**Treatment Options for type 2 Diabetes in Adolescents and Youth**

**TODAY2 PHASE 2 (T2P2)**

**LONG-TERM POST-INTERVENTION OBSERVATIONAL FOLLOW-UP**



Manual of Procedures

Control Echocardiogram and Blood Data Collection

Distributed by

TODAY Coordinating Center

George Washington University Biostatistics Center

6110 Executive Boulevard, Suite 750

Rockville, MD 20852

November 7, 2014

|  |
| --- |
| **CONFIDENTIAL** |

**Changes to MOP**

**Changes made on November 7, 2014**

**5.3, In–person Data Collection Visit**

Corrected the language regarding the types of CBL tubes used in collecting the serum and EDTA storage specimens.

**Table of Contents**

[1 Introduction 2](#_Toc399503993)

[2 Verification of Fasting for Blood Draw 2](#_Toc399503994)

[3 Blood Pressure 3](#_Toc399503995)

[4 Anthropometrics 5](#_Toc399503996)

[4.1 Height (cm) 5](#_Toc399503997)

[4.2 Weight (kg) 6](#_Toc399503998)

[4.3 Table of Weights by Heights for BMI of 18.5, 25, and 30 6](#_Toc399503999)

[5 Participant Eligibility, Screening, and Data collection 8](#_Toc399504000)

[5.1 Eligibility Criteria 8](#_Toc399504001)

[5.2 Screening Contact or Visit 8](#_Toc399504002)

[5.3 In –person Data Collection Visit 8](#_Toc399504003)

[6 Echo Control Imaging Protocol (Echocardiogram Views) 10](#_Toc399504004)

[7 Data collection and management 12](#_Toc399504005)

[7.1 Data Forms 13](#_Toc399504006)

[7.1.1 FRESH, CBL Fresh Specimen Transmittal Shipment 13](#_Toc399504007)

[7.1.2 FROZE, CBL Frozen Specimen Transmittal Shipment 13](#_Toc399504008)

[7.1.3 ECHODOC, Echocardiogram Documentation 13](#_Toc399504009)

[7.1.4 PTDATA, Eligibility and Participant Data 13](#_Toc399504010)

[8 Safety and alerts 14](#_Toc399504011)

[8.1 Immediate Safety Alert Actions 14](#_Toc399504012)

[8.2 Individual/PCP Notification of Safety Alerts 15](#_Toc399504013)

*Maintained by TODAY Coordinating Center*

*George Washington University Biostatistics Center*

# Introduction

In addition to this document, procedures are also described in the protocol and on the forms. Measurements are made so that the control data and the study data are comparable. The table summarizes sources for procedures for the various study activities.

|  |  |
| --- | --- |
| **Activity** | **Procedures** |
| recruitment and enrollment | Presented in the Protocol. |
| echocardiogram | Procedures same as in TODAY/TODAY2 provided by the Echocardiography Reading Center. Sonographers will undergo training and certification by the Echocardiography Reading Center. |
| blood draw | Per local practice, by appropriately trained and certified staff. If participant has volunteered and is eligible for a fasting draw, T/T2 procedures to verify fasting are given below. Those drawing, processing, and shipping blood must be certified. |
| blood processing and shipment | Manual of procedures provided by the T/T2 Central Biospecimen Laboratory. |
| blood pressure | Instructions are given below and on Form PTDATA. Standard clinic equipment is used. Clinic staff must be certified. |
| height | Instructions are given below and on Form PTDATA. Standard clinic equipment is used. Clinic staff must be certified. |
| weight | Instructions are given below and on Form PTDATA. Standard clinic equipment is used. Clinic staff must be certified. |
| forms | Instructions on form completion are included with each form. Additional instructions can be found in this document. |
| data entry  | Data collected is entered in the T/T2 web based data entry system. Keyers must be trained and certified. Additional information can be found in the MIDAS manual of procedures. |
| alerts and follow-up | Presented in the Protocol. |
| data management | Presented in the Protocol. |
| participant management | Presented in the Protocol. |

# Verification of Fasting for Blood Draw

Verify fasting state (8 hours since last caloric intake) with participant. It is important to question participants about consumption of caloric beverages, such as soda, lemonade, juice, sports drinks (e.g., Gatorade), flavored water, tonic water, milk, tea, and coffee, as well as easily forgotten caloric foods such as gum and cough drops, over the fasting period. The following probes may be used to determine whether a participant has been fasting:

* Have you had anything to eat or drink since *<times corresponding to 8 hours ago>* last night?
* What time did you eat dinner last night and what have you eaten since?
* What did you eat for breakfast this morning?
* What did you have to drink this morning when you woke up?
* Did you wake up and drink anything throughout the night?
* What time was your bedtime snack last night?

If the fast is less than 8 hours or more than 14 hours, it is recommended to reschedule the visit within a week, however the visit can be completed at any time. All study outcomes, the blood and echocardiogram, must be collected on the same day.

# Blood Pressure

1. The right arm is used unless not available.
2. Before starting the blood pressure procedure:
	1. The participant is seated quietly in the examination room, feet flat on the floor, outer jackets, sweaters, or bulky clothing removed, and sleeves loosely rolled to the shoulder so that two fingers may be placed under the sleeve without difficulty.
	2. Position the arm with the cubital fossa supported at heart level (see Figure 4).
	3. The participant’s arm should be resting on a table or other support with the palm upward.
	4. A small participant may need to be seated on a stool so that the arm is at heart level (approximately halfway between the shoulder and the waist), and a box under the feet to prevent dangling.
	5. Allow participant to rest for 5 minutes.
3. The blood pressure cuff is chosen and placed around the participant’s upper, right arm using the following guidelines:
4. The cuff bladder width should be approximately 40% of the circumference of the upper arm (Figures 1 and 2).
5. The cuff bladder, when applied, should cover 80-100% of the length of the upper arm (Figure 3).
6. A total of three measurements are taken. Once the participant is properly positioned and rested for 5 minutes, the first measurement is taken. Allow one full minute between measurements 1 and 2 and between measurements 2 and 3.
7. Record all three blood pressure measurements on Form PTDATA. If less than 3 measurements are collected, leave the 1st reading blank (or permanently missing) on the form and in MIDAS and enter the values using the 2nd and 3rd spaces. A comment explaining why the data was missed should be entered in MIDAS.
8. Blood pressure is calculated as the averages of the 2nd and 3rd systolic (SBP) and the 2nd and 3rd diastolic (DBP) measurements.

Figure 1: Dimensions of Bladder and Cuff Related to Arm Circumference



Figure 2: Determining Proper Cuff Size, Step 1



Figure 3: Determining Proper Cuff Size, Step 2



Figure 4: Positioning of Participant’s Arm



# Anthropometrics

Height and weight are measured and recorded twice. If the 1st and 2nd values differ by the accepted amount indicated on Form PTDATA, measure and record a 3rd value. Two of the recorded values must be within the accepted difference – if not continue to take additional measures until two readings are within the accepted difference range (see section on Height and Weight collection for additional information).

General set-up:

* Location should be screened, warm, well-lit, and offer privacy, with a secure place for storing participant valuables. The room must have access to a standard clinic stadiometer and clinic scale.
* Participants are advised to wear lightweight clothing, preferably a separate top/shirt and bottom/pants or shorts.
* Outer clothing and shoes are removed.
* Participants empty their bladder and bowels prior to any measurement.
* For measuring height, it is preferable to have participants with tall hairstyles take down their hair so the bar on the stadiometer can be used as designed.

## Height (cm)

1. Height is measured in centimeters using a stadiometer. For clinical work, participants must be measured with an accurate instrument and in a standard posture.
2. The basic components of an instrument for measuring stature are:
3. a firm horizontal surface on which the subject stands;
4. a rigid vertical surface that can be brought into contact with his/her back;
5. another horizontal surface (as distinct from a narrow rod) that can move up and down the vertical one, always at right-angles to it, and can be brought into contact with the top of the participant's head; and
6. a means of measuring the distance between the two horizontal surfaces.
7. a calibrated, reliable, clinic-based stadiometer is preferred.
8. The participant stands erect with the heels, buttocks, and shoulders tangentially against the vertical surface.
9. If the participant is unwilling to take down a tall hairstyle, the hairpiece is measured with a centimeter stick and the height of the hairpiece subtracted from the height measurement.
10. The heels are together with the feet at a 45 degree angle to each other in a comfortable stance.
11. The participant looks straight ahead.
12. The examiner positions the head erect with hands below the participant’s jaw.
13. The examiner makes sure that the heels are on the floor and in the correct position.
14. The participant is instructed to take a deep breath and make him/herself as tall as possible.
15. The sliding head projector is brought down firmly on the crown of the head and the stature is recorded to the nearest tenth (0.x) of a centimeter.
16. One measurement is taken and recorded on Form PTDATA with the participant stepping away from the stadiometer after measurement.
17. Repeat steps 2-10 for a second measurement.
18. Take the difference of the two measurements, ignoring positive or negative sign.
	* If the difference is >1 cm, repeat measurement procedures until two measures are <1 cm apart and record a third measurement.
19. Site staff should perform calibration as needed per manufacturer guidelines.

## Weight (kg)

1. Weight is measured in kilograms using the existing clinic scale.
2. The scale is placed on a flat level uncarpeted surface.
3. The examiner confirms that the scale is zeroed and zeroes if necessary.
4. The participant stands comfortably, arms at the sides, and looking straight ahead.
5. The participant’s feet are parallel but not touching and centered on the scale platform.
6. The weight is recorded on Form PTDATA to the nearest tenth (0.x) of a kilogram and the participant steps off the scale.
7. Repeat steps 3-6 for a second measurement.
8. Take the difference of the two measurements, ignoring positive or negative sign.
	* If the difference is >0.2 kg, repeat measurement procedures until two measures are <0.2 kg apart and record a third measurement.
9. Site staff should perform calibration as needed per manufacturer guidelines.

## Table of Weights by Heights for BMI of 18.5 – 25 and 30

Use the following table to quickly determine if the BMI is within range for the study samples

* during phone screening when the volunteer self-reports height and weight
* at the clinic visit when measurements are made by trained staff

|  |  |  |
| --- | --- | --- |
| Height | BMI 18.5-25, Range in Weights | BMI 30, Weight |
| inches (cm) | pounds (kg) | pounds (kg) |
| 48 (122)49 (124)50 (127)51 (130)52 (132)53 (135)54 (137)55 (140)56 (142)57 (145)58 (147)59 (150)60 (152)61 (155)62 (157)63 (160)64 (163)65 (165)66 (168)67 (170)68 (173)69 (175)70 (178)71 (180)72 (183)73 (185)74 (188)75 (191)76 (193)77 (196)78 (198)  |  60.6- 81.9 (27.5-37.2) 63.2- 85.4 (28.7-38.7) 65.8- 88.9 (29.8-40.3) 68.4- 92.5 (31.0-42.0) 71.2- 96.2 (32.3-43.6) 73.9- 99.9 (33.5-45.3) 76.7-103.7 (34.8-47.0) 79.6-107.6 (36.1-48.8) 82.5-111.5 (37.4-50.6) 85.5-115.5 (38.8-52.4) 88.5-119.6 (40.2-54.3) 91.6-123.8 (41.5-56.1) 94.7-128.0 (43.0-58.1) 97.9-132.3 (44.4-60.0)101.1-136.7 (45.9-62.0)104.4-141.1 (47.4-64.0)107.8-145.6 (48.9-66.1)111.2-150.2 (50.4-68.1)114.6-154.9 (52.0-70.3)118.1-159.6 (53.6-72.4)121.7-164.4 (55.2-74.6)125.3-169.3 (56.8-76.8)128.9-174.2 (58.5-79.0)132.6-179.3 (60.2-81.3)136.4-184.3 (61.9-83.6)140.2-189.5 (63.6-86.0)144.1-194.7 (65.4-88.3)148.0-200.0 (67.1-90.7)152.0-205.4 (68.9-93.2)156.0-210.8 (70.8-95.6)160.1-216.3 (72.6-98.1) |  98.3 (44.6)102.5 (46.5)106.7 (48.4)111.0 (50.3)115.4 (52.3)119.9 (54.4)124.4 (56.4)129.1 (58.5)133.8 (60.7)138.6 (62.9)143.5 (65.1)148.5 (67.4)153.6 (69.7)158.8 (72.0)164.0 (74.4)169.4 (76.8)174.8 (79.3)180.3 (81.8)185.9 (84.3)191.5 (86.9)197.3 (89.5)203.2 (92.1)209.1 (94.8)215.1 (97.6)221.2 (100.3)227.4 (103.1)233.7 (106.0)240.0 (108.9)246.5 (111.8)253.0 (114.8)259.6 (117.8) |

# Participant Eligibility, Screening, and Data collection

## Eligibility Criteria

Eligibility assessment begins with the screening contact or visit. Eligibility is determined by responses to questions on form PTDATA and lab analysis of HbA1c. Eligibility criteria are below:

Sample 1 Obese Controls Eligibility Criteria

Inclusion

1. Body mass index (BMI) >30 kg/m2.
2. Age 18-30 years.
3. Consent to blood draw for testing HbA1c and FGF-23.
4. Signed informed consent form.

Exclusion

1. Pregnant female.
2. Diagnosed with diabetes (either type 1 or type 2) or HbA1c >6.5% determined by central lab analysis of screening blood drawn.
3. Diagnosed with hypertension or taking anti-hypertensive medication or screening blood pressure ≥130/80.
4. Any non-removable orthopedics (e.g. cast).

Sample 2 Lean Controls Eligibility Criteria

Inclusion

1. Body mass index (BMI) 18.5-25 kg/m2.
2. Age 18-30 years.
3. Consent to blood draw for testing HbA1c and FGF-23.
4. Signed informed consent form.

Exclusion

1. Pregnant female.
2. Diagnosed with diabetes (either type 1 or type 2) or HbA1c >6.5% determined by central lab analysis of screening blood drawn.
3. Diagnosed with hypertension or taking anti-hypertensive medication or screening blood pressure ≥130/80.
4. Any non-removable orthopedics (e.g. cast).

## Screening Contact

Screening is performed over the phone using worksheet SCREEN to document responses and determine initial eligibility. Once an individual fails a screening criterion, the screening process STOPS. Procedures are:

Initial Contact

* Phone capture includes age, self report diagnosis of diabetes, hypertension, or taking an anti-hypertensive medication. Self reported height and weight are also captured to determine estimated BMI.
* Individuals who pass the inclusion criteria are invited to an in-person clinic visit. Participants are advised that if they are eligible and willing to undergo a blood draw at the visit, they must arrive fasting (nothing to eat or drink except water **8 hours prior to the visit**).

## In–person Data Collection Visit

Participants who meet the initial eligibility requirements are asked to come in for a blood draw and echocardiogram. Eligibility continues to be verified until the HbA1c results have been received. Additional information is documented on forms PTDATA, FRESH, FROZE, and ECHODOC. If at any time during the completion of form PTDATA the individual fails an eligibility criterion, the process STOPS.

In–person Clinic Visit

* Informed consent is obtained.
* Eligibility assessment continues using more invasive methods to measure height and weight to determine BMI and to measure blood pressure. Collected on form PTDATA.
* Individuals who pass the in-person criteria (signed informed consent, BMI in range, BP in range) continue with visit procedures including echocardiogram and blood draw.
* Blood is collected as follows:
	+ One 2 mL (purple top) EDTA blood sample is collected to analyze HbA1c to detect diabetes. Specimens are sent to the CBL using Form FRESH.
* One 5 mL (lavender top) EDTA blood sample is collected and stored at the site. Samples are batched and sent at periodic times during the study to Thomas Jefferson University and then forwarded to Lurie Children’s Hospital for analysis to determine Fibroblast Growth Factor-23 (FGF-23). FGF-23 is a biomarker for cardiovascular disease and is related to heart muscle growth.
	+ Optional blood is drawn and sent to CBL for storage and future testing in those who consent. Specimens are sent using form FROZE.
		- One 10 mL (red top) for serum storage
		- One 10 mL (purple top) for EDTA storage
* Participants who have the fasting blood draw are given a light breakfast/snack prior to the echocardiogram collection.
* Echocardiogram images are collected. Echocardiogram views are presented in section 6.

The blood and echocardiogram must be collected on the same date. If the participant is fasting less than 8 hours or more than 14 hours, it is recommended to reschedule the visit within a week, however the visit can be completed at any time. *All study outcomes, the blood and echocardiogram, must be collected on the same day.*

* The following incentive and visit reimbursement amounts are distributed:
	+ Individuals who attend an in-person clinic visit and sign informed consent form but are determined not eligible due to values of BMI or BP receive $25 for time and travel.
	+ Individuals who attend the in-person clinic visit, sign informed consent form, have an echocardiogram, provide blood for HbA1c and FGF-23, and complete study forms receive $75 for time and travel.
	+ Individuals who attend the in-person clinic visit, sign informed consent form, have an echocardiogram, provide blood for HbA1c and FGF-23, complete study forms, and provide additional blood for storage receive $100 for time and travel.

Post-Visit

* CBL returns the value of HbA1c to complete the eligibility process. If HbA1c >6.5% then the individual is ineligible and any data collected are removed from the CBL dataset via the TODAY Coordinating Center. Results can and should be shared with the participant.
* Echo and HbA1C findings are conveyed to participants and their designated healthcare provider in a follow-up letter. Alert values may initiate a more immediate response – see the section on Safety.

## Ineligible Participants

Once a participant is found to be ineligible, the visit stops.

Ineligible due to measured anthropometrics

The visit is complete once a participant is found ineligible due to BMI category or blood pressure as measured by certified staff. A participant is also ineligible if not all anthropometric measures are completed. For example, if a participant is only willing to give one height measurement, the visit stops. Subsequent questions on form PTDATA are marked permanently missing on the form and in MIDAS. The participant receives a $25 incentive for time and travel.

Blood Pressure. The procedure for measuring BP is (1) measure after 5 minutes sitting at rest, (2) measure 1 minute later, (3) measure 1 minute later.

* If the average of the 2nd and 3rd BP > 130/80, then note in the follow-up letter.
* If either the 2nd or 3rd BP > 140/100, then the clinic study MD asks the participant about symptoms and at his/her discretion either note in the follow-up letter or escort to ER or clinic for immediate follow-up.

HbA1c

HbA1c is the only eligibility criteria that must be analyzed by a laboratory. Eligibility is indicative of a result <6.5%. Once the results are returned from CBL (usually a week after shipment to CBL), site staff should enter the value on form PTDATA to confirm or negate eligibility. If the HbA1c result is >6.5%, the participant is ineligible. The echocardiogram is removed from the study dataset by site staff and the coordinating center contacts CBL to remove the blood results. The participant still receives the $75 incentive for completing the visit (+$25 for optional blood draw). The participant also receives the summary letter for the completed tests.

# Echo Control Imaging Protocol (Echocardiogram Views)

**Parasternal Long Axis View**

* View 1 - Two Dimensional Parasternal long axis view
	+ Interventricular septum should be perpendicular to ultrasound beam
* View 2 - Parasternal long axis with focus on the aortic root and ascending aorta
* View 3 – M mode of aorta/left atrium
* View 4 - M mode of left ventricle
	+ The cursor should be placed just past the tips of the mitral valve leaflets
	+ Edges should be clearly defined
* View 5 - Parasternal long axis view with color flow Doppler
	+ Assess foraortic or mitral valve insufficiency
* View 6 – Modified parasternal long axis view to show right ventricular inflow
* View 7 – Add color flow Doppler to view 6
	+ Assessfor tricuspid valve insufficiency
* View 8 - Add continuous wave Doppler to View 7
	+ Assess peak tricuspid insufficiency velocity

**Parasternal Short Axis**

* View 9 -Parasternal Short axis view at the aorta valve level
	+ Assess for anatomy of aortic valve (tricuspid, bicuspid, thickened…)
* View 10 - M mode of aorta/left atrium
* View 11 - Parasternal Short axis view at the aorta valve level with color flow Doppler of tricuspid valve and pulmonary valve
* View 12 - Pulsed wave Doppler of blood flow across the pulmonary valve
* View 13 - Parasternal Short axis view with color flow Doppler of the tricuspid valve
* View 14 - Continuous wave Doppler of the tricuspid insufficiency jet
	+ Assess peak tricuspid insufficiency velocity
* View 15 - Parasternal short axis of the left ventricle at the basal level
	+ Move transducer to ensure perpendicular cut
	+ Mitral valve level with left ventricular inferior wall remaining in view throughout cardiac cycle
	+ Have participant hold respiration while recording
* View 16 - Parasternal short axis of the left ventricle at the mid level
	+ Move transducer to ensure perpendicular cut
	+ Just below mitral valve leaflets
	+ Have participant hold respiration while recording
* View 17 - Parasternal short axis of the left ventricle at the apical level
	+ Move transducer to ensure perpendicular cut
	+ Have participant hold respiration while recording
* View 18 – M mode from the short axis of the left ventricle at the mid level
	+ The cursor should be placed just past the tips of the mitral valve leaflets
	+ Edges should be clearly defined

**Apical Four Chamber View**

* View 19 – Apical four chamber view
	+ All four chambers should be fully opened
	+ All walls should remain inside of sector throughout cardiac cycle
	+ Endocardium needs to be well defined
* View 20 - Apical four chamber view with focus on the mitral valve
* View 21 - Apical four chamber view with color flow Doppler of the mitral valve
	+ Assess for mitral insufficiency and mitral inflow
* View 22 – Pulsed wave Doppler at the tips of the mitral valve leaflets
* View 23 - Pulsed wave Doppler at the tips of the tricuspid valve leaflets
* View 24 - Apical four chamber view with tissue Doppler imaging at the lateral wall of the left ventricle
	+ Adjust scale and baseline so that the peak e,a and s waves are demonstrated
* View 25 - Apical four chamber view with tissue Doppler imaging at the interventricular septal wall
	+ Adjust scale and baseline so that the peak e,a and s waves are demonstrated
* View 26 - Apical four chamber view with tissue Doppler imaging at the free wall of the right ventricle
	+ Adjust scale and baseline so that the peak e,a and s waves are demonstrated
* View 27 - Apical four chamber view with focus on the right ventricle
	+ Right ventricle needs to be fully opened
	+ Define right ventricular endocardium and show apex
* View 28 - Place M mode cursor through the tricuspid annulus at the right ventricular free wall for TAPSE – Tricuspid Annular Plane Systolic Excursion
* View 29 – Apical four chamber with focus on the right ventricle with color flow Doppler
* View 30 – Continuous wave Doppler of tricuspid insufficiency
	+ Assess peak tricuspid insufficiency velocity

**Apical Two Chamber View**

* View 31 – Apical two chamber view
	+ Chambers should be fully opened
	+ All walls should remain inside of sector throughout cardiac cycle
	+ Endocardium needs to be well defined
* View 32 - Apical two chamber view with color flow Doppler
	+ Assess for mitral valve insufficiency

**Apical Long Axis**

* View 33 – Apical long axis view
	+ Chambers should be fully opened
	+ All walls should remain inside of sector throughout cardiac cycle
	+ Endocardium needs to be well defined
* View 34 - Apical long axis with color flow Doppler
	+ Assess for aortic valve insufficiency and turbulence across aortic valve
* View 35 – Apical long axis with the pulsed wave Doppler sample volume at the left ventricular outflow tract, proximal to the aortic valve
	+ Assess for left ventricular outflow tract obstruction
* View 36 - Apical long axis with the pulsed wave Doppler sample at the left ventricular outflow tract, distal to the aortic valve
	+ To assess for aortic valve stenosis

**Speckle Tracking Images**

* View 1a –Parasternal short axis – basal level
* View 1b - Parasternal short axis – mid level
* View 1c - Parasternal short axis – apical level
* View 2 – Apical four chamber with focus on the left ventricle
* View 3 – Apical short axis – “Apical cap”
* View 4 – Apical four chamber with focus on the left atrium
* View 5 – Apical two chamber view with focus on the left ventricle
* View 6 – Apical two chamber view with focus on the left atrium

**Optional Views**

* Subcostal transverse view
* Subcostal sagittal view
* Suprasternal notch view of aorta

# Data collection and management

Data are collected on study forms for screening and eligibility, to document the echocardiogram, to document the blood draw and shipment, and to characterize the participant in terms of gender, race-ethnicity, and smoking behaviors. The study forms are entered into the web-based data entry system (MIDAS) developed and maintained by the George Washington University TODAY Coordinating Center. See the MIDAS MOP for specific procedures on data entry.

The staff ID is a unique ID assigned to each certified staff member who collects study data and completes study forms. The ID consists of the first and last initial of the staff member followed by the number 1. For example, Jenni Berry 🡪 JB1. If there is another staff member with the same initials, use the subsequent number. For example, John Burke 🡪 JB2.

The technician ID is a unique ID assigned to each technician by the Echo reading center. Please contact Erin Rickets (erinricketts@jhu.edu) to request a technician ID.

Participants are assigned a unique and confidential study ID formatted as the following: the first 3 numbers are ‘**333**’ to indicate a participant in this data collection and the second set of 3 numbers is assigned to indicate the location the participant was enrolled.

* Johns Hopkins University: sequentially assign 001-299 as the second set of 3 numbers
	+ E.g., 333-001
* Nemours Children’s Clinic: sequentially assign 301-599 as the second set of 3 numbers
	+ E.g., 333-301
* Thomas Jefferson University: sequentially assign 601-899 as the second set of 3 numbers
	+ E.g., 333-601

All data are labeled with the study ID, including forms and specimens.

## Data Forms

Refer to specific completion instructions at the start of each form.

There are 4 forms completed by trained study staff:

* FRESH, CBL Fresh Specimen Shipment
* FROZE, CBL Frozen Specimen Shipment
* ECHODOC, Echocardiogram Documentation
* PTDATA, Eligibility and Participant Data

### FRESH, CBL Fresh Specimen Transmittal Shipment

This form is completed to document that the fresh specimen, HbA1c, was collected, processed, and shipped to CBL. A copy of this form is included with the specimen shipment to CBL. In the notes area, include any additional information that is relevant to the specimens and/or visit, also include the site name, site contact name, and site phone number.

### FROZE, CBL Frozen Specimen Transmittal Shipment

This form is completed to document that the frozen and storage specimens were collected, processed, and shipped to CBL. A copy of this form is included with the specimen shipment to CBL. In the notes area, include any additional information that is relevant to the specimens and/or visit, also include the site name, site contact name, and site phone number.

### ECHODOC, Echocardiogram Documentation

This form is used to document that the echocardiogram was attempted or collected and used as a checklist for the echo protocol completion.

The technician ID is a unique ID assigned to each technician by the Echo Reading Center. Please contact Erin Rickets (erinricketts@jhu.edu) to request a technician ID.

Participant information (height, weight, DOB, sex) is obtained from form PTDATA.

Each series/view of the echo is documented as obtained or not obtained. If a series/view is not collected, include a brief reason explaining why.

### PTDATA, Eligibility and Participant Data

This form is completed to determine the participant’s eligibility in the study. Once a question deems a participant ineligible, the process STOPS. Highlighted responses indicate the individual as ineligible.

* Item 2: enter the date of the in-person clinic visit. If the participant is not confirmed fasting, it is recommended to reschedule the visit within 1 week, however the visit can be completed at any time. When the participant returns for the echo and blood draw, the clinic visit date should be changed to the date of the actual visit.
* Items 3 through 8 are self-reported by the individual during the screening process. The remainder of the form is completed during the in-person clinic visit.
* Item 11: enter the measured height and weight, the BMI is auto-calculated and populated into MIDAS. A participant is ineligible due to anthropometrics if not all measures are completed.
* Item 14: enter this value using the CBL results report.

# Safety and alerts

These are alerts identified by the study and reported to the participant and his/her PCP (via the participant). Alerts are documented in the summary letter with recommendations for the participant to seek appropriate follow-up care with his/her PCP.

* + Blood Pressure
		- If the average of the 2nd and 3rd BP > 130/80, then note in the follow-up letter.
		- If either the 2nd or 3rd BP > 140/100, then the clinic study MD asks the participant about symptoms and at his/her discretion either note in the follow-up letter or escort to ER or clinic for immediate follow-up.
	+ HbA1c. The CBL notifies the clinic staff of alert levels as analyzed.
		- If value 5.8-6.5, then note in the follow-up letter with interpretation of pre-diabetes.
		- If value >6.5, then note in the follow-up letter with recommendation to be tested to confirm diagnosis of diabetes.
	+ Echocardiogram
		- Alerts and referrals are identified and confirmed by a Reading Center physician and are considered a research interpretation of the echocardiogram.
		- All results that meet criteria for a referral or alert are reported to the participant via a results letter after the visit.
		- Alerts include aortic aneurysm, flail leaflet, severe LV dysfunction, significant arrhythmia, suspected pericardial tamponade, thrombus, tumor, or vegetation.
		- The on-site sonographer may identify a condition during the echocardiogram; if so, the sonographer notifies the study MD and study staff. Because the study is performing this procedure to identify findings of immediate and urgent interest that may have clinical relevance, we are responsible for appropriate follow-up.
			* If there is a good well engaged primary care provider (PCP), the plan could be that the study MD calls the PCP and they decide together how to proceed.
			* If the participant is going to a free clinic, then the study MD needs to take responsibility for discussing with someone who can give a clinical judgment on the echo that was done and making a plan that is appropriate.
			* It may or may not be appropriate to send the echo to a referral clinic or have them talk to the Reading Center – the study echo may not be considered sufficient for clinical practice and a follow-up echo may be needed if indicated for clinical purposes.

## Immediate Safety Alert Actions

|  |
| --- |
| **Action: Immediate attention and plan for response.** |
| Left ventricular internal dimension in diastole * The most likely cause is obesity, regardless an LV this big is a risk factor for future heart failure.
 | > 6.0 cm |
| Interventricular septal thickness in diastole* Walls these thick are suggestive of chronic hypertension or possible cardiomyopathy
 | > 1.4 cm |
| Left ventricular posterior wall in diastole* Walls these thick are suggestive of chronic hypertension or possible cardiomyopathy
 | > 1.4 cm |
| Ejection fraction (fraction of blood pumped out of ventricles with each heart beat)* Values below this threshold are definite ventricular dysfunction and need cardiology assessment
 | ≤ 45% |
| Left ventricular dysfunction* See ejection fraction above, needs cardiology referral right away
 | Moderate or severe |
| Aortic root dimension* Values above this threshold are consistent with an ascending aortic aneurysm
 | > 4.5 cm |
| Left atrial dimension* Most likely causes are obesity, hypertension, and diabetes; could also be a marker for LV dysfunction
 | > 4.5 cm |

## Individual/PCP Notification of Safety Alerts

|  |
| --- |
| **Action: Note in letter to PCP for follow-up.** |
| Right ventricular systolic pressure* Could be indicative of PA hypertension, possibly secondary to sleep apnea, needs to be confirmed as these values often vary a lot day to day
 | > 40 mmHg |
| Mitral or aortic regurgitation * These findings would suggest intrinsic heart disease (unlikely this would be a new finding as these conditions have significant heart murmurs)
 | Moderate or severe |
| Stenosis of any valve | Mild, moderate, or severe |
| Mitral valve prolapse | Moderate or severe |
| Left ventricular hypertrophy * Might suggest the need for intensification of antihypertensive therapy (starting medication in a borderline individual or making sure BP is at goal in someone on treatment), otherwise the most likely cause is obesity.
 | ≥ 51 g/m2.7 |
| Clinical findings (i.e., pericardial effusion, wall motion abnormality, severe arrhythmias, bicuspid aortic valve, etc.)  | Significant |