GUEST EDITORIAL

Cardiovascular research in South Africa – Past, present, and future

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ABSTRACT

Cardiovascular diseases (CVD) remain one of the greatest global health challenges of our time. In the field of cardiology, South Africa (SA) produced several giants and champions whose contributions have been exceptional in their respective spheres. With the complexities required to reduce and prevent such illnesses, we draw inspiration and motivation from our history as we look to overcome future challenges. Here, we share some perspectives on future research priorities, including the usage of several facets of Artificial Intelligence (AI), such as AI-assisted echocardiography, which could unlock pathways to precision medicine, and adopting mobile health (mHealth) technology and wearable instruments for diagnostics, as well as clinical trials investigating the use of polypill interventions. This work echoes calls for health equity, recognising that the future strength of cardiovascular research will require initiatives that promote talent and provide opportunities to grow diverse capabilities within our country. Finally, we highlight the importance of community engagement and co-creation to foster trust and thereby enhance the uptake of interventions, including those aimed at promoting health literacy and education to support positive behaviour change in preventing CVDs and other non-communicable diseases (NCD).
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INTRODUCTION

Cardiovascular health research in SA has made substantial contributions to the field, with a significant global impact. However, research and innovation will need to continue adapting as the burden of CVDs in SA rises. The complexity of SA's CVD burden and the contributing social determinants and risk factors, including the multimorbidity of associated NCDs, makes this task ever more challenging. Multimorbidity can be considered a norm in SA, especially among older adults, with hypertension as the main driver.[1] Such illnesses are now evident not only in adults, but in children too. A recent systematic review and meta-analysis provided updated estimates of paediatric hypertension, suggesting a continued increase in prevalence across the continent, highlighting the potential role of increasing overweight/obesity.[2]

SA's young people also experience a persistent burden of rheumatic heart disease (RHD).[3] This is amidst a legacy of infrastructural disparities in diagnostics and care, with most of these services for CVDs (and others) located mainly in the private sector.[4] Consequently, the vast majority of individuals, especially in rural areas, are unable to access specialised services. There also remain gaps in awareness and education, as well as access to long-term follow-up. These provide opportunities to develop solutions, which will require strengthening multidisciplinary stakeholder engagement.

SA has benefited immensely from the contributions of stalwarts whose exceptional research expertise resulted in significant historical milestones in cardiovascular health, impacting not just our country but the world. If we are to tackle the task ahead, it is best to draw lessons from the past, to remind ourselves of what is possible. Isaac Newton's phrase springs to mind, "If I have seen further, it is by standing on the shoulders of giants." To that we add, "If you don't know where you've come from, how can you hope to know where you are going?" As we look towards the future of CVD research in SA, we offer a moment of reflection on what came before.

FIGURE 1: Cardiovascular research champions of the recent past and unfolding present.
Top, left to right: Prof. Chris Barnard, Prof. Donald Ross, Dr John Barlow, Prof. Lionel Opie, and Prof. Solomon Levin.
Bottom, left to right: Prof. Bongani Mayosi, Prof. Karen Sliwa-Hahnle, Prof. Ntobeko Ntusi, and Dr Martin Mpe.

A history of cardiothoracic surgery in SA has been well detailed by Schewitz.[5] Here we add to it briefly, mentioning some of the giants of the recent past and the unfolding present (Figure 1). These people have massively impacted the field and the current landscape and, to varying degrees, also our personal journeys and careers. As we endeavour to build on the established legacy, we aim to expand the field of cardiovascular research in ways that push scientific boundaries while remaining responsive to society's needs, to ensure the greatest impact for those who require it most. Considering the current cardiovascular research landscape, this work underscores its vital role in shaping the future, particularly in advancing universal health coverage (UHC) and contributing to the National Health Insurance (NHI).

The past – Pioneering foundations

Prof. Chris Barnard is perhaps one of the most notable figures in cardiac surgery in SA, with his special contribution of performing the world's first human heart transplant in 1967 at Groote Schuur Hospital, Cape Town, which caught global attention.[6] Alongside was a colleague, Prof. Donald Ross, an innovator in his own right, developing the Ross procedure, an aortic valve replacement technique that uses the patient's own pulmonary valve.[7] Another sterling contributor was Prof. Lionel Opie, later known as the father of cardiovascular medicine in SA, for pioneering research in heart metabolism and the pharmacological treatment of heart disease, and his advocacy efforts for evidence-based cardiovascular medicine contributed greatly to knowledge building in the field.[8-10] Dr John Barlow, another legend in SA, with his key contribution in linking abnormal heart sounds ("clicks" and murmurs) to mitral valve prolapse, also known as "Barlow syndrome" – a discovery that shaped how doctors worldwide diagnose and understand valve disease.[11] Lastly, though not the least, we remember Prof. Solomon Levin, who published over 120 papers and book chapters and trained hundreds of specialists, leaving an extraordinary legacy in child heart care.[12]

The present – At the heart of the matter

In the free and democratic society of SA, we remember another outstanding clinician, scientist, and teacher, Prof. Bongani Mayosi, whose commitment to academic excellence, collaboration, and social transformation influenced and continues to inspire many. His significant contributions to research, teaching, training, and health policy have deservedly been recognised nationally and internationally with numerous accolades. A champion of research capacity building and health equity, his contributions to the field also included the identification of a novel gene in 2017, which encodes for arrhythmogenic cardiomyopathy. This was recognised as one of the most important medical advances made by a South African scientific team since the first human heart transplant.[13]

Prof. Karen Sliwa-Hahnle is a widely recognised world expert in CVDs, whose efforts have strengthened the CVD research ecosystem in the country, with a special interest in reducing women's mortality, focusing on heart disease in pregnancy and peri-partum cardiomyopathy. She founded the Soweto Cardiovascular Research Unit, advancing knowledge on the intersection of CVDs and maternal health and leads several inter-African and global research projects, with a major impact on creating knowledge and shaping policy on CVDs common in Africa and other low- and middle-income countries (LMIC).[14-16]

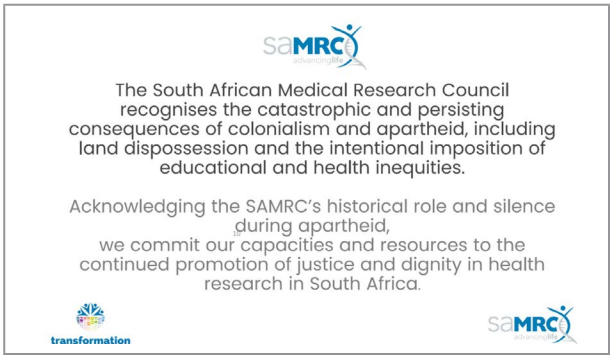

FIGURE 2: The board of the South African Medical Research Council (SAMRC) endorsed the adoption of an organisational declaration to raise awareness of persisting health inequities in South Africa, and in particular, their roots in our history of colonisation and apartheid.

Prof. Ntobeko Ntusi is a leading South African cardiologist whose most significant contributions include using advanced imaging and translational clinical research to deepen understanding of heart disease in African populations. He pioneered the use of cardiovascular magnetic resonance (CMR) imaging to characterise and understand heart disease – especially cardiomyopathy, inflammatory heart disease, and human immunodeficiency virus (HIV)-associated CVD.[17-19] Beyond his research, he serves in leadership and mentorship roles, training postgraduate students, supervising research, and is currently the president and chief executive officer of the South African Medical Research Council (SAMRC). His role encompasses influencing health policy, setting research priorities, and capacity building. In 2023, the SAMRC adopted a history and health statement to raise awareness of the persisting health inequities in SA, recognising their roots in our history of colonisation. The declaration acknowledges the organisation's role during apartheid and affirms its active commitment to addressing past injustices while advancing health equity (Figure 2).

Dr Martin Mpe is another noteworthy, distinguished cardiologist known for his leadership in interventional cardiology, cardiac pacing, and heart failure management. He also championed health promotion and education to raise awareness about CVD in under-resourced communities. As the current president of the South African Heart Association, his work combines cutting-edge clinical practice with a strong commitment to public health advocacy.

FUTURE RESEARCH PRIORITIES

SA is experiencing a high prevalence of hypertension, diabetes, and obesity. These are intricately bound to associated risk factors for other NCDs, including cancer and mental health disorders. Such chronic illnesses place an enormous burden on the already strained healthcare system. The consequence is a multimorbid epidemic, a lived experience for many people attempting to manage one or more of these illnesses simultaneously. Any progress to address these NCDs requires an approach that considers social health determinants, aiming to develop interventions that address their common risk factors. In terms of research and innovation, several plausible areas within cardiology can be prioritised. Several of these fields are described below.

Advancing cardiology – Unlocking precision medicine

Going forward, we need both precision and equitable care strategies. There are also calls for the inclusion of underrepresented populations in cardiovascular genetics and epidemiology, with novel genetic risk markers that can expand our current understanding and risk-stratification paradigms.[20] Further research considering genetic, environmental, and social health determinants will be required in developing culturally tailored prevention strategies. This opens the door to more personalised medicine (PM) approaches, which are lacking in SA and broadly across Africa. Adopting policies that incorporate a more PM approach could have a global impact, considering the uniqueness of African genetic diversity.

Furthermore, a study aimed at critically evaluating the current status quo of genetic counselling in SA by uncovering grey areas in their integration within the national healthcare system has highlighted the need for improved genetic education and healthcare inclusiveness to advance genomic medicine and precision healthcare for underserved populations.[21] By analysing policy frameworks, infrastructure, education, and initiatives, genetic counselling could advance patient knowledge and informed decision-making in SA. Despite significant challenges, these can be addressed through targeted research and education, while policy reforms will be critical for integrating genetic-related services into regional healthcare systems, which could be fundamental to improving healthcare strategies and patient outcomes across the continent.[21]

The SAMRC is a partner in the EU-Africa PerMed Consortium, which aims to identify areas of mutual interest and added value for future collaboration and to build sustainable links between Africa and Europe in PM research, development, innovation, and implementation, thereby better integrating the African continent into the global PM agenda. It is also noteworthy to mention the SAMRC's genomics platform and its next-generation sequencing (NGS) technology capability. Starting as a sequencing service with 9 human genomes completed in 2019, it has since developed into a core NGS facility for African genomics, precision medicine, pathogen surveillance, biomarker discovery, clinical trials, and training and mentoring of young scientists. The platform has reached a significant landmark achievement, completing the sequencing of its 10 000th sample, and is well poised to be a leader in advancing the PM agenda on the continent.

AI-assisted echocardiography

Remote interpretation and point-of-care diagnostics in rural areas have the potential to reduce diagnostic delays and human resource burdens. The accuracy of handheld echocardiography

(HAND) has been assessed against that of standard echocardiography (STAND), having the potential to usher in a new age of RHD screening in endemic areas.[22] HAND displayed good accuracy in detecting definite RHD only, and modest accuracy for detecting any RHD; however, it demonstrated poor accuracy in detecting borderline RHD alone. There is also some evidence for the potential of HAND to increase access to echocardiographic screening for RHD in resource-limited and remote settings; nevertheless, further research into the feasibility and cost-effectiveness of wide-scale screening is still required.[22]

Mobile health (mHealth) and wearables

In sub-Saharan Africa (SSA), where there is a high disease burden, a dearth of medical experts, and inadequate healthcare infrastructure, mHealth is particularly advantageous for real-time monitoring and behaviour modification. Behaviour change interventions are increasingly delivered via mHealth, using smartphone applications and wearables. These are believed to support healthy behaviours at the individual level in a low-threshold manner.[23] However, evidence is scarce for LMICs, as well as for people with different socio-economic and cultural backgrounds.

In practice, clinicians and healthcare practitioners could carefully consider the potential benefits, limitations, and evolving research when recommending smartphone applications to overweight or obese adolescents and adults.[23] With the fast adoption of mobile phones and the internet in the SSA region, mHealth technologies are projected to make a substantial contribution to the highly challenged SSA healthcare sector; however, greater efforts are required to integrate wearable sensors into mHealth platforms.[24] The potential impact of this development could be enormous.

Polypill studies

The polypill is a single-pill combination (SPC) therapy for primary and secondary prevention.[25-28] Despite the proven efficacy, safety, and economic benefits of the polypill protocol, pharmaceutical companies remain reluctant to invest in its development and testing. Furthermore, community-based trials to assess uptake and adherence, especially in SA, are still required. Overall, the polypill, combined with advice to improve lifestyles, can facilitate the implementation of worldwide programmes to limit the consequences of CVDs, which is considered the new pandemic of our century.[29]

Currently, there are SPCs for hypertension, which are effective and widely used, but only one formulation is currently licensed for CVD use in SA. Given the tremendous success of SPC antiretrovirals (ARVs) in this country, we have the potential to reduce CVD deaths substantially. According to estimates, only 50% polypill adoption could prevent approximately 2 million CVD deaths and 4 million cardiovascular events per year, which is crucial in attaining the World Health Organization's (WHO) Sustainable Development Goal of reducing global deaths from NCDs by 30% by 2030.[30]

CAPACITY BUILDING, DIVERSITY, AND LEADERSHIP

Increasing evidence suggests that health objectives are best achieved through a multisectoral approach. It requires multiple sectors to consider health and well-being as a central aspect of their policy development and implementation, recognising that numerous health determinants lie outside (or beyond the confines of) the health sector.[31] This needs to be in favour of a "One Health" approach, as opposed to dealing with these illnesses in isolation. Given that several programmes face similar challenges and associated risk factors, efforts aim to target common risk factors for these conditions, such as nutrition and physical inactivity.[32]

Furthermore, infrastructure that benefits a cardiovascular registry may also benefit a cancer registry. With so many people experiencing several of these illnesses, their information and data would likely need to be captured across these registries. As an example, the South African Population Research Infrastructure Network (SAPRIN)-enabled CVD registries/cohorts for real-world evidence and policy feedback loops could be considered.[33] This could facilitate the development of "Big Data" and the generation of standardised national datasets to inform policy and practice. In addition, training and mentoring the next generation of cardiovascular researchers, including strengthening expertise in biostatistics, AI, and implementation science, and investing in research infrastructure, will be necessary. This should include equitable funding mechanisms and initiatives that promote African-led collaborations across the continent.

A diverse workforce is increasingly recognised as paramount in SA's cardiovascular research ecosystem. The critical contributions of women, those from underrepresented groups, universities, and institutions to the cardiovascular research ecosystem in our country are being acknowledged. Of the past five presidents of SA Heart®, three were women, as were the current and recent presidents of the American College of Cardiology, the American Heart Association, and the European Society of Cardiology. Furthermore, increasing African leaders in clinical trials, journal editorships and boards, as well as funding agencies, will ensure a more resilient research landscape, with a focus on LMIC priorities.[34]

We echo calls for partnerships involving various sectors, including robust community engagement, to effectively deliver and sustain health-promoting policies and actions.[31] Regarding health systems research and reform, towards UHC, which is underpinned by cost-effective models for long-term care, decentralised and task-sharing approaches, more public-private academic collaborations are needed. It will be important to conduct policy-relevant research that influences not only CVD research strategies but also the national NCD strategy, given the interconnectedness and associated risks of these illnesses. Chronic condition management increasingly strains health systems, far exceeding acute care needs globally, necessitating adaptation.[35]

In this context, an analysis of clinical interventions targeted at adults aged 15+, with evidence of the direct costs of type 2 diabetes mellitus (T2DM), hypertension, and CVDs in SA, reported primary estimates of in- and out-of-hospital costs from a provider perspective.[36] Drugs and treatment of complications were major cost drivers for hypertension and T2DM, with hospitalisation driving CVD costs. It was found that 39% of identified CVD treatment costs used a private sector perspective, leaving significant research gaps in the public sector and the cheaper to treat hypertension and T2DM.[36]

Furthermore, a systematic review investigating the relationship between socio-economic inequalities and fatal and non-fatal cardiovascular events found that, although not statistically significant, women of low socio-economic status (SES) were at higher CVD risk than men. It was found that CVD risk was more relevant to educational than economic inequality.[37] These results support previous findings, which highlighted that low SES is linked to increased CVD risk in high-income countries, and that women with low SES had a relative risk of 2.24 for angina pectoris (chest pain or discomfort) compared to their high SES counterparts, whereas no significant difference was observed in men.[38,39] Additionally, given the high prevalence of central obesity in children that can ultimately result in cardiovascular risk factors and mental health issues, the need for systems jointly initiated by healthcare providers, policymakers, and general society is highlighted to reduce the burden of central obesity by introducing children and adolescents to health-promoting lifestyles.[40]

Community-level interventions, such as hypertension control, are considered useful for preventing cardiovascular and cerebrovascular events. Unfortunately, systematic evaluation of such community-level interventions among patients living in LMICs is scarce. Thus, community-based strategies are relevant in addressing the burden of hypertension and aid in decentralised hypertension care in LMICs, while confronting the gap in access to care, without diminishing the quality of hypertension control.[41] Thus, a similar approach can be used to ensure that interventions are culturally safe, having been co-designed by the people requiring these services themselves.

CONCLUSION

SA has a long, rich legacy of innovation and multiple global contributions to cardiovascular research. The field is growing with new scientists, basic clinicians, innovators, and trialists – many leading their respective fields. Future research efforts must be diverse, spanning from genetic studies to clinical trials and public health initiatives, with a particular emphasis on the unique challenges faced by our country and region. Addressing the rising burden of CVD requires bridging science, systems, and society. The future lies in equity-driven, data-informed, and technology-enabled solutions. The country needs to prioritise translational research, community and lived-experience partnerships, and the rapid advancement of skilled services, such as cardiac surgery. Overcoming the challenges posed not only by CVDs but by all related illnesses and associated risk factors will require a collective commitment from all of society.

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