, or laboratory finding in a study subject. 2. reportable event **rt: adverse reaction** *Usage note*: Not to be used interchangeably with adverse reaction.

adverse reaction *n* - Broadly, a reaction that has negative consequences or implications for the person experiencing the reaction. In the context of trials, such a reaction attributed to a study treatment; adverse drug reaction when the treatment involves a drug. *Usage note*: Not to be used interchangeably with adverse event. In the context of trials, adverse reactions represent that subset of adverse events attributable to study treatments.

adverse side effect *n* - A side effect that has adverse health implications. **rt: toxic side effect**

adverse treatment effect *n* - A treatment effect that has negative health implications; a treatment effect contrary to the one intended or desired. **ant: beneficial treatment effect**

advisory-review *adj* - Of or relating to providing advice and review; in relation to trials primarily in relation to the design and operation of the trial for the benefit of study investigators and sponsor and offered by persons or a committee independent of the investigators and sponsor.

advisory-review and treatment effects monitoring committee (ARTEMC) *n* - A committee that performs the functions of both an advisory-review committee and treatment effects monitoring committee.

advisory-review committee (ARC) *n* - [trials] A committee in the organizational structure of a trial responsible for reviewing the design and operations of the trial for the purpose of advising investigators related to the trial; voting members usually not involved in the execution of the trial or associated with any of the participating centers or sponsor of the trial. Selected investigators from the trial may serve as nonvoting members. A committee in the organizational structure of some multicenter treatment trials with method of appointment and route of reporting similar to that described for treatment effects monitoring committee. aka: advisory board, advisory committee, policy-advisory board, policy-advisory committee, policy board, policy committee.

advocacy representation construct *n* - [multicenter studies] A representation construct based on advocacy, e.g., one where membership on the steering committee includes persons external to the study chosen to advocate a position or to represent an interest. **rt: center representation construct, discipline representation construct, PI representation construct**

affiliate center *n* - A center, established or adopted by a parent center, responsible for performing specified functions in affiliation with or as an agent of the parent center. **rt: associate center, daughter center, satellite center, sibling center, sister center**

affiliate clinic *n* - A clinic, established or adopted by a parent clinic, that is responsible for performing specified functions in relation to patient enrollment, treatment, or followup in affiliation with or as an agent of the parent clinic. **rt: associate clinic, daughter clinic, satellite clinic, sibling clinic, sister clinic**

age *n* - A measure of time marked from the occurrence of some event, such as birth, to the present or some point in the past; when reported or recorded as years of age, a count

of the number of birthday anniversaries since birth; e.g., in the United States, 25 for a person born over 25 years ago but less than 26 years ago. **rt: birthdate, years of age** *Usage note*: The convention for reporting age varies. A child in her 19th month of life would be regarded as being 2 years of age by insurance companies or 1 or 2 years of age by her parents, depending on where they live. She would be reported as being 1 year of age in the United States and in most European countries and 2 years of age in some Asian countries. If age is important, e.g., as when used to determine eligibility for study, the determination should be made from birthdate not age.

age of assent *n* - In research involving minors, the age at which assent from the minor is required as a prerequisite to study; usually at or around the age 5, but IRBs have discretion as to when assent is required. **rt: age of consent**

age of consent *n* - In research, the age at which consent is required as a prerequisite to study; usually at or near the age of majority. **rt: age of assent, age of majority**

age of emancipation *n* - 1. age of majority 2. The age at which a minor is regarded as an adult in some sense legal or operational sense, e.g., in regard to an IRB, waiving requirements for parental consent in a study of contraceptive use by teenage girls.

age of majority *n* - The age at which full civil rights are accorded to a person; for U.S. states, this ranges from 18 to 21 years of age.

aggregate data *n* - 1. Data compiled by aggregating data from individuals to provide group data. 2. group data *Usage note*: Not to be confused with grouped data.

aggregate patient data (APD) *n* - Data aggregated by combining data from a group of patients, e.g., data for patients in a particular treatment group in a trial. **ant: individual patient data**

aggregate patient data meta-analysis *n* - A meta-analysis involving aggregate patient data.

alert limit *n* - 1. A limit in a trial specified for a treatment difference that serves to alert investigators to the possibility of stopping the trial or a treatment in the trial. 2. A limit specified for a laboratory test that, when exceeded, causes the test to be called to the attention of medical personnel, causes it to be repeated, or causes other tests or procedures to be performed. **rt: monitoring limit, normal limit**

alias *n* - In experimental design, a contrast that has the same form as another and, hence, indistinguishable from the other form. **rt: confounded effect**

allocation *n* - 1. A specified apportionment or distribution. 2. treatment assignment *Usage note*: Not recommended in the sense of defn 2; use treatment assignment instead for reasons indicated in usage note for assignment.

allopathic *adj* - Of or relating to remedies intended to cure or ameliorate disease by producing effects different from those of the disease itself.

allopathic medicine *n* - A medicine intended to cure or ameliorate disease by producing effects different from those of the disease itself; a medicine chosen because of its known or presumed allopathic properties. **ant: homeopathic medicine**

alpha *n* - First letter in Greek alphabet; lower case α; used to denote type I error in sample size calculations and tests of significance.

alpha error *n* - type I error, significance level

alpha spending function *n* - A function serving to apportion the amount of type I error spent per look when engaged in testing involving multiple looks at accumulating data, e.g., as in treatment effects monitoring, so as to preserve an overall type I error level; achieved by testing early on at high levels

of error protection and later on with lower levels of error protection such that the total error is at the level as specified at the outset.[55]

alternation treatment assignment *n* - Any systematic (nonrandom) method of treatment assignment in which assignments alternate, e.g., a scheme in which every other person enrolled is assigned to the test treatment; odd–even method of treatment assignment.

alternative care *n* - Care available to persons declining enrollment or withdrawing from a trial; one of a series of disclosures considered essential to informed consent (CFR Title 45, Part 46, §46.116 (4); http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm; accessed 18 Jun 2010).[200]

alternative hypothesis *n* - 1. A hypothesis stated as an alternative to the null hypothesis in which parameters, functions, traits, characteristics, or effects of interest are assigned non-null values. 2. In a test of hypothesis, the hypothesis that is accepted when the null hypothesis is rejected. 3. alternative treatment hypothesis. **rt: one-tailed alternative hypothesis, two-tailed alternative hypothesis**

alternative treatment *n* - 1. Treatment available to persons declining enrollment or withdrawing from a trial; one of a series of disclosures (§46.116 (4))[200] considered essential to informed consent. (http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html) 2. The treatment represented by a control treatment.

amended protocol *n* - 1. A protocol that has been changed. 2. A protocol change that has been reviewed and approved by an IRB.

analysis by administered treatment *n* - Data analysis in which treatment comparisons are based on administered treatment, e.g., as done by grouping results for patients who were assigned to the test treatment but refused the treatment with those for patients assigned to and receiving the control treatment in the case of a placebo-controlled trial; not a primary method of analysis; see analysis by assigned treatment. **syn: per protocol analysis ant: analysis by assigned treatment, per assignment analysis rt: analysis by level of treatment compliance**

analysis by assigned treatment *n* - Data analysis in which treatment comparisons are based on assigned treatment; primary method of analysis. **syn: analysis by intention to treat, per assignment analysis ant: analysis by administered treatment, per protocol analysis** *Usage note*: Term preferred to analysis by intention to treat because focus is on assignment rather than on what is intended.

analysis by intention to treat *n* - analysis by assigned treatment. **syn: per assignment analysis ant: per protocol analysis** *Usage note*: See intention to treat for comment.

analysis by level of treatment adherence *n* - In trials treatment comparisons by level of treatment adherence; typically done by performing treatment comparisons within subgroups of patients classified by level of treatment compliance or by use of regression models using measures of treatment adherence for deriving adjusted treatment comparisons. Not recommended as a primary method of analysis (see analysis by assigned treatment). **rt: analysis by administered treatment**

analysis center *n* - 1. data center 2. data coordinating center 3. coordinating center

analysis committee *n* - 1. A committee having responsibility for data analysis. 2. A committee within the organizational structure of a multidisciplinary collaborating group having responsibility for analysis of one or more aspects of the data generated by the group. **rt: committee, performance monitoring committee, treatment effects monitoring committee, writing committee**

analysis data edit *n* - A data edit that is the result of a data discrepancy, inconsistency, or error detected during data analysis. **rt: data edit**

analysis database *n* - The subset of data contained in the study database available for data analysis; data that have been keyed, edited, and stored electronically available for analysis.

analysis dataset *n* - The dataset used for an analysis, e.g., a dataset prepared for use in writing a results paper; typically involving a data freeze and assembly of data from various databases comprising the study database. **rt: dataset**

analysis of covariance (AnoCo, ANOCO, AoC, AOC) *n* - A method of adjustment involving regression procedures designed to remove the effect of a variable(s) related to the classifications, factors, or variables of interest in an analysis of variance. **rt: analysis of variance**

analysis of variance (AnoVa, ANOVA, AoV, AOV) *n* - A method of data analysis for determining the contribution of classifications or factors (e.g., treatment in a clinical trial) by partitioning the observed variance into component parts related to those classifications or factors. **rt: analysis of covariance**

analysis plan *n* - [trials] The plan for data analysis, especially that plan as set forth in the study protocol; including specification of outcomes to be assessed, designation of the primary outcome measure, listing of secondary outcomes to be evaluated, description of primary analysis procedures, and description of treatment effect monitoring procedures.

analysis principle *n* - A principle used to guide data analysis; principles for trials, as discussed by Meinert and Tonascia [1986],[172] include: (1) primary analysis to be by treatment assignment (regardless of course of treatment); (2) analysis to account for all persons enrolled; (3) all outcome events occurring after treatment assignment to be counted regardless of when they occur; (4) comparison of higher order outcomes or events (e.g., death) performed before performing comparisons of lower order outcomes or events (e.g., cause-specific mortality or fatal or nonfatal MI); (5) component parts (e.g., death and nonfatal MI) of a composite outcome measure analyzed separately; a composite outcome measure not to serve as the basis for a primary analysis if the analysis of the component parts yield conflicting or offsetting differences (e.g., a difference favoring one treatment group for death and a difference favoring the other treatment group for nonfatal MI). **rt: counting rule**

ancillary publication *n* - 1. A publication containing ancillary results. 2. A publication related to an ancillary aim of a research project; in the case of trials, usually publications from ancillary studies. **rt: primary publication, secondary publication**

ancillary result *n* - A result from an ancillary study; a result of ancillary importance to the primary objective of a study. **rt: primary result, secondary result**

ancillary study *n* - 1. A supplementary study done in association with a parent study. 2. A study done by personnel associated with a parent study. **rt: auxiliary study, daughter study, sister study, substudy**
Usage note: Subject to misuse; not to be confused with substudy. Ancillary studies are the result of the varying interests and pursuits of investigators in the parent study. Most multicenter trials have procedures for reviewing and approving proposals for ancillary studies. Generally, investigators must satisfy officers of the study or steering committee that a proposed study is impact neutral in regard to the parent study. Studies seen as having a likely adverse impact are not usually approved. Studies calling for the collection of additional data or the conduct of additional procedures on persons enrolled

in the parent study are not likely to be approved if seen as interfering with the parent study or if seen as increasing the risk of dropout or missing data. Ancillary studies are expected to be resource neutral from the perspective of the parent study. Studies calling for use of treatment-related data are assumed to be impact negative and are not approved, or are approved with the proviso that such data are not to be released or used until the parent study has been completed. Approvals are contingent on IRB approvals.

anniversary closing date *n* - In trials and followup studies, a date for close of followup based on when persons enrolled, e.g., separation of persons from a trial one year after enrollment; aka common followup period close-out. **rt: common closing date**

anniversary date close-out *n* - In trials, a method of close-out in which persons are separated from a trial on an anniversary date, e.g., separation after 26 weeks of followup. Operationally equivalent to common date close-out when enrollment occurs over a short period of time, otherwise the amount of followup person-time will be less than that for common date close-out. **rt: common date close-out**

anonymized data *n* - Data stripped of personal identifiers.

anonymous data *n* - unidentifiable data; unlinkable data; de-identified data **rt: anonymized data** *Usage note*: See usage note for linkable data.

antagonism *n* - 1. Opposition of a conflicting force, tendency, or principle. 2. Opposition in physiological action; the interaction of one substance with another causing the action of either substance to be lessened. **ant: synergism**

antagonist *n* - A substance, such as a drug or food, that opposes the action of another substance (e.g., milk opposing the action of tetracycline). **ant: synergist**

antagonistic treatment effect *n* - A treatment effect produced by the simultaneous use of two or more substances (e.g., two different drugs or a drug and a food) that is less than the sum of the effects of those substances acting alone. **ant: synergistic treatment effect**

apartheid treatment effects monitoring *n* - Treatment effects monitoring performed in such a way so as to keep study personnel and patients from seeing or knowing interim treatment results; typically done by constituting a treatment effects monitoring committee absent clinic personnel, by closed deliberations, and by proscription of dissemination or discussion of interim results until the trial is completed or until the monitoring body has produced a results-based recommendation for change for consideration by study investigators. *Usage note*: The origins of this form of monitoring comes from concerns of sponsors and investigators regarding risks of treatment-related feedback bias and the desire to shield clinic personnel from interim results to minimize conflicts of interest (defn 2) such knowledge may induce when approaching patients for enrollment. The apartheid notion is contained in recommendations from the NIH Clinical Trials Committee issued in 1979. The committee recommended (in regard to composition of monitoring committees in multicenter trials) *Physicians engaged in the care of study patients or directly responsible for evaluating clinical status are excluded*.[192]

applied research *n* - 1. Research concerned with application or use. 2. In medicine, research following preclinical work; broadly clinical research. **rt: basic research, translational research** *Usage note*: There is a certain futility in classifying research as applied or basic because the classification depends on perspective. Clinical trials are applied from one perspective (that of the preclinical researcher) and basic from another (that of the clinician or end user wanting to know

whether a treatment works in everyday practice).

appointed study chair *n* - A study chair appointed by the study sponsor or some other body or person. **rt: elected study chair, fiat study chair, rotating study chair, study chair external, study chair internal**

approved consent form *n* - A consent form approved by one's IRB; typically as evidenced by a date stamp indicating approval expiration date. **rt: consent form**

approved drug *n* - 1. A drug approved for a specified use or indication by a regulatory agency. 2. A drug approved by the Food and Drug Administration, based on a New Drug Application or other bases, e.g., via the Drug Efficacy Study Implementation (DESI). 3. Drugs listed in the *Physicians' Desk Reference*. 4. A drug listed in a recognized pharmacopeia or formulary. 5. licensed drug

approved protocol *n* - 1. A protocol that has been approved for implementation. 2. The protocol for an approved study. 3. A protocol that has been approved by an IRB.

approved protocol change *n* - 1. A protocol change approved by study investigators. 2. A protocol change approved by an IRB.

archive *n* - A place, such as a library, where documents are stored for access and use; public archive if access or use is open to the public or to a general class of people; repository. **rt: bank** *Usage note*: See repository.

aristocracy representation construct *n* - [multicenter studies] A representation construct limited to founding members, e.g., one where membership on the steering committee is limited to persons responsible for getting funding for the study. **rt: center representation construct, discipline representation construct, PI representation construct**

arithmetic mean *n* - The sum of a set of numeric values divided by the number of values in the set; usually denoted by $\bar{x}$ or $\bar{y}$ for sample means and by μ for population means.

ascertainment bias *n* - A bias in the way something is found or determined; e.g., in a randomized trial, a bias in classification of cause of death because circumstances of death are better described and documented in one treatment group than in another.

assent *n* - 1. The act of assenting; a permission granted. 2. An expression of acquiescence to something proposed. **rt: assent form, consent, oral assent, oral consent, post-assignment consent, signed assent, signed consent** *Usage note*: Not to be confused with consent. Generally in research, assent is required whenever consent is given by someone else on behalf of the person being studied provided the person has sufficient mental capacity to understand the nature and extent of what is being proposed. The starting age at which assent is required varies, but is usually 5 years of age or thereabouts. For persons unable to read, the assent may be oral after the person has been presented with an explanation of what is involved. For persons able to read (e.g., children aged 7 or 8 to the age of majority), the process may require the use of a written assent form and a signed assent before proceeding. The process, while used primarily in relation to children, extends as well to adults with limited but sufficient mental capacities to allow them to assent.

assent, assented, assenting, assents *v* - To express willingness to accept in relation to some proposal or plan, especially such expression after discussion and consideration; permission granted. **rt: consent** *Usage note*: Not to be confused with consent as used in research settings. One requires the assent of a child and the consent of the child's parent or guardian to enroll the child into a study. The *American Heritage Dictionary*[4] lists for assent (v)

agree, accede, acquiesce, accept, consent, concur, and subscribe as synonyms and indicates: *These verbs mean to go along with another's views, proposals, or actions. Assent implies saying "yes" in a formal, somewhat impersonal manner. Agree and accede are loosely related in the sense of assenting after discussion or persuasion. But agree suggests mutual accommodation in a meeting of minds, whereas accede implies yielding on the part of one person or group. Acquiesce suggests agreeing, despite reservations, because of unwillingness to oppose. Accept may indicate agreement with some reluctance. Consent indicates complete and voluntary personal commitment to a proposal or desire. Concur refers to agreement with another's position, and may suggest that one has reached the same conclusion independently. Subscribe indicates hearty consent or approval*.

assent form *n* - A written document presented to a child or to an adult with diminished mental capacity as a prelude to enrollment into a research project having the function of providing a written description (in language consistent with the age of the child or mental capacity of the adult) of the proposed research, of the nature of the commitment required, of the procedures to be performed and of the reasons for them, of the purpose of the research and why the person is being approached for enrollment, of the potential risks and benefits associated with participation, and of the right of the person to not agree to enrollment and of the right of the person to withdraw at anytime after enrollment without prejudice in regard to the nature or amount of care or treatment available to the person at the research site.

assigned to treatment *n* - The state of having been assigned to a treatment in a trial.

assigned treatment *n* - The treatment assigned to a person; not to be confused with administered treatment. **syn: treatment assignment rt: administered treatment**

assignment *n* - 1. Something assigned or designated, as a duty, task, or regimen. 2. The act of assigning. 3. treatment assignment *Usage note*: In regard to randomized trials, preferred to allocation in references to treatment assignment. Assignment is a more accurate characterization of the process involved than is allocation.

associate center *n* - [trials] A study center established or adopted by a parent center, that is responsible for performing specified functions in association with or as an agent of the parent; may or may not receive financial support from the parent. **rt: affiliate center, daughter center, satellite center, sibling center, sister center**

associate clinic *n* - A clinic, established or adopted by a parent clinic responsible for performing specified functions in association with or as an agent of the parent clinic; may or may not receive financial support from the parent. **rt: affiliate clinic, daughter clinic, satellite clinic, sibling clinic, sister clinic**

association *n* - [statistics] 1. An observed or postulated pattern of change of one variable (event, factor) to another, typically identified through exploratory data analysis, and assessed using statistical methods. 2. dependence **rt: correlation, dependent, independence, relationship, statistical association** *Usage note*: An association is considered to be present if the probability of occurrence of an event, trait, or characteristic depends on the occurrence of one or more other events, the presence of one or more characteristics, or on the value of one or more other variables. The relationship of two variables is characterized as positive if the change of one variable is associated with a change in the same direction for the other variable and negative if the change of one variable is associated with a change in the opposite direction of the other variable. Often used interchangeably with relationship, especially in uses in the

sense of defn 1. See also notes for correlation and cause and effect.

asymmetrical treatment effects monitoring *n* - Treatment effects monitoring sensitive to the sign of observed treatment differences; e.g., as practiced by having different criteria for recommending a stop or change for positive treatment effects than for negative treatment effects. **ant: symmetrical treatment effects monitoring rt: stopping guideline, stopping rule** *Usage note*: Clinical trials typically involve asymmetrical monitoring since they are done to determine whether a treatment is beneficial, not to determine harm. Masking the monitoring body has the effect of depriving monitoring body knowledge of the sign of the treatment difference forcing, in effect, symmetrical monitoring, but usually the mask is lifted if a treatment difference emerges.

attack rate *n* - The number of new cases of an illness, disease, or condition observed over a defined time period, divided by the number at risk of developing that illness, disease, or condition over that time period.

attributable risk *n* - [epidemiology] *The amount or proportion of disease incidence (or disease risk) that can be attributed to a specific exposure;*[103] usually the difference in incidence or associated morbidity or mortality in exposed persons versus persons not exposed. *Usage note*: Subject to varying uses; define when used; see Gordis[103] and Last.[143]

audit for cause *n* - An audit because of known or suspected aberrancies.

audit trail *n* - The sequence of transactions linking two events or actions. In data processing, the sequence of transactions linking data in a finished dataset to those recorded in source documents, such as data collection forms or medical records.

author *n* - 1. The writer or one of the writers of a document, such as a manuscript. 2. The source or originator of a notion or concept. **rt: authorship attribution** *Usage note*: See **Vancouver Convention**.

author citation *n* - 1. The listing of authors in the masthead or title page of a document, manuscript, or work; conventional author citation, corporate author citation. 2. The citing of authors in relation to a document, manuscript, or work of the authors, e.g., in a reference citation.

authorship attribution *n* - The persons, group, or agency to which a work is attributed. See conventional authorship and corporate authorship. **rt: authorship credit**

authorship credit *n* - Credit for authoring a manuscript as denoted in the masthead or elsewhere in a manuscript. **rt: authorship attribution** *Usage note*: Under the Uniform Requirements for Manuscripts Submitted to Biomedical Journals (also known as the Vancouver Convention) persons claiming authorship credit must be able to show substantial contributions to *(a) conception and design, or analysis and interpretation of data; and to (b) drafting the article or revising it critically for important intellectual content; and on (c) final approval of the version to be published. Conditions (a), (b), and (c) must all be met*.[117] Acquisition of funding, the collection of data, or general supervision of the research group do not, by themselves, justify authorship credit.[117] The most recent version of the requirements is typically posted to websites of subscribing journals or may be found at www.icmje.org.

authorship format *n* - The form of authorship attribution displayed in mastheads of publications; see conventional author citation, modified conventional author citation, corporate author citation, and modified corporate author citation for formats. **rt: masthead author listing**

autonomy, right of *n* - Right to be self-governing or self-directing without outside control. [study subjects] The right to consent and to withdraw without prejudice

from a research study; required as conditions for IRB approval.

auxiliary study *n* - 1. An ancillary study done by personnel not associated with a parent study. 2. A study involving data or material from a study, done independently of that study and by personnel not associated with it. **rt: ancillary study, substudy**

average *n* - 1. arithmetic mean 2. An estimation of or approximation to the arithmetic mean, such as provided by the median or mode or some other central tendency measure. 3. A typical or usual level, degree, or kind. **rt: median, mode** *Usage note*: Avoid in scientific writing, especially when referring to results based on a known measure of central tendency; use the proper term.

award statement *n* - [funding] A document confirming the fact of funding, amount, and time period covered.