PART II SPECIFIC PROTOCOLS

Section I The CCHN One protocol

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1. PROTOCOL OVERVIEW

The overall goal of the Community and Child Health Network (CCHN) is to gain new insights into the reasons for the disparities in maternal health and child development. The goals of the first study originating from the Network are 1) to examine the factors associated with maternal allostatic load (a possible factor in poor pregnancy outcomes), and 2) to evaluate the usefulness of community-partnered participatory research for conducting research on health disparities.

These goals will be achieved through a community-academic partnered, multi-center observational study with the following two specific aims:

1. To determine the factors associated with maternal allostatic load.
2. To explore the relationship between maternal allostatic load during the interconceptional period and birth/child health outcomes in a subsequent pregnancy.

This is a study about stress and resilience and their influences on maternal allostatic load as a mediator of birth outcomes and child health and development. In phase I of this study (known as CCHN One), we will examine the factors associated with allostatic load, with particular attention to two understudied areas: the influence of community and of paternal factors. We will also establish a framework for exploring the link between maternal allostatic load and birth/child health outcomes in subsequent phases of the study.

1.1. Definitions

Stress: demands that tax or exceed the coping resources of the individual, family or community.

Resilience: characteristics of individuals, families, and communities that provide strength in adversity and enable people to better manage their lives.

Allostasis: achieving stability through change. Allostasis refers to the body's adaptive processes that maintain homeostasis in the face of a challenge through the production of mediators such as adrenalin, glucocorticoids, cytokines and other chemical messengers.

Allostatic load: the cumulative physiological toll (wear-and-tear) of adaptation. Allostatic load refers to the price the body pays for being forced to adapt to adverse psychosocial or physical situations, and it represents physiological dysregulation of the body's adaptive systems as a result of chronic stress.

Preterm birth: Live birth of greater than or equal to 20 weeks but less than 37 completed weeks of gestational age (by spontaneous vaginal, instrumental, or Cesarean delivery).

Index child is the live birth of greater than or equal to 20 weeks of gestational age at the time of study enrollment to meet eligibility criteria.

Subsequent child is the live birth of greater than or equal to 20 weeks of gestational age occurring after study enrollment and during the study period.

Poor is having Medicaid, Medicaid pending, Local/Sate insurance or self-pay as health coverage at the time of enrollment AND/OR having received food stamps, WIC, and/or TANF within the 12 months prior to enrollment.

Non-poor is having private health insurance coverage AND/OR not having received food stamps, WIC, and/or TANF within the 12 months prior to enrollment.

1.2. Overview of Study Design

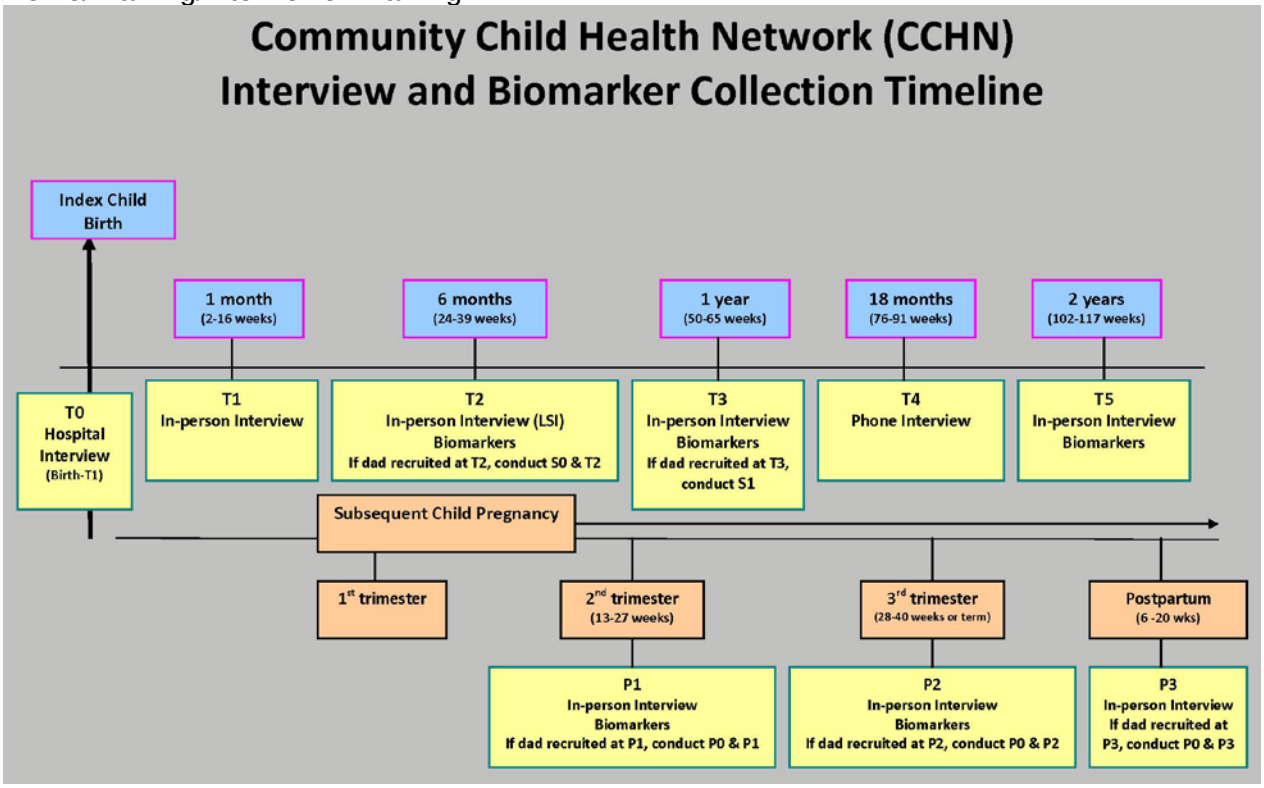
CCHN One is a five-year, multi-site, prospective cohort study of the influences of stress and resilience on maternal allostatic load and birth outcomes. A cohort in excess of 2,400 families will be recruited at delivery of the index child, such that at least 2,040 of the mothers complete the twelve-month interview (T3). There will be oversampling among African American and Hispanic women, as well as women with preterm birth. Periodic assessment of the mother, father/partner, and their relationship will occur *via* in-person visits at 1, 6, 12, and 24 months and per trimester during subsequent pregnancy (with an abbreviated telephone interview at 18 months); individual, family, community and institutional stressors and resilience factors will be recorded. Biomarkers will be collected at 6, 12, and 24 months. The influences of stress and resilience on maternal allostatic load will be analyzed using canonical correlation analyses, structural equation modeling and multilevel analyses. Study materials such as interview forms for the main study are designated by a T; example T0, T1, etc.

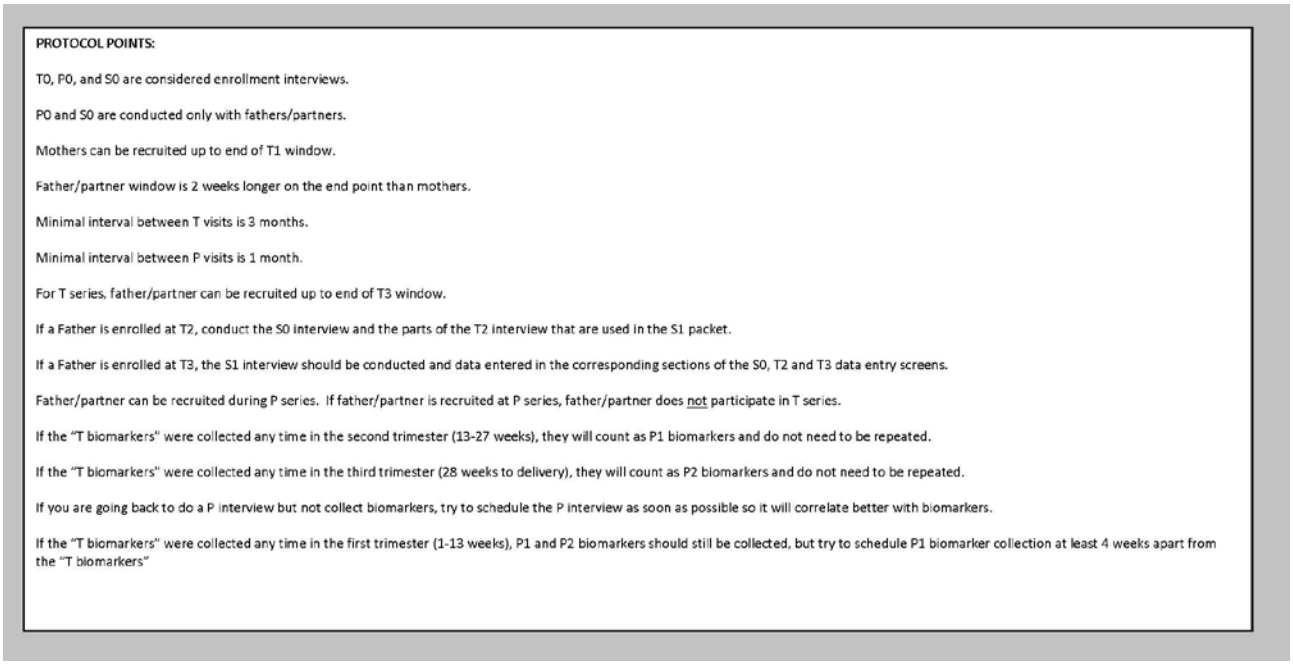
Subsequent Pregnancy study

Based on Baltimore Healthy Start experience, we estimate that 38% of mothers in the cohort will give birth to a subsequent child during the study period; the relationship between their allostatic load and subsequent birth outcomes will be explored. The sub-study for women who experience a second pregnancy while enrolled in the main study is known as the Subsequent Pregnancy study. This study has its own set of visit windows, interviews, and incentives that are different from the main study. All data for this study are in addition to data collected for the main study; forms are designated by a P—for example P1, P2, etc.

Biological forms are the same for both the T and P series.

The timeline for the study is shown below and can be accessed on the CCHN website at Home/Training/Interviewer Training.





2. STUDY PERSONNEL

There will be a variety of staffing patterns in the different sites. Some sites may have interviewers doing recruitment; others will have these as two separate jobs. Some sites will have the interviewers entering their own data; others may have separate data entry personnel. Staff titles will vary but each site will have one person who is the primarily responsible for coordinating all aspects of implementing the study at that site. Regardless of titles and how the work is divided, because local study personnel will collect data at the five sites, standardizing study procedures to the extent possible and requiring staff involved in data collection to demonstrate the required level of procedural knowledge and competency will reduce the likelihood of lost or unusable data. The following standards apply to CCHN One.

2.1. Responsibilities and Qualifications

Each site is responsible for ensuring that all study personnel are trained according to their local IRB standards and in compliance with the NIH. Staff training will be conducted locally at each site and monitored at regular intervals per local site procedures. Each site will document the methods they use to establish and monitor competency for each staff member throughout the study. In the case of personnel turnover during a study, replacement personnel shall complete the site's competency training (including Interviewer Training and Certification as appropriate) and DCAC application training prior to their participation in study activities.

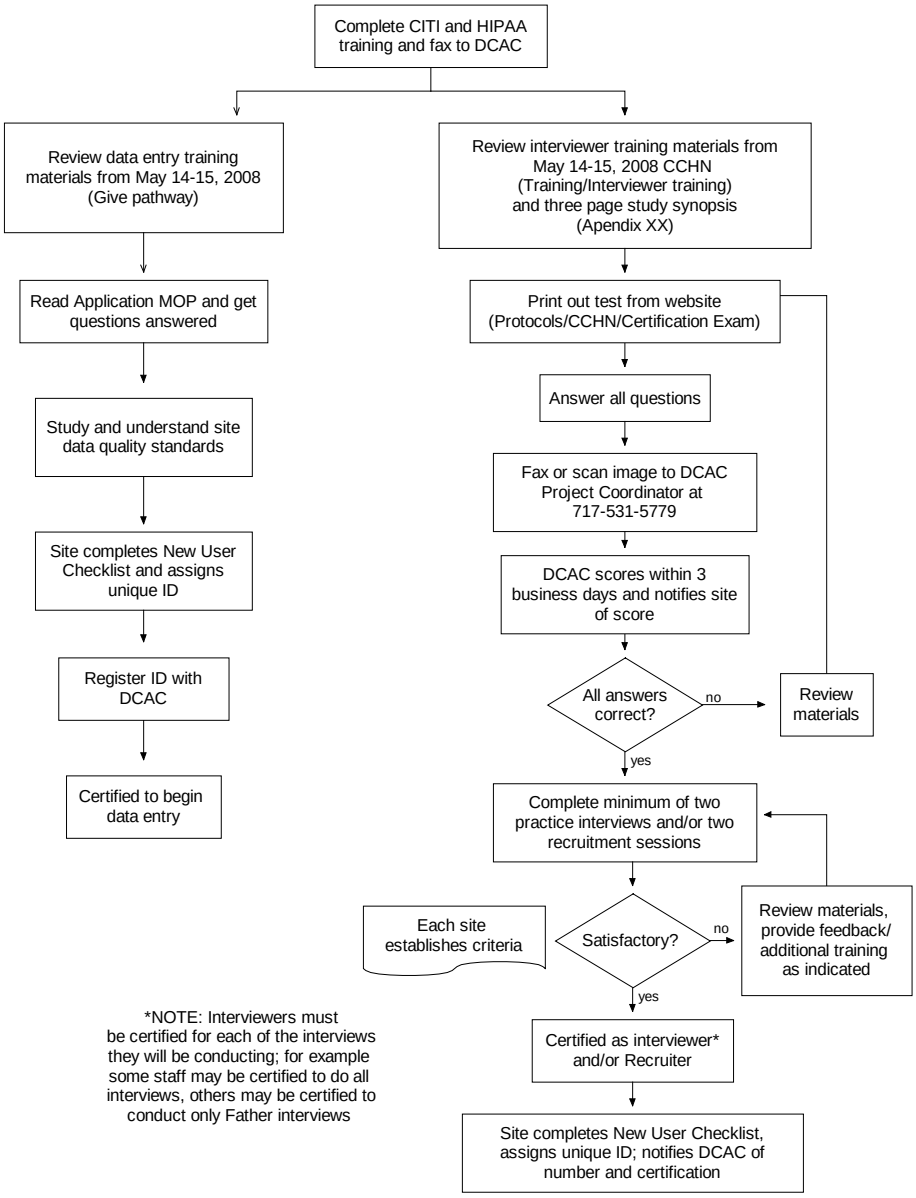
Although staff training may vary by sites and roles, all study personnel must complete the training required by their respective institutions for protection of human subjects from research risk (often this is CITI) and confidentiality of information as defined by the Health Insurance Portability and Accountability Act (HIPAA). CITI training and certification is available at www.citiprogram.org; local institutions may have their own version of the CITI training, and HIPAA training may or may not be incorporated as a module. Study staff should check with their institutions' Human Subject Protection Office (HSPO) to ensure they meet all their

institution's requirements prior to study personnel engaging in recruitment and enrollment activities. In addition, site staff members are required to comply with the certification process defined in Section B.2. Site staff must submit to the DCAC, either as a fax or a .pdf file, copies of documentation for the successful completion of all training and certification (institution and DCAC) required for CCHN One. **ORIGINAL training documents must be retained at the site and are considered part of the source documents for that site.**

2.2. Certification Process

Data entry personnel, recruiters, and interviewers must complete the certification process as shown in the diagram. All study personnel must complete the CITI and HIPAA training as described in Section 2.1. Interviewers and Recruiters will: 1) review the CCHN Training materials provided on the CCHN website (Training/Interviewer Training), 2) correctly answer all questions on the CCHN One Certification Quiz (CCHN website/Protocols/CCHN/ Certification Exam/CCHN One Certification Synopsis and Exam) and, 3) satisfactorily complete two practice interviews or recruitment sessions as defined by local site procedure. Study personnel will be required to pass additional site-specific training as determined by the sites in order to demonstrate adequate understanding and knowledge of CCHN One. A synopsis of the CCHN One design to assist study personnel is on the website. (Protocols/CCHN/Certification Exam/CCHN One Certification Synopsis and Exam). Study staff members doing data entry must review the materials on the CCHN website at Training/Application Training and familiarize themselves with the Applications MOP (CCHN website/Protocols/CCHN/MOP/Current/Application MOP) prior to

Interviewer/Recruiter and Data Entry Certification Process



doing data entry. When a staff member initially begins doing data entry, sites are advised to provide close supervision to ensure correct data entry from the start.

Personnel who have satisfactorily completed the training at the site are issued a unique ID number by the site, per local procedures. Each site is responsible for registering the individual by submitting a new user checklist to the DCAC. When the Interviewer's ID is entered, the action will trigger a back check to ensure that all training and documentation is complete for the Interviewer. If the Interviewer ID is unknown, the DCAC will forward a query to the site. If the Interviewer ID is known and the interviewer has not completed the training or has completed the training but the documentation has not been sent to the DCAC, the DCAC will issue a protocol excursion to the site.

The New User Checklist is an on-line, fillable form on the CCHN website home page in the Quick Reference section. This checklist must be completed and submitted on-line for each site staff member to gain access to the website and/or application. Refer to the Application MOP, Section 2.2.2 for more information

When there is turnover in a Project Coordinator, interviewer, recruiter or data entry staff position at a site, the site is responsible for training the new employee(s). Replacement personnel must complete standard training and certification as defined above prior to their participation in the study.

2.3. Re-certification for Inactive Staff

If a Project Coordinator/interviewer is inactivated for any reason, those individuals will need to review CCHN One procedures and have oversight/supervision by the Project Coordinator or other certified individual if they return to the study within two years.

3. RECRUITMENT AND ENROLLMENT

3.1. Sampling Strategy and Enrollment Goals—Main study

Participants are recruited into the study using the following hospital-based sampling scheme: Each site has defined a geographical area of interest sufficiently diverse to allow for analyses of racial-ethnic disparities and SES gradient. Geographic areas by site are shown in Table 1.

Table 1 Catchment areas by site

Site	Catchment Area
Baltimore	Baltimore City, MD
Chicago	Lake County, IL
North Carolina	7 counties: Edgecombe, Martin, Tyrrell, Greene, Washington, Pitt, Bertie
Los Angeles	Harbor Corridor, Los Angeles County
Washington D.C.	Washington, District of Columbia VA counties: Arlington, Fairfax, Loudon, Prince William MD counties: Montgomery, Prince George's, Anne Arundel, Charles

Each site has generated a list of delivery hospitals servicing women who reside within the geographical area of interest and will recruit women delivering at these hospitals to participate in the study, with selection for participation adjusted to satisfy criteria listed in Table 2.

Table 2 Recruitment of participants by racial/ethnic breakdown and poor/non-poor status by site

Baltimore

	Hispanic	African American	Caucasian	Total
Poor	0%	45%	35%	80%
Non-poor	0%	15%	5%	20%
Total	0%	60%	40%	100%

Chicago

	Hispanic	African American	Caucasian	Total
Poor	35%	15%	10%	60%
Non-poor	20%	5%	15%	40%
Total	55%	20%	25%	100%

Los Angeles

	Hispanic	African American	Caucasian	Total
Poor	45%	5%	5%	55%
Non-poor	20%	10%	15%	45%
Total	65%	15%	20%	100%

North Carolina

	Hispanic	African American	Caucasian	Total
Poor	0%	40%	40%	80%
Non-poor	0%	10%	10%	20%
Total	0%	50%	50%	100%

Washington DC

	Hispanic	African American	Caucasian	Total
Poor	20%	45%	10%	75%
Non-poor	10%	10%	5%	25%
Total	30%	55%	15%	100%

Aggregate

	Hispanic	African American	Caucasian	Total
Poor	20%	30%	20%	70%
Non-poor	10%	10%	10%	30%
Total	30%	40%	30%	100%

CCHN One investigators will over-sample mothers for preterm births according to Table 3.

Table 3 Preterm births versus term births by race/ethnicity

	% African American	% Hispanic	% Caucasian	Total
% Preterm Birth	13.3%	13.3%	6.7%	33.3%
% Term Birth	27.7%	27.7%	13.3%	66.7%
Total	40.0%	40.0%	20.0%	100.0%

Each site **must make every** attempt to enroll **per these guidelines** so that the final study sample (CCHN-wide) will be comprised of approximately

- 40% African American women, 30% Latina women, and 30% Caucasian women
- 70% poor households and 30% non-poor households (see definitions below)
- 33.3% preterm births and 66.7% term births

Poor is having Medicaid, Medicaid pending, Local/Sate insurance or self-pay as health coverage at the time of enrollment AND/OR having received food stamps, WIC, and/or TANF within the 12 months prior to enrollment.

Non-poor is having private health insurance coverage AND/OR not having received food stamps, WIC, and/or TANF within the 12 months prior to enrollment.

Preterm birth: Live birth of greater than or equal to 20 weeks but less than 37 completed weeks of gestational age (by spontaneous vaginal, instrumental, or Cesarean delivery).

Sites may decide to over-enroll initially. Each site has the flexibility to enroll under whatever schedule they feel is necessary to reach **the goal of 408 enrolled mothers who complete the 12-month interview (T3) for a total across sites of 2040 mothers who complete the 12-month interview.** Of the 2040 mothers completing the 12-month interview, we anticipate an additional attrition rate of 15%. This would leave approximately 347 mothers per site (1735 mothers total) by the end of the study. We estimate that on average, 38% of the 1735 women remaining in the study will give birth to a subsequent child during the study period. Given the anticipated drop-out rate of 15% during the first 12 months, and allowing for a 15% refusal/drop-out rate for those women who give birth to a subsequent child, a total sample size of approximately 660 women with subsequent births is expected.

Our goal is to minimize attrition rate to 15% per year. We have planned for equal rates of retention for fathers, anticipating that our community-academic partnership will facilitate retention and that, for some families, a second father or father-figure will enroll in the study. We will employ the full range of standard methods for tracking, encouraging and supporting participation and retention.

3.2. Inclusion Criteria

The following individuals are eligible for participation:

- Mothers 18 to 40 years of age
- Mothers self-identified as “Black or African American,” “Hispanic or Latina” and/or “White”
- Mothers who currently reside in the catchment area
- Men (or women who are designated by the mothers to be intimate partners) at least 18 years of age who are identified initially by the mother, and who meet the criteria in Section C.4
- Live birth of greater than or equal to 20 weeks of gestational age

3.3. Exclusion Criteria

The following individuals are ineligible for participation:

- Women or men who cannot give informed consent for themselves or their children;
- Mothers not self-identified as "Black or African American," "Hispanic or Latina" and/or "White"
- Women or men who are unable to fully understand requirements of the study in English or Spanish;
- Mothers for whom the index child is fourth or higher in birth order;
- Mothers who have resided in the center-specific geographical catchment area for < 6 months;
- Women or men who are incarcerated or otherwise unable to participate in the study in a home, community or clinical setting
- Mothers who plan to be surgically sterilized in the hospital following the delivery of the index child will be excluded.
    - Note: If the mother's partner is surgically sterilized but the mother is not and the mother does not desire to be surgically sterilized in the hospital following the delivery of the index child, the woman is still considered eligible for the study.
- Live birth of less than 20 weeks of gestational age
- CCHN study personnel (See Policy statement in Section XX in Part I)

3.4. Eligibility—Main study

Eligibility is determined by use of the T0 Eligibility Forms (CCHN website/Protocols/CCHN/Forms and Visits/Fillable Visit Packets). There are Eligibility Forms for both the Father and the Mother. NOTE: There is a separate form to use when a Father is recruited to the study for the first time at the T2 window for the main study; team members should use the S0 or Supplemental Father Packet (CCHN website/Protocols/CCHN/Forms and Visits/Visit Packets). This packet takes the place of the T0 and T1 interviews for a father enrolling for the first time at the T2 window. Fathers should not be enrolled after the T2 window for participation in the main study.

Subsequent Pregnancy Study

Women become eligible if/when they become pregnant again while enrolled in the main study. There are additional packets for these participants, known collectively as the "P series"—P1 (second trimester), P2 (third trimester), and P3 (post partum). Forms are on the web site; go to Protocols/CCHN/Forms and Visits/Visit Packets. At the time of the subsequent pregnancy, if there is a new father (different from the index child father/partner), enrolling at P1, study staff will need to use the P0 Father packet found on the CCHN website/ Protocols/CCHN/Forms and Visits/Visit Packets. **This packet contains eligibility information for a father enrolling for the first time during the subsequent pregnancy, whether the father is the father of the index child or not.**

Exceptions to eligibility must be cleared through the DCAC.

3.5. Baby's Father and/or Mother's Intimate Partner

Criteria for identification and enrollment of the baby's father and/or mother's intimate partner are in the Application MOP, Section 1.1.3.

3.6. Consent and Enrollment

Informed consent MUST BE OBTAINED from each subject according to the guidelines of each site's IRB and in accordance with all NIH specifications. Each site is responsible for maintaining its own consent form in compliance with the NIH and its local IRB standards. For each site except Baltimore, women will need to sign a separate consent to participate in the Subsequent Pregnancy study.

3.7. Unique Family ID Assignment

Once informed consent has been obtained, study staff MUST ENTER the individual into the CCHN Registry in keeping with the procedure outlined in the Applications MOP, Section 3.2 (CCHN website/Forms/Admin Forms/Registry). This will allow the site to assign the participant a unique family ID. For the Subsequent Pregnancy Study, the unique family ID will remain intact and the Moms will keep the same numbers. The T (main study) dads are assigned a number starting with 3 and new dads of a subsequent pregnancy (P dads) will get assigned a number starting with 5. If a dad participating in the subsequent pregnancy is the same dad who never got involved with the T series (father of index child), he will be assigned a number starting with 3 to allow for more accurate tracking of father accrual numbers.

4. DATA COLLECTION

4.1. Overview

This study employs three primary data collection mechanisms. One is a series of interviews conducted with the mother and the baby's father and/or mother's intimate partner at the specified times indicated in the study overview. Determination of who should be invited to participate is the responsibility of the local site in keeping with the policy outlined in Section 1.1.3 of the Application MOP. In some small number of cases, there may actually be three interviews at a given point: one with the mother, one with the baby's father, and one with the mother's intimate partner who may be different from the baby's father. Each should receive a separate ID number (see note in Section 3.6 for ID number assignment during the subsequent pregnancy study.

Subsequent pregnancy materials are known as the "P" visits. Time windows for visits for the subsequent pregnancy interviews are shown in the table below.

The second mechanism is a series of biological and clinical measures including samples of blood and saliva from the mother to analyze for markers of stress, anthropometric measures, blood pressure and heart rate. Sites have the option of collecting the biological/clinical data on fathers/partners. See table for a summary of times and windows.

The third mechanism is a chart review. Each of these is described more fully in Section 4. See the table and the Application MOP Section 1.1.1. for windows for all data collection points.

This study is focused primarily on African American, Hispanic, and white individuals, or individuals of mixed race who declare at least one of those three backgrounds. Race and/or ethnicity will be captured for recruitment monitoring and analysis purposes. Subjects have the option of choosing more than one category in order to best describe their racial/ethnic background. If a participant declares American Indian/Native American or Asian-American or Pacific Islander ONLY, doesn't know, or refuses, that person is ineligible. If a participant checks "multi-racial" he/she will be asked which race(s) apply. As long as the individual answers yes to

at least one of the three races of focus for the study (African American, Hispanic, white) that individual is eligible. Questions 4 and 4a on the T0 Eligibility forms capture this information and will be recorded as captured in the database.

4.2. Data Collection Points

4.2.1. General Information

Per agreement of the Steering Committee, all sites are doing interviews with paper copies of the forms for T0 and T1; however, sites have the option of collecting some data (such as the EPDS data for Time 1) as an interview, or inquiring if the participant prefers to self-administer the data collection form. A script for presenting options to the participant regarding the EPDS data is integrated into the corresponding interview document located on the CCHN website (Protocols/CCHN/Forms/Forms and Visit packets/T1 Mother Fillable). The EPDS Questionnaire form is at the end of the T1 Mother Fillable form.

Interviewers are expected to follow the questions on the data collection form as presented and in sequential order; all data must be entered into the CCHN One database maintained by the DCAC. Language to guide the interviewer in each of the sections of the interview is incorporated into each form.

NOTE: The use of paper copy or some other form of data collection for any remaining interviews will be addressed by the Steering Committee as each interview is developed and reported in future iterations of the MOP.

Windows—Main Study

CCHN Data Collection Time Points	**T0 Birth and/or Prenatal**	**T1 Home Visit #1**	**T2 Home Visit #2**	**T3 Home Visit #3**	**T4 Phone Interview**	**T5 Home Visit #4**
Dates/Window	**Birth to T1 interview**	**1 month (wk. 4) Window: 2-16 wks.**	**6 months (wk. 26) Window: 24-39 wks.**	**12 months (wk. 52) Window: 50-65 wks.**	**18 months (wk. 78) Window: 76-91 wks.**	**24 months (wk. 104) Window: 102-117 wks.**
Screening Participants	X					
Informed Consent & HIPAA Agreement	X					
Maternal Psychosocial Interview	X	X	X	X	X	X
Contact Information	X	X	X	X	X	X
Medical Chart Review (Mother & Newborn)	X					
Father/Partner Interview		X	X	X	X	X
Blood Spot (finger prick)			X	X		X
Saliva Collection			X	X		X

Anthropometry, Blood Pressure, Heart Rate			**X**	**X**		**X**

Exceptions

There is an exception window of four weeks for mothers and fathers on the T interviews. In other words, the mother T1 interview can be done as late as 20 weeks. Sites are encouraged to still collect data on study participants outside the four week exception window if it will help with subject retention, but an excursion from protocol will be noted. While there is a minimum interval between T visits of three months, if an interview is done within the extension window, sites should schedule subsequent T visits to get back to the original schedule as much as possible. For example, if T2 was done at 43 weeks, T3 should be scheduled at 55 weeks. This allows for the three month minimum interval and gets back to the original schedule of T3 occurring between 50-65 weeks.

The base window for fathers is two weeks longer on the end than the window for the mother; for example, the T1 mother window is 2-16 weeks, and the T1 father window is 2-18 weeks. In addition, fathers can be granted a four week extension, so with the extension the father T1 window is two to 22 weeks.

Windows—Subsequent Pregnancy study

CCHN Data Collection Time Points (Subsequent Pregnancy)	P0	Second trimester P1 Home visit 1P	Third trimester P2 Home visit 2P	Post Partum P3 Home visit P3
Dates/Windows	Subsequent pregnancy known	16-24 weeks gestation	28-36 weeks gestation	TBD
Enrollment	X			
Informed consent (except Baltimore)	X			
Medical Information (use Chart Review, passport, and/or interview to obtain*)		X	X	X
Mother interview		X P1 mother packet	X packet	X packet
Father/partner enrollment and consent	X P0 father packet			
Father/Partner interview		X P1 father packet	X packet	X packet

NOTE: Biomarkers for P3 are collected only at the Chicago and Washington DC sites				
Finger stick		X	X	X
Blood spot		X	X	X
Saliva		X	X	X
Anthropometric and BP		X	X	X

*Medical data will be collected throughout the subsequent pregnancy and when the baby is born using one of the three listed mechanisms, or a combination.

Exceptions
There are no exceptions for P1 or P2 visits.

4.2.2. Time 0 Data Collection (includes chart review)

The T0 document has several sections; information in the Eligibility for Mother Section may be obtained by interview, from chart review if approved by the local IRB, or from hospital personnel able to answer the questions correctly. In addition, there is a T0 Mother Birth Interview, T0 Eligibility for the Father, T0 Mother Chart Review, and T0 Mother Prior Pregnancies. Date of first prenatal visit, number of prenatal visits, and Mother Prior Pregnancies questions may be integrated into the T0 Mother Birth Interview per local site option. Time 0 forms are on the CCHN website (Protocols/CCHN/Forms/Forms and Visit Packets).

The T0 Newborn Chart Review is optional; all other information in the T0 document is required for the CCHN One protocol. For those sites electing to collect T0 information on the newborn, in the case of multiple births, the newborn chart review is to be completed only for the first born child. If there are discrepancies in the newborn's weight among the medical records, the delivery room weight is the correct one to document on the chart review form.

4.2.3. Time 1 Data Collection

Time 1 is a face to face interview for both the mother and the father/partner. The interview lasts approximately 90 minutes and is conducted in the home or a place of the participant's choosing, Time 1 information is collected when the index child is approximately one month of age. One section of the interview, Section 5 EPDS, may be completed as a questionnaire by the participant. Sites using this option are referred to the appropriate wording in the Interview form itself (CCHN/Forms/Forms and Visit Packets/T1 Mother Fillable/Section 5/Page 10). T1 forms are on the CCHN website (Protocols/CCHN/Forms/Forms and Visit Packets). Windows for collecting Time 1 data are shown in Section D above and in the Application MOP, Section 1.1.1.

The Time 1 Mother Interview may conducted at the same time as the Time 1 Father interview; however, sites reserve the right to conduct the Time 1 interview for either the mother or the father at a separate date, time, or place. The Time 1 Father interview may be conducted by another interviewer at the same time and place as the Time 1 Mother interview. It may be done by the same interviewer in the same place following or preceding the Mother interview, or it may be done at a separate time and place than the mother interview.

4.2.4. Time 2 Data Collection

Time 2 data collection includes three components: 1) an interview with both the mother and the baby's father and/or mother's intimate partner similar to those done at Time 1, 2) a qualitative interview called the Life Stress Interview to be done with both the mother and the baby's father

and/or mother's intimate partner and 3) biological/clinical measures on the mother only (optional for fathers per local protocol). Each component of Time 2 data collection is described more fully below, and the windows for collecting Time 2 data are shown in Section 4.2.1 above and in Section 1.1.1 of the Application MOP.

1) Interviews
Time 2 interviews are done face to face, in the participant's home or another place of his/her choosing just as for Time 1. This interview will take about 90 minutes and is conducted when the index child is approximately 6 month of age. Forms for the T2 interviews are on the CCHN website at (CCHN/Forms/Forms and Visit Packets). As it is in the Time 1 interviews, language to guide the interviewer is incorporated into the Time 2 interview forms.

2) Qualitative Interview
Time 2 interviews contain a qualitative component in the form of the Life Stress Interview. This interview does require special training and needs to be audio taped and scripted. Data collection and data entry procedures for this component will need to be established.

3) Biological and clinical data
Time 2 includes collection of biological specimens/clinical measures from the mother only (local option to collect biological specimens/clinical measures on fathers/partners) as shown in Section 4.2.1 and in the Applications MOP, Section 1.1.1. Study staff will collect blood samples via a finger stick and blood spots, provide instructions and materials to the mother for collection of saliva specimens, conduct the anthropometric measures, and measure blood pressure and heart rate. Saliva samples are to be mailed to the local study office and blood spots will be returned to the study office by the interviewer; all biological specimens must be catalogued in and placed in storage to be shipped to the designated laboratory at a later date as outlined in the Biological MOP (Part III). If a participant fails to send the saliva samples within a one-week window, she (he) is to receive one reminder phone call from study staff. Detailed procedures for all biological measures and forms for recording them are in Part III of this Manual of Procedures; electronic copy of forms for recording biological measures is located on the CCHN website (Protocols/CCHN/Forms/Forms and Visit Packets/Fillable Forms). Logs and Labels for Blood Spots and Saliva are on the website at Protocols/CCHN/Forms/Admin Forms.

NOTE: There is no limit on the number of days between the collection of the interview and biomarker data; however, the ideal time is 7 days or less and must be done within the time window for that data collection point. In order to create a concurrent assessment of stress at the time of biomarker collection, if biomarkers and interview are more than 7 days apart (but still within the time window for that data collection point), study staff will **repeat the PSS and only the PSS** from the interview at the time of the biomarkers collection.

4) Subsequent Pregnancy (P)
Women who are enrolled in the study may have a pregnancy subsequent to the birth of the index child; this pregnancy may occur as early as the T2 window of the main study (The Design Committee will consider what to do if subsequent pregnancy occurs earlier than T2). The subsequent pregnancy study involves a separate set of interviews to be conducted with both the father and the mother at three time periods: P1 is the second trimester, P2 is the third trimester, and P3 is the post partum period. Windows are shown in Table XX in Section 4.1. P0 is the name of the packet to be used for a father enrolling for the first time with the subsequent pregnancy. Study staff should continue with the schedule of face-to-face interviews for the index child (T series), and in addition, complete the interviews found in the P1 Mother and P1 Father Packets (CCHN website/Protocols/CCHN/Forms and Visits/Visit Packets) at the indicated times. If a participant has missed both of her P1 and {2 visits, then there is no value in

completing the P3 visit; therefore the mother should not complete the P3 visit. If a mother has a tubal ligation after her subsequent child (P series) she does not need to be withdrawn from the T series since she has already had the second child.

Father Interviews

The subsequent pregnancy is an opportunity to enroll a new dad (father of the subsequent pregnancy child who is different from the father of the index child or the father of the index child who declined to participate initially but who now agrees to participate in the subsequent pregnancy study). The P0 Father Interview packet should be used for any father who enrolls at the time of the Subsequent Pregnancy. This interview should be conducted as soon as the pregnancy is determined or during the second trimester (P1) interview. If they are not already enrolled in the main study, fathers recruited as part of the subsequent pregnancy study participate **only** in the P series, not the T series for the index child. Only as a last resort, these Father interviews are allowed to be conducted by telephone instead of in-person.

NOTE: If a father enrolls at the T2 window **in the absence of a subsequent pregnancy,** that father completes the S0 packet to catch up, then continues with the T series. If a Father is enrolled at T2, conduct the S0 interview and the parts of the T2 interview that are used in the S1 packet. Sections that are not completed can be put to "missing" when data are entered. If a Father is enrolled at T3, the S1 interview should be conducted and data entered in the corresponding sections of the S0, T2 and T3 data entry screens. Sections that are not completed can be put to "missing" when entering data.

Biological and clinical data for subsequent pregnancy

If T and P visits occur within three months of each other, biomarkers will be collected according to the P (subsequent pregnancy) visit schedule. If T and P visits occur more than three months apart, biomarkers will be collected during both visits; however, biomarkers for the P visits take precedence over biomarkers for the T visits. **Combining the T and P visits is specifically discouraged because this is considered to be too onerous for the participant; if combining interviews is absolutely essential, it should be treated as an exception to the protocol.**

4.2.5. Time 3 Data Collection

Time 3 data collection includes two components: 1) an interview with both the mother and the baby's father and/or mother's intimate partner similar to those done at Times 1 and 2, 2) biological/clinical measures on the mother only (optional on fathers per local protocol). Each component of Time 3 data collection is described more fully below, and the windows for collecting Time 3 data are shown in Section 4.2.1 above and in Section 1.1.1 of the Application MOP.

1) Interviews

Time 3 interviews are done face to face, in the participant's home or another place of his/her choosing just as for Times 1 and 2. The Time 3 interview will take about 90 minutes and is conducted when the index child is approximately 12 months of age. Forms for the T3 interviews are on the CCHN website at (CCHN/Forms/Forms and Visit Packets). As it is in the Time 1 and Time 2 interviews, language to guide the interviewer is incorporated into the Time 3 interview forms.

2) Biological and clinical data

Time 3 also includes collection of biological specimens/clinical measures from the mother only (local option to collect biological specimens/clinical measures on fathers/partners) as shown in Section 4.2.1 and in the Applications MOP, Section 1.1.1. Study staff will collect blood spots via a finger stick, provide instructions and materials to the mother for collection of saliva specimens,

conduct the anthropometric measures, and measure blood pressure and heart rate. Saliva samples are to be mailed to the local study office and blood spots will be returned to the study office by the interviewer; all biological specimens must be catalogued in and placed in storage to be shipped to the designated laboratory at a later date as outlined in the procedure (Part III of the MOP). If a participant fails to send the saliva samples within a one-week window, she (he) is to receive one reminder phone call from study staff. Detailed procedures for all biological measures and forms for recording them are in Part III of this Manual of Procedures; electronic copy of forms for recording biological measures is located on the CCHN website (Protocols/CCHN/Forms/Forms and Visit Packets/Fillable Forms). Logs and Labels for Blood Spots and Saliva are on the website at Protocols/CCHN/Forms/Admin Forms.

NOTE: There is no limit on the number of days between the collection of the interview and biomarker data; however, the ideal time is 7 days or less and must be done within the time window for that data collection point. Because the PSS is repeated as part of the T3 interviews, and in order to create a concurrent assessment of stress at the time of biomarker collection, if biomarkers and interview are more than 7 days apart (but still within the time window for that data collection point), study staff will **repeat the PSS and only the PSS** from the interview at the time of the biomarkers collection.

3) Subsequent Pregnancy (P)

Women who are enrolled in the study may have a pregnancy subsequent to the birth of the index child; if this pregnancy occurs at the T3 window of the main study, follow the same steps for the subsequent pregnancy study as outlined in Section 4.2.4, Item 4. The subsequent pregnancy study involves a separate set of interviews to be conducted with both the father and the mother at three time periods: P1 is the second trimester, P2 is the third trimester, and P3 is the post partum period. Windows are shown in the table in Section 4.2.1. P0 is the name of the packet to be used for a father enrolling for the first time with the subsequent pregnancy. Study staff should continue with the schedule of face-to-face interviews for the index child (T series), and in addition, complete the interviews found in the P1 Mother and P1 Father Packets (CCHN website/Protocols/CCHN/Forms and Visits/Visit Packets) at the indicated times.

Father Interviews

The subsequent pregnancy is an opportunity to enroll a new dad (father of the subsequent pregnancy child who is different from the father of the index child or the father of the index child who declined to participate initially but who now agrees to participate in the subsequent pregnancy study). The P0 Father Interview packet should be used for any father who enrolls at the time of the Subsequent Pregnancy. This interview should be conducted as soon as the pregnancy is determined or during the second trimester (P1) interview. If they are not already enrolled in the main study, fathers recruited as part of the subsequent pregnancy study participate **only** in the P series, not the T series for the index child. Only as a last resort, these Father interviews are allowed to be conducted by telephone instead of in-person.

NOTE: Fathers are only allowed to enroll in the study up to the T2 interview for the index child (if recruited at T2, conduct S0 and T2 interview) and allowed to enroll up to the P2 interview for the subsequent child (if recruited at P1, conduct P0 and P1; if recruited at P2, conduct P0 and P2).

Biological and clinical data for subsequent pregnancy

If T and P visits occur within three months of each other, biomarkers will be collected according to the P (subsequent pregnancy) visit schedule. If T and P visits occur more than three months apart, biomarkers will be collected during both visits; however, biomarkers for the P visits take precedence over biomarkers for the T visits. **Combining the T and P visits is specifically discouraged because this is considered to be too onerous for the participant; if**

combining interviews is absolutely essential, it should be treated as an exception to the protocol.

4.2.6 Time 4 Data Collection

Time 4 data collection is a telephone interview with no biological specimens collected.

4.2.7 Time 5 Data Collection

4.3. Incentives

4.3.2. Monetary incentives

Study participants are compensated for the following procedures: initial enrollment, each in-person assessment, and each biomarker collection; monetary compensation for the telephone interview is optional. The amounts of compensation may vary by site; however, each site should ensure their local IRB approves and update the Project Coordinators/MOP committee and the Steering Committee. A table showing incentives by site is located in Appendix XX; each site is responsible for updating their portion of the table.

Study participants in the Subsequent Pregnancy study are compensated over and above the compensation for participation in the main study. As with the main study, each site is responsible for determining their incentive structure, and for recording and updating it in Appendix XX.

4.3.3. Non-monetary incentives

Each site has the option of providing a variety of non-monetary compensations to their study participants. These are often used in conjunction with retention strategies and may consist of appropriate items that are donated, educational materials, magazines on parenting, and similar items. Non-monetary compensations do not need to be standard across sites. Project coordinators will periodically share with each other what their sites are doing in this regard, and ideas can be posted on the website in the Project Coordinator Committee folder.

5. DATA ENTRY AND QUALITY CONTROL

5.1. Data entry

Data entry is the responsibility of each site, following procedures outlined in the Applications MOP, Section 4, Data Collection, Data Entry and Data Quality Control.

5.2. Quality Control

Each site is responsible for developing a quality control plan to ensure the quality of data entered by their site. Quality control mechanisms must be documented by each site (to be placed on the website Committees/Project Coordination Committee) and will contain the following at a minimum: 1) a mechanism to ensure that interviews did happen, 2) a mechanism to verify what is on the paper copy of the interview matches what is in the data base (system not set up for double data entry), and 3) a mechanism for ensuring data is clean when it is entered (i.e. were skip patterns followed correctly, is all data entered, etc.). It is recommended that the

work of new interviewers be reviewed more closely with a lesser degree of review for interviewers whose accuracy and attention to detail has proven satisfactory.

5.3. Quality Control over time for interviewers/recruiters

As noted in the Certification process, Interviewers will need to be certified on each of the CCHN One interviews that they are/will be administering. In addition, each site's quality control plan must have a procedure for ensuring that interviewers and recruiters maintain their skills throughout the project. This can consist of periodic observations by the local trainer(s), re-training as needed, and/or repeat of practice interview/recruitment sessions. Local procedures must be defined and incorporated into the local site's MOP.

6. QUALITY AUDIT

6.1. Purpose

The purpose of a quality audit is to examine each site's adherence to the policies and procedures of the network (CCHN MOP Parts I and III) and the current protocol as defined in Part II of the CCHN Manual of Procedures (MOP). See MOP Part I for details. In addition to the CCHN MOP, each site must document their local processes and procedures. Sites are free to organize the documents in whatever way works best for them; however, each site must have immediate access (online or hard copy) to all documents named above and have a documented process for maintaining and updating all procedures and documents.

6.2. Site Visits

Each site will be audited during the five-year project period of CCHN One according to a schedule determined by the DCAC in conjunction with the Steering Committee. The Quality Audit team will consist of one representative of the NICHD and representatives from the DCAC. Other team members may include a PI or Project Coordinator from a site other than the one being visited. The Design Committee will assist the DCAC in planning and performing site visits.

Site visits are intended to achieve the following goals:

Assess the overall performance of the site, and adherence to procedures and processes
Assess the quality of data collection
Provide consultation in identifying and solving problems
Transfer effective approaches across sites

Components of the site visit will include but not be limited to: meeting with site personnel; examining facilities and data files; reviewing administrative organization within the site; reviewing source documents; evaluating conduct of special procedures; and comparing samples of completed interview forms with entered study data. Examples of specific tasks performed during a site visit:

- Checking whether query changes and data corrections were made to data collection forms
- Evaluating the center's data processing
- Verifying that the informed consent exists and is signed and dated for each subject
- Ensuring that the current version of the MOP is readily available (See note below on MOP)
- Checking for consistency in data collection forms

- Evaluating the organization of participant folders

Please refer to the Applications MOP Sections 1.3 and 1.4 for details on Source Documents and Exceptions, Protocol Excursions and Protocol Violations, and to Part I of the CCHN MOP for additional details on the network's Quality Audit process.

The DCAC will prepare a site visit report, which may include specific recommendations for the site. The report will be sent to the PI and Project Coordinator at the site where the visit occurred, NICHD, and the Chairperson of the Steering Committee. If serious problems are detected, the report will also be sent to the Design Committee for review.

6.3. Cost of Site Visits

Any site staff member who is traveling as part of an audit team pays for travel from the local site budget. The DCAC will pay for the DCAC staff travel expenses, and NICHD staff will cover their travel expenses.

7. WITHDRAWAL/COMPLETION OF STUDY PARTICIPATION

The Withdrawal/Completion Form must be completed per the instructions in Section 1.1.4 of the Application MOP and submitted to the DCAC to indicate a study end-point for each participant. A separate withdrawal form must be completed for both the T series and the P series. A Participant need not be withdrawn if she misses T1 and T2; however, if she misses T2 and T3, she will be missing required biological data and should be withdrawn. However, if an exception is requested, she can be maintained in the study, but her data may not be able to be used. If a Mother is withdrawn, a Father does not necessarily have to be withdrawn if he is interested in continuing in the study. If a mother has a tubal ligation after her subsequent child (P series) she does <u>not</u> need to be withdrawn from the T series since she has already had the second child.

The withdrawal form is located on the CCHN website/Protocols/CCHN/Forms/Forms and Visit Packets and in Section 1.1.4 of the application MOP.