THE BONGANI MAYOSI RESEARCH COLLABORATIVE

Work where angels fear to tread – tackling cardio-vascular diseases affecting the poor in Africa

The Bongani Mayosi Collaborative for Cardiovascular Disease Research Excellence in Africa is an interdisciplinary platform that brings together active research programmes in the area of cardiovascular disease.

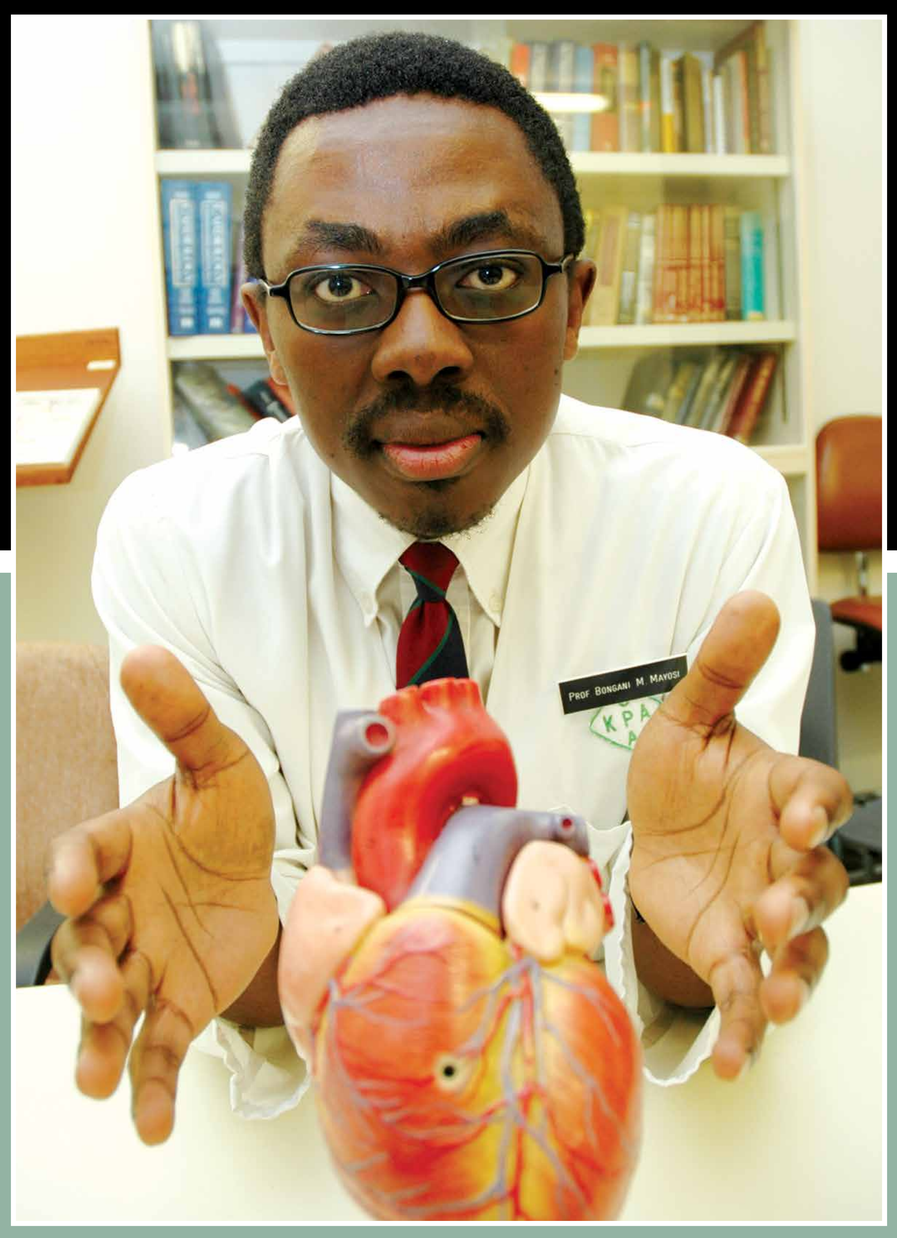
Fundamentally aligned with Professor Bongani Mawethu Mayosi's ethos and values, The Bongani Mayosi Research Collaborative seeks to strengthen and improve coordination between existing research initiatives on clinical, epidemiological and basic science approaches to cardiac research in Africa.

Through local and international partnerships, The Bongani Mayosi Research Collaborative's activities are designed to see Bongani Mayosi's vision to completion, and beyond. It is spearheaded by four of his doctoral graduates: Professor Liesl Zühlke, Professor Mpiko Ntsekhe, Professor Ntobeko Ntusi, and Professor Mark Engel, all of who are now well-established clinician scientists and epidemiologists.

The Bongani Mayosi Research Collaborative supports African research through the following activities:

- capacity development programs, including seminars and workshops, postgraduate student and research staff supervision, and training in research methodology and data management.
- the development of translational research infrastructure and the creation of a sustainable environment for ongoing research.
- centralised research coordination for the efficient management of resources, regulatory documentation, and processes that facilitate interactive and innovate research.

HEART FAILURE AND CARDIOMYOPATHY



Heart failure is the dominant form of cardiovascular disease in Africa.

Heart failure has great social and economic relevance owing to its high prevalence, mortality and impact on young, economically active individuals. Professor Bongani Mayosi single-handedly contributed to most of the scholarship of heart failure in sub-Saharan Africa. He led efforts to better understand its epidemiology at hospital and population level, unravelling its genetic underpinnings, studying its causes and mechanisms of development, its complications, and its long-term outcomes amongst Africans. Over a third of the articles he published were dedicated to improved understanding of heart failure in Africans.

As the prevalence of heart failure is expected to rise substantially in the continent, Bongani Mayosi called for population-based studies and registries of the epidemiology of heart failure in Africans and the urgent study of interventions that will decrease morbidity and mortality from the causes of heart failure.

The ambitious A*frican Cardiomyopathy and Myocarditis Registry Program* (IMHOTEP) was his brainchild – named after the Ancient Egyptian priest Imhotep (2650-2600 BC), the father of medicine and healing. IMHOTEP is a multi-centre, multi-national prospective cohort study. It will be a platform to study clinical characteristics, genetic features, causes, treatment practices and outcomes in cardiomyopathy and myocarditis in sub-Saharan Africa.

To date, the IMHOTEP pilot study has enrolled over 800 patients from six centres in South Africa and two centres in Mozambique. The study will be scaled up over the next five years to include over 10,000 African patients with heart failure. Planning for the second phase of the study is currently underway.

CONGENITAL HEART DISEASE

Congenital Heart Disease (CHD) affects nearly 1% of births and is a major cause of childhood death and disability.

CHD is a group of conditions in which the heart is not formed properly during a baby's development in the womb. In developed countries, there has been dramatic improvement in care and survival of CHD patients. In Africa, access to similar levels of care remain unavailable for the vast majority.

Challenges faced by African countries in caring for those affected by CHD are compounded by the lack of an African-specific evidence base. Evidence so far suggests that the CHD burden is substantially underestimated because of incomplete recording of poor early outcomes, but the little available evidence from Africa indicates that CHD has major health impacts. Improving knowledge about its epidemiology in sub-Saharan Africa is of immediate practical importance.

In order to address this crucial need, the PROTEA study (Partnerships in Congenital Heart Disease in Africa) was established by Professor Liesl Zühlke in 2017, with local and international partners including Professor Bongani Mayosi. It has enrolled over 2000 paediatric and adult patients with plans to perform full genetic studies with detailed phenotyping and state of the art computational fluid dynamic modelling. The study will be expanded to include several other countries in sub-Saharan Africa. Through the work of the PROTEA study, we anticipate that in the next five to ten years we can answer some of the key epidemiological and genetic aetiology questions facing the children and adults with congenital heart disease in sub-Saharan Africa; and will consider focused interventions to improve the survival rate to that of their counterparts in other parts of the world.

HIV/ART-ASSOCIATED CARDIAC DISEASE

Photograph, courtesy MRC

One-fifth of the population of sub-Saharan Africa live with HIV.

Over the last fifteen years, the development of antiretroviral therapy (ART) has transformed the disease from a certain death sentence to a chronic but manageable condition. Evidence from places where ART was rolled out earlier than in Africa indicate that a significant proportion of the current morbidity and mortality in people living with HIV is related to non-communicable diseases, and non-AIDS related complications such as diabetes and heart disease. It is unknown whether ART itself contributes to the risk of developing some of these conditions.

In South Africa, close to 9 million people are infected with HIV and nearly 330 000 of these are under the age of 15. The country also has the biggest ART program in the world. It is crucial that the medical community understands the burden, spectrum and causes of heart disease and other non-communicable diseases in order to continue to improve the lives of people living with HIV.

To help find answers to these important questions, The Bongani Mayosi Research Collaborative has embarked on a promising program of research. It works closely with local and global scientists, and with members of communities most affected by HIV. Over the next five to ten years we hope to provide insights and answers to help those living with HIV realize the promise of a near normal life expectancy free of preventable cardiac and other non-communicable diseases.

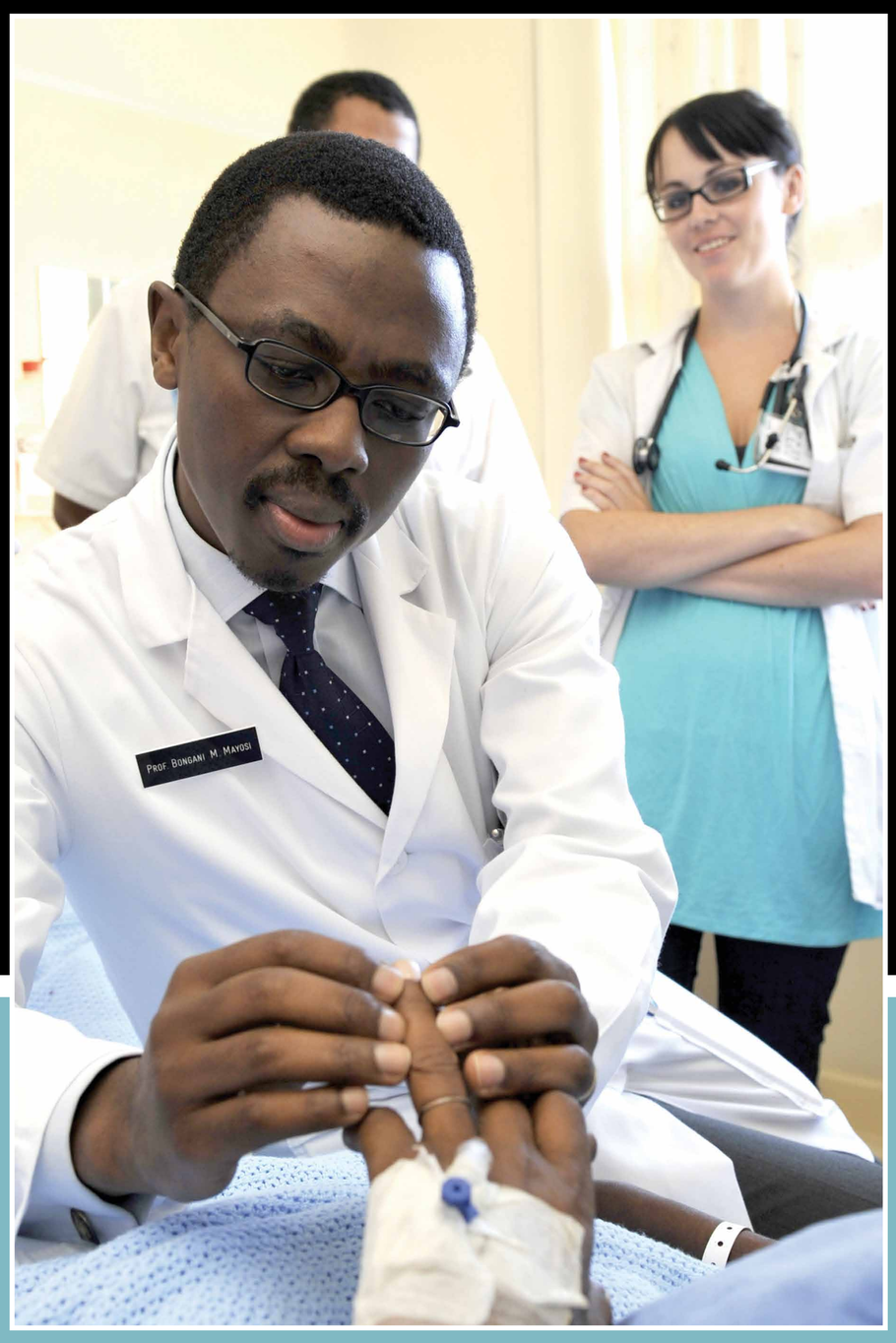
TUBERCULOSIS

In 2016, 2.5 million people in Africa fell ill with tuberculosis (TB), accounting for a quarter of new TB cases worldwide.

While cardiac TB was once relatively rare, the advent of HIV resulted in a resurgence of this aggressive and often fatal form of TB. Local and pan-African observational studies suggest that tuberculosis of the heart and its complications may account for 5-10% of the heart failure burden in regions such as the rural Eastern Cape.

Keen to improve outcomes of TB of the heart, Professor Bongani Mayosi and collaborators set up the Investigation of the Management of Pericarditis in Africa (IMPI) prospective research programme in 2003. IMPI aims to better understand the disease, addressing issues such as how and why it causes so much harm; how it can best be diagnosed; what the best treatment options are; and how its most devastating complications such as constrictive pericarditis can be prevented. The Bongani Mayosi Research Collaborative is working on these questions with the IMPI network and others.

A series of randomised controlled studies are ongoing to test new treatment strategies, with others in the pipeline. A host of studies are also underway and planned to investigate the immunopathogenesis, mechanisms of fibrosis and optimal diagnosis. Over the next five to ten years, we hope to improve the survival rate of patients with tuberculous heart disease and identify ways of preventing severe complications amongst survivors.



RHEUMATIC HEART DISEASE

Rheumatic heart disease (RHD) is the leading cause of heart disease in children and young adults world-wide.

RHD is highly prevalent in developing countries, including South Africa and throughout Africa. Acute rheumatic fever (ARF), and subsequent RHD, is a major public health problem linked to inadequate access to healthcare, poorly functioning health systems, and social inequality. A 2015 study of prevalence in two centres in Cape Town demonstrated a clear socio-economic gradient, with rates between 12-20 per 1000. The incidence of RHD in patients over 14 years old in Johannesburg is 23.5 per 100,000 people per year.

RHD remains a neglected and under-studied disease, especially considering its extremely high disability-adjusted life year (DALY) burden. In 2010 the Global Burden of Disease Study calculated that the DALY burden of RHA was higher than that of, for example, cervical cancer and measles. Consequently, RHD has been identified as a strategic research priority area of the South African Medical Research Council. The recent African Union Communique highlighted a strategic plan for the eradication of RHD on the continent, which was followed by a landmark WHO resolution against ARF and RHD. The fight against ARF and RHD was spearheaded and galvanised by the work and advocacy efforts of Professor Bongani Mayosi in his quest to “eradicate ARF/RHD in our lifetime”.

The Bongani Mayosi Research Collaborative seeks to understand the facilitators of, and barriers to, accessing healthcare for ARF/RHD. It has active research projects examining Streptococcus A, the antecedent infection, which is part of an international initiative to inform African-appropriate vaccines as well as studies to improve the understanding of factors related to the disease’s rapid progression and subsequent mortality and morbidity using advanced imaging and metabolomics. To this end, the AFROStrep Registry was established by Professor Mark Engel in 2016. To date, AFROStrep is being launched in South Africa as well as other Southern African countries.

BUILDING CAPACITY IN AFRICA

Photograph, courtesy MRC

Professor Bongani Mayosi believed that if the continent was to realise its vast potential and reclaim its history of discovery and development, then Africans need the skills and know-how to understand, define and prioritise their own problems and find the appropriate answers.

Central to this vision was the need to “grow our own timber”. This philosophy emphasises excellence, while nurturing and mentoring people with potential in order to create a pipeline of future African scientists and researchers. Looking at the future through this lens inspired Professor Bongani Mayosi’s conceptualisation of the 1000 PhDs project, which remain in place today as part of his extraordinary legacy.

With support from local and international partners, The Bongani Mayosi Research Collaborative aims to continue building on this vision by facilitating opportunities such as scholarships, fellowships, and visiting research programmes for African investigators and clinician scientists. They also plan to promote capacity development through seminars and workshops, postgraduate student and research staff supervision, and providing training in research methodology and data management.