

2020

Add Health Wave V Documentation



# Measures of Inflammation and Immune Function

**Report prepared by**

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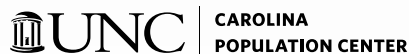
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This document summarizes the rationale, equipment, protocol assays, internal quality control, data cleaning, external quality control, and procedures for the measurement and classification of inflammation at the Wave V home exam. Whenever possible, data collection and methods in Wave V mirrored those of Wave IV to ensure comparability of data between waves, although **important inter-Wave differences exist and are grey-highlighted herein**. This document is one in a set of Wave V user guides. User guides are also available to describe protocols for the following biological measures in Wave V:

- Anthropometrics
- Cardiovascular Measures
- Medication Use – Home Exam
- Baroreflex Sensitivity & Hemodynamic Recovery
- Glucose Homeostasis
- Lipids
- Renal Function

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## Citation

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## 1. Introduction

Wave IV measures of inflammation were based on dried blood spots collected using capillary finger prick.<sup>1</sup> In contrast, Wave V measures of inflammation were based on venous blood collected via phlebotomy. The blood was collected by field examiners (FEs) certified in phlebotomy, chilled at 4°C during the remainder of the home exam, centrifuged immediately afterward, aliquoted into transport tubes, and then sent overnight to a laboratory for assay.

### Assayed Measures of Inflammation

- High Sensitivity C-Reactive Protein (hsCRP, mg/L)

Moreover, the restricted use Add Health Wave V data include eleven constructed measures designed to facilitate its analysis and interpretation:

- Classification of hsCRP<sup>2</sup>
- Count of common subclinical symptoms<sup>3</sup>
- Count of common infectious or inflammatory diseases
- NSAID/Salicylate medication use in the past 24 hours
- NSAID/Salicylate medication use in the past 4 weeks
- Cox-2 Inhibitor medication use in the past 4 weeks
- Inhaled Corticosteroid medication use in the past 4 weeks
- Corticotropin/Glucocorticoid medication use in the past 4 weeks
- Anti-rheumatic/Anti-psoriatic medication use in the past 4 weeks
- Immunosuppressive medication use in the past 4 weeks
- Any Anti-inflammatory medication use in the past 4 weeks

## 2. General Overview of Data Collection

All Wave V venous blood samples were collected during home exams performed by FEs from two Add Health data collection partners: Examination Management Services, Inc. (2016–2017) and Hooper Holmes, Inc. (2018–2019). All FEs were trained and certified using a custom program specific to the Add Health protocol. FEs used a 7" Samsung Galaxy Tab 4 tablet to record and transmit data. An Add Health data collection application (Open Data Kit or ODK) installed on the tablet guided the FEs through the home exam protocol. In addition, FEs received a series of job aids, both on paper and on the tablet, to serve as quick reference guides when completing the protocol. Each tablet also contained an in-depth Add Health training manual that could be accessed at any time.

FEs conducted home exams among previously consented respondents. All FEs were phlebotomy-certified and had at least two years of experience collecting venous blood. Before home exams, FEs were sent a Visit Supply Kit that included a box for shipping blood to the lab and a Blood Collection Kit containing most required materials for the blood collection. FEs supplied additional materials, as needed (see section 3.2). Protocols for blood collection were dictated to FEs by the handheld 7" Samsung tablet used during all home exams. The tablet gave step-by-step directions for the blood collection and required FEs to enter information about the blood draw for each respondent. All respondents had the

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option to decline part or all of the blood draw, although declining did not affect their ability to participate in the rest of the home exam. Overall, 91.8% of the respondents agreed to and completed the blood draw. Of the remainder, 6.5% refused, 1.3% agreed but the blood draw was unsuccessful, and < 1% had exams terminated before the blood draw (see the blood draw status variable **H5BLOOD** in the *bdemo5* data set and codebook).

Blood collection was the last step in the home exam. Afterwards, all collection tubes were inverted 8-10 times to distribute the blood and contents of the tubes and then chilled at 4° C (on ice or frozen cold packs) for up to two hours. Subsequent processing involved centrifuging specific tubes then aliquoting serum and plasma into color-coded transport tubes pre-labelled with unique barcode identifiers linking the blood to a particular respondent. Then the transport tubes were packaged in a Styrofoam Box with frozen cold packs and shipped overnight via FedEx to the Laboratory for Clinical Biochemistry Research (LCBR) at the University of Vermont. Overnight shipment enabled receipt by LCBR before 10:30 am the next morning. Upon receipt, LCBR documented the arrival of the transport tubes, evaluated their condition, processed them, and either assayed the specimens or aliquoted and archived them in -80°C freezers.

### 3. Whole Blood Collection

#### 3.1 Rationale

Venous blood was collected to provide Add Health with the biological specimens necessary to assay and interpret a pre-specified panel of metabolic, hematologic, inflammatory, immune, and renal biomarkers, including the measure of hsCRP described herein. It also was collected to establish an archive of serum, plasma, whole blood, RNA, and packed cells capable of supporting future assays and ancillary studies.

#### 3.2 Equipment

Before exams, FEs were shipped a Visit Supply Kit (Exhibit 1) including (1) a cardboard Shipping Box with an inner Styrofoam Box and two cold packs for shipping collected samples to LCBR, (2) a large Tyvek envelope in which to ship the Shipping Box, and (3) a Blood Collection Kit for collecting blood. The Blood Collection Kit contained:

- Biohazard-labelled Ziploc bag
- Latex-free gloves
- 2"x2" gauze
- Latex-free, Band-Aid type adhesive dressings
- Latex-free, strap tourniquet
- Alcohol prep pads, disposable pipets
- Single-use vacutainer (blood collection) tube holder
- 21-gauge Eclipse straight needle
- 21-gauge butterfly needle
- (3) disposable 3 ml graduated transfer pipets
- (2) 8.5 ml serum separation transport (SST) vacutainer tubes

- (1) 6 ml sodium fluoride/potassium oxalate (NaF/KOx)-containing vacutainer tube, if needed for the glucose sub-study (see Section 4.1.2.1)
- (1) 3- or 4- ml potassium ethylenediaminetetraacetic acid (EDTA)-containing vacutainer tube
- (1) 10 ml EDTA-containing vacutainer tube
- (1) 10 ml PAXgene vacutainer tube (containing 7.5 ml of preservative)
- (4) 10 ml transport tubes with color coded caps
- Extra barcode labels

BD Biosciences (San Jose, CA) supplied all the vacutainer and transport tubes. As of February 2018, their 3 ml EDTA vacutainer tube (Cat #367835) was no longer available, so Add Health switched to the 4 ml EDTA vacutainer tube (Cat #367844).



**Exhibit 1. Visit Supply and Blood Collection Kits**

FEs were responsible for providing ancillary materials for each home exam, including but not limited to a chux-type absorbent under pad, a sharps container, and a cooler with cold packs for keeping samples cold before packaging and shipping them to LCBR.

### 3.3 General Protocol

#### 3.3.1 Blood Collection

The blood draw was performed as the final stage of the home exam following collection of anthropometric, cardiovascular, and medication information. After confirming respondents were comfortable giving blood, respondents were asked to either sit or recline at their discretion. They also were asked if they had problems in the past with blood collection such as fainting, bleeding, or hard-to-find veins. FEs were instructed to ensure the blood collection area was private, uncluttered, and fully prepared before beginning the blood draw. Preparation involved placing the chux pad, organizing the vacutainer tubes/supplies, preparing the cooler to accept the blood samples, and scanning the barcode located on the outside of the Blood Collection Kit. Scanning it automatically captured a unique, eight-digit code, thereby linking the respondent to the transport tubes / labels within it, the corresponding ODK questionnaire data, and ultimately to LCBR results.

Following standard phlebotomy protocols, FEs asked respondents to identify an arm for collecting blood, applied the tourniquet to that arm, and identified a vein in the antecubital fossa for venipuncture. If no vein appeared suitable, FEs asked to try the opposite arm. Unless respondents had objections, venipuncture was performed on the best potential vein and whole blood was collected, as summarized below:

- Put on nitrile gloves.
- Have the respondent extend his/her arm on the protective pad, palm up and straight at the elbow.
- Inspect the arm. Do not draw blood from an arm that has a rash, open sore, is swollen or shows signs of a recent venipuncture or hematoma. Do not draw blood from an arm that contains an arterial access such as a fistula or shunt.
- Apply the tourniquet several inches above the elbow and palpate for a suitable vein.
- Select a vein that is palpable and well-fixed to surrounding tissue.
- Open the needle assembly unit and attach it to the vacutainer holder.
- Ask the respondent to make a tight fist. Cleanse the area with an alcohol wipe using a circular motion and allow the area to air dry.
- Remove the cover from the needle.
- The vein should be fixed or held taut during the puncture. Push the needle firmly and deliberately into the vein. When firmly in the vein, blood appears in the tubing of the needle assembly past the end of the needle.
- Quickly push the first vacutainer tube (using the sequence in the table above) onto the needle in the holder, puncturing the center of the stopper.
- Release the tourniquet after the flow is established or if the respondent becomes uncomfortable. The respondent may open his/her fist once blood flow is established.
- When the first vacutainer tube is filled to capacity, remove it from the holder and place the next vacutainer tube in the holder.
- Gently invert each vacutainer tube 8-10 times immediately upon removing each one and while filling the next one. Repeat until all the desired vacutainer tubes are filled.
- Place all filled vacutainer tubes directly into a cooler with ice or ice packs.
- When the last vacutainer tube is filled, remove the tourniquet, carefully withdraw the needle, and cover the venipuncture site with a sterile gauze pad.
- Never apply pressure to the gauze until the needle is clear of the puncture site and away from the arm.
- Have the respondent hold the gauze pad with mild pressure and sit quietly for a few minutes.
- Slide the needle safety guard forward to prevent an accidental needle stick. Discard the entire used needle assembly in a sharps container.
- Check the venipuncture site. If it is adequately clotted, remove the gauze and apply a bandage. If after a few minutes, bleeding continues keep direct pressure on the site for 5 minutes.
- Encourage the respondent to sit quietly for a few minutes. Due to a fasting blood draw encourage the respondent to eat a snack if needed.

When the first attempt at blood collection was unsuccessful, FEs were allowed to ask to draw blood from the opposite arm. However, no more than two blood collection attempts were permitted.

Moreover, only the antecubital fossa was acceptable for blood draw. FEs were not allowed to collect blood from any other sites, such as the back of the hand.

Either 5 or 6 tubes of blood were collected per respondent, depending on eligibility for a separate glucose sub-study (see Measures of Glucose Homeostasis User Guide, Section 4.1.2.1). Collection order, tube type, and processing information are listed below (Exhibit 2).

| Order | Tube Type      | Centrifuged | Resultant supernatant | Resultant precipitate | Use  |
|-------|----------------|-------------|-----------------------|-----------------------|--|
| 1     | 8.5 ml SST     | Yes         | Serum                 | Discarded             | Assays: glucose, total cholesterol, high- & low-density lipoprotein-cholesterol, triglycerides, high sensitivity C reactive protein, creatinine & cystatin C |
| 2     | 10 ml EDTA     | Yes         | Plasma                | RBC/buffy coat        | Archival: for future use   |
| 3     | 3 or 4 ml EDTA | No          | N/A                   | N/A                   | Assay: hemoglobin A1c<br>Archival: for future use  |
| 4     | 8.5 ml SST     | Yes         | Serum                 | Discarded             | Archival: for future use   |
| 5     | 6 ml NaFl/KOx  | Yes         | Plasma                | Discarded             | Assay: glucose sub-study   |
| 6     | 10 ml PAXgene  | No          | N/A                   | N/A                   | Archival: for future use   |

**Exhibit 2. Tubes of Blood Collected**

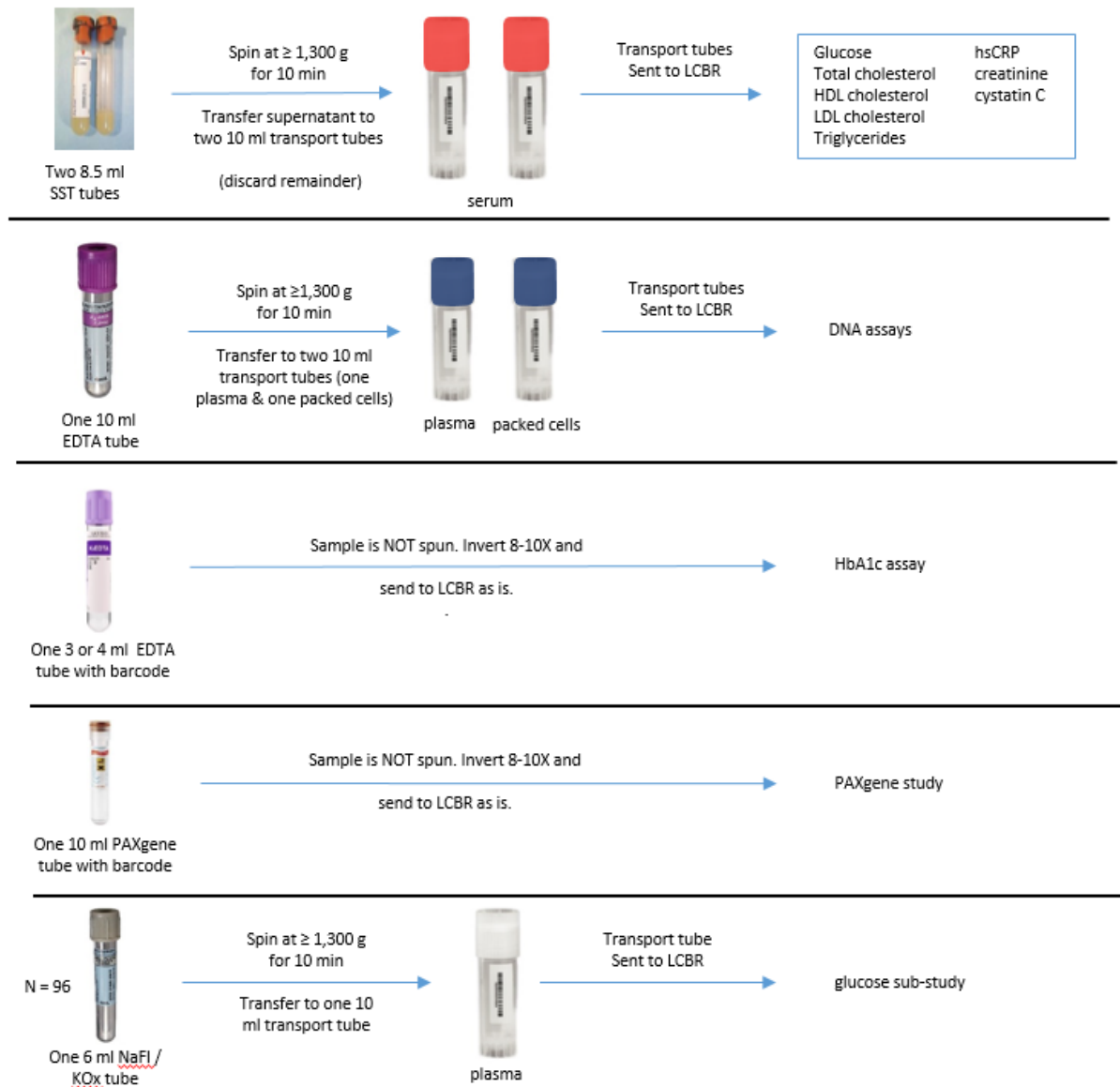
### 3.3.2 Blood Processing

The venous blood draw concluded the home exam. After cleaning up all supplies and equipment, FEs left the exam sites and were allowed a maximum of two hours before processing the blood which was chilled at 4° C (on ice or frozen cold packs) in the interim.

All FEs centrifuged specific blood collection tubes, including the 8.5 ml SST, 10 ml EDTA, and when collected, the 6 ml NaFl/KOx vacutainer tubes. The 3-4 ml EDTA vacutainer tube used for the HbA1c assay was *not* centrifuged. FEs centrifuged tubes for ≥ 10 min at ≥ 1300 g, depending on the capabilities of their centrifuge. After centrifugation, FEs used the graduated transfer pipettes included in the Blood Collection Kit to aliquot serum from the SST and (separately, when collected) plasma from the NaFl/KOx vacutainer tubes into 10 ml, round bottom, skirted transport tubes (BD Biosciences, NJ). FEs aliquoted as much supernatant as possible into the transport tubes but avoided disturbing the precipitate layer. A red cap identified transport tubes containing serum from the SST vacutainer tubes, a blue cap identified transport tubes containing plasma from the 10 ml EDTA vacutainer tube, and a white cap identified the



transport tube containing plasma from the Na/Fl/KOx tube. Transport tubes were chilled at 4° C (on ice or frozen cold packs) until packaged for shipment to LCBR. Exhibit 3 demonstrates the complete blood processing protocol.



### Exhibit 3. Blood Processing Protocol

After processing the blood, FEs took a loose barcode label provided in the Blood Collection Kit and affixed it to a paper manifest designed to accompany the transport tubes to LCBR. The loose barcode label matched the barcode labels on the transport tubes and the Shipping Box. FEs recorded all vacutainer tubes that were collected and identified all difficulties during blood draw or processing on the manifest as well as in the tablet. The barcode-labelled manifest was designed to be scanned on arrival at LCBR to associate it with an individual respondent's transport tubes.

### 3.3.3 Shipment of Samples

Immediately before shipment, FEs removed two cold packs from the freezer, sandwiched the transport tubes between them, enclosed the sandwich within the Styrofoam Box, placed the manifest on top of the Styrofoam Box, sealed the cardboard Shipping Box around it, put the cardboard Shipping Box inside the Tyvek envelope, applied a pre-printed FedEx shipping label to the envelope, carried it to a FedEx office, and handed it to a FedEx representative (*in person*) for Priority Overnight shipment to LCBR with arrival the following morning. FEs were not permitted to leave shipments at unattended FedEx drop boxes.

When overnight shipment was impossible, FEs noted this on the manifest and held unboxed transport tubes in a refrigerator approved for biological specimens or cooler with enough cold packs to keep them chilled at 4° C overnight without risk of freezing (or thawing), as is possible on wet or dry ice. The transport tubes were packaged and shipped the next day using freshly frozen cold packs.

### 3.3.4 Receipt of Samples at LCBR

LCBR technicians specifically trained for Add Health Wave V received and immediately processed samples each morning. They unpacked the shipping boxes one at a time, evaluated the volume and quality of each transport tube, and entered them into a custom-made laboratory information management system (LIMS) program.

After re-centrifuging the serum samples for hsCRP assays at 4° C for 10 min at 30,000 g, the technicians aspirated the supernatant, discarded all remaining precipitate, transferred the aspirate to pre-labelled tubes, and placed them in a biospecimen refrigerator for archival (in 1 ml aliquots at -80° C) or assay (200 ul aliquot). The LCBR technicians entered all aliquot information into the LIMS system.

## 4. Assay and Internal Quality Control

### 4.1 High Sensitivity C-Reactive Protein [H5CRP]

#### 4.1.1 Rationale

CRP is produced by the liver in response to inflammation. It also is a fairly stable protein that can be sensitively measured with precision using standardized laboratory procedures<sup>2</sup>. Moreover, in asymptomatic, intermediate-risk men aged ≤ 50 years and women ≤ 60 years, measurement of hsCRP may be useful in cardiovascular risk assessment.<sup>4</sup>

#### 4.1.2 Assay

All hsCRP assays were run on the same day of sample arrival at LCBR using the Siemens BNII / BN Prospec System (Siemens Healthcare Diagnostic Products GmbH, Marburg, Germany) and an hsCRP-specific particle enhanced immunonephelometric assay. Serum from venous blood collected using the SST vacutainer tubes was introduced into the Siemens system by placing sample vials holding 200 µl of serum into an automatic sampling tray, after which all processes were automatically performed and

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results output by the Siemens system. All samples were automatically run at a sample dilution of 1:20 with N diluent.

The Siemens system read barcodes on the vials to automatically determine which assays to run. In addition to hsCRP, Cystatin C also was run using the Siemens system. Only the hsCRP assay is described below. Assay protocols for Cystatin C can be found in the Add Health Renal Function User Guide.

In the hsCRP assay, polystyrene particles coated with monoclonal antibodies specific to human CRP were aggregated when mixed with serum containing CRP. These aggregates scattered a beam of light passed through the sample. The intensity of the scattered light was proportional to the concentration of the relevant protein in the sample. The result was evaluated by comparison with a standard of known concentration.<sup>5</sup>

Reference curves were generated by multi-point calibration. Serial dilutions of N Rheumatology Standard SL were automatically prepared by the instrument using N Diluent. The exact measuring range depended upon the concentration of the protein in each lot of N Rheumatology Standard SL. The analytical sensitivity of the assay was determined by the lower limit of the reference curve and therefore depended upon the concentration of the protein in the N Rheumatology Standard SL. A typical detection range for CRP was 0.175 – 9.75 mg/L for measurements performed using a sample dilution of 1:20. The following reagents and materials were used in the assay and supplied by Siemens Healthcare (Newark, DE).

- CardioPhase hsCRP; Cat. # OQIY21
- N Supplementary Reagent/Precipitation; Cat. # OUMU15
- N/T Rheumatology Control SL/1; Cat. # OQDB13
- N/T Rheumatology Control SL/2; Cat. # OQDC13
- Apolipoprotein Control Serum CHD; Cat. #OUPH07
- N Rheumatology Standard SL; Cat. # OQKZ13
- BNII Additive; Cat. # OQKY61
- N Diluent; Cat. # OUMT65
- Reaction Buffer; Cat. # OUMS65

#### 4.1.3 Internal Quality Control

The Siemens system was maintained daily by inspecting all tubing, connections, and syringes for leaks, kinks, cracks, or contamination. Reaction buffers, N diluent, and wash solutions were also replaced daily.

N/T Rheumatology Controls SL/1 and SL/2 and Apolipoprotein Control Serum was assayed after each establishment of a reference curve, the first use of a reagent vial as well as with each run of samples. LCBR also ran EDTA and serum controls as specimen samples each time a new standard curve was established. In addition to the daily quality control, LCBR used two pools of samples from twenty normal donors (US Biologicals, Salem, MA) in longitudinal quality control analyses. One pool was an EDTA plasma normal donor pool (Lot #E050115). The other pool was a serum normal donor pool (Lot #S042715). LCBR periodically assayed both pools over the course of Wave V. The plasma and serum hsCRP concentration mean (coefficient of variation) based on those assays was 4.6 µg/dl (6.3%) and 7.3 µg/dl (7.9%), respectively. When hsCRP concentrations exceeded acceptable parameters, the Siemens system was investigated and repaired.

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## 5. External Quality Control

### 5.1 Reliability

Within a race/ethnicity- and sex-stratified random sample of 94 Add Health respondents among whom venous blood was collected twice, on average 14.3 (95% confidence interval: 13.0-15.6) days apart, typically by the same FE and at approximately the same time of day, the reliability of hsCRP (mg/L) was estimated as an intra-class correlation coefficient (ICC, 95% confidence interval) [Exhibit 4]. The estimate suggests that the home exam venous blood collected at Add Health Wave V yields a more reliable measure of hsCRP than the dried capillary whole blood spots collected at Wave IV.

| Measure      | n  | ICC  | 95% CI       |
|--------------|----|------|--------------|
| hsCRP (mg/L) | 94 | 0.82 | (0.75, 0.89) |

**Exhibit 4. Reliability of hsCRP**

## 6. Constructed Measures

### 6.1 Classification of hsCRP [H5CCRP]

The classification of hsCRP concentrations among Add Health respondents was constructed without regard to fasting status, in accordance with the American Heart Association/Centers for Disease Control (AHA/CDC) clinical and public health practice recommendations regarding markers of inflammation and cardiovascular disease.<sup>2</sup> In keeping with the recommendations, classes of hsCRP were defined to approximate tertiles in the adult population, as tabulated below, although it should be noted that in many populations, only 5% of hsCRP concentrations exceed 10 mg/L (Exhibit 5):

| Classification | hsCRP (mg/L) | AHA/CDC Class |
|----------------|--------------|---------------|
| 1              | < 1          | Low           |
| 2              | 1 – 3        | Average       |
| 3              | > 3          | High          |

**Exhibit 5. Classification of hsCRP**

### 6.2 Count of Common Subclinical Symptoms [H5SUBCLN]

High hsCRP concentrations, particularly those exceeding 10 mg/L, should trigger searches for non-cardiovascular (e.g. infectious or inflammatory) diseases capable of seriously confounding hsCRP-based estimates of cardiovascular disease risk. Subclinical sources of infection or inflammation identified in Question 14 of the Wave V home exam also have potential to confound hsCRP-based estimates of cardiovascular disease risk in apparently healthy populations. Common symptoms identified by items H5Q014A – H5Q014G were therefore counted and categorized as previously described<sup>3,6,7</sup> for investigation or control of potential confounding in hsCRP analyses (Exhibit 6):

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| Code | Symptom Count* |
|------|----------------|
| 0    | 0              |
| 1    | 1              |
| 2    | 2              |
| 3    | ≥ 3            |

\* Subclinical sources of infection or inflammation in the last 2 weeks include the following: cold or flu-like symptoms [variable: H5Q014A = 1], Q014b fever [variable: H5Q014B = 1], night sweats [variable: H5Q014C = 1], nausea or vomiting or diarrhea [variable: H5Q014D = 1], blood in stool or feces or urine [variable:

**Exhibit 6. Count of Common Subclinical Symptoms**

### 6.3 Count of Common Infectious or Inflammatory Diseases [H5INFECT]

Although the infectious and inflammatory diseases identified in Question 13 of the Wave V home exam are not included in the symptom count tabulated above, they too may confound hsCRP-based estimates of cardiovascular disease risk. Therefore, responses to items H5Q013A – H5Q013F from this question were counted and categorized for investigation or control of potential confounding in hsCRP analyses (Exhibit 7). Please note that at Wave IV, the analogous constructed variable (C\_INFECT) included two other items in the count, namely “Asthma/Chronic Bronchitis/Emphysema” and “Hepatitis C,” which were not captured in the Wave V home exam.

| Code | Disease Count* |
|------|----------------|
| 0    | 0              |
| 1    | 1              |
| 2    | 2              |
| 3    | ≥ 3            |

\* Infectious and inflammatory diseases in the last 4 weeks include the following: gum disease/tooth loss [variable: H5Q013A = 1], active infection [variable: H5Q013B = 1], injury [variable: H5Q013C = 1], acute illness [variable: H5Q013D = 1], surgery [variable: H5Q013E = 1], and active seasonal allergies [variable: H5Q013F = 1].

**Exhibit 7. Count of Common Infectious or Inflammatory Diseases**

### 6.4 Medication Use Variables [H5CRP1 – H5CRP8]

Use of anti-inflammatory medications (and/or the diseases for which they are being taken) also may

confound hsCRP-based estimates of cardiovascular disease risk. These exposures were captured at Wave V in the home exam medication inventory, and for salicylates/nonsteroidal anti-inflammatory drugs (NSAIDs), in questions 69 and 70 of the home exam.<sup>8</sup> They should be used cautiously in the investigation or control of potential confounding in hsCRP analyses because the typical intermittency and brevity of anti-inflammatory medication use (e.g. for headache, menstrual cramps, muscle ache, etc.) and their short half-lives in the circulation reduce ability to accurately define exposure. Moreover, selection biases often threaten the study of non-randomized medication exposures. Respondents used  $\geq 1$  medication identified by  $\geq 1$  of the following questions, coded therapeutic classes, or active ingredients (Exhibit 8):

| Question / Class           | Label   | Variable |
|----------------------------|---|----------|
| Q069=yes<br>Q070=yes       | Salicylate past 24 hours or<br>Non-Steroidal Anti-Inflammatory Drug (NSAID)<br>past 24 hours  | H5CRP1   |
| 057-058-061<br>057-058-062 | NSAIDs past 4 weeks or<br>Salicylate past 4 weeks or<br>Any oral medication that contains NSAID or<br>Salicylate as an active ingredient* in a combination<br>medication past 4 weeks | H5CRP2   |
| 057-058-278                | Cyclooxygenase-2 (COX-2) Inhibitor past 4 weeks   | H5CRP3   |
| 122-130-296                | Inhaled Corticosteroids past 4 weeks  | H5CRP4   |
| 097-098-300<br>097-098-301 | Corticotropin or<br>Glucocorticoid past 4 weeks   | H5CRP5   |
| 105-192-***<br>105-270-*** | Anti-rheumatic or<br>Anti-psoriatic past 4 weeks  | H5CRP6   |
| 254-104-***<br>254-257-*** | Immunosuppressive agents or<br>Immunosuppressive monoclonal antibodies past 4<br>weeks  | H5CRP7   |
| Any of the above           | Any of the above anti-inflammatories  | H5CRP8   |

\*Active Ingredients:

#### **NSAIDS**

- Bromfenac
- Diclofenac
- Diflunisal
- Etodolac
- Fenoprofen
- Flurbiprofen
- Ibuprofen
- Indomethacin
- Ketoprofen
- Ketorolac
- Meclofenamate
- Mefenamic Acid
- Meloxicam
- Nabumetone
- Naproxen
- Oxaprozin
- Piroxicam
- Sulindac
- Tolmetin

#### **Salicylates**

- Aspirin
- Choline salicylate
- Magnesium salicylate
- Salsalate
- Sodium salicylate
- Thiosalicylate

### **Exhibit 8. Anti-Inflammatory Medications**

Add Health is a program project directed by Kathleen Mullan Harris and designed by J. Richard Udry, Peter S. Bearman, and Kathleen Mullan Harris at the University of North Carolina at Chapel Hill, and funded by grant P01-HD31921 from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, with cooperative funding from 23 other federal agencies and foundations. Information on how to obtain the Add Health data files is available on the Add Health website (<http://www.cpc.unc.edu/addhealth>).

## 7. The Inflammation and Immune Function Data File (bcrp5.xpt)

### 7.1. Structure

The structure of the disseminated inflammation and immune function data file is flat. This means that it is a respondent-level data file, where each respondent has one and only one record. The respondent's identifying number (the AID variable) will appear in the data file only once.

### 7.2. Contents

The inflammation and immune function data file includes the variables below, which are described in the corresponding codebook documentation that also contains frequencies.

| <b><u>Variable Name</u></b> | <b><u>Variable Description</u></b>                                    |
|-----------------------------|---|
| AID                         | Respondent Identifier   |
| H5CRP                       | hsCRP assay result (mg/L)   |
| H5CCRP                      | hsCRP AHA/CDC classification  |
| H5Q013A                     | Q013a Gum disease/tooth loss in last 4 weeks                          |
| H5Q013B                     | Q013b Active infection in last 4 weeks                                |
| H5Q013C                     | Q013c Injury in last 4 weeks  |
| H5Q013D                     | Q013d Acute illness in last 4 weeks                                   |
| H5Q013E                     | Q013e Surgery in last 4 weeks   |
| H5Q013F                     | Q013f Active seasonal allergies in last 4 weeks                       |
| H5INFECT                    | Q013 Count of infectious/inflammatory diseases                        |
| H5Q014A                     | Q014a Cold or Flu-like symptoms in last 2 weeks                       |
| H5Q014B                     | Q014b Fever in last 2 weeks   |
| H5Q014C                     | Q014c Night sweats in last 2 weeks                                    |
| H5Q014D                     | Q014d Nausea or vomiting or diarrhea in last 2 weeks                  |
| H5Q014E                     | Q014e Blood in stool or feces or urine in last 2 weeks                |
| H5Q014F                     | Q014f Frequent urination in last 2 weeks                              |
| H5Q014G                     | Q014g Skin rash or abscess in last 2 weeks                            |
| H5SUBCLN                    | Q014 Count of subclinical symptoms                                    |
| H5CRP1                      | Flag indicating NSAID/Salicylate medication use (24 hours)            |
| H5CRP2                      | Flag indicating NSAID/Salicylate medication use (4 weeks)             |
| H5CRP3                      | Flag indicating Cox-2 Inhibitor medication use (4 weeks)              |
| H5CRP4                      | Flag indicating Inhaled Corticosteroid medication use (4 weeks)       |
| H5CRP5                      | Flag indicating Corticotropin/Glucocorticoid medication use (4 weeks) |
| H5CRP6                      | Flag indicating Anti-rheumatic/Anti-psoriatic med use (4 weeks)       |
| H5CRP7                      | Flag indicating Immunosuppressive medication use (4 weeks)            |
| H5CRP8                      | Flag indicating any Anti-Inflammatory medication use (4 weeks)        |

## 8. References

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