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2 THE DIOXIN ASSAY

2.1 PARTICIPANTS SELECTED FOR DIOXIN MEASUREMENT

The eligibility for participants at the 1997 physical examination to have a blood measurement of dioxin was determined by assignment to one of three categories: (a) previous participants with a quantitative dioxin result who were selected for an additional blood measurement of dioxin to advance pharmacokinetic studies (1), (b) previous participants returning to the 1997 physical examination with no prior dioxin blood measurement or no previously quantitative dioxin results, and (c) first-time participants. Of the 2,121 participants at the 1997 follow-up examination, a total of 594 participants were asked to provide a blood sample for use in analysis of serum dioxin levels. Table 2-1 shows the number of participants selected for the 1997 dioxin blood measurement belonging to each category by exposure group (Ranch Hand, Comparison). Table 2-1 also gives the number of actual dioxin assay results obtained that belonged to each category by exposure group.

Table 2-1. Participants with a 1997 Blood Measurement of Dioxin

Category	Number Eligible			Number of Results		
	Ranch Hand	Comparison	Total	Ranch Hand	Comparison	Total
Returning participants with a previous quantitative dioxin result selected for another blood measurement of dioxin to advance pharmacokinetic studies	430	0	430	421	0	421
Returning participants who either attended the 1987 or 1992 follow-ups but had no previous dioxin blood measurement or no previous quantitative dioxin result	18	42	60	17	40	57
Participants who were selected for a dioxin blood measurement for the first time	11	93	104	5	80	85
Total	459	135	594	443	120	563

Table 2-2 displays the reasons why blood samples from 31 participants were not obtained. Nine participants were medically deferred because of pending surgery or a low hemoglobin level, and 22 participants refused the blood measurement of dioxin. Samples for the remaining 563 participants were shipped to the Centers for Disease Control and Prevention (CDC) for analysis.

Table 2-2. Participants Eligible for the 1997 Blood Measurement of Dioxin and Reasons for Participant Sample Exclusions

Distribution of Sample Exclusion	Ranch Hand	Comparison	Total
Total Eligible for Blood Measurement of Dioxin	459	135	594
Less:			
Medically Deferred	(7)	(2)	(9)
Refused	(9)	(13)	(22)
Total Specimens Sent to CDC	443	120	563

2.2 SAMPLE ACQUISITION

Following a CDC protocol, blood was drawn from consenting participants for the serum dioxin assay on the morning of the second day of the 1997 physical examination. The participants were instructed to fast after midnight (water was allowed), and samples were drawn with a 15-gauge needle into a blood pack unit without anticoagulant. CDC purchased blood bags in lots of 1,200, packaged in 50 boxes of 24 bags per box, and tested one bag per box to assess dioxin contamination. If the tested bag was found to be free of dioxin contamination, the box of 24 bags was shipped to the Air Force for use in the study.

Participants had 280 ml of blood drawn. After the draw, the bags were clamped, labeled, placed upright, and the samples were allowed to clot at room temperature for 7 hours.

The clotted samples were centrifuged for 15 minutes at 4,500 revolutions per minute between 4° and 10 °C. The serum was then transferred from the spun unit bag by a plasma extractor to transfer packs that also were tested and found to be free of dioxin. The transfer packs were then spun for 15 minutes at 4,500 revolutions per minute. The serum was placed into four Wheaton bottles: two 4-ounce bottles for the serum dioxin analysis, a 5 ml bottle for the lipid profile, and a 10 ml bottle for the reserve serum. Samples were catalogued and stored at –70 °C or colder until shipment. Appendix A contains the detailed procedures used by Scripps Clinic for the dioxin blood collection and processing. Frozen samples were packed in dry ice in Styrofoam boxes and shipped weekly from Scripps Clinic in La Jolla, California, to Brooks Air Force Base, Texas. At Brooks Air Force Base, inventory was taken and the specimens were stored at –70 °C until shipment to CDC. All samples were coded so that the CDC staff was blinded to the exposure group status (Ranch Hand, Comparison) of each specimen.

2.3 ANALYTICAL METHOD

The serum samples were analyzed for dioxin in groupings consisting of a method blank, three unknown samples, and a quality control (QC) pool sample (2, 3). Cholesterol esters, triglycerides, and high-density lipoprotein cholesterol were determined in duplicate by standard methods. Total phospholipids were determined in duplicate by modifying the Folch, et al., procedure (4, 5). Free cholesterol was determined in duplicate by an enzymatic method (6). For each analysis, the mean result of duplicate analyses was used to calculate the concentrations of total lipids using the summation method (7), low-density lipoprotein cholesterol, and very low-density lipoprotein cholesterol (8).

2.4 QUALITY CONTROL

Quality assurance was maintained with matrix-based materials well characterized for dioxin concentration and isotope ratios to ensure that the analytical system was in control. QC charts were maintained for each of these materials (five serum pools). The concentration in the QC sample from each analytical run was

required to be within established 99-percent confidence limits (9, 10). The unlabeled and carbon-13 labeled internal standard isotope ratios were required to be within 95-percent confidence limits. All analytical runs for the dioxin and lipid measurements were in control. No dioxin was detected in the blanks (on-column injection of 100 femtograms from a standard solution produces detectable signals greater than three times the background noise).

2.5 DATA DESCRIPTION

CDC delivered whole-weight and lipid-adjusted dioxin concentrations to the Air Force, together with the total sample weight, weights of lipid fractions, total lipid weight, detection limit, quantitation limit, and all associated QC information, including results from blank samples. The lipid-adjusted dioxin concentration was calculated using the whole-weight dioxin concentration and the total lipid weight. Details of the calculation are discussed subsequently in this chapter. Table 2-3 provides the results of the 1997 physical examination blood measurements of dioxin by exposure group and result comment. Result comments are based on whether the result was measurable, or good, (G); measurable, but below the limit of detection (GND) or below the limit of quantitation (GNQ); or no result was obtained (NR).

Table 2-3. Result Comments for the 1997 Blood Measurements of Dioxin

Result Comment	Ranch Hand	Comparison	Total
Good Result (G)	430	82	512
Good Result, Below Limit of Detection (GND)	11	35	46
Good Result, Below Limit of Quantitation (GNQ)	0	0	0
No Result (NR)	2	3	5
Total	443	120	563

Note: The two Ranch Hands with no result at the 1997 follow-up examination had a good result at a previous follow-up examination.

The Air Force Health Study (AFHS) dioxin database is a combination of the dioxin assay results from the 1987, 1992, and 1997 examinations. Table 2-4 shows the number of blood measurements of dioxin by year and illustrates the high percentage of study participants who have had dioxin measurements. Of the 2,121 fully compliant participants for the 1997 study, 2,101 (99.1%) had blood measurements of dioxin in 1997 or in a previous study.

Table 2-4. Dioxin Results for 1997 Physical Examination Participants

Years of Dioxin Blood Measurement Result	Ranch Hand	Comparison	Total
No Dioxin Blood Measurement	6	14	20
1987 Only	297	865	1,162
1992 Only	56	118	174
1997 Only	12	93	105
1987 and 1992	68	134	202
1987 and 1997	153	6	159
1992 and 1997	5	7	12
1987, 1992, and 1997	273	14	287
Total	870	1,251	2,121

Note: 1987 includes participants from both the 1987 pilot study and the 1987 follow-up physical examination.

Participants may have been assayed during any combination of four events: the pilot study conducted in April 1987 (9), the 1987 follow-up examination (May 1987 to March 1988), the 1992 follow-up examination (May 1992 to March 1993), or the 1997 follow-up examination (May 1997 to April 1998). The majority of participants had an assay in 1987, through either the pilot study or the 1987 follow-up examination. Consequently, 1987 was designated as the reference point for post-Southeast Asia (SEA) serum dioxin levels, termed "current dioxin" in previous AFHS reports and "1987 dioxin" subsequently in this report.

Each participant with a good (G or GND) dioxin result was given a "reference" dioxin assay result derived from the good result. When a participant had multiple assay results, first priority was given to the 1987 pilot-study dioxin results, second priority was given to results derived from serum collected at the 1987 physical examination, third priority was given to the 1992 results, and fourth priority was given to the 1997 results. Figure 2-1 outlines this decision process and shows that the first quantitative result was used.

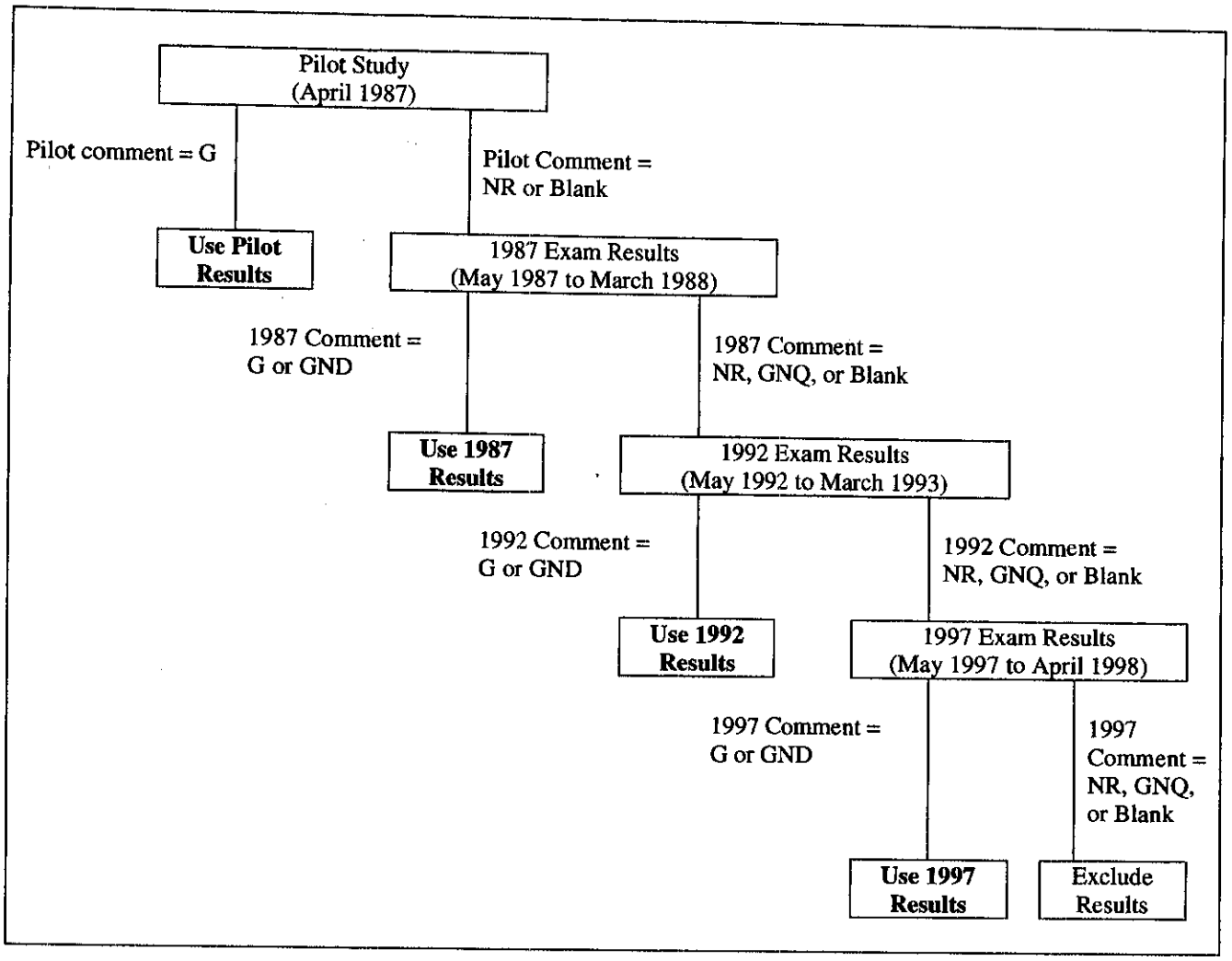

Figure 2-1. Decision Process for Determination of Dioxin Results for Analysis

Of the 2,121 fully compliant participants at the 1997 physical examination, 870 were Ranch Hands and 1,251 were Comparisons. Of the 2,121 participants, 20 had never had blood measured for dioxin. Six participants had missing dioxin results (result comment = NR) or nonquantitative dioxin results (result comment = GNQ). A total of 2,095 participants, consisting of 863 Ranch Hands and 1,232 Comparisons, had quantitative dioxin measurements. Table 2-5 summarizes the sample sizes by exposure group. The six participants with missing or nonquantitative dioxin results are cross-classified in Table 2-6 by result comment and exposure group.

Table 2-5. Results from Blood Measurements of Dioxin

Summary of Sample Size Reduction	Ranch Hand	Comparison	Total
1997 Follow-up Participants	870	1,251	2,121
Less: No Blood Measurement of Dioxin at any Physical Examination	(6)	(14)	(20)
1997 Follow-up Participants with a Dioxin Assay	864	1,237	2,101
Less: Missing or Nonquantitative (Good Result, but Below Limit of Quantitation or No Result)	(1)	(5)	(6)
1997 Follow-up Participants with Quantitative Dioxin Results	863	1,232	2,095

Table 2-6. Results from Blood Measurements of Dioxin with Missing or Nonquantitative Results

1987 Assay	1992 Assay	1997 Assay	Ranch Hand	Comparison	Total
GNQ			1	1	2
GNQ	GNQ		0	1	1
GNQ		NR	0	1	1
		NR	0	2	2
Total			1	5	6

Note: GNQ = Good result, below level of quantitation.
NR = No Result.

If the 1987 pilot study or follow-up measurement was not used, the 1987 dioxin level was derived for each participant in the following manner. If the 1992 measurement was used, the level was extrapolated to 1987 levels when the 1992 dioxin concentration surpassed 10 parts per trillion (ppt). These extrapolated lipid-adjusted dioxin values were calculated using a first-order elimination model with a half-life of 8.7 years and a background level of 4 ppt. Levels at or below 10 ppt were not extrapolated because the first-order elimination model was not considered to be valid at background levels (lipid-adjusted 1987 dioxin levels ≤10 ppt). If the 1997 measurement was used, the level was extrapolated to 1987 levels when the 1997 dioxin concentration surpassed 10 ppt. Details on the extrapolation method are given in Chapter 7, Statistical Methods. A summary detailing the year the measurement was used and whether the dioxin level was extrapolated to 1987 dioxin levels is provided in Table 2-7 by exposure group.

Table 2-7. Summary of Number of Assays Used for 1997 Follow-up Participant Dioxin Measures

Study	Ranch Hand		Comparison		Total	
Pilot (1987)	127		44		171	
1987 Follow-up	615		858		1,473	
1992 Follow-up	99		213		312	
Extrapolated to 1987		35		0		35
Not Extrapolated to 1987		64		213		277
1997 Follow-up	22		117		139	
Extrapolated to 1987		4		0		4
Not Extrapolated to 1987		18		117		135
Total	863		1,232		2,095	

2.6 LIPID-ADJUSTED AND WHOLE-WEIGHT CURRENT DIOXIN MEASUREMENTS

Serum dioxin is defined as the serum concentration of 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin). It can be expressed as a lipid-adjusted or a whole-weight measurement. The lipid-adjusted dioxin measurement, also called "current dioxin body burden," is a derived quantity calculated from the formula ppt = ppq·102.6/W, where ppt is the lipid-adjusted concentration, ppq (parts per quadrillion) is the actual weight of dioxin in the sample (also known as whole-weight dioxin) in femtograms, 102.6 corrects for the average density of serum, and W is the total lipid weight of the sample (10).

The correlation between the serum lipid-adjusted concentration and adipose tissue lipid-adjusted concentration of dioxin has been observed to be 0.98 in 50 persons from Missouri (11). Using the same data, Patterson, et al., calculated the partitioning ratio of dioxin between adipose tissue and serum on a lipid-adjusted basis as 1.09 (95% confidence interval: [0.97,1.21]). On the basis of these data, a one-to-one partitioning ratio of dioxin between lipids in adipose tissue and lipids in serum cannot be excluded. Measurements of dioxin in adipose tissue generally have been accepted as representing the body burden concentration of dioxin. The high correlation between serum dioxin levels and adipose tissue dioxin levels in the study by Patterson, et al., suggests that serum dioxin is also a valid measurement of dioxin body burden.

Figures 2-2 and 2-3 show the distribution of serum lipid-adjusted dioxin for the 863 Ranch Hands and 1,232 Comparisons whose results were used in analyses of 1987 dioxin versus health in this report. Figure 2-4 compares distributions of serum lipid-adjusted dioxin concentrations for Ranch Hands and Comparisons on the same scale (parts per trillion). Figure 2-5 compares distributions of the logarithm (base 2) of serum lipid-adjusted dioxin concentrations for Ranch Hands and Comparisons on the same scale.

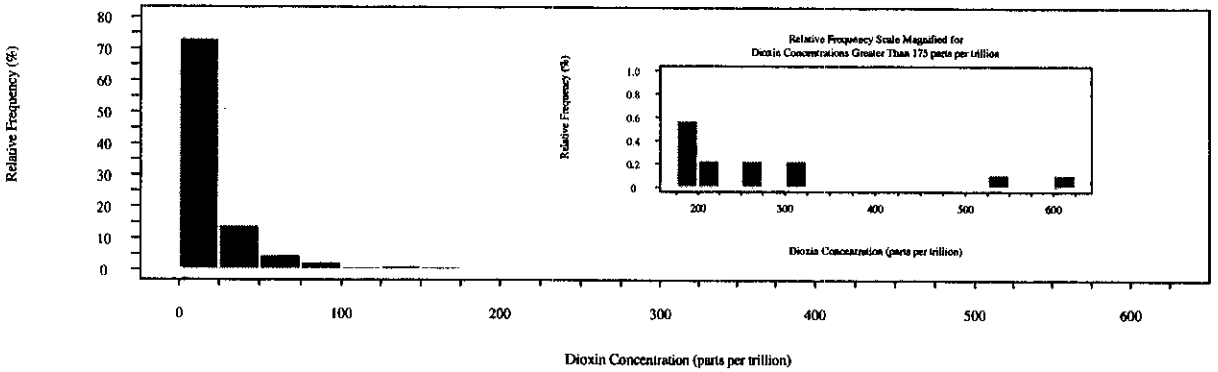

Figure 2-2. Relative Frequency Distribution of Lipid-adjusted Dioxin Concentrations for 863 Ranch Hands

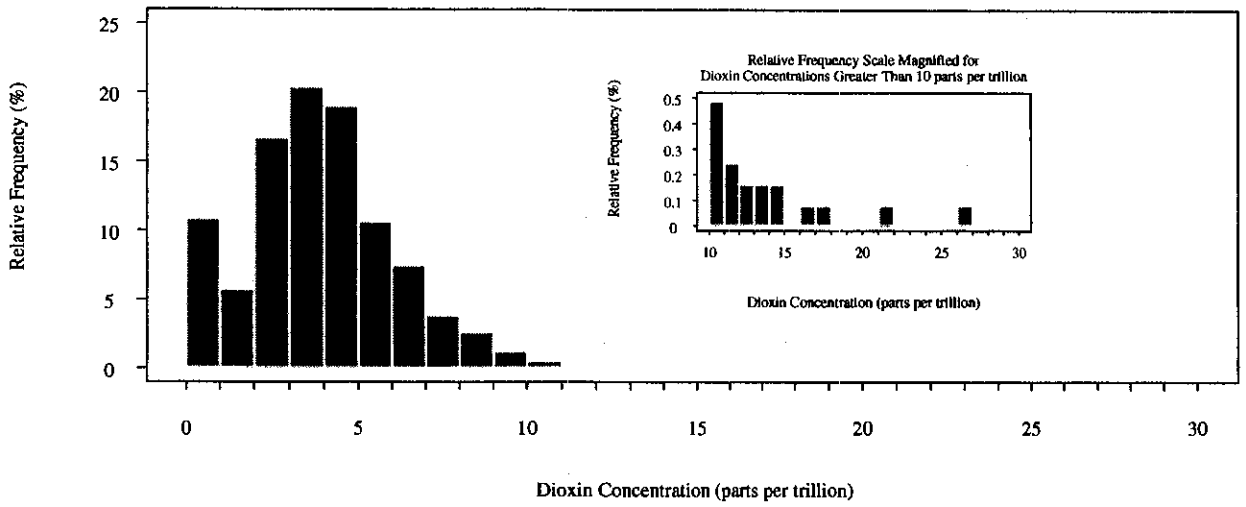

Figure 2-3. Relative Frequency Distribution of Lipid-adjusted Dioxin Concentrations for 1,232 Comparisons

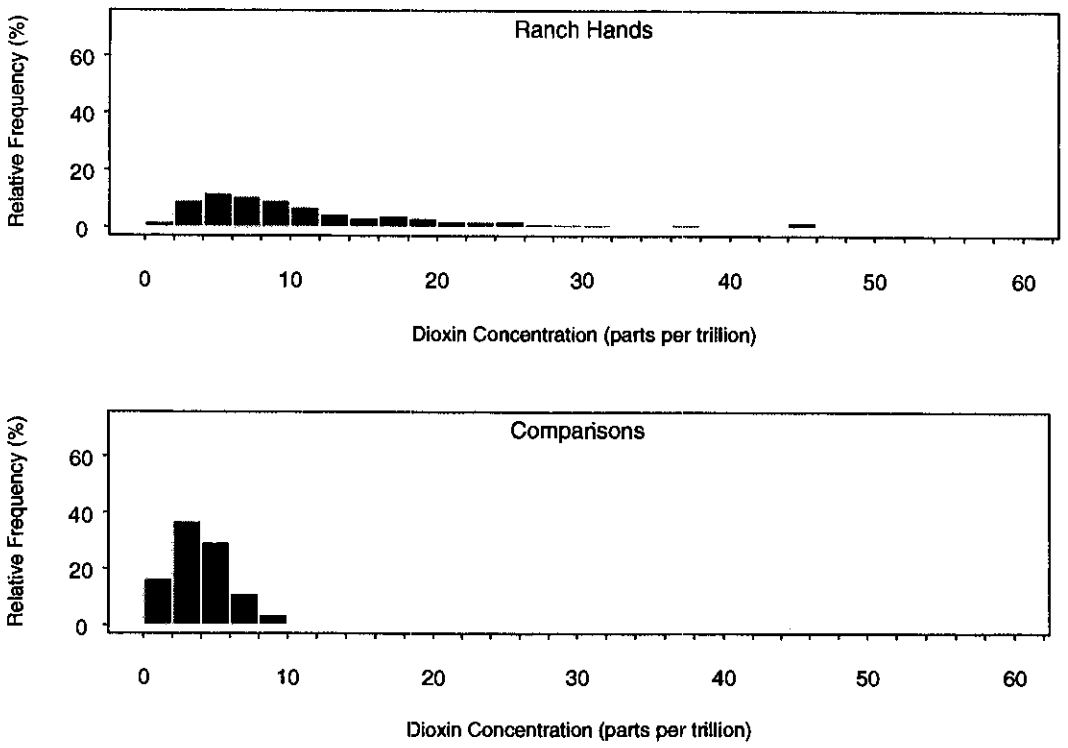

Figure 2-4. Relative Frequency Distribution of Lipid-adjusted Dioxin Concentrations

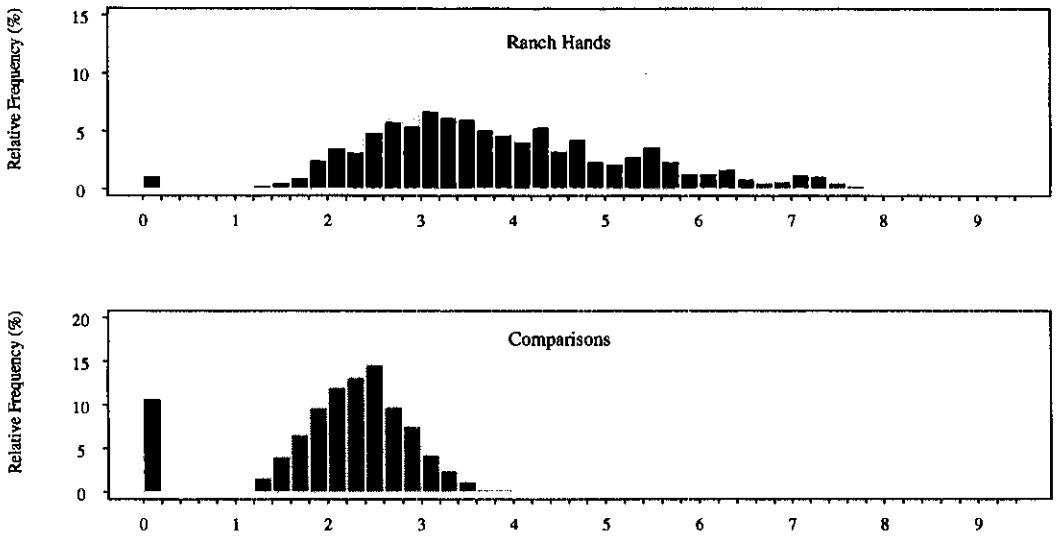

Figure 2-5. Relative Frequency Distribution of the Logarithm (Base 2) of Lipid-adjusted Dioxin Concentrations

Table 2-8 summarizes, by military occupation and exposure group, the serum lipid-adjusted dioxin results among the 863 Ranch Hands and 1,232 Comparisons whose results were used in the analyses of dioxin versus health in this report. For Ranch Hands, the median level was greatest for enlisted groundcrew and least for officers.

Table 2-8. Lipid-adjusted Dioxin Result Summary

Military Occupation	Ranch Hand n	Ranch Hand Median (ppt)	Ranch Hand Range (ppt)	Comparison n	Comparison Median (ppt)	Comparison Range (ppt)
Officer	197	7.4	0-36.0	486	4.0	0-17.3
Enlisted Flyer	151	16.4	0-195.5	186	3.8	0-12.8
Enlisted Groundcrew	375	24.0	0-617.8	560	3.6	0-26.6
Total	863	11.6	0-617.8	1,232	3.8	0-26.6

Note: ppt = parts per trillion.

2.7 SUMMARY

In summary, serum was collected for dioxin analysis for 563 participants at the 1997 follow-up at Scripps Clinic. The serum was shipped from Scripps Clinic to Brooks Air Force Base to CDC according to rigid protocols. The data collected from the 1997 follow-up assays were combined with data from the 1987 pilot study, 1987 follow-up examination, and 1992 follow-up examination for use in pharmacokinetic studies and for determining post-SEA dioxin levels. After combining data from this and previous follow-ups, a total of 863 of the 870 Ranch Hands (98.5%) and 1,232 of the 1,251 Comparisons (99.1%) attending the 1997 follow-up examination had quantitative dioxin assay results.

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3 QUESTIONNAIRE METHODOLOGY

This chapter describes the development and implementation of the two participant questionnaires used in the 1997 follow-up to the Air Force Health Study (AFHS): the 1997-98 Health Interval Questionnaire and the 1997-98 Study Subject Baseline Questionnaire. Both questionnaires were formatted and administered by the National Opinion Research Center (NORC), a social science research center at the University of Chicago.

The two 1997 questionnaires were comparable to those used in the baseline study and the 1985, 1987, and 1992 follow-up efforts. In the 1982 baseline study, interviews were conducted in the participants' homes. In the 1985, 1987, and 1992 studies, the follow-up interviews were conducted in person at the physical examination site. The latter method proved to be more efficient and subject to better quality control (QC). In all the examinations before 1997, the questionnaires were administered in hard copy, which was later edited and key-entered into the final SAS®[1] data set. For the 1997 follow-up, the interview responses were recorded electronically on laptop computers using a computer-assisted personal interviewing (CAPI) system. This method afforded an added measure of QC.

The baseline questionnaire was administered to any participant who had not previously completed that questionnaire. With the exception of the translation into the CAPI format, the baseline questionnaire has not changed since 1982. The interval questionnaire was designed to capture the participant's health history in the interval since participation in previous follow-up examinations. In addition, the interval questionnaire elicited general health measures needed by the debriefing physicians.

3.1 QUESTIONNAIRE DEVELOPMENT

An objective of questionnaire development in each follow-up year has been to maintain, to the maximum extent possible, the question wording, context, and procedures used in the 1982 baseline study. In addition, the interval questionnaire was often augmented to obtain data on new areas of inquiry. The central task of questionnaire development has been to obtain interval histories on questionnaire items, thereby updating the information provided in previous follow-up studies. For instance, if a study subject participated in the 1992 follow-up, the 1997-98 Health Interval Questionnaire elicited an interval history for the period from 1992 to 1997; however, if the subject last participated in the baseline study or the 1985 follow-up, the 1997-98 Health Interval Questionnaire elicited an interval history from those dates until 1997.

3.1.1 Baseline Questionnaire

The baseline questionnaire used during the 1997 examination was developed in 1982 and has never been changed. The 1982 Study Subject Baseline Questionnaire obtained information on demographics, education, occupation, medical history, study compliance, toxic exposures, and reproductive history. In general, responses to histories and other questions where the response does not change over time were obtained in the baseline questionnaire. Each participant completed the baseline questionnaire the first time he participated in the study. In the 1997 follow-up study, no changes were made to the content of the baseline questionnaire.

[1] SAS and all other SAS Institute, Inc., product and service names are registered trademarks or trademarks of SAS Institute, Inc., in the USA and other countries.

3.1.2 Interval Questionnaire

All participants were asked questions to update their history from previous interviews. These data were obtained in the interval questionnaire. For the 1985 follow-up, new questions on risk factors for skin cancer and personality type were added. Enhancements were added to the data collection procedures to include birth defects and drinking habits, and questions were included to obtain a more detailed smoking history. The interval questionnaire was expanded in 1987 to include detailed drinking history and sleep disorder questions. Because some of the study subjects did not participate in the 1985 follow-up, the 1987-88 Health Interval Questionnaire was structured to include one-time questions added in 1985, such as ethnic background and smoking history, for "rejoining" participants (i.e., those who completed a previous questionnaire but did not participate in all examinations).

The 1992-93 Health Interval Questionnaire added questions concerning occupational exposure to heavy metals and vibrating power tools, family health history (with particular reference to diabetes, heart trouble, and heart disease), further participant health inquiries (in particular, questions about diabetes, hepatitis B, intermittent claudication, and vascular insufficiency), and the participant's normal level of physical activity. In addition, the 1992 participants completed a Diet Assessment Questionnaire developed by Walter Willett at Harvard University (1).

With the exception of the diet assessment, which was discontinued for the 1997 follow-up, the 1997-98 Health Interval Questionnaire contained all of the questions in the 1992-93 Health Interval Questionnaire, the Interval Supplement Recording Book, and AFHS Forms 1, 1B, 2A, and 8 (the "self-administered" forms). The 1997-98 Health Interval Questionnaire also added the two following questions on herbicide exposure:

- What percentage of the missions that you flew as part of the aircrew during the Ranch Hand operation were herbicide spraying missions?
- It has been reported that some Vietnam veterans have intentionally drunk herbicides. Have you ever intentionally drunk herbicides?

Copies of the 1992-93 Health Interval Questionnaire and the Interval Supplement Recording Book are provided in Appendix B of the 1992 Final Report (2). AFHS Forms 1, 1B, 2A, and 8 are provided in Appendix C of the same report.

The goals in developing the CAPI Interval Questionnaire for the 1997 follow-up survey included the following:

1. To create one questionnaire encompassing the interval questionnaires and the "self-administered" forms. Questions from the additional forms were inserted throughout the questionnaire into sections covering similar subjects.
2. To print health history responses, previously available from the self-administered forms, onsite after the interview for use in participant debriefing.
3. To eliminate item nonresponse.
4. To use "bounded recall" techniques to improve participants' abilities to recall information. A longitudinal questionnaire is dependent on the respondent's ability to remember events and to place those events in time. Even when given a precise starting date, respondents frequently repeat information given earlier, neglect to report new information because they thought they had previously reported it, and otherwise misplace events in time or forget them completely. One

method of preventing such errors is through the use of "bounded recall," in which the respondent is reminded of information that he has already reported and asked to provide new information. For the 1992 interview, interviewers worked from a hard-copy information sheet containing summaries of key responses from the previous examination. These responses included date of birth, highest educational degree, military status at the last interview, marital status at the last interview, name of spouse or partner at the last interview, and a cumulative list of all children reported during previous interviews. This practice was replicated online for the 1997 questionnaire.

5. To minimize redundancies of items asked of participants and to avoid reminders of previously reported sensitive family history items during their interview. These goals were accomplished by including the items from the self-administered forms in the CAPI questionnaire and by programming the CAPI questionnaire to skip any sensitive family history items, such as parents or children previously reported as deceased.

6. To replicate, to the maximum extent possible, the 1992 variables, names, labels, and formats in the final SAS® data set.

7. To lessen the time burden on the participant for the administration of the questionnaires. By combining the self-administered forms with the interval questionnaire and reducing the redundancy of questions, the participants were able to complete this portion of their examinations in a timelier manner.

3.2 INTERVIEWER TRAINING

In April 1997, NORC's Chicago office staff trained eight interviewers and one field manager to administer the 1997-98 Health Interval and Study Subject Baseline Questionnaires. One interviewer and the Field Manager had administered questionnaires previously in the 1992 follow-up examination. The interviewers reported to the Field Manager, who in turn reported to the Data Collection Task Leader in Chicago. The Field Manager observed interviews by each interviewer and presented summaries of these assessments each quarter. The NORC Project Director made quarterly visits to the interviewing site. As part of the training process, the NORC interviewing staff was not informed of the exposure status of any study participant either before or after questionnaire completion.

3.3 DATA COLLECTION

Upon arrival at Scripps Clinic, the participant received a schedule that included the time and place for the interval interview (and, if appropriate, the baseline interview) and was assigned an interviewer. In all of the personal interviews conducted for the AFHS, interviewers were required to ask questions exactly as written, were not allowed to interpret questions or interject personal commentary, and were instructed to probe "Don't Know" responses at least once. As an added QC measure, the CAPI system did not permit them to skip around among sections of the questionnaire.

During the interview, participants signed both informed consent and medical records release forms. If a participant did not have all of the information with him to complete the medical release form during the interview, he was given blank medical records release forms and instructed to mail the completed forms to the Air Force. If the medical records required pertained to his now-adult children and required their signature, he was again given blank medical records release forms and instructed to mail the completed forms to the Air Force. During the course of the data collection, the interviewing procedures were amended so that medical release forms were not signed if the participant informed the interviewer that he

had brought the relevant records with him, that the records had already been submitted to the AFHS, or that the condition had been diagnosed at Scripps Clinic.

After each interview, interviewers used an onsite printing program that was built into the CAPI system to produce a six-page form containing items from the questionnaire that were needed for the participant debriefings. These forms were transferred to the participants' folders each day. Each evening, the completed interviews were uploaded via modem to the NORC home office in Chicago. At that time, new participant data and refinements to the questionnaire software also could be downloaded to the interviewing site.

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4 PHYSICAL EXAMINATION METHODOLOGY

The 1997 follow-up examination was given to 2,121 invited and scheduled participants, who traveled to the examination site at Scripps Clinic in La Jolla, California. The examination consisted of the following major elements:

- Adipose tissue extraction
- Laboratory testing
- Medical outbriefings
- Physical examination
- Psychological testing
- Specialized testing (e.g., phlebotomy for measurement of serum dioxin).

The Combat Experience Questionnaire and skin, hair, and eye color determinations (components of the 1985 follow-up examination) were administered to all participants who did not attend the 1985, 1987, and 1992 follow-up examinations.

The Air Force carefully prescribed the details of the above examination elements in the Examiners' Handbook, provided in Appendix B. All physical examination procedures were approved by the Air Force Research Laboratory Institutional Review Board (IRB) at Brooks Air Force Base and by the Scripps Clinic IRB. Clinical variations were neither desired nor authorized; all proposed examination procedural changes were reviewed in detail by Air Force technical and contractual personnel prior to the start of the examinations. An important objective of the entire physical examination process was to ensure that bias was not created by any procedural change. This objective was carried out successfully.

The requirement to maintain blind examinations was particularly stringent. The clinical staff was prohibited from knowing or seeking information as to the group identity (i.e., Ranch Hand, Comparison) of any participant. At the end of his examination, each participant was asked to note on the critique form whether such information was sought by any member of the clinical or paramedical staff. In 1997, nine participants indicated that an examining physician had asked them about specific duties in Southeast Asia (SEA). Two of these participants later stated that they had answered erroneously. Three participants stated that they had not been questioned but rather had volunteered information in casual conversation. The balance of the nine participants could not be identified because they chose to remain anonymous. In all known cases, the physician or technician involved was reminded to be more careful in his or her conversations.

4.1 EXAMINATION CONTENT

The examination content, as designed by the Air Force, emphasized detection of medical endpoints suspected of being associated with exposure to phenoxy herbicides, chlorophenols, or dioxin. In each follow-up study, the Air Force has used findings from the previous examination to refine the current examination.

The general content of the 1997 physical examination and psychological test battery is shown in Table 4-1. The complete laboratory test series accomplished at Scripps Clinic is displayed in Table 4-2.

Table 4-1. Elements of the 1997 Follow-up Physical Examination

Elements	Remarks
Adipose Tissue Extraction	313 Participants
Chest X Ray	Radiologist
Dermatologic Examination	Dermatologist
Doppler	Technician; Caffeine and Nicotine Abstinence
Electrocardiogram	Caffeine and Nicotine Abstinence
General Physical Examination	Internist
Immunologic Studies	40% Random Sample
Neurological Examination	Neurologist
Patient Outbriefing	Internist, Medical Diagnostician
Psychological Evaluation:	
Symptom Checklist 90-Revised (SCL-90-R)	
Jenkins Activity Survey	
Pulmonary Function	Internist with Subspecialty in Pulmonary Disease
Vibrotactile Threshold	Technician

Table 4-2. Laboratory Test Procedures Performed at Scripps Clinic

Chemistry

2-hour Postprandial Glucose (mg/dl)	Gamma Glutamyl Transferase (GGT) (U/l)
Alanine Aminotransferase (ALT) (U/l)	Glycated Hemoglobin (percent)
Alkaline Phosphatase (U/l)	High Density Lipoprotein (HDL) Cholesterol (mg/dl)
Amylase (U/l)	Serum Creatinine (mg/dl)
Aspartate Aminotransferase (AST) (U/l)	Serum Insulin (µIU/ml @ 2 hours after fasting glucose)
Cholesterol (mg/dl)	Total Bilirubin (mg/dl)
Creatine Kinase (U/l)	Total Lactic Dehydrogenase (LDH) (U/l)
Direct Bilirubin (mg/dl)	Triglycerides (mg/dl)
Fasting Glucose (mg/dl)	

Coagulation

Patient Prothrombin Time (seconds)

Hematology

Absolute Bands (thousand/mm^3)	Differential Segs (percent)
Absolute Basophils (thousand/mm^3)	Erythrocyte Sedimentation Rate (mm/hr)
Absolute Eosinophils (thousand/mm^3)	Hematocrit (percent)
Absolute Lymphocytes (thousand/mm^3)	Hemoglobin (gm/dl)
Absolute Monocytes (thousand/mm^3)	Mean Corpuscular Hemoglobin (MCH) (pg)
Absolute Reactive Lymphs (thousand/mm^3)	MCH Concentration (MCHC) (gm/dl)
Absolute Segs (thousand/mm^3)	Mean Corpuscular Volume (MCV) (cubic micra)
Differential Bands (percent)	Platelet Count (thousand/mm^3)
Differential Basophils (percent)	RBC Morphology
Differential Cells Counted	Red Blood Cell (RBC) Count (million/mm^3)
Differential Eosinophils (percent)	White Blood Cell (WBC) Count (thousand/mm^3)
Differential Lymphs (percent)	WBC Morphology
Differential Monocytes (percent)	Platelet Observation
Differential Reactive Lymphs (percent)	

Table 4-2. Laboratory Test Procedures Performed at Scripps Clinic (Continued)

Immunology	
Anti Delta Total Antibody	Hepatitis B Surface Antigen
Anti-Thyroid Antibody	Hepatitis B Surface Antigen Confirmatory
Hepatitis A Total Antibody	Hepatitis C Virus Antibody
Hepatitis B Core Antibody	
Lupus Panel	
Anti-Mitochondrial Antibody	Anti-Smooth Muscle Antibody
Anti-Nuclear Antibody	Latex Rheumatoid Factor (IU/ml)
Anti-Parietal Cell Antibody	Thyroid Microsomal Antibody
Fecal Studies	
Fecal Occult Blood	
Protein Profile	
α-1-Acid Glycoprotein (mg/dl)	Haptoglobin (mg/dl)
α-1-Antitrypsin (mg/dl)	IgA (mg/dl)
α-2-Macroglobulin (mg/dl)	IgG (mg/dl)
Albumin (mg/dl)	IgM (mg/dl)
Apolipoprotein B (mg/dl)	Prealbumin (mg/dl)
C3 Complement (mg/dl)	Transferrin (mg/dl)
C4 Complement (mg/dl)	
Radioimmunoassay	
Estradiol (pg/ml)	Prostate-Specific Antigen (ng/ml)
Follicle Stimulating Hormone (FSH) (mIU/ml)	T_4 (μg/dl)
Free Testosterone (pg/ml)	Thyroid Stimulating Hormone (TSH) (μIU/ml)
Luteinizing Hormone (mIU/ml)	Total Testosterone (ng/dl)
T & B Lymphocytes and Subsets (special immunology testing performed on 818 participants)	
CD20+ Cells (B cells) (percent)	Absolute CD16+56+ Cells (Natural Killer Cells) (per mm^3)
CD3+ Cells (T cells) (percent)	Absolute CD20+ Cells (B Cells) (per mm^3)
CD4+ Cells (Helper T Cells) (percent)	Absolute CD3+ Cells (T Cells) (per mm^3)
CD3+CD4+ Cells (Helper T Cells) (percent)	Absolute CD4+ Cells (Helper T Cells) (per mm^3)
CD8+ Cells (Suppressor T Cells) (percent)	Absolute CD3+CD4+ Cells (Helper T Cells) (per mm^3)
CD3+CD8+ Cells (Suppressor T Cells) (percent)	Absolute CD8+ Cells (Suppressor T Cells) (per mm^3)
CD45 Total Lymphs (Common Leukocyte Antigen) (percent)	Absolute CD3+CD8+ Cells (Suppressor T Cells) (per mm^3)
Lymphs (percent)	Absolute Lymphocytes (per mm^3)
	CD16+56+ Cells (Natural Killer Cells) (percent)
Urinalysis	
2-hour Postprandial Urine Glucose (g/dl)	Urinary Glucose (g/dl)
Leukocyte Esterase	Urinary Ketones (mg/dl)
Urinary Bacteria (per high-powered field)	Urinary Mucus (per high-powered field)
Urinary Bilirubin	Urinary Nitrites
Urinary Blood	Urinary pH
Urinary Casts (per low-powered field)	Urinary Protein (mg/dl)
Urinary Clarity	Urinary RBC (per high-powered field)
Urinary Color	Urinary WBC (per high-powered field)
Urinary Comment	Urine Specific Gravity
Urinary Crystals (per high-powered field)	Urobilinogen (Ehrlich unit/dl)
Urinary Epithelial Cells (per high-powered field)	

4.2 ADIPOSE TISSUE EXTRACTION

The follow-up results of the 1987 and 1992 Air Force Health Study (AFHS) showed a rise in the incidence of pre-diabetic indicators of type 2 diabetes, non-insulin-dependent diabetes mellitus (NIDDM), in the participants exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin). To examine the relation between dioxin exposure and glucose transporting activity in human adipose tissue cells, 313 participants volunteered to participate in a separate sub-study of the AFHS in which approximately 10 grams of adipose tissue were removed by liposuction and preserved for laboratory analysis. The information derived from the adipose tissue sub-study may help explain the positive association between dioxin body burden and diabetes mellitus in veterans of Operation Ranch Hand.

The Air Force designated 650 potential participants for adipose extraction by a random selection process within classifications of exposure, age, body fat, and diabetes. A consent form was provided to each adipose tissue-designated participant at the evening orientation. Over the course of the 1997 physical examination, a board-certified plastic surgeon extracted an adipose sample from 313 participants. The procedure lasted 30 minutes and required the use of a local anesthetic. The adipose tissue specimens were shipped to Brooks Air Force Base weekly for storage. The results of this study will be summarized in a separate report.

4.3 QUALITY CONTROL

As in the baseline and the 1985, 1987, and 1992 studies, quality control (QC) requirements for both laboratory testing and clinical procedures were extensive. Although details are provided in Chapter 6, the following categories summarize the extent of the emphasis on quality. For laboratory testing, Westgard rules (1_{2s}) were used throughout the study. Single reagent lots and control standards were used when practical, duplicate specimens were routinely and blindly retested, and testing overlaps were mandatory when test reagent lots were changed.

The Scripps clinical team was instructed to ensure clinician consistency. In total, 18 board-certified physicians in internal medicine, neurology, and dermatology participated in the general, specialty, and diagnostic examinations. In addition, 12 radiologists, 5 pulmonologists, and 4 cardiologists performed tests and interpreted results. To reduce observer variability, turnover in the clinical and paramedical staffs was minimized during the 11 months of examinations. One Scripps Clinic physician served as the Project Medical Director, responsible for the scheduling, conduct, and QC of the examinations. All examining physicians reviewed the mark-sense examination forms prior to a pre-examination test. To minimize recording errors, the layout of the form was designed to parallel the flow of the clinical examination. Because data transcription was not permitted, each physician was responsible for filling in the bubbled form. To a large extent, the use of these mark-sense forms and subsequent QC measures were the primary reason for a clean clinical data set. A complete set of forms is provided in Appendix B. Additional QC included the following elements:

- A detailed onsite quality control process was employed by Scripps Clinic, Science Applications International Corporation (SAIC), and Air Force physicians and personnel.
- Clinical quality assurance meetings were conducted to detect and correct problems.
- Examiners were unaware of the exposure status of the participants.
- Automated blood pressure recording was performed.

4.4 CONDUCT OF EXAMINATIONS

All examinations, from May 1997 to April 1998, were conducted in accordance with the Examiners' Handbook. Excluding weeks with national holidays, two groups of participants, averaging approximately 25 per group, were examined weekly.

A demanding logistics effort was required to contact, transport, and examine the 2,121 study participants. Pre-examination contact consisted of making telephone calls to recruit participants, determine special requirements (e.g., wheelchair assistance), and arrange transportation. Once scheduling was reasonably firm, the SAIC logistics coordinator sent each participant a detailed information package outlining dietary requirements, a stool occult blood testing kit (Hemoccult®), inbriefing schedules, important telephone numbers, a request for medical records, and local maps designating examination site dining and recreational facilities.

To encourage participation in future follow-up studies, some activities were continued in 1997. These included participant critique forms, an informational meeting open to any accompanying family members and friends, and preventive medicine examinations such as human immunodeficiency virus and prostate-specific antigen testing. Proctosigmoidoscopy, as well as treadmill tests, were made available to participants for a nominal fee. Accompanying family members also were offered the opportunity to use the clinic facilities at a discounted rate.

Each morning of the examinations, the current group of participants was transported to the Scripps Clinic, having fasted and abstained from nicotine and caffeine since midnight the previous evening. In addition, alcohol was strictly prohibited from 24 hours before the first day of the examination through the second day of the examination. On the first day, each participant was given an individualized 2-day schedule outlining his medical, interviewing, and laboratory appointments. The schedule carefully noted the specific required periods of caffeine and nicotine abstinence for generalized periods in relation to electrocardiograph testing. Although the clinic schedules generally were assigned at random, consideration was given to smokers and diabetics because of the fasting and abstinence restrictions. Figure 4-1 shows a typical 2-day schedule prepared for a participant. The participant depicted in this schedule was in good self-reported health, was a smoker, and was asked to participate in the blood measurement of dioxin on Day 2.

As in the previous examinations, schedules were printed with specific directions to aid participants in locating clinic departments, although for many tests, participants were escorted from the waiting room. Throughout the examination day, time was provided for waiting-room activities (i.e., renewal of past friendships, discussions of experiences in SEA, consumption of refreshments when permitted, and completion of paperwork). On the second day of the examination, the participants completed testing and examinations and received outbriefings from a medical diagnostician.

The psychological tests (the SCL-90-R and the Jenkins Activity Test) were self-administered and reviewed by a Scripps Clinic psychologist. If a problem was indicated, the participant was advised of the issue during his medical debrief. Upon completion of these debriefings, the participants were paid their stipend and reimbursed for travel expenses.

4.4.1 Blood Collection

On the first examination day, each participant had 160 ml of blood collected. Detailed immunology testing (see Table 4-2) was conducted on approximately 40 percent of the participants. These

AIR FORCE HEALTH STUDY

Participant Schedule for: Monday, May 05, 1997 and Tuesday, May 06, 1997

Case Number – group #

Participant's Full Name

Day: 1 Monday, May 05, 1997

Start Time	End Time				
0600		Meet in Hotel Lobby	Shuttle Bus	Transfer to Scripps	
0615		Bus to Scripps			
0630		Orientation and signing of consent forms	Green 2 N	Waiting Room	
0645	TBA*	Blood Draw 1 and 2	Green 2 W	Room W263 A	
0800		Physical Exam	AOP 3 A	Internal Medicine	Dr. Sargeant
0845		Dermatology	AOP 1 B	Dermatology	Dr. Cornell
1100		Chest X Ray	Green 1	Radiology	Please sign in
1200		Spirometry/ECG	Green 2 W	Room 264	
1300		Psychology Exam	Green 2 N	Room 231	
1415		Vibrotactile	AOP 3 A	Vascular Lab	Please sign in
1430		Doppler Exam	AOP 3 A	Internal Medicine	
1545		Bus to Hotel	Green 3 W	Outside Fountain	

TBA* = BLOOD DRAW 2 SCHEDULED 2 HOURS AFTER DRINKING GLUCOLA

NO FOOD, CAFFEINE, OR NICOTINE PRIOR TO BLOOD DRAWS 1 OR 2 ON DAY 1

NO CAFFEINE OR NICOTINE WITHIN 4 HOURS PRIOR TO DOPPLER EXAM, ECG, OR SPIROMETRY

MT01 smoker Good

Figure 4-1. Typical 2-Day Clinic Schedule

AIR FORCE HEALTH STUDY

Participant Schedule for: Monday, May 05, 1997 and Tuesday, May 06, 1997

Case Number – group #

Participant's Full Name

Day: 2 Tuesday, May 06, 1997

Start Time	End Time				
0615		Board Shuttle Bus	Hotel		
0630		Bus to Scripps			
0700		Blood Draw 3	Green 2 W	Room W263 A	
0800		Neurology Exam	AOP 3 A	Neurology – CHECK IN	Dr. Otis
0830		NORC Interview	Green 2 N	Room CP228	
1015		NIDR Dental Exam	Green 2 W	Room 213	
1315		Debriefing	AOP 3 A	Internal Medicine	Dr. Moore
1330		Exit Interview	Green 2 N	Waiting Room	Rita Taliaferro
1400		Bus to Hotel	Green 3 W	Outside Fountain	

TBA* = BLOOD DRAW 2 SCHEDULED 2 HOURS AFTER DRINKING GLUCOLA

NO FOOD, CAFFEINE, OR NICOTINE PRIOR TO BLOOD DRAWS 1 OR 2 ON DAY 1

NO CAFFEINE OR NICOTINE WITHIN 4 HOURS PRIOR TO DOPPLER EXAM, ECG, OR SPIROMETRY

MT01 smoker Good

Figure 4-1. Typical 2-Day Clinic Schedule (Continued)

participants were identified by the last digit of their participant study identification number used for previous testing, thus establishing a longitudinal connection between examinations. The immunologic tests were subjected to highly structured QC procedures set forth by the Air Force. Participants chosen for immunology testing had an additional 30 ml of blood collected. An additional blood collection of 10 ml was taken 2 hours after the first blood collection to assess 2-hour postprandial glucose and insulin. Blood bank chairs were used for maximum comfort and total body support in the event of a reaction. These chairs were selected because they could be shifted easily into the Trendelenburg position if a participant felt faint. Out of the 160 ml of blood collected from each participant, the Air Force was provided 40 cc of serum for archival purposes as well as human immunodeficiency virus and syphilis testing.

On the second day of the group examination, 563 participants were invited and provided a second blood collection for dioxin analysis at the Centers for Disease Control and Prevention. A total of 280 ml of blood was collected for these participants, unless the participant had blood collected for immunology testing the previous day. In this case, only 250 ml of blood was collected.

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5 STUDY SELECTION AND PARTICIPATION

5.1 INTRODUCTION

In this chapter, 1997 follow-up and cumulative study compliance are reviewed. Refusal rates are compared between Ranch Hands and Comparisons, as are the reasons for refusal. Reasons for refusal also are examined by age, race, and rank to detect any differences in refusal rates. All noncompliant Original Comparisons were to be replaced by Comparisons appropriately matched on age, race, rank, and self-reported health status. Adherence to the replacement strategy as defined in the study protocol (1) is assessed, and the health status of noncompliant Original Comparisons is compared to their Replacement Comparisons. Differences in the perception of health are evaluated by group, age, race, rank, and 1997 compliance status. Among fully compliant study participants, self-reported health status is compared. Because perception of health may differ between Ranch Hands and Comparisons, medication use and work loss are compared as possible surrogate measures of actual health status.

Throughout this chapter, several terms are used to describe veterans who did not participate in the 1997 examination. These terms include "passive refusal," "hostile refusal," and "final refusal." An individual who communicated a desire not to have any contact with or from the Air Force Health Study (AFHS) under any circumstances was classified as "hostile." Veterans who were classified as hostile in the past were not invited to the 1997 examinations (see Section 5.5.2.2). A veteran was classified as a "passive refusal" if he was scheduled for a physical examination but broke the appointment twice. He also could be classified as a passive refusal for other reasons, such as inability to contact him directly because of the presence of a "gatekeeper" (see Sections 5.5.2.1 and 5.5).

A veteran who was classified as hostile, or had refused to participate twice—passively or otherwise—was classified as a "final refusal." Prior to the second refusal, a "refusal conversion" attempt was made. The refusal conversion consisted of an attempt, made by a specially trained person, to convince the veteran to participate. If this conversion attempt failed, the veteran was classified as a final refusal.

5.2 FACTORS KNOWN OR SUSPECTED TO INFLUENCE STUDY PARTICIPATION

A multitude of factors may influence study participation. These may be broadly classified as health, logistics, demographic, operational, or publicity factors. For example, health factors are thought to include self-perception of health as well as demonstrable health indicators, such as medication use and work-days lost due to illness or injury. Logistics factors include distance to the examination site, reluctance to spend time away from family or job, income, and occupation. Demographic factors include flying status, age, race, or military duty status (active, retired, separated). Operational factors include any aspect of study operation that may cause differential compliance, such as differential treatment of participants during scheduling, physical examination, interview, or debriefing. Publicity factors are related to national attitudes and media presentations regarding the Agent Orange (Herbicide Orange) issue, the Vietnam War, veterans' health care, or health care in general. In addition, these considerations may influence Ranch Hands differently than Comparisons.

The decision to volunteer for this study is complex, making statistical assessment of compliance bias difficult and necessarily crude in that many of the factors contributing to self-selection cannot be measured directly. Instead, compliance bias was investigated at the 1997 follow-up with respect to self-perception of health, medication use, and work loss. Medication use and days lost from work due to

illness or injury were obtained from questionnaire and physical examination data and, therefore, were available only for fully compliant participants. In 1997, as in 1992, no partial compliance (defined as compliant to the questionnaire and noncompliant to the physical examination) occurred because both the physical examination and the questionnaire were administered at the examination site.

5.3 REPLACEMENT PROTOCOL

During the design phase of the AFHS, the authors of the study protocol anticipated that a loss of participants between follow-up examinations would pose the greatest threat to study validity. In particular, they expected differential compliance, with relatively more Ranch Hands choosing to return to the study than Comparisons and with health differences of unknown character between noncompliant Ranch Hands and noncompliant Comparisons. To partially correct the situation, the study design specified that noncompliant Comparisons would be replaced by Comparisons with the same values of the matching variables (age, race, and military occupation at the baseline examination) and the same health perception. Military occupation was stratified into the following five categories: (1) flying officer—pilot, (2) flying officer—non-pilot, (3) non-flying officer, (4) flying enlisted, and (5) non-flying enlisted (also referred to as enlisted groundcrew). In this way, the Replacement Comparisons would serve as surrogates for Comparisons who refused to participate. This method of replacement would tend to reduce bias resulting from refusal in the Comparison group and would maintain group size. No corresponding strategy for the Ranch Hands was possible because all living Ranch Hands had been identified and invited to participate.

The first Comparison in each randomized matched set who was asked to participate in the baseline questionnaire and physical examination was identified as the Original Comparison for his respective Ranch Hand (in accordance with the study protocol). If the Original Comparison was noncompliant, a "Replacement" Comparison was invited in his place. Noncompliance was determined if any of the following three conditions were met:

1. The Comparison refused to participate.
2. The Comparison was partially compliant (completed the baseline questionnaire but did not complete the baseline physical examination).
3. The Comparison was unlocatable.

Replacement Comparisons were identified as such in the database to satisfy the study protocol requirement that they be matched with the refusing Original Comparisons (also known as refusals) based on self-reported health (excellent, good, fair, or poor). Of course, in the case of an unlocatable Original Comparison, matching with regard to self-reported health was not possible. Original Comparisons who were partially compliant were replaced, but deceased Original Comparisons were not.

During the 1985 examination, a telephone questionnaire was administered to refusals and their potential replacements. This questionnaire served as the basis for health-matching required by the study protocol, and assessed self-perception of health, days lost from work due to illness, and medication use. Although the study protocol is not explicit on this point, it implies that the decision to include or exclude the replacements from the study should be based only on this health contrast. At the 1987 follow-up examination, instead of using a telephone questionnaire, refusals were asked during the scheduling process for their self-perception of health. During the 1992 and 1997 follow-up examinations, schedulers requested a current perception of health (compared to others their age) from all participants contacted by telephone. Health-matching of replacements was not used during the baseline examination but was implemented during the 1985, 1987, 1992, and 1997 follow-up examinations. Replacement Comparisons

were matched to noncompliant Original Comparisons with respect to age, race, rank, and military occupation at all examinations.

5.4 1997 FOLLOW-UP SCHEDULING AND REPLACEMENT OPERATION

5.4.1 Scheduling Strategy

The scheduling process included the following three objectives:

1. To maximize participation rates (in both the present and future follow-up studies)
2. To ensure that Ranch Hands and Comparisons were recruited using the same procedures and with the same effort
3. To ensure that, whenever possible, each Ranch Hand had at least one compliant Comparison who was matched with that Ranch Hand on age, race, and military occupation.

These objectives led to a set of conflicting priorities: maximizing participation rates meant giving each potential participant every opportunity and encouragement to participate, without being so persistent as to lose the cooperation of unwilling respondents in future follow-up examinations. This careful approach had to be balanced against the need to quickly identify noncompliant Comparisons. Until these noncompliant Comparisons were removed from the scheduling process, they could not be replaced. In general, prospective participants were contacted for scheduling in random order; however, priority was given to certain potential participants who needed to be contacted early in the scheduling period. These included the following:

- Veterans who live overseas, because they would be more difficult to contact and require more advance time to make travel arrangements
- Passive refusals or "no-shows" for previous physical examinations.

During the first 2 months of scheduling, an attempt was made to contact all veterans invited to previous examinations. In addition, all previously invited veterans were sent a refrigerator magnet that stated the date that scheduling would begin and the toll-free number of the scheduling operation.

Although every reasonable attempt was made to contact eligible veterans, accommodate unusual schedules, and convert refusals, experience in past examinations had shown that certain types of potential participants ultimately would not schedule appointments. To continue with the replacement of Comparisons, these cases needed to be closed early. Therefore, the following rules were observed to limit the number of calls to certain types of individuals who were not likely to participate:

- An individual classified as hostile to the study in previous follow-up examinations was not contacted in 1997.
- An individual who was extremely hostile in his refusal to initial scheduling contacts was coded as a final refusal with no refusal conversion attempts.
- If the scheduler did not get an answer on the telephone after eight attempts, a registered letter was sent to that individual. If there was direct evidence that the letter was received at the proper address and the individual did not respond to the registered letter, he was considered a passive refusal.
- An individual who broke two examination appointments ("passive refusal") was considered a final refusal.

- An individual who equivocated about attending the physical examinations twice during the first two contacts was considered a first refusal.
- One refusal conversion attempt was made for all first refusals.

Some potential participants were particularly difficult to reach because of the presence of a "gatekeeper" who did not allow the schedulers to speak directly to the potential participant. A potential participant was designated as a final passive refusal after a minimum of three contacts with a gatekeeper and failure to reach the participant by other means. These contact methods included varying calling times, leaving messages, or sending a certified letter. Up to eight gatekeeper contacts were allowed if the scheduling supervisor decided additional attempts were still warranted (e.g., if an individual had previously scheduled and canceled, if it seemed reasonable that he might reschedule). After these gatekeeper contacts had been exhausted, the individuals were designated as final passive refusals and, if eligible for replacement, replaced. Potential participants who were designated as final refusals at any stage in the scheduling process were provided with the toll-free number for the study and allowed to volunteer to participate at any time.

The percentage of persons completing the 1997 physical examination is plotted by calendar date in Figure 5-1 for Ranch Hands, Original Comparisons, Replacement Comparisons, and all Comparisons. These patterns are similar to those seen at previous follow-up examinations and reflect the study protocol specification that scheduling be random with respect to group. Completion rates are similar between Ranch Hands and Original Comparisons. Replacement Comparisons completed the physical examinations later in the scheduling process, as would be expected.

5.4.2 Replacement Strategy

All Comparisons who had been invited to participate in the baseline, 1985, 1987, or 1992 studies were invited to participate in the 1997 examination. If no previously invited Comparisons for a particular Ranch Hand agreed to participate in 1997, schedulers attempted to recruit a replacement. These replacements were selected from a set of up to 10 candidate Comparisons, matched by age, race, rank, and military occupation, whose self-reported health status in 1997 matched that of the noncompliant Original Comparison for a given Ranch Hand. Health status was recorded in four categories: excellent, good, fair, or poor. If a willing, health-matched participant was not found in the matched set, self-reported perceptions of health status were dichotomized into "excellent or good" and "fair or poor" categories, and these dichotomized health statuses were matched. If this second method for identifying a suitable replacement failed, no replacement was made.

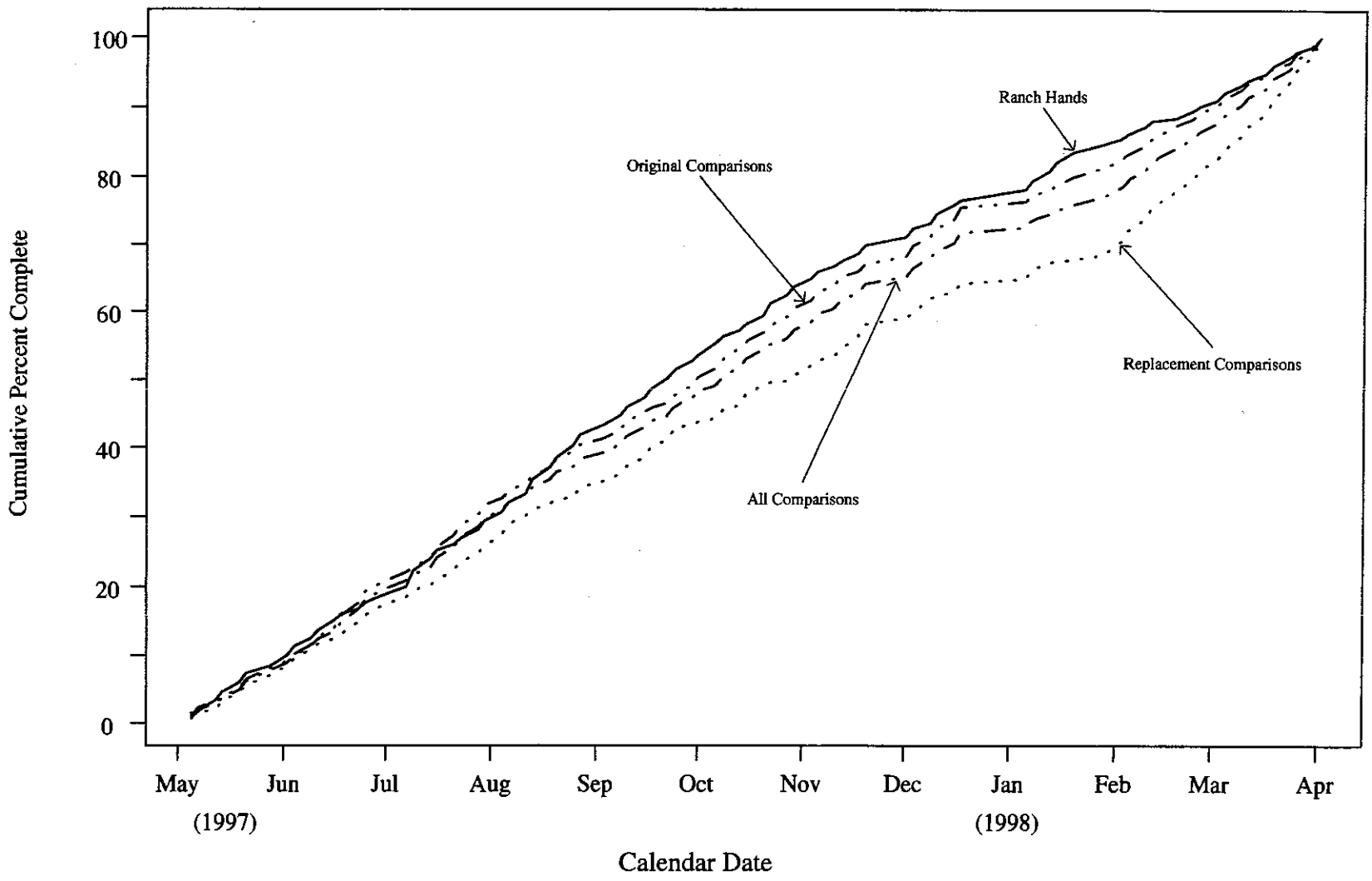

Figure 5-1. Cumulative Percent Completed Physical Examination by Calendar Date

There were two exceptions to the replacement strategy. First, the study protocol required that the noncompliant Original Comparisons report their health status during the scheduling effort so that they could be used to recruit Replacement Comparisons with the same health status. On occasion, Original Comparisons refused to speak with the scheduler or respond to questions. In these cases, a Replacement Comparison for the Original Comparison was recruited in the order in which he was listed in the randomized matched set. This strategy also was used for unlocatable and hostile Original Comparisons. Second, as specified in the study protocol, no replacement was made if all formerly invited Comparisons in a matched set were deceased.

5.5 COMPLIANCE

Of the 1,101 eligible Ranch Hands, 870 (79.0%) participated in the 1997 follow-up examination, while 839 (72.8%) of the 1,151 eligible Original Comparisons participated. Of the 768 Replacement Comparisons eligible for the 1997 follow-up, 412 (53.6%) chose to attend the examination. Table 5-1 provides compliance counts for Ranch Hands, all Comparisons as a group, and Original and Replacement Comparisons. Appendix C contains tables that describe these counts by compliance at the baseline examination. Table C-1 provides counts for the Ranch Hands. Total Comparison counts are summarized in Table C-2. Original Comparison counts are presented in Table C-3, and Replacement Comparison counts are provided in Table C-4.

In Table 5-1 and Appendix C, the "New to Study" rows include potential Replacement Comparisons who were found to be deceased when contact was attempted. The same deceased potential replacements are then accounted for in the rows marked "Died." Undefined categories are indicated by dashes. For example, in the Appendix C tables, dashes are shown when partially compliant participants at the baseline examination could not be partially compliant at a later examination. Partial compliance only occurred when a participant agreed to the baseline questionnaire but refused to attend the physical exam. As stated previously, no partial compliance occurred in 1992 or 1997 because both the baseline questionnaire and physical examination were given at the same site. As shown in Appendix C, Tables C-1 and C-2, 86 percent (819 of 949) of living Ranch Hands and 87 percent (976 of 1,116) of living Comparisons who were fully compliant at the baseline examination returned for the 1997 follow-up examination.

Table 5-2 describes the newly compliant participants in terms of their compliance at previous examinations. Two Ranch Hands, 9 Original Comparisons, and 69 Replacement Comparisons were fully compliant and examined for the first time at the 1997 follow-up examination. One Original Comparison and 52 Replacement Comparisons had not been invited previously to participate. The one Original Comparison who had not been invited previously to participate replaced an Original Comparison who was reclassified as a Ranch Hand (see Section 5.5.1). Two Ranch Hands, seven Original Comparisons, and five Replacement Comparisons had been previously invited and had refused to participate in one or more previous examinations.

Table 5-1. Compliance by Group and Examination Year

Time Period	Disposition	Group			
		Ranch Hands	All Comparisons	Original Comparisons	Replacement Comparisons
Baseline		***1,209***	***1,666***	***1,235***	***431***
1985 Examination	***Eligible***	***1,209***	***1,666***	***1,235***	***431***
Between Baseline & 1985 Examination	New to Study	9	73	17	56
	Died	(19)	(26)	(21)	(5)
	Remaining Eligible	***1,199***	***1,713***	***1,231***	***482***
	Subject Unlocatable	(39)	(65)	(48)	(17)
	Refused	(134)	(326)	(220)	(106)
	Partially Compliant	(9)	(30)	(9)	(21)
	Fully Compliant	***1,017***	***1,292***	***954***	***338***
1987 Examination	***Eligible***	***1,199***	***1,713***	***1,231***	***482***
Between 1985 & 1987 Examinations	New to Study	4	33	4	29
	Died	(15)	(16)	(13)	(3)
	Remaining Eligible	***1,188***	***1,730***	***1,222***	***508***
	Subject Unlocatable	(20)	(47)	(31)	(16)
	Refused	(171)	(358)	(242)	(116)
	Partially Compliant	(1)	(27)	(11)	(16)
	Fully Compliant	***996***	***1,298***	***938***	***360***
1992 Examination	***Eligible***	***1,188***	***1,730***	***1,222***	***508***
Between 1987 & 1992 Examinations	New to Study	(0)	83	2	81
	Died	(39)	(52)	(33)	(19)
	Remaining Eligible	***1,149***	***1,761***	***1,191***	***570***
	Subject Unlocatable	(12)	(56)	(15)	(41)
	No Health-Match	--	(11)	--	(11)
	Refused	(184)	(414)	(264)	(150)
	Fully Compliant	***953***	***1,280***	***912***	***368***
1997 Examination	***Eligible***	***1,149***	***1,761***	***1,191***	***570***
Between 1992 & 1997 Examinations	New to Study	(0)	236	2	234
	No Health-Match in 1992	--	(11)	--	(11)
	Died	(48)	(67)	(42)	(25)
	Remaining Eligible	***1,101***	***1,919***	***1,151***	***768***
	Subject Unlocatable	(4)	(29)	(10)	(19)
	No Health-Match	--	(91)	--	(91)
	Refused	(227)	(548)	(302)	(246)
	Fully Compliant	***870***	***1,251***	***839***	***412***

Table 5-2. Participants Newly Compliant in 1997 and Their Previous Compliance Pattern

Previous Compliance Pattern							
Baseline	1985	1997	1992	Ranch Hand	Original Comparison	Replacement Comparison	Grand Total
Partial	Refused	Refused	Refused	2	2	0	4
Partial	Refused	Unlocated	Refused	0	1	0	1
Partial	Refused	Unlocated	Unlocated	0	0	1	1
Partial	Unlocated	Unlocated	Refused	0	1	0	1
Partial	Unlocated	Unlocated	Unlocated	0	1	0	1
Refused	Partial	Refused	Refused	0	0	1	1
Refused	Refused	Refused	Refused	0	2	0	2
Refused	Refused	Refused	Unlocated	0	1	0	1
			Refused	0	0	3	3
			Unlocated	0	0	11	11
			No Health-Match	0	0	1	1
			New 1997	0	1	52	53
			Total	2	9	69	80

5.5.1 Corrections to Previously Reported Study Compliance Totals

Some changes were made to the historical cell counts shown in Table 5-1 (and the tables in Appendix C) so that they now differ from compliance tables presented during previous examinations (in particular, Tables 5-1 through 5-4 of the 1992 follow-up report). The differences are due to the following independent events:

1. One Original Comparison, who had been fully compliant since the baseline examination, was reclassified as a Ranch Hand. This participant was discovered to be part of stateside testing of Operation Ranch Hand and was assigned, on temporary duty, to the unit that transported Operation Ranch Hand equipment to SEA. This participant also was eligible as a Comparison because of a later assignment. The Ranch Hand assignment took precedence over the assignment as a Comparison. This change affects Tables 5-1, C-1, C-2, and C-3.
2. In the 1992 follow-up report, 3 Original Comparisons and 27 Replacement Comparisons who were new to the study since the baseline examination were classified as refusals for the 1985 follow-up examination. These numbers have been revised to indicate that 4 Original Comparisons and 26 Replacement Comparisons who were new to the study since the baseline examination were refusals at the 1985 follow-up examination. This change was due to the misclassification of one Original Comparison as a Replacement Comparison. This change affects Tables 5-1, C-3, and C-4.
3. In the 1992 follow-up report, two Original Comparisons and four Replacement Comparisons who were new to the study since the baseline examination were classified as partially compliant for the 1985 follow-up examination. These numbers have been revised to indicate that one Original Comparison and five Replacement Comparisons who were new to the study since the baseline examination were partially compliant for the 1985 follow-up examination. This change was due to the misclassification of one Replacement Comparison as an Original Comparison. This change affects Tables 5-1, C-3, and C-4.

4. In the 1992 follow-up report, 5 Original Comparisons and 28 Replacement Comparisons who were new to the study since the baseline examination were classified as new to the study between the 1985 and 1987 follow-up examinations. These numbers have been revised to indicate that 4 Original Comparisons and 29 Replacement Comparisons who were new to the study since the baseline examination were new to the study between the 1985 and 1987 follow-up examinations. This change was due to the misclassification of one Replacement Comparison as an Original Comparison. This change affects Tables 5-1, C-3, and C-4.

5. In the 1992 follow-up report, two Original Comparisons and five Replacement Comparisons who were new to the study since the baseline examination were classified as unlocatable at the 1987 follow-up examination. These numbers have been revised to indicate that one Original Comparison and six Replacement Comparisons who were new to the study since the baseline examination were unlocatable at the 1987 follow-up examination. This change was due to the misclassification of one Replacement Comparison as an Original Comparison. This change affects Tables 5-1, C-3, and C-4.

6. In the 1992 follow-up report, 4 Original Comparisons and 78 Replacement Comparisons who were new to the study since the baseline examination were classified as new to the study between the 1987 and 1992 follow-up examinations. In addition, three Replacement Comparisons who were new to the study since the baseline examination were classified as deceased between the 1987 and 1992 follow-up examinations. These numbers have been revised to indicate that 2 Original Comparisons and 81 Replacement Comparisons who were new to the study since the baseline examination were new to the study between the 1985 and 1987 follow-up examinations. In addition, the number of Replacement Comparisons who were new to the study since the baseline examination and classified as deceased between the 1987 and 1992 follow-up examinations has been revised from three to four. This change was due to the misclassification of two Replacement Comparisons as Original Comparisons and the addition of one deceased Replacement Comparison to the "New to Study" classification. This change affects Tables 5-1, C-2, C-3, and C-4.

7. In the 1992 follow-up report, 2 Original Comparisons and 27 Replacement Comparisons who were new to the study since the baseline examination were classified as unlocatable for the 1992 follow-up examination. These numbers have been revised to indicate that no Original Comparisons and 29 Replacement Comparisons who were new to the study since the baseline examination were unlocatable at the 1992 follow-up examination. This change was due to the misclassification of two Replacement Comparisons as Original Comparisons. This change affects Tables 5-1, C-3, and C-4.

8. In the 1992 follow-up report, 8 Original Comparisons and 44 Replacement Comparisons who were new to the study since the baseline examination were classified as refusals for the 1992 follow-up examination. These numbers have been revised to indicate that 6 Original Comparisons and 46 Replacement Comparisons who were new to the study since the baseline examination were refusals at the 1992 follow-up examination. This change was due to the misclassification of two Replacement Comparisons as Original Comparisons. This change affects Tables 5-1, C-3, and C-4.

5.5.2 Analysis of Refusals

Of the 1,101 Ranch Hands and 1,919 Comparisons eligible for the 1997 follow-up examination, 227 Ranch Hands and 548 Comparisons (302 Original and 246 Replacement) chose not to attend. Their reasons for refusal are summarized in Table 5-3. The 91 "no health-match" potential Replacement Comparisons included in Table 5-1 are not shown in Table 5-3. They also are not used in the analysis of refusals that follows because they were willing to participate but were excluded by the specifications of the study protocol.

Table 5-3. Reasons for Refusal by Group

Reason	Ranch Hands		Comparisons				Total	
			Original		Replacement			
	n	%[a]	n	%[a]	n	%[a]	n	%[a]
Health Reasons	42	3.8	38	3.3	28	3.6	108	3.6
Job Commitment	33	3.0	49	4.3	55	7.2	137	4.5
No Time	26	2.4	35	3.0	39	5.1	100	3.3
Travel Distance, Family	14	1.3	21	1.8	21	2.7	56	1.9
Confidentiality	5	0.5	3	0.3	2	0.3	10	0.3
Financial Hardship	1	0.1	1	0.1	0	0.0	2	0.1
Passive Refusal	23	2.1	24	2.1	18	2.3	65	2.2
Hostile	55	5.0	96	8.3	49	6.4	200	6.6
Fear of Physical Exam	1	0.1	1	0.1	1	0.1	3	0.1
Dissatisfaction with USAF	1	0.1	6	0.5	0	0.0	7	0.2
Dissatisfaction with AFHS	3	0.3	4	0.3	4	0.5	11	0.4
Dissatisfaction with Previous Exam	5	0.5	5	0.4	1	0.1	11	0.4
Other	18	1.6	19	1.7	28	3.6	65	2.2
Total	227	20.6	302	26.2	246	32.0	775	25.7
Total Invited	1,101		1,151		768		3,020	

[a] Percent of persons invited.

Table 5-3 shows that a greater percentage of Comparisons than Ranch Hands refused, and a greater percentage of Replacement Comparisons than Original Comparisons refused (32.0% vs. 26.2%). Of the total invited, nearly the same percentages of Ranch Hands, Original Comparisons, and Replacement Comparisons refused due to health reasons (3.8%, 3.3%, and 3.6%, respectively). The percentages were also nearly the same for passive refusals (2.1%, 2.1%, and 2.3%, respectively). More Replacement Comparisons than Ranch Hands or Original Comparisons declined due to "job commitments" or "no time." More Original Comparisons were hostile refusals (8.3%) than either Replacement Comparisons (6.4%) or Ranch Hands (5.0%).

Table 5-4 summarizes reasons for refusal by group, age, rank, and race. Reasons for refusal have been collapsed to the following five categories:

1. Health (health reasons)
2. Logistics (job commitment, no time or interest, travel distance or family constraints, confidentiality, or financial hardship)
3. Passive (passive refusal)
4. Hostile (hostile refusal)
5. Other (fear of physical examination; dissatisfaction with the U.S. Air Force, U.S. Government, the AFHS, or previous examinations; or other reasons).

Table 5-4. Reasons for Refusal by Group, Age, Rank, and Race

Category	Total Refusals	Reasons for Refusal: Health n	Health %	Logistics n	Logistics %	Passive n	Passive %	Hostile n	Hostile %	Other n	Other %	Unadjusted p-Value
Ranch Hand	227	42	18.5	79	34.8	23	10.1	55	24.2	28	12.3	0.092
Comparison	548	66	12.0	226	41.2	42	7.7	145	26.5	69	12.6	
Birth Year <1942	389	85	21.9	128	32.9	20	5.1	103	26.5	53	13.6	<0.001
Birth Year ≥1942	386	23	6.0	177	45.8	45	11.7	97	25.1	44	11.4	
Officer	248	29	11.7	81	32.7	18	7.3	94	37.9	26	10.5	<0.001
Enlisted	527	79	15.0	224	42.5	47	8.9	106	20.1	71	13.5	
Black	46	7	15.2	17	37.0	7	15.2	9	19.6	6	13.0	0.463
Non-Black	729	101	13.9	288	39.5	58	8.0	191	26.2	91	12.5	
Total	775	108		305		65		200		97		

Note: Percentages represent the percent of total refusals.

Age, rank, and race have been dichotomized for analysis purposes (born before 1942 and born in or after 1942; officer and enlisted; Black and non-Black, respectively). Without adjustment for age, rank, or race, the association between reason for refusal and group was not significant (p=0.092). There was a significant association between reason for refusal and age (p<0.001) and between reason for refusal and rank (p<0.001). Younger participants were less likely to refuse for health reasons than older participants (6.0% vs. 21.9%). Younger participants were more likely to refuse passively (11.7% vs. 5.1%) or for logistics reasons (45.8% vs. 32.9%). Officers were more likely to be hostile refusals than enlisted men (37.9% vs. 20.1%) and were less likely to refuse because of logistics reasons than enlisted men (32.7% vs. 42.5%). No significant association was found between reason for refusal and race (p=0.463).

A test of association between reason for refusal and group (adjusted for age, rank, and race) was performed and found to be not significant (p=0.132). The adjusted association between reason for refusal and age was significant (p<0.001), as was the association between reason for refusal and rank (p<0.001). No significant association was found for race (p=0.521).

5.5.2.1 *Passive Refusals*

A potential participant was classified as a passive refusal if he was scheduled for a physical examination but broke the appointment twice. A potential participant also was classified as a passive refusal for other reasons, including the inability to contact the participant directly because of the presence of a "gatekeeper" (see Section 5.5). Although passive refusal was the most common type of refusal (second only to hostile attitude) during the 1992 study, this type of refusal was far less prevalent in the 1997 follow-up. Passively refusing Ranch Hands, Original Comparisons, and Replacement Comparisons accounted for only 8.4 percent of the refusals (65 passive refusals, 775 total refusals) (see Table 5-3).

5.5.2.2 *Hostile Refusals*

Hostile refusals accounted for approximately 25 percent of both refusing Ranch Hands and refusing Comparisons. As shown in Table 5-5, 197 veterans were classified as hostile refusals during the 1992 physical examination process. Five additional veterans were added to the list of hostile individuals after the 1992 report was completed to bring the total to 202 individuals. Of these five, two were previously designated as refusals for the 1992 examination because of no interest in the AFHS, and three were dissatisfied with previous examinations. Between the 1992 and 1997 examinations, this list of 202 veterans was reviewed and some individuals were re-designated as refusals that should be contacted for the 1997 follow-up examination. Some hostile individuals on this list also contacted the Air Force and expressed a desire to participate in the 1997 follow-up examination. Consequently, 17 veterans were removed from the list of hostile individuals. Three of these previously hostile veterans participated in the 1997 follow-up examination, and the remaining 14 veterans refused to participate in the 1997 examination. Six additional veterans on the list of hostile individuals died between the 1992 and 1997 follow-up examinations. The list of 202 hostile individuals was therefore reduced to 179 veterans that were not to be contacted by schedulers for the 1997 examination. During the course of the 1992 examination, 21 additional veterans were designated as "newly" hostile individuals, resulting in a total of 200 veterans designated as hostile for the 1997 follow-up examination, as shown in Table 5-5.

5.5.2.3 *Reasons for Refusal Across AFHS Examinations*

The reasons for refusal for the baseline, 1987, 1992, and 1997 examinations are shown in Table 5-5, and are presented separately for Ranch Hands and Comparisons. The reasons for refusal to participate in the 1985 examination are not addressed in Table 5-5 because the data were not collected in a manner consistent with that in the other examinations. In 1985, the data were collected verbatim as part of the record of telephone contacts. Therefore, no meaningful comparisons can be made between the 1985 study data on refusals and other years. Table 5-5 shows a slight but consistent increase in total refusals across time. Of particular note is the steady increase in refusals for health reasons. Passive refusals decreased in the 1997 examination. This may be attributable to the aggressive efforts to maintain communication with veterans who were expected to become passive refusals.

Table 5-5. Reasons for Refusal by Group and Year

Reason	Baseline				1987				1992				1997			
	Ranch Hands		Comparisons		Ranch Hands		Comparisons		Ranch Hands		Comparisons		Ranch Hands		Comparisons	
	n	%[a]	n	%[a]	n	%[a]	n	%[a]	n	%[a]	n	%[a]	n	%[a]	n	%[a]
Fear of Physical Exam	6	0.5	6	0.4	1	0.0	4	0.2	0	0.0	3	0.2	1	0.1	2	0.1
Job Commitment	29	2.4	80	4.8	32	2.7	61	3.5	31	2.7	53	3.0	33	3.0	104	5.4
Dissatisfaction with USAF	5	0.4	0	0.0	10	0.8	11	0.6	6	0.5	10	0.6	1	0.1	6	0.3
No Time	53	4.4	154	9.3	28	2.4	79	4.6	13	1.1	50	2.8	26	2.4	74	3.9
Travel Distance, Family	4	0.3	21	1.3	5	0.4	17	1.0	8	0.7	17	1.0	14	1.3	42	2.2
Confidentiality	11	0.9	15	0.9	1	0.1	4	0.2	1	0.1	2	0.1	5	0.5	5	0.3
Health Reasons	10	0.8	7	0.4	11	0.9	16	0.9	19	1.7	21	1.2	42	3.8	66	3.4
Passive Refusal	9	0.7	15	0.9	40	3.4	78	4.5	41	3.6	96	5.5	23	2.1	42	2.2
Dissatisfaction with Previous Exam	n/a	0.0	n/a	0.0	0	0.0	1	0.1	3	0.3	5	0.3	5	0.5	6	0.3
Financial Hardship	n/a	0.0	n/a	0.0	1	0.1	1	0.1	2	0.2	2	0.1	1	0.1	1	0.1
Hostile	n/a	0.0	n/a	0.0	n/a	0.0	n/a	0.0	58	5.0	139	7.9	55	5.0	145	7.6
Dissatisfaction with AFHS	n/a	0.0	n/a	0.0	n/a	0.0	n/a	0.0	n/a	0.0	n/a	0.0	3	0.3	8	0.4
Other	0	0.0	3	0.2	42	3.5	88	5.1	2	0.2	16	0.9	18	1.6	47	2.4
Total	127		3010		171		360		184		414		227		548	
Total Invited	1,207		1,657		1,188		1,730		1,149		1,761		1,101		1,919	

[a] Percent of persons invited to participate.

5.5.3 Replacement Comparisons

As stated previously, matching replacements for refusing Original Comparisons based on health status, as well as age, race, rank, and occupation, was maintained at the 1997 follow-up. The reported health status of new replacements was obtained at the time of telephone scheduling. At the 1997 follow-up, 412 Replacement Comparisons were fully compliant (see Table 5-1). The health-matching results for the 52 Replacement Comparisons invited to the study for the first time in 1997 (see Table 5-2) and their replaced Original Comparisons are summarized in Table 5-6.

Table 5-6. Self-reported Health Status of Original Comparisons and Their Replacements

Replacement's Reported Health	Original Comparison's Reported Health					
	Excellent	Good	Fair	Poor	Unknown[a]	Total
Excellent	7	2	0	0	3	12
Good	2	22	0	0	6	30
Fair	0	0	3	1	4	8
Poor	0	0	0	0	0	0
Unknown	0	0	0	0	2	2
Total	9	24	3	1	15	52

[a] Includes 11 hostile respondents and 4 respondents who reported "Don't Know" for health status; one Replacement Comparison replaced a Replacement Comparison instead of an Original Comparison.

Thirty-two of the 52 Replacement Comparisons were matched perfectly on health status to the Original Comparisons. Five additional Replacement Comparisons were matched according to the dichotomized health status indicated in the study protocol. Fifteen Original Comparisons (labeled "Unknown") refused to give a self-perception of health or said they did not know how their health compared with that of others. The health status of these 15 Replacement Comparisons is shown in Table 5-6.

At the 1997 follow-up, 421 Original Comparisons were either deceased or noncompliant (see Table 5-7). The entire matched set of replacement candidates for each noncompliant Original Comparison was reviewed to determine if the appropriate replacement strategy was followed. Results are presented in Table 5-7. Of the 421 noncompliant (refusing, unlocatable, or deceased) Original Comparisons at the 1997 follow-up, 284 compliant replacements were found. Ninety-nine matched sets were closed because all previously invited Comparisons were deceased and, consistent with the protocol, no replacements were to be contacted, or because all replacements were contacted and no replacements were found that were willing to participate or were able to be health-matched. No Replacement Comparisons were contacted for 11 of the noncompliant Original Comparisons. A review of the record of telephone calls showed that all 11 had declined late in the scheduling process. For 27 of the noncompliant Original Comparisons, some replacements, but not all, were contacted and none complied. A review of the cohort of the 27 Original Comparisons, where replacement contact was not fully exhausted, showed that the Original Comparison or one or more of the Replacement Comparisons also had declined late in the process.

Table 5-7. Matched Set Compliance of Noncompliant Original Comparisons

Matched Set Compliance	Original Comparison's Compliance			
	Refusal	Unlocatable	Deceased	Total
At Least One Compliant Replacement	250	10	24	284
All Contacted Replacements Noncompliant and No Uncontacted Comparisons Remain in the Matched Set or All Previously Contacted Comparisons are Deceased	16	0	83	99
All Contacted Replacements Noncompliant and Other Uncontacted Comparisons Remain in the Matched Set	25	0	2	27
No Replacement Comparisons Contacted	11	0	0	11
Total	302	10	109	421

5.6 MATCHING OF SELF-REPORTED HEALTH STATUS

5.6.1 Self-reported Health Status of Refusals

Of the 775 refusals, reported health status, as obtained by telephone at the time of scheduling, was available for a total of 423 Ranch Hands and Comparisons. Table 5-8 summarizes their responses. Data were obtained from 125 (55.1%) of 227 refusing Ranch Hands and 298 (54.4%) of 548 refusing Comparisons. Among the 423 refusals responding to the health status question, there was no significant association between group and reported health (p=0.155).

Table 5-8. Reported Health Status of Refusals

Reported Health Status	Ranch Hands		Comparisons		Total		p-Value
	n	%	n	%	n	%	
Excellent	33	26.4	97	32.6	130	30.7	0.155
Good	64	51.2	152	51.0	216	51.1	
Fair	27	21.6	42	14.1	69	16.3	
Poor	1	0.8	7	2.3	8	1.9	
Total	125		298		423		

Note: Does not include 47 Ranch Hands and 107 Comparisons who reported "Don't Know" or refused to answer health status, and does not include 55 Ranch Hands and 143 Comparisons who were hostile.

Ideally, compliance bias between the groups should be assessed by comparing the health of refusing veterans to fully compliant participants with adjustment for the matching variables. The only current data available on the refusing veterans are self-reported responses to the health status question asked during the scheduling procedure. These data are missing for all hostile refusals. Almost three-quarters

(48 of 65, or 73.8%) of the passive refusals did not give their reported health status during scheduling. A summary of reported health status for 17 passive refusals that reported their health status during scheduling is shown in Table 5-9.

Table 5-9. Reported Health Status of Passive Refusals

Reported Health Status	Ranch Hands		Group: Original Comparisons		Group: Replacement Comparisons		Total	
	n	%	n	%	n	%		%
Excellent	0	0.0	1	25.0	1	20.0	2	11.8
Good	6	75.0	2	50.0	3	60.0	11	64.7
Fair	2	25.0	1	25.0	1	20.0	4	23.5
Poor	0	0.0	0	0.0	0	0.0	0	0.0
Total	8		4		5		17	

Note: Does not include 15 Ranch Hands, 20 Original Comparisons, and 13 Replacement Comparisons who reported "Don't Know" for health status.

A test of association between reported health status and group, age, rank, compliance, and race was performed, and the results are shown in Table 5-10. For analysis purposes, reported health status was classified into two categories: excellent or good, and fair or poor. The covariates age, rank, compliance, and race were dichotomized (born before 1942 and born in or after 1942; officer and enlisted; fully compliant and refusal; Black and non-Black, respectively). No significant association was found between race and reported health status ($p=0.824$). Without adjustment, age ($p<0.001$), rank ($p<0.001$), and compliance ($p<0.001$) were associated significantly with reported health. Ranch Hands were more likely to report fair or poor health than were Comparisons (14.1% vs. 11.1%). Enlisted men were more likely to report fair or poor health than were officers (15.1% vs. 7.6%). As expected, refusals (18.2%) and older participants (14.9%) were more likely to report fair or poor health than were fully compliant (11.0%) or younger participants (9.1%).

The association between reported health status and group, adjusted for age, rank, compliance, and race was significant ($p=0.011$). The adjusted association between reported health status and compliance was statistically significant ($p<0.001$), as were the adjusted associations between health status and age ($p<0.001$) and rank ($p<0.001$).

Table 5-11 shows the reported health status versus compliance separately by group. For both Ranch Hands and Comparisons, significantly more refusals reported fair or poor health ($p=0.007$ and $p=0.001$, respectively) than fully compliant participants. A higher percentage of compliant Ranch Hands reported fair or poor health (12.9%) than compliant Comparisons (9.7%). When adjusted for age, race, and occupation, the relation between health status and compliance did not change significantly with group ($p=0.876$). This result showed that the difference in health status between refusals and fully compliant participants was similar between Ranch Hands and Comparisons.

Table 5-10. Reported Health Status by Group, Age, Rank, Compliance, and Race

Group	Total	Reported Health Status: Excellent/Good #	Excellent/Good %	Fair/Poor #	Fair/Poor %	Unadjusted p-Value
Ranch Hand	963	827	85.9	136	14.1	0.028
Comparison	1,509	1,342	88.9	167	11.1	
Birth Year <1942	1,351	1,150	85.1	201	14.9	<0.001
Birth Year ≥1942	1,121	1,019	90.9	102	9.1	
Officer	935	864	92.4	71	7.6	<0.001
Enlisted	1,537	1,305	84.9	232	15.1	
Fully Compliant	2,049	1,823	89.0	226	11.0	<0.001
Refusal	423	346	81.8	77	18.2	
Black	144	125	86.8	19	13.2	0.824
Non-Black	2,328	2,044	87.8	284	12.2	
Total	2,472	2,169		303		

Table 5-11. Reported Health Status by Group

Group	Compliance Status	Total	Reported Health Status: Excellent/Good #	Excellent/Good %	Fair/Poor #	Fair/Poor %	p-Value
Ranch Hand	Fully Compliant	838	730	87.1	108	12.9	0.007
	Refusal	125	97	77.6	28	22.4	
Comparison	Fully Compliant	1,211	1,093	90.3	118	9.7	<0.001
	Refusal	298	249	83.6	49	16.4	

5.6.2 Self-reported Health Status of Fully Compliant Participants

Tables 5-12 through 5-14 summarize the reported health status, medication use, and work loss of the 2,121 fully compliant participants at the 1997 follow-up examination. Table 5-12 summarizes the reported health status of participants fully compliant to the 1997 physical examination. Among fully compliant participants, a marginally significant association was found between reported health at the time of scheduling and group (Ranch Hand, Comparison) (p=0.076). More Ranch Hands reported their health as fair (12.9%) than did Comparisons (9.7%).

Table 5-12. Reported Health Status of Fully Compliant Participants

Reported Health Status	Group						
	Ranch Hands		Comparisons				
	n[a]	%	n[a]	%	Total	%	p-Value
Excellent	287	34.2	440	36.3	727	35.5	0.076
Good	443	52.9	653	53.9	1,096	53.5	
Fair	108	12.9	118	9.7	226	11.0	
Poor	0	0.0	0	0.0	0	0.0	
Total	838		1,211		2,049		

[a] Does not include 32 Ranch Hands and 40 Comparisons who answered "Don't Know."

Table 5-13. Reported Medication Use of Fully Compliant Participants

Medication Use	Group						
	Ranch Hands		Comparisons				
	n[a]	%	n	%	Total	%	p-Value
Yes	512	58.9	688	55.0	1,200	56.6	0.081
No	357	41.1	563	45.0	920	43.4	
Total	869		1,251		2,120		

[a] One Ranch Hand did not report on medication use.

Table 5-14. Reported Work Loss of Fully Compliant Participants

Work Loss	Group						
	Ranch Hands		Comparisons				
	n	%	n	%	Total	%	p-Value
Yes	105	16.7	148	16.5	253	16.6	0.968
No	524	83.3	750	83.5	1,274	83.4	
Total	629		898		1,527		

Note: Does not include the following: 22 unemployed (9 Ranch Hands, 13 Comparisons)
564 retired (231 Ranch Hands, 333 Comparisons)
8 who did not answer (1 Ranch Hand, 7 Comparisons).