The heart of Africa: succeeding against the odds

Karen Sliwa

South Africa and other areas of sub-Saharan Africa have in the past 20 years undergone rapid demographical changes, largely due to urbanisation and changes in lifestyle. This rapid change has led to a marked increase in specific cardiac conditions, such as hypertensive heart disease and coronary artery disease (with the highest prevalence in the middle-aged population), in conjunction with a range of other heart diseases, which are historically common in Africa—eg, rheumatic heart disease, cardiomyopathies, and unoperated congenital heart disease. The short supply of well-equipped screening facilities, late diagnosis, and inadequate care at primary, secondary, and tertiary levels have led to a large burden of patients with poorly treated heart failure. Excellent progress has been made in the understanding of the epidemiology, sociodemographical factors, effect of urbanisation, and pathophysiology of cardiac conditions, such as peripartum cardiomyopathy, rheumatic heart disease, and tuberculous pericarditis, which are common in sub-Saharan Africa. This progress has been achieved largely through several studies, such as the Heart of Soweto, THESUS, REMEDY, BA-HEF, Abeokuta-HF, and the PAPUCO studies. Studies on the suitable therapeutic management of several heart conditions have also been done or are underway. In this Lecture, I provide a personal perspective on the evolving burden of cardiac disease, as witnessed since my appointment at Chris Hani Baragwanath Hospital, in Soweto, South Africa, in 1992, which was also the year that the referendum to end apartheid in South Africa was held. Subsequently, a network of cardiologists was formed under the umbrella of the Heart of Africa Studies and the Pan African Cardiac Society. Furthermore, I summarise the major gaps in the health-care system dealing with the colliding epidemic of communicable and non-communicable heart diseases, including cardiac diseases common in peripartum women. I also touch on the fantastic opportunities available for doing meaningful research with enthusiastic colleagues and, thereby, having a large effect, despite the need to be highly innovative in finding much needed funding support.

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Cardiovascular risk and heart disease in urban African settings: the Heart of Soweto Study

When I started as a Senior House Officer in 1992, Chris Hani Baragwanath Hospital in Soweto, South Africa, was the largest hospital in sub-Saharan Africa with more than 3000 beds. South Africa had just freed itself from apartheid, and the world famous township of Soweto was the epicentre of South Africa's struggle against apartheid. In Vilakazi Street, Soweto, not far from Chris Hani Baragwanath Hospital, two Nobel Peace Prize winners—namely, Nelson Mandela (Inaugural President of the free South Africa) and Archbishop Desmond Tutu (who is still today considered to be the moral compass of the country)—had their homes. The instability in the country at this stage led to horrendous crimes, often endless queues of victims of gun shots and stabbings, and even more horrible crimes were seen at the hospital. We saw less than one myocardial infarction per month at Chris Hani Baragwanath Hospital, and little attention was given to cardiovascular diseases (CVDs), against the backdrop of a large burden of communicable diseases.

At the beginning of the 20th century and throughout the following decade, Soweto, together with other urban communities on the continent, underwent epidemiological transition as the shift in political and economic transformation led to a profound change in lifestyle. Through an activity of *The Lancet* in 2005, *The Future of Academic Medicine*, I met David Wilkinson and Simon Stewart, my future long-term Australian collaborators, and we jointly set up a series of studies. A screening project was initiated at the Soweto Taxi Ranks as, at that time, almost all inhabitants of Soweto used public transport and commuters often had to wait for long periods. Overall, 1691 patients were screened over nine so-called heart awareness days.[1] Strikingly, obesity was by far the most prevalent risk factor for future CVD, with 1184 (70%) patients found to be overweight and 727 (43%) considered obese. The overall prevalence of obesity was significantly lower in men than in women (23% *vs* 55%; odds ratio [OR] 0·24, 95% CI 0·19–0·30; p<0·001). This simple study, aptly named "A time bomb of risk in an urban community" led to the planning of the Heart of Soweto Study,[2] which is now regarded as a landmark study in our attempts to understand the evolving burden of heart disease in the region. We faced enormous challenges setting up this major project, because funders, hospitals, and the overall health–political arena had little awareness of, or simply no interest in, the antecedent risk factors for non-communicable forms of heart disease and stroke in this community or elsewhere in Africa. The Heart of Soweto Study generated a series of more than 20 reports describing various aspects of the range of heart disease, with many of those reports being first of its kind in the African context. During 2006–08, data that consisted of high-level profiling (including echocardiography) were subsequently captured on 6006 de-novo presentations at the Cardiology Unit of the Chris Hani Baragwanath Hospital. Of these cases, 678 (11·3%) were found to not have any form of CVD or major risk factors. Those cases were used to define the normal electrocardiogram in Africans[3] and determine normal echocardiographic parameters compared with other population groups.[4] Of the 5328 remaining cases, 401 (7·5%) were derived from

emergency case presentations, 367 (6·9%) from external referrals from local primary care clinics, 1992 (37·4%) from internal referrals as a hospital inpatient, and 2568 (48·2%) from referrals from other outpatient clinics. The publication *Standing at the crossroads between new and historically prevalent heart disease: effects of migration and socio-economic factors*[5] highlighted the high burden of complex cases in young individuals and women (a pattern rarely seen in high-income countries), and also the intrinsic balance between historically prevalent and emergent forms of heart disease. In South Africa and sub-Saharan Africa, the range and manifestation of CVDs are markedly different compared with that of high-income countries, because rheumatic heart disease (RHD), tuberculous pericarditis, and the cardiomyopathies remain common and often present at an advanced stage due to cardiac failure.[6,7] Subsequently, we described the high prevalence of RHD diagnosed in adulthood,[8] the complex effect of HIV/AIDS on CVDs,[9] and the broad range of conditions leading to right heart failure.[10] Several other studies in South Africa, such as the THUSA study[11,12] and the CRIBSA study in Cape Town, South Africa,[13,14] reported on metabolic risk factors, with the SABPA Study[15] exploring the effect of those risk factors on end organ damage.

From Heart of Soweto to the Heart of Africa Studies

Through innovative pathways, we were successful in obtaining funding for larger studies under very difficult conditions. I expanded my research (under the umbrella of the Heart of Africa studies) to other African countries by linking up with like-minded colleagues on the continent and, thereby, forming a strong network of researchers. The Pan-African Society of Cardiology (PASCAR), established in 1981, is an organisation of physicians from across Africa involved in the prevention and treatment of CVDs.[16] In the past few years, under the leadership of Bongani Mayosi and the Executive Board, PASCAR has strengthened its role in promoting research relevant to CVDs in Africa. The PASCAR-Heart failure task force (chaired by myself) had several meetings and symposia in sub-Saharan Africa, which formed the basis of several heart failure research projects.

The first of many large, multicentre, multi-country cardiovascular studies done in Africa within the past decade was The Sub-Saharan Africa Survey of Heart Failure (THESUS-HF) study,[17] guided by the leadership of Albertino Damasceno. The aim of the study was to determine the pattern, morbidity, and mortality of acute heart failure in sub-Saharan Africans, and to investigate the causes and available treatment.[17] THESUS-HF was done during 2007–10, and included 1011 patients with acute heart failure, presenting at 12 cardiology centres in nine African countries. The predominant causes of heart failure was hypertension (453 [45·4%] of 998 cases), followed by idiopathic dilated cardiomyopathy (188 [18·8%] of 998), and RHD (143 [14·3%] of 997). Peripartum cardiomyopathy (PPCM) and heart failure due to ischaemic heart disease was equally common (77 [7·7%] of 999 and 1002), followed in frequency by tuberculous pericardial effusion tamponade (68 [6·8%] of 999), HIV-related cardiomyopathy (26 [2·6%] of 1000), and endomyocardial fibrosis (13 [1·3%] of 1000); altogether these findings show a very different range of causes compared with high-income countries.[18]

The 6-month mortality was 17·8%, similar to that of other populations diagnosed with acute heart failure.[19] The specific characteristics of patients with acute heart failure in this cohort differed to other cohorts according to sex, with acute heart failure being more common in women younger than 50 years[20] and, therefore, at odds with data from other parts of the world—eg, Europe.[21] Contemporary profiling of acute heart failure from Nigeria, the Abeokuta heart failure Study,[22] revealed that 452 (10%) of all medical admissions presenting within 1 year to the Federal Medical Centre in Abeokuta, Nigeria, had acute heart failure, with hypertensive heart failure found in 335 (78·5%) patients. The Abuja Heart Society Cohort of urban Nigerians[23] compared data for 1586 consecutive patients referred for the first time to the Cardiology Unit at Abuja Teaching Hospital, Nigeria, from 2006 to 2010, with data for the Heart of Soweto cohort collected at the same time. Data from the Nigerian study showed hypertension as the primary diagnosis in more than half of the study patients, with more women than men having this diagnosis. However, right heart failure was much rarer in the Abuja study than in the Soweto cohort (2·5% *vs* 27%). This difference could probably be explained by the higher rate of smoking (41% *vs* 7·5%) and higher exposure to industrial pollutants in Soweto than in Abuja. These studies, together with studies from other regions such as Tanzania[24] and Cameroon,[25] highlight the need to implement primary prevention and health promotion strategies to combat hypertension in sub-Saharan Africa. A 2014 analysis led by Ogah and colleagues[22] investigated the economic burden of heart failure in the Abeokuta cohort, southwest Nigeria. On the basis of studies in the region, it is estimated that 7–10% of medical admissions, affecting mainly the breadwinner and carer generation (aged <55 years),[6,20] are due to heart failure. In view of the paucity of data describing the costs of acute and chronic forms of heart failure, this study[22] is of particular importance as it is the first systematic attempt to estimate costs of heart failure in Nigeria or other sub-Saharan African countries. The proportional contribution of inpatient costs was 46% and outpatient costs was 54%, with transport costs for clinic visits contributing to 46% of the direct outpatient costs. Overall, the total costs of heart failure or cost per patient annually was enormous, considering the context of a developing economy where out-of-pocket expenses are the main means of funding. Tim Evans and

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Ariel Pablos-Mendez, from the World Bank Group, have highlighted that high out-of-pocket spending among those who fall ill contributes the largest share of health expenditure in most low-income and middle-income countries, where people fall or remain trapped in poverty.[26] There is thus an urgent need to develop community-based heart failure care in sub-Saharan Africa, because this type of care will reduce the costs of frequent transport to major health-care facilities.

In 2009, the Pan African Pulmonary Hypertension Cohort (PAPUCO) study[27,28] was set up by Friedrich Thienemann, Ana Olga Mocumbi, and myself. The aim of this study was to describe the presentation, causes, and comorbidities of pulmonary hypertension in Africa. Specific objectives were to determine the overall 6-month survival. More broadly, the registry endeavours were to develop sustainable clinical and research capacity across the African continent, and raise awareness of pulmonary hypertension and its risk factors. Because this study had minimal financial support, a tailor-made database needed to be developed by the study team to fulfil the study requirements. Open-source technology was used to develop the web-based system that allowed the investigators to collect, store, and analyse research data in various formats. It provided hierarchical permissions and validations at the point of entry, and most importantly ownership of the data to the centres. For this study,[27] we developed a diagnostic algorithm to diagnose pulmonary hypertension in resource-limited settings that did not have access to right heart catheterisation. There were 209 adults (median age 48 years; IQR 35–64) and 11 children (aged 1–17 years). Most adults had advanced disease (66% WHO functional class III–IV) and a median right ventricular systolic pressure of 58 mm Hg. Adults comprised 16% pulmonary arterial hypertension, 69% pulmonary hypertension due to left heart disease, 11% pulmonary hypertension due to lung disease or hypoxia (or both), 2% chronic thromboembolic pulmonary hypertension, and 2% pulmonary hypertension with unclear multifactorial mechanism. At 6 months, 21% of the adults with follow-up data had died. This study provides new insights into pulmonary hypertension from an African perspective, with clear opportunities to improve its prevention, treatment, and outcomes.

In the past year, the large burden of newly diagnosed RHD, diagnosed only in adulthood, was reported by many studies in Africa.[8] In the REMEDY study,[29] patients with RHD—from 12 African countries, India, and Yemen—were young (median age 28 years), largely women, and mostly severely affected.[29] RHD is closely associated with childhood poverty and highlights the poor access to basic preventive health-care measures, such as antibiotics for a throat infection. There is clearly an inadequacy in awareness of the so-called backlog effect of acute rheumatic fever, which affects millions of people globally, with the subsequent development of subclinical RHD that often presents only in adulthood with increasingly substantial valve disease and heart failure. Many cases present during pregnancy with an increased heart rate and cardiac output unmasking subclinical RHD.[30]

Multicentre, multi-country, CVD interventional studies in Africa

On the basis of a carefully done cohort study, two larger, multi-country, and multicentre interventional cardiovascular studies were done in Africa. Ntsekhe and colleagues,[31] and Mayosi and colleagues[32–34] did several studies highlighting the importance of tuberculous pericarditis, with and without HIV, leading to effusive pericarditis with and without tamponade and constrictive pericarditis in sub-Saharan Africa. Evidence from earlier studies[33] of patients with tuberculous pericarditis suggested that corticosteroids might improve outcome by decreasing inflammation and subsequent reduction in pericardial constriction and tamponade. On the basis of this finding, Mayosi and colleagues embarked on an innovative, complex, and ambitious study by undertaking the Investigation of the Management of Pericarditis (IMPI) randomised controlled trial[34] of the efficacy and safety of adjunctive immunotherapy for patients with tuberculous pericarditis. It was hypothesised that adjunctive prednisolone, supressing intrapericardial inflammation, or intradermal *Mycobacterium indicus pranii*, by modifying local immune response, would show a benefit compared with the placebo in a 2×2 factorial study design. Overall, neither prednisone nor *Mycobacterium indicus pranii* reduced the primary composite outcome of constrictive pericarditis, cardiac tamponade, or mortality. Prednisone reduced numbers of admission to hospital and constrictive pericarditis in HIV-positive and HIV-negative patients. However, when both interventions were given jointly, an increased incidence of HIV-related cancer in the study population was found.

The combination treatment with hydralazine-nitrates versus placebo in Africans admitted with Acute HEart Failure (BA-HEF) was the first interventional multicentre, multi-country, randomised heart failure study[35] undertaken in Africa. This study was developed on the information obtained from the THESUS study,[17] which found that patients with acute heart failure in Africa are rarely being treated with a hydralazine-nitrates combination. On the basis of screening and enrolment rates in the THESUS registry, the BA-HEF study planned to enrol 500 patients during an acute heart failure admission over 12 months, and to test whether administration of hydralazine-nitrates would reduce the risk of death or heart failure readmission over 6 months. Regretfully, despite our best efforts, after 4 years we managed to enrol fewer than 150 patients and, because of the expiration of the study drug, the study could not continue. Patients were randomised in a double-blind

manner to receive 50 mg hydralazine and 20 mg nitrates three times a day, or matching placebo for 24 weeks followed by open-label hydralazine-nitrates for all patients. The primary endpoint of death or heart failure readmission through 24 weeks showed no significant difference between groups (hazard ratio [HR] 1·05; 95% CI 0·48–2·27; p=0·90) in the 133 randomised patients included in the analyses.

However, despite this small dataset, results for several secondary outcomes were consistent with expected effects of hydralazine-nitrates, including a lower rate of cardiovascular mortality through 24 weeks, a non-significantly lower number of heart failure and all-cause admissions per patient and death, and days dead or in hospital in the active group than in the placebo group. There were non-significant effects in favour of hydralazine-nitrates in secondary endpoints including change in dyspnoea severity at day 7 or discharge, decrease in systolic blood pressure, greater decrease in weight, and increase in performance in the 6-min walk test at week 24. There were also small changes in echocardiographic indices of cardiac size and function in favour of hydralazine-nitrates but none were significant. There are many reasons for the poor recruitment into this study. Only 133 (21·5%) of 619 screened patients were eligible for enrolment into the study, which reflects the difficulty of recruiting patients for acute heart failure trials in general. It also made us aware that the study was underfunded, because there were no dedicated funds for screening patients. Many of the sites had insufficient clinical research facilities, such as Good Clinical Practice trained nurses, dedicated research officers, research equipment, and clinical staff with dedicated time available to do research. We noted that these factors made the recruitment of patients within the specified time interval of 96 h extremely challenging. Another limiting factor was obtaining ethics approval for centres that had little experience with a placebo-controlled, multicentre, randomised trial, causing delays for up to 2 years at some sites. All the centres had previously participated in registries, which do not have these short recruitment time intervals or administer study medication, and were still possible under these circumstances. For registries, successful recruitment was possible with enthusiasm and large investment of overtime hours as shown by the REMEDY study on RHD,[29] the Heart of Soweto Study,[2] and THESUS.[17]

Maternal heart health in African women

During the past decade, a steady increase in institutional maternal mortality rate for cardiac disease in South Africa has been reported.[36,37] After non-pregnancy related infections, cardiac disease is the second most common cause of indirect maternal death, with PPCM and complications due to RHD contributing to more than 50% of the cases. The mortality occurred typically in the post-partum period beyond the standard date of recording of maternal death, as we highlighted in a recent Comment in *The Lancet*.[38] The fact that most of the deaths occurred post-partum is noteworthy. It implies that the death rate in South Africa—already estimated to be 176 per 100 000 (about ten-times higher than that in high-income countries)—is probably grossly underestimated, because death was only reported until 42 days postpartum.[38,39] On the basis of a recent meeting with the Minister of Health Aaron Motsoaledi and Melvyn Freeman (Cluster Manager, Non-communicable Diseases, National Department of Health, South Africa), we have embarked on projects to address these issues, in the hope that this will lead not only to a better understanding of the burden of late maternal death but also to interventions to reduce the contributing factors.

PPCM is one of the cardiac conditions from which a substantial amount of information came from research done in South Africa with fruitful long-term international collaborations with centres in Germany, France, and the USA.[40–42] A publication in *The Lancet*[43] highlighted the fact that despite this condition occurring in about one in 1000 women in South Africa, with a reported mortality range of 12–28%, it is poorly researched and underreported globally. As per the Working Group on Peripartum Cardiomyopathy of the Heart Failure Association of the European Society of Cardiology, PPCM is defined as an idiopathic cardiomyopathy presenting with heart failure secondary to left ventricular systolic dysfunction (left ventricular ejection fraction <45%) towards the end of pregnancy, or in the months following delivery, for which no other cause of heart failure is found.[44] Because no specific test exists to confirm PPCM, it remains a diagnosis of exclusion.[45]

On the basis of a PPCM heart failure Working Group proposal, the European Cardiac Society Research Observational Program approved substantial funding for a global registry on 1000 patients with PPCM.[46] More than 450 patients from 38 countries have been enrolled so far, showing that the condition occurs globally but is particularly common in Africa, the Middle East, Pakistan, Indonesia, and the UK, and has led to a recent position paper of the Working Group on acute care of patients with this condition.[47] Careful clinical observations by our South African team[48] has led to several experiments by Hilfiker-Kleiner and colleagues,[41,49–51] (Hannover University, Germany) in animal models, which were later confirmed in human serum and tissue samples. The mechanisms of disease on PPCM were dissected and led to a promising new and affordable medication,[52] which is currently being tested in a larger randomised study.[53] Our experimental data strongly suggested a detrimental effect of prolactin, which is cleaved into an antiangiogenic and pro-apoptotic 16 kDa isoform destroying endothelial cells and leading to apoptosis and heart failure (figure 1).

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Responding to challenges and succeeding against the odds

Increasing health research productivity

Uthman and colleagues[54] assessed the profile and determinants of health research productivity in Africa since 2000. For the WHO Africa region, the percent share of first authors from Africa contributing to worldwide research publications per year increased from 0·7% in 2000, to 1·3% in 2014, with South Africa, Nigeria, and Kenya contributing to 52% of the publications. This increase is encouraging. The authors highlighted that although there is a clear need for improving the performance of health researchers on the continent, African health decision makers should use the available research evidence to guide policy, strengthen practice, and maximise use of resources to improve care.

In South Africa, in response to the fact that the academic health workforce is shrinking and that there is a decline in clinical research capacity and output, two new research training tracks within the professional MBChB programme have been created. These programmes are the intercalated BSc (Med) Hons/MBChB track and the integrated MBChB/PhD track.[55] Additionally, Aaron Motsoaledi, South African Minister of Health, has pledged to train 1000 clinician PhDs through the National Health Scholars Programme in the next 10 years, providing scholarships equivalent to the salaries of health professionals employed by the Department of Health.[55] Pharmaceutical companies and the medical industry support several training posts in South Africa, which is an example of a successful public–private partnerships on research and clinical training.

There have also been many externally supported programmes to create the next generation of cardiovascular researchers. The National Institute of Health (NIH) Fogarty Wits Non-communicable Disease Research Leadership Training Programme, which was established in 2010, is a unique project with principle investigators from different areas—namely, Michelle Ramsay (genetics), Kerstin Klipstein-Grobusch (public health), Nigel Crowther (biochemistry), and myself (cardiology). The specific aim of the training programme is to develop a group of well-trained researchers at the Masters, PhD, and post-doctoral levels that will facilitate the cross-cutting need to examine in-depth social, genetic, epigenetic, clinical, and physiological factors of CVD and metabolic disease. These researchers will contribute to the understanding of the prevalence of these diseases in southern Africa and provide evidence to monitor and understand the underlying causes to develop effective intervention programmes. Biannual symposia and other meetings aim to generate research capacity through a network of young leaders in the field of non-communicable diseases. Several of the PhD and post-doctoral fellows have been elected to be part of the World Heart Federation Emerging Leadership programme, which has been established by the current president Salim Yusuf. This leadership programme aims to form a long-term cadre of experts who collaborate, research, and act to reduce premature mortality from CVD globally by at least 25% by 2025, as targeted by the World Heart Federation and WHO. The Human Heredity and Health in Africa consortium supported by the NIH and Welcome Trust was established in response to global efforts to apply genomic science and associated technologies to further the understanding of health and disease in different populations. Training in various aspects of biomedical research provides an important component of this project.

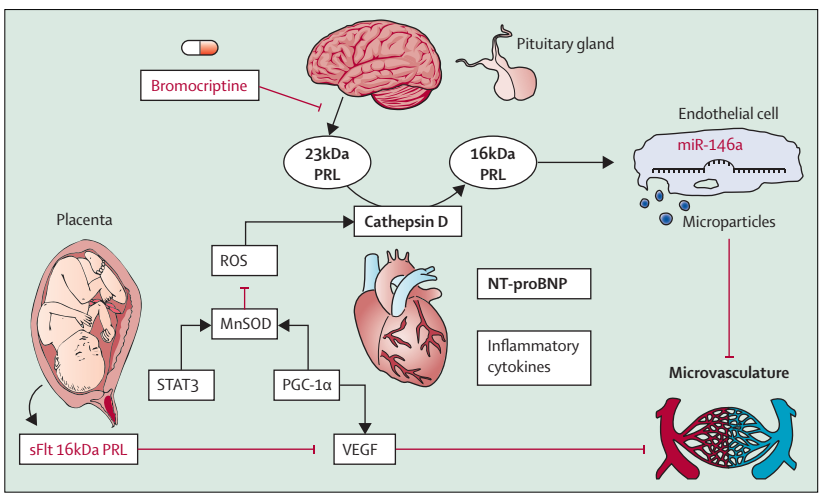

Figure 1: **Hypothesis for the pathogenesis of PPCM**
PPCM=peripartum cardiomyopathy. PRL=prolactin. miR=micro RNA. ROS=reactive oxygen species. NT-proBNP=N-terminal pro-b-type natriuretic peptide. MnSOD=manganese superoxide dismutase. STAT3=signal transducer and activator of transcription 3. PGC-1α=peroxisome proliferator-activated receptor γ coactivator 1-α. sFlt=soluble fms-like tyrosine kinase. VEGF=vascular endothelial growth factor.

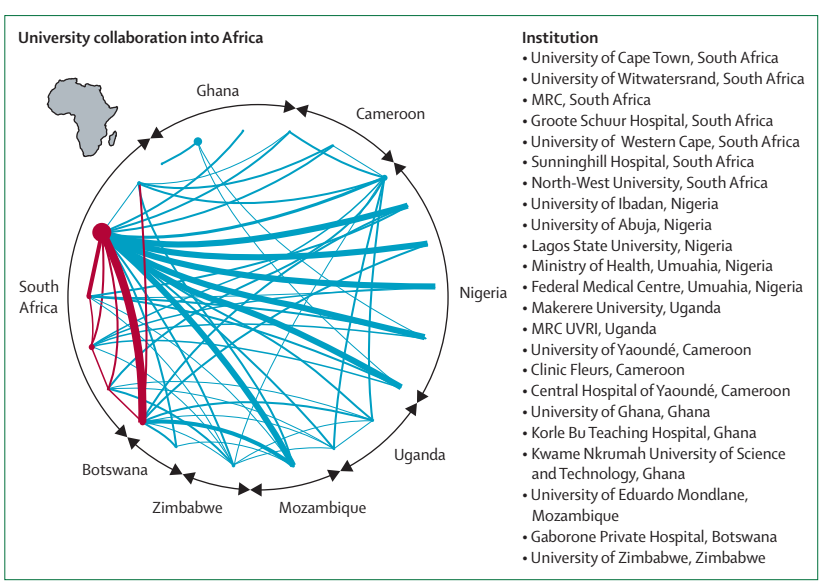

Figure 2: **Institution level collaboration in cardiovascular research in sub-Saharan Africa**
MRC=Medical Research Council. UVRI=Uganda Virus Research Institute. Adapted from Ettarh,[60] by permission of AME Publishing Company.

For the **Wits NCD Research Leadership Training Programme** see http://www.ncdleadership training.org/

For the **World Health Federation** see http://www.world-heart-federation.org

One specific project—The RHDGen Network—focuses on the genetics of RHD.

To facilitate the exchange of new knowledge on cardiovascular research done during the past decade in Africa, Simon Stewart and colleagues have compiled a book, *The Heart of Africa*,[56] that is endorsed by the Pan African Society of cardiology. This book will hopefully find wide dissemination through a broad readership as it will be made available for a nominal fee as an e-book via the PASCAR website.

For **PASCAR** see http://www.pascar.org

Addressing poor research infrastructure and accessing funding

The poor research infrastructure in many centres wanting to do cardiovascular research and the paucity of suitable funding schemes have provided major challenges.

For the Heart of Soweto Study,[2] we had, with the help of an unconditional research grant from Adcock Ingram South Africa, to demolish and rebuild the waiting area and clinical rooms of the cardiac clinic at Chris Hani Baragwanath Hospital in 2005, to make it suitable to do research on 8000 consecutive patients.

For the **National Research Foundation** see http://www.nrf.ac.za

To ensure minimal loss of follow-up (<10%), during 6 years, of the more than 200 African patients from Soweto recruited into the HOPE III study,[57–59] we had to be extremely proactive and unconventional. Together with my PhD student at that time, Sandra Pretorius, we organised annual events in the form of "braais" (the South African term for barbecue) for all the patients in the study, and small Christmas gifts that had to be delivered by the study nurses to their homes to ensure that the patients felt that they were part of the HOPE community. Even more crucial was the service of a respected elderly gentleman, Selby Mathinja, who did home visits after-hours to trace patients who were lost to follow-up.

However, access to funding for research in CVD has been tremendously difficult up to now for all African research groups. National funding bodies such as the South African National Research Foundation and South African Medical Research Council mainly supported national projects with funding of less than €100 000 (maximum) per annum. Up to 2014, the focus was almost entirely on communicable diseases, such as HIV/AIDS and tuberculosis. Since 2013, a funding scheme between two sub-Saharan countries (eg, South Africa and Mozambique) has been supported by bilateral agreements of the National Research Foundation that also funded non-communicable disease projects. None of those sub-Saharan or international funding schemes allowed for multicentre, multi-country research in Africa without a high income principal investigator. Therefore, projects such as the Heart of Soweto, THESUS, PAPUCO, BA-HEF, IMPI, and REMEDY needed innovative fund raising, and were mainly supported by local universities (in-house support via salaries), local smaller funding agencies, foundations, and unconditional research grants from pharmaceutical and mining companies among many other.

In a 2015 published analysis[60] of institutional-level collaboration in cardiovascular research in sub-Saharan Africa by Remare Ettarh, the Hatter Institute for Cardiovascular Research in Africa (HICRA), University of Cape Town, South Africa, and the Chris Hani Baragwanath Hospital (Soweto Cardiovascular Research Unit), affiliated with the University of Witwatersrand, South Africa, are the leading hubs for cardiovascular research collaboration in sub-Saharan Africa (figure 2). The study highlighted that HICRA has the expertise required to support high-quality research on CVD, and that through several multi-country studies, other countries in sub-Saharan Africa have benefitted from the partnerships by HICRA's support of graduate trainees at remote institutions nationally and within Africa. The report mentioned the substantial collaboration with the Eduardo Mondlane University, Mozambique, which collaborated frequently with the University of Cape Town, despite the difference in the languages in the two countries.

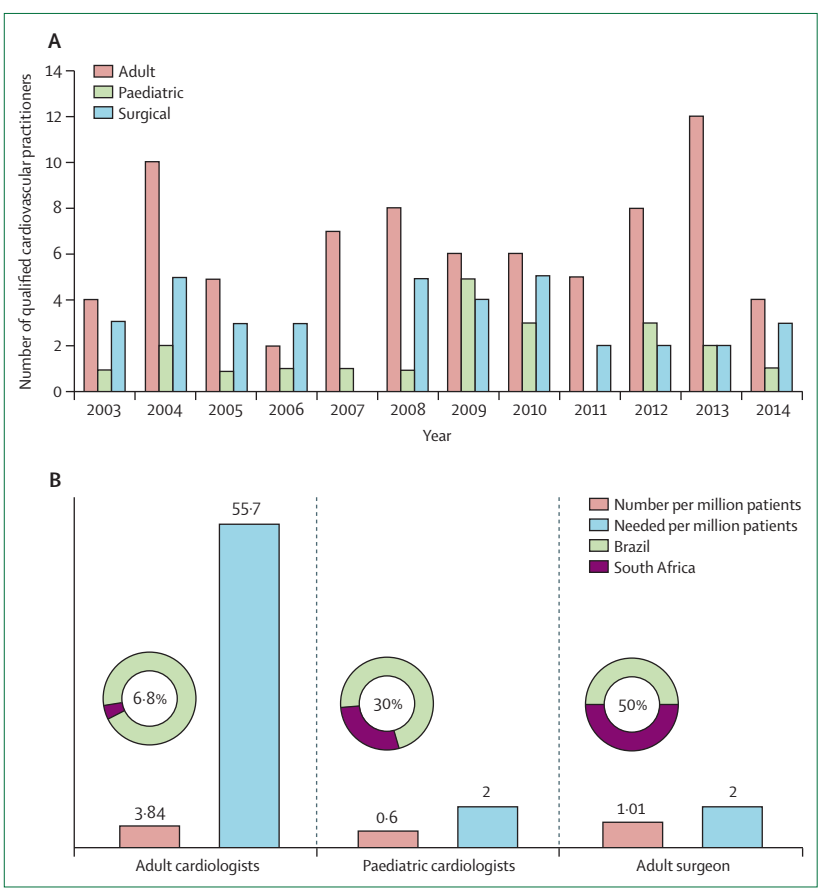

Figure 3: **Number of cardiovascular practitioners in South Africa**
(A) Number of cardiologists, paediatric cardiologists, and cardiothoracic surgeons qualified in South Africa between 2003 and 2014 per annum. (B) Registered specialists in South Africa versus needed number of specialists per million patients compared with Brazil, one of the BRIC countries with similar cardiovascular health issues to South Africa. Adapted from Sliwa and colleagues,[61] by permission of Clinics Cardive Publishing. BRIC=Brazil, Russia, India, and China.

Addressing the shortage of health-care providers

The South African Heart Association has summarised in a position paper the tremendous shortage of cardiologists, paediatric cardiologists, and cardiothoracic surgeons (figure 3).[61] Several novel approaches have been attempted to remedy the shortage of clinical services. The Walter Sisulu Centre of Africa, South Africa, attempts to fill this gap. The African Paediatric Fellowship Programme serves to train paediatricians from across Africa, including paediatric cardiologists and surgeons, and facilitate collaborations between countries, such as South Africa and Ethiopia, that have used task shifting to build capacity.[62] To address this urgent need for cardiac pacing, the PASCAR Fellowship in Cardiac Pacing, supported by Medtronic, which facilitates training in pacing of non-cardiologists, has been established.

To facilitate earlier disease detection in pregnant women with previously undiagnosed heart disease (eg, RHD or cardiomyopathy), obstetricians could receive training in screening for cardiac diseases, which is already in place since 2010 at the weekly maternity clinic for cardiac disease at Groote Schuur Hospital, South Africa. Obstetricians have good ultrasound skills, and the detection of turbulence over a rheumatic valve, a myopathic heart, or a pericardial effusion would lead to quicker referral to cardiologists or cardiothoracic surgery for appropriate intervention. This workflow could be expanded by training medical students and a larger group of health-care workers in the appropriate use of simple, hand-held ultrasound devices.[61,63] The screening for relevant diseases requiring referral to secondary and tertiary facilities could lead not only to earlier detection of major disease but would also reduce costly unnecessary referrals.

It is encouraging that the Department of Health, South Africa, has started pilot projects on integrated care of patients with multi-morbidity due to communicable (eg, HIV/AIDS) and non-communicable diseases (eg, hypertension), with use of community health-care workers at several local clinics. The polypill project, promoted by the World Heart Federation will hopefully facilitate compliance and adherence for patients with several co-morbidities. Africa and other low-income regions do not necessarily need novel drugs to treat common conditions such as hypertension or heart failure, but requires readily available, affordable, and good-quality medication.[64] Investigators from a study of the PURE data showed that the median monthly combined cost of four commonly used cardiovascular medicines, as a percentage of a household's capacity to pay, made the medication unaffordable to more than 20% of patients in low-income and middle-income regions.[64]

The way forward

Health authorities face enormous challenges dealing with CVD in South Africa and other parts of sub-Saharan Africa. The overall needs are tremendous and, to some extent, poor management due to inadequate leadership skills, poor infrastructure, and also burgeoning layers of bureaucracy, have had a catastrophic effect on the delivery of health care in many regions. African cardiologists and other clinicians dealing with CVD should seek engagement with health authorities, and vice versa, for the common goal to improve care in a difficult setup.

Better epidemiological data for CVD need to be an integral part of the health system to strengthen strategies, and more investment per gross domestic product is needed.[65] True partnerships within Africa, via South–South collaborations and globally supported by national governments and research funding bodies, need to be strengthened in the next decade. It has to be recognised that each side can learn from the other and that those partnerships must be built on mutual respect and not dictated by the partner having better access to funding.

In my opinion, we have to go back a step and not forget the strength of curiosity-driven research and the enjoyment derived from research done as part of an enthusiastic team. Often novel research and approaches will only be recognised a decade later and will thus not lead to instant gratification. I feel that too much emphasis is on a number of research output parameters—making us forget that research is about improving knowledge—and accepting that not all research will have positive results but should eventually lead to better patient care.

For the **Fellowship Programme** see http://www.paediatrics.uct.ac.za/scah/apfp

Declaration of interests

I declare no competing interests.

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