Great Plains IDeA-CTR

Gleb R Haynatzki, PhD, DSc
Professor of Biostatistics

Introduction to Biostatistics in Comparative Research:

Making Sense of Statistics in Clinical Trial Reports

LEARNING OBJECTIVES:

1. Review the basic study designs
2. Review the approaches to reporting biostatistics for clinical trials

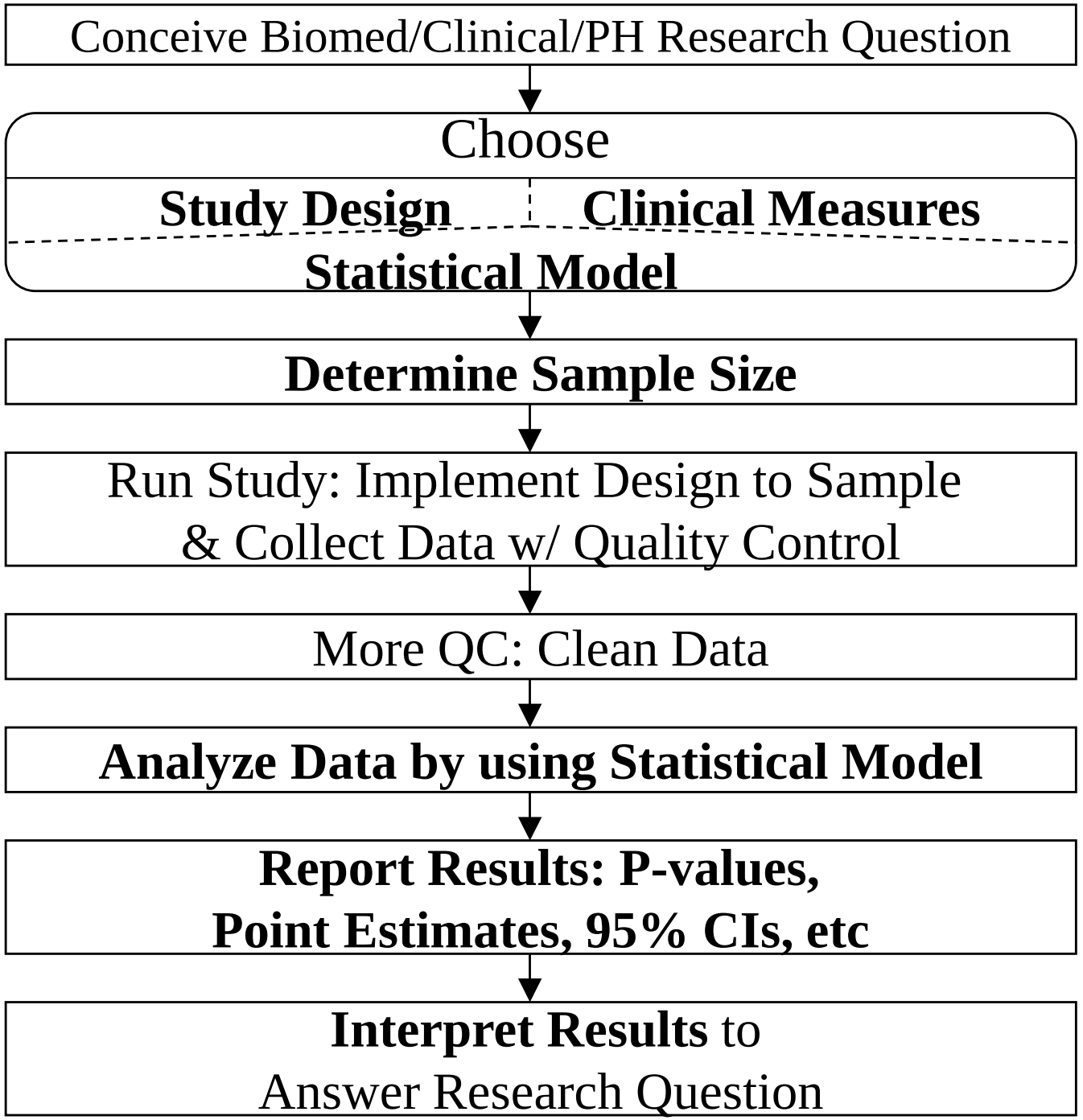
Outline

- Unraveling the complexities of statistical presentation — why it is important
- Steps in a research project — how is statistics involved in each step?
- Conducting and reporting research
- Basic study designs — review
- Making sense of statistics in clinical trial reports — the essentials of statistical analysis
- Displaying results in tables and figures
- Estimates of treatment effects and their confidence intervals (CIs)
- P-values and their interpretation
- Conclusions

Unraveling the Complexities of Statistical Presentation — Why It Is Important

- P-values can be grossly misinterpreted
- Authors often present the *relative risk* rather than the *absolute risk difference*, although the latter has more value to patients
- Ex 1: The decrease of an event rate from 4% to 2% is often reported as a “50% decrease”, which is the *relative* risk reduction, but the *absolute* decrease is just 2%.
- Ex 2: SPRINT (Systolic BP Intervention Trial), NEJM:
  - “Trial participants assigned to the lower SBP target (**intensive**-treatment group), as compared with those assigned to the higher target (**standard**-treatment group), had a 25% *lower relative risk* of the primary outcome.“
  - Actually, this is an absolute risk reduction of just 1.6%, in % of patients with a primary outcome from 6.8% (for the standard-trt group) to 5.2% (for the intensive-trt group) over a median 3.26-year follow-up.

Steps in a research project—how is **statistics** involved in each step?



Conducting and Reporting Research

Research Question (Hypothesis)

Introduction Section

Research Design/Methods

Methods Section

Data Summaries and Analyses Results

Results Section

Conclusions

Conclusions/Discussion Section

Basic Study Designs — Review (1)

I. Descriptive/qualitative studies

Case Report and **Case Series**

II. Explanatory/quantitative studies

A. Experimental

Randomized (controlled) clinical trial (RCT)*

B. Observational

1. **Cohort***
2. **Case-control** (retrospective)
3. **Cross-sectional** (at a single time point)

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*prospective study

Basic Study Designs — Review (2)
Explanatory Studies

- sample(s) $\xrightarrow{\text{inference}}$ population(s)
- group comparison

Experimental (Clinical trial): the researcher *does* something (ie, assigns treatments) to the subjects and observes the results; and *controls* random allocation of subjects to treatments; conclusion about causation is often possible

Observational (Cohort, Case-control, Cross-sectional): the researcher *observes* an existing situation but has *no* control over allocation of subjects to treatments, and *no* conclusion about causation can be made w/o additional info

Making Sense of Statistics in Clinical Trial Reports: The Essentials of Statistical Analysis (1)

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THE PRESENT AND FUTURE

STATE-OF-THE-ART REVIEW

Making Sense of Statistics in Clinical Trial Reports

Part 1 of a 4-Part Series on Statistics for Clinical Trials

Stuart J. Pocock, PhD,* John J.V. McMurray, MD,† Tim J. Collier, MSc*

Making Sense of Statistics in Clinical Trial Reports:
The Essentials of Statistical Analysis (2)

The main steps in data analysis (Pocock *et al, JACC*, 2015) are:

1. Displaying results in tables and figures
2. Quantifying any associations (eg, estimates of treatment differences in patient outcomes)
3. Expressing the uncertainty in those associations by use of confidence intervals (CIs)
4. Assessing the strength of evidence that the association is “real” (ie, more than could be expected by random chance) by using *p*-values (for statistical tests of significance)

Making Sense of Statistics in Clinical Trial Reports:
The Essentials of Statistical Analysis (3)

Abbreviations and Acronyms:

ANCOVA = Analysis of Covariance
CABG = Coronary Artery Bypass Grafting
CI = Confidence Interval
PCI = Percutaneous Coronary Intervention
RCT = Randomized Clinical Trial
SBP = Systolic Blood Pressure
SD = Standard Deviation
SE = Standard Error
IQR = Inter-Quartile Range

Displaying Results in Tables and Figures: Table of Baseline Data

PARADIGM-HF = Prospective Comparison of Angiotensin Receptor–Neprilysin Inhibitor with Angiotensin Converting–Enzyme Inhibitor to Determine Impact on Global Mortality and Morbidity in Heart Failure

TABLE 1 Characteristics of the Patients at Baseline in the PARADIGM-HF Trial

	LCZ696 (N = 4187)	Enalapril (N = 4212)
Age, yrs	63.8 ± 11.5	63.8 ± 11.3
Female	879 (21.0)	953 (22.6)
Race or ethnic group		
White	2,763 (66.0)	2,781 (66.0)
Black	213 (5.1)	215 (5.1)
Asian	759 (18.1)	750 (17.8)
Other	452 (10.8)	466 (11.1)
Region		
North America	310 (7.4)	292 (6.9)
Latin America	713 (17.0)	720 (17.1)
Western Europe and other	1,026 (24.5)	1,025 (24.3)
Central Europe	1,393 (33.3)	1,433 (34.0)
Asia-Pacific	745 (17.8)	742 (17.6)
Systolic blood pressure, mm Hg	122 ± 15	121 ± 15
Heart rate, beats/min	72 ± 12	73 ± 12
Body mass index	28.1 ± 5.5	28.2 ± 5.5
Serum creatinine, mg/dl	1.13 ± 0.3	1.12 ± 0.3

PARADIGM-HF = Prospective Comparison of Angiotensin Receptor–Neprilysin Inhibitor with Angiotensin Converting–Enzyme Inhibitor to Determine Impact on Global Mortality and Morbidity in Heart Failure

Table 1. (Cont'd) - the "middle" part of the table is not shown here.

Treatments at randomization		
Diuretic agent	3,363 (80.3)	3,375 (80.1)
Digitalis	1,223 (29.2)	1,316 (31.2)
Beta-blocker	3,899 (93.1)	3,912 (92.9)
Mineralocorticoid antagonist	2,271 (54.2)	2,400 (57.0)
Implantable cardioverter-defibrillator	623 (14.9)	620 (14.7)
Cardiac resynchronization therapy	292 (7.0)	282 (6.7)

Values are mean ± SD, n (%), or median (interquartile range). Table summarizing the characteristics at the baseline visit for patients in the PARADIGM-HF trial by treatment allocation. Adapted with permission from McMurray et al. (1).

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; NYHA = New York Heart Association; PARADIGM-HF = Prospective Comparison of Angiotensin Receptor-Neprilysin Inhibitor with Angiotensin-Converting-Enzyme Inhibitor to Determine Impact on Global Mortality and Morbidity in Heart Failure.

Displaying Results in Tables and Figures: Table of Main Outcome Events

SAVOR-TIMI 53 = Saxagliptin Assessment of Vascular Outcomes Recorded in Patients with DM–Thrombolysis In Myocardial Infarction 53

TABLE 2 Pre-Specified Clinical Endpoints in the SAVOR-TIMI 53 Trial

	Saxagliptin (n = 8,280)	Placebo (n = 8,212)	Hazard Ratio (95% CI)	p Value
Cardiovascular death, myocardial infarction, or stroke: primary efficacy endpoint	613 (7.3)	609 (7.2)	1.00 (0.89–1.12)	0.99
Cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, heart failure, or coronary revascularization: secondary efficacy endpoint	1,059 (12.8)	1,034 (12.4)	1.02 (0.94–1.11)	0.66
Death from any cause	420 (4.9)	378 (4.2)	1.11 (0.96–1.27)	0.15
Death from cardiovascular causes	269 (3.2)	260 (2.9)	1.03 (0.87–1.22)	0.72
Myocardial infarction	265 (3.2)	278 (3.4)	0.95 (0.80–1.12)	0.52
Ischemic stroke	157 (1.9)	141 (1.7)	1.11 (0.88–1.39)	0.38
Hospitalization for unstable angina	97 (1.2)	81 (1.0)	1.19 (0.89–1.60)	0.24
Hospitalization for heart failure	289 (3.5)	228 (2.8)	1.27 (1.07–1.51)	0.007
Hospitalization for coronary revascularization	423 (5.2)	459 (5.6)	0.91 (0.80–1.04)	0.18

SAVOR-TIMI 53 = Saxagliptin Assessment of Vascular Outcomes Recorded in Patients with DM–Thrombolysis In Myocardial Infarction 53

Table 2. (Cont'd).

Doubling of creatinine level, initiation of dialysis, renal transplantation, or creatinine >6.0 mg/dl (530 µmol/l)	194 (2.2)	178 (2.0)	1.08 (0.88-1.32)	0.46
Hospitalization for hypoglycemia	53 (0.6)	43 (0.5)	1.22 (0.82-1.83)	0.33

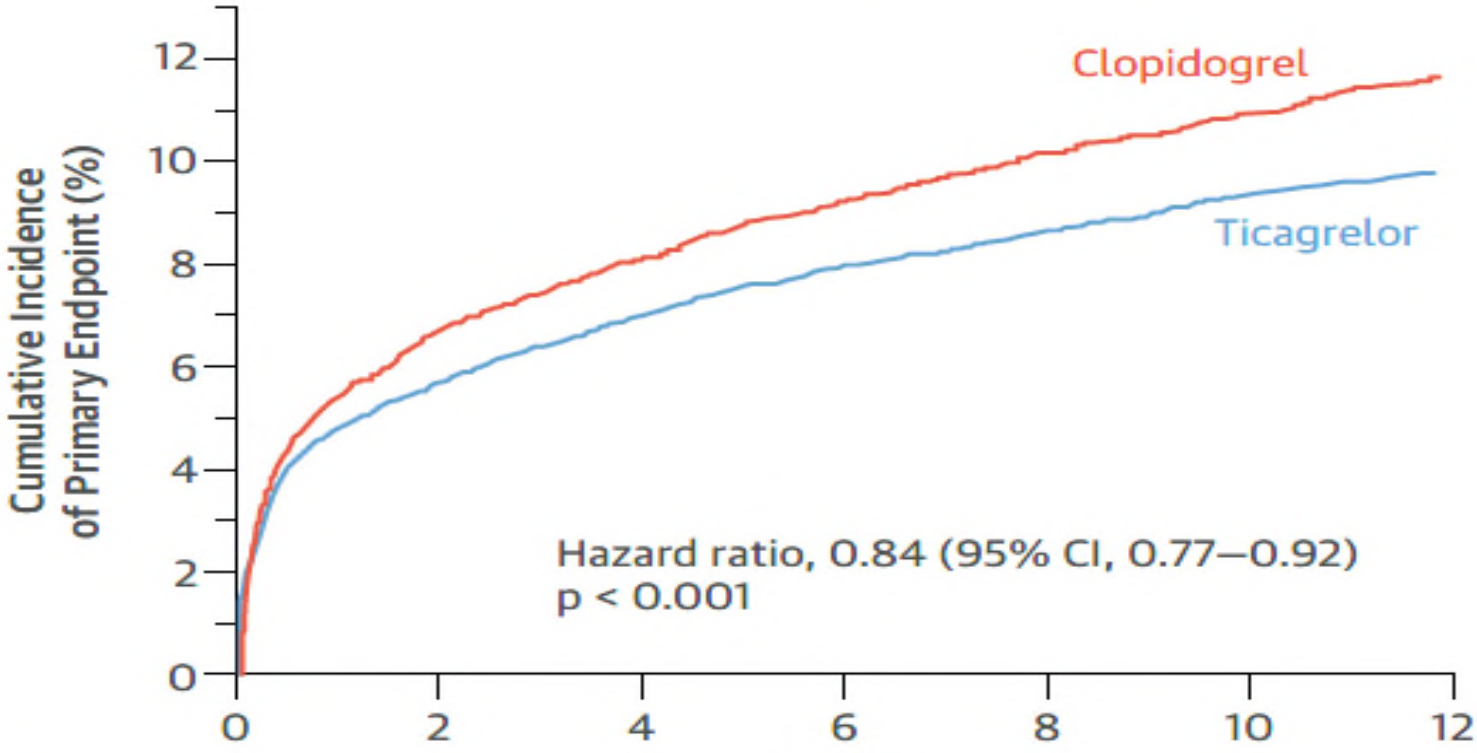
Values are n (%), unless otherwise indicated. 2-year Kaplan-Meier estimates and hazard ratios (95% confidence intervals [CIs]) for pre-specified clinical endpoints in the SAVOR-TIMI 53 trial. Percentages are 2-year Kaplan-Meier estimates. Adapted from Scirica et al. (2).

SAVOR-TIMI 53 = Saxagliptin Assessment of Vascular Outcomes Recorded in Patients with Diabetes Mellitus-Thrombolysis In Myocardial Infarction 53.

Displaying Results in Tables and Figures: Kaplan-Meier Plot

PLATO = Study of Platelet Inhibition and Patient Outcomes

FIGURE 1 Kaplan-Meier Estimates of the Cumulative Incidence Over Time of the First Adjudicated Occurrence of the Primary Efficacy Endpoint in the PLATO Trial

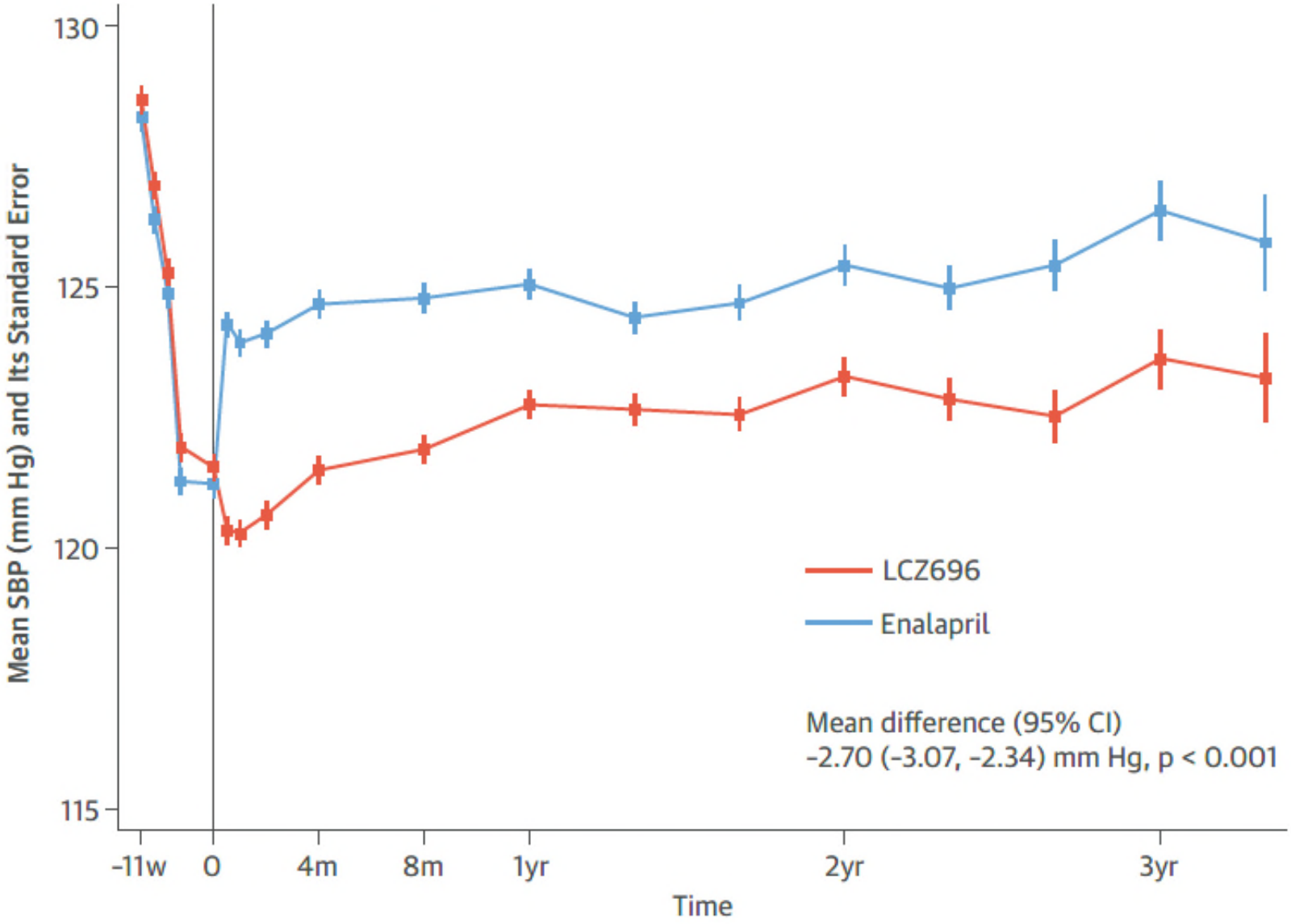


No. at Risk							
Ticagrelor	9333	8628	8460	8219	6743	5161	4147
Clopidogrel	9291	8521	8362	8124	6650	5096	4047

Cumulative incidence of the primary endpoint—a composite of death from vascular causes, myocardial infarction, or stroke—was significantly lower in the ticagrelor group than in the clopidogrel group (9.8% vs. 11.7% at 12 months; hazard ratio: 0.84; 95% confidence interval [CI]: 0.77 to 0.92; $p < 0.001$). PLATO = The Study of Platelet Inhibition and Patient Outcomes. Reprinted with permission from Wallentin et al. (5).

Displaying Results in Tables and Figures: Repeated Measures Over Time

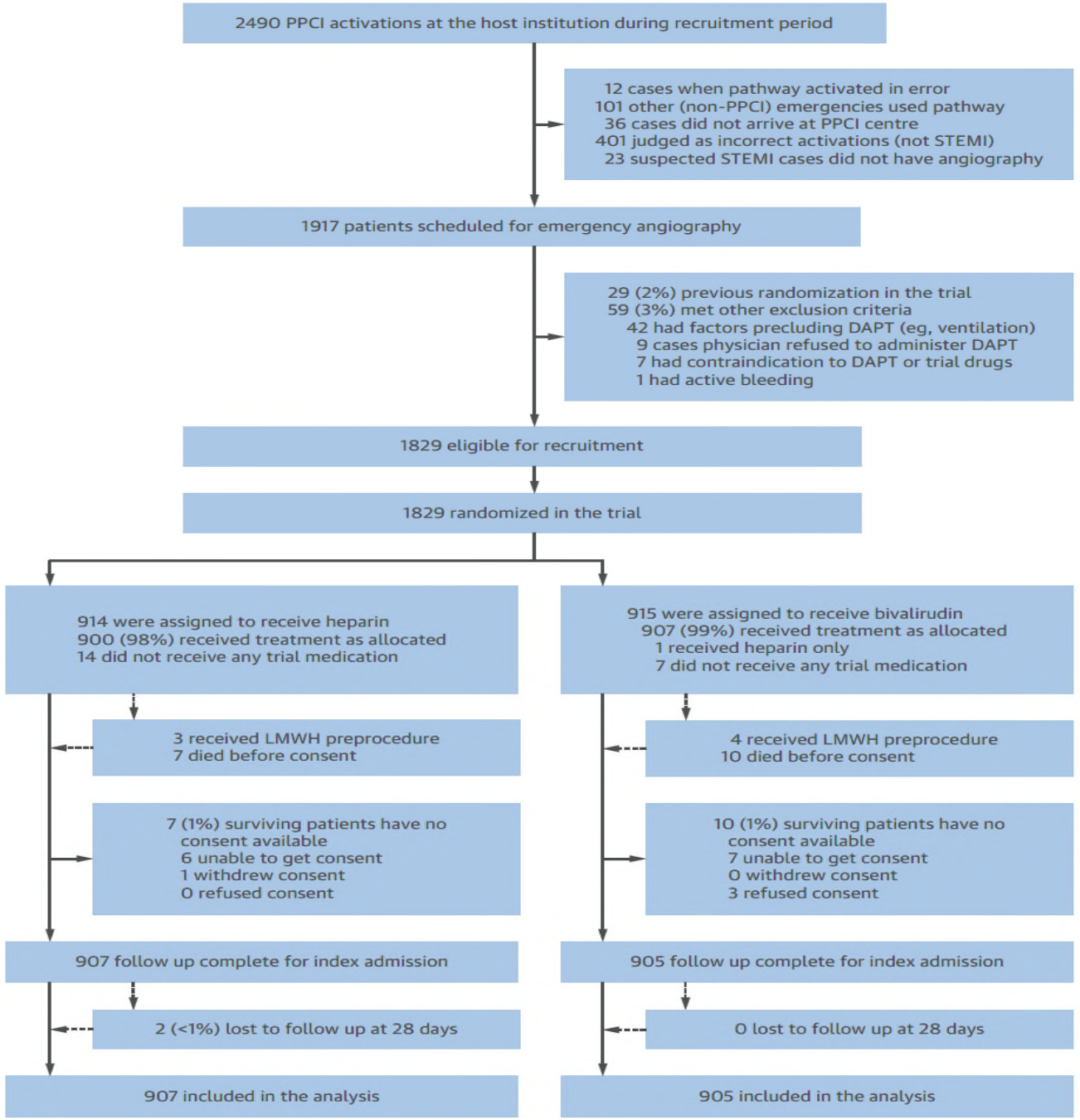
FIGURE 2 **Systolic Blood Pressure During Run-In And After Randomization in the PARADIGM-HF Trial**



Mean systolic blood pressure (SBP) by visit and treatment group, and overall mean difference (95% confidence interval [CI]) in the PARADIGM-HF trial. PARADIGM-HF = Prospective Comparison of Angiotensin Receptor-Neprilysin Inhibitor with Angiotensin-Converting-Enzyme Inhibitor to Determine Impact on Global Mortality and Morbidity in Heart Failure. Reprinted, with permission, from McMurray et al. (1).

Displaying Results in Tables and Figures: Trial Profile

FIGURE 3 **Trial Profile of the HEAT-PPCI Trial**



Trial profile for HEAT-PPCI summarizing the flow of patients through the trial from the pre-randomization recruitment period to the post-randomization follow-up and analysis. Reprinted with permission from Shahzad et al. (8). DAPT = dual antiplatelet therapy; HEAT-PPCI = How Effective Are Antithrombotic Therapies in Primary PCI; LMWH = low-molecular-weight heparin; PPCI = primary percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

Estimates of Treatment Effects and Their Confidence Intervals (CIs)

Estimates of Treatment Effects and Their Confidence Intervals (CIs): General Ideas

-1) Obtain a *point estimate*, ie, the actual difference observed.
-2) Express the *degree of uncertainty* present in the data, ie, the bigger the trial, the more precise the point estimate; usually expressed as a 95% *CI*.

The type of estimate depends on the nature of the patient outcome:

1. A *binary* (yes/no) *response*, eg, success or failure, dead or alive, or the composite in a trial ("death, MI, ischemia-driven revascularization, or stent thrombosis"; ie, did any of these occur within 48 h of randomization in percutaneous coronary intervention [PCI] patients, yes or no?
2. A *time-to-event outcome*, for example, time-to-death, time-to-symptom relief, or in a trial, the time-to-"first hospitalization for heart failure or cardiovascular death", whichever (if either) happens first.
3. A *quantitative outcome*, eg, change in SBP from randomization to 6 months later.

Estimates of Treatment Effects and Their Confidence Intervals (CIs): Estimates Based on Percentages

TABLE 3 Estimates Based on the Comparison of 2 Percentages, Illustrated by the Primary Outcome* of the CHAMPION-PHOENIX Trial

	Cangrelor	Clopidogrel
Randomized patients, n	5,470	5,469
Patients with primary outcome, n (%)	257 (4.698)†	322 (5.888)†

Estimate	Formula	Result
Relative risk (95% CI)	$\frac{4.698}{5.888}$	= 0.798 (0.680 to 0.936)
Relative risk reduction (95% CI)	$(1 - 0.798) \times 100$	= 20.2% (6.4% to 32.0%)
Relative odds (95% CI)	$\frac{4.698/(100 - 4.698)}{5.888/(100 - 5.888)}$	= 0.788 (0.666 to 0.932)
Difference in percentages (95% CI)	$4.698 - 5.888$	= −1.19% (−0.35% to −2.03%)
Number needed to treat (95% CI)	$\frac{100}{1.19}$	= 84.0 (49.3 to 285.7)

Number and percentage of patients with a primary outcome (death, myocardial infarction, ischemia driven revascularization, or stent thrombosis within 48 h of randomization) in the CHAMPION-PHOENIX trial along with various estimates of treatment effect. *Primary composite outcome is death, myocardial infarction, ischemia-driven revascularization, or stent thrombosis within 48 h of randomization. †In the middle of all numerical calculations, any values (e.g., percentages) should be precise (e.g., to ≥3 decimal places). Only at the final step should values be rounded for convenience of expression.

CHAMPION-PHOENIX = Cangrelor versus Standard Therapy to Achieve Optimal Management of Platelet Inhibition PHOENIX trial; CI = confidence interval.

Estimates of Treatment Effects and Their Confidence Intervals (CIs): Expressing Uncertainty Using CIs

TABLE 3 Estimates Based on the Comparison of 2 Percentages, Illustrated by the Primary Outcome* of the CHAMPION-PHOENIX Trial

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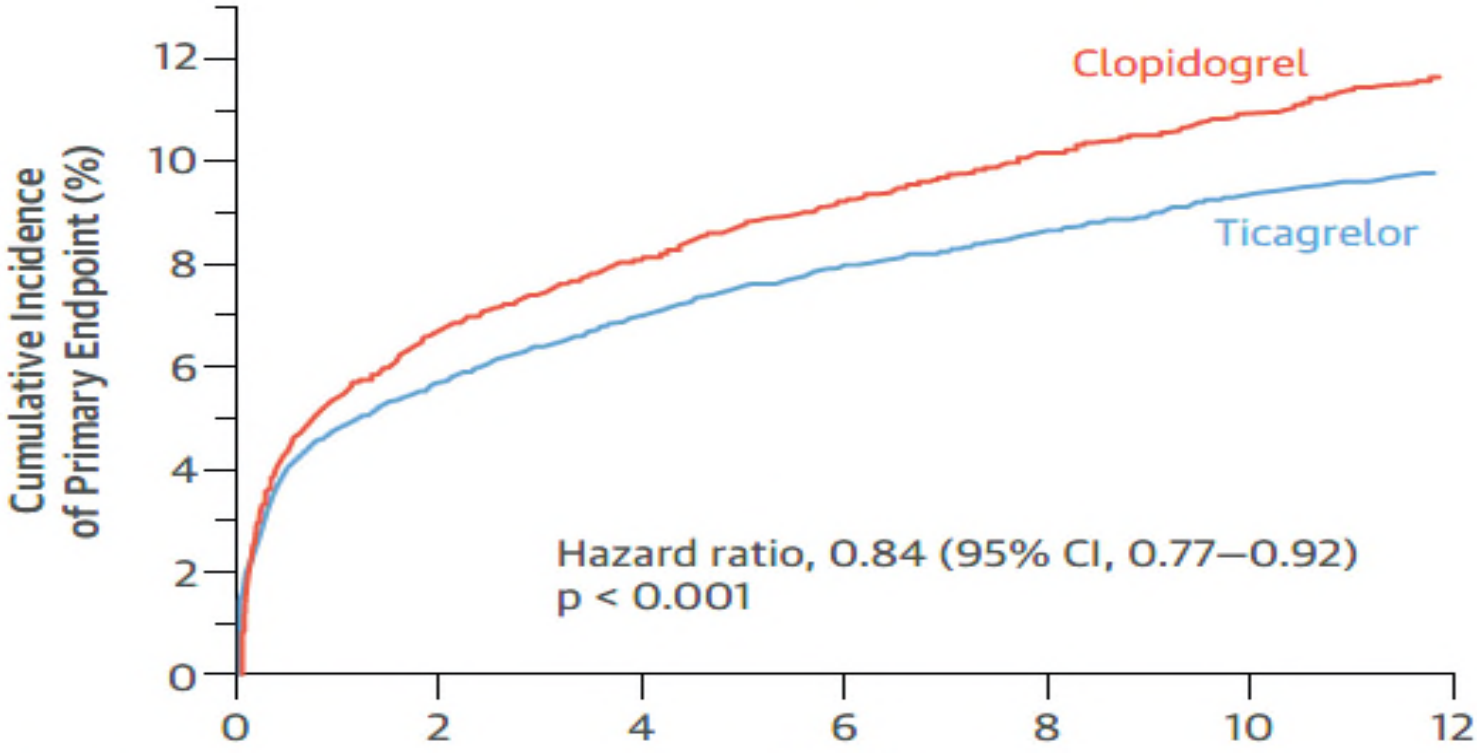
Estimates of Treatment Effects and Their Confidence Intervals (CIs): Estimates for Time-to-Event Outcomes

PLATO = Study of Platelet Inhibition and Patient Outcomes

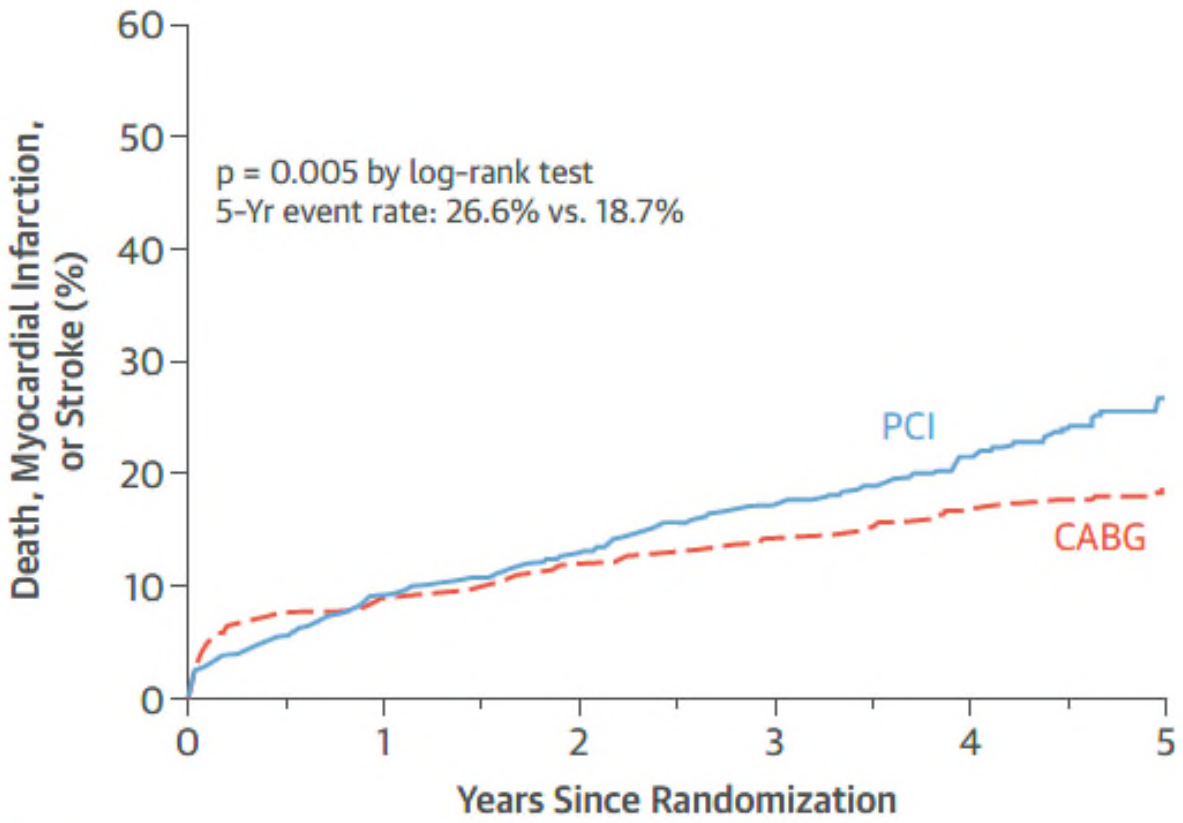
FIGURE 1 Kaplan-Meier Estimates of the Cumulative Incidence Over Time of the First Adjudicated Occurrence of the Primary Efficacy Endpoint in the PLATO Trial



No. at Risk							
Ticagrelor	9333	8628	8460	8219	6743	5161	4147
Clopidogrel	9291	8521	8362	8124	6650	5096	4047

Cumulative incidence of the primary endpoint—a composite of death from vascular causes, myocardial infarction, or stroke—was significantly lower in the ticagrelor group than in the clopidogrel group (9.8% vs. 11.7% at 12 months; hazard ratio: 0.84; 95% confidence interval [CI]: 0.77 to 0.92; $p < 0.001$). PLATO = The Study of Platelet Inhibition and Patient Outcomes. Reprinted with permission from Wallentin et al. (5).

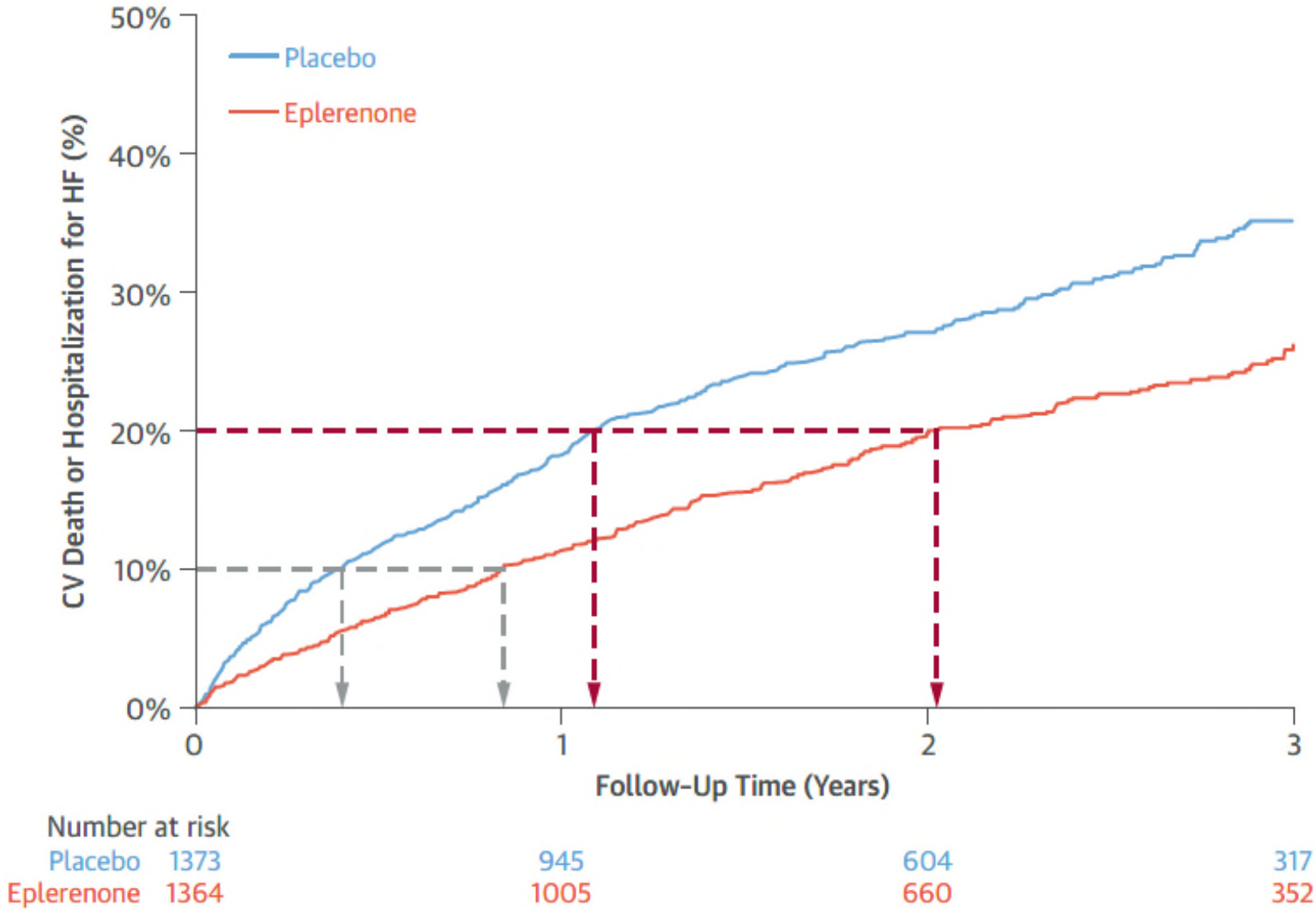
FIGURE 4 **Kaplan-Meier Estimates of the Cumulative Incidence Over Time of the Primary Efficacy Endpoint in the FREEDOM Trial**



No. at Risk						
PCI	953	848	788	625	416	219
CABG	947	814	758	613	422	221

Kaplan-Meier estimates of the cumulative incidence of the primary efficacy endpoint (death, myocardial infarction, or stroke) by treatment group in the FREEDOM trial. FREEDOM = Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease. Reprinted with permission from Tepel et al. (25). CABG = coronary artery bypass graft; PCI = percutaneous coronary intervention.

FIGURE 5 Time to Primary Event in the EMPHASIS-HF Trial



Kaplan-Meier cumulative incidence of cardiovascular (CV) death or hospitalization for heart failure (HF) in the EMPHASIS-HF trial. The eplerenone and placebo groups reach 10% incidence at 0.84 and 0.40 years, respectively, a time ratio of 2.10. The 20% incidence occurs at 2.02 and 1.09 years, respectively, a time ratio of 1.86. EMPHASIS-HF = Eplerenone in Mild Patients Hospitalization and Survival Study in Heart Failure.

Estimates of Treatment Effects and Their Confidence Intervals (CIs): Estimates for Quantitative Outcomes

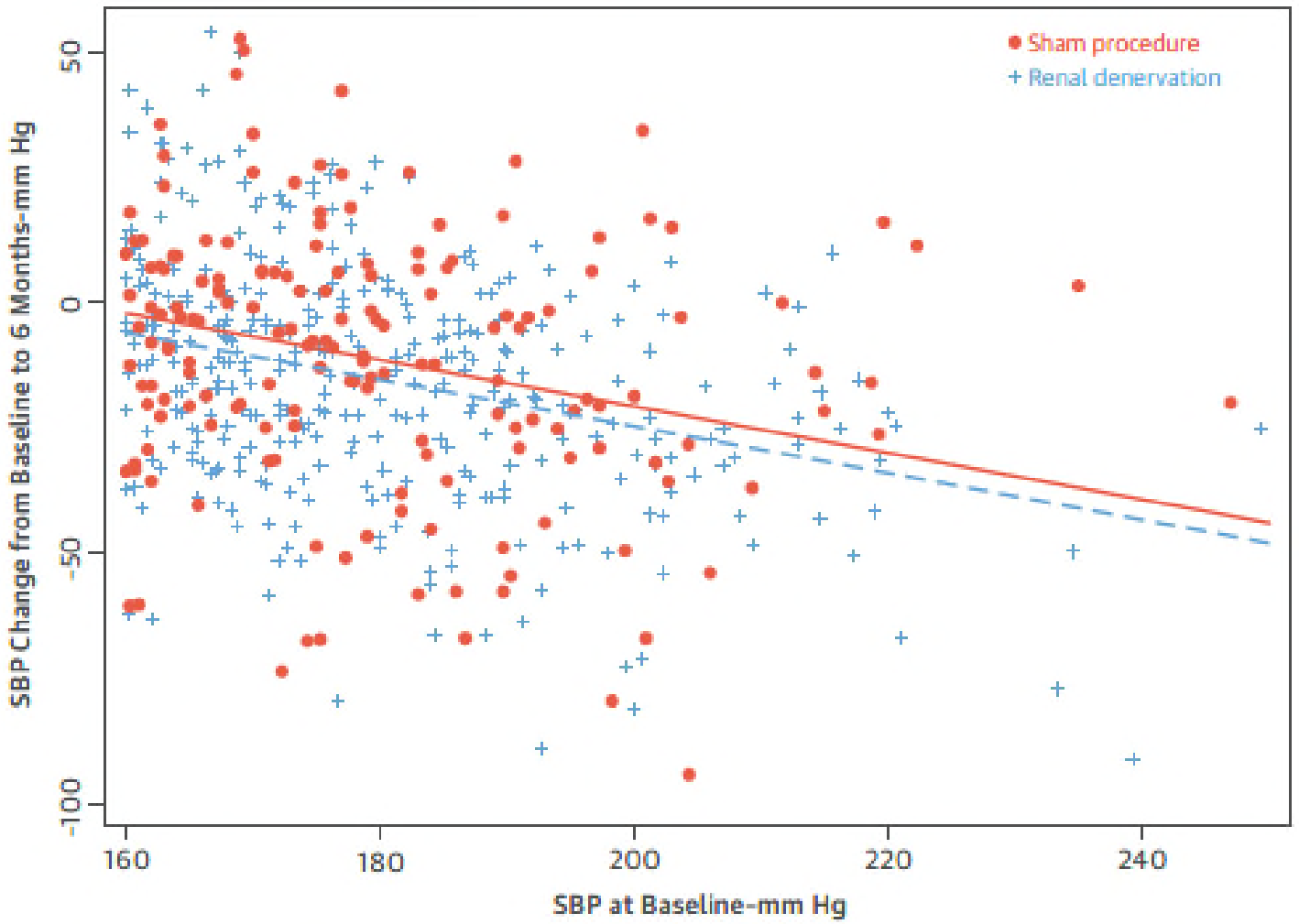
TABLE 4 6-Month Results From the SYMPLICITY HTN-3 Trial

SBP at 6 months	−4.20 (−9.17 to +0.77)
6-month change in SBP	−4.07 (−8.63 to +0.49)
6-month change in SBP adjusted for baseline SBP using ANCOVA	−4.11 (−8.44 to +0.22)

Values are mean treatment difference (95% confidence interval) in mm Hg. Three different methods of analyzing 6-month systolic blood pressure (SBP) results from the SYMPLICITY HTN-3 trial of renal denervation versus a sham procedure.

ANCOVA = analysis of covariance; SYMPLICITY HTN-3 = Renal Denervation in Patients With Uncontrolled Hypertension.

FIGURE 6 **Analysis of Covariance for Change in SBP in the SYMPLICITY HTN-3 Trial**



Individual 6-month change in systolic blood pressure (SBP) by baseline SBP by treatment group from the SYMPLICITY 3 trial. The **2 drawn parallel regression lines** show the anticipated regression to the mean, that is, patients with a higher baseline SBP (in both treatment groups) tend to have a greater blood pressure reduction compared with those nearer the minimum inclusion criteria of 160 mm Hg. The vertical distance between the 2 regression lines is 4.11 mm Hg, the mean treatment effect adjusted for baseline. SYMPLICITY HTN-3 = Renal Denervation in Patients With Uncontrolled Hypertension.

P-values and Their Interpretation: General Ideas

P-values and Their Interpretation: General Ideas

-Explaining p-values until after descriptive statistics, estimation, and CIs, is both natural and also an attempt to counter the obsessive tendency for people to classify a clinical trial into “positive” or “negative” depending on whether or not the primary endpoint achieves $p < 0.05$.

-Such oversimplification is an abuse of the p-value, which can be a valuable statistical tool when interpreted appropriately.

-Alongside an estimate of a treatment difference and its 95% CI, the corresponding p-value is the most succinct direct way to express the extent to which it is a real treatment effect (or, rather, an artefact).

-At the core of any (superiority) significance test is the *null hypothesis* that the 2 treatments are identical in their effect on the outcome.

-The p-value is the probability of obtaining a treatment difference at least as great (in either direction) as that actually observed if the null hypothesis were true. The smaller the p-value, the stronger the evidence against the null hypothesis; ie, the more convincing the evidence that a genuine treatment difference exists.

P-values and Their Interpretation: Some Details

P-values and Their Interpretation: Some Details (1)

Interpretation of a “positive” trial rests on more than just a significant – value.

1. Give the actual p-value (ie, p = 0.042 rather than p < 0.05 or crudely “significant,” or p = 0.061 rather than “not significant”).
2. Recognize the link between the p-value and the 95% CI for the treatment difference. If the 95% CI includes no difference, that is, 0 on an absolute scale (eg, % or mean difference) or 1 on ratio scale (eg, relative risk or hazard ratio), then we know p > 0.05. Conversely, if the 95% CI does not contain the null value, then we know p < 0.05.
3. It is best to use 2-sided p-values. That is, under the null hypothesis, p is the probability of getting a difference in either direction as big as (or bigger) than that observed. Occasionally, people will argue that they are only interested in 1 direction of treatment effect (new treatment superior) and, hence, should be allowed to halve the p value *via* a 1-sided test. This practice produces an inconsistency across trial reports and makes it too easy to achieve p < 0.05.
4. A small p-value clarifies that an observed treatment difference appears greater than what could be attributed to chance, but this does not automatically mean that a real treatment effect is occurring.

P-values and Their Interpretation: Some Details (2)

5. There is an important distinction between *statistical significance* and *clinical relevance* of a treatment effect. Here, the magnitude of treatment difference and its CI are a guide as to whether the benefit of a new treatment is sufficiently great to merit its use in clinical practice.
6. For a *small trial* to reach a statistically significant treatment effect, the magnitude of treatment difference needs to be very large. For instance, a trial of acetylcysteine versus placebo to prevent contrast-induced nephropathy reported 1 of 41 and 9 of 42 acute reductions in renal failure ($p = 0.01$). This finding has a risk ratio of 0.11 with a very wide 95% CI: 0.015 to 0.859. The observed result is “too good to be true.” A comparable small trial with a nonsignificant finding would doubtless not have been published in a major journal. Thus, publication bias, that is, the tendency for published trials to exaggerate treatment effects, is accentuated when trials are small.
7. Here we discuss the interpretation of p-values (and CIs) for trials whose purpose is to determine if one treatment is superior to another (aka *superiority trial*). For *non-inferiority trials*, with the goal of seeing if a new treatment is as good as the control, interpretation is somewhat different.

P-values and Their Interpretation: Examples

TABLE 7 4 Examples Using z

Trial Name (Ref. #)	Patients With an Event (n)				
	Control (a)	New Treatment (b)	z $\frac{a-b}{\sqrt{a+b}}$	p Value	Interpretation
PARADIGM-HF (1)	1,117	914	4.50	<0.00001	Overwhelming evidence
CHAMPION-PHOENIX (9)	322	257	2.70	0.007	Strong evidence
IMPROVE-IT (20)	2,742	2,572	2.33	0.02	Some evidence
ASTRONAUT (21)	214	201	0.64	0.52	No evidence

ASTRONAUT = Aliskiren Trial on Acute Heart Failure Outcomes; IMPROVE-IT = Examining Outcomes in Subjects With Acute Coronary Syndrome: Vytorin (Ezetimibe/Simvastatin) vs Simvastatin (P04103); other abbreviations as in Tables 1 and 3.

TABLE 4 6-Month Results From the SYMPLICITY HTN-3 Trial

SBP at 6 months	−4.20 (−9.17 to +0.77)
6-month change in SBP	−4.07 (−8.63 to +0.49)
6-month change in SBP adjusted for baseline SBP using ANCOVA	−4.11 (−8.44 to +0.22)

Values are mean treatment difference (95% confidence interval) in mm Hg. Three different methods of analyzing 6-month systolic blood pressure (SBP) results from the SYMPLICITY HTN-3 trial of renal denervation versus a sham procedure.

ANCOVA = analysis of covariance; SYMPLICITY HTN-3 = Renal Denervation in Patients With Uncontrolled Hypertension.

Conclusions

CENTRAL ILLUSTRATION **Practical Guide to the Essentials for Statistical Analysis and Reporting of Randomized Clinical Trials**

THE FOUR MAIN STEPS IN DATA ANALYSIS AND REPORTING FOR CLINICAL TRIALS

1 What to include in result tables and figures

Characteristic
Age (yrs)
Female, n (%)
Previous myocardial infarction (MI), n (%)
Race, n (%)
Black, white, asian, other...

Table of Baseline Data

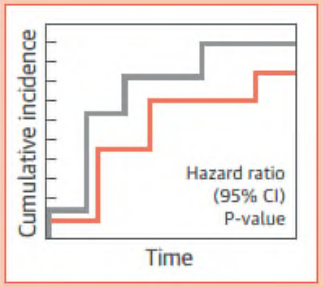
First table for any clinical trial report

- Total nos. of patients per group
- Key demographic variables
- Related medical history
- Other endpoint-related variables

Endpoint
Cardiovascular death
Death from any cause
MI
Ischemic stroke
Repeat hospitalization
Hospitalization for heart failure

Table of Main Outcome Events

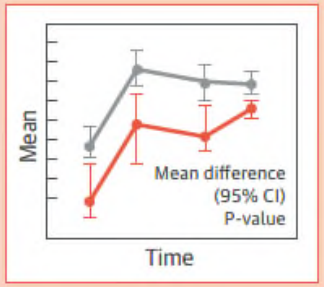
- Main outcome by group
- Nos. (%) experiencing endpoint by group
- For composite endpoints report nos. (%) experiencing each component event
- Analysis of first and subsequent events



Kaplan-Meier Plot of cumulative incidence over time, by group

Common figure in major trial reports

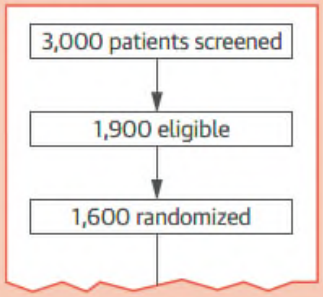
- Focus on cumulative incidence
- Sensible vertical axis range
- Report number at risk over follow-up time



Repeated Measures Over Time

Figure to show change in mean over time by group

- Standard error bars to express uncertainty



Trial Profile

Flow of patients through trial

- Nos. of eligible patients identified
- Nos. randomized into trial
- Nos. lost to follow-up
- Nos. included in analysis

2 Quantify associations

Estimate treatment effect (numerous methods):

- Relative risk/relative odds for binary outcomes
- Relative risk reduction
- Absolute difference in percentage
- Number Needed to Treat (NNT)
- Hazard ratio for time-to-event outcomes
- Mean difference using ANCOVA for quantitative outcomes

3 Express uncertainty

Confidence interval

Estimates will always have built-in imprecision because of the finite sample of patients studied

- Always acknowledge a degree of uncertainty (95% confidence interval, "95% CI")
- Larger studies provide more reliable estimates with tighter confidence intervals (i.e., 99% CI)

4 Assess evidence

P values and interpretation

Determine whether there is real treatment effect

The *smaller* the value of P the *stronger* the evidence to contradict the null hypothesis of no true treatment difference

- Report actual p value, i.e., p = 0.042
- Note if p value meets significance level ($p < 0.05$)
- Use two-sided p values

Pocock, S.J. et al. J Am Coll Cardiol. 2015; 66(22):2536-49.

ANCOVA = analysis of covariance; CI = confidence interval; NNT = number needed to treat.

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