CVD Toolkit Guideline v2.0

Instruments

Toolkit Purpose

A collection of measures to capture essential phenotypes for biomedical research related to cardiovascular diseases (CVD).

Guideline Description

The CVD toolkit can be used to collect essential phenotypes associated with CVD related research, including; Anthropometrics, CVD History (Angina, Heart Attack, Congestive Heart Failure, Thyroid Disease) and more. This document establishes guidelines (particularly applicable in Africa) on how to use the toolkit and collect detailed, relevant and harmonized phenotype and exposure data for research.

As listed below, the CVD toolkit consists of 6 Instruments, labelled Instruments 1 to 6.

Instrument	**Phenotypes**	**Instrument**	**Phenotypes**
1	Angina	4	Thyroid Disease
2	Heart Attack	5	Cardiac Blood Flow
3	Congestive Heart Failure	6	Blood Biomarkers

Important Notes

1. The toolkit employs branching logic, therefore, we recommend that it is completed in order, as some variables may or may not appear OR accept input based on the input of previously listed variables.

2. Some branching logic (specifically related to date of birth/age and biological sex) affect the display of items relevant to adult or paediatric participants across multiple instruments.

3. Any addition or removal of variables may also affect branching logic so editing of variables should be carefully positioned so as not to interrupt branching logic conditions with related variables.

4. The toolkit is recommended to be used in conjunction with the Core Phenotypes toolkit (https://github.com/h3abionet/h3aphenstds). Crucial CVD information is included in the Core Phenotypes toolkit and, therefore, not repeated here in the CVD toolkit.

5. Although not highlighted below, each instrument requires a collection date, which can be collected either manually or automatically.

6. Consistent codes are recommended for the identification of missing data, and these are incorporated into all Instruments discussed below. We recommend the use of 'Temporarily unavailable' for pending results in Instrument 8.

7. Codes for Missing Data are specified below.

Code	Value Label
-991	No information
-992	Asked but unknown
-993	Temporarily unavailable
-994	Not asked
-995	Refused
-998	Not applicable

8. We recommend that when a participant responds with an "I don't know" to a question that the interviewer firstly ensures that the participant understands the question clearly and secondly is gently encouraged to reconsider their response if possible. If "I don't know" is still the response we make use of the 'Asked but unknown' missing code. Questions where "I don't know" is a highly anticipated and valid response will have a checkbox for Unknown included - it should be noted that this will not be recognised as missing data in statistical software.

Recommendations

Instrument 1: Angina

This instrument enables the retrospective and self-reported collection of information related to a research participant's medical history and experience of Angina.

Questions	[Has the participant ever been told by a doctor, nurse, or other healthcare workers that they have angina (chest pain due to heart disease)? Has the participant ever received treatment for chest pain due to heart disease prescribed by a doctor, nurse or other healthcare workers?

	Is the participant currently taking any medication for angina prescribed by a doctor or other healthcare worker? Is the participant currently taking any herbal or traditional remedy for angina?] **Response Options**: Yes; No (If Yes) Specify prescribed medication or herbal/traditional remedies being used for angina:
Notes	- **Angina** - A chest pain that is caused when your heart muscle doesn't get enough oxygen-rich blood. - If available, the above information may be retrieved from or cross-checked with a participant's hospital and(or) patient records. - If possible, encourage the participant to bring along any prescribed medication for cross-reference.
Questions	[During the last 12 months, has the participant experienced any pain or discomfort in their chest, or pain going to the left arm or neck when they walk uphill or hurry? Is the pain or discomfort relieved if the participant stands still?] **Response Options**: Yes; No

Instrument 2: Heart Attack

The instrument enables the retrospective and self-reported collection of information related to a research participant's medical history and experience of Heart Attack.

Questions	[Has the participant ever been told by a doctor, nurse, or other healthcare workers that they have had a heart attack? Has the participant ever received medical treatment for a heart attack? Is the participant currently on treatment to prevent heart attack prescribed by a doctor, nurse, or other healthcare worker? Is the participant currently taking any herbal or traditional remedy for a heart attack?] **Response Options**: Yes; No (If Yes) Specify prescribed medication or herbal/traditional remedies being used for heart attack:
Notes	- **Heart attack** - Necrosis of the myocardium caused by an obstruction of the blood supply to the heart and often associated with chest pain, shortness of breath, palpitations, and anxiety as well as characteristic EKG findings and elevation of serum markers including creatine kinase-MB fraction and troponin. - If available, the above information may be retrieved from or cross-checked with a participant's hospital and (or) patient records. - If possible, encourage the participant to bring along any prescribed medication for cross-reference.

Instrument 3: Congestive Heart Failure

This instrument enables the retrospective and self-reported collection of information related to a research participant's medical history and experience of Congestive Heart Failure.

Questions	[Has the participant ever been told by a doctor, nurse, or other healthcare workers that they have heart failure? Has the participant ever received medical treatment for heart failure prescribed by a doctor, nurse, or other healthcare worker? Is the participant currently on treatment for heart failure prescribed by a doctor, nurse, or other healthcare worker? Is the participant currently taking any herbal or traditional remedy for heart failure?] **Response Options**: Yes; No (If Yes) Specify prescribed medication or herbal/traditional remedies being used for congestive heart failure:
Notes	- **Congestive heart failure** (CHF) - Failure of the heart to pump a sufficient amount of blood to meet the needs of the body tissues, resulting in tissue congestion and edema. Signs and symptoms include shortness of breath, pitting edema, enlarged tender liver, engorged neck veins, and pulmonary rales. - If available, the above information may be retrieved from or cross-checked with a participant's hospital and (or) patient records. - If possible, encourage the participant to bring along any prescribed medication for cross-reference.

Instrument 4: Thyroid Disease

The instrument enables the retrospective and self-reported collection of information related to a research participant's medical history and experience of Thyroid Disease.

Questions	Has a doctor ever told the participant that they have thyroid disease? **Response Options**: Yes; No (If Yes) Type of thyroid disease known? **Response Options**: Yes; No (If Yes) Specify type of thyroid disease: **Response Options**: Hyperthyroidism; Hypothyroidism; Hashimoto's thyroiditis; Graves' disease; Goiter; Thyroid nodules; Other (If Other) Specify other type of thyroid disease:

Notes	- **Thyroid disease** - A disease involving the thyroid gland. - **Hyperthyroidism** - Overactivity of the thyroid gland resulting in overproduction of thyroid hormone and increased metabolic rate. The symptoms are related to the increased metabolic rate and include weight loss, fatigue, heat intolerance, excessive sweating, diarrhea, tachycardia, insomnia, muscle weakness, and tremor. - **Hypothyroidism** - A condition in which the thyroid gland doesn't produce enough thyroid hormone. Hypothyroidism is a deficiency of thyroid hormones that can disrupt such things as heart rate, body temperature and all aspects of metabolism. Major symptoms include fatigue, cold sensitivity, constipation, dry skin and unexplained weight gain. - **Hashimoto's thyroiditis** - An autoimmune disorder caused by the production of autoantibodies against thyroid tissue. There is progressive destruction of the thyroid follicles leading to hypothyroidism. - **Graves' disease** - Hyperthyroidism associated with diffuse hyperplasia of the thyroid gland (goiter), resulting from production of antibodies that are directed against the thyrotropin receptor complex of the follicular epithelial cells. As a result, the thyroid gland enlarges and secrets increased amounts of thyroid hormones. - **Goiter** - Enlargement of the thyroid gland usually caused by lack of iodine in the diet, hyperthyroidism, or thyroid nodules. Symptoms include difficulty in breathing and swallowing. - **Thyroid nodules** - A nodular lesion that develops in the thyroid gland. The term "thyroid nodule" refers to any abnormal growth that forms a lump in the thyroid gland. - If available, the above information may be retrieved from or cross-checked with a participant’s hospital and (or) patient records. - If possible, encourage the participant to bring along any prescribed medication for cross-reference.
Questions	Has the participant ever been treated for thyroid disease? **Response Options**: Yes; No (If Yes) Specify treatment used for thyroid disease: **Response Options**: Antithyroid drugs; Radioactive Iodine; Surgery; Thyroid hormone; Other (If Other) Specify other treatment used: Have either of the participant's parents ever had thyroid disease? **Response Options**: Yes; No
Notes	- **Antithyroid drugs** (also called thionamides) are most often used to treat an overactive thyroid (hyperthyroidism). These drugs block the formation of thyroid hormone by the thyroid gland. - **Radioactive iodine** is used to treat hyperthyroidism by gradually shrinking the thyroid. - **Thyroid hormone** therapy is the use of manmade thyroid hormones to raise abnormally low levels of natural thyroid hormones in the body. - If available, the above information may be retrieved from or cross-checked with a participant’s hospital and (or) patient records. - If possible, encourage the participant to bring along any prescribed medication for cross-reference.

Instrument 5: Cardiac Blood Flow

This instrument enables the collection of information related to a research participant's cardiac blood flow i.e. blood flow through the heart. The information in this instrument should strictly be collected by a qualified healthcare professional.

Questions	Doppler Reading - Average cIMT on the right (mm): Doppler Reading - Average cIMT on the left (mm): Pulse rate:
Notes	- A **Doppler** ultrasound is a noninvasive test that can be used to estimate the blood flow through your blood vessels by bouncing high-frequency sound waves (ultrasound) off circulating red blood cells. - The **pulse rate** is a measurement of the heart rate or the number of times the heart beats per minute.

Instrument 6: Blood Biomarkers

This Protocol enables the recording of a research participant's laboratory results with regards to CVD Blood Biomarkers. The information recorded in this Protocol needs to be gained from qualified medical laboratory facilities with trained and qualified laboratory staff.

Questions	Fasting plasma glucose: HbA1c: High-density lipoprotein: Low-density lipoprotein: Insulin: Total cholesterol: Triglycerides:
Notes	- Dates should be collected in the following format - DD-MM-YYYY - **Fasting plasma glucose** refers to an individual's blood sugar level after fasting or not eating anything for at least 8 hours. - **HbA1c** refers to glycated haemoglobin i.e. the amount of blood sugar (glucose) attached to haemoglobin. - **High-density lipoprotein** refers to lipoprotein which absorbs cholesterol and carries it back to the liver. - **Insulin** is a peptide hormone that regulates the metabolism of carbohydrates, fats and protein by promoting the absorption of glucose from the blood into the liver, fat and skeletal muscle cells. - **Low-density lipoprotein** refers to lipoprotein which leads to build-up of cholesterol in arteries. - **Total cholesterol** is a measure of the total amount of cholesterol in your blood. - **Triglycerides** refer to the major form of fat stored by the body.

Abbreviations

cIMT: Carotid Intima-Media Thickness Test

CHF: Congestive Heart Failure
CVD: Cardiovascular Disease
EKG: Electrocardiogram
HbA1c: Hemoglobin A1c Test
SCD: Sickle Cell Disease

Administration

Mode of Administration

	Instruments					
	1	2	3	4	5	6
Interview OR Self-administered questionnaire	X	X	X	X		
Clinical assessment					X	
Bioassay/Lab- based assessment						X

Life Stage

	Instruments					
	1	2	3	4	7	8
Infancy (0 - 12 months)					X	X
Toddler (13 - 24 months)					X	X
Childhood (2-11 years)					X	X
Adolescence (12 - 18 years)	X	X	X	X	X	X
Adult (18 and older)	X	X	X	X	X	X

Personnel and Training Required

Instruments 1 to 4 may be implemented as either self-reported questionnaires or interviewer-administered questionnaires. If interviewer-administered, interviews should be conducted by trained study coordinators or data collectors who speak the native/local language of the target population. Information in these instruments may also be recorded from and (or) cross-checked with hospital and (or) patient records. The information recorded in **Instrument 5** needs to be collected by qualified healthcare professionals, while information recorded in **Instrument 6** needs to be gained from qualified medical laboratory facilities, with trained and qualified laboratory staff.

References

The CVD toolkit is based on and aligned with several existing standards, to facilitate data harmonisation. These resources are listed below:

1. Instrument - Angina (https://www.phenxtoolkit.org/protocols/view/40601)
2. Instrument - Myocardial Infarction (https://www.phenxtoolkit.org/protocols/view/40801)
3. AWI-Gen Collaborative Centre - Cardiometabolic Disease Research Instruments
4. Stroke Investigative Research & Educational Network (SIREN) Instruments
5. Owolabi MO, Akpa OM, Made F, Adebamowo SN, Ojo A, Adu D, Motala AA, Mayosi BM, Ovbiagele B, Adebamowo C, Tayo B, Rotimi C, Akinyemi R, Gebregziabher M, Sarfo F, Wahab KW, Parekh RS, Engel ME, Chisala C, Peprah E, Mensah G, Wiley K, Troyer J, Ramsay M; as members of the CVD Working Group of the H3Africa Consortium. Data Resource Profile: Cardiovascular H3Africa Innovation Resource (CHAIR). Int J Epidemiol. 2019 Apr 1;48(2):366-367g. doi: 10.1093/ije/dyy261. PMID: 30535409; PMCID: PMC6469307.

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Contact Us

For queries related to this standard and guideline, users can log a ticket to the Phenotypes Standards queue in the H3ABioNet Helpdesk. User feedback and improvements on the current toolkit are welcome and encouraged. These can also be submitted through the Helpdesk, or on our GitHub Issues page.