

Driving a greater understanding of non-communicable diseases in Africa through collaborative research: the experience of the GSK Africa NCD Open Lab

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Background The majority of premature deaths from non-communicable diseases (NCDs) occur in low-income countries. However, clinical research in these patient populations is generally lacking. Thus, many treatment paradigms for NCDs are either absent or extrapolated from populations with different genetics, health needs, and socio-economic circumstances.

Methods The objective of the study was to evaluate the outcomes from the first call for proposals from the GSK Africa NCD Open Lab. Funding was offered to research projects aiming to improve understanding and generate new knowledge of NCDs in African populations. Proposals were sought for projects relating to cancer, cardiovascular disease, diabetes, chronic respiratory disease or chronic kidney diseases. The proposal had to be led by African scientists from Cameroon, The Gambia, Ghana, Kenya, Côte d'Ivoire, Malawi, Nigeria or Uganda and include a capacity building component.

Results The 155 eligible proposals covered oncology (31.0%), cardiovascular disease (27.1%), metabolic disorders such as diabetes (20.6%), chronic respiratory disease (9.7%) and chronic kidney disease (6.5%). Most applications were from Nigeria (37.8%), Kenya (17.3%) and Uganda (13.5%). Following initial review, 23 proposals were considered by a Scientific Advisory Board, and ten were invited to submit full applications. Five projects were funded in cardiovascular disease, the interaction between cardiovascular disease and HIV infection, breast cancer, asthma and chronic kidney disease/diabetes. Principal investigators were from Nigeria, Uganda and Malawi with collaborators from Cameroon, Ethiopia, Kenya, Mozambique, South Africa, the UK, USA and the Netherlands. All of the projects involved research capacity strengthening elements.

Conclusions These projects have the potential to improve the understanding of the aetiology and natural history of specific NCDs, while also informing the development of clinical guidelines for the effective management of disease. However, far more needs to be done to address capacity building and funding for NCD research in Africa.

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Non-communicable diseases (NCDs), including cardiovascular disease, chronic respiratory disease, diabetes and cancer are major causes of morbidity and mortality worldwide (1). The majority of premature NCD deaths (82%) occur in low- and middle-income countries, including countries in sub-Saharan Africa where age-standardised mortality rates from NCDs have been shown to be higher than in high-income countries and projected to increase even further (1-3). Sub-Saharan Africa is currently experiencing a dual burden of disease resulting from an increasing burden of NCDs and a persistence of certain communicable diseases including malaria, tuberculosis and HIV, with significant population health, health systems and economic implications (4, 5). NCDs have a huge negative economic impact and can significantly impede social development, reduce productivity and contribute to poverty (6-8). The economic impact of NCDs is likely to be high in Africa, as these diseases appear to occur at younger ages and be associated with poorer outcomes (3, 9).

Addressing the increasing burden of NCDs in sub-Saharan Africa requires relevant research assessing population-specific disease burdens and trends, and understanding of unique local risk factors, as well as genetic heterogeneity in the African population. Findings from such research are necessary to stimulate political will for health promotion and improvement in the health system response to NCDs, and to inform effective preventive and management strategies (10, 11).

NCDs as challenges to development was recognised in the 2030 Agenda for Sustainable Development adopted by the United Nations Summit on Sustainable Development in September 2015 (12). Heads of State and Government agreed to develop national responses to implement the Sustainable Development Goals, including specific measures to address NCDs. In particular, they agreed to support the research and development of vaccines and medicines for NCDs that affect developing countries.

However, there currently exists a wide gap between the burden of NCDs in sub-Saharan Africa and the research response, possibly owing to limited resources for such activities and prioritisation of infectious diseases over NCDs (2, 13, 14). Compared to the rest of the world, Africa produces the lowest number of biomedical publications in general (less than 1%) with relatively little published on NCDs (2, 15-17). Research findings from high-income countries may not always be generalizable to Africa, considering the unique environmental and genetic determinants of disease, highlighting the importance of conducting Africa-specific NCD research.

The GlaxoSmithKline (GSK) Africa NCD Open Lab was established in 2014 to help address NCDs, a major healthcare problem in Africa, by working with multiple partners including world-class academic centres globally and African research centres to deliver high quality and impactful research into NCDs, and to strengthen African research capability (18). To kick start these research efforts, the first call for proposals was published in November 2014 with up to £4 million (US \$5.6 million) available to fund projects. The purpose of this paper is to outline the processes involved in launching and facilitating the first call for proposals, the outcome of the call, including brief descriptions of the successful proposals, lessons learned and the scope for future calls for funding NCD research in Africa.

Objective

The GSK Africa NCD Open Lab aims to improve the understanding of the unique attributes of NCDs in Africa and the treatment response in African patients. It provides financial support and engages scientifically with African researchers to answer locally relevant research questions pertinent to NCDs. There is also the ambition to encourage sustainable NCD research capability that will attract and retain the next generation of scientific talent within Africa, by supporting the education and training of African scientific researchers in various disciplines.

The goal for the first call for proposals was to fund research projects that aimed to improve understanding and generate new knowledge on the unique disease mechanisms, pathophysiology and aetiology of NCDs in African populations, which would subsequently inform in-

terventions for the prevention and treatment of NCDs. Proposals had to address at least one of the priority NCD areas, ie, cancer, cardiovascular disease, diabetes, or chronic respiratory disease (19). Chronic kidney diseases and the interplay between these NCDs and infectious diseases were also in scope.

The proposal had to be led by African scientists. The first call for proposals was open to African researchers based in academic or research institutions in the following countries covering Western, Eastern and Southern Africa: Cameroon, The Gambia, Ghana, Kenya, Côte d'Ivoire, Malawi, Nigeria and Uganda. Decisions on the design and scope of the call for proposals were made in consultation with the Scientific Advisory Board members appointed to provide input and guidance on the strategy of the Africa NCD Open Lab. The Scientific Advisory Board consists of twelve leading scientists (see acknowledgements), the majority of whom are Africans.

METHODS

The call for proposals, launched in November 2014, was advertised on www.gsk.com and in the included countries, with significant input from GSK country medical directors. The advertisements reached 17 countries and resulted in a total of 171 pieces of media coverage, including local newspapers and scientific journals.

Proposals were subject to a two-stage application process: preliminary and full application stages.

Figure 1 shows a flow diagram of the application and review processes and the outcome at each stage. At the preliminary stage, applicants submitted an outline of their proposed study electronically, indicating the knowledge gap and research questions, study objectives and the potential impact of the project, study design and proposed methods. The applications were checked for eligibility against the guidance documents that had been issued with the call for proposals, before being entered into a two-stage review process. At first review, scientific and clinical specialty experts and statisticians from GSK reviewed and scored the proposals against agreed, consistent criteria. These included the scope and scientific merit of the proposed project, its significance, feasibility and impact, the training and experience of the research team to successfully complete the proposed project, the appropriate consideration of ethical issues, the suitability of the host environment and the potential for GSK to engage in scientific collaboration for capacity strengthening. Following this initial screening, shortlisted applicants were invited to submit a full proposal providing more details on the proposed project, methods, budget and the *curriculum vitae* of all investigators. GSK clinical speciality experts offered support to the applicants at this stage and provided scientific and statistical input to applicants on request. The aim was to strengthen the proposals and make them more competitive for the next phase of review, or for submission to other funding agencies if unsuccessful. Applicants were given a six-week period to submit their full proposals. These were reviewed and scored by the Africa NCD Open Lab Scientific Advisory Board members. The reviewers assessed the significance and impact, the research team, the approach or methods described and the research

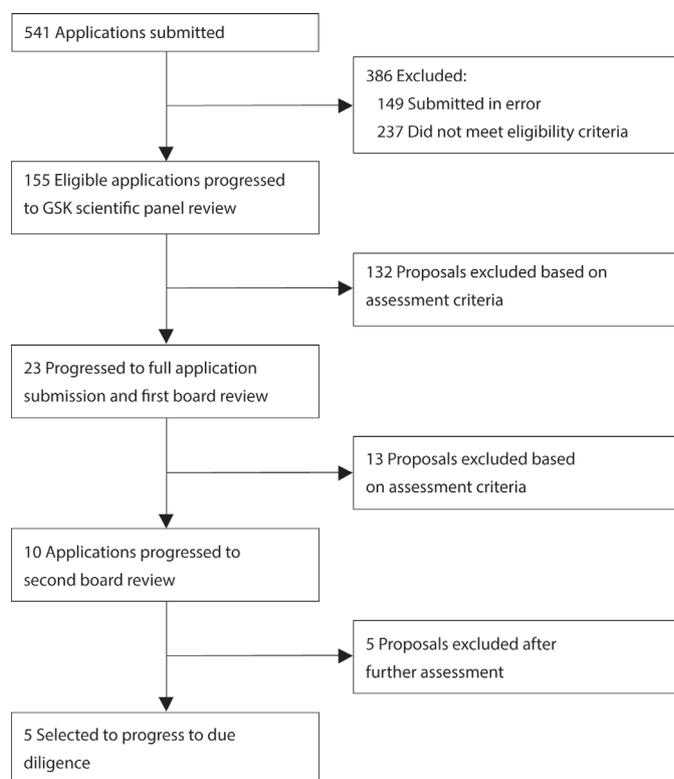


Figure 1. The review process and progression of applications.

environment of the applicants. The proposals were then ranked according to the scores obtained and discussed at a final panel meeting involving the Scientific Advisory Board and key Africa NCD Open Lab team members. Panel members were encouraged to read through all the proposals even when they were not the lead discussants. Every effort was made to ensure that any apparent or potential conflicts of interest were disclosed and eliminated throughout the review process.

Following the multi-stage review process of full applications, the five highest scoring proposals were recommended for funding and were progressed to due diligence prior to the signing of research collaboration agreements and the release of funding.

RESULTS

Of the 392 submitted proposals (after removing those submitted in error and duplicates), 155 met the eligibility criteria (39.5%) and were entered into the review process. The proposals covered a wide range of NCDs including oncology (31.0%), cardiovascular disease (27.1%), metabolic disorders such as diabetes (20.6%), chronic respiratory disease (9.7%) and chronic kidney disease (6.5%). The highest number of applications were submitted by scientists from Nigeria (37.8%) followed by Kenya (17.3%) and Uganda (13.5%). The progression of these applications through the various stages of review is shown by disease area and country of the principal investigator in

Figure 2 and Figure 3.

The main reasons for ineligibility of proposals were applications that were out of scope (as outlined in the guidance document issued along with the call), including those focusing on health promotion, health policy, environmental science or behavioural science, proposals that did not address the priority NCD disease areas, or principal investigators from countries not included in the call. Overall, 23 proposals (6% of all submitted applications and 15% of all eligible applications) were progressed to first Scientific Advisory Board panel review and ten of these were invited to submit full applications.

Projects funded by the call for proposals

A brief description of the five projects that were funded is shown in Table 1. These projects covered different NCD areas including cardiovascular disease, the interaction between cardiovascular disease and HIV infection, oncology (breast cancer), chronic respiratory disease (asthma) and chronic kidney disease/diabetes. The principal investiga-

tors of the final selected proposals were from Nigeria, Uganda and Malawi but the projects involved collaborations with other African countries including Cameroon, Ethiopia, Kenya, Malawi, Mozambique and South Africa as well as international collaborations involving researchers from the UK, USA, and the Netherlands. All of the projects involved research capacity strengthening elements including training of MSc and PhD students in fields such as biostatistics and acquisition of clinical skills in various specialised areas. These projects if completed have the potential to improve the understanding of the aetiology and natural history of specific NCDs, while also informing the development of clinical guidelines for the effective management of disease.

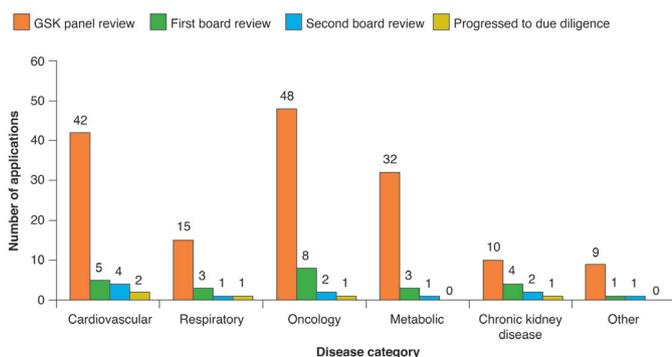


Figure 2. Progression of applications by disease category.

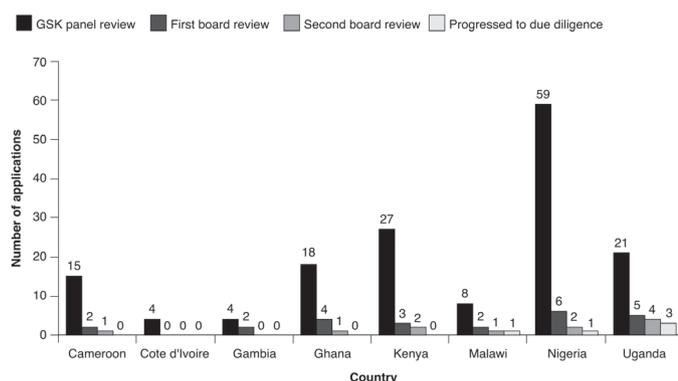


Figure 3. Progression of applications by country of principal investigator.

Table 1. Summary of funded studies

Project	The African Severe Asthma Project.
Countries	Uganda, Kenya, Ethiopia & The Netherlands.
Aims	To identify and characterise severe asthma in Eastern Africa and to determine the frequency of genes related to treatment-resistant severe asthma in 1676 asthma patients aged ≥12 years.
Potential impact	The findings of the study may improve the understanding of the natural history, asthma-related burden, and unmet needs in patients with severe and difficult-to-treat asthma in this understudied population. It will also identify important subgroups and possible asthma phenotypes unique to the study population including clinical features and response to therapy, which may help improve asthma management and outcome in the population and among African patients in general.
Project	Defining the molecular profile of breast cancer in Uganda and its clinical implications.
Countries	Uganda & United States of America.
Aims	To characterise the molecular profile and determine the prevalence of breast cancer subtypes in 100 women ≥18 years presenting with an initial diagnosis of breast cancer and evaluate the robustness of reverse transcription polymerase chain reaction (RT-PCR), widely available in Africa primarily used to monitor HIV management, to diagnose the receptor status of patients with breast cancer.
Potential impact	Optimal breast cancer management depends on knowledge of hormone-receptor status. This project will potentially improve the understanding of tumour biology, prevention targets and prognosis of breast cancer in Uganda. Knowledge of the distribution of tumour receptor subtypes and specific molecular aberrations that may be unique to black African patients may inform the development of new targeted drugs or better deployment of existing therapies in the longer term.
Project	The identification of modifiable viral and inflammatory risk factors for cerebrovascular and cardiovascular disease (CBD/CVD) in HIV-infected Malawian adults.
Countries	Malawi & United Kingdom.
Aims	To determine if chronic immune activation driven by HIV and viral antigenaemia increases the risk of cerebrovascular/cardiovascular disease (CBD/CVD) in HIV infected adults on anti-retroviral therapy (ART) in sub-Saharan Africa.
Potential impact	Findings from the study may improve the understanding of the contribution of HIV viremia, inflammation, chronic immune activation, other latent viral infections, traditional CVD risk factors, and ART on the development of atherosclerosis and CBD/CVD. These findings will potentially inform prevention strategies in sub-Saharan Africa among HIV patients and also inform the development of clinical guidelines for the effective management of HIV patients identified to be at high risk of developing CBD/CVD.
Project	Comparison of three combination therapies in lowering blood pressure in black Africans (CREOLE).
Countries	Nigeria, South Africa, Cameroon, Kenya, Mozambique, Uganda & United Kingdom.
Aims	To compare the efficacy of three different combinations of two antihypertensive drugs (amlodipine/hydrochlorothiazide amlodipine/perindopril or perindopril /hydrochlorothiazide) on 24-hour ambulatory blood pressure (BP) levels and other BP and cardiovascular risk parameters (including clinic measured systolic and diastolic BP, BP control, albuminuria, blood lipids and blood glucose) in black African patients.
Potential impact	The best antihypertensive drug combinations for treatment of hypertension in Africa is currently unknown and the findings of the proposed study may potentially provide the required evidence to inform clinical guidelines and protocols for the effective management of essential hypertension in black populations in Africa and globally.
Project	The identification and characterisation of chronic kidney disease (CKD) in Uganda and Malawi.
Countries	Uganda, Malawi & United Kingdom.
Aims	To identify the most accurate way of estimating renal function in adults in Uganda and Malawi and to determine the prevalence of CKD in these populations and the risk factors associated with CKD.
Potential impact	Equations for estimating glomerular filtration rate (GFR) have not been validated in sub-Saharan African populations, and data on GFR in Africa are few. The proposed study will examine the accuracy of different equations for calculating eGFR by comparing results to directly measured GFR using iohexol.

DISCUSSION

The GSK Africa NCD Open Lab's first call for proposals involving eight African countries generated a huge interest among researchers with 392 applications submitted. The high response from African scientists suggests a widespread interest in conducting NCD research in Africa, possibly reflecting the growing burden of NCDs as an important health priority. It may also reflect the limited funding opportunities for NCD research in Africa.

NCDs are an important cause of morbidity and mortality globally, occurring alongside an ongoing epidemic of infectious diseases in Africa. Current projections indicate that Africa and other low and middle income countries will have the largest increase in NCD mortality by 2020 (19). In 2012 the World Health Assembly endorsed a global health goal to reduce premature mortality from NCDs by 25% by 2025 (20). Research is crucial to inform diagnostic and preventive strategies and to improve the primary care response that will ensure that

African countries are able to meet this goal, yet the region has the least resources for an effective response (11). Most research funding in the African region is from external sources and usually focused on infectious diseases such as HIV/AIDS, tuberculosis and malaria (21). It is, therefore, apparent that there is a pronounced gap in NCD research funding and it is important for funding initiatives, both local and international, to be sustained and to ensure the availability of resources for NCD research in the future whilst responding effectively to the changing health needs of local relevance to Africa (22, 23).

The level of response to the call varied among the included countries, possibly indicating differences in the level of interest in NCD research or in the research capacity and capability in these different countries. Interestingly, the country response to the call correlated well with the health research output pattern reported from the Africa region (24). The response to the call for proposals and the quality of the submitted proposals suggested that institutions with significant prior experience in obtaining research funding and those with experience of international collaborative research were over represented in the final selection process. These findings highlight a need for funding agencies to consider including training on grant application processes and proposal writing in future research funding opportunities for less experienced institutions and researchers as a means of making their proposals more competitive. The opportunity given in this call to offer scientific input by GSK scientists was highly utilised, with many researchers seeking guidance to strengthen aspects of their application, particularly in the areas of biostatistics, genetics and molecular biology. It is expected that, even if such proposals do not get funded, any improvements will make them more competitive for submission to other funders, hence increasing their chance of ultimately being funded.

The conditions for applicants in the GSK call explicitly requested investigators to include plans in their proposals for strengthening capacity in various areas of NCD research. Ensuring that all investigators highlight their plans for providing relevant training on conducting NCD research in Africa is important in promoting research sustainability efforts in the region and equipping the next generation of African NCD researchers with the skills required to conduct translational research. Building the skills for managing and delivering health research is essential for development, and for ensuring that African researchers own and drive their specific health research agendas (25). It may be useful for funding agencies to ask researchers to explicitly outline their plans for building research capacity in all submitted proposals. Greater national and international investment in capacity building in low-income countries has the greatest potential for securing dynamic knowledge systems that can deliver better health and equity, now and in the future (13).

The majority of proposals that were submitted in response to the GSK call more often involved international collaborations. Although collaborations with researchers from high-income countries have been shown to be important in transferring skills to African partners, they have been reported to sometimes generate a power imbalance, where the high-income partners end up directing the research agenda without equal collaboration from the African partners (13, 26). It is important to encourage South-South collaborations, as these can strengthen the ability of researchers from low-income countries to identify their own problems and needs, and to enable them to design solutions to those problems (27). Efforts to promote inter-organisational collaborations within Africa aimed at addressing a broader NCD research agenda should be encouraged.

There were variations in the disease areas of proposals submitted in response to the GSK call for proposals, with a large number of applications in oncology and fewer covering chronic respiratory diseases. The prevalence of NCDs and risk factors have been reported to vary considerably between African countries (2). The high mortality rates often associated with cancers in Africa may have led to the increased interest in oncology (28). Overall across the disease areas, the spread of research proposals submitted mirrored that of the prevalence of the major groups of NCDs.

It is evident that initiatives such as the GSK call for research proposals directed at funding NCD research in Africa and increasing local African research capability, are urgently required. To ensure the availability of locally relevant evidence-based research, such initiatives should highlight the need to include research capacity strengthening in the proposal and promote South–South research partnerships and collaborations.

Geolocation: Cameroon, The Gambia, Ghana, Kenya, Côte d'Ivoire, Malawi, Nigeria and Uganda.

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