SDAC Sample Report

Beta-Blocker Heart Attack Trial (BHAT)

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Statistical Data Analysis Center

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Contents

List of Figures

Part I

Introduction

1 BHAT Protocol and Procedures

The β-Blocker Heart Attack Trial (BHAT) was a National Heart, Lung and Blood Institute (NHLBI) sponsored, randomized, double-blind, placebo-controlled, multi-center trial designed to test whether the regular administration of propranolol hydrochloride to men and women who had experienced at least one myocardial infarction (MI) would result in a significant reduction in total mortality during a two- to four-year follow-up period. The BHAT results were initially published in the 1982 paper:

> "β-Blocker Heart Attack Trial Research Group: A Randomized Trial of Propranolol in Patients with Acute Myocardial Infarction. I. Mortality Results. β-Blocker Heart Attack Trial–Final Report." *Journal of the American Medical Association (JAMA)* 247:1707-1714, 1982.

This sample report, prepared by the Statistical Data Analysis Center (SDAC) at the University of Wisconsin–Madison, is based on the data available at the final closing of the database in June, 1984.

Treatment Arms

A total of 3,837 patients were enrolled and randomized to one of the following groups:

- Propranolol hydrochloride, oral tablets, 20 mg initial dose followed by 40 mg tid for one month, then titrated to 60 mg tid or 80 mg tid based on serum propranolol level
- Placebo, oral tablets, titrated in a similar fashion to maintain blind.

Primary Outcome

The primary outcome of the study was all-cause mortality. The primary analysis compared survival times of patients in the two treatment groups through the study duration, using a logrank test.

Study Procedures

Screening for study participants began in June, 1978 and continued through October, 1980. Patients were recruited by 31 clinical centers from 134 participating hospitals (coronary care units). Candidates for enrollment were men and women between the ages of 30 and 69 who were hospitalized with a documented acute MI and who survived at least five days after admission. Patients were excluded from the study if they had contraindications to the use of propranolol; a life-threatening illness other than coronary heart disease (CHD); had undergone or were likely to undergo cardiac surgery; were already taking β-blockers or were likely to have β-blockers prescribed to them; or if the qualifying MI resulted from a non-atherosclerotic cause.

Eligible patients who gave consent to participate were given a baseline reference examination prior to hospital discharge, but not later than 21 days following admission. Upon completion of the exam, patients were randomized to either the propranolol or placebo group. An oral tablet (20 mg of propranolol hydrochloride or matching placebo) was given immediately; if no adverse reactions were noted, the dose was increased to 40 mg every eight hours. After a minimum of six consecutive doses on this schedule, blood was drawn and sent to a central laboratory for a determination of serum propranolol level. Based on this level, patients were prescribed a dose of either 60 mg or 80 mg three times a day. (Placebo patients were given similar regimens in proportion to the dose assignments in the propranolol group.) Of the 3,837 enrolled patients, 82% were assigned the 180-mg/day regimen and 18% were assigned the 240-mg/day regimen.

The initial post-discharge visit took place one month following randomization, at which time the health status of the patient was evaluated and the assigned dosing schedule was introduced. Subsequent visits were scheduled for six weeks and three months following randomization, and every three months thereafter. At each visit, adherence to study drug, side effects, health status, the use of non-study medication and occurrence of non-fatal events were monitored.

Data Flow

A Clinic Coordinator at each of the participating Clinical Centers was responsible for appointment scheduling, maintaining good patient adherence, checking the completeness of the BHAT study forms and monitoring the shipment of blood samples and ECGs. A single Central Laboratory (Bio-Science Laboratories; Van Nuys, CA) performed all laboratory tests for the study. A Resting ECG Reading Center (University of Minnesota; Minneapolis, MN) read and coded all of the standard ECGs collected during the study, while an Ambulatory ECT Reading Center (Anthropometrics Heart Clinic; Haddonfield, NJ) read and coded the baseline Holter recordings. A Coordinating Center, located at the University of Texas in Houston, had the responsibility of collecting, editing, analyzing and storing all data from the Clinical Centers, ECG Reading Centers and Central Laboratory.

Clinical Centers were responsible for notifying the Coordinating Center of the deaths of patients within 48 hours of their discovery. A Mortality Classification Subcommittee adjudicated, with treatment group masked, the cause of death in all patients (for secondary endpoint analyses).

Interim Analysis

Approximately every six months during the conduct of the trial, the Coordinating Center prepared confidential interim analyses of the accumulating study data for a Data Monitoring Committee (in this study, referred to as the Policy and Data Monitoring Board, or PDMB). The PDMB was responsible for reviewing the study results by treatment group and evaluating the study treatment for beneficial and adverse effects.

Seven scheduled interim analyses of efficacy (all-cause mortality) were planned. To account for repeated testing, the logrank statistic for the primary endpoint analysis was compared to critical

values corresponding to an O'Brien-Fleming interim monitoring boundary with an overall two-sided significance level of 5%, based on equivalent numbers of deaths between each of the seven analyses. At the sixth interim analysis in October, 1981, the logrank statistic for the difference in mortality exceeded the O'Brien-Fleming boundary for the first time. After consideration of a number of other issues, including the magnitude of the effect, consistency of results across subgroups and completeness of follow-up, the PDMB recommended to the NHLBI that the trial be terminated early due to an observed beneficial treatment effect.

2 Overview of Report

This report has been prepared by the Statistical Data Analysis Center (SDAC) at the University of Wisconsin, Department of Biostatistics and Medical Informatics. The purpose of this report is to demonstrate the structure and content of a typical interim monitoring report prepared by SDAC with an illustrative subset of graphics and analyses. It is not intended to be a comprehensive presentation of the BHAT data.

Report Production

Analyses for the report were performed using SAS (SAS Institute Inc.). Results were processed with S-PLUS (MathSoft Inc.) to create the figures and with LaTeX (Leslie Lamport, *LaTeX: A Document Preparation System*, Addison-Wesley, 1986) to compile the report.

Report Versions

There are typically two versions of an interim monitoring report. The *Open* Session Report summarizes the data without regard to assigned treatment and is intended for use in an open session or by anyone involved in the conduct of the study at the discretion of the sponsors or the Data Monitoring Committee (DMC). The *Closed* Session Report includes comparisons by assigned treatment and should only be viewed in closed session by the DMC, the statistical analysis (or coordinating) center, or others determined by the DMC.

This sample report includes analyses by assigned treatment and is representative of a Closed Session Report. Part IV, *Ancillary Material*, contains examples of graphical displays that would appear in an Open Session Report.

Abbreviated Report Outline

- Introduction
- Accrual
- Baseline Characteristics

- Adverse Events
- Primary Endpoint Analysis
- Additional Follow-Up Measures
- Supporting Material
- Ancillary Material

List of Abbreviations

AE	Adverse Event
ASHD	Atherosclerotic Heart Disease
BHAT	β-Blocker Heart Attack Trial
BP	Blood Pressure
CHD	Coronary Heart Disease
CRF	Case Report Form
CV	Cardiovascular
DMC	Data Monitoring Committee
ECG	Electrocardiogram
mg tid	milligrams three times daily
MI	Myocardial Infarction
NHLBI	National Heart, Lung and Blood Institute
PDMB	Policy and Data Monitoring Board
SAE	Serious Adverse Event
SDAC	Statistical Data Analysis Center
WBC	White Blood Count

Sources of Data Included in Report

This report is based on a single dataset supplied by the NHLBI consisting of data available at the final closing of the BHAT database in June, 1984.

During an ongoing clinical trial, the study database is comprised of many individual datasets, which are frozen and transferred to SDAC at a point in time for the preparation of an interim monitoring report. The date and source of the data transfer, the names of datasets included in the transfer, and the specific CRFs associated with each of the datasets would be described in this section of the *Introduction.* Any other sources of data utilized in the report (such as endpoint information received independently at SDAC as a form of verification) would also be described here.

3 Report Structure

Treatment Labels

In a typical Closed Session Report, treatment groups are indicated by “A” and “B”. The assignment of code to study drug is not usually provided in the report, but is consistent throughout the trial.

In this sample report, the treatment group designations are as follows:

- Group A – propranolol hydrochloride ($n = 1,916$)
- Group B – placebo ($n = 1,921$).

P-values

P-values for treatment comparisons are given as “pA.B”. These p-values should be interpreted cautiously, since no adjustment has been made for multiple comparisons. Given the large number of comparisons considered, we would expect that a number of p-values would appear statistically significant (< 0.05) simply by chance. In studies with more than two treatment arms, p-values for multiple contrasts can be displayed.

P-values for continuous data are computed using the non-parametric Wilcoxon Rank Sum test with no stratification by site. This test is appropriate for data with non-normal distributions and has power near that of the Student t-test when the data are normal. Wilcoxon tests are also used for data which are ordered categorical (e.g., amount of cigarette smoking). For dichotomous and unordered categorical data (e.g., location of MI), the Pearson chi-square test is used. A logrank test is used to compare the distributions of survival times when Kaplan-Meier survival curves are displayed.

Graphical Conventions

The primary mode of presentation in this report is graphical. The visual presentation is intended to allow the reviewer to examine easily the distribution of the variables and characterize the study population at a glance. Treatment comparisons, both at baseline and over time, are easily examined, as are time-related trends in the data. The majority of figures present categorical data as bar charts representing the percent of patients falling into a particular category, or continuous data represented as boxplots.

Bar chart. Bar charts indicate for categorical data the number or percent of patients by category. Several types of bar charts are used. Simple bar charts display categorical variables with mutually exclusive categories, as in the plots for gender and location of MI in Figure BASE–1 on page 18.

Multiple bar chart. Bar charts of related dichotomous variables are sometimes grouped together to form a multiple bar chart, as in the graphic for medical history of coronary artery disease, Figure BASE–2 on page 19.

Stacked bar chart. A more detailed bar chart is used to display the cumulative frequency distribution of subjects across a set of ordered or nested categories, as in the display of cigarette smoking by follow-up year, Figure FU–4 on page 33.

Boxplot. Boxplots indicate the distribution of continuous data by means of percentiles. The top and bottom edges of the box represent the 25^{th} and 75^{th} percentiles of the data. The 5^{th} and 95^{th} percentiles are represented by the "whiskers" extending from the top and bottom of the box. The plotting symbol inside the box represents the median of the data. An example is the boxplot for age in Figure BASE–1 on page 18.

Kaplan-Meier plot. Dichotomous response variables with variable lengths of follow-up are often displayed as Kaplan-Meier (product-limit) "survival" curves across time. These curves indicate the cumulative probability of remaining event-free as a function of time since the study start, as in Figure MORT–1 on page 24. The total numbers of events appear on the plot, as do the numbers of patients at risk (event-free and uncensored) at various points of follow-up.

Relative risk graphic. A relative risk graphic, for example Figure MORT–4 on page 27, is used to efficiently summarize subgroup analyses of a treatment group difference. This type of graphic displays point estimates and nominal 95% confidence intervals for the relative risk of an event in one treatment group compared to another treatment group. Consistency of a treatment effect across subgroups defined by baseline characteristics is easily assessed with this graphic.

Change from baseline. For variables which are measured at several fixed time points, change from baseline is usually provided below the figure for the observed data. For continuous variables, change can be given either in the original units or as percent change (see Figure FU–1, page 30). For dichotomous variables, change from baseline can be indicated by displaying follow-up data separately for each baseline group (as in Figure AE–2, page 22).

Annotations. All figures indicate the number of patients used for the analysis, either directly under the corresponding portion of the plot, or labeled as "nA" or "nB" at the bottom of the panel. P-values corresponding to the comparisons of the two treatment groups are included, where applicable. In a typical interim report, figures are also annotated with the data source (names of datasets used and date of data transfer).

Figure identifier. Figures are identified by mnemonic labels in the top right corner of each page. These identifiers, which are listed alphabetically in the index at the back of the report, normally would not change over the course of the study and hence can be useful for locating corresponding figures in future or past reports.

4 Notes on Chapter Contents

General Conventions

This report is based on data available from NHLBI after the final closing of the database in June, 1984.

The graphics and analyses in this report include all randomized patients ($N = 3,837$). For displays in Chapter 2, *Baseline Characteristics*, Chapter 3, *Adverse Events*, and Chapter 5, *Additional Follow-Up Measures*, the denominators for each graphic are the number of patients with non-missing data for the variable(s) being displayed. For analyses in Chapter 4, *Primary Endpoint Analysis*, the denominator (or risk set) is the set of all randomized patients. In time-to-event analyses, patients with no event (death) are censored on the "date last known alive" reported in the NHLBI database.

Follow-up visits were scheduled to occur quarterly with the exception of the first two, which took place approximately one month and six weeks after randomization. Patients were followed a minimum of 12 months and a maximum of 40 months (average follow-up 25 months). In the database made available to SDAC, much of the information collected at regular study visits was limited to the baseline examination and the visits occurring one year, two years, and three years after randomization. Therefore, displays which include patient follow-up information (such as the follow-up status of enrolled patients in Figure ACCR–3 on page 16, and all displays in Chapters 3 and 5) are based upon a limited amount of data.

Interim analyses are frequently based on incomplete and inconsistent data. The assumptions, computations and conventions designed to handle the data problems encountered during preparation of the report would be described in this section, or in the more detailed chapter notes below.

Accrual

Enrollment began in June, 1978 and ended in October, 1980. A total of 3,837 patients were enrolled at 31 clinical centers in the United States. Patient accrual over time is displayed in Figure ACCR–1 on page 14. Figure ACCR–2 on page 15 displays patient accrual at each clinical center, by assigned treatment group. Displays (not shown) of the number of clinical centers enrolling patients over time (based on date of first patient enrollment) are often included in this chapter. For multinational studies, accrual by country, continent, or other geographic region could be displayed.

Information on data availability or follow-up status of enrolled patients, as in Figure ACCR–3 on page 16, is also presented. These graphics can be designed to help assess the timeliness of data collection and entry.

Baseline Characteristics

The BHAT exam at baseline included a clinical history, physical examination, 12-lead resting electrocardiogram (ECG), chest x-ray, urinalysis, and other laboratory tests. A typical report would display treatment group comparisons for all baseline variables (except those items which appear in the database only as verbatim listings). In this sample report, only a few variables from the baseline examination are presented in this chapter. Some additional baseline measures are displayed along with follow-up data over time in Chapter 3, *Follow-Up*.

Eligibility for BHAT required a documented MI. ECGs for the qualifying MI were initially read at the clinical center, and later confirmed by the Resting ECG Reading Center. A number of randomized patients with a clinical diagnosis of MI did not fulfill the strict BHAT criteria for an MI. These patients remained in the trial, and are characterized as “Non-BHAT MI” in the display of the location of the BHAT MI in Figure BASE–1 on page 18.

Adverse Events

At each study visit, patients were asked about adverse events they may have experienced since the previous visit (or within a three-month period prior to the baseline examination). This chapter displays adverse events reported at baseline or at the first, second or third annual follow-up visits.

The BHAT database did not include severity levels for reported AEs, nor was there a comprehensive, hierarchical set of coded AEs. In reports for industry-sponsored trials, AEs are typically displayed both at the body system level and at the level of preferred term, with stacked bars indicating severity.

In many clinical trials there is a separate mechanism for expedited reporting and data management of serious adverse events (SAEs) for regulatory purposes, with a later reporting of the event on a study form. Because of the difficulty of merging data from different sources, information obtained from a separate SAE database would usually be displayed in a separate chapter. Information on the occurrence of SAEs was not included in the BHAT database, but is generally an important component of interim monitoring reports because of its greater timeliness and clinical significance.

Primary Endpoint Analysis

With the exception of a single graphic of interim analysis results (Figure MORT–2 on page 25), the graphical displays in this chapter are based on data available from NHLBI after the final closing of the database. The interim analysis results for the primary endpoint analysis were published in:

> DeMets DL, Hardy R, Friedman LM and Lan KKG. “Statistical Aspects of Early Termination in the Beta-Blocker Heart Attack Trial.” *Controlled Clinical Trials* 5:362-372, 1984.

The Kaplan-Meier plot in Figure MORT–1 on page 24 displays all-cause mortality. Based on the final dataset, there were 138 deaths (7.2%) in the propranolol group, and 188 deaths (9.8%) in the placebo group. The Z–score from this final analysis is 2.90. The trial was stopped early after the Z–score from the interim analysis of all-cause mortality exceeded the monitoring boundary at the sixth planned analysis (displayed in Figure MORT–2 on page 25).

A more extensive report would include separate Kaplan-Meier plots for the primary endpoint analysis in patient subgroups of particular interest, as in Figure MORT–3 on page 26. Figure MORT–4 on page 27 is an example of a relative risk graphic assessing the treatment effect for various subgroups. Estimates of the hazard ratios and 95% confidence intervals were obtained using the Cox proportional hazards model.

Figure MORT–5 on page 28 presents information on mortality according to cause of death. All deaths were classified by the mortality classification subcommittee without knowledge of the treatment assignment. Secondary objectives of the study included ascertainment of the effect of propranolol on coronary heart disease mortality and sudden cardiac death. More extensive analyses of secondary endpoints would usually be included in this chapter of a report.

Additional Follow-Up Measures

Patient follow-up data may be collected by logging specified types of events (e.g., adverse events, hospitalizations, changes in dosing or concomitant medication), or by assessing patient status at designated visits or time points over the course of the follow-up period. The BHAT dataset contained information gathered at baseline, and at the first, second and third annual follow-up visits.

Follow-up information can be displayed with bars representing the percent of patients under observation who meet certain criteria at specified timepoints (e.g., Figure FU–3 on page 32) or with a boxplot to illustrate the distribution of continuous measures. Change from baseline for given cohorts is often presented on the same page as displayed in Figure FU–1 on page 30. For other types of data, such as concomitant medication in Figure FU–5 on page 34, the report summarizes information collected over the entire period of observation.

Additional Analytic Considerations (not included in this report)

In a typical interim report, this chapter would include analyses of issues not addressed elsewhere that are relevant to the DMC deliberations concerning study conduct. The following analyses could be addressed in this section: comparisons of observed with expected accrual, and of observed with expected event rates; implications for study power and design if observed rates are lower (or higher) than expected; evaluation of changes in characteristics of enrolled patients over time; and conditional power calculations.

Supporting Material

Part III, *Supporting Material*, includes backup tables of univariate statistics and detailed frequency counts for the graphical displays of the previous chapters. These tables are cross-referenced to and from the corresponding graphical pages.

Ancillary Material

Additional information relevant to the interpretation of a report can be included as Ancillary Material. Early in a trial, copies of key study forms are often included to illustrate the source of certain data items or the data collection process in general. Detailed listings of patient accrual at each clinical center, reported serious adverse events, or other data may also be provided.

In this section of the sample report we have included four example graphics from an Open Session Report. Figure ANCI–1 on page 54 is the aggregate version of the display of baseline information in Figure BASE–1 on page 18. An aggregate version of the laboratory measurements displayed in Figure FU–2 on page 31 is included as Figure ANCI–2 on page 55. Figure ANCI–3 on page 56 is the aggregate version of the display of cigarette smoking in Figure FU–4 on page 33. Figure ANCI–4 on page 57 is the aggregate presentation of the survival curve comparison in Figure MORT–1 on page 24.

5 Contact Information

In an actual report, this section would include names and contact information for the members of the DMC, the Executive Committee Chair, SDAC staff associated with the study, and sponsor-affiliated study personnel. In this sample report, we provide contact information for SDAC.

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A copy of this *Sample Report* is available in Adobe Acrobat format via our Web site at:

http://www.biostat.wisc.edu/clintrials/sdac/sdacpdf.html

Part II

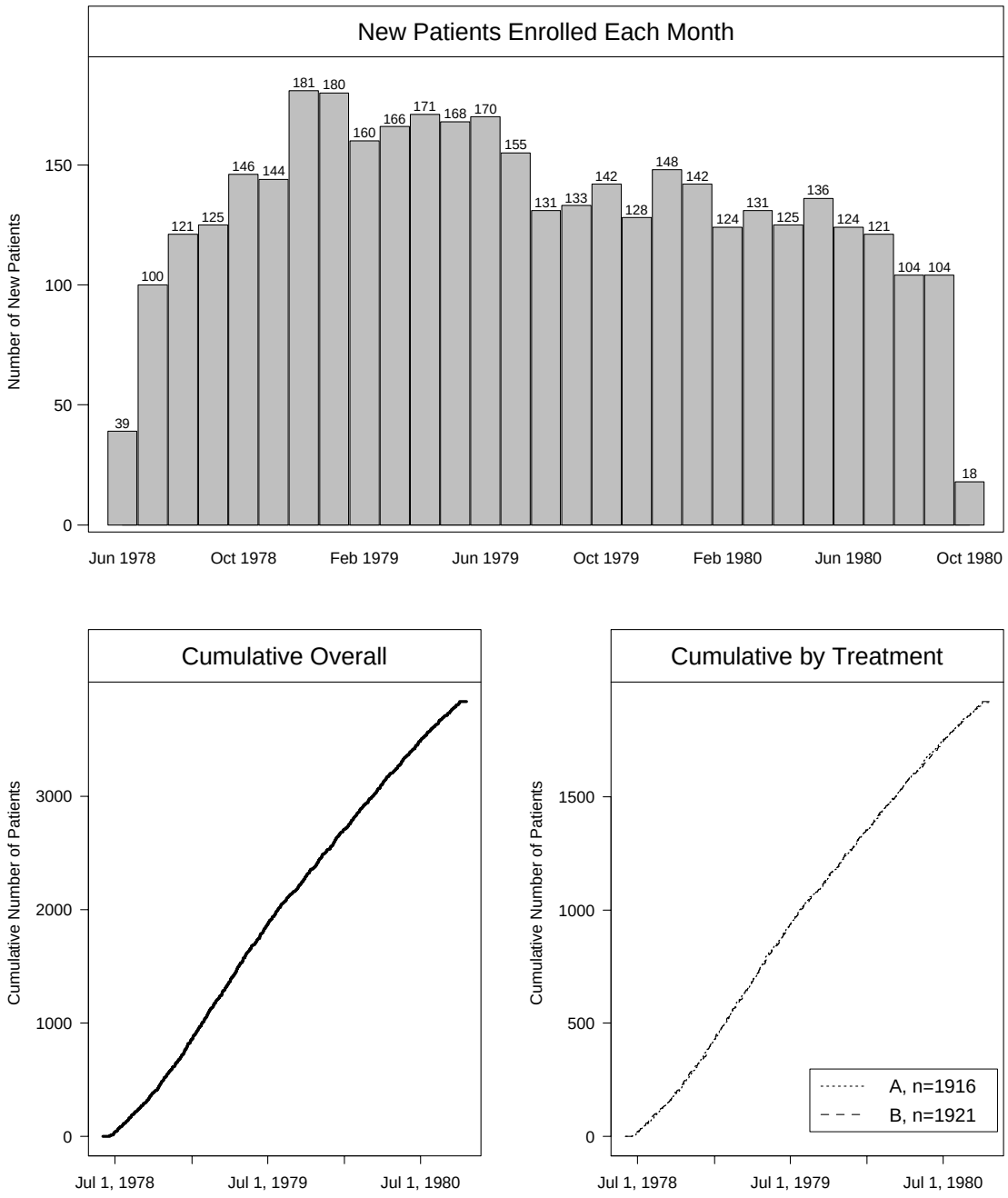
Main Material

Chapter 1

Accrual

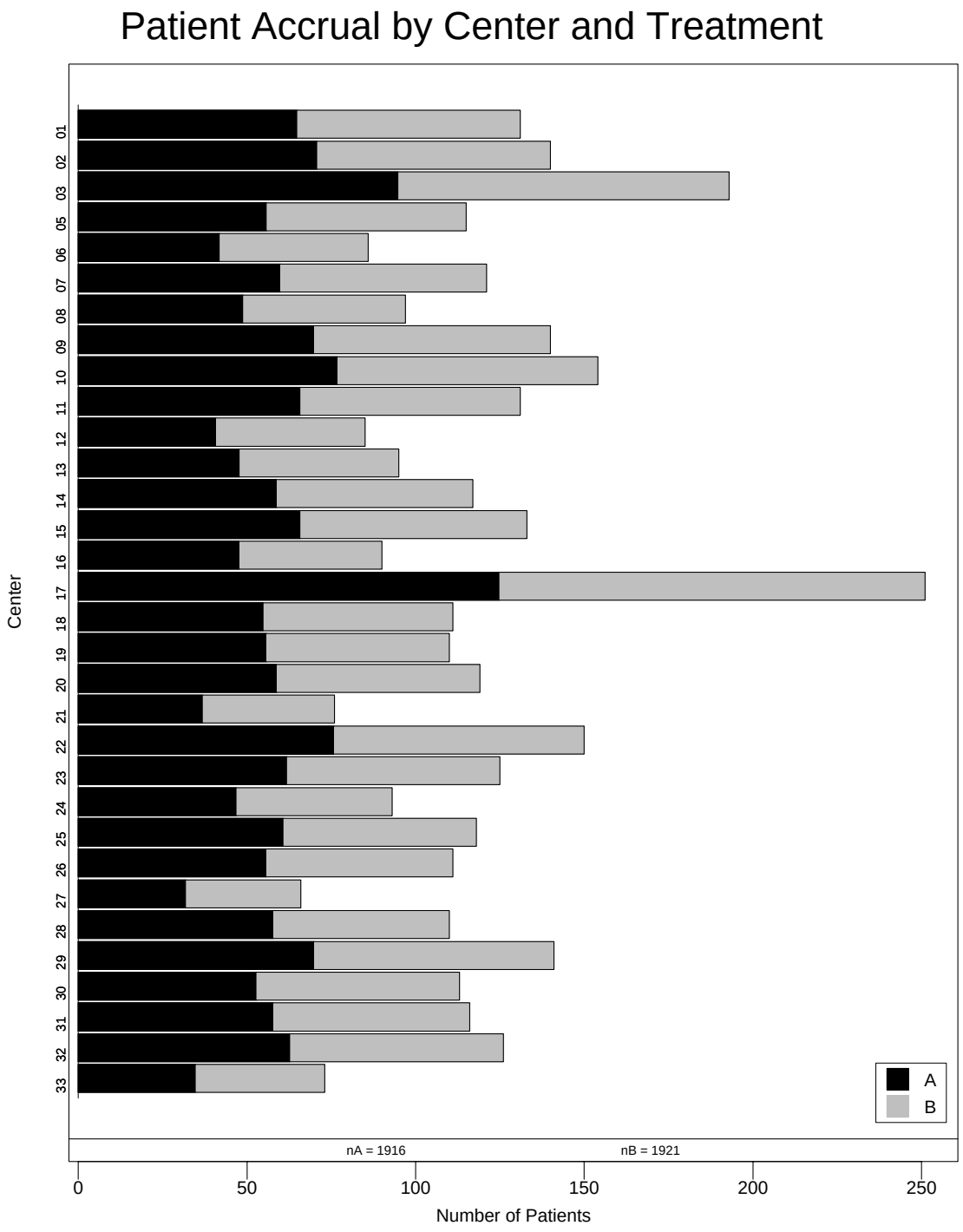
Figure ACCR–1

Patient Accrual over Time



Top panel displays the number of new patients accrued each month from June, 1978 to October, 1980. Bottom panel displays cumulative accrual, overall and by treatment group. A total of 3,837 patients were enrolled in BHAT.

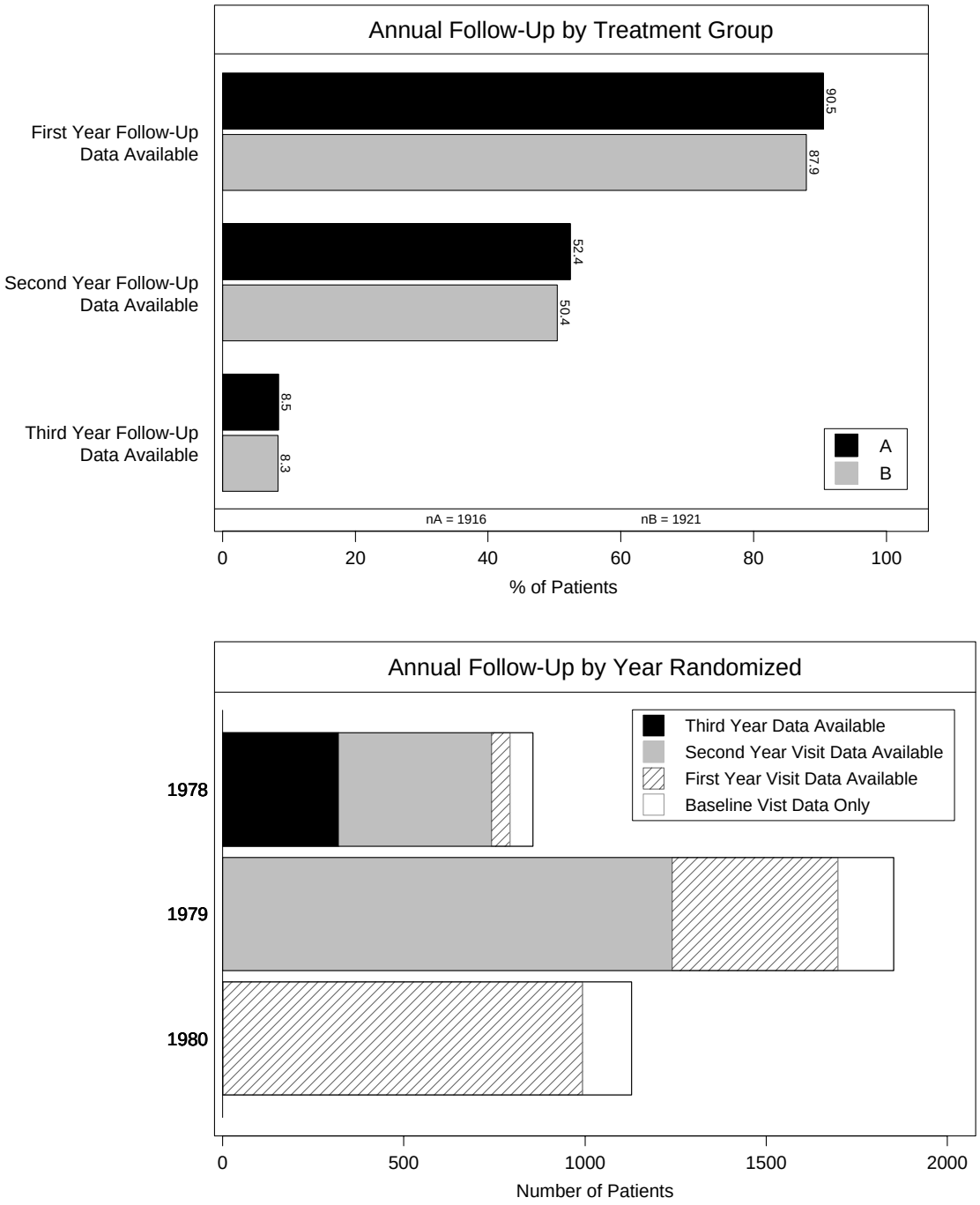
Figure ACCR–2



Display shows the total number of new patients enrolled from each clinical center over the course of the study, according to assigned treatment group.

Figure ACCR–3

Accrual and Follow-Up Data Availability



Displays show the availability of follow-up data by treatment group and by year randomized. (Note that only data from the annual follow-up visits were made available to SDAC.) The trial was terminated in October, 1981, less than a year after the last patient entry. The upper panel displays the percent of randomized patients with the designated annual follow-up visits. In the lower panel, patients are subdivided by the year of randomization and assigned to the first applicable category of data availability.

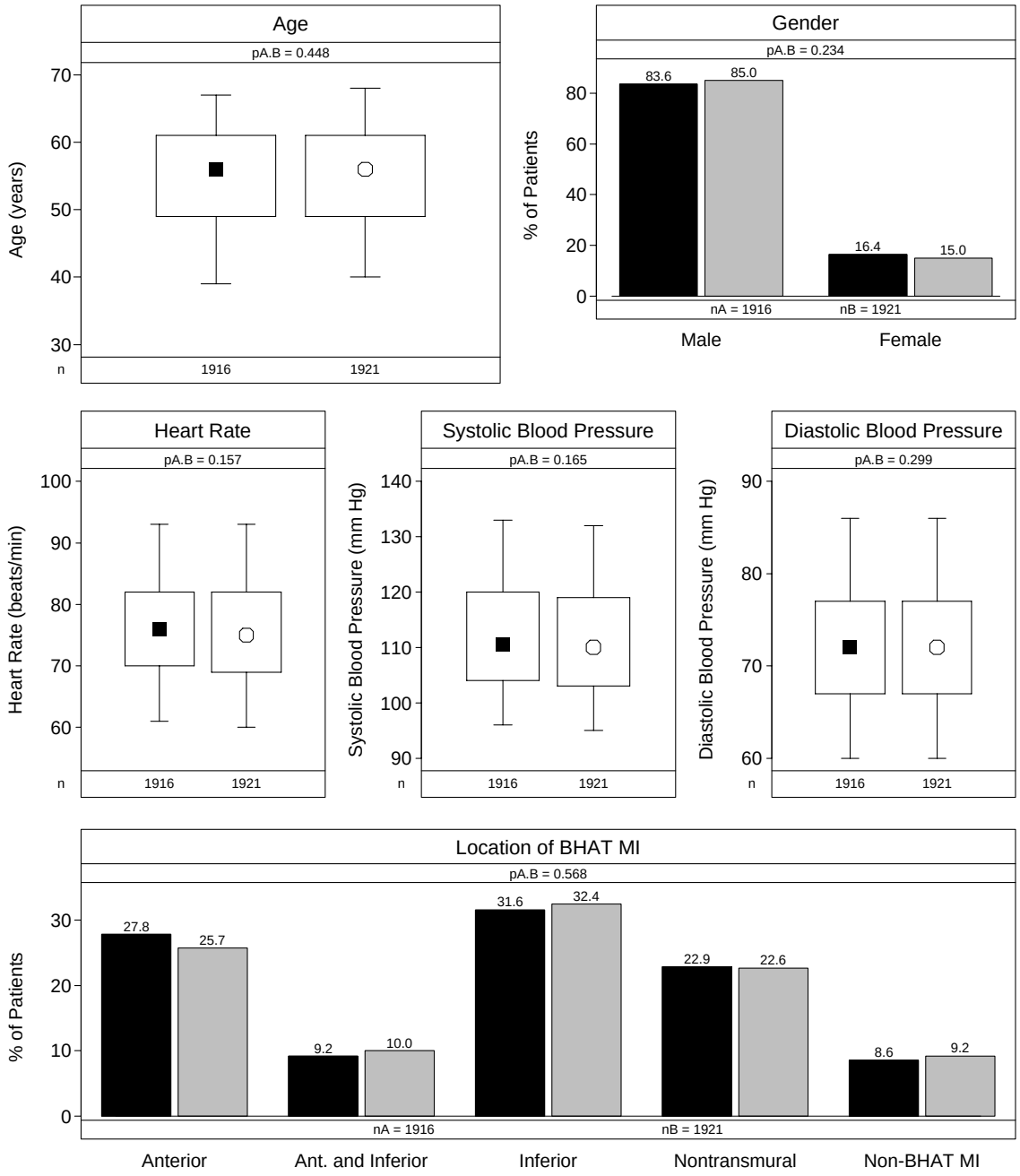
See Table Set ACCR–3 on page 36.

Chapter 2

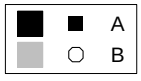
Baseline Characteristics

Figure BASE–1

Baseline Demographics



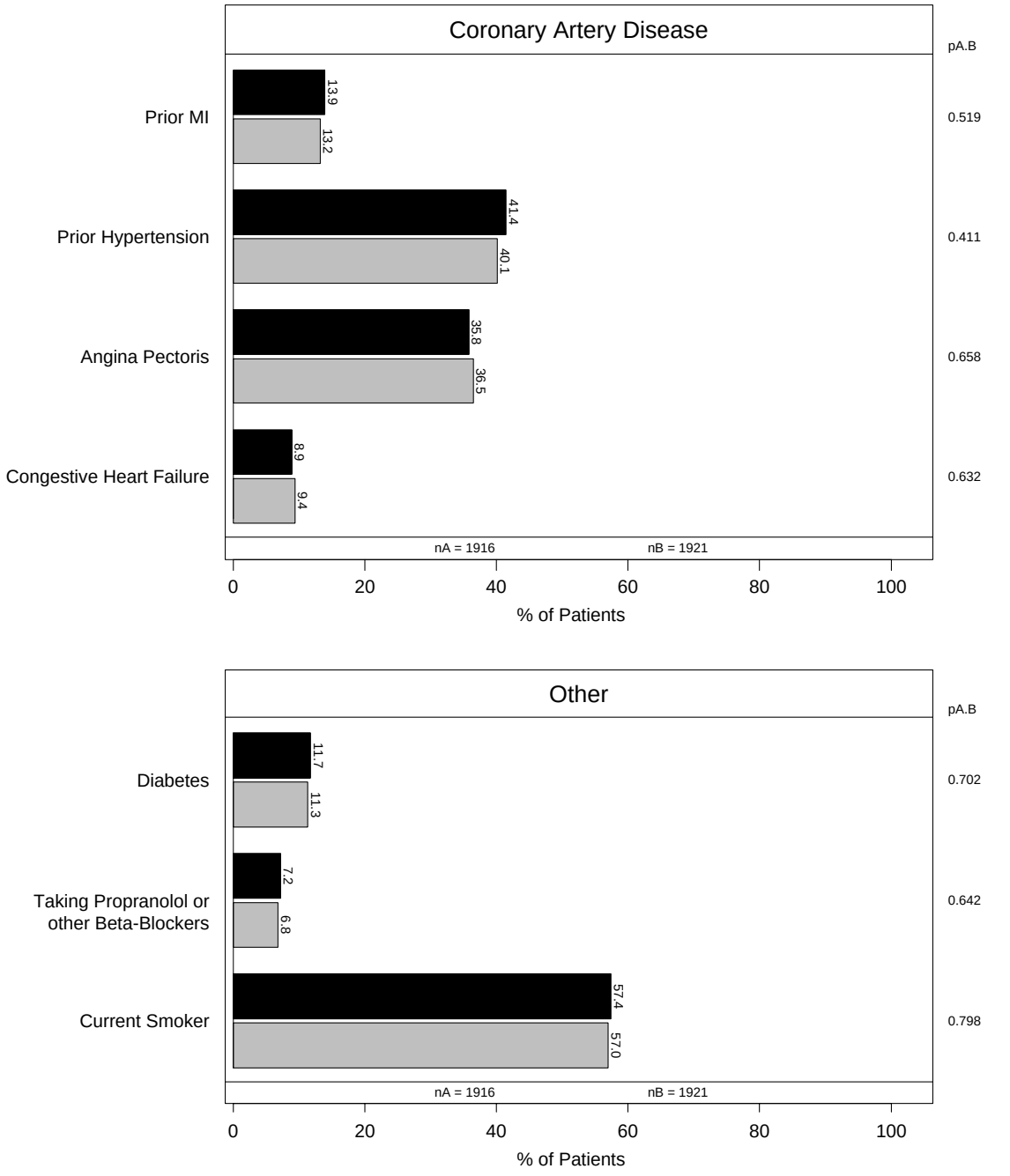
Information determined by baseline interview, physical examination, and ECG administered prior to randomization. See the *Introduction* for a discussion of "Non-BHAT MI" classification. Figure ANCI–1 on page 54 displays an Open Session Report version of this page. (See Table 1: *JAMA* 247:1708, 1982.)



See Table Set BASE–1 on page 37.

Figure BASE–2

Medical History



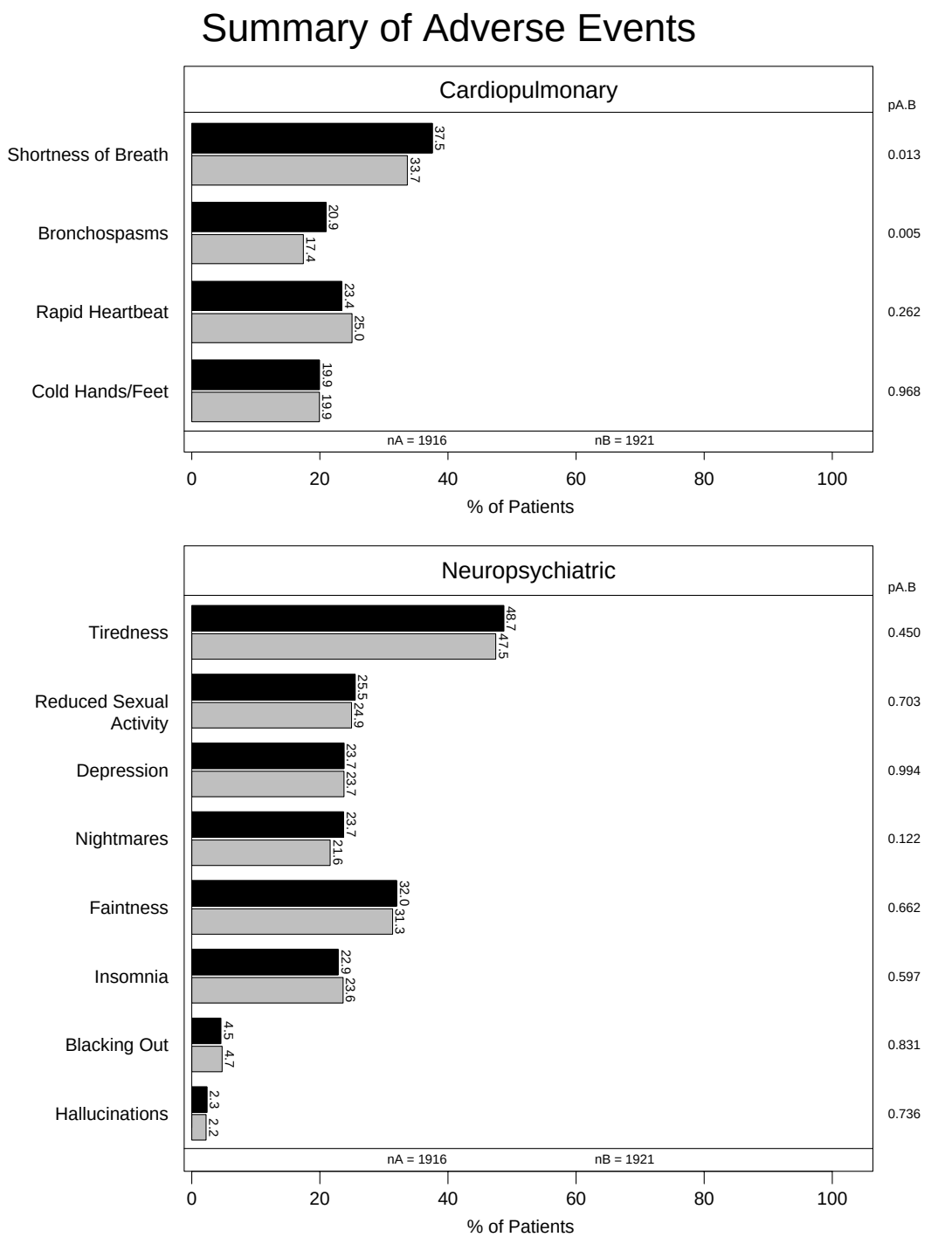
Top panel shows the percent of patients reporting a history of several conditions related to coronary artery disease. Bottom panel shows the percent of patients reporting other relevant conditions. Multiple conditions may be present. Values indicate the percentage of patients indicating “Yes” at the baseline examination out of all patients randomized. (See Table 1: *JAMA* 247:1708, 1982.)

See Table Set BASE–2 on page 38.

Chapter 3

Adverse Events

Figure AE–1

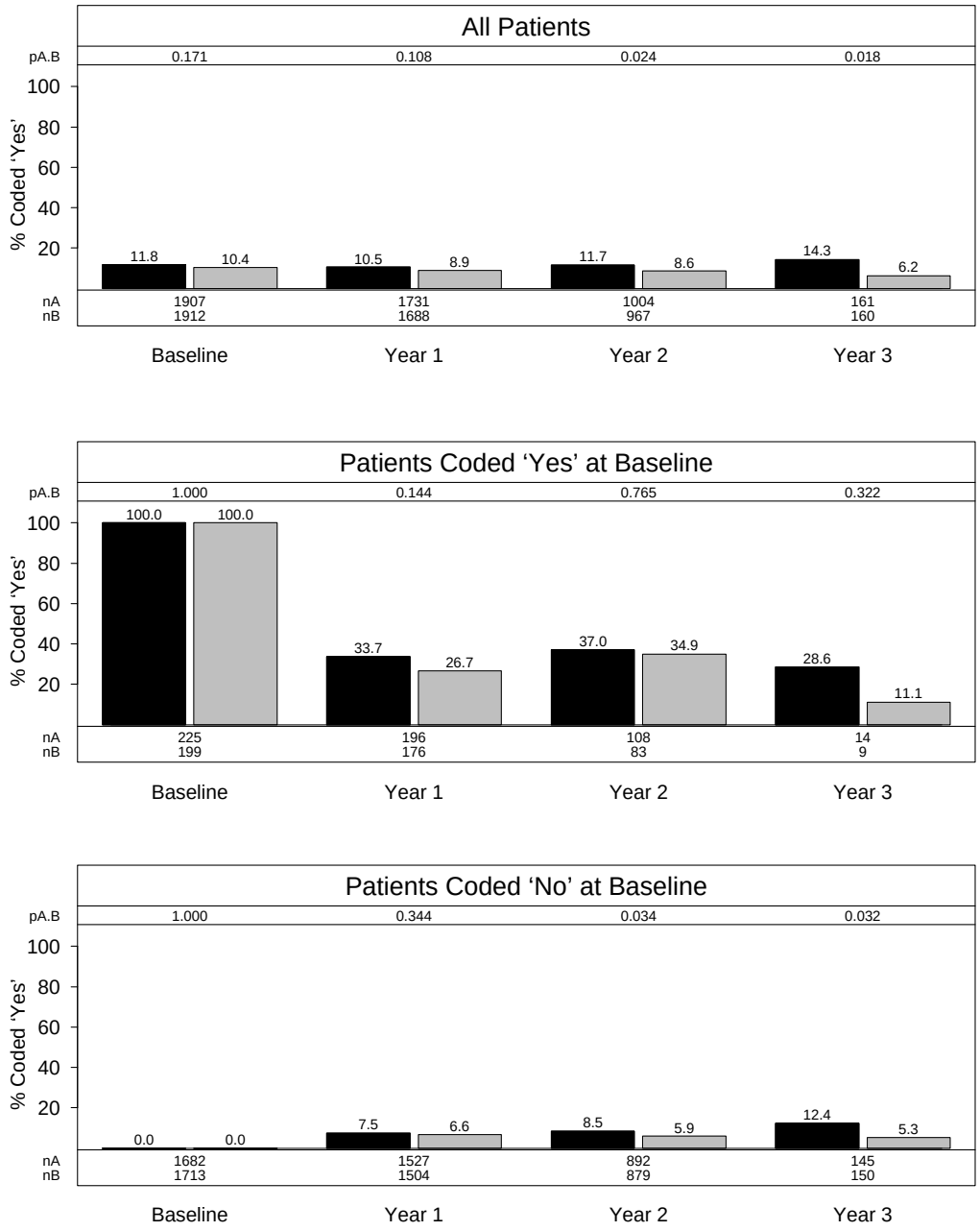


Information from the baseline examination and from visits scheduled after one, two, and three years of follow-up. At each study visit, patients were asked about the adverse events they may have experienced since the previous visit (or within the past three months, at the baseline exam). Because this display is based on data from a limited number of visits, the overall incidence of reported adverse events may be underrepresented. (For comprehensive information, see Table 6: *JAMA* 247:1711, 1982.)

See Table Set AE–1 on page 39.

Figure AE–2

Bronchospasms, by Follow-Up Year



Information from the baseline examination and from visits scheduled after one, two, and three years of follow-up. At each study visit, patients were asked whether they had experienced recurrent bronchospasm (wheezing in the chest) since the most recent visit (or within the past three months, at the baseline exam). The top panel shows the percent of patients responding "Yes" at each visit; the middle panel shows the response at each visit for patients who reported bronchospasms at baseline; the bottom panel shows the response at each visit for patients who did not report bronchospasms at baseline.

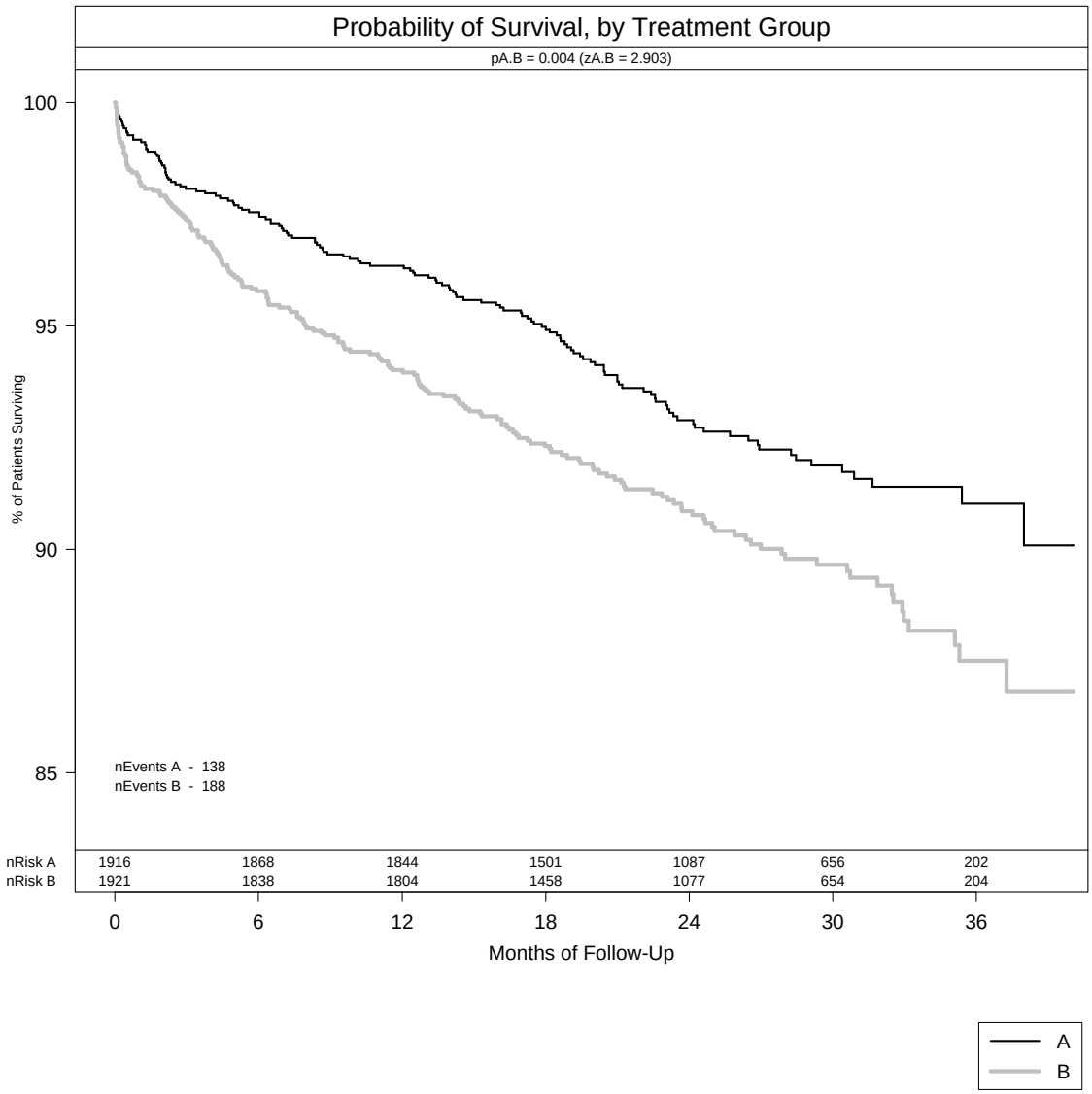
See Table Set AE–2 on page 40.

Chapter 4

Primary Endpoint Analysis

Figure MORT–1

All-Cause Mortality over Time

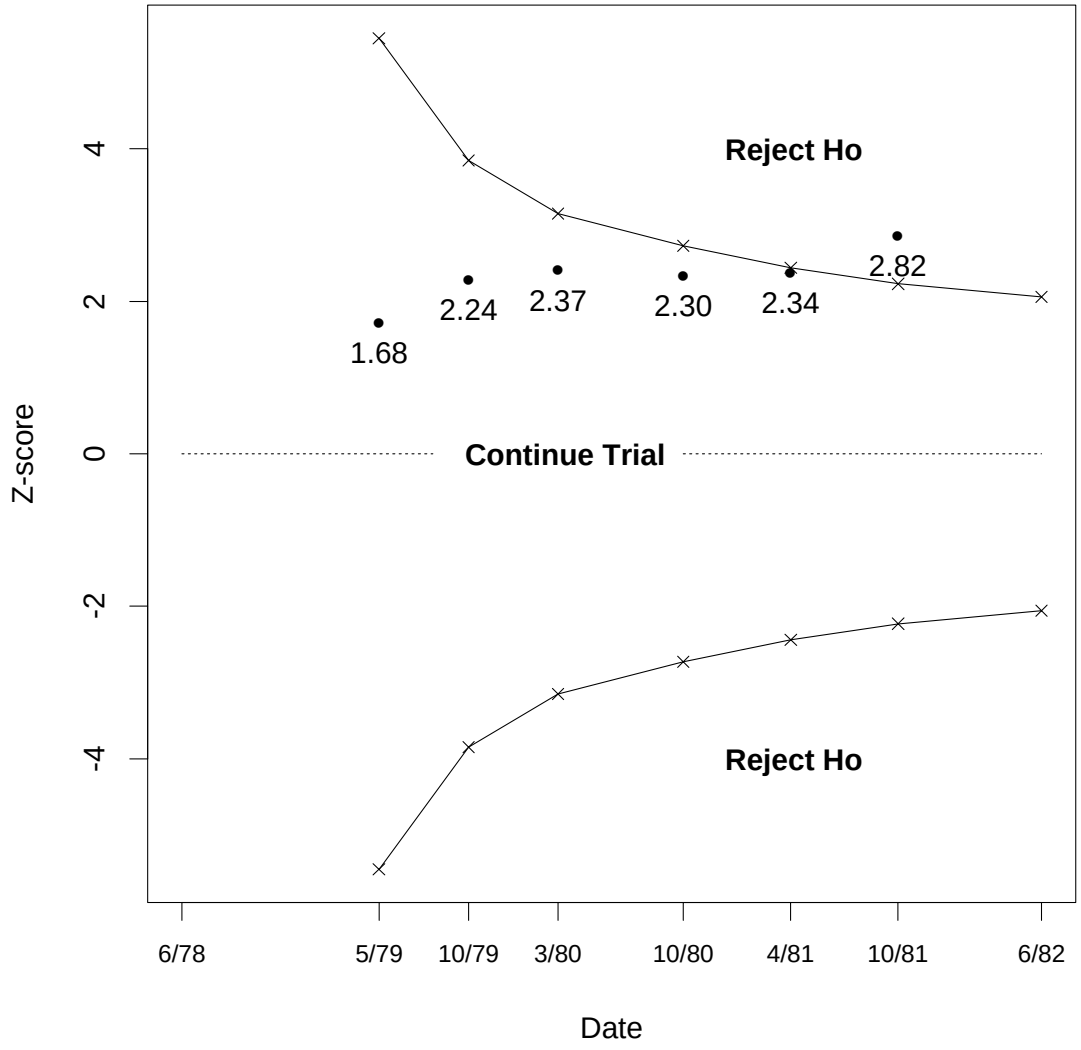


All-cause mortality by assigned treatment group. The total number of deaths appear on the plot ("nEvents"), as do the numbers of patients at risk (event-free and uncensored) at various points of follow-up. Surviving patients were censored as described in the *Introduction* on page 8. Figure ANCI–4 on page 57 displays an Open Session Report version of this page. (See Figure 1 and Table 2: *JAMA* 247:1709, 1982.)

See Table Set MORT–1 on page 42.

Figure MORT–2

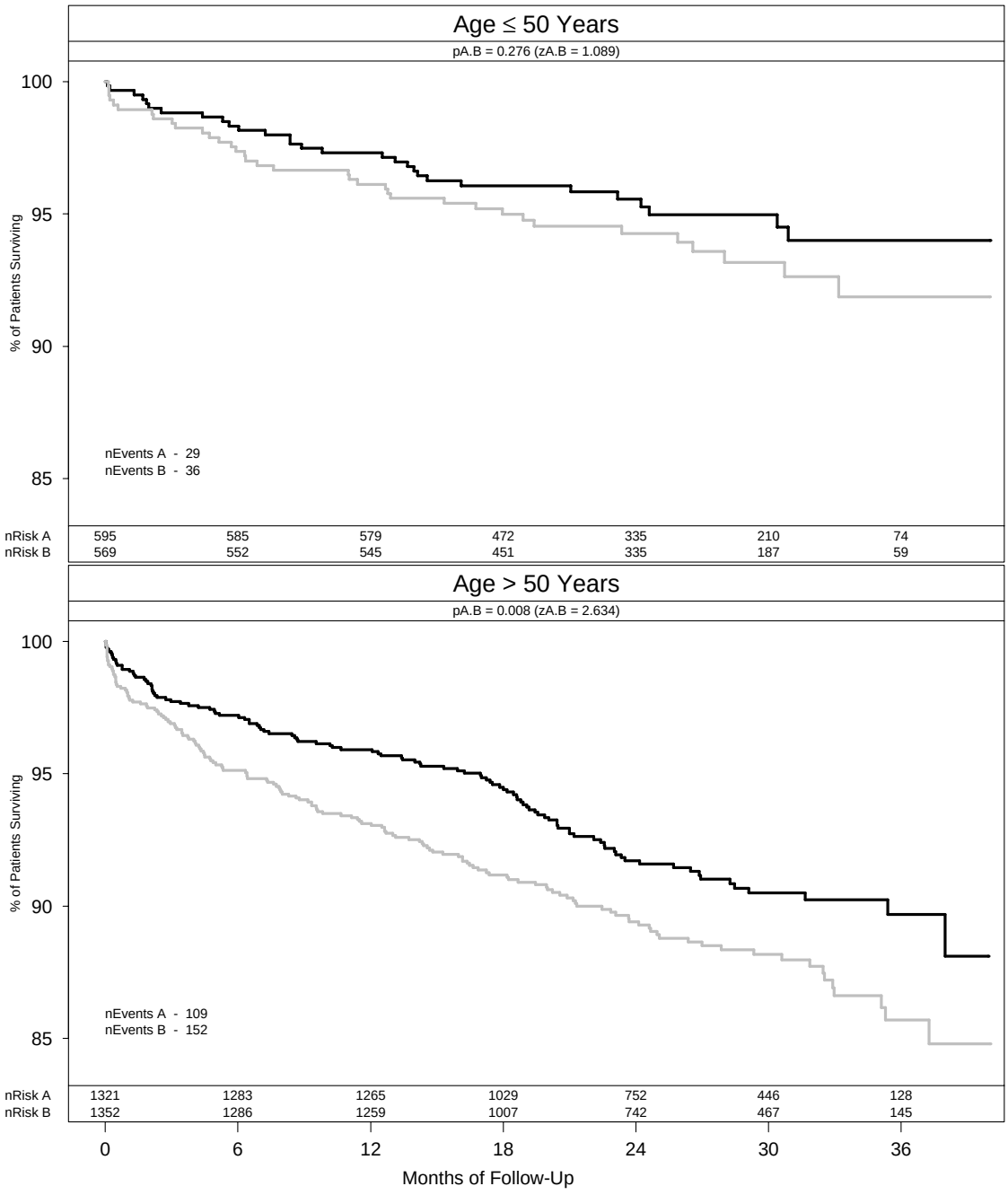
Interim Monitoring Boundary for All-Cause Mortality



O'Brien-Fleming interim monitoring boundary for the primary endpoint based on seven planned interim analyses with overall type I error of α=0.05. Also shown are the Z-scores for the comparison of treatment groups at the first six interim analyses. A Z-score greater than 0 corresponds to excess events in group B. The trial was stopped early after the Z-score at the sixth planned analysis exceeded the monitoring boundary. The Z-score from the analysis of the final data, presented in Figure MORT–1, is 2.90. (See Figure 2: *CCT* 5:366, 1984.)

Figure MORT–3

All-Cause Mortality over Time by Age Group

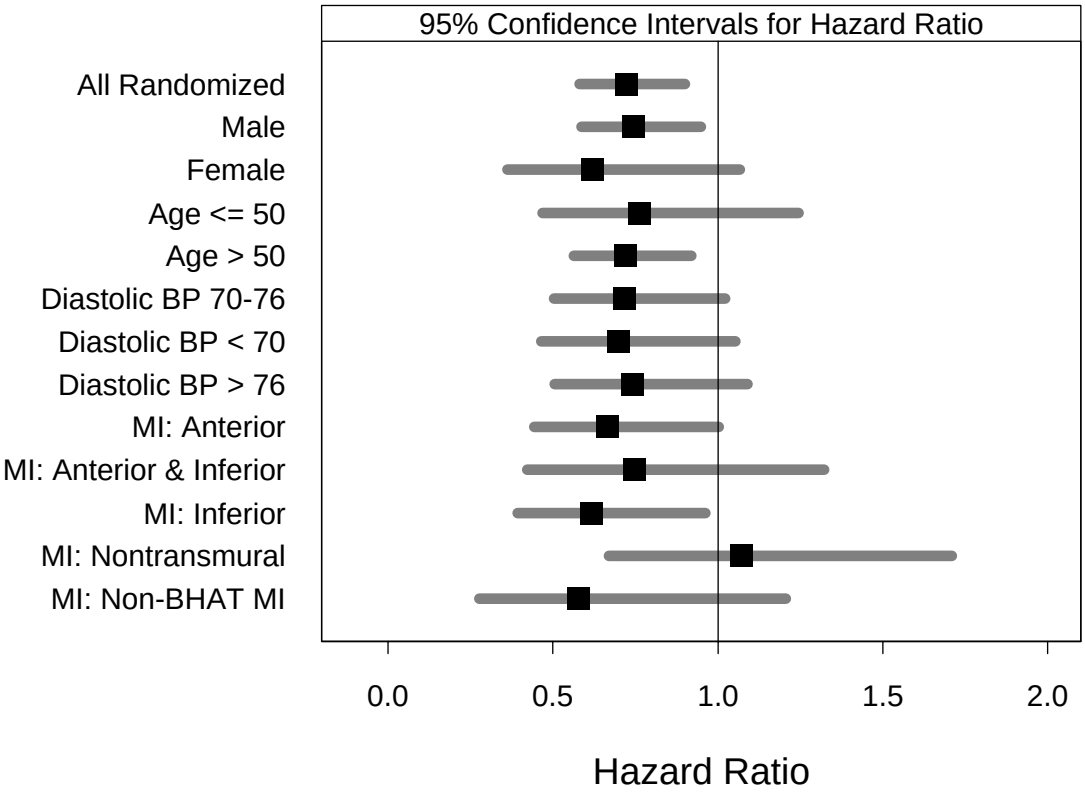


All-cause mortality by assigned treatment group. The total number of deaths appear on the plot ("nEvents"), as do the numbers of patients at risk (event-free and uncensored) at various points of follow-up. Surviving patients were censored as described in the *Introduction* on page 8. The patient population was subdivided at 50 years of age to evaluate differences in survival by age and treatment.

See Table Set MORT–3 on page 43.

Figure MORT-4

Hazard Ratios for All-Cause Mortality

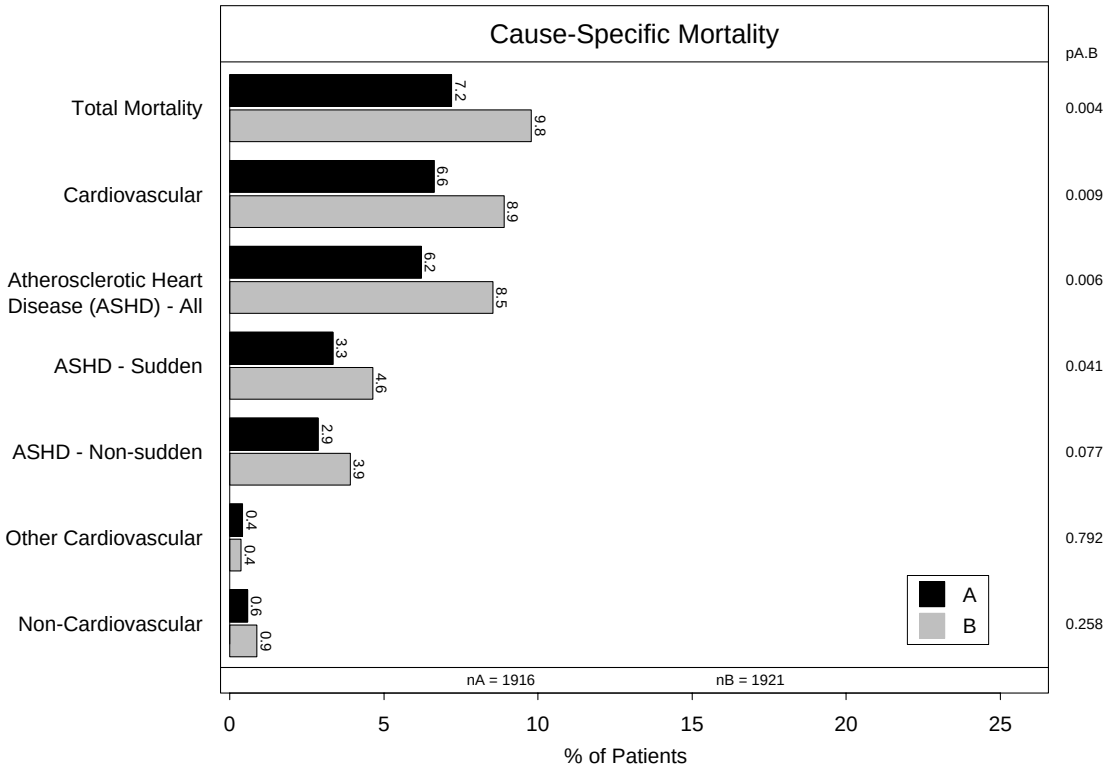


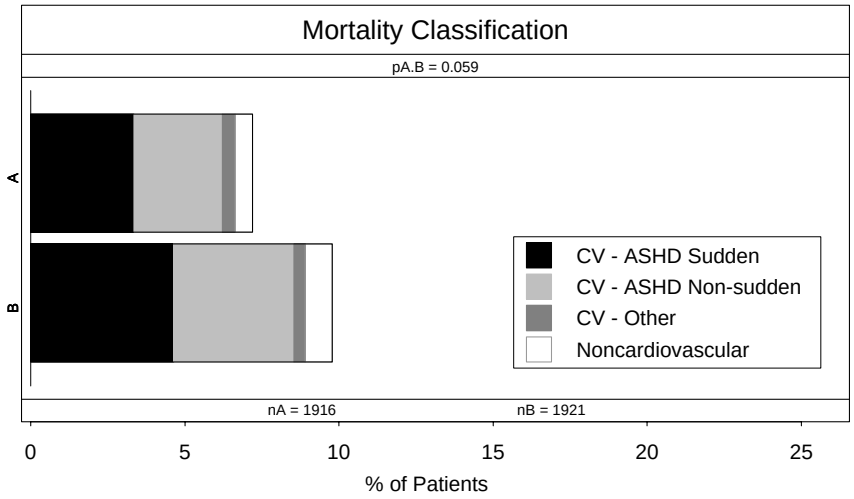
Subgroup	Events/N Pats (%) Tot		A		B		Hazard Ratio	(95% CI)	P Value
All Randomized	326/3837	8.5%	138/1916	7.2%	188/1921	9.8%	0.72	(0.58,0.90)	0.004
Male	271/3235	8.4%	116/1602	7.2%	155/1633	9.5%	0.75	(0.59,0.95)	0.017
Female	55/602	9.1%	22/314	7.0%	33/288	11.5%	0.62	(0.36,1.07)	0.084
Age $\leq$ 50	65/1164	5.6%	29/595	4.9%	36/569	6.3%	0.76	(0.47,1.24)	0.278
Age $>$ 50	261/2673	9.8%	109/1321	8.3%	152/1352	11.2%	0.72	(0.56,0.92)	0.009
Diastolic BP 70-76	126/1375	9.2%	53/679	7.8%	73/696	10.5%	0.72	(0.50,1.02)	0.066
Diastolic BP $<$ 70	95/1340	7.1%	39/667	5.8%	56/673	8.3%	0.70	(0.46,1.05)	0.086
Diastolic BP $>$ 76	105/1122	9.4%	46/570	8.1%	59/552	10.7%	0.74	(0.50,1.09)	0.129
MI: Anterior	94/1027	9.2%	40/533	7.5%	54/494	10.9%	0.67	(0.44,1.00)	0.052
MI: Anterior & Inferior	49/368	13.3%	20/176	11.4%	29/192	15.1%	0.75	(0.42,1.32)	0.317
MI: Inferior	82/1228	6.7%	31/605	5.1%	51/623	8.2%	0.62	(0.39,0.96)	0.033
MI: Nontransmural	70/873	8.0%	36/438	8.2%	34/435	7.8%	1.07	(0.67,1.71)	0.778
MI: Non-BHAT MI	31/341	9.1%	11/164	6.7%	20/177	11.3%	0.58	(0.28,1.21)	0.144

Relative risks for treatment A vs. treatment B, based on univariate analysis using the Cox proportional hazards model. Each black box indicates the point estimate of the relative risk, and shaded lines indicate the nominal 95% confidence intervals. Boxes to the left of the vertical line at 1.0 indicate excess events in group B. Information used to define patient subgroups was taken from the baseline examination. (See Table 4: *JAMA* 247:1710, 1982)

Figure MORT–5

Mortality by Adjudicated Cause of Death





Deaths were classified by the Mortality Classification Subcommittee as being due to atherosclerotic heart disease (ASHD), cardiovascular disease other than ASHD, or non-cardiovascular cause, and with ASHD deaths further classified as being sudden or non-sudden (sudden death defined as death within 24 hours of onset of acute symptoms or unexpected collapse without warning symptoms). (See Table 3: *JAMA* 247:1710, 1982.)

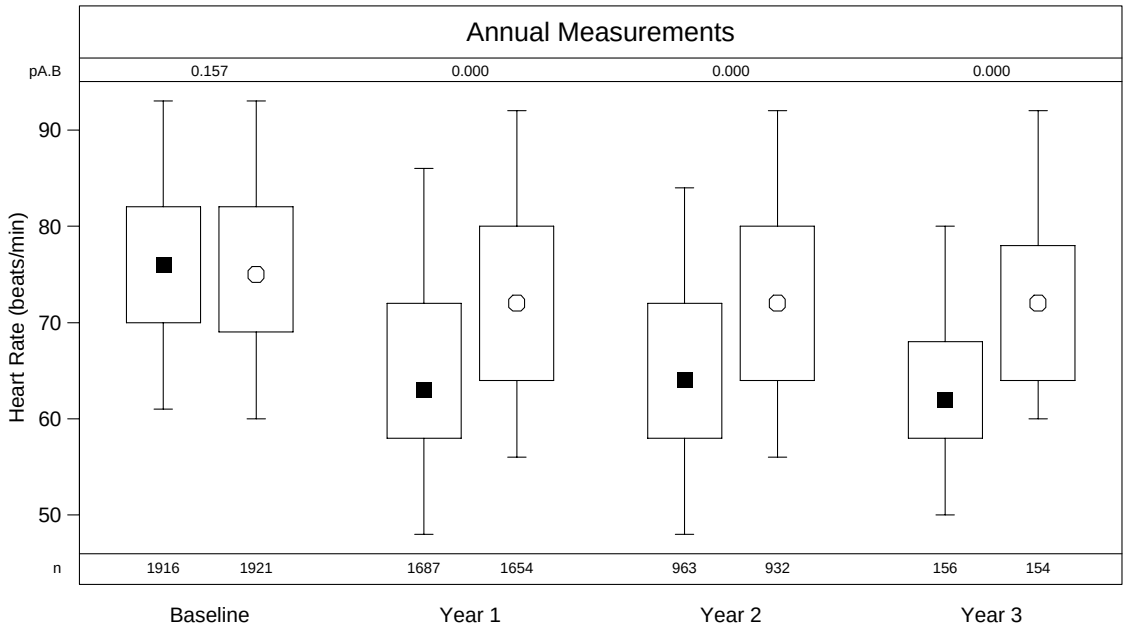
See Table Set MORT–5 on page 45.

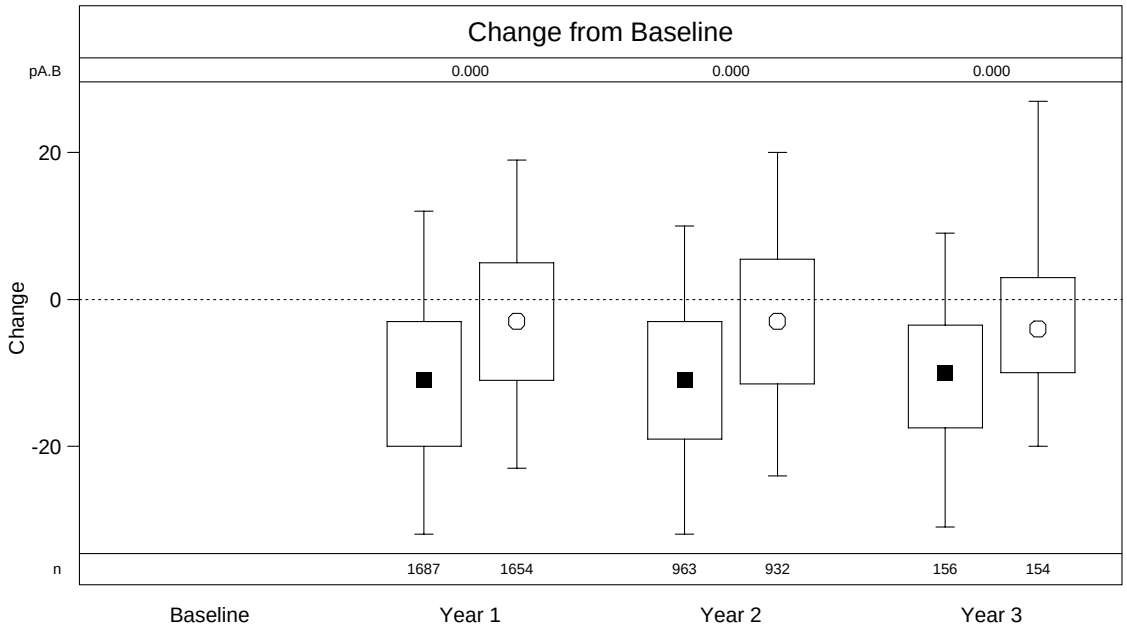
Chapter 5

Additional Follow-Up Measures

Figure FU–1

Heart Rate



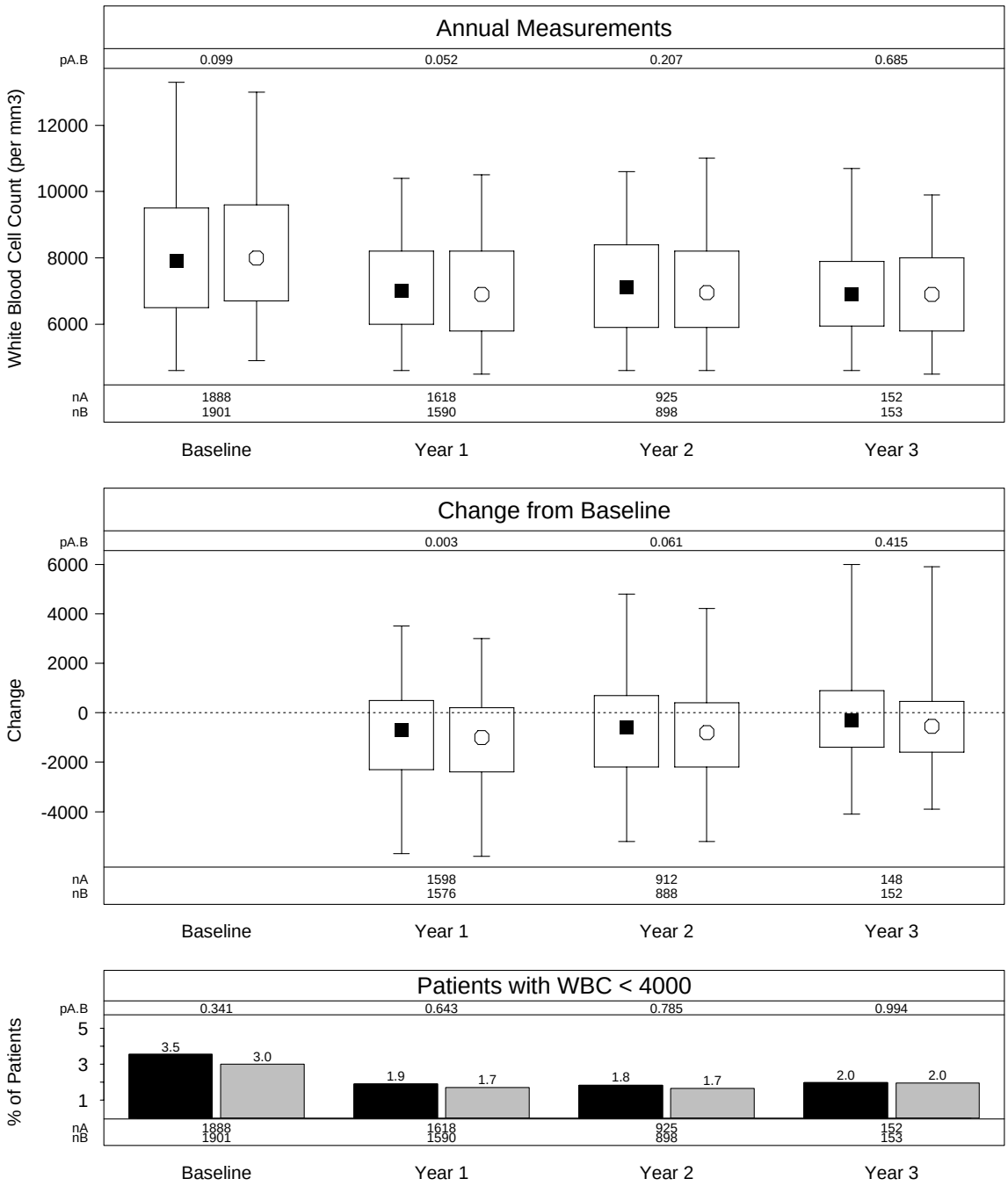


Information from the baseline examination and from visits scheduled after one, two, and three years of follow-up. A physical examination was performed at every study visit; measurements at selected visits and absolute change from baseline are shown.

See Table Set FU–1 on page 46.

Figure FU–2

White Blood Cell Count

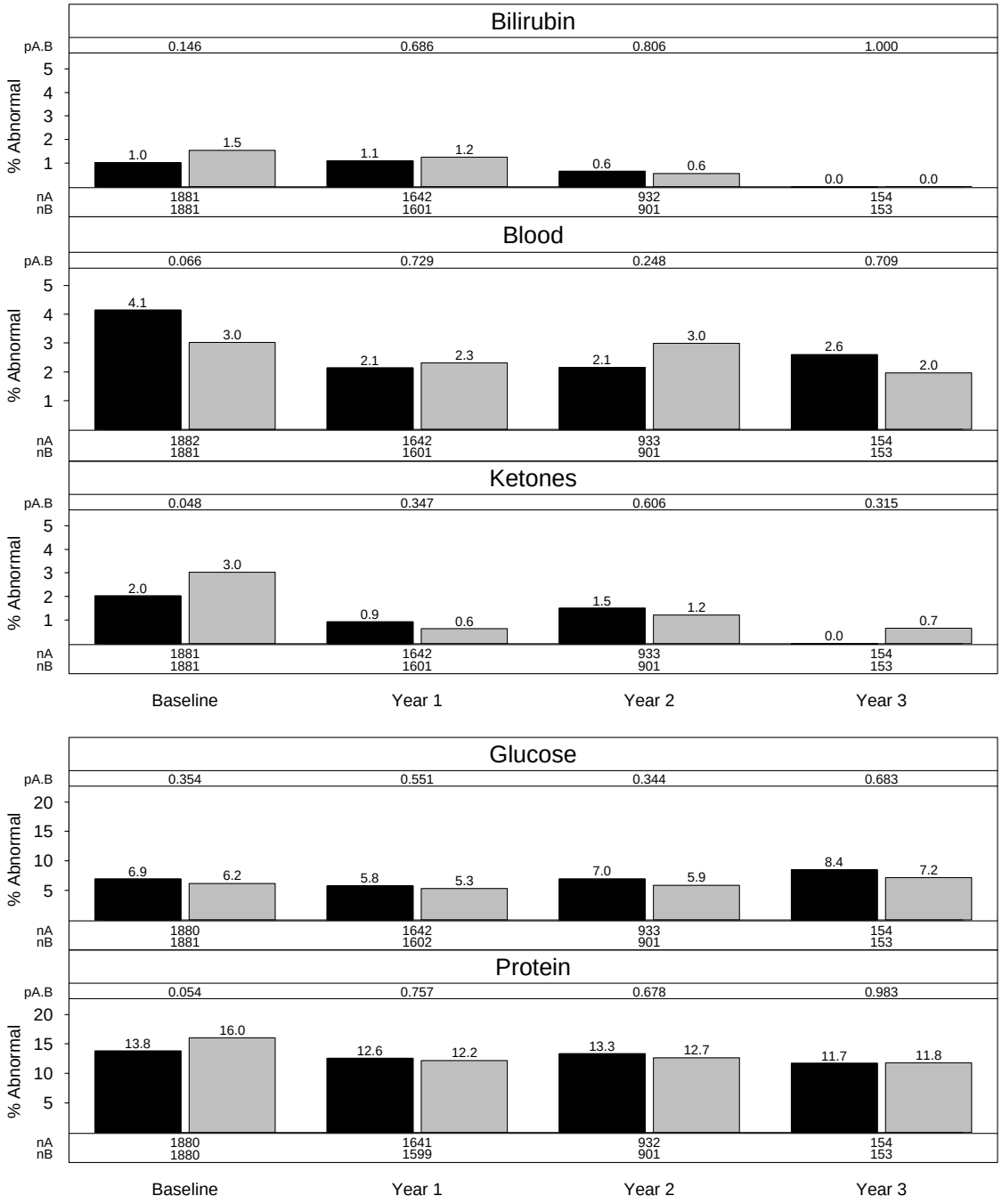


Information from the baseline examination and from visits scheduled after one, two, and three years of follow-up. Panels show measurements at each visit, absolute change from baseline, and percent of patients with white blood cell (WBC) counts < 4000. See also Figure ANCI–2 on page 55 for the Open Session Report version of this page.

See Table Set FU–2 on page 47.

Figure FU–3

Urinalysis Findings



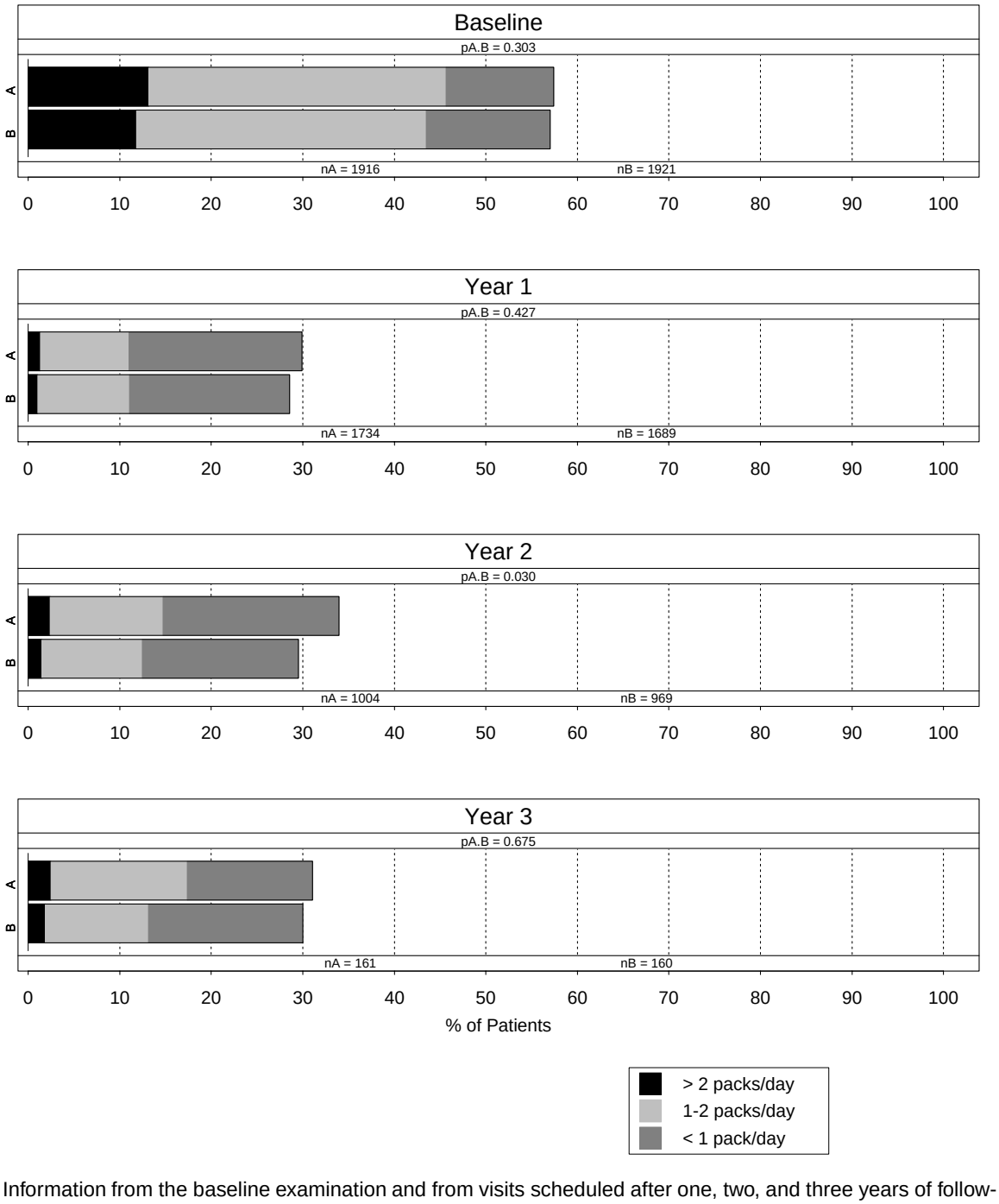
Information from the baseline examination and from visits scheduled after one, two, and three years of follow-up. Panels show the percent of patients at each visit with abnormal values reported for the indicated measurements.

A
B

See Table Set FU–3 on page 48.

Figure FU–4

Cigarette Smoking

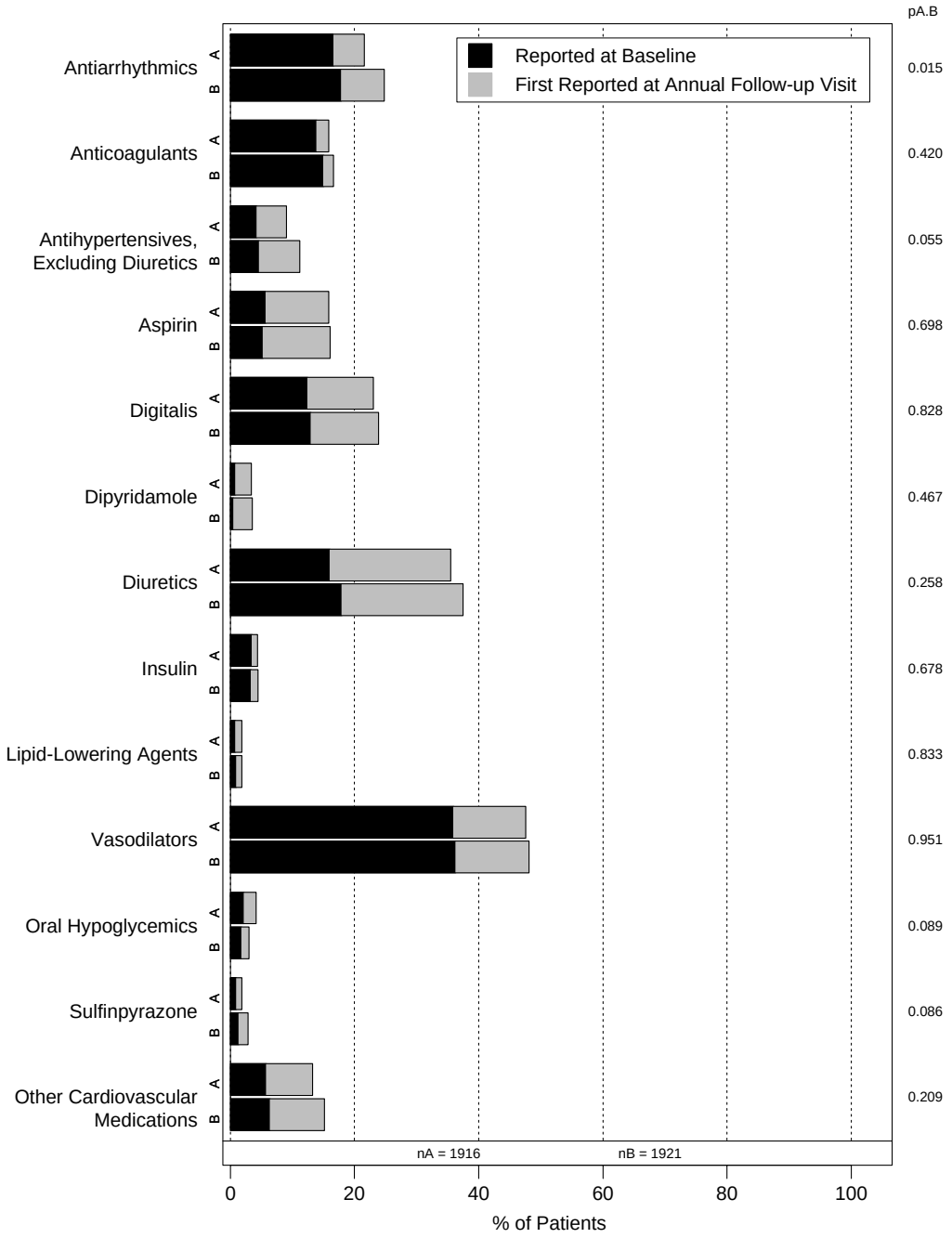


Information from the baseline examination and from visits scheduled after one, two, and three years of follow-up. Panels show the percent of patients at each visit categorized as heavy, moderate, or light smokers based on interview results. See also Figure ANCI–3 on page 56 for the Open Session Report version of this page.

See Table Set FU–4 on page 49.

Figure FU–5

Concomitant Medication Usage



Information from the baseline examination and from visits scheduled after one, two, and three years of follow-up. Panels show whether each type of medication was reported at baseline examination, or was reported later at any of the included visits. Because this display is based on data from a limited number of visits, the overall incidence of medication use may be underrepresented. (For comprehensive information, see Table 7: *JAMA* 247:1711, 1982.)

See Table Set FU–5 on page 50.

Part III

Supporting Material

Chapter 1

Accrual

1.3 Availability of Follow-up Data

Table Set ACCR–3

Accrual and Follow-Up Data Availability: Annual Follow-Up by Treatment Group

See Figure ACCR–3 on page 16.

			Value			
		Total	Yes			P-
	Trt	Pats	N	%	Contrast	Value
First Year Follow-Up Data Available	A	1916	1734	90.50	A.B	0.010
	B	1921	1689	87.92		
Second Year Follow-Up Data Available	A	1916	1004	52.40	A.B	0.225
	B	1921	969	50.44		
Third Year Follow-Up Data Available	A	1916	162	8.46	A.B	0.888
	B	1921	160	8.33		

Chapter 2

Baseline Characteristics

2.1 Demographics

Table Set BASE–1

Baseline Demographics: Age

See Figure BASE–1 on page 18.

Trt	Total Pats	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
A	1916	54.69	8.48	56.00	49.00	61.00	39.00	67.00	A.B	0.45
B	1921	54.93	8.41	56.00	49.00	61.00	40.00	68.00		

Baseline Demographics: Gender

See Figure BASE–1 on page 18.

	Treatment Group					
	A		B			P-
	N	%	N	%	Contrast	Value
Total Patients	1916		1921		A.B	0.23
Male	1602	83.61	1633	85.01		
Female	314	16.39	288	14.99		

Baseline Demographics: Heart Rate

See Figure BASE–1 on page 18.

Trt	Total Pats	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
A	1916	76.17	9.80	76.00	70.00	82.00	61.00	93.00	A.B	0.16
B	1921	75.73	9.83	75.00	69.00	82.00	60.00	93.00		

Baseline Demographics: Systolic Blood Pressure

See Figure BASE–1 on page 18.

Trt	Total Pats	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
A	1916	112.3	11.6	110.5	104.0	120.0	96.0	133.0	A.B	0.16
B	1921	111.7	11.6	110.0	103.0	119.0	95.0	132.0		

Baseline Demographics: Diastolic Blood Pressure

See Figure BASE–1 on page 18.

Trt	Total Pats	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
A	1916	72.55	7.79	72.00	67.00	77.00	60.00	86.00	A.B	0.30
B	1921	72.31	7.87	72.00	67.00	77.00	60.00	86.00		

Baseline Demographics: Location of BHAT MI

See Figure BASE–1 on page 18.

	Treatment Group A N	A %	Treatment Group B N	B %	Contrast	P-Value
Total Patients	1916		1921		A.B	0.57
Anterior	533	27.82	494	25.72		
Ant. and Inferior	176	9.19	192	9.99		
Inferior	605	31.58	623	32.43		
Nontransmural	438	22.86	435	22.64		
Non-BHAT MI	164	8.56	177	9.21		

2.2 Medical History

Table Set BASE–2

Medical History: Coronary Artery Disease

See Figure BASE–2 on page 19.

	Trt	Total Pats	Value Yes N	Yes %	Contrast	P-Value
Prior MI	A	1916	267	13.94	A.B	0.52
	B	1921	254	13.22		
Prior Hypertension	A	1916	794	41.44	A.B	0.41
	B	1921	771	40.14		
Angina Pectoris	A	1916	686	35.80	A.B	0.66
	B	1921	701	36.49		
Congestive Heart Failure	A	1916	171	8.92	A.B	0.63
	B	1921	180	9.37		

Medical History: Other

See Figure BASE–2 on page 19.

	Trt	Total Pats	Value Yes N	Yes %	Contrast	P-Value
Diabetes	A	1916	225	11.74	A.B	0.70
	B	1921	218	11.35		
Taking Propranolol or other Beta-Blockers	A	1916	138	7.20	A.B	0.64
	B	1921	131	6.82		
Current Smoker	A	1916	1100	57.41	A.B	0.80
	B	1921	1095	57.00		

Chapter 3

Adverse Events

3.1 Summary of Adverse Events

Table Set AE–1

Summary of Adverse Events: Cardiopulmonary

See Figure AE–1 on page 21.

			Value			
		Total	Experienced Event			P-
	Trt	Pats	N	%	Contrast	Value
Shortness of Breath	A	1916	719	37.53	A.B	0.0129
	B	1921	647	33.68		
Bronchospasms	A	1916	401	20.93	A.B	0.0053
	B	1921	334	17.39		
Rapid Heartbeat	A	1916	449	23.43	A.B	0.2616
	B	1921	480	24.99		
Cold Hands/Feet	A	1916	382	19.94	A.B	0.9679
	B	1921	382	19.89		

Summary of Adverse Events: Neuropsychiatric

See Figure AE–1 on page 21.

			Value			
		Total	Experienced Event			P-
	Trt	Pats	N	%	Contrast	Value
Tiredness	A	1916	933	48.70	A.B	0.45
	B	1921	912	47.48		
Reduced Sexual Activity	A	1916	488	25.47	A.B	0.70
	B	1921	479	24.93		
Depression	A	1916	455	23.75	A.B	0.99
	B	1921	456	23.74		
Nightmares	A	1916	454	23.70	A.B	0.12
	B	1921	415	21.60		
Faintness	A	1916	613	31.99	A.B	0.66

(Continued on next page.)

(Continued from previous page.)

Summary of Adverse Events: Neuropsychiatric

See Figure AE–1 on page 21.

			Value			
		Total	Experienced Event			P-
	Trt	Pats	N	%	Contrast	Value
	B	1921	602	31.34		
Insomnia	A	1916	438	22.86	A.B	0.60
	B	1921	453	23.58		
Blacking Out	A	1916	87	4.54	A.B	0.83
	B	1921	90	4.69		
Hallucinations	A	1916	45	2.35	A.B	0.74
	B	1921	42	2.19		

3.2 Adverse Events by Follow-Up Year

Table Set AE–2

Bronchospasms, by Follow-Up Year: All Patients

See Figure AE–2 on page 22.

			Value					
		Total	Yes		No			P-
	Trt	Pats	N	%	N	%	Contrast	Value
Baseline	A	1907	225	11.80	1682	88.20	A.B	0.171
	B	1912	199	10.41	1713	89.59		
Year 1	A	1731	182	10.51	1549	89.49	A.B	0.108
	B	1688	150	8.89	1538	91.11		
Year 2	A	1004	117	11.65	887	88.35	A.B	0.024
	B	967	83	8.58	884	91.42		
Year 3	A	161	23	14.29	138	85.71	A.B	0.018
	B	160	10	6.25	150	93.75		

Bronchospasms, by Follow-Up Year: Patients Coded ‘Yes’ at Baseline

See Figure AE–2 on page 22.

			Value					
		Total	Yes		No			P-
	Trt	Pats	N	%	N	%	Contrast	Value
Baseline	A	225	225	100.00	0	0.00	A.B	1.00
	B	199	199	100.00	0	0.00		
Year 1	A	196	66	33.67	130	66.33	A.B	0.14
	B	176	47	26.70	129	73.30		
Year 2	A	108	40	37.04	68	62.96	A.B	0.76
	B	83	29	34.94	54	65.06		
Year 3	A	14	4	28.57	10	71.43	A.B	0.32
	B	9	1	11.11	8	88.89		

Bronchospasms, by Follow-Up Year: Patients Coded 'No' at Baseline

See Figure AE–2 on page 22.

			Value					
		Total	Yes		No			P-
	Trt	Pats	N	%	N	%	Contrast	Value
Baseline	A	1682	0	0.00	1682	100.00	A.B	1.000
	B	1713	0	0.00	1713	100.00		
Year 1	A	1527	115	7.53	1412	92.47	A.B	0.344
	B	1504	100	6.65	1404	93.35		
Year 2	A	892	76	8.52	816	91.48	A.B	0.034
	B	879	52	5.92	827	94.08		
Year 3	A	145	18	12.41	127	87.59	A.B	0.032
	B	150	8	5.33	142	94.67		

Chapter 4

Primary Endpoint Analysis

4.1 All-Cause Mortality over Time

Table Set MORT–1

All-Cause Mortality over Time: Probability of Survival, by Treatment Group

See Figure MORT–1 on page 24.

Treatment A						
	Number	Number	Survival	Std	95% Confidence Limits	
Days	at Risk	of Events	%	Error	Lower	Upper
0	1916	0	100.0	0.0	100.0	100.0
30	1899	16	99.2	0.2	98.8	99.6
60	1888	11	98.6	0.3	98.1	99.1
90	1878	10	98.1	0.3	97.5	98.7
120	1876	2	98.0	0.3	97.3	98.6
150	1871	5	97.7	0.3	97.0	98.4
180	1868	3	97.5	0.4	96.9	98.2
270	1850	18	96.6	0.4	95.8	97.4
360	1844	5	96.3	0.4	95.5	97.2
540	1501	25	94.9	0.5	93.9	95.9
720	1087	28	92.9	0.6	91.7	94.1
900	656	10	91.9	0.7	90.5	93.3
1080	202	4	91.0	0.8	89.4	92.7
1200	2	1	90.1	1.2	87.7	92.6

All-Cause Mortality over Time: Probability of Survival, by Treatment Group

See Figure MORT–1 on page 24.

Treatment B						
	Number	Number	Survival	Std	95% Confidence Limits	
Days	at Risk	of Events	%	Error	Lower	Upper
0	1921	0	100.0	0.0	100.0	100.0
30	1888	34	98.2	0.3	97.6	98.8
60	1879	6	97.9	0.3	97.3	98.6
90	1869	10	97.4	0.4	96.7	98.1
120	1859	11	96.8	0.4	96.0	97.6
150	1845	14	96.1	0.4	95.2	97.0
180	1838	6	95.8	0.5	94.9	96.7
270	1819	19	94.8	0.5	93.8	95.8
360	1804	15	94.0	0.5	93.0	95.1
540	1458	30	92.3	0.6	91.1	93.5
720	1077	20	90.9	0.7	89.5	92.2
900	654	12	89.7	0.8	88.2	91.2
1080	204	10	87.5	1.0	85.5	89.5
1200	5	1	86.8	1.2	84.4	89.3

4.3 All-Cause Mortality over Time for Selected Subgroups

Table Set MORT–3

All-Cause Mortality over Time by Age Group: Age $\leq$ 50 Years

See Figure MORT–3 on page 26.

Treatment A						
	Number	Number	Survival	Std	95% Confidence Limits	
Days	at Risk	of Events	%	Error	Lower	Upper
0	595	0	100.0	0.0	100.0	100.0
30	593	2	99.7	0.2	99.2	100.0
60	589	4	99.0	0.4	98.2	99.8
90	588	1	98.8	0.4	98.0	99.7
120	588	0	98.8	0.4	98.0	99.7
150	587	1	98.7	0.5	97.7	99.6
180	585	2	98.3	0.5	97.3	99.4
270	580	5	97.5	0.6	96.2	98.7
360	579	1	97.3	0.7	96.0	98.6
540	472	7	96.1	0.8	94.5	97.7
720	335	2	95.6	0.9	93.9	97.3
900	210	2	95.0	1.0	93.1	96.9
1080	74	2	94.0	1.2	91.7	96.3
1200	2	0	94.0	1.2	91.7	96.3

All-Cause Mortality over Time by Age Group: Age $\leq$ 50 Years

See Figure MORT–3 on page 26.

Treatment B						
	Number	Number	Survival	Std	95% Confidence Limits	
Days	at Risk	of Events	%	Error	Lower	Upper
0	569	0	100.0	0.0	100.0	100.0
30	562	6	98.9	0.4	98.1	99.8
60	561	0	98.9	0.4	98.1	99.8
90	559	2	98.6	0.5	97.6	99.6
120	557	2	98.2	0.6	97.2	99.3
150	555	2	97.9	0.6	96.7	99.1
180	552	3	97.4	0.7	96.0	98.7
270	548	4	96.7	0.8	95.2	98.1
360	545	3	96.1	0.8	94.5	97.7
540	451	6	95.0	0.9	93.2	96.8
720	335	3	94.3	1.0	92.3	96.3
900	187	3	93.2	1.2	90.9	95.5
1080	59	2	91.9	1.5	89.0	94.8
1200	1	0	91.9	1.5	89.0	94.8

All-Cause Mortality over Time by Age Group: Age $>$ 50 Years

See Figure MORT–3 on page 26.

Treatment A						
	Number	Number	Survival	Std	95% Confidence Limits	
Days	at Risk	of Events	%	Error	Lower	Upper
0	1321	0	100.0	0.0	100.0	100.0
30	1306	14	98.9	0.3	98.4	99.5
60	1299	7	98.4	0.3	97.7	99.1
90	1290	9	97.7	0.4	96.9	98.5
120	1288	2	97.6	0.4	96.7	98.4
150	1284	4	97.3	0.4	96.4	98.2
180	1283	1	97.2	0.5	96.3	98.1
270	1270	13	96.2	0.5	95.2	97.2
360	1265	4	95.9	0.5	94.8	97.0
540	1029	18	94.4	0.6	93.1	95.7
720	752	26	91.7	0.8	90.1	93.3
900	446	8	90.5	0.9	88.7	92.3
1080	128	2	89.7	1.1	87.6	91.8

All-Cause Mortality over Time by Age Group: Age $>$ 50 Years

See Figure MORT–3 on page 26.

Treatment B						
	Number	Number	Survival	Std	95% Confidence Limits	
Days	at Risk	of Events	%	Error	Lower	Upper
0	1352	1	100.0	0.0	100.0	100.0
30	1326	28	97.9	0.4	97.2	98.7
60	1318	6	97.5	0.4	96.7	98.3
90	1310	8	96.9	0.5	96.0	97.8
120	1302	9	96.2	0.5	95.2	97.2
150	1290	12	95.3	0.6	94.2	96.5
180	1286	3	95.1	0.6	94.0	96.3
270	1271	15	94.0	0.6	92.8	95.3
360	1259	12	93.1	0.7	91.8	94.5
540	1007	24	91.2	0.8	89.7	92.7
720	742	17	89.4	0.9	87.7	91.1
900	467	9	88.2	1.0	86.3	90.1
1080	145	8	85.7	1.3	83.2	88.3
1200	4	1	84.8	1.6	81.8	87.9

4.5 Mortality by Adjudicated Cause of Death

Table Set MORT–5

Mortality by Adjudicated Cause of Death: Mortality Classification

See Figure MORT–5 on page 28.

	Treatment Group					
	A		B			P-
	N	%	N	%	Contrast	Value
Total Patients	1916		1921		A.B	0.059
AHD - Sudden	64	3.34	89	4.63		
AHD - Non-sudden	55	2.87	75	3.90		
Other Cardiovascular	8	0.42	7	0.36		
Non-Cardiovascular	11	0.57	17	0.88		

Mortality by Adjudicated Cause of Death: Cause-Specific Mortality

See Figure MORT–5 on page 28.

		Treatment Group					
		A		B			P-
		N	%	N	%	Contrast	Value
Total Mortality	Total Patients	1916		1921		A.B	0.0041
	Yes	138	7.20	188	9.79		
Cardiovascular	Total Patients	1916		1921		A.B	0.0085
	Yes	127	6.63	171	8.90		
Atherosclerotic Heart Disease (ASHD) - All	Total Patients	1916		1921		A.B	0.0058
	Yes	119	6.21	164	8.54		
ASHD - Sudden	Total Patients	1916		1921		A.B	0.0407
	Yes	64	3.34	89	4.63		
ASHD - Non-sudden	Total Patients	1916		1921		A.B	0.0768
	Yes	55	2.87	75	3.90		
Other Cardiovascular	Total Patients	1916		1921		A.B	0.7920
	Yes	8	0.42	7	0.36		
Non-Cardiovascular	Total Patients	1916		1921		A.B	0.2580
	Yes	11	0.57	17	0.88		

Chapter 5

Additional Follow-Up Measures

5.1 Vital Signs

Table Set FU–1

Heart Rate: Annual Measurements

See Figure FU–1 on page 30.

	Trt	Total Pats	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Baseline	A	1916	76.17	9.80	76.00	70.00	82.00	61.00	93.00	A.B	0.15697
	B	1921	75.73	9.83	75.00	69.00	82.00	60.00	93.00		
Year 1	A	1687	64.84	11.44	63.00	58.00	72.00	48.00	86.00	A.B	0.00000
	B	1654	72.73	11.20	72.00	64.00	80.00	56.00	92.00		
Year 2	A	963	64.95	11.73	64.00	58.00	72.00	48.00	84.00	A.B	0.00000
	B	932	72.67	11.12	72.00	64.00	80.00	56.00	92.00		
Year 3	A	156	63.35	9.58	62.00	58.00	68.00	50.00	80.00	A.B	0.00000
	B	154	73.01	10.56	72.00	64.00	78.00	60.00	92.00		

Heart Rate: Change from Baseline

See Figure FU–1 on page 30.

	Trt	Total Pats	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Year 1	A	1687	-11.1	13.3	-11.0	-20.0	-3.0	-32.0	12.0	A.B	0.00000
	B	1654	-2.7	12.7	-3.0	-11.0	5.0	-23.0	19.0		
Year 2	A	963	-11.0	13.7	-11.0	-19.0	-3.0	-32.0	10.0	A.B	0.00000
	B	932	-2.8	13.3	-3.0	-11.5	5.5	-24.0	20.0		
Year 3	A	156	-10.6	12.2	-10.0	-17.5	-3.5	-31.0	9.0	A.B	0.00000
	B	154	-2.4	12.6	-4.0	-10.0	3.0	-20.0	27.0		

5.2 Laboratory Data

Table Set FU–2

White Blood Cell Count: Annual Measurements

See Figure FU–2 on page 31.

	Trt	Total Pats	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Baseline	A	1888	8142	2848	7900	6500	9500	4600	13300	A.B	0.099
	B	1901	8298	3216	8000	6700	9600	4900	13000		
Year 1	A	1618	7212	1938	7000	6000	8200	4600	10400	A.B	0.052
	B	1590	7148	2122	6900	5800	8200	4500	10500		
Year 2	A	925	7356	3094	7100	5900	8400	4600	10600	A.B	0.207
	B	898	7218	2027	6950	5900	8200	4600	11000		
Year 3	A	152	7122	1792	6900	5950	7900	4600	10700	A.B	0.685
	B	153	7022	1965	6900	5800	8000	4500	9900		

White Blood Cell Count: Change from Baseline

See Figure FU–2 on page 31.

	Trt	Total Pats	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Year 1	A	1598	-897	2963	-700	-2300	500	-5700	3500	A.B	0.003
	B	1576	-1171	3360	-1000	-2400	200	-5800	3000		
Year 2	A	912	-603	3021	-600	-2200	700	-5200	4800	A.B	0.061
	B	888	-835	3186	-800	-2200	400	-5200	4210		
Year 3	A	148	-183	3208	-300	-1400	900	-4100	6000	A.B	0.415
	B	152	-218	2704	-550	-1600	450	-3900	5900		

White Blood Cell Count: Patients with WBC $<$ 4000

See Figure FU–2 on page 31.

			Value			
		Total	Yes			P-
	Trt	Pats	N	%	Contrast	Value
Baseline	A	1888	67	3.55	A.B	0.34
	B	1901	57	3.00		
Year 1	A	1618	31	1.92	A.B	0.64
	B	1590	27	1.70		
Year 2	A	925	17	1.84	A.B	0.79
	B	898	15	1.67		
Year 3	A	152	3	1.97	A.B	0.99
	B	153	3	1.96		

Table Set FU–3

Urinalysis Findings: Bilirubin

See Figure FU–3 on page 32.

			Value			
		Total	Positive			P-
	Trt	Pats	N	%	Contrast	Value
Baseline	A	1881	19	1.01	A.B	0.15
	B	1881	29	1.54		
Year 1	A	1642	18	1.10	A.B	0.69
	B	1601	20	1.25		
Year 2	A	932	6	0.64	A.B	0.81
	B	901	5	0.55		
Year 3	A	154	0	0.00	A.B	1.00
	B	153	0	0.00		

Urinalysis Findings: Blood

See Figure FU–3 on page 32.

			Value			
		Total	Positive			P-
	Trt	Pats	N	%	Contrast	Value
Baseline	A	1882	78	4.14	A.B	0.07
	B	1881	57	3.03		
Year 1	A	1642	35	2.13	A.B	0.73
	B	1601	37	2.31		
Year 2	A	933	20	2.14	A.B	0.25
	B	901	27	3.00		
Year 3	A	154	4	2.60	A.B	0.71
	B	153	3	1.96		

Urinalysis Findings: Ketones

See Figure FU–3 on page 32.

			Value			
		Total	Positive			P-
	Trt	Pats	N	%	Contrast	Value
Baseline	A	1881	38	2.02	A.B	0.05
	B	1881	57	3.03		
Year 1	A	1642	15	0.91	A.B	0.35
	B	1601	10	0.62		
Year 2	A	933	14	1.50	A.B	0.61
	B	901	11	1.22		
Year 3	A	154	0	0.00	A.B	0.31
	B	153	1	0.65		

Urinalysis Findings: Glucose

See Figure FU–3 on page 32.

			Value			
		Total	Positive			P-
	Trt	Pats	N	%	Contrast	Value
Baseline	A	1880	130	6.91	A.B	0.35
	B	1881	116	6.17		
Year 1	A	1642	95	5.79	A.B	0.55
	B	1602	85	5.31		
Year 2	A	933	65	6.97	A.B	0.34
	B	901	53	5.88		
Year 3	A	154	13	8.44	A.B	0.68
	B	153	11	7.19		

Urinalysis Findings: Protein

See Figure FU–3 on page 32.

			Value			
		Total	Positive			P-
	Trt	Pats	N	%	Contrast	Value
Baseline	A	1880	259	13.78	A.B	0.05
	B	1880	301	16.01		
Year 1	A	1641	206	12.55	A.B	0.76
	B	1599	195	12.20		
Year 2	A	932	124	13.30	A.B	0.68
	B	901	114	12.65		
Year 3	A	154	18	11.69	A.B	0.98
	B	153	18	11.76		

5.3 Cigarette Smoking

Table Set FU–4

Cigarette Smoking: Baseline

See Figure FU–4 on page 33.

	Treatment Group					
	A		B			P-
	N	%	N	%	Contrast	Value
Total Patients	1916		1921		A.B	0.30
> 2 packs	253	13.20	228	11.87		
1-2 packs	622	32.46	607	31.60		
< 1 pack	225	11.74	260	13.53		

Cigarette Smoking: Year 1

See Figure FU–4 on page 33.

	Treatment Group					
	A		B			P-
	N	%	N	%	Contrast	Value
Total Patients	1734		1689		A.B	0.43
> 2 packs	23	1.33	18	1.07		
1-2 packs	168	9.69	169	10.01		
< 1 pack	328	18.92	295	17.47		

Cigarette Smoking: Year 2

See Figure FU–4 on page 33.

	Treatment Group					
	A		B			P-
	N	%	N	%	Contrast	Value
Total Patients	1004		969		A.B	0.030
> 2 packs	24	2.39	15	1.55		
1-2 packs	124	12.35	106	10.94		
< 1 pack	193	19.22	165	17.03		

Cigarette Smoking: Year 3

See Figure FU–4 on page 33.

	Treatment Group					
	A		B			P-
	N	%	N	%	Contrast	Value
Total Patients	161		160		A.B	0.67
> 2 packs	4	2.48	3	1.88		
1-2 packs	24	14.91	18	11.25		
< 1 pack	22	13.66	27	16.88		

5.4 Concomitant Medication

Table Set FU–5

Concomitant Medication Usage

See Figure FU–5 on page 34.

			Value					
		Total	First Present at Baseline		Present After Randomization			P-
	Trt	Pats	N	%	N	%	Contrast	Value
Antiarrhythmics	A	1916	319	16.65	94	4.91	A.B	0.015
	B	1921	344	17.91	132	6.87		
Anticoagulants	A	1916	267	13.94	36	1.88	A.B	0.420
	B	1921	290	15.10	29	1.51		
Antihypertensives, Excluding Diuretics	A	1916	82	4.28	91	4.75	A.B	0.055
	B	1921	90	4.69	124	6.45		
Aspirin	A	1916	110	5.74	193	10.07	A.B	0.698
	B	1921	102	5.31	206	10.72		
Digitalis	A	1916	239	12.47	202	10.54	A.B	0.828
	B	1921	250	13.01	208	10.83		

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Concomitant Medication Usage

See Figure FU–5 on page 34.

			Value					
		Total	First Present at Baseline		Present After Randomization			P-
	Trt	Pats	N	%	N	%	Contrast	Value
Dipyridamole	A	1916	16	0.84	49	2.56	A.B	0.467
	B	1921	11	0.57	57	2.97		
Diuretics	A	1916	308	16.08	372	19.42	A.B	0.258
	B	1921	346	18.01	374	19.47		
Insulin	A	1916	68	3.55	15	0.78	A.B	0.678
	B	1921	65	3.38	20	1.04		
Lipid-Lowering Agents	A	1916	16	0.84	19	0.99	A.B	0.833
	B	1921	19	0.99	17	0.88		
Vasodilators	A	1916	690	36.01	222	11.59	A.B	0.951
	B	1921	698	36.34	226	11.76		
Oral Hypoglycemics	A	1916	43	2.24	37	1.93	A.B	0.089
	B	1921	35	1.82	22	1.15		
Sulfinpyrazone	A	1916	19	0.99	16	0.84	A.B	0.086
	B	1921	26	1.35	29	1.51		
Other Cardiovascular Medications	A	1916	112	5.85	141	7.36	A.B	0.209
	B	1921	124	6.45	167	8.69		

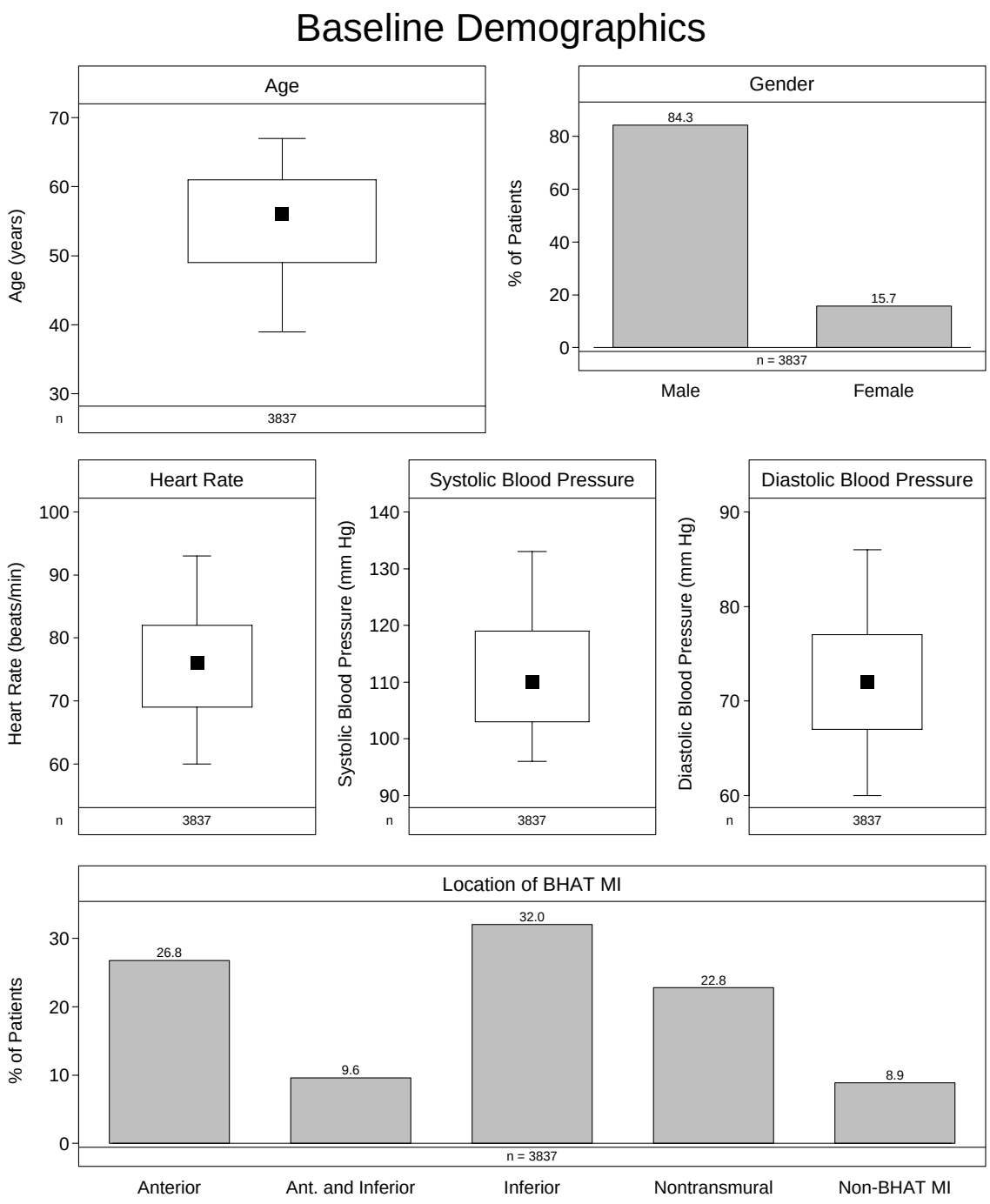
Part IV

Ancillary Material

Chapter 1

Open Session Report Style Plots

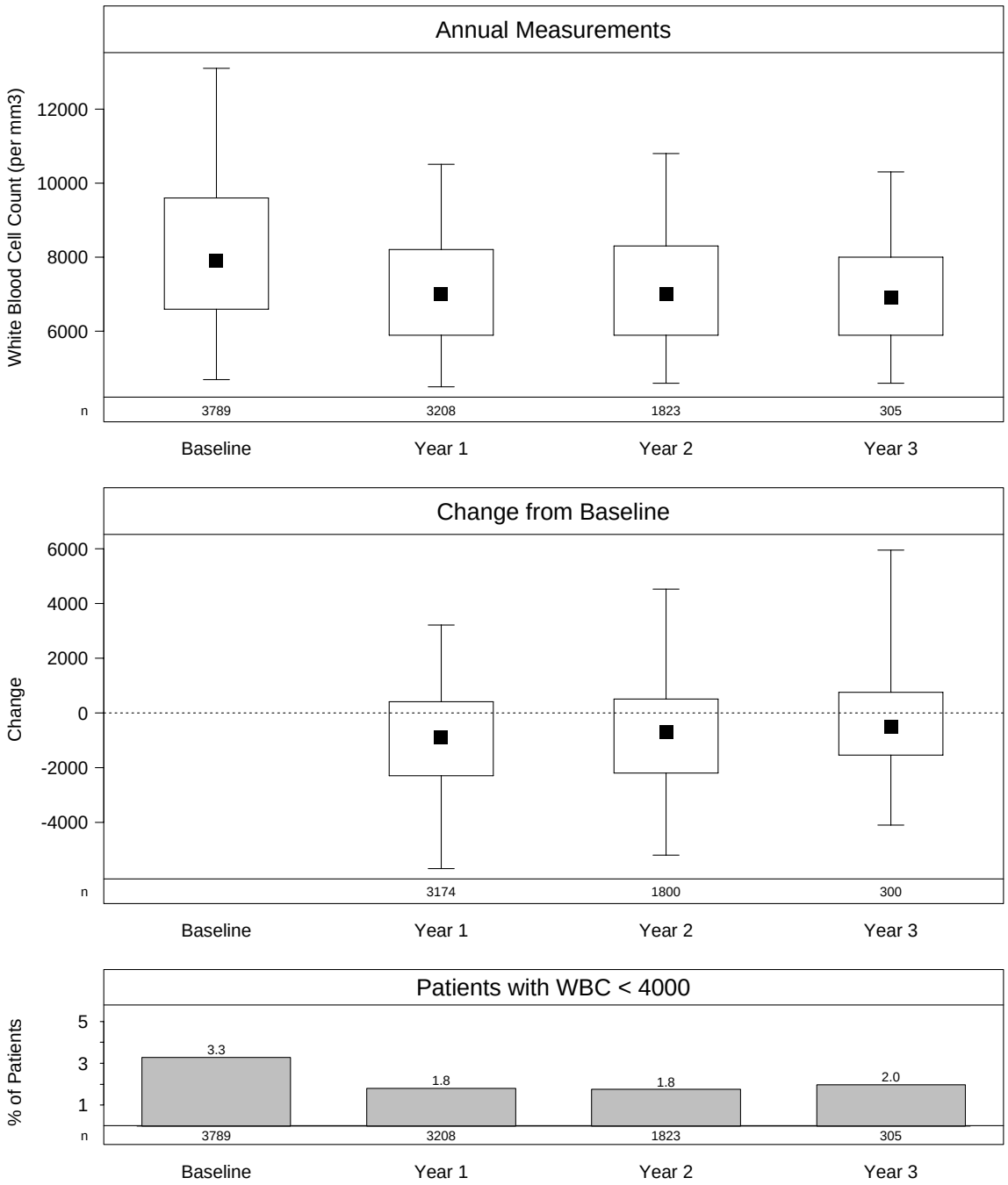
Figure ANCI–1



Information determined by baseline interview, physical examination, and ECG administered prior to randomization. ECGs for the BHAT qualifying MI were initially read at the clinical center, and later confirmed by the Resting ECG Reading Center. See the *Introduction*, page 9, for discussion of “Non-BHAT MI” classification. See also Figure BASE–1 on page 18 for the Closed Session Report version of this page.

Figure ANCI–2

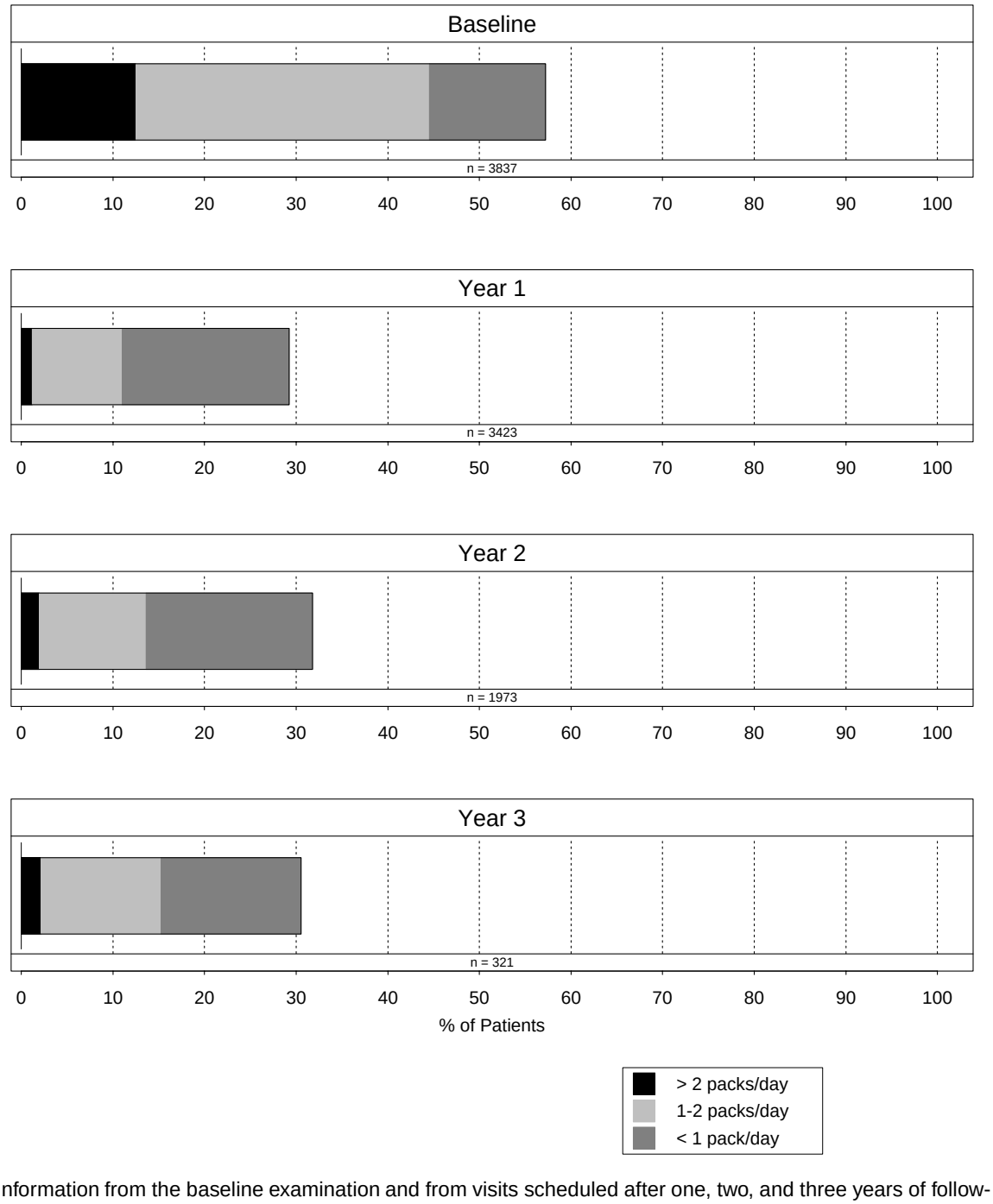
White Blood Cell Count



Information from the baseline examination and from visits scheduled after one, two, and three years of follow-up. Panels show measurements at each visit, absolute change from baseline, and percent of patients with white blood cell (WBC) count $<$ 4000. See also Figure FU–2 on page 31 for the Closed Session Report version of this page.

Figure ANCI–3

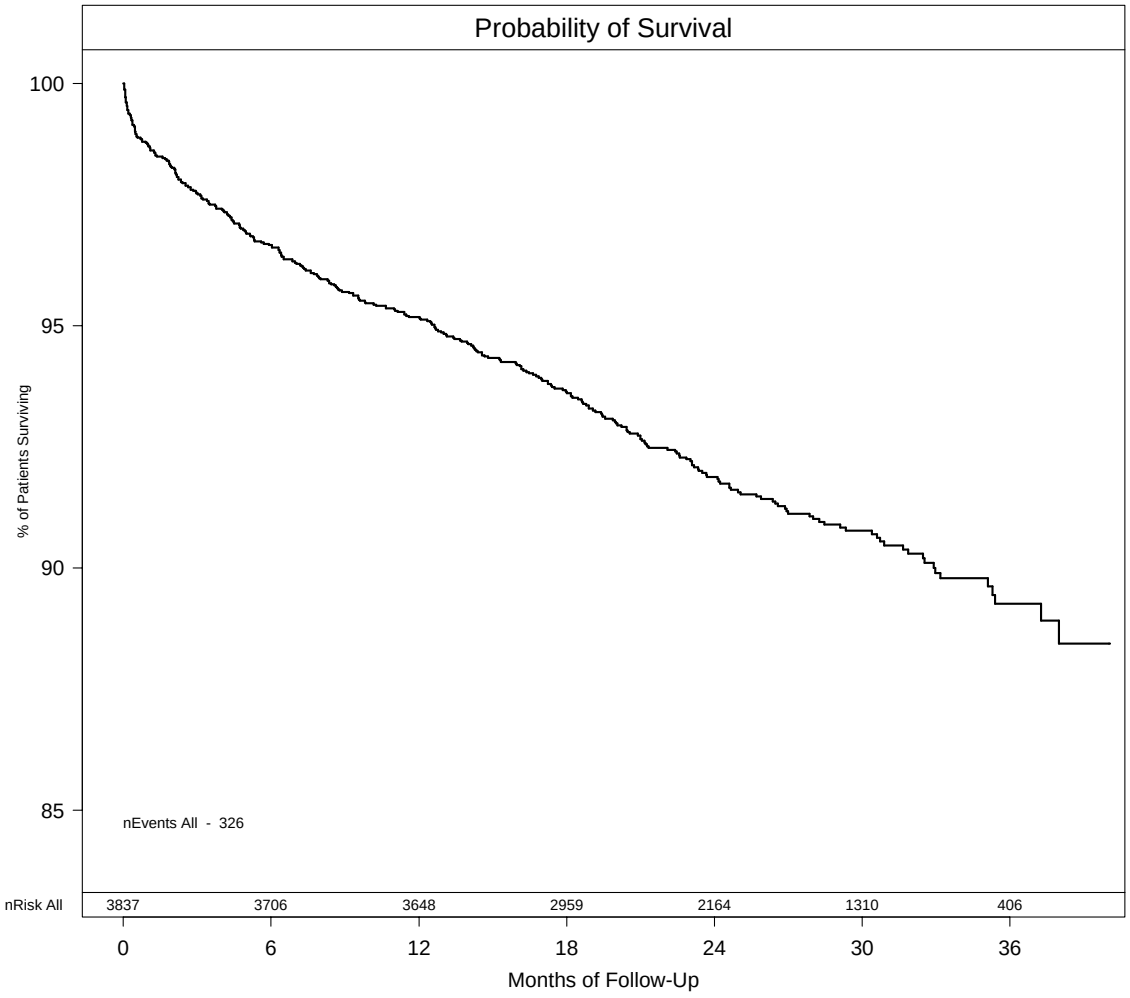
Cigarette Smoking



Information from the baseline examination and from visits scheduled after one, two, and three years of follow-up. Panels show the percent of patients at each visit categorized as heavy, moderate, or light smokers based on interview results. See also Figure FU–4 on page 33 for the Closed Session Report version of this page.

Figure ANCI–4

All-Cause Mortality over Time



All-cause mortality collapsed over assigned treatment groups. The total number of deaths appear on the plot ("nEvents"), as do the numbers of patients at risk (event-free and uncensored) at various points of follow-up. Surviving patients were censored as described in the *Introduction* on page 8. See also Figure MORT–1 on page 24 for the Closed Session Report version of this page.

Index of Figures and Tables

Page numbers for main material appear in normal (unslanted) type; page numbers for supporting material, if any, are given in italics.