Family History Toolkit Guideline v2.0

Instruments

Toolkit Purpose

A collection of measures to capture essential phenotypes associated with Family History (FH) related biomedical research.

Guideline Description

The FH toolkit can be used to collect essential information pertaining to the medical history of a research participant's family. First, we define the types of relationships within the family, as we acknowledge that some family composition is not always biological. We then break down the various medical information we wish to glean into their various body systems, such as respiratory system, musculoskeletal system, nervous system etc. The following 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 FH toolkit consists of 15 Instruments, labeled Instruments 1 to 15:

Instrument	**Phenotypes**	**Instrument**	**Phenotypes**
1	Family Composition	9	FH: Urogenital System Disorders
2	FH: Chronic Infectious Diseases	10	FH: Endocrine System Disorders
3	FH: Mental Disorders	11	FH: Circulatory System Disorders
4	FH: Nervous System Disorders	12	FH: Musculoskeletal System Disorders
5	FH: Vision and Hearing Disorders	13	FH: Integumentary System Disorders
6	FH: Respiratory System Disorders	14	FH: Developmental Disorders
7	FH: Cardiovascular System Disorders	15	FH: Traumatic Life Events
8	FH: Digestive System Disorders		

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 current pregnancy) affects 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).

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.

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.

9. The instruments listed in this toolkit can be administered to either the research participants themselves, or, in the case of young research participants, to their parents or guardians.

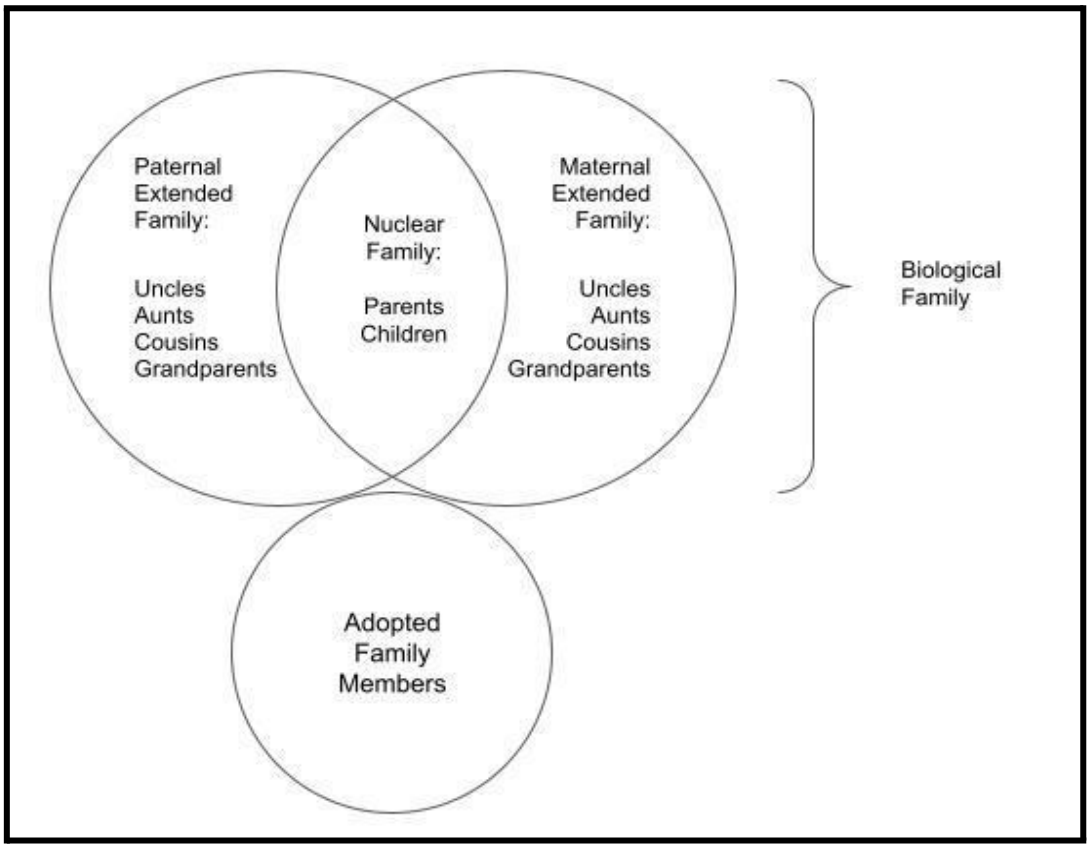
10. Important terms and concepts to be clarified for the use of the toolkit:

    Biological Family - Family and its members who are related by blood. The concept may be discussed in terms of a person's blood relations or relatives as opposed to family relations acquired by marriage, adoption, or fostering.

    Adopted Family - Family that contains at least one adopted child and at least one adoptive parent i.e. a person(s) assumes the parenting of another, from that person's biological parents.

    Nuclear Family - A family group consisting of a research participant, their biological parents and children.

    Extended Family - A family that extends beyond the nuclear family, consisting of aunts, uncles, grandparents, and cousins.



Recommendations

Instrument 1: Family Composition

The instrument enables the collection of a research participant's family composition.

<table>
<tr><td>Questions</td><td>It has been confirmed that the participant understands the following family relational terms:
Response Options:
Biological; Adopted; Nuclear; Extended
Does the participant have biological siblings with whom they share at least one parent? (half siblings and those who have passed away are included)
Response Options: Yes; No; Not Sure
Does the participant have 'siblings' with whom they do not share any parents? (those who have passed away are included)
Response Options: Yes; No; Not Sure</td></tr>
<tr><td>Notes</td><td>- ‘Siblings’ with whom participants do not share a parent with, should be excluded from further questions related to nuclear family members, and should only be included in extended family questions if the participant knows the biological relation.</td></tr>
<tr><td>Questions</td><td>How many biological siblings (including those passed away) does the participant have?
Does the participant have any stepchildren or adopted children?
How many biological children does the participant have?
How many of the participant's nuclear family members are alive?
How many of the participant's nuclear family members have passed away?
(If ANY) Indicate the health conditions that may have contributed to their death/s:
Response Options:
Cancer;
Cardiovascular System Disorder;
Circulatory System Disorder;
Digestive System Disorder;
Endocrine System Disorder;
Infectious Disease;
Integumentary System Disorder;
Mental Disorder;
Musculoskeletal System Disorder;
Nervous System Disorder;
Respiratory System Disorder;
Other
(If Other) Specify other health condition/s contributing to cause of death/s:
If known, provide the specific health condition/s contributing to cause of death/s:
Provide a brief narrative about the participant's overall nuclear and extended family health:</td></tr>
<tr><td>Notes</td><td>- Adopted and stepchildren should be excluded from further questions related to nuclear and extended families in subsequent questions instruments.
- A family health narrative is collected to tease out family health history of which a participant is less sure of the exact details, or can't communicate it efficiently.
- Disease Examples:
<table>
<tr><td>Disease</td><td>Description</td></tr>
<tr><td>Infectious Disease</td><td>TB; HIV; Malaria</td></tr>
<tr><td>Musculoskeletal Disease</td><td>Arthritis; Gout; Fibromyalgia</td></tr>
</table></td></tr>
</table>

Nervous System Disease	Alzheimer's; Parkinson's; Dementia; Epilepsy
Cardiovascular Disease	Congenital Heart Disease; Arrhythmia; Heart failure
Endocrine System Disease	Type 1 Diabetes; Type 2 Diabetes; Hyperthyroidism
Mental Disorders	Anxiety Disorder; Bipolar Disorder; PTSD
Digestive System Disease	Inflammatory Bowel Disease; Liver disease
Respiratory System Diseases	Asthma; Emphysema; Cystic Fibrosis
Urogenital System Diseases	Chronic Kidney Disease; Kidney Stones
Circulatory System Diseases	Sickle Cell Disease; Haemophilia; Anemia
Integumentary System Diseases	Psoriasis; Eczema; Vitiligo

Instrument 2: FH - Chronic Infectious Diseases

The instrument enables the self-report collection of a research participant's family history of infectious diseases.

Questions	How many nuclear family members have had a chronic infectious disease? (If ANY) Specify the chronic infectious disease/s: **Response Options**: see Notes (Disease descriptions) (If Other) Specify other chronic infectious disease/s: How many extended family members have had a chronic infectious disease?
Notes	- Disease descriptions:

Disease	Description
Hepatitis	Inflammation of the liver; usually from a viral infection, but sometimes from toxic agents.
HIV	Includes the spectrum of human immunodeficiency virus infections that range from asymptomatic seropositivity, thru AIDS-related complex, to acquired immunodeficiency syndrome (AIDS).
HPV	HPV is the most common sexually transmitted infection. Many people with HPV don't develop any symptoms but can still infect others through sexual contact. Symptoms may include warts on the genitals or surrounding skin.
Malaria	A life-threatening parasitic disease caused by Plasmodium parasites that are transmitted by Anophles mosquito bites to humans and is typically clinically characterized by attacks of fever, headache, chills and vomiting.

	Trypanosomiasis	A parasitic disorder caused by protozoa of the Trypanosoma brucei species. It is transmitted by flies and is endemic in various regions of Sub-Saharan Africa. Signs and symptoms include fever, joint pain, headache, and significant swelling of the lymph nodes. If left untreated, the parasitic infection causes anemia, heart, kidney, and endocrine failure, and neurologic damage. Subsequently patients develop confusion, disruption of the sleep cycle, and mental deterioration.
	Tuberculosis	A chronic, recurrent infection caused by the bacterium Mycobacterium tuberculosis. Tuberculosis (TB) may affect almost any tissue or organ of the body with the lungs being the most common site of infection.

Instrument 3: FH - Mental Disorders

The instrument enables the self-report collection of a research participant's family history of mental disorders.

Questions	How many nuclear family members have had a mental disorder? (If ANY) Specify the mental disorder/s: **Response Options**: see Notes (Disease descriptions) (If Other) Specify other mental disorder/s: How many extended family members have had a mental disorder?
Notes	- Disease descriptions:

Disease	Description
Anxiety Disorder	A category of psychiatric disorders which are characterized by anxious feelings or fear often accompanied by physical symptoms associated with anxiety.
Bipolar Disorder	A disorder associated with episodes of mood swings ranging from depressive lows to manic highs. Manic episodes may include symptoms such as high energy, reduced need for sleep and loss of touch with reality. Depressive episodes may include symptoms such as low energy, low motivation, and loss of interest in daily activities. Mood episodes last days to months at a time and may also be associated with suicidal thoughts.
Depression	A mood disorder that causes a persistent feeling of sadness and loss of interest and can interfere with your daily functioning.
Eating Disorder	A range of psychological conditions that cause unhealthy eating habits to develop. In severe cases, eating disorders can cause serious health consequences and may even result in death. Anorexia symptoms include trying to maintain a below-normal weight through starvation or too much exercise. Bulimia is an eating disorder marked by bingeing, followed by methods to avoid weight gain such as vomiting (purging).

Impulse Control Disorder	A class of psychiatric disorders characterized by impulsivity – failure to resist a temptation, an urge, or an impulse; or having the inability to not speak on a thought. There are five types: kleptomania (excessive stealing), pyromania (setting things on fire), intermittent explosive disorder (episodes of sudden expressions of anger), pathological gambling and trichotillomania (excessive hair pulling).
Posttraumatic Stress Disorder (PTSD)	A disorder arising from experiencing or witnessing a terrifying event. The condition may last months or years, with triggers that can bring back memories of the trauma accompanied by intense emotional and physical reactions. Symptoms may include nightmares or flashbacks, avoidance of situations that bring back the trauma, heightened reactivity to stimuli, anxiety, or depressed mood.
Personality Disorder	A mental disorder in which you have a rigid and unhealthy pattern of thinking, functioning, and behaving. A person with a personality disorder has trouble perceiving and relating to situations and people. This causes significant problems and limitations in relationships, social activities, work and school.
Substance Abuse Disorder	A disease that affects a person's brain and behaviour and leads to an inability to control the use of a legal or illegal drug or medication
Tourette Syndrome	Tourette Syndrome (TS) is a condition of the nervous system. TS causes people to have “tics”. Tics are sudden twitches, movements, or sounds that people do repeatedly. People who have tics cannot stop their body from doing these things.

Instrument 4: FH - Nervous System Disorders

The instrument enables the self-report collection of a research participant’s family history of nervous system disorders.

Questions	How many nuclear family members have had a nervous system disorder? (If ANY) Specify the nervous system disorder/s: **Response Options**: see Notes (Disease descriptions) (If Other) Specify other nervous system disorder/s: How many extended family members have had a nervous system disorder/s?
Notes	- Disease descriptions:

Disease	Description
Alzheimer’s Disease	A progressive disease that destroys memory and other important mental functions. Brain cell connections and the cells themselves degenerate and die, eventually destroying memory and other

	important mental functions. Memory loss and confusion are the main symptoms.
Cerebral Palsy	A group of disorders that affect a person's ability to move and maintain balance and posture. CP is the most common motor disability in childhood. Cerebral means having to do with the brain. Palsy means weakness or problems with using the muscles.
Dementia	A group of thinking and social symptoms that interferes with daily functioning, characterised by impairment of at least two brain functions, such as memory loss and judgement. Symptoms include forgetfulness, limited social skills and thinking abilities so impaired that it interferes with daily functioning.
Epilepsy	A disorder in which nerve cell activity in the brain is disturbed, causing seizures. Epilepsy may occur as a result of a genetic disorder or an acquired brain injury, such as a trauma or stroke. During a seizure, a person experiences abnormal behaviour, symptoms and sensations, sometimes including loss of consciousness.
Motor Neuron Disease	A nervous system disease that weakens muscles and impacts physical function. In this disease, nerve cells break down, which reduces functionality in the muscles that they supply. The cause is unknown. The main symptom is muscle weakness.
Multiple Sclerosis (MS)	A disease in which the immune system eats away at the protective covering of nerves. In MS, resulting nerve damage disrupts communication between the brain and the body. MS causes many different symptoms, including vision loss, pain, fatigue and impaired coordination. The symptoms, severity and duration can vary from person to person.
Parkinson's Disease	A disorder of the central nervous system that affects movement, often including tremors. Nerve cell damage in the brain causes dopamine levels to drop, leading to the symptoms of Parkinson's. Parkinson's often starts with a tremor in one hand. Other symptoms are slow movement, stiffness, and loss of balance.
Peripheral Neuropathy	Conditions that result when nerves that carry messages to and from the brain and spinal cord from and to the rest of the body are damaged or diseased.
Stroke	Sudden impairment of blood flow to a part of the brain due to occlusion or rupture of an artery to the brain.

Instrument 5: FH - Vision & Hearing Disorders

The instrument enables the self-report collection of a research participant's family history of musculoskeletal system diseases.

<table>
<tr><td>Questions</td><td>How many nuclear family members have had a vision or hearing disorder?
(If ANY) Specify the vision and hearing disorder/s:
Response Options: see Notes (Disease descriptions)
(If Other) Specify the other vision and/or hearing disorder/s:
How many extended family members have had a vision or hearing disorder?</td></tr>
<tr><td>Notes</td><td>- Disease descriptions:
<table>
<tr><th>Disease</th><th>Description</th></tr>
<tr><td>Blindness/ Visual Impairment</td><td>A decreased ability to see to a degree that causes problems not fixable by usual means, such as glasses OR a complete loss of vision.</td></tr>
<tr><td>Cataracts</td><td>The clouding of the lens of your eye, which is normally clear. Most cataracts develop slowly over time, causing symptoms such as blurry vision. Cataracts can be surgically removed through an outpatient procedure that restores vision in nearly everyone.</td></tr>
<tr><td>Deafness/ Hearing Impairment</td><td>Occurs when there's a problem with, or damage to, one or more parts of the ear. Also refers to complete loss of hearing.</td></tr>
<tr><td>Diplopia</td><td>Double vision occurs when a person sees a double image where there should only be one. The two images can be side by side, on top of one another, or both.</td></tr>
<tr><td>Glaucoma</td><td>A group of eye conditions that damage the optic nerve, the health of which is vital for good vision. This damage is often caused by an abnormally high pressure in your eye.</td></tr>
<tr><td>Hyperopia</td><td>A common vision condition in which you can see distant objects clearly, but objects nearby may be blurry. The degree of your farsightedness influences your focusing ability.</td></tr>
<tr><td>Myopia</td><td>A condition in which the individual does not see far distances clearly.</td></tr>
<tr><td>Strabismus</td><td>A condition in which the eyes do not properly align with each other when looking at an object.</td></tr>
<tr><td>Tinnitus</td><td>Ringing or buzzing noise in one or both ears that may be constant or come and go, often associated with hearing loss.</td></tr>
<tr><td>Vertigo</td><td>Vertigo is a dizziness characterized by a specific type of dizziness, a major symptom of a balance disorder. It is the sensation of spinning or swaying while the body is stationary with respect to the surroundings.</td></tr>
</table></td></tr>
</table>

Instrument 6: FH - Respiratory System Disorders

The instrument enables the self-report collection of a research participant's family history of respiratory system disorders.

<table>
<tr><td>Questions</td><td>How many nuclear family members have had a respiratory system disorder?
(If ANY) Specify the respiratory system disorder/s:
Response Options: see Notes (Disease descriptions)
(If Other) Specify the other respiratory system disorder/s:
How many extended family members have had a respiratory system disorder?</td></tr>
<tr><td>Notes</td><td>- Disease descriptions:
<table>
<tr><td>Disease</td><td>Description</td></tr>
<tr><td>Asthma</td><td>A chronic respiratory disease manifested as difficulty breathing due to the narrowing of bronchial passageways.</td></tr>
<tr><td>Chronic Bronchitis</td><td>Inflammation of the lining of your bronchial tubes, which carry air to and from your lungs. People who have bronchitis often cough up thickened mucus, which can be discoloured.</td></tr>
<tr><td>COPD</td><td>An anomaly that is characterized progressive airflow obstruction that is only partly reversible, inflammation in the airways, and systemic effects or comorbidities.</td></tr>
<tr><td>Cystic Fibrosis</td><td>A congenital metabolic disorder affecting the exocrine glands. Symptoms usually appear in childhood, and include meconium ileus, poor growth despite good appetite, malabsorption and foul bulky stools, chronic bronchitis with cough, recurrent pneumonia, bronchiectasis, and emphysema.</td></tr>
<tr><td>Emphysema</td><td>A lung condition that causes shortness of breath. In people with emphysema, the air sacs in the lungs (alveoli) are damaged. Over time, the inner walls of the air sacs weaken and rupture — creating larger air spaces instead of many small ones.</td></tr>
<tr><td>Sleep Apnea</td><td>A disorder characterized by multiple cessations of respirations during sleep that induce partial arousals and interfere with the maintenance of sleep.</td></tr>
</table></td></tr>
</table>

Instrument 7: FH - Cardiovascular System Disorders

The instrument enables the self-report collection of a research participant's family history of cardiovascular system disorders.

<table>
<tr><td>Questions</td><td>How many nuclear family members have had a cardiovascular system disorder/s?
(If ANY) Specify the cardiovascular system disorder/s:
Response Options: see Notes (Disease descriptions)
(If Other) Specify other cardiovascular system disorder/s:</td></tr>
</table>

	How many extended family members have had a cardiovascular system disorder?
Notes	- Disease descriptions:

Disease	Description
Arrhythmia	Any disturbances of the normal rhythmic beating of the heart or MYOCARDIAL CONTRACTION. Cardiac arrhythmias can be classified by the abnormalities in HEART RATE, disorders of electrical impulse generation, or impulse conduction.
Angina	A chest pain that is caused when your heart muscle doesn't get enough oxygen-rich blood.
Congenital Heart Disease	An abnormality in the heart that develops before birth. Congenital heart defect is one of the most common types of birth defects. Symptoms include abnormal heart rhythms, blue-tinted skin, shortness of breath, failure to feed or develop normally, and swollen body tissue or organ.
Congestive Heart Failure	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.
Hypertension	Persistently high systemic arterial BLOOD PRESSURE. Based on multiple readings (BLOOD PRESSURE DETERMINATION), hypertension is currently defined as when SYSTOLIC PRESSURE is consistently greater than 140 mm Hg or when DIASTOLIC PRESSURE is consistently 90 mm Hg or more.
Ischemic Disease	Ischemic Vascular Disease is where a waxy substance called plaque builds up inside blood vessels, and restricts the normal flow of blood.
Myocardial Infarction / Heart attack (Type 1)	A myocardial infarction (commonly called a heart attack) is an extremely dangerous condition caused by a lack of blood flow to your heart muscle. Type 1 is caused by coronary thrombosis at the site of plaque rupture or erosion that partially or completely occludes coronary blood flow.
Myocardial Infarction / Heart attack (Type 2)	A myocardial infarction (commonly called a heart attack) is an extremely dangerous condition caused by a lack of blood flow to your heart muscle. Type 2 is defined by a rise and fall of cardiac biomarkers and evidence of ischemia without unstable coronary artery disease (CAD), due to a mismatch in myocardial oxygen supply and demand.
Obesity	A status with BODY WEIGHT that is grossly above the acceptable or desirable weight, usually due to accumulation of excess FATS in the body. The standards may vary with age, sex, genetic or cultural background. In the BODY MASS INDEX, a BMI greater

	than 30.0 kg/m2 is considered obese, and a BMI greater than 40.0 kg/m2 is considered morbidly obese
Peripheral Vascular Disease	Any disorder affecting blood flow through the veins or arteries outside of the heart.
Pulmonary Stenosis	A condition characterized by obstruction to blood flow from the right ventricle to the pulmonary artery. This obstruction is caused by narrowing (stenosis) at one or more points from the right ventricle to the pulmonary artery.
Valve Disease	In heart valve disease, one or more of the valves in the heart doesn't work properly.

Instrument 8: FH - Digestive System Disorders

The instrument enables the self-report collection of a research participant's family history of digestive system disorders.

Questions	How many nuclear family members have had a digestive system disorder? (If ANY) Specify the digestive system disorder/s: **Response Options**: see Notes (Disease descriptions) (If Other) Specify other digestive system disorder/s: How many extended family members have had a digestive system disorder?
Notes	- Disease descriptions:

Disease	Description
Coeliac Disease	A condition where your immune system attacks your own tissues when you eat gluten.
Diverticulitis	The infection or inflammation of pouches that can form in your intestines. These pouches are called diverticula.
Gallstones	The impairment of bile flow, gallstones in the biliary tract, infections, and neoplasms
Gastroesophageal Reflux Disease	A digestive disorder that occurs when acidic stomach juices, or food and fluids back up from the stomach into the esophagus. GERD affects people of all ages—from infants to older adults.
Hemorrhoids	Swollen and inflamed veins in the rectum and anus that cause discomfort and bleeding. Haemorrhoids are usually caused by straining during bowel movements, obesity or pregnancy. Discomfort is a common symptom, especially during bowel movements or when sitting. Other symptoms include itching and bleeding.

Hepato-Splenomagaly	A condition that causes swelling and enlargement of the liver and spleen.
Hiatus Hernia	A condition in which part of the stomach pushes up through the diaphragm muscle.
Inflammatory Bowel Disease	A group of conditions that cause the digestive system to become inflamed (red, swollen, and sometimes painful). The most common types of IBD are ulcerative colitis and Crohn's disease. These cause similar symptoms, including diarrhea, abdominal pain, and fever.
Liver Disease	Pathological processes of the liver. Symptoms may include, yellowish skin and eyes (jaundice), abdominal pain swelling, swelling in the legs and ankle, dark urine color, pale stool color and chronic fatigue.
Malabsorption Syndrome	A number of disorders in which the small intestine can't absorb enough of certain nutrients and fluids.
Pancreatitis	An inflammation of the pancreas. Pancreatitis may start suddenly and last for days or it can occur over many years. It has many causes, including gallstones and chronic, heavy alcohol use. Symptoms include upper abdominal pain, nausea and vomiting.
Peptic Ulcers	Open sores that develop on the inside lining of your stomach and the upper portion of your small intestine. The most common symptom of a peptic ulcer is stomach pain.

Instrument 9: FH - Urogenital System Disorders

The instrument enables the self-report collection of a research participant's family history of urogenital system disorders.

Questions	How many nuclear family members have had a urogenital system disorder? (If ANY) Specify the urogenital system disorder/s: **Response Options**: see Notes (Disease descriptions) (If Other) Specify the other urogenital system disorder/s: How many extended family members have had a urogenital system disorder?

- Disease descriptions:

Disease	Description
Chronic Kidney Disease	A condition characterized by a gradual loss of kidney function over time.
Inguinal Hernia	Also known as groin hernia, occurs when tissue, such as part of

	the intestine, protrudes through a weak spot in the abdominal muscles. The resulting bulge can be painful, especially when you cough, bend over or lift a heavy object.
Kidney Stones	Hard deposits made of minerals and salts that form inside your kidneys. Diet, excess body weight, some medical conditions, and certain supplements and medications are among the many causes of kidney stones.
Urinary Incontinence	The involuntary leakage of urine. It means a person urinates when they do not want to. Control over the urinary sphincter is either lost or weakened.
Urethral stricture	Involves scarring that narrows the tube that carries urine out of your body (urethra). A stricture restricts the flow of urine from the bladder and can cause a variety of medical problems in the urinary tract, including inflammation or infection.
Urinary Retention	A condition in which you cannot empty all the urine from your bladder. Urinary retention can be acute—a sudden inability to urinate, or chronic—a gradual inability to completely empty the bladder of urine.

Instrument 10: FH - Endocrine System Disorders

The instrument enables the self-report collection of a research participant's family history of endocrine system disorders.

Questions	How many nuclear family members have had an endocrine system disorder? (If ANY) Specify the endocrine system disorder/s: **Response Options**: see Notes (Disease descriptions) (If Other) Specify other endocrine system disorder/s: How many extended family members have had an endocrine system disorder?
Notes	- Disease descriptions:

Disease	Description
Cushing's disorder	A condition that occurs from exposure to high cortisol levels for a long time. The most common cause is the use of steroid drugs, but it can also occur from overproduction of cortisol by the adrenal glands.
Growth Hormone Deficiency	Also known as dwarfism or pituitary dwarfism, a condition caused by insufficient amounts of growth hormone in the body.
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.

Hypogonadism	A failure of the gonads, testes in men and ovaries in women, to function properly.
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.
Pituitary adenoma	Non-cancerous tumours in the pituitary gland that don't spread beyond the skull.
Polycystic ovary Syndrome (PCOS)	A hormonal disorder common among women of reproductive age.
Type I Diabetes	A chronic condition in which the pancreas produces little or no insulin. Type I diabetes mellitus is manifested by the sudden onset of severe hyperglycemia with rapid progression to diabetic ketoacidosis unless treated with insulin.
Type II Diabetes	A type of diabetes mellitus initially characterized by insulin resistance and hyperinsulinemia and subsequently by glucose intolerance and hyperglycemia.

Instrument 11: FH - Circulatory System Disorders

The instrument enables the self-report collection of a research participant's family history of circulatory system disorders.

Questions	How many nuclear family members have had a circulatory system disorder? (If ANY) Specify the circulatory system disorder/s: **Response Options**: see Notes (Disease descriptions) (If Other) Specify the other circulatory system disorder/s: How many extended family members have had a circulatory system disorder?
Notes	- Disease descriptions:

Disease	Description
Anemia	A condition in which you lack enough healthy red blood cells to carry adequate oxygen to your body's tissues. Having anemia can make you feel tired and weak. There are many forms of anemia, each with its own cause. Anemia can be temporary or long term, and it can range from mild to severe.
Haemophilia	A mostly inherited genetic disorder that impairs the body's ability to make blood clots, a process needed to stop bleeding. This results in people bleeding for a longer time after an injury, easy bruising, and an increased risk of bleeding inside joints or the brain.

	Podoconiosis — A chronic inflammatory, geochemical skin disease caused by prolonged exposure to irritant red clay soils derived from volcanic rocks and causes bilateral asymmetrical swelling of the lower legs.
	Rheumatoid Arthritis — An autoimmune disease that can cause joint pain and damage throughout your body. The joint damage that RA causes usually happens on both sides of the body. So, if a joint is affected in one of your arms or legs, the same joint in the other arm or leg will probably be affected, too.
	SCID — An inherited primary immunodeficiency disease that typically presents in infancy results in profound immune deficiency condition resulting in a weak immune system that is unable to fight off even mild infections.
	Sickle Cell Disease — A pleiotropic inherited disorder of the blood, characterised by the appearance of sickle-shaped red blood cells and anemia.
	Systemic Lupus Erythematosus — An autoimmune disease. In this disease, the immune system of the body mistakenly attacks healthy tissue. It can affect the skin, joints, kidneys, brain, and other organs.
	Thalassemia — A blood disorder passed down through families (inherited) in which the body makes an abnormal form or inadequate amount of hemoglobin.
	Thrombocytopenia — A condition in which you have a low blood platelet count. Platelets (thrombocytes) are colorless blood cells that help blood clot. Platelets stop bleeding by clumping and forming plugs in blood vessel injuries.
	Thrombophilia — A condition in which there's an imbalance in naturally occurring blood-clotting proteins, or clotting factors. This can put you at risk of developing blood clots.

Instrument 12: FH - Musculoskeletal System Disorders

The instrument enables the self-report collection of a research participant's family history of musculoskeletal system disorders.

Questions	How many nuclear family members have had a musculoskeletal system disorder? (If ANY) Specify the musculoskeletal system disorder/s: **Response Options**: see Notes (Disease descriptions) (If Other) Specify the other musculoskeletal system disorder/s: How many extended family members have had a musculoskeletal system disorder?

Notes

- Disease descriptions:

Disease	Description
Arthritis	The swelling and tenderness of one or more of your joints. The main symptoms of arthritis are joint pain and stiffness, which typically worsen with age.
Bone Fracture	A complete or partial break in a bone. Causes of bone fractures include trauma, overuse and diseases that weaken bones. The main symptom is pain. There may also be loss of functionality depending on the area affected. Treatment often involves resetting the bone in place and immobilising it in a cast or splint to allow time to heal. Sometimes, surgery or metal rods may be required to reset the bone.
Carpal Tunnel	Carpal Tunnel is a narrow passageway surrounded by bones and ligaments on the palm side of your hand. When the median nerve is compressed, the symptoms can include numbness, tingling and weakness in the hand and arm.
Fibromyalgia	A disorder characterized by widespread musculoskeletal pain accompanied by fatigue, sleep, memory and mood issues. Researchers believe that fibromyalgia amplifies painful sensations by affecting the way your brain and spinal cord process painful and non-painful signals.
Gout	A condition caused by a build-up of uric acid usually affecting your feet. Symptoms include swelling and pain in the joints of your foot, particularly your big toe. Sudden and intense pain.
Guillain Barre syndrome	A rare disorder in which your body's immune system attacks your nerves. Weakness and tingling in your extremities are usually the first symptoms.These sensations can quickly spread, eventually paralyzing your whole body.
Ligament Injury	Ligament injuries may be caused by twisting or landing awkwardly, and they are most common when the ligaments around a joint are stretched fully, causing them to tear away from the bone.
Muscular Dystrophy	A group of inherited diseases that damage and weaken your muscles over time. This damage and weakness is due to the lack of a protein called dystrophin, which is necessary for normal muscle function. The absence of this protein can cause problems with walking, swallowing, and muscle coordination.
Osteoporosis	A bone disease that occurs when the body loses too much bone, makes too little bone, or both. As a result, bones become weak and may break from a fall or, in serious cases, from sneezing or minor bumps.
Rickets	A softening and weakening of bones in children, usually due to inadequate vitamin D.
Scoliosis	Scoliosis is a sideways curvature of the spine that occurs most often during the growth spurt just before puberty.

	Tendonitis — inflammation of a tendon. It happens when a person overuses or injures a tendon, for example, during sport. It is normally linked to an acute injury with inflammation. It often affects the elbow, wrist, finger, thigh, and other parts of the body.

Instrument 13: FH - Integumentary System Disorders

The instrument enables the self-report collection of a research participant's family history of integumentary system disorders.

Questions	How many nuclear family members have had an integumentary system disorder? (If ANY) Specify the integumentary system disorder/s: **Response Options**: see Notes (Disease descriptions) (If Other) Specify other integumentary system disorder/s: How many extended family members have had an integumentary system disorder?
Notes	- Disease descriptions:

Disease	Description
Albinism	A rare group of genetic disorders that cause the skin, hair, or eyes to have little or no color. Albinism is also associated with vision problems.
Atopic Dermatitis	A chronic inflammatory genetically determined disease of the skin marked by increased ability to form reagin, with increased susceptibility to allergic rhinitis and asthma, and hereditary disposition to a lowered threshold for pruritus. It is manifested by lichenification, excoriation, and crusting, mainly on the flexural surfaces of the elbow and knee.
Eczema	Eczema, also called atopic dermatitis, is a common skin condition marked by itchy and inflamed patches of skin.
Haemangioma	A birthmark often appearing as a rubbery, bright red nodule of extra blood vessels. Haemangiomas are seen more frequently among premature infants.
Neurofibromatosis	A condition characterized by changes in skin coloring (pigmentation) and the growth of tumors along nerves in the skin, brain, and other parts of the body
Psoriasis	Psoriasis is a skin disease that causes red, itchy scaly patches, most commonly on the knees, elbows, trunk and scalp. Psoriasis is a common, long-term (chronic) disease with no cure. It tends to go through cycles, flaring for a few weeks or months, then subsiding for a while or going into remission.
Vitiligo	A condition in which the skin loses its pigment cells. This can

	result in discolored patches in different areas of the body, including the skin, hair and mucous membranes. Vitiligo is a disease that causes loss of skin color in patches.

Instrument 14: FH - Developmental Disorders

The instrument enables the self-report collection of a research participant's family history of developmental disorders.

Questions	How many nuclear family members have had a developmental disorder? (If ANY) Specify the developmental disorder/s: **Response Options**: see Notes (Disease descriptions) (If Other) Specify other developmental disorder/s: How many extended family members have had a developmental disorder?
Notes	- Disease descriptions:

Disease	Description
ADHD	A disorder that can cause above-normal levels of hyperactive and impulsive behaviors. People with ADHD may also have trouble focusing their attention on a single task or sitting still for long periods of time
Autism Spectrum Disorder	A disorder beginning in childhood. It is marked by the presence of markedly abnormal or impaired development in social interaction and communication and a markedly restricted repertoire of activity and interest. Manifestations of the disorder vary greatly depending on the developmental level and chronological age of the individual.
Developmental Delay/Intellectual Disability (DD/ID)	Disorders in which there is a delay in development based on that expected for a given age level or stage of development. These impairments or disabilities originate before age 18, may be expected to continue indefinitely, and constitute a substantial impairment
Down Syndrome	A chromosomal dysgenesis syndrome resulting from a triplication or translocation of chromosome 21. Down syndrome occurs in approximately 1:700 live births. Abnormalities are variable from individual to individual and may include slowed mental development, slowed growth, flat hypoplastic face with short nose, prominent epicanthic skin folds, small low-set ears with prominent antihelix, fissured and thickened tongue, laxness of joint ligaments, pelvic dysplasia, broad hands and feet, stubby fingers, transverse palmar crease, lenticular opacities and heart disease.
Fetal Alcohol Syndrome	A disorder caused by a prenatal exposure to maternal consumption of alcohol leading to a range of behavioral, cognitive and neurological deficits in the offspring. It is characterized by physical growth problems, distinct facies, and

	varying psycho-neurological issues.
Fragile X Syndrome	A genetic syndrome caused by mutations in the FMR1 gene which is responsible for the expression of the fragile X mental retardation 1 protein. This protein participates in neural development. This syndrome is manifested with mental, emotional, behavioral, physical, and learning disabilities.
Learning Disorder	A group of disorders that affect a person's ability to learn or process specific types of information which is in contrast to his/her apparent level of intellect.

Instrument 15: FH - Traumatic Life Events

The instrument is optional and enables the self-report collection of a research participant's family history of traumatic life events.

Questions	[Have either of the participant's biological parents been exposed to 'specified traumatic life event' disaster? Have either of the participant's biological grandparents been exposed to 'specified traumatic life event' disaster?] **Response options:** Yes; No Traumatic Life Events: Natural disaster/s Military combat or a war zone Serious accident (e.g. fire or explosion) Imprisonment Racial segregation Physical assault Epidemic or pandemic

Abbreviations

ADHD: Attention Deficit Hyperactivity Disorder
AIDS: Acquired Immunodeficiency Syndrome
BMI: Body Mass Index
CHF: Congestive Heart Failure
COVID-19: Coronavirus 2019
DD: Developmental Disability
FH: Family History
EKG: Electrocardiogram
HIV: Human Immunodeficiency Virus
HPV: Human papillomavirus

ID: Intellectual Disability
MS: Multiple Sclerosis
PCO: Polycystic Ovary
PTSD: Post-traumatic Stress Disorder
SCID: Severe Combined Immunodeficiency
STD: Sexually Transmitted Disease
TB: Tuberculosis

Administration

Mode of Administration

	Instruments														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Interview OR Self-administered questionnaire	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Clinical assessment															
Bioassay/Lab-based assessment															

Life Stage

	Instruments														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Infancy (0 - 12 months)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Toddler (13 - 24 months)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Childhood (2-11 years)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Adolescence (12 - 18 years)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Adult (18 and older)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Personnel and Training Required

Instruments 1 to 15 may be implemented as either self-reported questionnaires or interviewer-administered questionnaires. If interviewer-administered, interviews should be conducted by trained or study coordinators or data collectors who speak the native/local language of the target population.

References

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

1. AWI-Gen Collaborative Centre - Cardiometabolic Disease Research Instruments
2. GA4GH Family History Tools Inventory

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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.