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A collaborative effort across Africa to investigate risk factors and outcomes of premature acute coronary syndrome: Protocol for the EAS Lipid Registry of Africa (LIPRA)

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ABSTRACT

Data on acute coronary syndrome (ACS) is lacking in Africa where cases of premature ACS seem to be on the rise. Africa would benefit from an epidemiological assessment of premature ACS to determine its risk factors and management in this demographic to inform guidelines and practice. The European Atherosclerosis Society recognised this urgency and formed a growing network across 11 African countries to create the Lipid Registry of

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Africa (EAS-LIPRA). This article is based on the EAS-LIPRA protocol and presents the aims, concept and methodological considerations, and the operations and collaborative governance structure of this project. EAS-LIPRA aims to report risk factors and outcomes of premature ACS in Africa to further understand its prevalence and management via collating and pooling multinational prospective data on premature ACS across multiple sites in Africa into a standardised registry. Data will be stratified into subgroups based on country-level income as defined by the World Bank, and within country residence of urban versus rural areas. Valid statistical procedures will be employed to compare and observe trends in the pooled data based on demographics, clinical and laboratory variables, and disparities in its management. Being the first multinational lipid registry in Africa, it is envisaged that the network will expand to other African countries and sites yet to participate, facilitate other epidemiological studies in preventive cardiology, and set a precedent for other developing countries and regions.

1. Background and rationale

The first clinical manifestation of cardiovascular disease (CVD) is often acute coronary syndrome (ACS), which umbrellas a variety of conditions pertaining to either unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI), or ST-segment elevation myocardial infarction (STEMI) [1]. These conditions are typically classified based on 12-lead electrocardiogram (ECG) changes and cardiac troponin elevation at presentation of clinical signs or symptoms ranging from chest pain/discomfort to cardiac arrest, which informs triaging and risk stratification together with its management [1]. A main culprit of ACS is atherosclerosis which often develops with age [2] hence the risk of ACS is usually greater in the elderly.

Although ACS is less frequent in young adults (≤55 years old), recent studies on the Egyptian Cardio-Risk project [3] and the Portuguese registry of ACS (Pro-ACS) [4] reported that above 25 % of ACS cases were premature ACS. These data in this example also demonstrate that premature ACS is somewhat double the prevalence in a populous African country compared to a Western country. Those with premature ACS in the Portuguese cohort mostly presented with STEMI whereas those in the Egyptian cohort presented with STEMI in men, of which 51 % underwent primary percutaneous coronary intervention, and UA or NSTEMI in women. Furthermore, a global registry of acute coronary events (GRACE) which ran from 1999 to 2009 included participation from 154 hospitals in 14 countries across North and South America, and Europe, Australia and New Zealand that resulted in enrollment of 102, 341 ACS patients and the development of a risk score [5]. This global data provided valuable insights into the characteristics and short-term outcomes of comparatively young adults hospitalised with premature ACS [6] in the Western world.

Data on ACS is lacking in the African continent, where cases of premature ACS seem to be on the rise [7,8], and the medical community in the Eastern world would benefit from an epidemiological assessment of premature ACS to determine its risk factors and management in this demographic to inform guidelines and practice. A 10-year systematic review on ACS in Sub-Saharan Africa recently reported disparities in clinical outcomes including mortality amongst the countries studied [9] which further supports the priority for a multisite regional study of the African continent to reliably collect and pool multinational data into a standardised registry. Members of the European Atherosclerosis Society (EAS) in collaboration with the Egyptian Association of Vascular Biology and Atherosclerosis (EAVA) recognised this urgency, so the EAS formed a growing network across multiple African countries to create the Lipid Registry of Africa (EAS-LIPRA) with the Coordinating Centre based in Egypt. Being the first multinational lipid registry across Africa, it is envisaged that the network will expand to other African countries and sites yet to participate, facilitate other epidemiological studies in preventive cardiology, and set a precedent for other developing countries and regions.

Our paper is based on the EAS-LIPRA protocol and presents the aims, concept and methodological considerations, and the operations and collaborative governance structure of this project.

2. Study aims and objectives

This first EAS-LIPRA observational study aims to report the risk factors and outcomes of premature ACS in patients indigenous to and residing in Africa to further understand the prevalence and risk of UA, NSTEMI and STEMI, and their management to inform and improve standardised healthcare practices across Africa. The objectives of this study are to acquire multinational prospective data from premature ACS patients recruited voluntarily from clinical recruitment sites across Africa and pool these data into a standardised registry to compare characteristics based on demographics and disparities in its management.

Data will also be stratified into subgroups based on country-level income as defined by the World Bank [10], and within country residence of urban versus rural areas because disparities in healthcare could arguably be explained by differences in wealth of African countries.

3. EAS-LIPRA collaborative governance structure

The EAS-LIPRA project brings together researchers and clinicians from multiple countries across Africa with support from various regions of the Western world with an interest in ACS and patient care to form the

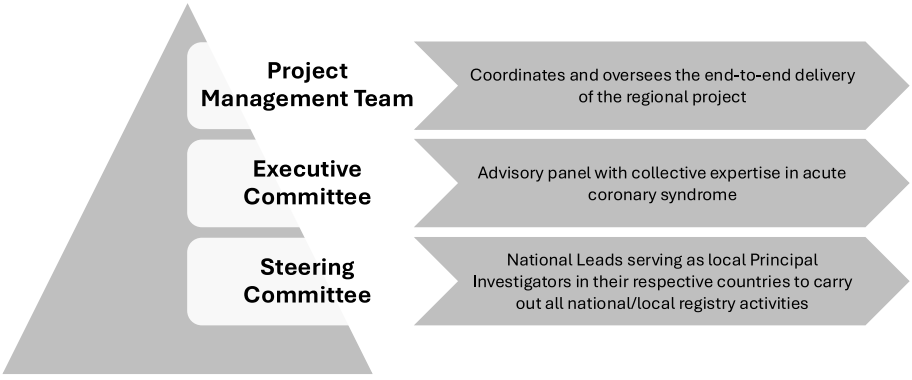

Fig. 1. EAS-LIPRA collaborative governance structure.

Box 1
List of African countries currently participating in EAS-LIPRA.

Botswana	Mozambique
Cameroon	Nigeria
Egypt	Sudan
Ethiopia	Tanzania
Ghana	Tunisia
Kenya	

collaborative governance structure illustrated in Fig. 1. The senior decision-makers comprises the Project Management Team responsible for overseeing the end-to-end planning and delivery of the regional project. The Coordinating Centre via the vendor ICOM-Group in Egypt acts as the central point for regional data collection, cleaning and processing, and to address data queries.

The Project Management Team are supported by an Executive Committee comprising an academic panel with interest and expertise in preventive cardiology to act as an advisory group to help ensure the success and regional expansion of the project. The Executive Committee also helps recruit local Principal Investigators in African countries to be appointed by the Project Management Team as National Lead Investigators (NLI) of their respective countries.

NLIs are responsible for the end-to-end planning and delivery of the project on a national level via coordinating patient recruitment, data collection, and contributing data to the regional registry in accordance with ethical and consensual laws, policies and regulations. NLIs by default of their appointment form the Steering Committee to further support and interact with the Project Management Team on the running of the project.

The lists of committees and their members are available in the Appendix. All committees are expected to play an active, collaborative role in raising awareness for the EAS-LIPRA project and disseminating published material that arises from this collaboration. Box 1 lists the eleven countries currently participating in EAS-LIPRA to demonstrate the span of the project across Africa. The Project Management Team welcomes expressions of interest via email to the corresponding author for further collaboration across the continent, particularly in African countries and sites yet to participate in EAS-LIPRA.

4. Methodological considerations

4.1. Ethical considerations and intellectual property

Ethical approval for the regional EAS-LIPRA study (pooling data) has been granted on 7th July 2024 by the Research Ethics Committee of the General Organisation for Teaching Hospitals and Institutes, Egypt. The EAS-LIPRA protocol has been registered as an observational study on clinicaltrails.gov (NCT06238375). Local ethical approvals are being sought by NLIs and their respective teams for all participating local sites across Africa to consent and enroll participants and to collect and share source data. All participants will be treated and managed in accordance with the Declaration of Helsinki. Participants may withdraw from the study without being obligated to provide a reason, at any stage without prejudice or consequence to their medical care.

All source data collected will be pseudo-anonymised via a unique code and identifiers will be limited to gender, age and year of birth with all other obvious identifiers removed by NLIs prior to sharing the data with EAS-LIPRA's regional database. Stringent data security protocols will be employed to safeguard the privacy and confidentiality of participants in accordance with data protection laws. Individual-level data shared with the regional EAS-LIPRA database will strictly not be shared with third parties.

The source data will remain property of the individual sites where it was originally collected. The participating sites may withdraw from the study at any stage without being obligated to provide a reason at the discretion of the respective NLIs whom will inform the Project Management Team of their decision to withdraw with instructions to either allow EAS-LIPRA to retain or delete their respective source data

Box 2
List of study core variables.

Premature ACS in African population.

- Demographics/characteristics.
- ACS diagnosis.
- ECG changes.
- ACS laboratory derived biomarkers.
- Lipid profiles.
- Other routine clinical data.
- Medical history.
- Management including interventions (medical and/or surgical).
- Risk factors associated with CVD particularly coronary artery disease (CAD).
- Co-morbidities (including items of the Dutch Lipid Clinic Network Score (DLCNS) for clinical diagnosis of the genetical condition familial hypercholesterolemia, which accelerates atherosclerosis ref. [12].
- Factors contributing to the onset of ACS.
- Disparities between African countries for all the above.

contributed thus far. The overall pooled regional dataset will remain property of EAS-LIPRA where stringent data security protocols will also apply in accordance with data protection laws.

4.2. Study design and population

This first EAS-LIPRA observational study is a multi-site, cross-sectional assessment of African adult volunteers (aged ≥18 years) diagnosed with premature ACS, defined as ACS occurring in men aged ≤55 years and in women aged ≤65 years [11], at the time of admission to a clinical recruitment site. Upon admission, patients suspected of having an ACS will receive routine diagnostic tests followed by appropriate routine treatment for their diagnosis of either UA, NSTEMI or STEMI in accordance with standard clinical guidelines [1]. Once a diagnosis of an ACS has been confirmed by the treating clinician, the patient will be deemed eligible to participate in this study. Eligible patients will be provided with an information letter containing details of this study and how their data will be stored and used for the purposes of conducting this study. Then the patients will be given the opportunity to ask the recruiting clinician any questions they may have regarding this study, and then invited to enroll as a study participant. Upon recruitment, patients of autonomous mind will provide written informed consent to participate in this study with the understanding that they may withdraw from the study without being obligated to provide a reason, at any stage without prejudice or consequence to their medical care.

A secure web-based portal for one-way source data capture via electronic case report files (e-CRFs) has been customised and is managed by the ICOM-Group vendor, Egypt, on behalf of the EAS-LIPRA Coordinating Centre, Egypt. Clinicians at the participating recruitment sites upload the completed e-CRFs (containing study core variables listed in Box 2) to this portal which essentially forms the EAS-LIPRA regional database. Source data uploaded will then be inspected for accuracy and completeness during the data cleaning process, and any queries will be returned to the NLIs of their respective countries and sites to address. NLIs will have restricted access to the pooled data on a national level for the sites in their respective countries, whereas, the Coordinating Centre will have access to the entire African regional database to conduct the study in compliance with data protection policies (see section 4.1).

4.3. Statistical analysis plan

Following cleaning and processing of the source data, valid statistical procedures will be employed to provide descriptive summaries of the study population to explore trends and differences overall and between subgroups. Subgroups will be stratified based on, for example, income-level of the respective African countries as defined by The World Bank [10], within country residency of rural versus urban areas, gender, age groups, and other demographics that may require assessment as inquires evolve. Variability in the source data from the different African countries and within country rural/urban residence will facilitate the assessment of potential variation based on different geographic settings pertaining to prevalence, risk factors, outcomes and management, which may reflect unstandardised healthcare practices and lifestyle habits across Africa.

Descriptive estimates of continuous variables will be reported as mean (SD) for normally distributed data or median (IQR) for asymmetrical data. Categorical variables will be reported as absolute numbers and relative frequencies (%) of the total number of participants for the given variable. Following exploratory analysis, between group comparison tests will be conducted accordingly to assess differences between subgroups and where appropriate, odds ratios and 95 % CI will be estimated using regression models to assess the association between outcomes and exposures.

5. Publication and dissemination of results

The Project Management Team and active members of the Coordinating Centre, and the Executive and Steering Committees will form the writing group of the EAS-LIPRA results manuscript together with any other individuals that contributes directly to the scientific content of the manuscripts. An appendix of acknowledgements under the group name ‘EAS-LIPRA Investigators’ in the manuscripts is reserved for individuals that, although do not directly contribute to scientific content of manuscripts, contribute local data that pools into the regional registry used to generate results. NLIs are expected to provide the names of their active team members contributing such data for acknowledgment in the appendix of the papers to the Project Management Team.

The EAS-LIPRA public-facing website available at https://eas-society.org/collaborations-outreach/lipra/has been launched to raise global awareness of the project and awaits uploads of future publications to freely disseminate the findings to the community.

6. Conclusions

The planning and set up of EAS-LIPRA began in June 2023, led by the Project Management Team, and has since gained support from its Executive Committee members, NLIs and their local teams in 11 African countries thus far. The mission of this project is to establish a multinational consortium of experts with an interest in atherosclerosis to develop the EAS-LIPRA project with the initial goal to examine novel epidemiological data to further understand and address the risk factors and outcomes of premature ACS in Africa. Being the first multinational lipid registry in Africa, it is envisaged that the network will expand to other African countries and sites yet to participate, facilitate other epidemiological studies in preventive cardiology, and set a precedent for other developing countries and regions.

Author contributions

All authors conceptualised the project and designed the study. Reda A, Bendary, A and Tselepis, A wrote the first draft. All authors critically reviewed the manuscript. Lyons, ARM wrote the final draft. All authors approved the manuscript.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.athplu.2024.10.002.

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