Guidance for Industry

Clinical Studies Section of Labeling for Human Prescription Drug and Biological Products — Content and Format

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
January 2006
Labeling

Contains Nonbinding Recommendations

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Guidance for Industry[1]

Clinical Studies Section of Labeling for Prescription Drug and Biological Products — Content and Format

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I. INTRODUCTION

This guidance is intended to assist applicants in deciding (1) what studies should be included in the CLINICAL STUDIES section of prescription drug[2] labeling, (2) how to describe individual studies, and (3) how to present study data, including presentation of data in graphs and tables. This guidance is intended to make the CLINICAL STUDIES section of labeling, as described in the final rule amending the requirements for the content and format of labeling for human prescription drug and biological products (21 CFR 201.56 and 201.57),[3] more useful, and to promote consistency in the content and format of the section across drug product classes and within drug classes and indications. This guidance also calls attention to the advertising and promotional implications of data and statements contained in the CLINICAL STUDIES section.

The principal objective of labeling is to provide the information that is most useful to prescribers in treating their patients. In some cases, making the information in the CLINICAL STUDIES section of labeling more useful to prescribers could warrant significant departures from past labeling practices.

FDA's guidance documents, including this guidance, do not establish legally enforceable

[1] This guidance has been prepared by the Medical Policy Coordinating Committees in the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) at the Food and Drug Administration.

[2] This guidance applies to drug products, including biological drug products. For purposes of this guidance, *drug* or *drug product* will be used to refer to human prescription drug and biological products that are regulated as drugs.

[3] See the final rule "Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products" published in the *Federal Register* in January 2006.

responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. IDENTIFYING STUDIES FOR INCLUSION IN THE CLINICAL STUDIES SECTION

The CLINICAL STUDIES section of labeling must discuss those clinical studies that facilitate an understanding of how to use the drug safely and effectively (21 CFR 201.57(c)(15)). This is usually accomplished by providing concise, accurate summaries of information from studies concerning a drug's effectiveness (and sometimes safety) that practitioners consider important to clinical decision making. Generally, this should include information from the adequate and well-controlled studies that demonstrate the effectiveness of the drug for its approved indication. This section of the labeling is not intended to describe all available effectiveness data. Additional studies that reach the same conclusion should be omitted or described briefly without detail. If there are multiple studies that address the same effectiveness issue, the subset selected for presentation should ordinarily reflect the overall conclusions derived from the database as a whole (e.g., not suggest a larger treatment effect than the database as a whole).

A. Studies To Include in the Clinical Studies Section

The following are the types of adequate and well-controlled studies[4] that should usually be included in the CLINICAL STUDIES section.

1. Clinical studies that provide primary support for effectiveness

2. Clinical studies that provide other important information about a drug's effectiveness not furnished by the studies that provide primary support for effectiveness, such as:

    - Studies that suggest differential effects in population subsets (e.g., women vs. men, presence or absence of concomitant illness or medications)
    - Studies that suggest lack of effectiveness in a clinical situation or lack of effect on a particular endpoint where the drug might have been expected to work
    - Studies that provide information relevant to dose selection or adjustment (e.g., dose-response studies or studies in nonresponders to a particular dose)
    - Studies that provide information about the nature and size of the treatment effect, particularly where the effect is small

3. Clinical studies that prospectively evaluate an important safety endpoint

[4] See 21 CFR 314.126.

B. Studies *Not* To Include in the Clinical Studies Section

The following are the types of studies that should usually not be included in the CLINICAL STUDIES section, unless they also meet one of the factors in II.A (above). If an exception is made, the limitations of the study and the reasons for inclusion should be stated.

1. Clinical studies with results that imply effectiveness for an unapproved indication, use, or dosing regimen

2. Active control clinical studies that imply comparative effectiveness or safety claims not supported by substantial evidence

3. Studies that are not adequate and well-controlled within the meaning of 21 CFR 314.126.

III. DESCRIBING STUDIES IN THE CLINICAL STUDIES SECTION

A. General Principles

1. Focus on Effectiveness Data

The primary objective of the CLINICAL STUDIES section is to summarize (1) the evidence supporting effectiveness in the subjects who were studied, (2) the critical design aspects of the studies, including the populations studied and endpoints measured, and (3) the important limitations of the available evidence. Ordinarily, safety data are described in the ADVERSE REACTIONS section. However, in some cases it may be appropriate to present important information about safety in the CLINICAL STUDIES section (e.g., if the safety data are best understood when presented with a detailed study description or in the context of effectiveness results). The section should also include safety data from controlled studies specifically designed to evaluate a safety endpoint. If safety data are presented in the CLINICAL STUDIES section, they must be cross-referenced in the ADVERSE REACTIONS section and other sections, as appropriate (21 CFR 201.57(c)(15)(ii)).

2. Amount of Detail

In general, the amount of detail needed to provide a useful description of a study and its results will depend on the indication, the trial design, the understanding of the drug or drug class, and the extent to which the information adds to an understanding of the clinical effects of the drug and how the drug should be used. The amount of detail appropriate for a given study or dataset is inevitably a matter of judgment, but some general principles can be described.

Ordinarily, applicants should include more detail when:

- The study responses measured are of critical health importance. In most cases, such responses would be direct measures of a meaningful clinical outcome (e.g., mortality, stroke, acute myocardial infarction rates, fracture rates, symptom alleviation, or functional improvement), but could also include effects on important surrogate endpoints (e.g., cholesterol or hemoglobin A1c).

- The study results demonstrate that a new agent offers a clear advantage over existing therapy (see section III.A.4 for a discussion of comparative claims).

- The study results represent a significant advance in the treatment of a disease or condition, or provide important information about a drug's activities relative to its therapeutic class.

- The study enrolled a very specific population or used a very specific concomitant regimen, and the results may not be applicable to other populations.

- The study results are not what would be expected for that drug class and indication — for example, when the study results demonstrate a particularly marginal response or a response for which the clinical meaning or implications are unclear.

- The study uses an unfamiliar endpoint (e.g., a novel surrogate endpoint), or there are important limitations and uncertainties associated with an endpoint.

Applicants should include less detail when:

- The new drug appears to have effects that are typical of its class.

- The magnitude of the effect on clinical endpoints measured in the study is not readily translatable into effects in clinical practice. For example, exercise testing in a study of heart failure can demonstrate effectiveness, but does not translate to a quantifiable clinical outcome. Similarly, changes in HAM-D scores can be used to demonstrate effectiveness of an antidepressant, but the results for a given study are population- and probably site-specific, and thus, do not necessarily translate to a numerically similar outcome in clinical practice.

In these cases, it could be useful to describe the study in general terms (e.g., population, duration, endpoints measured, and qualitative outcome) without providing detailed results.

3. Endpoints

The CLINICAL STUDIES section should present those endpoints that establish the effectiveness of the drug or show the limitations of effectiveness. This includes

endpoints the Agency has accepted as evidence of effectiveness, or closely related endpoints that may be more easily understood. When it would be informative, the CLINICAL STUDIES section can also discuss other endpoints shown to be affected by the drug and endpoints that might have been expected to be influenced by the drug, but were not.

- **Composite Endpoints:**[5] In general, the results for all components of a composite endpoint should be presented. Presentation of all components reveals which components are driving the result and which components may be unaffected, or even adversely affected, by treatment with the drug. When there is a range of effects on the components of a composite endpoint, selectively presenting only a single component of the composite endpoint, or presenting only the change in the composite endpoint, can be misleading. In most cases, discussion of a component of a composite endpoint should be only descriptive (i.e., not be presented with statistical analyses) unless the component has been assessed as a separate endpoint with a prospectively defined hypothesis and analysis plan.

- **Primary and Secondary Endpoints:** The terms *primary endpoint* and *secondary endpoint* are used so variably that they are rarely helpful. The appropriate inquiry is whether there is a well-documented, statistically and clinically meaningful effect on a prospectively defined endpoint, not whether the endpoint was identified as primary or secondary.

- **Closely Related Endpoints:** If two or more endpoints are closely related and convey essentially the same information, only one should generally be presented.

4. Comparative Data

If the effectiveness of a drug can be determined by comparison to placebo, data comparing the effects of the drug to an active comparator should generally not be included in labeling unless the data are adequate to support an explicit comparative claim (either a superiority or similar effectiveness claim). For example, when describing a clinical trial with three treatment arms (study drug, active control, and placebo) in which the comparison of study drug to placebo yields important effectiveness information and the active control was present only to confirm assay sensitivity, the identity of the active control and the results from that arm should be omitted if those data are not adequate to support a comparative claim and are not otherwise important to a clinician's understanding of the drug's effect.

If effectiveness can be determined only by comparison to an active control (superiority or non-inferiority trial) and the identity of the active comparator is important to a clinician's

[5] Note that composite endpoint refers to combined morbidity and mortality endpoints that could potentially be evaluated separately, not to the separate components of standard evaluative scales (e.g., HAM-D for depression, BPRS for schizophrenia, nasal symptoms score).

understanding of the drug's effects, the active control data and identity of the comparator should be included in labeling. In such cases, the labeling should make clear that no comparative claim has been established (if it has not been) and should disclose any limitations of the comparative data (e.g., if the comparator was administered in a suboptimal or unapproved regimen).

An explicit claim of superior or similar effectiveness must be supported by substantial evidence (21 CFR 201.56(a)(3)). For superiority claims, such evidence would include adequate and well-controlled trials designed to establish superiority of one treatment over another. For claims of similar effectiveness, such evidence would include adequate and well-controlled trials designed to demonstrate that one treatment is not inferior to another and that the difference between the two is not clinically significant. Thus, the non-inferiority margin used would have to be smaller than the margin needed to merely establish effectiveness. For example, a non-inferiority trial designed to show that a new drug has at least 50 percent of the effect of the active control can provide adequate evidence of effectiveness, but a 50 percent non-inferiority margin would ordinarily be too large to support a claim of similar effectiveness. For each type of trial, the active control should be used at an appropriate dose and regimen, generally the highest recommended dose, and in an appropriate patient population. [6]

B. Describing the Study Design

The following elements are recommended when describing the study design.

1. Major Design Characteristics

The major design characteristics should be identified, including level of blinding (e.g., double-blinded, partially blinded, open-label), type of controls (e.g., placebo, active, historical), duration of the study, method of allocation to treatment groups (e.g., randomization), and use of a run-in period to identify potential responders or eliminate placebo responders from subsequent phases of the study. Often, many of these factors can be summarized in a phrase such as "randomized, double-blind, placebo-controlled study."

2. Treatment Arms

The dose, regimens, and any titration procedure should be identified for each trial arm.

3. Concomitant Therapy

Information about concomitant therapies should be included to the extent it helps to

[6] International Conference on Harmonization (ICH) guidance E10 (*Choice of Control Group and Related Issues in Clinical Trials)* considers fairness of comparisons intended to show superiority or equivalence of one treatment to another. The guidance discusses how to design a trial that does not inappropriately favor one treatment over another (see section on Fairness of Comparisons in ICH E10).

understand the use of the study drug or its effects.

4. Study Population

The description of the study population should identify those characteristics that are important for understanding how to interpret and apply the study results. The description thus should identify important inclusion and exclusion criteria, the demographic characteristics of the studied population, baseline values of any clinically relevant variables important for understanding the treatment effect, and other characteristics of the population that have important implications for the extent to which results can be generalized. For example, the description should discuss enrollment factors that exclude subjects prone to adverse effects, the age distribution of the study population, a baseline value that results in a study population that is more or less sick than usual, or a study population enriched by a study design that eliminates nonresponders.

5. Critical Endpoints

Endpoints critical to establishing effectiveness should be identified, and those that are not commonly understood should be defined.

C. Summarizing Study Findings

When including a detailed summary of study findings (see section III.A.2 for a discussion of when more detail is important), the following elements should be addressed to the extent they contribute to practitioners' understanding of drug effectiveness.

1. Disposition of Subjects

It is generally recommended that the discussion of disposition of subjects include the following:

- The number of subjects enrolled
- The number of subjects completing the study
- The number of subjects discontinuing the study and the reasons for discontinuation
- For a study with a run-in period or other distinct phases, the number of subjects entering each phase and the number of subjects not progressing to the next phase

2. Treatment Effect[7]

[7] *Treatment effect* means the effect that can be attributed to the drug. It is typically derived from a comparison of two prospectively identified treatment arms. Examples of such comparisons include differences in proportions of patients achieving some treatment goal, differences in mean change from baseline, or hazard ratios.

It is recommended that the summary of findings describe the clinical outcome of the treatment relative to the comparator (e.g., placebo or active).

- **Absolute vs. Relative Difference:** When presenting differences between study group and comparator, it is important to present the absolute difference between treatment groups for the endpoint measured, as well as the relative difference (e.g., relative risk reduction or hazard ratio). For example, if mortality is 6 percent in one study arm and 8 percent in the other, the absolute difference (2 percent) should be presented along with the 25 percent relative risk reduction.

- **Group Results and Individual Subject Data:** In most cases, the treatment effect is presented as a mean or median result accompanied by a measure of uncertainty or distribution of results for the treated groups. However, providing individual subject data for all treatment groups can be a useful alternative for describing the clinical effect of a drug. This can be done by including a graphical presentation of the distribution or cumulative distribution of responses among individual subjects (see Appendix for examples of graphical methods for presenting individual subject data). Individual data can also be presented as categorical outcomes (e.g., the proportion of patients reaching a prospectively defined goal, such as systolic blood pressure of 120 mmHg).

- **Combined Data:** In certain situations, analyses of data combined from multiple effectiveness studies can be useful for estimating the treatment effect. These analyses should be included only when they are scientifically appropriate and better characterize the treatment effect. Meta-analytic graphs (see Appendix) can be useful for displaying confidence intervals from several studies.

- **Uncertainty of Treatment Effect:** A confidence interval and a p-value provide complementary information, and both should usually be provided when describing uncertainty of the treatment effect. A confidence interval provides a better numerical description of the uncertainty of the treatment effect and provides some information about its size. A p-value better conveys the strength of the finding (i.e., how likely it is that the observed treatment effect is a chance finding). However, it is generally better not to use a p-value alone.

3. Describing Results Within Treatment Groups

In controlled trials, the change from baseline in a treatment group is usually not by itself informative. The comparison of the change from baseline *between* treatment groups is critical for understanding the treatment effect. Therefore, results for both the study drug and comparator should almost always be presented because the magnitude of the treatment effect is conveyed by the comparison. Presentation of results for both study drug and comparator is especially important for studies with large effects in the placebo group, where presentation of results uncorrected for the placebo group response can be highly misleading. When results from active control arms are discussed, a comparative claim should not be implied where one is not supported. The relevant statistical

comparisons are those comparing the groups, not the comparison of the treated and baseline value within a group.

For continuous data, the presentation of results within a treatment group should include, where appropriate, information about the variability of individual subject responses within the treatment group. This variability can be described with standard deviations and illustrated with box plots (see Appendix for examples of graphical methods for presenting results within treatment groups).

4. Demographic and Other Subgroups

The CLINICAL STUDIES section should include a summary statement about the results of required explorations of treatment effects in age, gender, and racial subgroups (21 CFR 314.50(d)(5)(v)). The summary statement should report the findings of analyses that had a reasonable ability to detect subgroup differences and should note when analyses were not useful because of inadequate sample size. The following are examples of appropriate summary statements.

- The database was not large enough to assess whether there were differences in effects in age, gender, or race subgroups.

- Examination of age and gender subgroups did not identify differences in response to (study drug) among these subgroups. There were too few African-American subjects to adequately assess differences in effects in that population.

- Examination of age and gender subgroups suggested a larger treatment effect in women (possibly resulting from the larger mg/kg dose in women), but no age-related differences. There were too few African-American subjects to adequately assess differences in effects in that population.

Compelling results from analyses of other subgroups of established interest should also be presented, with a caution statement, where appropriate, about the inherent risks of unplanned subgroup analyses.

D. Presenting Data for Different Types of Outcomes

Data on outcomes of treatment should be presented only if the outcome is of clinical significance.

1. Categorical Outcomes (e.g., success or failure)

For categorical outcomes, the number (or percentage) of outcomes for randomized subjects should be shown. For example, the total sample size for the treatment group, the number of successes, the number of failures, and the number of unknown status should be provided. Where informative, those subjects whose outcome status is unknown can be further differentiated by including the number who dropped out due to adverse events,

the number who were lost to follow-up, or any other pertinent distinction. If only percentages are reported, the denominator should be included.

2. Continuous Variables

For continuous variables, measures of central tendency (e.g., mean, median), accompanied by a measure of distribution, are the usual methods for presenting data. When means or medians are used, the number of subjects remaining in the study at each time point should be provided. Because means or medians, even when accompanied by descriptions of variability, may not adequately convey the variability of responses, it might be useful to display individual responses (e.g., by graphical representation of the cumulative distribution of responses — see Appendix). It is important to include the baseline value when reporting any change (either numerical or percent change) from that baseline.

3. Time-to-Event Endpoints

When time-to-event endpoints (e.g., mortality) are used, median or mean survival alone is not usually an adequate descriptor. Survival curves (or event-free survival curves) and hazard ratios are often effective ways to display such data. Data can also be summarized at specific times (e.g., prevalence at 3, 6, 9, 12 months) or at specific event frequency (e.g., time to 25 percent, 50 percent, and 75 percent prevalence of events). The number of subjects evaluated at a given interval or frequency should be specified. Note again the need to convey both absolute and relative difference (see III.C.2).

4. Graphs or Tables

Graphs and/or tables are often more effective than text alone in communicating study results, and one or the other should be used when presenting study results in the CLINICAL STUDIES section. See the Appendix for guidance on the use of graphs and tables in the CLINICAL STUDIES section of labeling.

E. Implied Claims and Advertising and Promotional Considerations

The CLINICAL STUDIES section must not suggest or imply indications, uses or dosing regimens not stated in the INDICATIONS AND USAGE or DOSAGE AND ADMINISTRATION section (21 CFR 201.57(c)(15)(i)). Words or phrases that lack a commonly understood meaning (e.g., imprecise quantitative terms), are not easily defined, are vague, misleading, or promotional in tone should be avoided. Examples include *large* or *small* (instead, use actual size or amount), *well-designed* (instead, provide specifics about the study design), *extensively studied* (instead, provide specifics about the database), *rapid* (instead, specify change/unit time), *trend* (instead, provide specifics about the outcome), *potent* (instead, give the size of the effect), *pivotal study* (instead, describe as major effectiveness study), and *highly significant* (instead, provide the confidence interval).

Advertising and promotion make frequent use of statements or data appearing in the CLINICAL STUDIES section. Sponsors are reminded that any claim of effectiveness made in prescription drug promotion, including comparative effectiveness, must be supported by substantial evidence (21 CFR 201.56(a)(3)) or substantial clinical experience (see e.g., 21 CFR 202.1(e)(6)(i)).

F. Updating the Clinical Studies Section

The CLINICAL STUDIES section must be updated when new information becomes available (21 CFR 201.56(a)(2)) that causes the labeling to become inaccurate, false or misleading. Such outdated information must be promptly revised or deleted.

APPENDIX

Presenting Study Results in Tables and Graphs

INTRODUCTION

When clinical data are to be presented in some detail in the CLINICAL STUDIES section, tables and graphs are often better than text alone because they can convey the desired information more effectively. The following general principles should be applied to the use of tables and graphs:

- Depict study results clearly, fairly, and accurately.
- Do not repeat in accompanying text, information that would be clear from viewing the table or graph, although the text can point out the most important data presented. Often the statement, "Results are found in Table X," is sufficient.
- Small tables can be embedded in the text. Do not place larger tables and graphs next to any explanatory text.
- Use clear titles and clearly labeled axes to limit the need for any explanatory text.

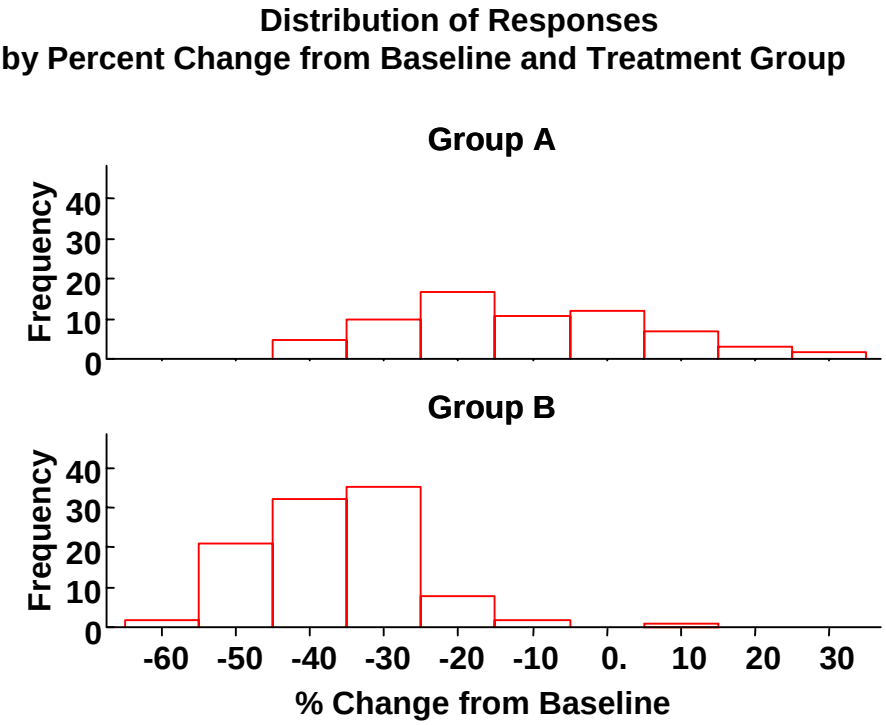
GRAPHS

A. Common Uses of Graphs

- To present a large amount of data, such as individual subject data points (e.g., distribution of responses)
- To show effects of treatment on major events or survival over time (Kaplan-Meier curves)
- To illustrate changes over time
- To illustrate differences in magnitude of response, particularly where more than two treatment groups are being compared
- To convey dose-response information

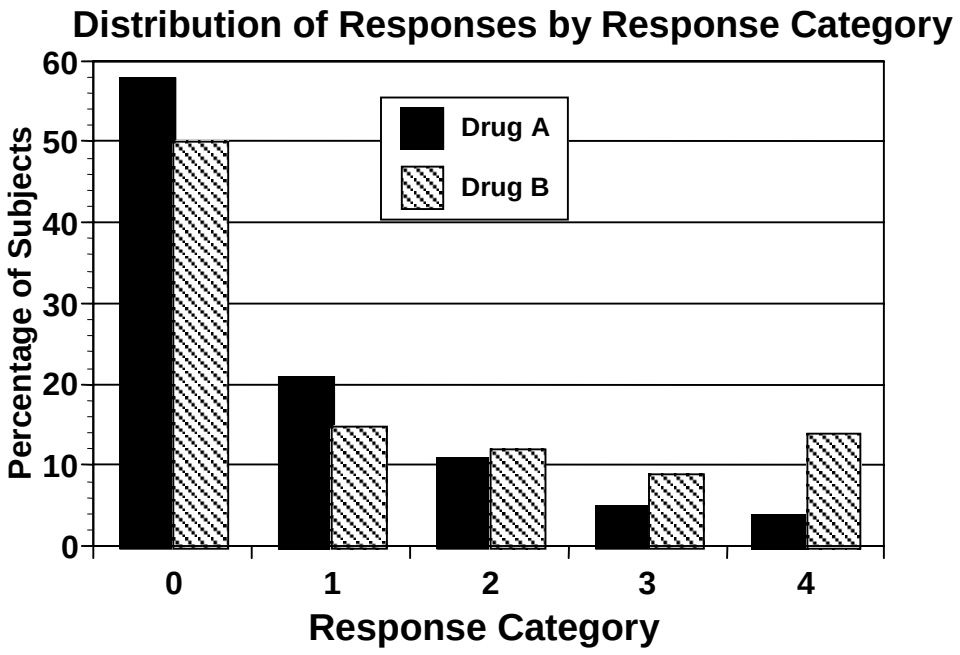
B. Graphs Most Commonly Used in the Description of Clinical Trial Effectiveness Data

Histogram



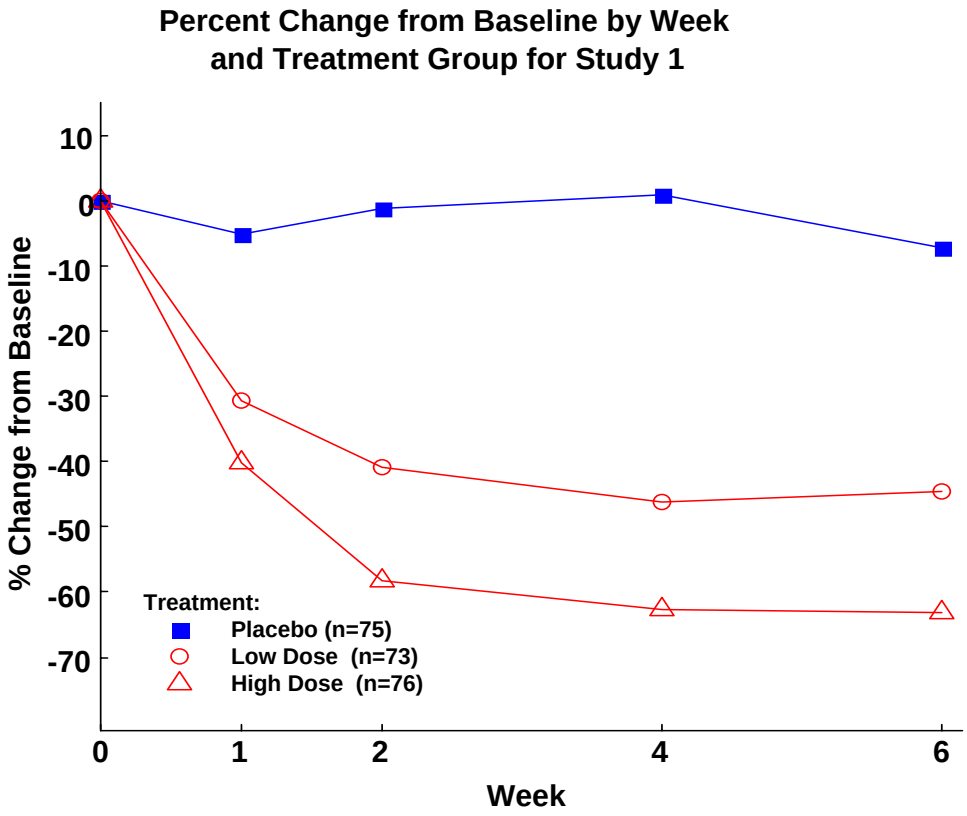
A histogram illustrates results of a trial by presenting the number or percentage of subjects (y-axis) exhibiting a given response (x-axis) over the whole response range.

Bar Graph



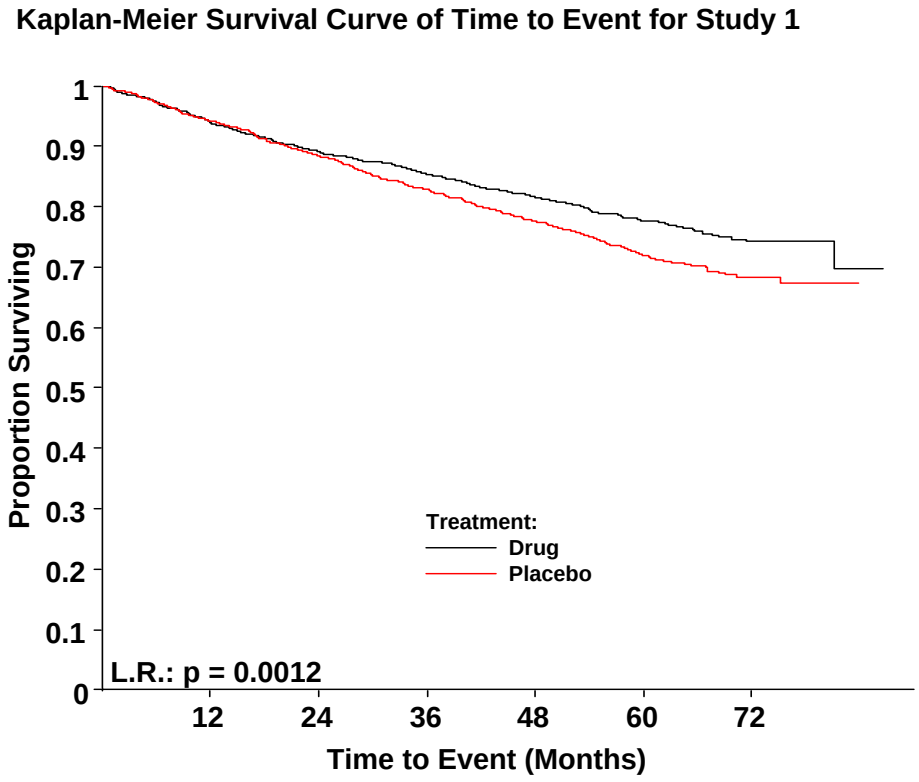
In a bar graph, the length of the bar (the y-axis) represents the group response for the outcome variable or the percentage or frequency of subjects exhibiting a categorical response. Similar graphs can be useful for comparing effects among subgroups. In this case, the response would appear on the y-axis, with various subgroups on the x-axis. In most cases, it is helpful to include error bars. A bar graph should not be used to illustrate just a few numbers that could be summarized better in a table. Graphs in 3-D should be avoided because the values for the bars are difficult to read. Stippling or other small patterns in bars should also be avoided because the bars can be difficult to differentiate after reduction or reproduction.

Line Graph



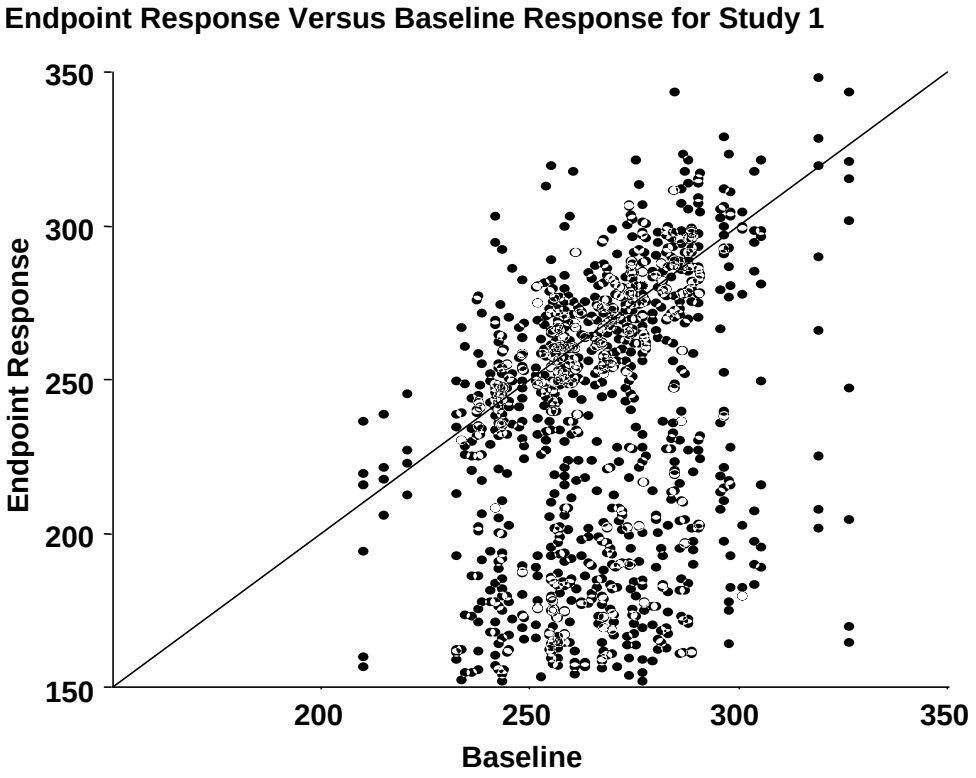
A line graph most often illustrates responses (y-axis) over time (x-axis) where each line represents the data for a defined group of subjects (e.g., a treatment group, a subgroup). It is helpful in some cases to include error bars and number of subjects remaining on study treatment at each time point. Similar graphs can be used to show dose response with response on the y-axis and dose on the x-axis.

Survival Curve



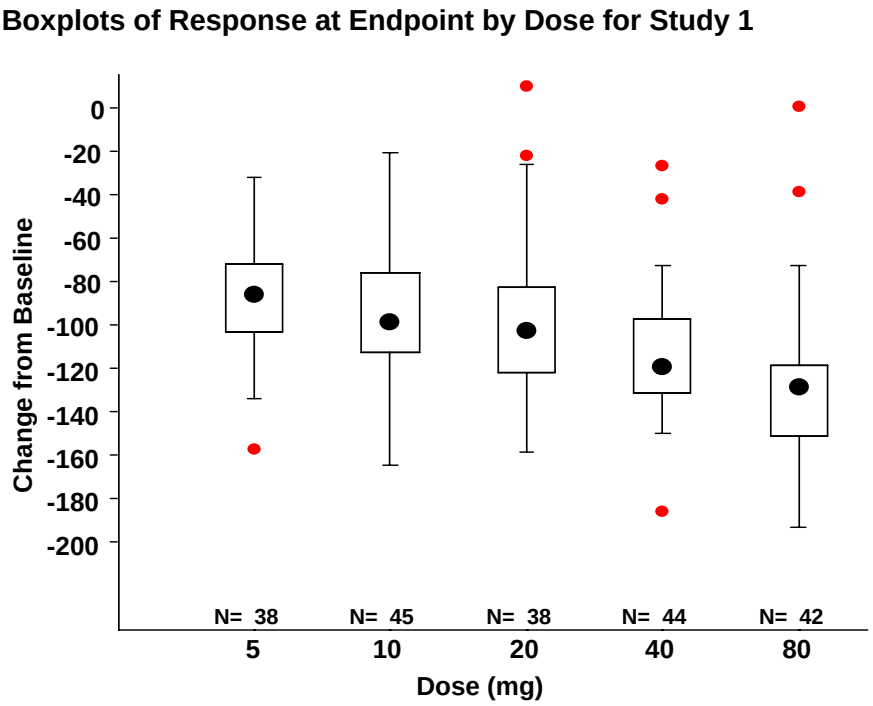
A survival curve depicts time-to-event data for events like death or recurrence of disease. Usually, Kaplan-Meier estimates of the proportion of patients surviving at any time as a fraction of people still in the study at that point are plotted, but some survival plots show the raw cumulative incidence rates as a fraction of patients randomized over time.

Scatter Plot



A scatter plot shows the relationship between two (usually continuous) variables for individual patients (e.g., response (y-axis) related to a baseline value (x-axis)).

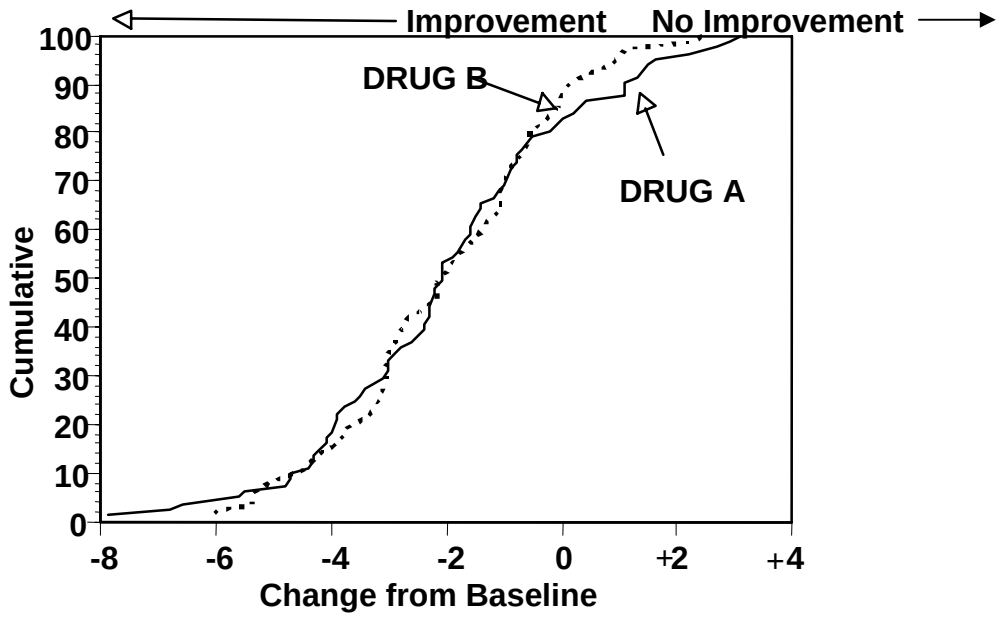
Boxplot



A boxplot illustrates the distribution of data for a single group. Several plots in a single graph are useful for comparing distributions. Boxes in this example represent the range of values from the 25th percentile to the 75th percentile. The median may be represented by a line or symbol. The definition for the length of the whiskers (lines extending out from each end of the box) varies with software packages and should be defined with the plot (e.g., the ends represent the 10th and 90th percentile).

Cumulative Distribution Plot

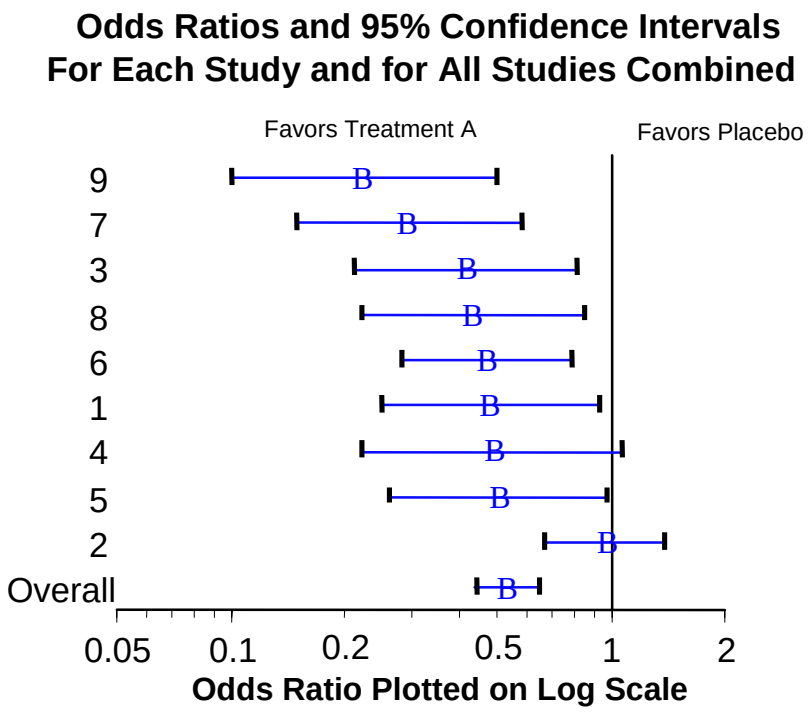
Cumulative Distribution Plot of Change From Baseline for Study 1



This graph shows the percentage of subjects (y-axis) attaining a change from baseline less than or equal to the value on the x-axis. A curve that shifts to the left indicates a better response.

A cumulative distribution plot shows the percentage of subjects with a change value equal to or less than the value on the x-axis. These distributions can be graphed using connected points, bars, or steps. A cumulative distribution plot may need a footnote and additional text in the body of the label describing how to read the graph. For example, the following text could accompany the graph shown above: "Approximately 50% of the patients in each group had a decrease of at least 2 mg/dL at endpoint."

Meta-Analytic Graph



A meta-analytic graph depicts summary results (usually a treatment difference or ratio) for several studies (or centers) on one graph. The x-axis displays the difference or ratio with a reference line at zero or one. The results are usually given with their variance or confidence interval. This graph is useful for illustrating consistency or lack of consistency across studies. Ordering the responses by magnitude or sample size enhances the visualization of the effects. Similar displays can show results in demographic or other subsets (e.g., disease severity, background therapy, country, or region) of a population.

C. Features of a Good Graph

- **Title:** The title should include the name of the study, the type of data, the timepoint, and important features of the patient population (e.g., intent-to-treat, evaluable, age range if relevant). For ease of reading, the first letter of each word should be capitalized, not every letter in the title.

- **Axis Label/Title:** Label each axis and include units of measurement.

- **Ticks and Grids:** Label selected ticks for each axis. A graph will appear less cluttered if ticks face away from the graph and if grids are eliminated.

- **Axis Scale:** Ensure that the scale of measurement (generally the y-axis) does not exaggerate the treatment effect or any other variable being measured (e.g., by interruptions). In general, make the scales for like graphs consistent within the labeling.

- **Symbols:** Distinguish symbols by size, shape, or fill (e.g., open symbols for placebo and closed symbols for treatment).

- **Footnotes:** Use a footnote if further information would be helpful to explain the content of the graph (e.g., the meaning of a term used, the meaning of a symbol). Statements directly interpreting the graph, however, should not be in a footnote, but in the text accompanying the graph.

- **Error Bars:** Measures of variability or uncertainty are represented in graphs by error bars or sometimes by shading. Make it clear from the graph which measure of variability is used to define the error bars (e.g., standard deviation, standard error, percentiles). Accompany treatment differences or ratios with confidence intervals.

- **Legend:** Ensure that the legend does not overpower the graph. Labels directly on the graph are preferable to a legend.

- **Sample Size:** Including sample sizes for each group often helps the reader interpret the graph. Sample sizes can be identified in text within the graph or in a small table just below the graph.

- **P-values:** The text or a table accompanying the graph usually will include p-values when describing the significance of the results, so it is generally not necessary or desirable to include p-values in a graph. One exception may be the plot of Kaplan-Meier survival curves where a p-value may be preferred to confidence bands and may enhance interpretation of the graph.

- **Additional Graph Descriptors:** To aid in interpretation of the graph, show reference lines for no change or no difference. Descriptors that denote change, such as an arrow labeled "Improvement" may be useful to the reader.

III. TABLES

A. Use of Tables

- To present simple, descriptive statistics such as medians, means, standard deviations, and sample sizes by treatment group
- To present comparative statistics such as treatment differences, confidence intervals, and p-values
- To summarize data from more than one effectiveness variable
- To present exact values, if that information is desirable

B. Features of a Good Table

- **Title:** Include the name of the study, the type of data, the timepoint, and the patient population (intent-to-treat, evaluable). For ease of reading, capitalize the first letter of each word, not every letter in the title.
- **Units:** Include the units of measurement for the data presented, either in the title or column headings. When presenting percentages, it is helpful to include the percent sign, particularly when several numbers are included on one line (such as mean percentages and sample sizes). Only include the number of digits after the decimal that are significant or meaningful.
- **Sample Size:** Include the sample size for each treatment group in the table.
- **Baseline Data:** Include baseline data whenever applicable.