Assessing and Improving the Care of Heart Failure Patients in Ghana: A National Network of Heart Failure Management Centers and Teams

Protocol title: Assessing and Improving the Care of Heart Failure Patients in Ghana: A National Network of Heart Failure Management Centers And Teams

Date: 05 August 2023

Name and address of the sponsor:

Deutsche Gesellschaft für Internationale Zusammenarbeit (GIZ) GmbH

GIZ International Office

P.O. BOX KA 9698
Accra, Ghana

Principal investigators

1. Prof Isaac K Owusu, Komfo Anokye Teaching Hospital, P.O.Box 1934 Adum-Kumasi
2. Dr Alfred Doku, Korle Bu Teaching Hospital, P. O. Box 77, Korle Bu, Accra

Institutions involved in the research.

1. Bono Regional Hospital, Sunyani
2. Presbyterian Hospital- Agogo, Agogo
3. Kumasi South Hospital, Kumasi
4. Effia Nkwanta Regional Hospital, Sekondi
5. Korle Bu Teaching Hospital, Accra
6. Komfo Anokye Teaching Hospital, Kumasi
7. Tamale Teaching Hospital, Tamale
8. Ho Teaching Hospital, Ho
9. Cape Coast Teaching Hospital, Cape Coast

Contents

i. LIST OF ABBREVIATIONS

ACE-I	Angiotensin converting enzyme inhibitor
ARB	Angiotensin receptor blocker
ARNI	Angiotensin receptor neprilysin inhibitor
ASD	Atrial septal defect
AV	Aortic valve
BB	Beta blockers
BNP	Brain natriuretic peptide
CABG	Coronary artery bypass graft
CAD	Coronary artery disease
CCS	Chronic coronary syndrome
CRP	C-reactive protein
CRT	Cardiac resynchronisation therapy
CRT-D	Cardiac resynchronisation therapy with defibrillator
CRT-P	Cardiac resynchronisation therapy pacemaker
CVD	Cardiovascular disease
DHIMS2	District Health Information Systems 2
EACTS	European Association of Cardiothoracic Surgeons
ECG	Electrocardiography
EMF	Endomyocardial fibrosis
ESC	European Society of Cardiology
HF	Heart failure
HFmrEF	Heart failure with mildly-reduced ejection fraction

HFpEF	Heart failure with preserved ejection fraction
HFrEF	Heart failure with reduced ejection fraction
HRQoL	Health-related quality of life
HTX	Heart transplant
ICD	Implantable cardioverter defibrillator
INTER-CHF	International congestive heart failure study
IVS	Interventricular septal thickness in diastole
JVP	Jugular venous pressure
KATH	Komfo Anokye teaching hospital
KBTH	Korle-Bu Teaching Hospital
LEVF	Left ventricular ejection fraction
LMWH	Low molecular weight heparin
LVADs	Left ventricular assist device
LVH	Left ventricular hypertrophy
LVIDd	Left ventricular end-diastolic diameter
LVIDs	Left ventricular end-systolic diameter
LVPW	Left ventricular posterior wall thickness in diastole
MRA	Mineralocorticoid receptor antagonist
MRI	Magnetic resonance imaging
MV	Mitral valve
NSTEMI	Non-ST elevation myocardial infarction
NT-proBNP	N-terminal pro-brain natriuretic peptide
NYHA	New York Heart Association

OPD	Outpatient department
PDA	Patent ductus arteriosus
PV	Pulmonary valve
PVC	Premature ventricular contraction
QOL	Quality of life
SR	Sinus rhythm
SSA	Sub-Saharan Africa
STEMI	ST elevation myocardial infarction
SVT	Supraventricular tachycardia
TAPSE	Tricuspid annular plane systolic excursion
TOF	Tetralogy of Fallot
TSH	Thyroid stimulating hormone
TV	Tricuspid valve
UH	Unfractionated heparin
VSD	Ventricular septal defect
VT	Ventricular tachycardia
WHF	World Heart Federation

ii. LIST OF TABLES AND FIGURES

List of tables

List of figures

iii. ABSTRACT

Background

Heart failure is a leading cause of morbidity and mortality globally, with a high disease burden. The prevalence of heart failure in Ghana is increasing rapidly, but epidemiological profiles, treatment patterns, and survival data are scarce. In addition, the expertise and tools for diagnosing and appropriately managing heart failure are limited.

There is, therefore, a need to build capacity at both secondary and tertiary levels of care to identify and manage heart failure promptly and appropriately to mitigate the burgeoning epidemic, especially when risk factors for heart failure are rising.

General Aim

To determine the epidemiology and medium-term outcome of heart failure in Ghana.

Methodology

This study is a prospective, multicentre, observational study of patients with heart failure. Patients will be recruited and administered guideline-directed management of heart failure after diagnosis has been confirmed following history, physical examination and investigation, including electrocardiogram, chest x-ray, echocardiography, and laboratory investigations. Patients' data will then be collated into a heart failure registry for continuous assessment and monitoring. Patients will be followed prospectively for one (1) year to assess the medium-term outcomes of interventions.

Expected Outcome

At the end of the study, a significant gap in the landscape of HF management and research will be filled. In addition, this study will provide data on the management and outcomes of patients with HF, yielding the most extensive contemporary HF data in Ghana.

1.0 INTRODUCTION

1.1 Background

Heart failure (HF) is a complex, multi-faceted and life-threatening syndrome characterised by significant morbidity and mortality, poor functional capacity and quality of life, and high costs.
HF has been an emerging epidemic in Africa, with significantly increasing trends often presenting as an emergency. HF is a dominant form of cardiovascular disease based on hospital-based studies associated with significant hospitalisations.[12]
Africa has the highest heart failure mortality rates globally.[3] The incidence of HF in Africa and, by extension, Ghana is likely to continue rising due to the increasing prevalence of risk factors for cardiovascular diseases such as type 2 diabetes mellitus, hypertension and obesity, and continuing presence of causes of heart failure such as rheumatic heart disease and endomyocardial fibrosis.[4]

The pathophysiology of heart failure causes and management has evolved with a clearer understanding and better outcomes in developed countries.

Prompt case identification, evaluation, and appropriate management with disease-modifying drugs have improved outcomes.[5] However, management teams are largely absent in most African countries.[6] Heart failure may simulate respiratory, hepatic, or renal diseases leading to wrong diagnosis and management. Empowering health professionals with diagnostic tools, training, and management protocols will help improve patient outcomes.[7] Whilst efforts are being made to identify and manage the leading risk factor for heart failure in Africa: hypertension, there is an urgent need to build capacity at both secondary and tertiary levels of care to identify and manage heart failure promptly and appropriately to improve morbidity and mortality outcomes.[7]

Apart from building capacity in the diagnosis and management of heart failure in Ghana, there is the need to accrue epidemiological evidence on HF characteristics, management, and outcomes to understand the clinical course of heart failure in Ghana. Additionally, while most HF survival rate data worldwide are based on national registries, there are few available reliable epidemiologic statistical information to estimate the incidence, prevalence, and survival rates of HF in Ghana.

Currently, extensive data regarding demographic characteristics, prognosis, and quality of care of patients with HF in Ghana are non-existent.

Therefore, the main objective of this study is to determine the epidemiology and medium-term outcome of heart failure in Ghana.

1.2 Problem Statement

Heart failure is a significant contributor to the cardiovascular disease burden in Ghana, with a worse prognosis and a more malignant course.[8,9] It is a costly health care epidemic, bedeviled with inadequate resources to diagnose the disease, frequent undertreatment, frequent hospitalisations, poor quality of life and poor prognosis. The situation is especially dire when the risk factors for heart failure in Ghana are on a steep increase, hence, a predictable rise in incidence and burden of heart failure among the populace.[10,11]

The cardiac diagnostic capability in Ghana is limited to only a few teaching and regional hospitals. Lack of cardiac diagnostics, especially echocardiograms, means patients with heart failure or suspected heart failure will have to travel several hundred kilometres to confirm an HF diagnosis.

Healthcare workers also lack knowledge and skills in managing HF; in most cases, patients are referred to regional and teaching hospitals for further care.

Furthermore, Ghana has few cardiologists in 6 out of 16 regions, with most of these specialists in the teaching or regional hospitals.

The importance of data on the patterns and management of heart failure in Ghana cannot be overemphasised; it is relevant for comprehensive and prospective assessment of the demographic, clinical and prognostic characteristics of patients with HF to improve HF diagnosis and clinical care and as a tool for advocacy and lobbying for resource funding for heart failure care and capacity building in Ghana.

1.3 Relevance of the study

Available data on HF in Ghana is limited to individual centres. Our approach to HF management in Ghana relies on research data that have been observed and published from registries developed in advanced countries with different patient demographics and clinical profiles, diagnostic algorithms and therapeutic strategies that are most often difficult to implement because of a lack of resources and different population dynamics.

Documented information about the outcome of treatments for patients with HF, including follow-up, is very scarce in Ghana.

A study of the patterns and management of HF in Ghana will serve as a pedestal to create a national HF registry.

Establishing an HF registry will improve and develop the care of patients with HF and the diagnosis of HF by providing continuous information about the diagnosis and therapy. Additionally, an HF registry will be a valuable tool for improving the management of patients with HF since it enables participating centres to focus on improving diagnosis and medical treatment through regular updates and guidance from mentors or cardiologists.

Through this pragmatic study, diagnostic equipment for heart failure will become available as the study is integrated into routine clinics, improve the knowledge and skills of health personnel in managing HF, and ultimately improve the morbidity and mortality outcomes of HF patients in Ghana.

1.4 General objective

The general objective of this study is to determine the epidemiology and medium-term outcome of heart failure in Ghana.

1.4.1 Specific objectives

i. Describe the clinical characteristics of heart failure patients in Ghana.

ii. Determine the aetiology of HF in Ghana.

iii. Determine the rate of heart failure rehospitalisation in Ghana

iv. Determine the number of deaths in patients with heart failure in Ghana.

v. Determine the predictors of rehospitilisation and death in patients with heart failure in Ghana.

2.0 LITERATURE REVIEW

2.1 Introduction and epidemiology

Heart failure is one of the leading causes of death in Ghana. Data from the DHIMS2 (District Health Information Systems 2) positions stroke and heart failure; most are from hypertension, the two leading causes of death in adult Ghanaians.[12]

Heart failure is the ultimate pathway of many cardiovascular diseases (CVDs) and is a significant public health problem in Ghana and globally.[13] Considered the new epidemic since 1995, more than 60 million people suffer from heart failure globally, of whom 29.5 million are males, and 34.8 million are female. [13,14] The global prevalence rate per 100 000 people is estimated at 831.0, with an increasing prevalence rate peaking at ages 70–74 years in males and 75–79 years in females. [13] The age-standardised prevalence of HF varies substantially across countries and regions but was reported to be the highest in Central Europe, North Africa, and the Middle East ranging from 1133–1196 per 100 000 people in 2017. [15]

Heart failure is a growing problem in sub-Saharan Africa, but to date, there are no population-based studies estimating prevalence and incidence in Northern and sub-Saharan Africa.[16] However, several hospital-based studies have evaluated the epidemiology of HF from all medical admissions or admission to cardiac units or emergency departments. [1]

In SSA, HF epidemiology from all medical admissions varied widely, from 9.4% to 42.5% in Nigeria and 12.2% in Tanzania[1]. Additionally, a meta-analysis showed that 25.6% and 30% of admissions to cardiac units were attributable to HF in SSA. [9,17]

Albeit, a retrospective study from 2004 to 2014 in Kumasi showed that 88% of CVD admissions were attributable to HF. [8]

HF is predominantly a disease of middle age in Africa; it is most common between the third and sixth decades of life, with a mean age of 36 to 62.4 years in SSA. [17]

The prevalence and incidence of heart failure in Ghana are unknown. Hypertensive heart disease and other heart diseases were Ghana's leading cause of death, accounting for 15.34% and 4.83%, respectively, in 2017. [12,18] Additionally, a five-year retrospective study looking at heart failure

outcomes found that 32.6% died during this period, with survival rates at 1, 2 and 5 years to 90.3%, 64.7% and 38.4%, respectively. [9]

A review of autopsy cases recorded by the Department of Pathology of the Korle-Bu Teaching Hospital (KBTH), Ghana's premier health care facility, identified that among 19,289 autopsy cases completed, deaths due to CVDs accounted for about one-fifth (22.5%). [19]

Single-centre studies have reported a high prevalence of heart failure in Ghana. Data from patients attending a cardiac clinic at Komfo Anokye Teaching Hospital, Kumasi, showed a prevalence of 76%. Another study from the same institution assessing trends in cardiovascular disease admissions revealed that heart failure constituted 88.3% of all CVD disease admissions over ten years. [8]

In addition, HF is estimated to have a high disease burden, high mortality and rehospitalisation rates, impaired quality of life, and a significant economic burden, mainly due to frequent readmissions with a median hospital stay of 11-13 days in Sub-Saharan Africa. [20]

2.2 Definition of heart failure

Heart failure is a clinical syndrome rather than a specific disease with diverse aetiologies and pathology, which has made the definition of heart failure a complex and elusive undertaking.[21] Heart failure is a clinical syndrome consisting of cardinal symptoms such as breathlessness, ankle swelling, and fatigue that may be accompanied by signs such as elevated jugular venous pressure, pulmonary crackles, and peripheral oedema. It is due to a structural or functional abnormality of the heart that results in elevated intracardiac pressures and/or inadequate cardiac output at rest and/or during exercise. [22] Thus, from a clinical perspective, HF is mainly characterised by symptoms such as dyspnoea, fatigue, and fluid retention.

Heart failure can broadly be classified into distinct phenotypes based on the left ventricular ejection fraction. (LEVF) as heart failure with reduced ejection fraction, LVEF <40% or heart failure with mid-range ejection fraction, LVEF 40–49% or preserved ejection fraction (HFpEF; LVEF ≥50%). [22]

2.3 Causes of heart failure

HF is a final common pathway for many conditions affecting the heart. The risk factors and causal factors for HF have been thoroughly elucidated in literature, but their epidemiology varies according to geographic region, with hypertensive heart disease being the most common in SSA.[3,8,23]

The main aetiologies of heart failure in Ghana are hypertension, which is the leading cause in Ghana rheumatic heart disease, cardiomyopathy, degenerative valvular disease, and ischemic heart disease. [8,23,24]

Other causes of heart failure are myocarditis, congenital heart disease, pericardial disease, pulmonary hypertension, alcoholic cardiomyopathy, metabolic arrhythmias, and drug-induced and infiltrative heart disease. [22,25]

2.4 Clinical presentation of heart failure

The signs and symptoms of HF result from the clinical sequelae of inadequate cardiac output and lack of efficient venous return. [26] The typical symptoms of HF are breathlessness, orthopnoea, paroxysmal nocturnal dyspnoea, reduced effort tolerance, fatigue, and ankle swelling. [22] Other symptoms of heart failure include nocturnal cough, wheezing, bloated feeling, loss of appetite, confusion, depression, palpitation, dizziness, syncope, bendopnea, abdominal distention and right hypochondrial pain.

The symptoms are usually insidious for several weeks to months before presentation to the healthcare worker. Patients who experience a rapid deterioration in HF usually have more pronounced symptoms, resulting in an urgent visit to a hospital emergency ward.[22]

Clinical signs of heart failure are tachycardia, tachypnoea, pedal oedema, increased jugular venous pressure (JVP), lung crackles, displaced apical impulse, wheezes, S3 gallop, hepatojugular reflux, ascites and hepatomegaly.

2.5 Diagnosis of heart failure

A complete medical history and focused physical examination are essential in diagnosing heart failure, providing vital information regarding aetiology of HF and possible exacerbating factors, and offering fundamental data for proper management of patients.

The diagnosis of HF can be difficult since symptoms and clinical findings typical of HF are non-specific. HF requires the presence of typical symptoms of heart failure, which may not always be present and evidence of cardiac dysfunction (Figure 1). [22] Although these criteria are concrete and explicit, diagnosing can still be challenging.[22]

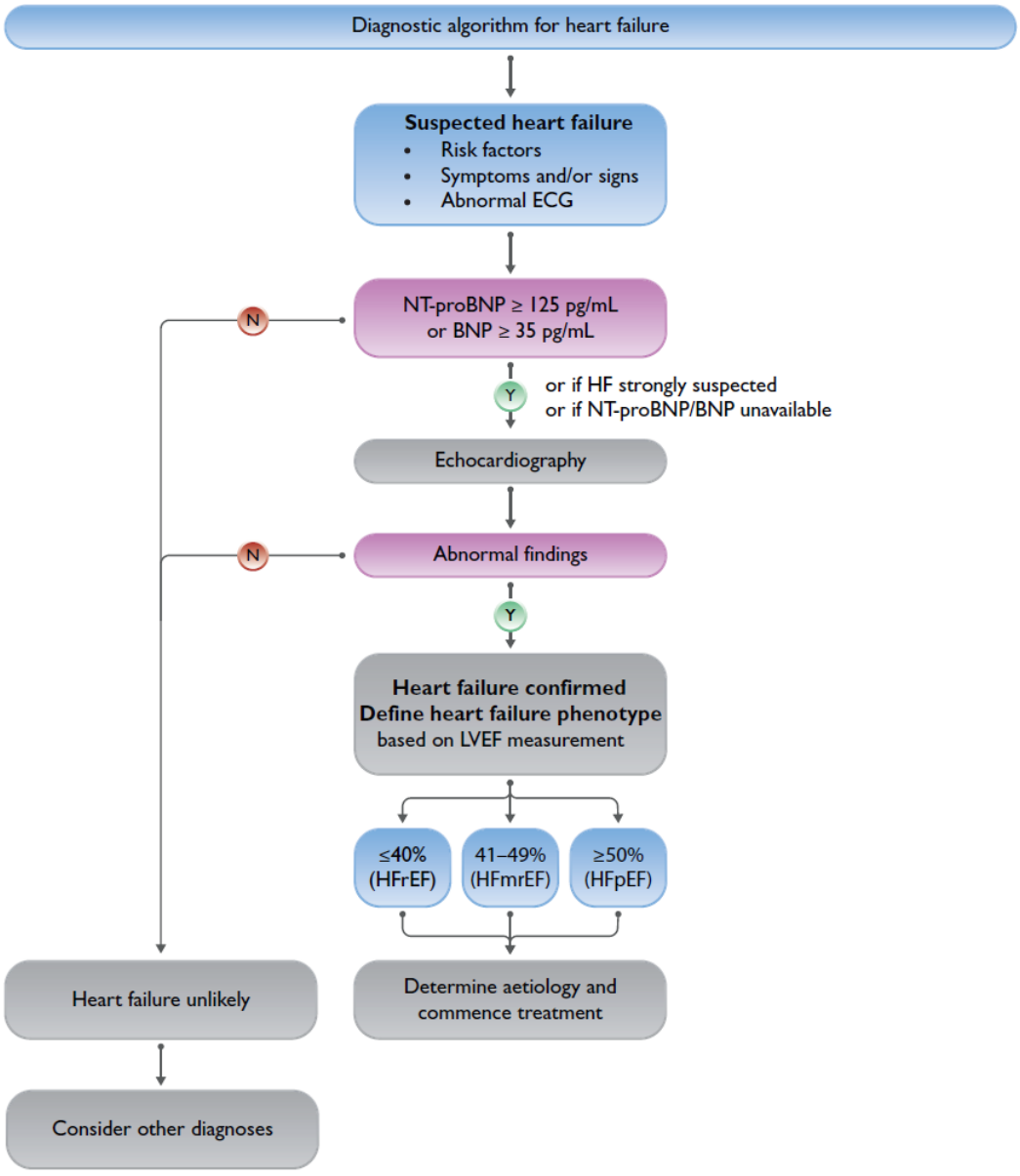


Figure 1. Diagnostic algorithm for diagnosis of heart failure, 2021 European Society of Cardiology Guidelines for diagnosis of chronic HF.

2.6 Management of heart failure

The primary purposes of the treatment of HF are to reduce signs and symptoms, improve HRQoL, prevent hospitalisation and improve survival.

The main approaches to treating heart failure include non-pharmacologic treatment, medications, and device treatment. The treatment of HF usually requires a multidisciplinary team, at least a cardiologist, an HF nurse dedicated to managing HF, and, if available, a physiotherapist, a dietician, and a primary physician.

Non-pharmacological treatment includes educating the HF patient regarding symptoms and information on appropriate diets, sodium and fluid intake and the importance of the physical activity to improve the patient's self-care behaviour. It also includes the importance of smoking cessation, reducing alcohol consumption, and vaccination recommendations.

The pharmacological treatment of the HF patient is complex, with different combinations of pharmacological agents, which include angiotensin-converting-enzyme inhibitor (ACEI), angiotensin receptor blocker (ARB), angiotensin receptor neprilysin inhibitor (ARNI), beta-receptor blocker (BB), mineralocorticoid receptor antagonist (MRA), diuretics and digoxin.

Device therapy consists of cardiac resynchronisation therapy (CRT), implantable cardioverter defibrillators (ICD), and left ventricular assist devices (LVADs). Heart transplantation (HTX) is done in select patients with severe HF refractory of all types of treatment.

2.7 Prognosis of heart failure

HF is associated with a poor prognosis, high mortality, morbidity, disability, and reduced quality of life. Globally, the one-year mortality is approximately 15-30 %, while the 5-year mortality is approximately 50-75 % in population-based studies. [15] The INTER-CHF study has shown that mortality rates are highest in Africa (34%). [6]

3.0 METHODOLOGY

3.1 Study sites

This study will be conducted in nine collaborating hospitals, including five teaching hospitals, two regional hospitals, one metropolitan hospital and one municipal hospital.

Korle Bu Teaching Hospital

The Korle Bu Teaching Hospital (KBTH) in Accra is the leading national referral centre in Ghana, with 2000 beds and an average daily attendance of about 1500 patients. The hospital currently serves as a training and research facility for various institutions, including the College of Health Sciences of the University of Ghana, Ghana Postgraduate College of Physicians and Surgeons, West African College of Physicians and West African College of Surgeons.

Komfo Anokye Teaching Hospital

The Komfo Anokye teaching hospital (KATH) is located in Kumasi, the capital of the Ashanti region. It is a 1,200-bed hospital, and referrals are from Upper East, Upper West, Savannah, North East, Northern, Ashanti, Bono, Ahafo, Bono East, Central, Western, Western North and Eastern.

KATH is currently a major centre for the training of postgraduate medical and dental practitioners in various specialities and the training of undergraduate personnel in Pharmacy, Nursing and many Allied Health Professions.

Cape Coast Teaching Hospital

Cape Coast Teaching Hospital, located in the Cape Coast, the regional capital of the central region, is a 400-bed capacity referral Hospital situated in the Northern part of Cape Coast. The Hospital serves as a teaching hospital for the School of Medical Sciences at the University of Cape Coast and is accredited by the Ghana College of Physicians and Surgeons for postgraduate training.

Ho Teaching Hospital

Ho Teaching Hospital is the fifth public Teaching Hospital in Ghana. It is a 300-bed hospital in Ho and provides specialised health care services to the people of the Volta Region and beyond.

The hospital is also patronised by clients from the Republic of Togo, Benin and the Federal Republic of Nigeria.

Tamale Teaching Hospital

The Tamale Teaching Hospital, located in the Tamale metropolis, provides health care services to the people of Tamale and its environs. It serves as the leading medical referral centre for the country's Northern Sector, including Upper East and West regions. It is the only tertiary health provider in the Savanna region with four hundred and eighty-four (484) beds.

Bono Regional Hospital

Brong Ahafo Regional Hospital, located in Sunyani, the Brong Ahafo Region, has 250 beds and a 10-bed accident and emergency ward. It is a secondary-level hospital serving the Bono and surrounding regions, including the Ashanti and Savanah regions.

Presbyterian Hospital- Agogo

Presbyterian Hospital- Agogo is a Municipal hospital located in the Ashanti-Akim North Municipality. The hospital has a bed capacity of 350 beds accredited for postgraduate medical training by the Ghana College of Physicians and Surgeons and has been a research site for several research projects: Africa for Malaria Vaccine Trial and the only site in Ghana for Typhoid Conjugate Trial.

Kumasi South Hospital

Kumasi South is a municipal hospital located at Atonsu-Agogo in the Kumasi metropolis and serves as the Ashanti Regional hospital. It is a secondary level hospital.

Effia Nkwanta Regional Hospital

Effia Nkwanta Regional Hospital is a secondary level 300-bed health facility in the Western and Western North Regions of Ghana. It is located in the Sekondi-Takoradi Metropolis. It receives referrals from the entire Western corridor of the Country.

3.2 Study participants

The study participants include patients aged 13 years and above who present with heart failure admitted to the medical wards or referred to the cardiology clinic of the collaborating hospitals. Participants who meet the inclusion criteria and consent will be recruited for the study.

3.3 Study design

This study is a prospective, multicentre, multilevel, observational study of patients with heart failure admitted through the emergency room or cardiology clinics from February 2023 to January 2024. The study will begin in the Korle-Bu Teaching Hospital and the Komfo Anokye Teaching Hospital in February 2023 and run for 6 (six) whilst the remaining 7 (seven) study sites will start in August 2023. All sites will then run concurrently for 6 months till January 2024.

3.4 Participants selection

3.4.1 Inclusion criteria

i. Subjects with confirmed heart failure.
ii. Patients 13 years or older.
iii. Willingness to participate in the study.

3.4.2 Exclusion criteria

i. Participants who are unwilling to participate in the study.

3.5 Variables

Variables measured or extracted are summarised below in Tables 1, 2 and 3.

Table 1 Diagnostic investigations

Variable	Definition	Type of variable	Scale of measurement
Resting ECG	ECG at enrollment or follow-up	Independent	Categorical
Chest x-ray	Chest x-ray (PA) at enrollment	Independent	Categorical
NYHA	Degree of breathlessness at rest and on exertion	Independent	Categorical • Class I • Class II • Class III • Class IV
BNP	Point of care testing during enrollment	Independent	Binary • Normal • Elevated
TSH	Participant's serum TSH	Independent	Continuous
URIC ACID	Participant's serum uric acid	Independent	Continuous
D-DIMER	Participant's D-dimer	Independent	Continuous
Hs-CRP	Participant's hs-CRP	Independent	Continuous
Heart failure	Confirmed diagnosis of heart failure using ESC algorithm for diagnosis of heart failure.	Dependent	Binary • Acute • Chronic
Acute heart failure	Confirmed diagnosis of decompensated heart failure	Dependent	Binary • De novo • Decompensated

Heart failure phenotype	Classification of HF based on LVEF LVEF ≥ 50% = HFpEF LVEF 40-49% = HFmrEF LVEF < 40% = HFrEF	Dependent	Categorical • HFrEF • HFmrEF • HFpEF

Table 2 Heart failure aetiology

Variable	Definition	Type of variable	Scale of measurement
Hypertensive heart disease	Hypertension cause of heart failure	Independent	Binary • Yes • No
Arrhythmia	Arrhythmia cause of heart failure	Independent	Categorical • Atrial fibrillation • Atrial flutter • SVT • VT
CAD	CAD cause of heart failure	Independent	Categorical • STEMI • NSTEMI • Unstable angina • Stable angina/ CCS
Rheumatic valve disease	Rheumatic valve disease cause of HF	Independent	Categorical • No • MS • MR • AS • AR
Infective endocarditis	Infective endocarditis cause of HF	Independent	Categorical • No • MV • AV • TV • PV
Congenital heart disease	Congenital heart disease cause of HF	Independent	Categorical • No • ASD • VSD

			• PDA • TOF • Others
EMF	EMF cause of heart failure	Independent	Binary • Yes • No
Cor pulmonale	Chronic lung conditions cause of HF	Independent	Binary • Yes • No
Pericardial disease	Pericardial disease cause of HF	Independent	Binary • Yes • No
Pulmonary embolism	PE cause of heart failure	Independent	Binary • Yes • No
Dilated cardiomyopathy	Dilated cardiomyopathy cause of HF	Independent	Binary • Yes • No

Table 3 Therapy

Variable	Definition	Type of variable	Scale of measurement
Therapy employed	Treatment participant receiving	Independent	Categorical • Medical therapy • Minimally invasive • Surgical therapy
Acute treatment	Acute/inotropic support/intravenous	Independent	Categorical • No • Furosemide • Dobutamine • Dopamine • Noradrenaline • Verapamil • Adenosine • Amiodarone • Labetalol • Hydralazine • Morphine • Nitroglycerine • UH • LMWH
Discharge/follow-up medications	At patient discharge during hospitalisation or outpatient follow-up	Independent	Categorical • Calcium channel blockers • Diuretics • Beta-blockers • Vasodilators • ACE- inhibitors • ARB • ARNI • Centrally acting

			• Mineralocorticoids • Oral anticoagulants • Antiplatelets • Statins • Device therapy • Other
Device therapy	Device therapy patient has received for heart failure treatment		Categorical • Pacemaker • ICD • CRT
Surgical therapy	Cardiac surgery patient has undergone	Independent	Categorical • Heart surgery • Congenital heart disease • Valvular heart disease • Pericardial • CABG • AV fistula • Stent placement • VAD placement • Aortic dissection • Other
Rehabilitation	Cardiac rehabilitation	Independent	Binary • Yes • No

3.6 Data management

3.6.1 Data collection and tools

Research Physicians and Cardiologists will record patients' data during the hospital stay, initial outpatient consultations, and designated visits after discharge. Data will be collected using an electronic data collection form (Appendix 1, Heart Failure Registry) design using KoboCollect toolbox v2022.4.4.

Blood samples will be obtained at admission and follow-up after discharge. Oral medications will be evaluated at admission, discharge, and follow-up visits.

In-hospital data will be collected during admission before discharge.

3.6.2 Heart failure registry

A structured electronic data collection form (Heart Failure Registry) will be used to collect all predetermined data. The data collection form has the first section containing the participant's unique identification number, facility number, entry point and entry date, and admission category.

The second section consists of data items regarding patient sociodemographic profile, participant risk factors and family history.

The third section of the data capture sheet explores participants presenting symptoms, whilst the fourth and fifth parts explore physical examination findings and results of diagnostic investigations.

The last two sections will collect data on therapies employed and follow-up findings of participants.

3.6.3 Patient demographics and heart failure characteristics

We will collect data on age, sex, height, weight, body mass index, nationality, ethnicity, religion, educational level, marital status, employment, monthly income, dietary patterns, personal health status, lifestyle, family history of heart failure risk factors and family history of sudden death.

Data on comorbidities including hypertension, diabetes mellitus, dyslipidaemia, smoking, alcohol consumption, hyperuricaemia, chronic kidney disease, history of hospitalisation for heart failure, prior myocardial infarction and prior stroke will also be collected.

Also, data regarding symptoms of heart failure, New York Heart Association (NYHA) functional classification, physical examination findings, blood pressure (systolic, diastolic), heart rate, peripheral capillary oxygen saturation (SpO_2; room air), investigations, interventions, and medications will also be collected.

In addition, data regarding patients' heart failure medications will also be collated. Anticoagulants, antiarrhythmic drugs, statins, glucose-lowering drugs and uric acid-lowering drugs on admission, at discharge and during follow-up after discharge will also be captured.

3.6.4 Laboratory data

Laboratory data will be obtained during admission or initial consultation and follow-up. Laboratory data include a complete blood count and serum chemistry. Serum chemistry includes renal and liver tests, lipid profile, fasting blood sugar, glycated haemoglobin, tests for electrolytes, uric acid, d-dimer, high-sensitive C-reactive protein (hs-CRP) and thyroid stimulating hormone (TSH). A point of care BNP test would also be made for patients with symptoms of heart failure and an ejection fraction of $\geq 50\%$.

3.6.5 Transthoracic echocardiogram, chest x-ray and ECG

Transthoracic echocardiographic parameters will be obtained for all patients immediately after admission or at the earliest possibility when recruited through the OPD.

Echocardiograms will be performed by Cardiologists using a GE Logic e Ultrasound machine equipped with a 3.0 MHz sector probe; after evaluating patient history and risk factors for heart failure and ECG.

Standard parasternal, short-axis, and apical views will be obtained, and all measurements done will be based on the recommendations of the American Society of Echocardiography.[27] M-mode, 2D, colour doppler, pulsed-wave doppler, pulsed wave tissue doppler, and tissue doppler imaging data will be obtained after image contrast, frequency, depth, and sector size adjustment for an adequate frame rate and optimal image visualisation.

2-Dimensional/ 2-Dimensional oriented M-mode guided measurements of interventricular septal thickness in diastole (IVS), left ventricular posterior wall thickness in diastole (LVPW), and left ventricular end-diastolic diameter (LVIDd) and left ventricular end-systolic diameter (LVIDs) would be recorded. Other parameters include aortic root diameter, atrial diameter, left atrial

volume index, right atrial area, mitral annular diameter and TAPSE (tricuspid annular plane systolic excursion).

LV ejection fraction (LVEF) will be calculated using the modified Simpson's method, and LV mass index will be calculated and recorded. Afterwards, HF will be classified as HF with preserved (HFpEF), mildly reduced (HFmrEF) and reduced ejection fraction (HFrEF).[22]

We will also collect data on standard 12-lead ECG and chest X-ray during admission before discharge and at the earliest possible after initial contact at the OPD.

The ECG will document abnormalities such as atrial fibrillation or other arrhythmia, Q waves, LV hypertrophy (LVH), and a widened QRS complex that may increase the likelihood of HF diagnosis, determine HF aetiology, and guide therapy. The heart rate, rhythm, PR interval, QRS axis and duration will be recorded, and the presence or absence of left atrial abnormalities, ventricular hypertrophy, bundle branch blocks, atrioventricular blocks, arrhythmia and ischaemia will be documented.

A chest X-ray may show pulmonary congestion and cardiomegaly to support a diagnosis of heart failure or rule out other potential causes of breathlessness (e.g. pulmonary disease). The presence or absence of cardiomegaly will be recorded based on the cardiothoracic ratio of > 50%. Other x-ray findings will also be recorded.

3.6.6 Diagnosis of heart failure

A modified diagnostic algorithm adopted from the 2021 ESC Guidelines for diagnosing and treating acute and chronic heart failure (Figure 2) will be used to confirm a diagnosis of heart failure in patients with suspected heart failure. [22]

The diagnosis of heart failure requires the presence of symptoms of heart failure (at rest or during exercise) and objective evidence of cardiac dysfunction. [22]

Heart failure with reduced ejection fraction (HFrEF)

The diagnosis of HFrEF requires the presence of symptoms and/or signs of HF and a reduced ejection fraction (LVEF ≤ 40%).

Heart failure with mildly reduced ejection fraction

The diagnosis of HFmrEF requires the presence of symptoms and/or signs of HF and a mildly reduced EF (41-49%).

The presence of elevated natriuretic peptides (NPs) (brain natriuretic peptides (BNP) ≥ 35 pg/mL or N-terminal pro-brain natriuretic peptides (NT-proBNP) ≥ 125 pg/mL) and other evidence of structural heart disease (increased left atrial (LA) size, LVH or echocardiographic measures of LV filling) make the diagnosis more likely but are not mandatory for diagnosis if there is certainty regarding the measurement of LVEF.

Heart failure with preserved ejection fraction

The diagnosis of HFpEF requires the presence of symptoms and signs of HF, an LVEF ≥50% and objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of LV diastolic dysfunction/ raised LV filling pressures including raised natriuretic peptides. Objective evidence of structural or functional abnormalities include

i. LV mass index ≥ 95 g/m^2 (Female), ≥ 115 g/m^2 (Male) and a relative wall thickness >0.42.
ii. Left atrial volume index >34 mL/m^2 in sinus rhythm (SR) and the presence of atrial fibrillation (AF) left atrial volume >40 mL/m^2.
iii. E/e' ratio at rest >9.
iv. NT-proBNP >125 (SR) or >365 (AF) pg/mL OR BNP >35 (SR) or >105 (AF) pg/mL
v. Pulmonary artery systolic pressure >35 mmHg or tricuspid regurgitant velocity at rest >2.8 m/s

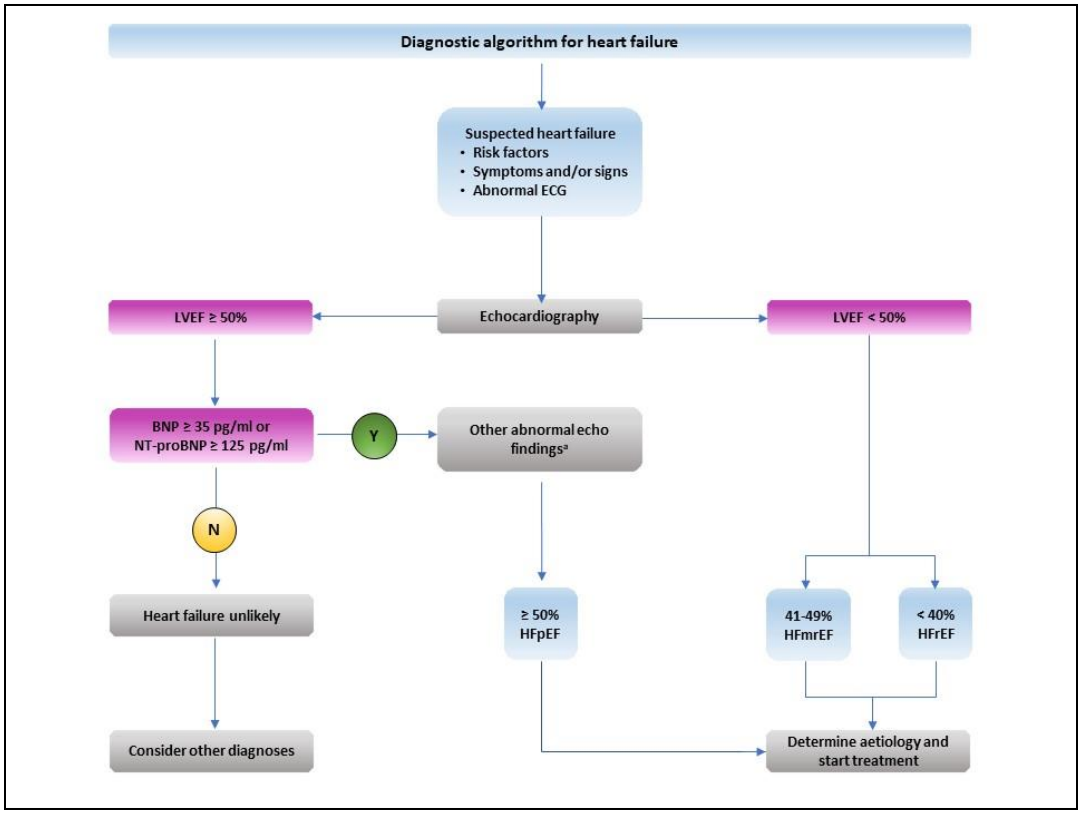


Figure 2. Modified diagnostic algorithm for heart failure. Adopted from ESC guidelines.

3.6.7 Aetiology of heart failure

The cause of heart failure will be determined based on clinical, laboratory, electrocardiographic and echocardiographic examinations.

Hypertension

Hypertension will be diagnosed in the presence of a persistent elevated systolic blood pressure ≥ 140 mmHg and diastolic blood pressure ≥ 90 mmHg in patients aged 18 years and above or presence of hypertensive retinopathy and/or the use of antihypertensive drugs and/or past medical history of hypertension drugs.[28] The presence of left ventricular diastolic dysfunction and/or left ventricular systolic dysfunction (ejection fraction < 50%), left ventricular hypertrophy, and dilated left atrium; left atrial diameter volume index > 34ml/m^2 or > 40ml/m^2 if patient has atrial fibrillation would confirm hypertensive as the aetiology of heart failure.

Coronary artery disease

An aetiology of ischaemic heart disease will be considered the cause of HF if there is evidence of definite myocardial infarction from history and clinical evaluation or if there is a long history of chronic stable angina/chronic coronary syndrome with concurrent consistent findings on echocardiogram or coronary angiogram or other imaging.

Valvular heart disease

Valvular heart disease diagnosis will be based on joint ESC/EACTS guidelines on managing valvular heart disease. It will be considered the primary cause of HF when echocardiographic evidence of primary valvular heart disease is of more than moderate severity.[29]

Rheumatic heart disease

The presence of any morphological valvular pathology as per World Heart Federation (WHF) criteria or evidence/ previous documentation of acute rheumatic heart disease.[30]

Dilated cardiomyopathy

Dilated cardiomyopathy will be diagnosed as the cause of HF based on the presence of dilated cardiac chambers with increased left ventricular mass and normal wall thickness in the absence of documented hypertension (in the past, on medication for hypertension or elevated blood pressure, i.e. systolic BP ≥ 140 mmHg and diastolic BP ≥ 90 mmHg on two or more occasions) or criteria for hypertensive heart disease and features suggestive of other causes such as valvular heart disease and ischemic heart disease.[31]

Arrhythmia-induced cardiomyopathy

Arrhythmia-induced cardiomyopathy should be suspected in patients with mean HR above 100 bpm, AF and/or PVCs burden equal to or greater than 10% and when no other cause of LV dysfunction is identified. Reversal of cardiomyopathy by eliminating the arrhythmia by effective rate or rhythm control, typically within four weeks, confirms the diagnosis. Active search for prolonged tachyarrhythmia, i.e. atrial fibrillation or other tachycardia documented in the patient's records at the first diagnosis of heart failure, should be undertaken.[32]

Congenital heart disease

History of congenital heart disease or incidental diagnosis of congenital heart defects such as atrial septal defect (ASD) or ventricular septal defect (VSD), patent ductus arteriosus (PDA) or tetralogy

of Fallot during the investigation for heart failure, considered to be of hemodynamic/clinical significance.

Others

Other clinical features diagnostic of restrictive cardiomyopathy, peripartum cardiomyopathy, endomyocardial fibrosis, cor pulmonale, pericardial disease, left ventricular noncompaction cardiomyopathy and toxin-induced cardiomyopathy.

Unknown causes

No apparent cause or cause of heart failure is unclear or awaiting additional examination results such as biopsy or MRI.

3.6.8 Treatment of heart failure

A modified diagnostic algorithm adopted from the 2021 ESC Guidelines for treating acute and chronic heart failure (Figure 3) will be employed in the treatment of patients. [22]

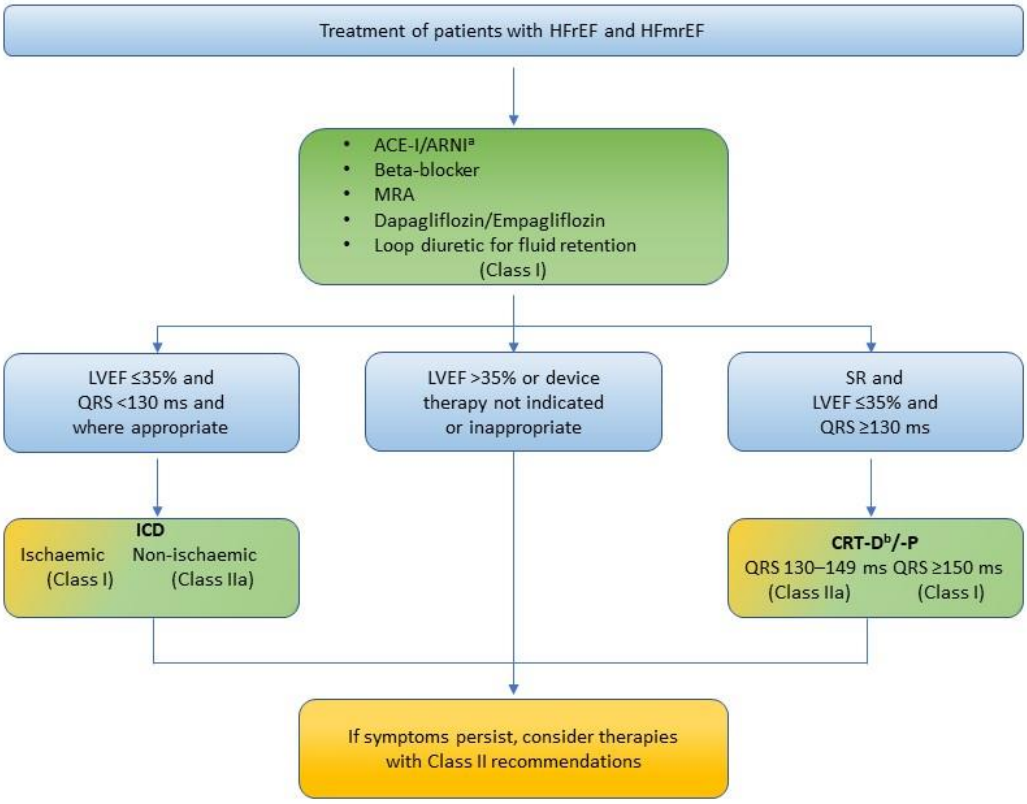


Figure 3 Therapeutic algorithm for a patient with HFrEF and HFmrEF. ***a*** as a replacement for ACE-I. ***b*** where appropriate. Class I=green. Class IIa=Yellow.

3.7 Data handling and record keeping

1. Data collection will be the responsibility of the clinical trial staff at the site under the supervision of the site Team Lead.
2. The Team Lead. will ensure reported data's accuracy, completeness, legibility, and timely capture.
3. All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data.
4. To enable audits and evaluations by regulatory authorities, the principal investigator shall keep records (essential documents) of the study for ten (10) years after study completion.

a. This includes any source data related to the study, the patient identification list (with patient numbers, full names and addresses) and the original signed Informed Consent forms.

3.8 Data analysis

KoboCollect toolbox v2022.4.4 will be used to capture data and upload it onto a cloud database which is only accessible to the principal investigator and the data manager. Collated data will be exported into the SPSS software package 2016 for statistical analysis. Tables, bar charts and pie charts will be used to present data. For continuous variables, central tendency and spread measures will be calculated using mean, standard deviation, and interquartile range. Categorical variables will be reported as numbers and percentages. Multivariable regression models will be used explore the relationships between variables and rehospitalisation and death. We will perform a Kaplan-Meier analysis to estimate the survival and death rate of patients with heart failure. The Cox regression analysis will determine the relationship between the risk of death and hospitalisation in an individual and selected variable and the significance of these variables. Missing values will be handled based on the type and frequency of missing values. A p-value <0.05 will be considered statistically significant.

3.9 Quality assurance

The study site Team Lead will ensure that study personnel are appropriately trained to obtain, store and capture data correctly.

Each clinical site will perform internal quality management of study conduct, data, documentation, and completion. Any quality issues found at the site will be documented and reported to the PI.

Quality control will be applied to each stage of data handling to ensure that data are accurate, reliable and processed properly.

All data collection sheets will be screened by site Team Leads before the data is captured in the data capture software (Excel) to ensure relevance, adequacy, completeness and consistency. Data will be entered twice and validated to ensure accuracy and completeness.

Data quality checks will also be run on the central database at agreed intervals. Any missing data or anomalies will be communicated to the site(s) for clarification/resolution.

In addition, visits to study sites to perform audits/inspections, including source data verification will done intermittently.

3.10 Ethical approval

The study will be conducted per the protocol, applicable regulatory requirements, and the ethical principles of the Declaration of Helsinki.

All the participants will be informed about the study, its objectives, and the data collection method by the recruiting research staff. Consent will be obtained from participants who agree to be part of the study and will be assured of strict confidentiality and anonymity. The developed consent form explains the study's rationale and why the subject has been asked to participate.

Individuals will not be pressured to participate in a study. They will continue to receive all services at the clinic whether they choose to participate in the study or otherwise. The patients will be notified of their voluntary participation and freedom to withdraw from the study at any time and without giving any particular reason. Patients will also be informed that withdrawing from the study will not affect the medical care or treatment they are entitled.

A unique study number will be assigned to each subject. Only this number will be used on study documents related to the subject.

A copy of the patient's information and the Informed Consent form will be given to the patient. The principal investigator or the designated representative who obtained consent from the patient shall sign the Informed Consent form. The Principal Investigator will file the signed Informed Consent forms in the Investigator's File for possible future audits and inspections.

The patient information and consent form (Appendix 2) will be submitted with the protocol for review and approval by the Ethical Review Committee of the Ghana Health Service for Kumasi South Hospital, Presby Hospital-Agogo, Bono Regional Hospital and Effia Nkwanta Hospital. Ethical approval for the remaining institutions which are teaching hospitals Komfo Anokye Teaching Hospital, Korle Bu Teaching Hospital, Ho Teaching Hospital and Tamale Teaching Hospital will be sought from their respective teaching hospitals institutional ethical review boards.

The data gathered will be shared between the collaborators and the sponsoring agency (Ghana Heart Initiative). The outcomes/results from this study will be published by the Principal

Investigator and Co-investigators as well as forwarded to stakeholders in health in Ghana (Ministry of Health and Ghana Health Service).

No conflict of interest is to be declared.

3.11 Risk and Benefits to participants

3.11.1 Potential risks

Heart failure medications licensed for heart failure will be prescribed as standard treatment to all patients. No experimental or drugs unapproved by the Food and Drugs Authority of Ghana will be administered to any patients. The most common risk of heart failure medications are drug-specific side effects that may include hypotension, hyponatraemia, hypokalaemia, hyperkalemia, headache, drowsiness, lethargy, cramps, bleeding, gastritis, vomiting, anorexia, nausea, rash, pruritus, and urticaria.

Careful evaluation of pre-disposing factors for drug side effects will be done, and close monitoring will be done during treatment as usual standard care to reduced or mitigate the risk of side-effects.

Other potential stressful events include extensive data collection and investigative procedures such as echocardiography and patients waiting for these diagnostic procedures.

3.11.2 Potential benefits

The study will improve the quality and care of patients with HF in the participating institutions because diagnostic equipment for heart failure will become available as the study is integrated into routine clinics, and the improvement in knowledge and skills of health personnel managing HF patients. Additionally, patients will benefit from some financial relief since echocardiography studies, ECG and NT pro-BNP will be done at zero cost to patients.

3.12 Expected outcomes of the study

Expected outcomes include.

1. Development of Advanced Heart Failure Management documents
2. Establishment of Heart Failure Registry
3. Establishment of 9 Heart Failure centres of excellence in Ghana
4. Provide data on Heart Failure in Ghana covering cross-sectional data as well as prospective data showing outcomes

5. Development of a framework to integrate the Heart Failure centres into normal service provision at the various hospitals
6. Improve heart failure outcomes in Ghana.

3.13 COVID-19 Prevention guidelines

General guidelines

1. Research staff will be required to wear a face mask whilst attending to research participants and in the healthcare facility.
2. Participants will also be encouraged to wear a face mask during encounters with research staff and whilst in health facilities.
3. Staff will be advised to **carry a mask with them at all times** in the event they are in one of the above situations.

Meeting and trainings

1. All staff meetings will be held virtually.
2. In-person trainings will be done with strict enforcement of preventive protocols.
3. All participants of training sessions in healthcare facilities must always wear face masks.
4. Hand sanitizers and handwashing facilities will be made available at all training venues.

Examination and diagnostic procedures

1. Participants will be encouraged to wear their facemask during all examination and procedures such as echocardiography and ECG procedures.
2. Crowding will be minimised during examination and procedures. A maximum of two people will be allowed in the echocardiography room including the echocardiographer during studies.
3. The number of study participants at all sites at any point in time will be limited to avoid overcrowding using an appointment system.
4. Symptom monitoring and testing. All research staff will be educated on COVID-19 prevention, monitored, and tested if they have symptoms of COVID-19.
5. All research staff will also be vaccinated against COVID-19.
6. Research participants will also be encouraged to take the COVID-19 vaccination.

COVID-19 researcher toolkit

All research staff undertaking research activities close to participants, will carry a "COVID-19 researcher toolkit". This should include:

- Two or more facemasks (might need several if spending the whole day and having to remove it in between data collection with participants).
- Carry additional masks for participants who may not have masks.
- Alcohol-based hand sanitizer.

3.14 Duration of the project and workplan

Table 4 Timelines

	2022	2023												2024								
	Oct-Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep
Protocol development																						
IRB application																						
Training																						
Awareness creations																						
Establish HF clinics																						
Enrolment and data collection																						
Follow-up																						
Monthly meetings																						
Data analysis																						
Report																						

4.0 BUDGET

Table 5 Budget

Item	Unit cost (Euros)	Quantity	Number of months	Total (Euros)
Protocol development and IRB application	50	1	1	50
Honorarium for team leads	150	9	12	16,200
Echocardiogram probes	4,500	9	-	40,500
Point of care BNP test and reagents	500	9	-	4,500
Awareness workshops	500	8	-	4,000
Transport cost for Master Trainers	100	8	-	800
Accommodation cost for Master Trainers	60	8	-	480
Total				**66,530.00**

5.0 PROJECT TEAM

All study team members are responsible for ensuring that the conduct of the study is compliant with institutional and state guidelines and regulations.

Principal investigators

1. Professor Isaac Kofi Owusu – Principal investigator
2. Dr Alfre Doku – Co - Principal investigator

Protocol and Institutional Review Board Team

1. Professor Isaac Kofi Owusu – Principal investigator
2. Dr Alfre Doku – Co - Principal investigator
3. Dr Felix R Awindaogo
4. Dr Emmanuel Achamfour Akowuah –

Regulatory and protocol coordinators

1. Dr Felix Awindaogo
2. Dr Emmanuel Achamfour Akowuah

Study site Team Leads

1. Dr Francis Agyekum - Korle Bu Teaching Hospital
2. Dr Collins Kokuro - Komfo Anokye Teaching Hospital
3. Dr Evans MacCready - Cape Coast Teaching Hospital
4. Dr Aba Folson - Ho Teaching Hospital
5. Dr Subuir Yakubu - Tamale Teaching Hospital
6. Dr Henry Andoh - Bono Regional Hospital
7. Dr Rexford Agu Gyamfi - Presbyterian Hospital- Agogo
8. Dr Daniel Minkah - Kumasi South Hospital
9. Dr George Peprah - Effia Nkwanta Regional Hospital

6.0 REFERENCES

1. Gtif I, Bouzid F, Charfeddine S, Abid L, Kharrat N. Heart failure disease: An African perspective. *Arch Cardiovasc Dis*. 2021;114(10):680-690. doi:10.1016/J.ACVD.2021.07.001

2. Kraus S, Ogunbanjo G, Sliwa K, Ntusi NAB. Heart failure in sub-Saharan Africa: A clinical approach. *SAMJ South African Med J*. 2016;106(1):23-31. doi:10.7196/SAMJ.2016.V106I1.10325

3. Karaye KM, Dokainish H, ElSayed A, et al. Clinical Profiles and Outcomes of Heart Failure in Five African Countries: Results from INTER-CHF Study. *Glob Heart*. 2021;16(1):50. doi:10.5334/GH.940/METRICS/

4. Gallagher J, McDonald K, Ledwidge M, Watson CJ. Heart Failure in Sub-Saharan Africa. *Card Fail Rev*. 2018;4(1):1. doi:10.15420/CFR.2018:4:1

5. Njoroge JN, Teerlink JR. Pathophysiology and Therapeutic Approaches to Acute Decompensated Heart Failure. *Circ Res*. 2021;128:1468-1486. doi:10.1161/CIRCRESAHA.121.318186

6. Dokainish H, Teo K, Zhu J, et al. Heart Failure in Africa, Asia, the Middle East and South America: The INTER-CHF study. *Int J Cardiol*. 2016;204:133-141. doi:10.1016/J.IJCARD.2015.11.183

7. Damasceno A, Mayosi BM, Sani M, et al. The causes, treatment, and outcome of acute heart failure in 1006 Africans from 9 countries: Results of the sub-Saharan Africa survey of heart failure. *Arch Intern Med*. 2012;172(18):1386-1394. doi:10.1001/ARCHINTERNMED.2012.3310

8. Appiah LT, Sarfo FS, Agyemang C, et al. Current trends in admissions and outcomes of cardiac diseases in Ghana. *Clin Cardiol*. 2017;40(10):783-788. doi:10.1002/clc.22753

9. Bonsu KO, Owusu IK, Buabeng KO, Reidpath DD, Kadirvelu A. Clinical characteristics and prognosis of patients admitted for heart failure: A 5-year retrospective study of African patients. *Int J Cardiol*. 2017;238:128-135. doi:10.1016/j.ijcard.2017.03.014

10. Ofori-Asenso R, Garcia D. Cardiovascular diseases in Ghana within the context of globalisation. *Cardiovasc Diagn Ther*. 2016;6(1):67-77. doi:10.3978/j.issn.2223-3652.2015.09.02

11. Owusu IK, Adu-Boakye Y, Boadu RK. Cardiovascular Risk Profile Of Patients Seen At A Cardiac Clinic In Kumasi, Ghana. *Internet J Heal*. 2013;14(1):1-5.

12. Owusu AY, Kushitor SB, Ofosu AA, Kushitor MK, Ayi A, Awoonor-Williams JK. Institutional mortality rate and cause of death at health facilities in Ghana between 2014 and 2018. *PLoS One*. 2021;16(9):e0256515. doi:10.1371/JOURNAL.PONE.0256515

13. Bragazzi NL, Zhong W, Shu J, et al. Burden of heart failure and underlying causes in 195 countries and territories from 1990 to 2017. *Eur J Prev Cardiol*. 2021;28(15):1682-1690. doi:10.1093/EURJPC/ZWAA147

14. Braunwald E. Cardiovascular Medicine at the Turn of the Millennium: Triumphs, Concerns, and Opportunities. *N Engl J Med*. 1997;337(19):1360-1369. doi:10.1056/NEJM199711063371906

15. Savarese G, Moritz Becher P, Lund LH, et al. Global burden of heart failure: a comprehensive and updated review of epidemiology. *Cardiovasc Res*. Published online February 12, 2022. doi:10.1093/CVR/CVAC013

16. Roger VL, Groenewegen A, Rutten FH, Mosterd A, Hoes AW. Epidemiology of heart failure. *Eur J Heart Fail*. 2020;22(8):1342-1356. doi:10.1002/EJHF.1858

17. Agbor VN, Essouma M, Ntusi NAB, Nyaga UF, Bigna JJ, Noubiap JJ. Heart failure in sub-Saharan Africa: A contemporaneous systematic review and meta-analysis. *Int J Cardiol*. 2018;257:207-215. doi:10.1016/J.IJCARD.2017.12.048

18. Ghana Health Service. The Health Sector in Ghana: Facts and Figures 2018. *Minist Heal Ghana*. Published online 2018:1-50.

19. Sanuade OA, Anarfi JK, de-Graft Aikins A, Koram KA. PATTERNS OF CARDIOVASCULAR DISEASE MORTALITY IN GHANA: A 5-YEAR REVIEW OF AUTOPSY CASES AT KORLE-BU TEACHING HOSPITAL. *Ethn Dis*. 201AD;24(1):55-59.

20. Ogah OS, Adebiyi A, Sliwa K. Heart Failure in Sub-Saharan Africa. *Top Hear Fail Manag*. Published online May 20, 2019. doi:10.5772/INTECHOPEN.82416

21. Bozkurt B, Coats AJS, Tsutsui H, et al. Universal definition and classification of heart failure: a report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing

Committee of the Universal Definition o. *Eur J Heart Fail*. 2021;23(3):352-380. doi:10.1002/EJHF.2115

22. McDonagh TA, Metra M, Adamo M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. 2021;42(36):3599-3726. doi:10.1093/eurheartj/ehab368

23. Owusu IK, Adu-Boakye Y. Prevalence and Aetiology of Heart Failure in Patients Seen at a Teaching Hospital in Ghana. *J Cardiovasc Dis Diagnosis*. 2013;01(05). doi:10.4172/2329-9517.1000131

24. Amoah AGB, Kallen C. Aetiology of heart failure as seen from a National Cardiac Referral Centre in Africa. *Cardiology*. 2000;93(1-2):11-18. doi:10.1159/000006996

25. Bragazzi NL, Zhong W, Shu J, et al. Burden of heart failure and underlying causes in 195 countries and territories from 1990 to 2017. *Eur J Prev Cardiol*. 2021;28(15):1682-1690. doi:10.1093/EURJPC/ZWAA147

26. Dassanayaka S, Jones SP. Recent Developments in Heart Failure. *Circ Res*. 2015;117(7):e58-e63. doi:10.1161/CIRCRESAHA.115.305765

27. Mitchell C, Rahko PS, Blauwet LA, et al. Guidelines for Performing a Comprehensive Transthoracic Echocardiographic Examination in Adults: Recommendations from the American Society of Echocardiography. *J Am Soc Echocardiogr*. Published online 2018. doi:10.1016/j.echo.2018.06.004

28. Mancia G, Dominiczak A. The new International Society of Hypertension guidelines on hypertension. *J Hypertens*. 2020;38(6):981. doi:10.1097/HJH.0000000000002490

29. Vahanian A, Beyersdorf F, Praz F, et al. 2021 ESC/EACTS Guidelines for the management of valvular heart disease Developed by the Task Force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J*. 2022;43(7):561-632. doi:10.1093/EURHEARTJ/EHAB395

30. Reméanyi B, Wilson N, Steer A, et al. World Heart Federation criteria for echocardiographic diagnosis of rheumatic heart disease—an evidence-based guideline. *Nat Rev Cardiol 2012 95*. 2012;9(5):297-309. doi:10.1038/nrcardio.2012.7

31. Japp AG, Gulati A, Cook SA, Cowie MR, Prasad SK. The Diagnosis and Evaluation of

Dilated Cardiomyopathy. *J Am Coll Cardiol*. 2016;67(25):2996-3010. doi:10.1016/J.JACC.2016.03.590/SUPPL_FILE/MMC1.DOC

32. Huizar JF, Ellenbogen KA, Tan AY, Kaszala K. Arrhythmia-Induced Cardiomyopathy: JACC State-of-the-Art Review HHS Public Access. *J Am Coll Cardiol*. 2019;73(18):2328-2344. doi:10.1016/j.jacc.2019.02.045

7.0 APPENDICES

APPENDIX 1 CONSENT AND AGREEMENT FORMS

PARTICIPANT INFORMATION SHEET

Title of study- Assessing and Improving the Care of Heart Failure Patients in Ghana: A National Network of Heart Failure Management Centers and Teams

Introduction: This is a study being conducted by Prof Isaac Owusu (Cardiologist at Komfo Anokye Teaching Hospital in collaboration with Dr. Alfred Doku (Cardiologist at Korle-Bu Teaching Hospital).

Background and purpose of research- Heart failure refers to a condition in which the heart is unable to pump blood around the body properly. This is because the heart has become too weak to pump blood or stiff to relax and receive blood for pumping. Another name for heart failure is congestive heart failure (CCF).

Symptoms of heart failure include breathlessness on exertion and fatigue, breathlessness on lying flat, fluid retention (which may cause weight gain, ankle swelling, or a bloating sensation), cough or wheezing at night, and light-headedness or syncope and poor appetite.

This study seeks to determine the epidemiology and medium-term outcome of heart failure in Ghana. The study aims to describe the epidemiological and clinical profile of heart failure patients in Ghana and determine the aetiology, medium-term outcomes and the predictors of heart failure in Ghana.

Nature of research: This study is a prospective, multicentre, multilevel, observational study of patients with heart failure admitted through the emergency room or attended to in the cardiology clinics from February 2023 to January 2024.

Participants' involvement: This study is for a period of 1 year. The study participants include patients aged 13 years and above who present with heart failure admitted to the medical wards or referred to the cardiology clinic of the collaborating hospitals.

Potential Risk: No potential risks are involved.

Benefits: Immediate benefits to participants include improved heart failure care and a medium-term reduction in hospitalisation and death.

Costs- There will be no costs incurred to participants due to this study. Costs incurred by participants will be a result of their usual care.

Compensation- There will be no compensation for participation in this study.

Confidentiality: The information collected from this research will be kept confidential. You will not be identified by your name but by a number. Completed forms and charts will be stored in secured cabinets with password-protected access systems. All consent forms will be kept securely under lock and key and only accessible to the research staff and Ethics Review Committee for a period of 10 years.

Voluntary participation/withdrawal: Participation is voluntary, and participants have the right to withdraw from the study at any time without penalty and without having to give any reasons.

Outcome and Feedback: At the end of the study, information on the management and outcomes of heart failure will be obtained and guide the management of heart failure in Ghana.

Funding information: This study is sponsored by the Ghana Heart Initiative. The data collated with be shared between the collaborators as well as with the sponsoring agency.

Conflict of Interest: The data collated will be shared between the collaborators and the sponsoring agency (Ghana Heart Initiative). The outcomes/results from this study will be published by the Principal Investigator and Co-investigators as well as forwarded to stakeholders in health in Ghana (Ministry of Health and Ghana Health Service).

Please note that a copy of this Information Sheet will be given to you after it has been signed or thumb-printed to take home.

For further clarification about participation in this study, please contact

Prof Isaac Owusu (Principal Investigator)
Komfo Anokye Teaching Hospital
Kumasi
Telephone number- 0244565702/ 0206420059
Email: ikeowusu@yahoo.com

For further clarification about ethical issues and rights as a participant of this study, please contact

GHS Ethics Review Committee
Telephone number- 0503539896
Email: ethics.research@ghs.gov.gh

CONSENT FORM

1. **Participants' statement and signature:**

I acknowledge that I have had the purpose and contents of the Participants Information Sheet read and satisfactorily explained to me in a language I understand (English □/Twi □/Ga □). I fully understand the contents and any potential implications as well as my right to change my mind (that is, withdraw from the research) even after I have signed this form.

I voluntarily agree to be part of this research.

Title: …… Name: ……...

Address: ……...

Contact number: …….

Participant's Signature: ……or Thumbprint……

Mark …….

Date: …….

2. **Interpreter's statement:**

I interpreted the purpose and contents of the Participants information Sheet to the above-named participant to the best of my ability in (Twi □/Ga □) language to his/her proper understanding. All questions, appropriate clarifications sought by the participant and answers were also duly interpreted to his/her satisfaction.

Name of interpreter: …….

Signature of interpreter: ……. Date: ……

Contact Details: ……...

3. **Statement of Witness:**

I was present when the purpose and contents of the Participant Information Sheet was read and explained satisfactorily to participant in the language, he/she understood (English □/Twi□ /Ga □)

I confirm that he/she was given the opportunity to ask questions/seek clarifications and same were duly answered to his/her satisfaction before voluntarily agreeing to be part of the research.

Name of witness: …….

Signature: ……Or Thumbprint: ……. Mark: ……

Date: ……..

4. **Statement and Signature of Investigator:**

I certify that the participant has been given ample time to read and learn about the study. All questions and clarifications raised by the participant have been addressed.

Researcher's name: …….

Signature: …….

Date: ……....

PARTICIPANT INFORMATION SHEET AND ASSENT FORM FOR CHILDREN 15 – 17 YEARS

Title of study- Assessing and Improving the Care of Heart Failure Patients in Ghana: A National Network of Heart Failure Management Centers and Teams

Introduction: This is a study conducted by Prof Isaac Owusu (Cardiologist at Komfo Anokye Teaching Hospital in collaboration with Dr Alfred Doku (Cardiologist at Korle-Bu Teaching Hospital).

I will give you information and invite you to be part of a research study. You can choose whether or not you want to participate. We have discussed this research with your parent(s)/guardian, and they know that we are also asking you for your agreement. If you are going to participate in the research, your parent(s)/guardian must agree. However, if you do not wish to take part in the research, you do not have to, even if your parents have agreed.

You may discuss anything in this form with your parents, friends, or anyone you feel comfortable talking to. You can decide whether to participate or not after you have talked it over. You do not have to decide immediately.

There may be some words you don't understand or things that you want me to explain more about because you are interested or concerned. Please ask me to stop at any time, and I will take the time to explain.

Background and research purpose- Heart failure refers to a condition in which the heart cannot pump blood around the body properly. This is because the heart has become too weak to pump blood or stiff to relax and receive blood for pumping. Another name for heart failure is congestive heart failure (CCF).

Symptoms of heart failure include breathlessness on exertion and fatigue, breathlessness on lying flat, fluid retention (which may cause weight gain, ankle swelling, or a bloating sensation), cough or wheezing at night, light-headedness or syncope and poor appetite.

This study wants to determine the epidemiology and medium-term outcome of heart failure in Ghana. The study aims to describe the epidemiological and clinical profile of heart failure patients in Ghana and determine the aetiology, medium-term outcomes and predictors of heart failure in Ghana.

Nature of research: This study is a prospective, multicentre, multilevel, observational study of patients with heart failure admitted through the emergency room or attended to in the heart clinics from February 2023 to January 2024.

Participants' involvement: This study is for a period of 1 year. The study involves children who are 13 years and above and grown-ups who present with heart failure and are admitted to the medical wards or come to the heart clinic.

Potential Risk: No potential risks are involved.

Benefits: Immediate benefits to you include better care of your heart and making you feel better so that you will not be kept in hospital or die.

Costs- Your parents don't have to pay more because of this research. Costs suffered by your parents will be a result of your usual care.

Compensation- There will be no payment or gifts for you in this study.

Confidentiality: The information collected from this research will be kept confidential. You will not be identified by your name but by a number. Completed forms and charts will be stored in secured cabinets with password-protected access systems. All consent forms will be kept securely under lock and key and only accessible to the research staff and Ethics Review Committee for a period of 10 years.

Voluntary participation/withdrawal: Your taking part in this study is up to you. If you decide not to be in this research, it's okay. This is still your clinic, and everything stays the same as before. Even if you say "yes" now, you can change your mind later, and it's still okay.

I have checked with the child, and they understand that participation is voluntary _____(initial).

Outcome and Feedback: At the end of the study, information on the management and outcomes of heart failure will be obtained and guide the management of heart failure in Ghana.

Funding information: This study is sponsored by Ghana Heart Initiative. The data collated with be shared between the collaborators as well as with the sponsoring agency.

Conflict of Interest: The data collated will be shared between the collaborators and the sponsoring agency (Ghana Heart Initiative). The outcomes/results from this study will be

published by the Principal Investigator and Co-investigators as well as forwarded to stakeholders in health in Ghana (Ministry of Health and Ghana Health Service).

Please note that a copy of this Information Sheet will be given to you after it has been signed or thumb-printed to take home.

For further clarification about participation in this study, please contact

Prof Isaac Owusu (Principal Investigator)
Komfo Anokye Teaching Hospital
Kumasi
Telephone number- 0244565702/ 0206420059
Email: ikeowusu@yahoo.com

For further clarification about ethical issues and rights as a participant of this study, please contact

GHS Ethics Review Committee
Telephone number- 0503539896
Email: ethics.research@ghs.gov.gh

ASSENT FORM

1. **Child's statement and signature:**

I have read this information. I have had my questions answered and know that I can ask questions later if I have them.

I agree to take part in the research.

OR

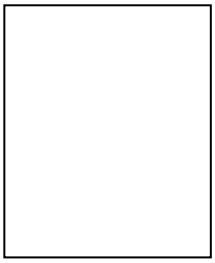
I do not wish to take part in the research, and I have not signed the assent below_____(initials of child/minor)

Only if child assents

Child's name ……

Signature of child ……... or Thumbprint

Date: …….



2. **Interpreter's statement:**

I interpreted the purpose and contents of the Participants information Sheet to the above-named participant to the best of my ability in (Twi □/Ga □) language to his/her proper understanding. All questions, appropriate clarifications sought by the participant and answers were also duly interpreted to his/her satisfaction.

Name of interpreter: ……

Signature of interpreter: …….. Date: ……

Contact Details: ……..

3. **Statement of Witness:**

I have witnessed the accurate reading of the assent form to the child, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely. I was

present when the purpose and contents of the Participant Information Sheet was read and explained satisfactorily to the child in the language he/she understood (English □/Twi □/Ga □/Other ……..).

Name of witness: …….

Signature: …… Or Thumbprint

Date: ……

4. Statement and Signature of Investigator:

I certify that the child has been given ample time to read and learn about the study. All questions and clarifications raised by the child have been addressed.

Researcher's name: …….

Signature: …….

Date: ……....

Copy provided to the participant _____ (initialed by researcher/assistant).

The parent/guardian has signed an informed consent.

Yes [ ] No [ ] _____(initialed by researcher/assistant)

PARTICIPANT INFORMATION SHEET AND PAARENTAL CONSENT FORM FOR CHILDREN < 15 YEARS

Title of study- Assessing and Improving the Care of Heart Failure Patients in Ghana: A National Network of Heart Failure Management Centers and Teams

Introduction: This is a study being conducted by Prof Isaac Owusu (Cardiologist at Komfo Anokye Teaching Hospital in collaboration with Dr. Alfred Doku (Cardiologist at Korle-Bu Teaching Hospital).

Background and research purpose- Heart failure refers to a condition in which the heart cannot pump blood around the body properly. This is because the heart has become too weak to pump blood or stiff to relax and receive blood for pumping. Another name for heart failure is congestive heart failure (CCF).

Symptoms of heart failure include breathlessness on exertion and fatigue, breathlessness on lying flat, fluid retention (which may cause weight gain, ankle swelling, or a bloating sensation), cough or wheezing at night, and light-headedness or syncope and poor appetite.

This study seeks to determine the epidemiology and medium-term outcome of heart failure in Ghana. The study aims to describe the epidemiological and clinical profile of heart failure patients in Ghana and determine the aetiology, medium-term outcomes and the predictors of heart failure in Ghana.

Nature of research: This study is a prospective, multicentre, multilevel, observational study of patients with heart failure admitted through the emergency room or attended to in the cardiology clinics from February 2023 to January 2024.

Participants' involvement: This study is for a period of 1 year. The study participants include patients aged 13 years and above who present with heart failure admitted to the medical wards or referred to the cardiology clinic of the collaborating hospitals.

Potential Risk: No potential risks to your child.

Benefits: Immediate benefits to your child include improved heart failure care and a medium-term reduction in hospitalisation and death.

Costs- There will be no costs incurred to you as a parent due to this study. Costs incurred by you will result from your child's usual care.

Compensation- There will be no compensation for you and your child for participating in this study.

Confidentiality: The information collected from this research will be kept confidential. Your child will not be identified by his or her name but by a number. Completed forms and charts will be stored in secured cabinets with password-protected access systems. All consent forms will be kept securely under lock and key and only accessible to the research staff and Ethics Review Committee for a period of 10 years.

Voluntary participation/withdrawal: Your child's participation is voluntary, and you or your child have the right to withdraw from the study at any time without penalty and without giving any reasons.

Outcome and Feedback: At the end of the study, information on the management and outcomes of heart failure will be obtained and guide the management of heart failure in Ghana.

Funding information: This study is sponsored by Ghana Heart Initiative. The data collated with be shared between the collaborators as well as with the sponsoring agency.

Conflict of Interest: The data collated will be shared between the collaborators and the sponsoring agency (Ghana Heart Initiative). The outcomes/results from this study will be published by the Principal Investigator and Co-investigators as well as forwarded to stakeholders in health in Ghana (Ministry of Health and Ghana Health Service).

Please note that a copy of this Information Sheet will be given to you after it has been signed or thumb-printed to take home.

For further clarification about participation in this study, please contact

Prof Isaac Owusu (Principal Investigator)
Komfo Anokye Teaching Hospital
Kumasi
Telephone number- 0244565702/ 0206420059
Email: ikeowusu@yahoo.com

For further clarification about ethical issues and rights as a participant of this study, please contact

GHS Ethics Review Committee

Telephone number- 0503539896

Email: ethics.research@ghs.gov.gh

CONSENT FORM

1. **Participants' statement and signature:**

I have been asked to give consent for my daughter/son to participate in this research study which will involve her completing one interview and questionnaire, physical examination and some investigations being conducted. I have read the foregoing information. I have had the opportunity to ask questions about it, and any questions that I have asked, have been answered to my satisfaction. I consent voluntarily for my child to participate as a participant in this study.

Print Name of Parent/Guardian ……

Signature of Parent/Guardian ……or Mark: …… or Thumbprint

Date ……

Day/month/year

If illiterate

I acknowledge that I have had the purpose and contents of the Participants Information Sheet read and satisfactorily explained to me in a language I understand (English □/Twi □/Ga □/Other ……..). I fully understand the contents and any potential implications as well as my right to change my mind (that is, withdraw from the research) even after I have signed this form. I consent voluntarily for my child to participate as a participant in this study.

Print Name of Parent/Guardian ……

Signature of Parent/Guardian ……or Mark: …… or Thumbprint

Date ……

2. **Interpreter's statement:**

I interpreted the purpose and contents of the Participants information Sheet to the above-named guardian/child to the best of my ability in (English □/Twi □/Ga □/Other

…….). language to his/her proper understanding. All questions, appropriate clarifications sought by the participant and answers were also duly interpreted to his/her satisfaction.

Name of interpreter …….

Signature of interpreter …….. Date: ……

Contact Details: ……

……

3. Statement of Witness:

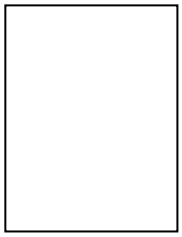
I was present when the purpose and contents of the Participant Information Sheet was read and explained satisfactorily to participant in the language he/she understood (English □/Twi□ / Ga □)

I confirm that he/she was given the opportunity to ask questions/seek clarifications and same were duly answered to his/her satisfaction before voluntarily agreeing to be part of the research.

Name of witness: …….

Signature: …… or Mark: …… or Thumbprint

Date: ……



4. Statement and Signature of Investigator:

I certify that the participant has been given ample time to read and learn about the study. All questions and clarifications raised by the participant have been addressed.

Researcher's name: …….

Signature: …….

Date: ……....

APPENDIX 3

COVID-19 PARTICIPANT INFORMATION AND PREVENTION GUIDELINES.

Thank you for volunteering to be a part of this research study. This sheet provides you with the necessary information about COVID-19 and the research study you are being asked to participate in. This information is in addition to the information you've been provided in the main study consent form. Your participation continues to be voluntary. You may choose not to participate or may withdraw your consent to participate at any time, and for any reason, without affecting your future care at this institution or your relationship with your study doctor.

Please, be assured that your safety is very important to us, and we also want to ensure that you are fully informed when you agree to be part of a study. There is still an existing risk of contracting COVID-19. We believe that your risk of contracting COVID-19 by participating in this research is no more than your risk of contracting this disease from going to another indoor public location.

Risk of COVID-19 infection

Risk to the participant

- Infected by research staff or fellow research participants that might be asymptomatic/symptomatic during a visit to the study site.
- Infected by handling objects contaminated by the virus.
- Carrying the virus from the research site into the home or community.

Risk to the research staff

- Research staff infected due to contact with an asymptomatic/symptomatic colleague research staff or research participant.

- Research staff infected by handling objects contaminated by the virus and infecting co-researchers and family members/ community members.

COVID-19 Prevention

7. You are always encouraged to wear your facemask whilst at the study sites.
8. Hand hygiene: frequent washing of hands with soap and water or use of 70% alcohol-based sanitiser is advised.
9. Cough etiquette: coughing or sneezing into a tissue or elbow is also advised.
10. Crowing will be minimised. A maximum of three people will be allowed in the echocardiography room. The number of participants at any point in time will be limited to avoid overcrowding by an appointment system.
11. Symptom monitoring and testing. All research staff will be educated on COVID-19 prevention, monitored, and tested if they have symptoms of COVID-19.
12. All research staff will also be vaccinated against COVID-19.
13. Research participants will also be encouraged to take the COVID-19 vaccination.

What is COVID-19?

COVID-19 is a respiratory illness caused by a new or "novel" coronavirus. Coronaviruses cause respiratory illnesses, such as the common cold.

How does it spread?

The virus spreads most commonly from person-to-person or through respiratory droplets when an infected person coughs, sneezes, or talks. COVID-19 can sometimes spread by airborne transmission and may be able to infect people who are more than 6 feet away from the infected person or after the person has left an enclosed space with inadequate ventilation. The virus may also spread in other ways, such as touching a surface or object that has the virus on it and then touching your mouth, nose, or possibly your eyes.

What are the symptoms?

The main symptoms of COVID-19 are fever, coughing, and shortness of breath. Some people also experience body aches, headaches, runny nose, loss of sense of smell and sore throats.

Who is most at risk?

Older adults, people of any age with other medical conditions such as heart disease, chronic kidney disease, type 2 diabetes, chronic obstructive pulmonary disease (COPD), sickle cell disease, obesity, HIV infection, asthma, cystic fibrosis, type 1 diabetes, or high blood pressure may be at higher risk for severe illness from COVID-19.

Diagnosis

Diagnosis is made through specific testing. The Polymerase Chain Reaction (PCR) test is most accurate and widely used. A swab is collected from the nose and throat. Results can take hours or days.

Rapid Diagnostic Test (RDT) is less accurate than PCR but the result is available within minutes. Tests can be done at the "point of care", at work, or at home. A swab is taken from the nose, or a saliva sample is used.

Treatment

Mildly sick patients can be managed at home with rest, plenty of fluids and medications to relieve symptoms.

However, severely sick individuals require hospitalisation, which can be managed with oxygen, intravenous fluids, and specific intravenous medication. They may require extensive support in intensive care with mechanical ventilation.

Prevention

- COVID-19 vaccination, including a booster dose, is recommended to reduce the risk of infection.
- Maintenance physical distance, at least 1 metre away from others, even if they appear well.
- Wearing a well-fitting face mask (or cloth covering nose and mouth) in closed spaces or when it is difficult to maintain social distance.
- Washing of hands frequently with soap and water. Use alcohol-based hand sanitiser when soap and water are not readily available.
- Ensuring adequate ventilation, especially in confined, enclosed spaces and crowded places.
- Avoiding crowded areas and public gatherings.
- Limiting face-to-face interactions.