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NHLBI GROWTH AND HEALTH STUDY

PROTOCOL

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TABLE OF CONTENTS

TABLE OF CONTENTS (Continued)

TABLE OF CONTENTS (Continued)

TABLE OF CONTENTS (Continued)

TABLE OF CONTENTS (Continued)

CHAPTER 1

BACKGROUND AND REVIEW OF LITERATURE

1.1 Introduction

Obesity has far reaching health and social implications. An important proportion of adult obesity has its origins in childhood, although many of the resulting serious medical problems may be deferred to adult life. Several studies have indicated that the degree of adiposity in infancy is predictive of obesity in childhood, and childhood adiposity, in turn, is correlated with adult obesity. The pre-adolescent period between ages 7 and 11 attracts particular attention because juvenile obesity often begin during this interval of accelerated growth (1). The determinants of childhood obesity are numerous and not well defined. They include physiological, nutritional, and social-psychological influences. In addition, the impact of these factors may not be the same for all racial and cultural groups.

1.2 Definition of Obesity

The National Center for Health Statistics (NCHS) has presented one ponderal index (height/weightl/3) (also called Sheldon's inversion of the ponderal index) as a measure of obesity suitable for group comparisons (2). The NCHS also presented a body mass index ($weight/height^2$) as suitable for group comparisons of cholesterol concentration (3). It has presented another index ($weight/height^{1.5}$) as being more appropriate for women (4) and also used a power function with $weight/height^2$ for males.

The various indices of obesity appear to be closely related. Criqui et al. have compared a variety of measures of obesity to find height/ weight$^{1/3}$, weight/height, and weight$^{1/3}$ height highly correlated with each other (0.95 to 0.99). These authors found weight/ height^2 and relative weight (obesity defined as a fixed percentage over "ideal" weight) very highly correlated (0.999) (5). One problem in defining obesity as relative weight is that ideal standards for such definitions have changed with time (6-8). The same difficulty is found in the measurement of skinfold thickness (9), and is part of the larger problem of defining normal and abnormal standards (10,11).

1.3 Relationship of Obesity and Race to Possible CHD Risk Factors

1.3.1 Race

Implicit in most public health Research on black/white differences is the U.S. Census approach-- that of self-definition of race by individuals. Most of the studies on black/white differences in obesity and coronary heart disease (CHD) risk factors discussed here were done on self-defining populations.

Of particular interest are the reported differentials in the Quetelet Index between black and white females beginning with the 6-11 age group and becoming progressively greater with advancing age. (NOTE: can B.H. supply this ref from Westat RFP) (12). The importance of these differentials to the health of black American women is demonstrated in the U.S. mortality statistics for 1980 by age, race, and sex. For women 35-44 the death rate from cardiovascular diseases (CVD) was 90.1 per 100,000 among blacks and 24.7 per 100,000 among whites. The difference between blacks and whites works out to an excess of 1,000 CVD deaths annually among 35-44 year old black women.

Similar calculations for white and black women aged 45-54 produces 3,200 excess CVD deaths annually among black women; for black women 55-64 the excess was about 4,200 deaths annually. Thus, the total number of excess CVD deaths annually among black women under 65 was about 8,400 in 1980.

1.3.2 Personality/Behavior

Among possible coronary-prone behaviors, Friedman and Rosenman's Type A behavior has been the best accepted and demonstrated (13,14). However, the psychological correlates of CHD risk factors, obesity, and black/white differences have not been adequately explored (15,16). Much that is known about the psychology of specific risk factors, e.g., smoking (17,18) and health attitudes and behavior in youths, have been found in NHANES to vary by race, SES, and geography (19).

1.3.3 Social Support

A number of studies have reported differences among ethnic groups in general child rearing practices. Black parents expected earlier assumption of responsibility by their children than whites (20,21). This appears to be especially true of the black mother's expectation that daughters should be independent and responsible (22,23). Black parents have been shown to be less permissive and more authoritarian than white parents (24), to place greater emphasis on physical rather than verbal punishment (25), and to be less supportive than white parents (26).

1.3.4 Nutrition

The hypothesis that CHD is associated with diet is over 30 years old (27). Moreover, evidence that serum cholesterol is an important

risk factor is quite strong (28-30). Harlan et al. found blood pressure to be related to alcohol, calcium, and phosphorus intake (31). In the Western Electric Study a positive association was found between reported intake of cholesterol and polyunsaturated fats and serum cholesterol (32). Crawford et al reported significant correlations between dietary cholesterol and serum cholesterol levels in six year old Berkeley, California children (33). In Kansas school age children, Foley et al. found that nutrition-related habits were associated with nutrition-related attitude scores (34).

Cultural differences in eating habits have been documented in a few studies. It has been reported that meat, poultry, and fish accounted for a larger share of the food dollar in black than white households (35,36). Kerr et al. showed that low income blacks in Houston consumed much more candy and sweetened beverages than whites or blacks who were better off financially (37). There is also known ethnic variation in salt purchase (38) and other dietary behaviors (3,39).

1.3.5 Exercise

Physical activity as a means of consuming calories influences the development of obesity. The relationship of exercise to CHD has been controversial, especially since it is a correlate of many known CHD risk factors (40,41,42). When physical activity in black and white females was compared, frequent leisure time exercise habits were found to be less common in black females over 21. However, 12-20 year old black females reported significantly more habitual physical activity than whites (43). Questionnaires measuring physical activity have been standardized (44-46), but have not yet been equated with calories spent (45). Of further use are objective methods to validate questionnaire

responses. LaPorte et al. have developed one such method in 12-14 year old boys (47).

1.3.6 Physical Maturation and Puberty

Normal pubertal development depends on appropriate nutrition and is highly correlated with changes in height and weight (48). As a child progresses through the Tanner stages of maturity they also grow at different rates (49). Differences in the age of menarche for black and white girls in the United States have been demonstrated (50).

1.4 Relationship of Obesity to Established Coronary Heart Disease Risk Factors

Over the last four decades cohort studies, case-control studies, cross-sectional studies and randomized clinical trials have established a variety of risk factors for coronary heart disease (CHD) that are closely associated with obesity. At the same time, autopsy studies of young adults dying of trauma have shown that coronary heart disease can be found in its early stages decades before clinical manifestations appear (51,52). Cross-sectional studies of young populations have also established that risk factors for CHD can be found in children and adolescents (53). Furthermore, longitudinal studies of young populations show that for hypertension, discrepancies between individuals tend to grow with the passage of time (54).

1.4.1 Hypertension

Hypertension is a well established risk factor for CHD in adults. It is more common among obese than lean populations (31,55-58). It is more common in blacks (59,60), particularly in black females in whom it is two to three times more prevalent than among whites, and where it is

more severe and less amenable to therapy (61). In addition, there is support for the hypothesis that certain forms of drug treatment of hypertension increase the risk of CHD (62).

Cross-sectional data from the Lipid Research Clinics (LRC) collaborative prevalence study indicates that (1) before age 15 there are not consistent male-female differences in systolic or diastolic blood pressure, but (2) during adolescence there are marked increases in blood pressure in both sexes which parallel increases in height and weight, and (3) mean diastolic blood pressure in males increases consistently from age 15 to 19, most of the increase being accomplished by age 30. Data from the LRC as well as from the National Health and Nutrition Examination Survey (NHANES) (63) indicate no consistent racial differences in blood pressure between ages 6 and 17.

1.4.2 Diabetes/Hyperglycemia

It is well recognized that diabetes is associated with an increased risk of CHD and that females with diabetes experience CHD at a higher rate than nondiabetic females. The etiology of Type II (non-insulin dependent diabetes) remains unknown although intake of excessive calories leading to weight gain and obesity is an important factor. Type II accounts for approximately 80 to 90 percent of the diabetic patients in the United States. The prevalence of Type II diabetes is higher among blacks, Hispanics and American Indians (64).

A major complication for diabetics is accelerated atherosclerosis involving the coronary, cerebrovascular, and peripheral vessels occurring at an earlier age and with greater frequency than in non-diabetics. In the United States, diabetics are twice as likely as non-diabetics to die from coronary artery disease, and their average annual incidence of cardiovascular sequelae is increased at least two-

fold. The prevalence of diabetes is twice as high among black females as it is among white females (64).

1.4.3 Lipids

Serum cholesterol has been strongly related to CHD (28-30). Among the serum cholesterol components, however, high density lipoprotein cholesterol (HDL-C) is associated with protection from CHD while low density lipoprotein cholesterol and very low density lipoprotein cholesterol are associated with increased risk (65,66). Serum triglycerides have been associated with CHD, but not after adjustment for cholesterol (28,67). Apolipoproteins play a key role in cholesterol metabolism and may be an important contribution to atherosclerosis (68). They have been found to be differentially distributed in blacks and whites (69).

Lipid components in the blood are related to body mass in children and adults (70). Black females have been shown to have higher serum cholesterol levels than white females over all levels of income. Serum cholesterol tended to increase in children with increasing family income in NHANES (71). The role of lipids in hypertension therapy is known, but the impact of such therapy on coronary heart disease has been the subject of debate (62,72). The excess of ~~HLD~~ HDL-C in blacks as compared to whites may be of importance, but its relation to diet and exercise has not yet been thoroughly explored (73).

1.4.4 Family History

The familial tendency to CHD is also well established, and has been further analyzed to identify genetic aspects (74,75). The tendency to CHD within families may be mediated by genetic tendencies to known risk factors (76).

Garn et al. (77) looked at obesity relative to family lines and found that children with two obese parents tended to be fattest. The presence of one obese parent, whether it was the mother or father, was also shown to affect the degree of obesity in the child. In general, spouses resembled each other in degree of obesity. These results led Garn et al. (77) to suggest that obesity was primarily the result of living together and only secondarily the outcome of genes held in common. They also postulated that there might be a critical period during which children learn to copy the eating and activity patterns of the parents they live with.

1.4.5 Smoking

There is a vast literature that shows cigarette smoking to be a risk factor for CHD. Cigarette smoking is also associated with other CHD risk factors including hyperlipidemia, hypertension and lack of exercise (40). Smoking has come to be more prevalent among black than white females and has increased markedly among adolescent females (73,78). Quitting cigarette smoking is associated with weight gain (79).

1.4.6 Socioeconomic Status

Moore and Stunkard (80) demonstrated in the mid-sixties in New York City that a strong inverse relationship existed between socio-economic status (SES) and obesity. Obesity was six times more prevalent among women of lower than upper SES. However, the relationship of CHD disease, SES and racial differences is more difficult to interpret (81).

Stunkard et al. (82), in a later study of white school children, used skinfold thickness to establish the age at which the influence of

SES on obesity becomes apparent. They found that as early as age six, there was a marked prevalence of obesity in the lower class relative to the upper class. Garn (77) found that income was positively related to obesity in females from childhood into adolescence, but negatively related in girls during later adolescence and in adult women at all ages. Correcting the data for income, black girls were still leaner than white girls and black women still fatter than white women. SES has been found to correlate positively with serum cholesterol in adults (3), with no consistent significant relationship in children. Blood pressure in children has not been associated with SES (83). However, food consumption profiles have been associated with income (84).

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CHAPTER 2

OVERVIEW OF THE MAJOR DESIGN FEATURES

2.1 Study Name

The official name of the study is the National Heart, Lung, and Blood Institute (NHLBI) Growth and Health Study (hereafter abbreviated as NGHS).

2.2 Study Objectives

The primary objective of the NGHS is to determine whether, and to what degree, black-white differences in the development of obesity in females during pubescence can be explained by differences in dietary habits, patterns of physical activity, socioeconomic status or psychosocial factors. A secondary objective is to determine whether differences in the development of obesity are associated with black-white differences in other coronary heart disease risk factors, such as blood pressure, blood lipids/lipoproteins and apolipoproteins.

2.3 Participating Units

The units participating in NGHS include the NHLBI project and contract offices; a coordinating center at Maryland Medical Research Institute in Baltimore, Maryland; three clinical centers located at the University of California at Berkeley, the University of Cincinnati, and WESTAT - Group Health Association in Washington, D.C; a central lipid laboratory at Johns Hopkins University in Baltimore; and a nutrition coding center at University of Minnesota. The study is governed by a Steering Committee comprised of two representatives from the project office, coordinating center, and each clinical center, and a Data Monitoring Committee comprised of scientists not directly associated with the NGHS.

2.4 Size and Nature of Participant Group and Eligibility Criteria

The NGHS will enroll approximately 1,100 black and 1,100 white girls (non-institutionalized) ages 9 and 10 at the time of first examination. In addition, the girls must have at least one parent or caretaker who is willing to provide certain basic family demographic information to the study as well as consent for the child's participation. A possible reason for ineligibility would be the family's plan to move away from the study area within 12 months after entry into the study. An attempt will be made to enroll one or both parents/guardians of each girl into the study as well.

2.5 Visit Schedule and Types of Information Collected

The participating children will be interviewed and examined at entry (Year 1) and each year for four years. The participating adults will be examined at entry (Year 1) and at Years 2 and 5 and will be given or sent study questionnaires to complete at home each year. The interviews for the child will include basic demographic information, psychosocial questionnaires, nutrition and physical activity patterns questionnaires, and review of three-day dietary and physical activity records. The child's clinical exam will consist of various body measurements, including height, weight, skinfold, girth and blood pressure measurements, assessment of stage of sexual maturity, and a bioelectrical impedance measurement. During the clinical exam, blood will be drawn for laboratory tests (i.e., lipid and apolipoprotein measures) at baseline (Year 1) and at the Years 2 and 5. Information obtained on the parents/guardians includes demographic and household information, medical history, body measurements (including height, weight, blood pressure, and skinfold and girth measurements), plasma lipid and apolipoprotein measurements (baseline only), household nutrition patterns, and various psychosocial patterns.

CHAPTER 3

STUDY OBJECTIVES AND RESEARCH QUESTIONS

3.1 Study Objectives

The primary objective of the NGHS is to determine whether, and to what degree, black-white differences in the development of obesity in females during pubescence can be explained by differences in dietary habits, patterns of physical activity, socioeconomic status or psychosocial factors. A secondary objective is to determine whether differences in the development of obesity are associated with black-white differences in other coronary heart disease risk factors, such as blood pressure and blood lipids/lipoproteins apolipoproteins.

3.2 Research Questions

The primary questions to be addressed, and hopefully answered, by the NGHS are the following:

1. Can the cross-sectional NHANES II findings that more black girls age 12-20 are classified as obese than white girls at the same age be confirmed by this new longitudinal follow-up study of a cohort of black and white girls. If so, what is the mean age at which the prevalence of obesity in black girls begins to diverge from that in white girls? For these purposes, the primary outcome variables will be change in adiposity as measured by (a) triceps skinfold, (b) subscapular skinfold, (c) suprailiac skinfold, (d) a summarization of these three skinfolds, and (e) a body mass index based on height and weight.
2. If the NGHS confirms that more black girls can be classified as obese than white girls, can this difference be explained by

different food intake and/or physical activity patterns between the black and white girls, or by differences in balance between food intake and physical activity patterns? To answer these questions it is necessary to obtain detailed dietary and physical activity histories from the children in addition to the body measurements indicated in #1 above.

3. Are there any socioeconomic factors that might help to explain the black-white difference in development of obesity and/or black-white differences in dietary and activity patterns? For this reason, in addition to the household food pattern information it will be necessary to collect information on total household income, level of education, and occupation of the parents/guardians.

4. Are there social or psychological factors that are in play in the family that contribute to the development of obesity? These include type of family interaction, household environment, style of parenting in the family, communications in the family, attitudes about activity, and cultural attitudes toward body build and diet.

5. If there are different dietary and/or activity patterns between blacks and whites, are these patterns familial (i.e., found similarly in the parents or guardians)? For this purpose, certain information must be obtained on physical activity patterns and on eating patterns and attitudes about food and body size in the parents/guardians.

6. Are there other factors, measured on the young girls, associated with the black-white difference in development in obesity, e.g., cigarette smoking, alcohol consumption, use of medications, age at menarche, or early biological maturation?

7. Are black-white differences in the development of obesity associated early on with black-white differences with respect to blood pressure and plasma lipid/lipoprotein levels which may be precursors of coronary heart disease?
8. Are there differing pathophysiologic ramifications of the development of obesity in black and white school girls, specifically in the assessment of the effects of obesity on lipids, lipoproteins, apolipoproteins, and blood pressure?
9. Are there biobehavioral differences in predictors of obesity in black and white girls? Does the development of obesity have differential effects on developmental and behavior patterns in black and white girls?
10. Is there a racial differential in the relative importance of parental obesity on the development of obesity in children, given the central importance of family environment as an explanatory variable?
11. Is it more socioculturally acceptable for black girls to be obese than white girls?
12. A longitudinal documentation of black/white differences in determinants of obesity would allow development of intervention policies based on causality. By better understanding the physiologic ramifications of obesity in black and white school girls by comparing and examining lipids, lipoproteins, apolipoproteins, and blood pressure, we would be able to better understand how obesity in black girls affects CHD risk factors. We would determine how development of obesity might ultimately affect race-sex-specific CHD morbidity and mortality, and in addition, we would be able to provide new, data-based targets for CHD risk factor

intervention. We would also be able to provide "hard" data relative to the hypothesis that it is socioculturally acceptable for black but not for white girls to be obese.

CHAPTER 4

ADMINISTRATIVE STRUCTURE

4.1 Introduction

The NGHS is divided into a one-year planning phase (Phase I), a five-year data collection phase (Phase II), and a two-year data analysis and report writing phase (Phase III). Three clinical centers, each recruiting black and white participants between the ages of 9 and 10 years and their caretakers, will participate in accordance with the uniform protocol developed in collaboration with the coordinating center and the NHLBI project office. The organizational structure described below will be assembled during Phase I and will continue to function during the projected five years of Phase II.

4.2 NHLBI Project Office/Contract Office

NGHS is supported by contracts from the National Heart, Lung, and Blood Institute (NHLBI). NHLBI project office staff in the Division of Epidemiology and Clinical Applications (DECA) will work closely with the NGHS coordinating center staff and the staff of participating clinical centers to provide necessary scientific communication and direction and assure the quality of the work to be performed under the provisions of the contracts with the NHLBI. An NHLBI biostatistician serves as a liaison from the Biostatistics Research Branch of DECA and works closely with the project office and Steering Committee on design and analysis issues. The contract officer will work closely with the project officer in order to handle the financial aspects of the NGHS including consideration of cost effectiveness of activities.

The NHLBI project office serves as a direct link from the organization of NGHS to the Director of the NHLBI to channel inquiries, recommendations and policy directives. Under the contract mechanism, NHLBI is the final authority for determining program policy.

4.3 Clinical Centers

The three NGHS clinical centers are:

1. University of Cincinnati, Cincinnati, OH.
2. WESTAT, Rockville, MD.
3. University of California, Berkeley, CA.

The role of the clinical centers includes the following functions:

1. Developing the study Protocol, Manual of Operations, and data forms in collaboration with other study investigators.
2. Implementing the approved Protocol at each clinical site by identifying and enrolling approximately 600-900 females aged 9-10 years, approximately equally divided between blacks and whites. Parents or guardians of the girls will also be enrolled.
3. Conducting baseline and follow-up examinations of the study population.
4. Collecting, entering, editing, and transmitting data obtained in accordance with the Protocol and Manual of Operations to the coordinating center. Working with the coordinating center to maintain the quality of the data collected.

5. Evaluating the progress of their clinic in carrying out the protocol and alerting the coordinating center and Steering Committee to major problems.
6. Preparing publications of study results in collaboration with other investigators and NHLBI staff.

4.4 Coordinating Center

The coordinating center is located at Maryland Medical Research Institute, Baltimore, MD. The coordinating center will be responsible for the following tasks:

1. Developing the study Protocol, Manual of Operations, and data forms in collaboration with the other study investigators.
2. Developing, pretesting, implementing, and maintaining a distributed database management system.
3. Coordinating training, certification, and recertification of clinical center staff in examination and data collection processes.
4. Contracting with and monitoring a central laboratory for the analysis of blood samples and a central facility for nutrient composition coding of three day food records. Pretesting and coordinating the collection of laboratory results and three day food record coding and integrating these into the main database.
5. Carrying out quality assurance procedures in conjunction with clinical centers. Maintaining audit trails on data entry, reviewing adherence to schedules, and verifying completeness of data collection, and notifying clinics of error rates and deficiencies. Cooperating with other investigators in obtaining inter- and intra-observer reliability measures for question-

naires and procedures so that information can be incorporated in analyses.

6. Convening meetings of the Steering Committee, writing and distributing minutes. Preparing periodic progress and quality control reports.
7. Providing support for the forms development and clearance process.
8. Providing leadership for the analysis of study data in collaboration with the Steering Committee and NHLBI project office.
9. Delivering data to clinical centers for specific analyses as directed by the Steering Committee and project office.
10. Assisting in the organization and conduct of site visits to each clinical center in conjunction with NHLBI and the working groups to insure compliance with the provisions of the Protocol and Manual of Operations.
11. Notifying principal investigators of any special local problems in performance, or the project officer if a timely resolution of the problem is not possible.

4.5 Central Laboratories

The central lipid laboratory is located at Johns Hopkins University, Baltimore, MD. This unit will be responsible for making determinations of total cholesterol, HDL cholesterol, triglycerides, apoprotein A-I, and LDL apoprotein B on serum specimens obtained on children and adults at the three NGHS clinical centers. This unit will also store at -70 c through the end of the study two vials of 0.5 ml serum each for each specimen obtained from the children, and one vial of 0.5 ml serum each for each specimen obtained from the adults (except

that for 400 of these adult specimens this will be used for apoprotein determinations during the first year -- see Section 8.7 for more information on this).

Another central laboratory located at the University of Michigan, Ann Arbor, MI, will make determinations of glucose and insulin on serum specimens obtained on children at the three NGHS clinical centers.

4.6 Nutrition Coding Center

The NGHS nutrition coding center is located at the Nutrition Coordinating Center (NCC), University of Minnesota in Minneapolis. Three day food records for each child which have been reviewed and clarified by NGHS nutritionists will be sent to the NCC for centralized coding.

The NCC will return to the NGHS Coordinating Center a computer file containing a line-by-line analysis for each food item on each food record and also a MLRC food group code for each item. Detailed information on each food item will be as follows:

1-participant ID
2-participant name code
3-visit number
4-date of interview
5-interviewer ID
6-reviewer ID
7-whether record is original or replacement
8-type of day (typical, sick, travel, special event, other)
9-date of food consumption
10-day of week of food consumption
11-place of food consumption
12-NCC food code for item
13-brief description of item
14-amount consumed
15-MLRC food group code
16-nutrient content - 74 nutrients
17-type default (yes, no)
18-amount default (yes, no)

4.7 Committees and Working Groups

4.7.1 Steering Committee

The Steering Committee is made up of two voting members from each of the three clinical centers, the coordinating center, and the project office. The NHLBI contract officer will serve ex-officio as a non-voting member. If a vote is taken it will require a two-thirds majority of the non-abstention votes. If one voting member of a study center is absent, the other voting member of that center may cast both votes.

The Steering Committee will meet regularly to review study progress. It provides overall scientific direction for the study through consideration of recommendations from the working groups and others. The Steering Committee will guide the development of the study Protocol and Manual of Operations, reviewing and approving major changes. It will review and approve ancillary studies, provide advice and assistance to all centers and NHLBI on operational matters, and resolve problems submitted by any center involved in the study. The Steering Committee will also monitor the performance of clinical centers through site visits. The Steering Committee Chairman is appointed by the NHLBI project office. Minutes will be taken, prepared and distributed by coordinating center staff.

4.7.2 Working Groups

Several NGHS working groups have been established by the Steering Committee to take responsibility during the first year of the study for selection and/or development of data forms and writing assigned sections of the NGHS Protocol and Manual of Operations as well as training and certification guidelines in specific areas. Each working group is composed of one or more representatives from each clinical center, the coordinating center, and the NHLBI project office. The

working groups are listed below along with the specific role and area of concern of each.

1. The Growth, Biochemical and Clinical Measures Working Group is concerned with clinical and anthropometric measurements, assessment of biologic maturation, lipid/lipoprotein and other biochemical determinations, medical history, family history, and smoking and medication histories.
2. The Dietary and Physical Activity Working Group is concerned with methods of assessment of dietary intake, food patterns, nutrition knowledge and attitudes, and physical activity patterns.
3. The Psychosocial Measures Working Group deals with the areas of demographic measures, family dynamics and support, psychological measures in children and adults, perceptions of obesity, and family behavior regarding food intake, physical activity, and nutrition knowledge.
4. The Design and Analysis Working Group oversees the formulation of hypotheses, the specification of study outcome variables, definitions of key terms (such as "race"), and formulation of rules for participant eligibility and selection.
5. The Recruitment and Cohort Maintenance Working Group directs the "marketing" of the study and deals with problems of participant recruitment, maintenance of follow-up in the study, and the monitoring of center performance.

4.7.3 Data Monitoring Committee

The Data Monitoring Committee is a body external to NGHS -- not directly involved in the NGHS -- consisting of experts in the areas of biostatistics, epidemiology, clinical medicine, pediatrics, behavioral

science, and nutrition. It has been appointed by NHLBI to provide a fresh, independent review of the NGHS data and will meet at least once each year. This Committee will review the protocol, the epidemiologic data, the quality control data, and the data on performance of the study units, and will make recommendations to the NHLBI project office and to the NGHS Steering Committee for modifying study procedures to improve performance or quality, and for further data analyses to help explicate the study research questions.

Each meeting of this Committee will be attended by at least one representative from the coordinating center (including the principal investigator or his designate), the Chairman of the Steering Committee, and at least two representatives from the project office.

CHAPTER 5

POLICY MATTERS

5.1 Informed Consent

Obtaining consent is an important part of the recruitment procedure. The process will begin when an introductory letter and information sheet are sent to the parents of prospective participants. Consent forms will be presented by an interviewer during the first clinical contact and will be signed by both the child and her caretaker. They will contain an explanation of the purpose of the study, what is being measured, the examination schedule and methods, steps taken to insure confidentiality and safety, information about later withdrawal from participation, and an offer to answer any questions about study procedures.

Any modifications required by Institutional Review Boards of the local clinical centers will be reviewed by the Steering Committee. Those which do not detract from the content of the suggested documents will be approved.

5.2 Publications and Presentations

5.2.1 Approval

All final mainstream abstracts and manuscripts (including substudies, local and ancillary studies) must be approved by the Steering Committee and the NHLBI project office before being submitted to any national or international organization or journal for presentation or publication. In addition, abstracts including tables and charts should be reproduced in complete sets so that copies will be available to all centers.

5.2.2 Authorship

It is anticipated that there will be one or two initial NGHS publications that will present the overall study design and methods and primary results of the study. These papers will be authored by the "NGHS Research Group," with the complete list of NGHS personnel from the clinical centers, coordinating center, and project office given in an appendix. Each of the remaining papers will be authored by the 3-6 persons who have participated on the writing team and/or have contributed most to the writing, reviewing, and editing of the manuscript. In general, papers will be initiated and writing teams designated according to the following guidelines:

1. The Steering Committee's scientific interests will be announced in formal meetings and recorded in the minutes and through informal conversations.
2. Other proposals will be submitted to the Steering Committee and should include supporting literature, a clear statement of research hypotheses, a description of the data to be used, analytical methods, and any proposed collaborators or outside expertise.
3. The Steering Committee can select authors for a particular area of study and appoint a paper writing committee. Other authors may be recommended by principal investigators for approval by the Steering Committee.
4. First authorship will be assigned by the Steering Committee on the basis of effort contributed. The selection of writing committee members should be equitable and fair to all involved. Presenters will be nominated by the writing committees and approved by the Steering Committee.

5. Finished papers will be reviewed by the entire Steering Committee, with two Steering Committee members appointed by the chairman as primary reviewers, as well as by the NHLBI project office.
6. No data will be published on incomplete pooled data sets. Presentations on incomplete data sets can be made with prior approval of the Steering Committee.
7. The Steering Committee reserves the right to reassign first authorship if reasonable progress on completing an abstract or manuscript within a predesignated time frame has not been made.
8. Graduate students associated with NGHS through a sponsoring principal investigators or co-investigator may use NGHS data if the subject of the investigation is judged by the Steering Committee and NHLBI to be unrelated to core areas. The student must acknowledge use of NGHS data in the written dissertation, but include a statement saying that opinions, ideas, and interpretations are the student's alone. Further work on the project may be carried out by an NGHS paper writing team appointed by the Steering Committee and NHLBI with the student as convener.

5.3 Privacy of Records

Confidentiality of stored records will be maintained with implementation of the following policies:

1. All records will be kept by assigned I.D. numbers.
2. No personal identifiers of NGHS participants will be sent to the coordinating center or any other study unit. Only I.D. number and six-letter namecode will be used to identify study participants on the data forms.

3. Clinical centers will store the data forms in locked files and permit access only by authorized individuals.
4. Final results will be presented for review in conferences and journals in the form of statistical analyses with no disclosures of specific individuals.

In addition, access to the database is limited to certain clinic personnel through security software installed on the clinic systems. In addition to controlling access to the database, this security software, called WatchDog, will control access to operating system commands. All access to the system, which must be done through user identification and passwords, and all activity on the system will be electronically recorded for reference.

5.4 Ancillary Studies

An ancillary study will be defined, for NGHS purposes, as a set of procedures to be performed and/or data to be collected on NGHS participants over and above the procedures and data stipulated in the NGHS Protocol. Either one, two, or all three NGHS clinical centers may participate in a particular ancillary study. The coordinating center retains the option of participating or not participating in a particular ancillary study. The coordinating center will not be expected to provide data entry and editing systems nor data analysis for ancillary studies unless it agrees to participate as a full scientific partner. Funding for an ancillary study must be obtained from sources other than the funds contracted for NGHS.

Proposals for ancillary studies will be submitted first to the Steering Committee for review. Those proposals that are approved by the Steering Committee will then be reviewed by the Data Monitoring Board and must be approved by that Board before the study is

undertaken. In general, it will also be necessary to submit an ordinary research grant proposal to NIH or some other agency in order to obtain funding for the ancillary study.

The Steering Committee's primary criterion for judging the acceptability of a proposed ancillary study is its effect on the conduct and goals of the parent NGHS study. An ancillary study that conflicts or interferes with the objects of NGHS will normally not be approved. Interference may take a variety of forms: excessive burdens of exam time or decreased acceptability of the exam for individual participants are two examples. All publications, presentations, and abstracts from an ancillary study must be reviewed and approved by the Steering Committee prior to submission.

5.5 Referral Policy

Using criteria of the 1984 Report of the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure, elevated systolic and diastolic blood pressure levels in adults will be reported by clinical center personnel to the adults with referrals to the family physician for evaluation. The following criteria will be used:

1. If systolic is under 140 and diastolic is 85-89, the person is asked to have blood pressure rechecked by a physician within the next year.
2. If systolic is under 140 and diastolic is 90-104, or if systolic is 140-159 and diastolic is under 105, the person is asked to have blood pressure rechecked by a physician within the next two months.
3. If systolic is under 160 and diastolic is 105-114, or if systolic is 160 or over and diastolic is under 115, the person is asked

to have blood pressure rechecked by a physician within the next two weeks.

4. If diastolic is 115 or over, the person is asked to have blood pressure rechecked by a physician or at a clinic or hospital emergency room that very day.

Using criteria of the 1986 Report of the Second Task Force on Blood Pressure Control in Children, elevated systolic and diastolic blood pressure levels in children will be reported by clinical center personnel to the parents/guardians of the children with referrals to the family physician for evaluation. The following criteria will be used:

1. If systolic is under 118 (9 years) or under 120 (10 years) and diastolic is 80-85, or if systolic is 118-129 (9 years) or 120-129 (10 years) and diastolic is under 86, the parent/guardian is asked to have the child's blood pressure rechecked by a physician within the next year.
2. If systolic is under 130 and diastolic is 86-95, or if systolic is 130-143 and diastolic is under 96, the parent/guardian is asked to have the child's blood pressure rechecked by a physician with the next several weeks.
3. If systolic is 144 or over or diastolic is 96 or over, the parent/guardian is asked to have the child's blood pressure rechecked by a physician or at a clinic or hospital emergency room within the next two days.

Adult participants with serum total cholesterol levels above 250 mg/dl will be notified by letter and asked to have their cholesterol rechecked by their physician within the next few months.

Any condition which in the best judgment of the NGHS physician or nurse requires attention will be referred to the family physician for evaluation.

5.6 Copyrights and the Use of Standardized Instruments

When instruments used in NGHS are copyrighted, two different estimates of the costs involved in their use should be made. In most instances outright purchase of necessary materials from vendors will not be prohibitively expensive, even for a large sample. Nevertheless, companies should be contacted and asked about fees charged for photocopying privileges, especially in the reproduction of answer sheets which cannot be reused. Attempts should be made to explain to them the wide-scale exposure that the instrument will receive in NGHS, and the fact that the study is government sponsored and non-profit.

In instances where an instrument has not been copyrighted and sold commercially, NGHS should extend to authors the courtesy of contacting them and keeping them informed of the instrument's use. If minor modifications of the instruments have been made in order to adapt them to the NGHS population, copies of the revised test should be sent to the original authors after pretesting is complete.

CHAPTER 6

PARTICIPANT ELIGIBILITY

6.1 Eligibility/Exclusion Criteria for Children

6.1.1 Age and Sex Criteria

To be eligible for participation in the NGHS, a child must be female, age 9 or 10 years old at last birthday. In a substantial proportion of cases, the child will have her ninth or eleventh birthday during the period encompassing the initial contact and the initial examination. Since the day of the baseline clinical examination/ interviews (or the first of such days if the examination is stretched out over several days) marks the child's official date of entry into the NGHS, ideally the child should be 9 or 10 years old as of this date. However, because of the occasional need to re-schedule an examination due to absence of a child, a grace period of plus or minus fourteen days will be permitted. Thus, if a child has her eleventh birthday within five days prior to the first day of the baseline exam, or will have her ninth birthday no more than five days after the first day of the baseline exam, she will be counted eligible for the study.

6.1.2 Race Criteria

For NGHS, each center will give priority to enrolling children who are designated by a parent or guardian on the NGHS Household Information Form as "black" or "white" with homogeneous black or white biological parentage and living with homogeneous black or white guardians. In other words, these are black children with both biological parents black and living with either a single guardian who is black or with two guardians, both of whom are black; similarly for

white children. If the race of one of the biological parents is unknown but the child's race is concordant with the race of the other biological parent and with that of her guardian(s), such a child will be eligible. In such cases, further attempts will be made at the follow-up visits to ascertain the hitherto unknown race of the one biological parent. If the child is identified by her guardian as "mixed race", "part black and part white," or in any way other than "black" or "white", she will not be eligible for the study. For NGHS, children will not be eligible if they or their parents or guardians are designated as Hispanic, Asian/Pacific Islander, or American Indian/Alaskan Native. However, a child will not be disqualified if one parent or guardian admits to having up to 50% Hispanic or Asian/Pacific Islander or American Indian/Alaskan Native blood but still considers him(her)self as "black" or "white." Finally, if a child divides her time living with two or more sets of guardians, she will still be eligible if she spends no more than 25% of the time with Hispanic, Asian/Pacific Islander, or American Indian/Alaskan Native guardians.

6.1.3 Availability of Household Information

A child need not have any parents/guardians enrolled in the study to be eligible herself. However, it is essential that a certain minimum amount of demographic information about the household be obtained from a parent or guardian of the child. For a child to be eligible, the following information must be provided on the Household Information Form (NGHS Form 02):

1. The child's date of birth (Q 3).
2. Child's race (Q 4A/B).
3. Plans to move (Q 7).

4. Relationships of female and male guardians to child (Q 10B and 13B).
5. Either (a) education of female guardian (Q 10) or (b) education of male guardian (Q 13), or household income (Q 20). (However, every attempt should be made to obtain all three of these pieces of information.)
6. Race of female and male guardians (Q 10 F/G and 13 F/G).
7. Race of either biological mother (Q 11 A/B) or biological father (Q 14 A/B).
8. Name, address, and telephone number of person completing Form 02 (Q 21).
9. Name, address, and telephone number of at least one, and preferably two, close relatives or friends (Q 22 and 23).

6.1.4 Other Exclusion Criteria

Other conditions that would exclude a child from participation in the NGHS are the following:

1. Intention of the family to move outside the study area within 12 months.
2. A missing parental or guardian consent for the child's participation in the NGHS.

There are no other exclusions since it is intended that the whole range of participant characteristics should be represented in the study, (except in Washington where the child must be enrolled in the HMO at the time of recruitment). Further, exclusions could hamper recruitment in schools where it is planned to enroll entire classes. Some girls formally excluded on age, racial or other grounds may be tested in the interest of good relations between the schools and the

NGHS clinics. However, their data will not become part of the main database and the parents/guardians of these children will not be enrolled.

6.2 Eligibility Criteria for Adults

Given that a girl is eligible for participation in NGHS, the selection of her parent(s)/guardian(s) to be enrolled in the study will follow these guidelines:

1. If the child lives with either (a) the biological B-mother and B-father, or (b) the B-mother and step-father, or (c) the B-father and step-mother, or (d) an adoptive mother and father an attempt should be made to enroll both of these "parents" (whether biological, step, or adoptive) into the study.
2. If the child lives with one B-parent and at least one other non-parent adult at least 21 years old, an attempt should be made to enroll the B-parent plus the one other adult who, in the judgment of the B-parent, spends the most time with the NGHS child.
3. If the Child lives with neither B-parent, an attempt should be made to enroll the child's guardian(s) or the adult listed in school records as responsible for the child. A second adult who is at least 21 years of age may also be enrolled if in the guardian's judgment he/she has a significant role in the child's care.
4. In general, enrolled B-parents should participate in the follow-up interviews and examinations regardless of whether they continue to live with the NGHS child. However, non-B-parents or other adults who leave the household of the

NGHS child should not be continued in the study. In the case where there is change caretaker status after the initial examination, a second adult, or two adults if both enrolled caretakers change, should be invited to participate.

The above-stated guidelines imply that it is theoretically possible for there to be as many as four adults (i.e., two B-parents and two non-B parents) enrolled for a given child. Caretakers will be designated as those adults actually living with the child. These guidelines may not cover all possible situations. Judgment must be used in enrolling adults in situations not covered above. The coordinating center should be notified of each situation not covered by these guidelines so that additional guidelines can be formulated for the Protocol.

CHAPTER 7

RECRUITMENT OF STUDY PARTICIPANTS

7.1 Overview of All Centers

The potential respondent universe for the NGHS is non-institutionalized black and white females ages 9 and 10 at time of the enrollment exam in three clinical centers in Richmond, CA, Cincinnati, OH, and Washington, DC. For two of the clinical centers (Richmond and Cincinnati) the girls will be enrolled from elementary schools. Public and parochial schools have been selected from both urban and suburban areas to encompass a broad range of socioeconomic status (SES) for both blacks and whites. For the third clinical center (WESTAT), girls will be recruited from families that are members of the Group Health Association (GHA) HMO in the urban and suburban Washington, DC area. A random sample stratified by race and household income will be selected of those families having 9 and 10 year old girls. Inclusion of a wide range of SES for both blacks and whites will be effected by this means.

Clearly, the NGHS participants will not represent a random sample of all black and white girls in the Richmond, CA, Cincinnati, OH, and Washington, DC areas (although it may come close to including all 9-10 year old black and white girls in Richmond), but is expected to have a good representation of the overall population in Richmond, Cincinnati, and Washington of black and white girls, covering a broad range of SES levels in both racial groups. In Cincinnati, the three geographical divisions covered (inner city -- HUD target area, urban residential, and suburban) were not fully coterminous with SES categories of lower, middle, and upper. A check of the urban residential schools indicated

that their student population includes black and white students from all three SES categories.

The estimated numbers of children eligible for and to be enrolled in the NGHS are given in Table 7.1 by clinical center, race, and SES level. These numbers were provided in the centers' initial RFP responses and are based on somewhat different definitions of SES among the centers. In Richmond and Cincinnati it is estimated that about 70% of the age-race eligible girls will be enrolled. In Washington, DC, an initial random sample of 25% of the black households and 44% of the white households in the HMO with 9-10 year old girls will be invited to participate, with the expectation again that about 70% of these will enroll in the NGHS.

Specific approaches employed by the three clinical centers for recruiting schools and proposed approaches for sampling and recruiting NGHS participants are discussed in the following sections.

7.2 University of Cincinnati

7.2.1 Introduction

Schools in the Greater Cincinnati area were selected for the NGHS from the inner city, urban residential neighborhoods, and suburban districts using available information on racial composition of each school in the Greater Cincinnati area and knowledge as to SES in the different geographical areas of the region. As the first step in selecting schools, an endorsement of the study and a letter of support were obtained from the school administration. Copies of this letter were sent to the principals of the individual elementary schools along with a detailed description of the study and its purposes. Follow-up phone calls were made to the principals to obtain a demographic description of their student body. After the specific schools were

selected, another letter was sent to the school principals advising them of the current plans for the girl's examinations in their schools. In the third year of the study, as some of the NGHS children are preparing to enter junior high schools, a similar procedure will be followed to elicit the cooperation of the administrators of these schools. From their experience conducting similar studies in the schools in Greater Cincinnati and following students who have transferred to new schools, the investigators anticipate that the cooperation of new (i.e., junior high school) principals for the NGHS will be easily obtained.

7.2.2 Cincinnati Public Schools

The Cincinnati Board of Education operates a system of "alternative schools" offering such educational programs as Montessori elementary education, individually graded instruction, and schools specializing in math and science, in the creative and performing arts, and in French, German, or Spanish (starting in Grade 1) as well as schools offering "additional" educational instruction. Racial balance in enrollment is maintained in the alternative schools. Further, many of the alternative programs have been located in racially integrated areas of the city to enhance the racial integration of the schools. Finally, the Board has adopted an open-enrollment policy under which a child may attend any school in the system that has an opening, provided his/her attendance will improve the racial balance of that school. While it does remain true that, for the most part, inner-city public schools enroll primarily inner-city children, the reverse is not true, and low income children do attend schools in other residential areas of the city.

Six traditional neighborhood schools and six alternative schools were selected for NGHS. All alternative schools are integrated; the six neighborhood schools include one fully integrated, two predominantly white, and three predominantly black schools.

7.2.3 Parochial Schools

There are two large, integrated parochial high schools serving parishes and elementary schools located in all three geographic areas of Greater Cincinnati (i.e., inner city, urban residential, and suburban). These two schools (Roger Bacon and Purcell-Marian) had cooperated with previous studies by the Cincinnati Lipid Research Clinic and they and the elementary schools "feeding" them were selected to participate in NGHS.

7.2.4 Suburban Schools

In addition to the availability of public school children from the City of Cincinnati, public school children from the suburb of Forest Park will also be enrolled. Forest Park was developed 25 years ago as a greenbelt, planned community. The total population of Forest Park is 18,675, of which 68.9% are white and 29.6% are black.

7.3 University of California

The NGHS clinical center at the University of California, Berkeley chose to utilize schools in a nearby city, Richmond, CA. The selection of schools in the Richmond area was simpler than for Cincinnati. Every one of the 37 public elementary schools in the Richmond Unified School District and all six of the parochial elementary schools in Richmond with more than 200 pupils were invited to participate in the NGHS, and all accepted.

As a first step, project staff met with the Superintendent and staff of the Richmond Unified School District and provided a detailed description of the proposed project. The Superintendent gave administrative approval to conduct the study in all 37 public elementary schools (as well as the junior high schools later in the study) in the district. The study was then presented at one of the monthly meetings of the public school principals and an NGHS fact sheet was distributed. Subsequently, each principal was contacted individually advising them of the current plans of the girl's examinations in their schools. In addition, the administrators of the six parochial schools were visited, informed of the study verbally and with the NGHS fact sheet, and invited to participate.

7.4 WESTAT/GHA

For this center, girls will be recruited from families that are members of the Group Health Association (GHA) HMO in the Washington, DC area. GHA has clinics serving over 138,000 members throughout the Washington metropolitan area. An analysis of GHA's membership files indicates an estimated 2,714 families with a female child 9 or 10 years of age when recruitment is expected to take place, and that approximately 64% of these families are black and 36% are white. A random sample of about 17% (i.e., 25% invited with 70% acceptance) of the black families and about 31% (i.e., 44% invited with 70% acceptance) of the white families will be selected to achieve the enrollment goal for this clinical center of 300 black and 300 white girls.

In preparation for taking this sample a telephone survey will be conducted on a random sample of 1,500 of the 2,714 GHA families with 9-10 year old girls in order to ascertain race and household income. At the time of this survey, a determination will be made on the basis

of the race and household income information whether to invite the family to participate in the study. In this way the WESTAT/GHA center should end up enrolling approximately equal numbers of blacks and whites within each stratum of household income.

7.5 Maintenance of Participation

(to be written)

TABLE 7.1

Estimated Number of Children Eligible for and to be Enrolled in the NGHS

Clinical Center	SES Level	No. Eligible Black	No. Eligible White	Expected To be enrolled No. Eligible Black	White	All
Richmond, CA	Lower	184	161	129	112	241
	Middle	400	386	279	270	549
	Upper	31	96	22	68	90
	All	615	643	430	450	880
Cincinnati, OH	Lower	212	60	146	45	191
	Middle	301	300	260	227	433
	Upper	77	240	53	182	235
	All	590	600	405	454	859
Washington, DC	Lower	488	97	80	60	140
	Middle	820	446	120	120	240
	Upper	436	427	100	120	220
	All	1744	970	300	300	600
All	Lower	884	318	355	217	572
	Middle	1521	1132	605	617	1222
	Upper	544	763	175	370	545
	All	2949	2213	1135	1204	2339

CHAPTER 8

INFORMATION TO BE OBTAINED ON NGHS PARTICIPANTS

8.1 Introduction

This chapter provides an overview of the demographic, household, medical, dietary, physical activity, and psychosocial information to be collected on NGHS child and adult participants.

8.2 Demographic, Household, and Medical History Information

Demographic information collected on the children includes age and birthdate, grade in school, and race. Information on health habits and history of the children includes onset of menstruation and cigarette-smoking and alcohol-drinking habits. In addition, in Years 1, 3, and 5 the child's parent(s) will be asked to provide information on the child's medical history with respect to diabetes, hypertension, high cholesterol, and other conditions. In Years 2 and 4 children will be asked to confirm their current address and update health habits and history information on the start of menstruation, smoking, birth control, and chronic medical problems.

Demographic and household information obtained from the adult participants in Years 1, 3, and 5 includes age, race, marital status, education, occupation, relationship to NGHS child, personal income, household income, and household composition. The information on education, occupation, and household income will be used to classify the participant household with respect to socioeconomic status. Information on health habits and medical history of the adults includes cigarette-smoking and alcohol-drinking habits and history, a brief physical activity profile, onset of menstruation and number of preg-

nancies (women only), history of major diseases or medical conditions, and current prescription of specific medications. Parents/guardians will not be interviewed in Years 2 and 4.

8.3 Blood Pressure and Anthropometric Measures

The following measurements are obtained on the child participants at baseline (Year 1) and each annual follow-up examination (Year 2-5): systolic blood pressure, diastolic blood pressure (both fourth phase and fifth phase), pulse rate, height, weight, triceps, subscapular, and suprailiac skinfolds, arm and upper thigh circumferences, bioelectrical impedance, and maturation staging. Beginning in Year 2, a waist and maximum below waist circumference measure will also be taken.

Prior to taking blood pressure, the right arm circumference is measured in order to select the appropriate blood pressure cuff size. Three blood pressure measurements are taken at 60 second intervals, with the child in a sitting position, using a Baum desktop standard mercury sphygmomanometer. In general, all three measurements are made by the same person. The mean of the second and third measurement is used as the child's blood pressure for that exam. For a 10% sample of the children, a second blood pressure measurer will take an additional set of blood pressure readings for quality assessment purposes. A 30 second pulse rate is measured once.

Height is measured using a special-order stadiometer, weight using a Detecto Health o Meter electronic scale, and skinfolds using Holtain calipers. Each of these measurements is performed twice by the same observer. A third measurement is made by the same observer only if the second measure differs from the first measure by more than 0.5 cm for height, 0.3 kg for weight, 1.0 mm for each of the three skin-

folds, or 0.5 cm for each of the circumferences. The mean of the two or three skinfold measurements is used for data analysis purposes. A single measurement of bioelectrical impedance is made using an RJL bioelectrical impedance analyzer.

Biological maturation staging of the areolae and pubic hair is assessed using plates prepared by Dr. Stanley Garn.

For adults, systolic and diastolic (fifth phase) blood pressure is measured three times at 60 second intervals, with the participant in a sitting position. Height, weight, and triceps skinfold are measured twice, with a third measurement made if the first two differ by amounts specified above. These measurements will be obtained at Year 1 (baseline) and in Years 3 and 5 for adults.

8.4 Nutrition Information

An examination of the food and nutrient intakes of the girls in the NGHS is an essential component of their growth and health assessment. In selecting the appropriate methodology for this portion of the study, the desire was to gain knowledge of the food consumption patterns from which intake levels of certain nutrients may be calculated. The methodology should be particularly sensitive to the intake levels of energy from carbohydrates, proteins and fats, and should reflect the intakes of saturated and polyunsaturated fatty acids as well as cholesterol. For this purpose, a three-day dietary record will be used for the girls at baseline and each annual follow-up visit. In addition, it is necessary to obtain basic information from girls and parents concerning the circumstances surrounding food selection by the individual participants in the study as well as by households of these participants. For this reason, additional questions will be included to collect information on food habits and customs, also on food

procurement and preparation procedures. This will be done at baseline and each annual follow-up visit. In Years 1, 3, and 5 more extensive information on nutrition patterns will gathered from children and their parent/guardians. In Years 2 and 4, only selected questions from Year 1 will be repeated on children, and no nutrition information will be taken from parents.

Recording the food consumed, in household measures, for periods of three to seven days, has been widely regarded as a good descriptive measure of the individual's current intake. Three days is often considered a desirable length for a record inasmuch as it is less demanding and less likely to influence customary food choices than a longer record. A three-day record is believed to give a reasonable estimate of the general quality of the individual diet superior to that obtained from a 24 hour recall or a food frequency (1). The three-day diet record is considered to be a very acceptable and efficient means of collecting dietary data for 11 year old school children participating in a large-scale longitudinal study (2).

Further examination of methods for obtaining information about food intake of individuals points out some serious weaknesses in the 24-hour recall method. In a study (3) which compared nutrient intake of meals served to 10 and 12 year olds, observed by a dietitian and subsequently recalled by the children, a large and significant difference was found between observed and recalled intakes of calories and protein. The author questions the usefulness of dietary recall for 10 to 12 year old children. Beaton (4) points out that a number of studies may have failed to show a relationship between 24 hour dietary intakes and serum lipid levels due to methodological limitation. He says that only by increasing the number of observations of dietary intake can the estimate of the usual intake of an individual be

improved. Garn (5) agrees with him as he discusses the limitations to 24 hour dietary records, primarily the problem of using one-day diets to interpret intakes of individuals.

There is need to verify for each study the validity and reliability of the method for the participant's age and education level. In light of the paucity of references relating to diet methods in this specific age group (6), was it considered essential to test the methods under consideration for this study. This was done for the NGHS on a population of sixty 9 and 10 year old black and white girls at both the Berkeley and the Cincinnati centers. The participants were divided into three diet methodology groups. Twenty girls completed a five-day food frequency form, 20 girls kept a three-day diet record, and 20 completed a 24-hour recall. Lunchtime eating was discreetly observed by trained observers. Observed dietary lunchtime intake was compared to recalled intake for each method. The study showed that the three-day record was the most accurate method of dietary data collection for these black and white 9 and 10 year old girls. Underreporting as well as overreporting of foods was minimized by this method. Reported intakes of all dietary factors including calories, protein, carbohydrate, fat, saturated fatty acids, polyunsaturated fatty acids and cholesterol were closest to actual observed intakes using the three-day diet record.

A serious limitation of the administration of the three-day diet record to 9 and 10 year old girls is the issue of compliance. Improved validity is of little value if the children are not willing to keep the diet records. To address this issue a feasibility study was initiated by the Cincinnati Center. Sixty-five black and white 9 and 10 year old girls were recruited to be part of a dietary study. Girls were offered a five dollar expense compensation for participating in the study.

Eighty-two percent returned their consent form and agreed to keep a three-day diet record. Ninety-one percent of those completed the study indicating that most girls in this age are willing to keep this kind of record for a period of three days. Careful review of these records indicated, however, that as many as 25% of the records may be unreliable, due to lack of understanding of measuring, unavailability of measuring equipment, failure to record meals, recording of questionable types of foods, or lack of recall concerning foods on the record. However, all methods may suffer from similar drawbacks, and it is imperative that NGHS staff develop an improved instructional program for keeping dietary records which would minimize these errors.

Thus the three-day records appear to be reasonably valid and feasible for use with the target population. The method relies on instructing the participants in the intricacies of measuring and recording the amounts and types of food and drink they ingest on three recent days (two weekdays and one weekend day), then interviewing them using trained nutrition interviews to insure the detailed completion and the reliability of their food records. The skill of the interviewers and their intimate knowledge of foods and their nutrient contribution to diets are essential features to optimize the validity, reliability and objectivity of the information obtained.

Estimates of the amounts of food and drink ingested will be in household measures. Each child will be given a six inch ruler, a graduated measuring cup, and a standard teaspoon and tablespoon with which to measure foods and beverages. In addition, each child will receive a booklet with geometric three-dimensional food size models to aid in accurate quantification of portion sizes. Food and drink and their corresponding quantities will be coded centrally for the entire study to facilitate computation of nutrient intake and food consumption

patterns. It is recognized, however, that each clinical center may be called upon by the nutrition coding center to provide additional specific information about certain food items which may be indigenous to the location and missing from the food composition data file. Each dietary interviewer will need to be familiar with the dietary coding system used by the nutrition coding center.

In addition to the three-day food record completed by the participating girls, a questionnaire will be completed by their parents or guardians in Years 1, 3, and 5 on the food customs and patterns prevailing in the household, and on the food procurement and preparation procedures followed by that household. The dietary interviewer will need to be particularly sensitive to information that may have a bearing on the correct coding of the information to obtain accurate dietary data.

8.5 Physical Activity Information

8.5.1 Physical Activity Record

8.5.1.1 Goals

The three-day physical activity record will be used to collect physical activity information from girls at Year 1 (baseline) and at each annual follow-up visit. A general activity level (low, moderate, high) will be assessed for each participant using a self-administered three-day physical activity record consisting of two consecutive weekdays followed or preceded by a weekend day, i.e., Thursday, Friday, and Saturday or Sunday, Monday and Tuesday. These days will be the same days as those for which the three-day food record is completed. As opposed to a single day, the three-day, physical activity record is designed to obtain an average of the usual physical activities

performed, to reduce within subject variance and to allow a reasonable estimate of individual activity levels (low, moderate, high).

Data collected will be used to investigate similarities and differences in activity levels between subgroups of girls studied, and the interrelationships of physical activity components with CHD risk factor variables.

A major objective of the protocol is to maintain reproducibility of the three-day activity record. The accuracy and reliability of the data can be aided by the use of standardized interviewing and probing techniques by physical activity interviewers, by educating the children on accurate documentation of their physical activities, and by periodic monitoring and retraining of physical activity interviewers.

8.5.1.2 Procedures

A trained individual will give group instruction in a school classroom to the girls enrolled in the NGHS in Cincinnati and Richmond. They will be briefly instructed on how to identify and mark activities. Westat/GHA will mail instructional materials and the records prior to giving each child individual telephone instruction by an interviewer. The diary is divided into morning, afternoon, and evening sections to help children in completing it.

Each physical activity interviewer needs to familiarize her/himself with any special physical activities which are popular as well as the local physical activities available to their population. Examples of these activities will be covered in a video that will be made available to the centers and included as part of the standard certification procedure for physical activity. Experience in the Cincinnati School System during the three-day physical activity recall pilot study indicated that some girls did not understand the concept of time.

Children will be given a watch for use in the study, which should enhance accurate recording of time. The children should be encouraged to keep the records themselves, but assistance by parents and other siblings will not be disallowed.

At the conclusion of the classroom instruction, each girl will be told to begin her record on the following morning (if the instruction occurs on Wednesday.) A weekend telephone reminder will be given to those girls who are instructed Friday and are to start their records on Sunday.

The physical activity data retrieval will be scheduled on days prior to or following the physical examinations and venipuncture in order to avoid recording unusual patterns during the fasting period. Following completion of the record, each child will return her record to the school and a trained physical activity interviewer will document the completeness, specificity, and acceptability of each girl's three-day record.

If a child fills out the record at a later date, the child will be reminded by telephone the day before the records are to be kept. Children will be asked to bring their completed records with them to the clinic/school. The child's record will be reviewed at the clinic/school with her by a physical activity interviewer. This will occur no later than fifteen days after the last recording day.

8.5.1.3 Determining Acceptability of the Physical Activity Record

A physical activity record will be considered "unacceptable" if either of the following conditions apply:

1. It contains no information at all (i.e., no activities checked).
2. The child is unwilling or unable to review the physical activity record with the interviewer within 15 days of the date of the physical activity record.

8.5.1.4 Asking a Child to Keep Another Physical Activity Record

A child will be asked to keep another physical activity record if:

1. The first record is left blank, and child is willing and able to complete another physical activity record.

2. It is a sick day defined as: child volunteers that she was sick and day's activities are markedly altered.

3. The child has missed keeping the record.

8.5.2 Physical Activity Patterns Questionnaire

In addition to the activity record, the child will complete a physical activity patterns questionnaire at baseline (Year 1) and at Years 3 and 5. The interviewer will impress upon the participant that there are no right or wrong, good or bad answers. They will be asked to report exactly what physical activities they usually do. The physical activity patterns questionnaire will be interviewer administered at all three clinic sites. Interviewers will ask a series of questions about the child's activity, attitudes and patterns, including habitual, as well as leisure time, activity and television watching habits. They will list activities and record the frequency of activities. The child will also be asked to answer questions about her parent/guardian's usual activities.

8.6 Psychosocial Information

8.6.1 Introduction

The goals of the psychosocial component of the exam will be:

1. To collect baseline attitudinal, perceptual, behavioral and social information with which to describe the NGHS study population of children and adults.

2. To describe the development of the above psychosocial or social factors over the follow-up period of four years.
3. To identify psychosocial and social factors which are predictive of the development of obesity in the study cohort and examine whether they are associated with and differences in obesity between black and white girls.

Psychosocial characteristics to be measured in children and adults were chosen for their reported and postulated associations with obesity and were judged by NGHS investigators as being the most important to evaluate (see Chapter 1). Instrument selection was based on appropriateness in terms of age, socioeconomic status, and literacy requirements. Attention was given to the length of forms as well as their documented use in prior research. Basic psychosocial characteristics for both children and adults include assessment of attitudes, self-perceptions, behaviors, social environment, familial interactions, eating behaviors, coping behaviors, and perceived stress.

8.6.2 Psychosocial Information on Children

A core of two psychosocial instruments--"What I Am Like" Profile (7), and Health Beliefs and Attitudes Questionnaire for Children--will be classroom- or interviewer-administered to the children at all three clinical centers. The first ("What I Am Like") will be given at baseline and at Years 3 and 5. The Health Beliefs and Attitudes Questionnaire will be administered at baseline and at each of the four follow-up exams. An abbreviated version will be given in Years 2 and 4.

At least two of the clinical centers (Cincinnati and Washington) also plan to administer additional instruments to the children according to the following schedule: My Feelings (eating disorder risk

factors) at baseline and Years 3 and 5, and FACES III (10), Perceived Stress Inventory (11), and Coping Strategies Inventory (12) at follow-up Years 2 and 4. In Cincinnati these will be classroom-administered and at Westat/GHA they will be self-administered.

All six instruments are standardized instruments or downward age extensions of instruments, except for the Health Beliefs and Attitudes Questionnaire developed by NGHS investigators to cover areas for which no pre-existing instruments could be identified. The seven psycho-social instruments for children are listed below:

	Psychosocial Characteristic	Instrument	Estimated Administration Time
1.	Self-concept	"What I am Like" (Harter, 1985).	25 min.
2.	Body image, attitudinal, behavioral and self-perceptions	Health Beliefs and Attitudes Questionnaire for Children (NGHS, 1986).	15 min.
3.	Family interaction	FACES III (Olson, Portner, Lavee, 1985).	5 min.
4.	Perceived stress	Perceived Stress Measure: Children's Version (adapted from adult version).	5 min.
5.	Coping strategies	Coping Strategies Inventory: Children's Version (adapted from adult version).	5 min.
6.	Eating disorder risk factors	My Feelings Inventory) (adapted from adult instruments.)	10 min.

8.6.3 Psychosocial Information on Adults

Seven different psychosocial forms have been selected for the children's parents/guardians who are enrolled in the study at the time of the initial exam. The Family Environment Scale (13), the Health Beliefs and Attitudes Questionnaire for Adults, and the Family Adaptability and Cohesion Scale (FACES III) (10) constitute the core of

the adult psychosocial evaluation and will be completed at all three clinical centers. The first two of these will be given at baseline and Years 3 and 5 and the third at follow-up Years 3 and 5. An abbreviated version of the Health Beliefs and Attitudes Questionnaire will also be given in Years 2 and 4. At least two of the clinical centers (Cincinnati and Washington) also plan to give or send the other four instruments to the adults to complete at home and mail back to the clinical center. The eating Disorder Inventory (9), Restrained Eating Questionnaire, Perceived Stress Inventory (11), and Coping Strategies Inventory (12) will be given at Years 3 and 5. All of these forms are standardized psychosocial instruments, except for the Health Beliefs and Attitudes Questionnaire, which was developed by NGHS investigators to cover areas for which no pre-existing instruments could be identified. The seven psychosocial instruments for adults are listed below:

Psychosocial Characteristic	Instrument	Estimated Administration Time
1. Family environment	Family Environment Scale (Moos, 1974).	15 min.
2. Body image, attitudinal, behavioral, and self-perceptions	The Health Beliefs and Attitudes Questionnaire for Adults (NGHS, 1986).	10 min.
3. Family interaction	FACES III (Olson, Portner, Lavee, 1985).	5 min.
4. Perceived stress	Perceived Stress Inventory: Adult Version (Cohen et al, 1983).	10 min.
5. Coping strategies	Coping Strategies Inventory: Adult Version (Tobin, 1985).	10 min.
6. Eating disorders	Eating Disorder Inventory (Garner, Olmstead, Polivy, 1984).	10 min.
7. Eating restraint	Restrained Eating Questionnaire. (Herman and Polivy, 1975)	5 min.

8.6.4 Validation of Psychosocial Instruments

Previously published instruments chosen for the NGHS study have already been demonstrated to have construct validity. For a number of these instruments, age- sex- race-specific norms are available. Data for the study cohort can be compared to published norms to determine whether data are consistent with those from prior investigations.

For the NGHS-developed questionnaires there is no standard against which to validate. Questions were developed to cover topics which were deemed important for the study and for which no tested instruments could be identified.

As Reynolds and Richmond pointed out, "test validation is a common term, yet if rigidly interpreted is a misnomer. We do not validate tests; we can only seek validation of the meanings we attach to the scores derived from the test." For the NGHS-designed survey instruments for assessing attitudes, perceptions and beliefs, rating or evaluation scales have not been constructed. In the analysis the relation of combinations of questions or derived scores to the development of obesity or any differences in the two racial groups will be examined. These relationships could be further substantiated in the subsequent follow-up periods. It should be emphasized that the evaluation of any survey instrument of the type designed for this study is a dynamic ongoing process of constant assessment and re-evaluation. Information learned from the analysis of the study findings may lead to changes in the instruments in the follow-up years. Continuing review of published research findings and discussions with colleagues by the Psychosocial Measures Subcommittee may also lead to the identification of new topics or the elimination of presently considered items.

One way to "validate" the questionnaires is to check for internal consistency. Are items that ask the same or similar questions being answered consistently? Questions that measure the same, or opposite, concepts should be highly correlated. The NGHS-developed questionnaire will be analyzed for consistency of response. For example, the participant is asked their belief about the role of both thinness and fatness on health. It should be expected that a high negative correlation exists between the two responses. In a similar way, an individual professing unhappiness about most of their body parts would be unlikely to claim that they are very happy about the way their body looks. The Psychosocial Measures Subcommittee has designed the instrument to allow for a number of consistency checks.

In the analysis the behavior of the ratings or scales with respect to the hypotheses will be examined. Differences in the measures between girls of various weights can be contrasted. However, caution in interpretation will need to be exercised since the variables of interest may have different cross-sectional and longitudinal relationships to the outcome measures.

8.7 Biochemical Measures

A 30 ml fasting blood specimen is collected from the children at baseline and Years 3 and 5, and from the adults at baseline only. A portion of the serum obtained from the child's blood sample is sent to the NGHS central laboratory at Johns Hopkins University for determinations of total cholesterol, high density lipoprotein (HDL) cholesterol, triglycerides, apoprotein A-I and LDL apoprotein B, and for long-term storage of two 0.5 ml aliquots. Low density lipoprotein (LDL) and very low density lipoprotein (VLDL) cholesterol are estimated by formula from total cholesterol, HDL cholesterol, and triglycerides.

The other portion of serum is sent to the University of Michigan for determinations of glucose and insulin. The serum obtained from the adult's blood sample is sent to the NGHS central laboratory for determinations of total cholesterol, HDL cholesterol, and triglycerides, and for long-term storage of the remaining serum. LDL and VLDL cholesterol are estimated by formula from total cholesterol, HDL cholesterol, and triglyceride values.

8.8 References

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CHAPTER 9

SCHEDULE OF INFORMATION COLLECTED

9.1 Visit Schedule

The children and their parent(s) or guardian(s) will be enrolled in the study during a period of recruitment of one year in duration. The child participants will be seen every year thereafter at approximately one year intervals. The adults will be seen every other year, at baseline (Year 1) and Years 3, and 5.

9.2 Schedule of Information Collected

	Baseline	Follow-up Years			
Item	1	2	3	4	5
History information					
Body image	C,A*	C	C	C	C
Parental body image	C	C	C	C	C
Smoking/alcohol history	C,A	C	C,A	C	C,A
Sexual maturation	C	C	C	C	C
Medical history	C,A	C	C,A	C	C,A
Demographic information					
Race	C,A				
Socioeconomic status (income, education, occupation)	A		A		A
Household composition	A		A		A
Physical examination					
Blood pressure	C,A	C	C,A	C	C,A
Height/weight	C,A	C	C,A	C	C,A
Skinfold thickness					
Triceps	C,A	C	C,A	C	C,A
Subscapular, suprailiac	C	C	C	C	C
Arm/thigh circumference	C	C	C	C	C
Waist/Max Below Waist Circumference		C	C	C	C
Bioelectrical impedance	C	C	C	C	C
Maturation staging	C	C	C	C	C
Lipid measurements	C,A		C		C

*C=Children, A=Adults

Item	Baseline 1	Follow-up Years 2	3	4	5
Dietary assessment					
3-Day food record	C	C	C	C	C
Nutrition patterns	C,A	C	C,A	C	C,A
Physical activity assessment					
Activity diary	C	C	C	C	C
Activity patterns	C		C		C
Psychosocial information					
"What I Am Like"	C		C		C
Family Environment Scale	A		A		A
Psychosocial Questionnaire	C,A	C	C,A	C	C,A
FACES III			C,A		C,A
Eating Disorders	C		C,A		C,A
Perceived Stress Measure		C		C	
Coping Strategies Inventory		C		C	
Restrained Eating Questionnaire			A		A

CHAPTER 10

TRAINING, CERTIFICATION, AND RECERTIFICATION

10.1 Introduction

In a collaborative study with multiple field centers collecting data, it is important that the personnel performing similar tasks among the field centers all be trained in a uniform manner to carry out those tasks. Thus, for certain data collection tasks in the NGHS -- i.e., blood pressure and skinfold measurements, and dietary assessment interviews, as well as for other tasks such as data entry --, the NGHS coordinating center, in concert with the NHLBI project office and the clinical center investigators, will conduct a series of training sessions prior to the beginning of data collection in the NGHS. Personnel who join the study after its initiation will generally be trained by the local field center supervisor for a given task. However, if several persons from different field centers require training at about the same time (such as at the beginning of a new school year), it may be expeditious to have them all trained centrally at one time.

In addition to the training sessions themselves, it is important to determine in as objective a fashion as possible whether the study personnel have been properly trained. Tests will be given to the trainees with passing grades required before they can be certified to carry out the given tasks in the NGHS.

Since the NGHS is a five-year study, a single certification prior to the beginning of the study will not suffice. Periodic monitoring of performance, at least annually, will be required for most tasks for which certification is required.

The field center itself must be certified before data collection can begin. To be certified, a field center must have at least one certified person to do each task requiring certification and provide evidence of satisfactorily adhering to inspection and maintenance procedures for all equipment. All field centers must be monitored on these procedures periodically.

10.2 Training of Study Personnel

Special training, using uniform training methods and common training materials will be required for the following tasks:

1. Blood pressure measurement
2. Skinfold, weight, height, circumferences and bioelectrical impedance measurements
3. Biologic maturation assessment
4. Medical history interviews (general interviewing)
5. Food record instruction and interviews
6. Physical activity diary debriefing
7. Psychosocial interviews
8. Data entry
9. Computer operator
10. Preparation of plasma specimens

The training sessions will be conducted by persons with extensive experience in carrying out the tasks in the context of similar research projects. Such a person should also, preferably, have had experience training others in the particular task. At each field center, if more than one person is trained and certified for a particular task, one of those persons will be designated by the field center director as the task supervisor. To qualify for designation as supervisor, one must either have had at least six months of active experience in the NGHS

performing the task, or else at least six months experience in a nearly identical task for another project. Personnel who join an NGHS field center after the study is underway must either be trained at a special NGHS training session, or by the local field center supervisor, by one of the other field center supervisors for a given task.

10.3 Certification/Monitoring of Study Personnel

Each person trained in one or more of the tasks listed in Section 10.2 above must be certified in that task before he/she can be permitted to carry out that task in the NGHS. A person may be certified in several tasks. Such a person may be designated as supervisor of one or more of those tasks, but not necessarily as supervisor of all of the tasks in which he/she is certified. A person certified in one task may not carry out another task in NGHS for which he/she has not been certified.

All NGHS field center personnel must be certified, as having basic knowledge of the study even if they will not be carrying out any of the tasks listed in Section 10.2. Such persons may include the field center director and clinic coordinator.

All persons to be certified must have a knowledge and understanding of the NGHS Protocol. Clinics will be supplied with a general NGHS Knowledge Assessment Form which can be used as a training tool. The test covers the candidate's understanding of the NGHS and knowledge of relevant epidemiologic data which led to and influenced the design of the NGHS, thereby promoting an adequate appreciation of the potential import of the study. In addition, all persons desiring to be certified for one of the tasks listed in Section 10.2 must, as a minimum, either attend an NGHS training session for that task or receive training from

an NGHS supervisor for that task. Certification in a particular task may entail other specific requirements, such as successfully completing blood pressure test tapes for the task of blood pressure measurement. Specific requirements for certification in each task are given in the NGHS Manual of Operations.

Annual monitoring of clinic procedures and measurements taken will be required for each of the areas listed in Section 10.2. Monitoring of all NGHS personnel will take place once each year of the study. If a new staff member has just been certified initially during the year, it will not be necessary for that person to be monitored until the following year.

The NGHS data forms require identification of the person who has measured, observed, or collected each type of information, and the coordinating center will routinely check to make sure that the persons who have collected or keyed the information have proper initial certification and are being monitored at appropriate intervals. Documentation of initial certification in the form of Personnel Certification Form 90 for each individual must be sent to the Coordinating Center. The Coordinating Center will check these against certification numbers appearing on database forms and send the clinics a list of all numbers on data forms which are missing a companion certification Form 90. Clinics will review the list, and return an accounting to the Coordinating Center. Recertification monitoring will only be carried out on those clinic personnel who have had a Personnel Certification Form 90 returned to the Coordinating Center.

10.4 Equipment Inspection and Maintenance

Detailed procedures for periodic inspection and maintenance of key measurement instruments used by the field centers are provided in the

NGHS Manual of Operations. Types of equipment for which these procedures must be followed include standard mercury sphygmomanometers, stature measuring board, beam balance, bioelectrical impedance analyzers, and skinfold calipers. An NGHS equipment Inspection and Maintenance Log will be developed for recording the carrying out of these procedures. These logs will be collected periodically by the coordinating center.

10.5 Certification/Recertification of Field Centers

In addition to individual persons being certified to carry out specific tasks in NGHS, each field center as a whole must also be certified before data collection can be initiated at that center and must be periodically recertified. In order for a field center to be certified/recertified, at least one person in that clinic must be certified and monitored for each of the tasks that require certification. In addition, for recertification of a field center, there must be evidence of satisfactory adherence to equipment inspection and maintenance procedures. Field center recertification will take place once a year.

CHAPTER 11

QUALITY ASSESSMENT PROCEDURES

11.1 Introduction

A primary concern of the NGHS will be to assure the quality of the data being collected and analyzed. The validity of the reports and results produced and published by the study will depend upon the integrity of the data submitted by the clinical centers, central laboratory, and nutrition coding center, and upon the appropriateness, thoroughness, and correctness of the data processing and data analysis procedures carried out at the coordinating center. The first step in assuring quality data is to have the data collectors and measurers properly trained, certified, and periodically recertified (see Chapter 10). This will then be supplemented with various procedures to monitor the performance of these groups with respect to the quality of the study data reported by them. Procedures for monitoring the performance of the clinical centers, central laboratory, nutrition coding center, and coordinating center are given in the following sections.

11.2 Quality Assessment of the Clinical Centers

Performance of the clinical centers will be assessed by consideration of the following at periodic intervals:

1. Number of participants enrolled to date and ratio of this number to the number who should have been enrolled to date given the scheduled recruitment period already completed.
2. Percentage of participants with missed examinations and percentage who have dropped out of the study, i.e., are no longer willing or able to have their annual examinations.

3. Number of study forms for which the data are past due at the coordinating center based on each participant's date of the baseline exam. In this regard, a time window for completion of each annual exam has been defined as the date of the baseline exam plus or minus 3 months.
4. Percentage of serum specimens found to be hemolyzed, thawed, or of insufficient volume upon receipt by the central laboratory.
5. Number of protocol violations, such as enrolling participants who do not meet all of the eligibility criteria or who have not provided informed consent, performing follow-up exams outside the proper time window, not following the study rules for designating "parents," etc.

For a random sample of 5 to 10% of all study participants--both children and adults--at baseline and each follow-up visit, blood pressures and anthropometric measurements will be repeated by an independent observer, blinded to the findings of the first observer. These results will be reported to the coordinating center which will periodically report the between-observer standard deviations in each measure by clinic and by pairs of observers. These standard deviations will be computed both for the total cumulative experience to date and for measurements made in successive six month periods to assess changes over time in inter-observer reliability.

Quality of the blood pressure and anthropometric measurements will also be assessed periodically by sending an expert measurer to each clinical center to do independent repeats of measurements for each clinical center measurer.

In addition to preparing periodic clinic monitoring reports of the measures listed above, the coordinating center will, twice a year, request hard copies of a random sample of data forms from each clinical center. The data on these forms will be compared manually against the data transmitted from the clinical centers and residing on the main data base at the coordinating center.

These monitoring and auditing activities will be supplemented by periodic site visits by coordinating center staff to the clinical centers, and by annual recertification of clinical center personnel responsible for key areas of data collection and entry.

11.3 Quality Assessment of the Central Laboratory

The purpose of a central laboratory for a multicenter longitudinal study like the NGHS is twofold: (1) to provide biochemical determinations in a uniform manner on specimens received from several different clinical centers; and (2) to provide determinations that are stable over a period of several years. One of the stipulations in selecting a central laboratory for this study is that it agree to use the same analytical methods and equipment throughout the course of the study, and that it participate in the Centers for Disease Control Quality Assurance Program for Lipid Determinations. The laboratory should also agree to send the coordinating center, at periodic intervals, quality control reports on each study determination, including special events such as change of standard and control pools, and change of reagents.

The coordinating center will establish an external quality assessment program for the central laboratory that will call for the clinical centers to obtain twice the usual amount of blood from a random sample of participants throughout the course of the study and

submit duplicate specimens to the laboratory in separate shipments. Procedures for carrying out such programs, including the blinding of the identity of the duplicate specimens to the central laboratory are well established.[1]

The external quality assessment program just described will provide estimates of the technical error of the various laboratory measurements. Even more important is an assessment of the long-term variation over time in the laboratory determinations. If the distribution of a given analyte is found to change over time, it must be determined if this reflects a biochemical change going on in the participants or if it reflects secular drift in the laboratory determinations. For this purpose it is proposed that pints of blood be obtained from donors, dividing the specimens into several lots, storing them at -70 C, and sending a lot to the central laboratory every two months. By overlapping the donor pools it will be possible to determine patterns of secular trends in the laboratory determinations. Since the NGHS laboratory determinations are scheduled for baseline and follow-up Years 3 and 5, it will be important to continue the secular trend quality control program throughout the follow-up period.

11.4 Quality Assessment of the Nutrition Coding Center

It is planned that three-day food records will be collected annually on the children in the NGHS. These records will be sent to a nutrition coding center for coding, keying, and nutrient analysis. In addition to the coding center's own internal quality control programs, an external quality control program will be established by the NGHS coordinating center to check periodically on the validity and reliability of the coding by sending to the nutrition coding center, in

a blinded fashion, NGHS participant food records previously coded at the center.

11.5 Quality Assessment of the Coordinating Center

The most difficult quality assessment task of all is monitoring coordinating center performance. The following are some of the activities the NGHS coordinating center will carry out that will help to enhance the quality of the data and analyses:

1. Persons (such as study manager and principal or co-investigators) not involved in the preparation of the data editing programs will fill out the study data forms, making deliberate errors. These forms will be keyed and processed through the data editing system to see if all of the errors were caught by the computer system.
2. The audit of a sample of original data forms against the data on the coordinating center computer (as described above in conjunction with quality control of the clinical centers) will be used not only to detect data entry errors at the clinical centers, but also to detect problems with the data entry and editing software prepared and provided by the coordinating center and problems with merging the data onto the main study data base at the coordinating center.
3. For each variable on the data base a point frequency distribution -- i.e., a tabulation of the frequency of occurrence of every distinct value -- will be obtained. This will help to identify many types of anomalies in the data such as: (a) illegal codes, (b) measurements given to more decimal places than provided by the measuring instrument, (c) digit

preferences, (d) biomodality or other bizarre form of the distribution, and (e) outliers, i.e., extreme values distinctly separate from the rest of the distribution. Once an observation has been identified as a true outlier, the first step is to go back to the original records and determine whether a recording or keying error was made. If such a value is verified as correct, then the question of whether or not to include the value in the data analysis depends upon the nature of each participant analysis. There is no reason to exclude the value if the analysis is a count of the number of participants having a value exceeding a given cut point. However, if means and standard deviations are being computed, or if correlation or regression analyses are being carried out, and the outlier value is such that it could have an undue impact on the mean and standard deviation, t-test, regression analysis, etc., then it should either be excluded or given a less extreme value (a procedure known by statisticians as Winsorization[2]) for purposes of the analysis.

4. New analysis programs (including runs using statistical packages such as SAS and BMDP) will be tested by running against a small subfile of 10 or 20 participants and independently producing the tabulations and statistical calculations manually from the original data. This will help to make sure the correct variables have been picked up from the analysis file, the variables and cut-points have been defined properly, transformations of the original variables on the analysis file have been formulated correctly, and the

correct variables have been extracted from the main data base onto the analysis file.

5. When preparing data reports, different tables, which may have resulted from a variety of analysis programs, will be checked for consistency of denominators. A discrepancy of as little as one participant among the denominators in different tables may be an indication of a much larger problem.

11.6 References

1. Canner PL, Krol WF, Forman SA: External quality control programs. Controlled Clin Trials 4:441-466, 1983.
2. Barnett V, Lewis T: Outliers in Statistical Data. New York, Wiley and Sons, 1978.

CHAPTER 12

DATA MANAGEMENT

12.1 Introduction and Overview

The data management system for NGHS is a distributed system based on microcomputers installed at the clinical centers. The coordinating center is responsible for the development and implementation of the system. The system is designed to provide the following capabilities to the clinics:

1. Direct data entry into a formatted screen with range checks and sophisticated consistency checks to eliminate, as early as possible in the data processing cycle, any problems with the coding of the data.
2. Batch edits (edits run in a batch mode) to check for consistency between all forms/data collected at a particular visit and between visits for a subject.
3. Identification of missing visits and missing data within a visit as well as scheduling of future visits.
4. Local capability of report generation (tabular with summary figures) for within clinic reports. This would be used for a clinic to prepare necessary reports for internal use and for study reporting purposes to the funding agency. Further, the clinics would have the capability of generating ad hoc reports and queries to the data base to identify certain subjects or groups of subjects for additional checking.
5. Preparation of data for monthly transmission to the coordinating center; on a monthly basis, any new or revised data would be extracted from the data base for transmission, electronically to the coordinating center.

6. Maintenance of an audit trail of all transactions to the data base. The audit trail file would be transmitted to the coordinating center along with the new or revised data. The data and the audit trail files should confirm each other.
7. Maintenance of the entire clinic data base for reference and reporting purposes. This would be necessary for clinical center administrative activities as well as for constant data cleaning activity. In addition, it is anticipated that the coordinating center, as interim analyses progress, would query certain items on a clinic data base. Finally, the possibilities of ancillary studies and of 'conditional' processing of laboratory specimens make it imperative that the entire data base remain available to the clinics. This is also the simplest approach to data maintenance; any other approach would require the constant reloading and unloading of segments of the data base.

12.2 Computer Hardware and Software

The computer hardware configuration for each NGHS clinical center is as follows:

1. IBM PC/AT microcomputer
    a. 640 Kbyte memory (using 512 Kbyte IBM memory and 128 Kbyte with Intel Above Board)
    b. 30 Mbyte hard disk drive (Seagate)
    c. Intel 80287 math coprocessor
    d. Princeton Max-12 Amber Monitor with Hercules monochrome adaptor card
    e. 1.2 Mbyte diskette drive

2. IOMEGA Bernoulli Box (double 20 Mbyte) disk cartridge system
3. Ven-Tel 2400 baud internal modem
4. Epson LQ1000 dot matrix printer

The data base management package which is used in the development of the distributed system is INFORMIX-SQL with INFORMIX-4GL (fourth generation language). System security is provided by the WATCHDOG software package.

12.2 Data Entry

Data entry is by trained and certified clinic personnel. The data entry process involves keying in data from study data collection forms into the microcomputer at the clinical center. The data entry software developed by the coordinating center consists of screens formatted to look similar to the forms being processed. The data entry operator key's the data into the appropriate area on the screen as indicated by the software.

Entry to the data entry system, as well as the other components of the system, is controlled by the security software. Only pre-authorized personnel have access to the system and to the data base.

Two levels of audit trails are kept by the system. The first level is to monitor all activity on the system itself. This audit trail records the identification of anyone entering the system and what operating system commands or programs they executed. The second level of audit trail records all changes (i.e., additions, modifications and deletions) to the study data base. This audit trail is transmitted to the coordinating center and maintained as part of the study data and supporting material.

12.3 Data Editing

Four levels of data editing are carried out by the system. The first level of editing is to prevent an illegal code from being entered. For example, if a question can only be answered 'Yes' (code 1) or 'No' (code 2) and a user tried to enter a code 3, then the system will flag an error and force the user to enter a legal code.

The second level of editing is to question values that are out-of-normal range. These normal ranges, which will be primarily medical/anthropometric measurements and laboratory values, will be established by medical personnel. For example, if a user enters 225 pounds for weight, the software will flag the data as out-of-normal range. The data entry software is written so that if the user subsequently verifies that a value is correct even if it is out-of-normal range, then the software will accept it. For example, if a participant weighs 250 pounds and the normal upper limit is set at 200 pounds, the program accepts 250 pounds if the user verifies the weight in response to a prompt by the software.

The third level of checking is for consistency within the form. For example, the software would query the user if the date of the participant's visit was entered as two months after the current date or if it is reported that a fasting blood specimen was obtained but another item indicates that blood could not be drawn. This type of error would require that new data be entered for one or more data items to resolve the discrepancy.

The fourth level of editing is for conditional inconsistencies. For example, the software would query the user if the data entered indicates that the participant was not taking any prescription drugs but a drug brand name was then entered. In this example, it is not clear which data item is wrong. Unless all responses and non-responses

on the form are entered into the data base, the software cannot accurately check for inconsistencies.

12.4 Data Transfer

On a monthly basis, the clinical center executes a batch procedure to extract any new or modified data from the data base for transmittal to the coordinating center. This procedure also prepares the audit trail for transmittal. The coordinating center computer calls up the clinical center computer and transfers the data back to the main study data base at the coordinating center. Data is transmitted using an 'error-correcting' method to assure accuracy of the data received.

12.5 Data Base Back-up

The clinical center executes a batch procedure daily to back-up any new or modified data onto a disk cartridge in the Bernoulli Box. Once a week, a full archive of the data base is done onto a disk cartridge in the Bernoulli Box. The disk cartridges containing the back-ups of the data base is stored in a secure location away from the computer itself. The data base maintained at the coordinating center also serves as another level of back-up.

12.6 Data Management at the Coordinating Center

The data management system at the coordinating center will be implemented on the Data General MV/2000 on-site. The primary purpose of this system is for data extraction, data handling and data analysis. All analysis is done at the coordinating center using standard statistical analysis software (i.e., SAS, BMDP, SPSS, IMSL) and customwritten programs as necessary.

CHAPTER 13

STATISTICAL POWER CONSIDERATIONS

For the outcome measure of subscapular skinfold, data from NHANES I indicate that for girls of ages 9 to 13, the standard deviation of the measure averaged 5.97 units, and the observed black-white difference in change in skinfold from 9 to 13 years old ($\bar{d}$) was 0.6 units. Assume that the standard deviation of this measure in the NGHS will likewise be 5.97, with a correlation of 0.75 between age 9 and age 13 skinfolds. Also assume that 1,135 black and 1,204 white children will be initially enrolled (Table 7.1), and that 80% of the children in each group (908 and 963, respectively) will have both baseline and year 4 skinfold measurements. Given these assumptions, a 95% confidence interval estimate of the true black-white difference in skinfold change from 9 to 13 years of age is $\bar{d} \pm 1.96(2)^{1/2}(5.97)(1-0.75)^{1/2}(908^{-1}+963^{-1})^{1/2}$ or $\bar{d} \pm 0.38$. Thus, if $\bar{d} = 0.6$ (as observed in NHANES I), the 95% confidence interval is far from overlapping zero.

A test of the null hypothesis that there is no black-white difference in change in subscapular skinfold from age 9 to age 13 has 87% power to detect a true difference of 0.6, given a two-sided significance level of 0.05 along with the other assumptions given above. For a true difference of 0.7 the power is 95%. The regression coefficient for the regression of skinfold on race has similar precision, as do partial regression coefficients for the regression of skinfold on race controlling for a variety of covariates.

CHAPTER 14

DATA ANALYSIS

14.1 Introduction

Data analysis will be carried out in this study for two main purposes. One is to monitor the clinical centers and other study units for performance with respect to participant recruitment and follow-up, adherence to study protocol, and correctness and completeness of study data, and to evaluate data from external quality control programs. For this purpose, it is anticipated that performance monitoring reports will be generated every two or three months early in the study, and eventually settle down to every six months after the initial 12-18 months of the study.

The second main purpose for data analysis is to seek answers to the research questions and objectives of this study. It is anticipated that research data reports will be generated at about six month intervals throughout the study, with the first report generated six to eight months after the initiation of patient recruitment.

14.2 Data Analysis of Quality Assessment Data

The data on performance of the clinical centers with respect to participant recruitment and follow-up, completeness of data, etc., will consist primarily of simple tabulations of counts and percentages. During the participant enrollment period, each clinical center will be assessed as to the characteristics of the black and white participants being enrolled and whether the black and white groups of each clinic are comparable with respect to certain characteristics. This will be done by the comparison of the percentage of blacks and the percentage of whites having each characteristic (for characteristics with discrete

values) or by the comparison of a measure of central tendency for the characteristic in the black children and in the white children (for characteristics with a continuous distribution of values).

The data from the split duplicate analyses by the central laboratory will be paired together and the differences computed so that the following can be calculated for each laboratory test:

1. The mean of the 2n determinations.
2. The between sample standard deviation of the n pairs of determinations.
3. The mean absolute difference of the n pairs.
4. The average error (100 times the ratio of the mean absolute difference to the mean of the 2n determinations).
5. The coefficient of variation (100 times the ratio of the standard deviation to the mean of the 2n determinations).

These results will be used to determine how much the within-person variability is increased by measurement error in the biochemical determinations. If the measurement error of a particular biochemical determination is so large as to increase the within-person standard deviation substantially, this would have a substantial impact on significance test or confidence intervals computed for this variable. In this case, it would be important to perform multiple analyses of this determinant and use the mean (or some other measure of central tendency) of the determinations in order to reduce the measurement error.

Analysis of the quality assessment data for secular trends will require the repeated submission of specimens from a donor pool. These specimens would be submitted at intervals throughout the study and results compared to identify any trends over time. The analysis would

utilize a multiple regression model containing a term for each time period, representing the amount of change in the value of the specimen due to secular trends in the laboratory determinations for that period, and a term for each time period representing the amount of change in the value of the specimen due to deterioration of the frozen sample for that period.

Analyses of the quality assessment data for food coders will be similar to those described above for technical error of laboratory determinations and will also include for each nutrient for each coder scatter diagrams of the values based on the two independent codings of the food records.

14.3 Data Analyses Relating to Research Questions

14.3.1 Preliminary Analyses

Before attempting to begin analyses directly relating to the research questions of this study, it will be necessary to carry out a number of preliminary analyses of the data. These will include the following:

1. Generation of a point frequency distribution (that is, a distribution including each distinct value observed or measured for each variable on the data base.
2. Detection of outlier values in the univariate data followed by attempting to determine a reason for the extreme value and deciding how to handle the outlier value in the analyses.
3. Evaluation of skewness and kurtosis of the distributions of each of the continuous variables and an assessment of whether a logarithmic or other "Gaussianizing" transformation may be warranted.

4. Definition of response variables like socioeconomic status, psychosocial status and particularly the primary response variable for this study, obesity. The NGHS will have several measures of skinfold thickness as well as height and weight.
5. Searching for variables totally or nearly totally confounded with black-white differences, e.g., certain nutrients, aspects of socioeconomic status, or certain psychosocial characteristics. It is important that any such variables be identified early in the study as they may have a profound effect on the conclusions that can be derived from this study. The same analysis will also be carried out on pairs of characteristics, using as a starting point single variables that are highly correlated with race. Along these same lines, a stepwise multiple regression analysis will be run with race as the dependent variable and the other study variables as ~~independent variable and the other study variables as~~ independent variables to determine how well we can distinguish 9-10 year old black females from 9-10 year old white females on the basis of other characteristics measured at entry.
6. As a preliminary to carrying out regression analyses, generating scatterplots to each dependent-independent variable combination and looking for bivariate outliers.

19.3.2 Analyses of Research Questions

The primary research questions are presented in Section 3.2. Although analysis plans typically are developed and expanded based on preliminary findings, initial analyses are outlined below for each of the research questions.

1. Can the cross-sectional NHANES II findings that black girls age 12-20 have more obesity than white girls at the same age be confirmed by the NGHS longitudinal findings from ages 9-10 to ages 13-14? The initial analysis will involve taking the final follow-up year minus baseline difference in obesity measure(s) for each girl, determining the distributions of these differences for blacks and whites, and performing a parametric (such as a t-test) or a non-parametric (such as a Wilcoxon test) test of the differences of the black and white distributions. Further analyses, e.g., multiple regression, will be carried out to characterize temporal patterns in development of obesity over the four years for blacks and whites. Given the association of sexual maturation with obesity, interaction terms for sexual maturation with age and sexual maturation with obesity will be included in the regression model. The mean age at which the prevalence of obesity in black girls begins to diverge from that in white girls can be identified by using the other follow-up years to calculate the difference in the obesity measures(s).
2. If the NGHS confirms that black girls have more obesity than white girls, can this difference be explained by different food intake and/or physical activity patterns between the black and white girls or by differences in balance between food intake and physical activity patterns? For this question, the difference between the obesity measures(s) at follow-up year 4 and baseline will be used as the dependent variable in a multiple regression and a variety of nutrition/physical activity measurements included as independent

variables. These nutrition/physical activity measurements could be included as variables summarizing the information over the entire follow-up period or as separate variables for each year. Other follow-up years could be used instead of follow-up year 4. The interactions of each variable with race will be important and will be included in the stepping procedure.

3. Are there any socioeconomic factors that might help to explain the black-white difference in development of obesity and/or black-white differences in dietary and activity patterns? The analytic approach to this question will be similar to that outlined in Question 2 above. In addition, outcome measures will need to be defined for dietary and activity patterns before multivariate analyses are undertaken with those measures as dependent variables.
4. Are there social or psychological factors that are in play in the family that contribute to the development of obesity? Summary measures will have to be defined for the social and psychological factors as measured by the study. These factors and summary measures will be used as independent variables in the analytic approach outlined in Question 2 above.
5. If there are different dietary and/or activity patterns between black and whites, are these patterns familial? This question may best be approached through contingency table analysis using log-linear models and through correlation analysis. The analysis would concentrate on measures of dietary and activity patterns as identified on the Nutrition Patterns Form and on the Physical Activity Patterns Form, both

of which are collected for both children and parents throughout the study. The interaction between these patterns and race will be important.

6. Are there other factors, measured on the young girls, associated with the black-white differences in the development of obesity? The analytic approach to this question will be similar to the approach outlined for Question 2 above.

7. How does the development of obesity affect other CHD risk factors in blacks and whites, such as blood pressure and serum lipid levels? The initial analyses will involve correlating year 4 minus baseline changes in blood pressure, serum lipids, and other variables with changes in obesity using scatter plots and regression analyses. It will be determined whether change in obesity over a four-year period correlates more highly with change in blood pressure, serum lipids, etc.; more in-depth analyses will be carried out to elucidate temporal patterns in these changes. For example, it will be determined whether blood pressure changes tended to occur earlier, later, or concurrently with obesity changes.