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In Memoriam Professor Bongani Mayosi, 1967 to 2018



George A. Mensah, MD

rofessor Bongani Mawethu Mayosi, Dean of the Faculty of Health Sciences at the University of Cape Town (UCT) and professor and former head of the Department of Medicine at Groote Schuur Hospital and UCT, was born in uMthatha in South Africa's Eastern Cape Province on January 28, 1967. He died in Cape Town on July 27, 2018. As his family disclosed, Professor Mayosi took his life after a battle with clinical depression in the preceding 2 years (1). He was only 51 years of age and was already a recipient of the Order of Mapungubwe in 2009, the highest honor awarded to South African citizens for "achievements that have impacted internationally and served the interests of the Republic of South Africa" (2). Other distinguished recipients of this award include former South African president Nelson Mandela for his achievements in national reconciliation and nation-building. This memorial tribute provides a brief review of Professor Mayosi's background and remarkable contributions to biomedical research, research training and mentorship, and the spirit of forging and nurturing international collaborations for health.

Professor Mayosi was 1 of 5 siblings. His father, Dr. George Timketson Sikhumbuzo Mayosi, was a regional district surgeon in the Eastern Cape Province and later a specialist in obstetrics and gynecology. His mother, Mrs. Nontle Mayosi, was a nurse who suspended her own career for 14 years to start a school with help from other mothers who were teachers in the village of Ngqamakhwe in the former Transkei (3). Professor Mayosi's humility, devotion to his family and community, and commitment to create opportunities for the underserved stem from his early experiences in the village of Ngqamakhwe. His love of the practice of medicine, however, came from childhood Saturdays spent in the backseat of his doctor father's Landover as his father "drove to patient after patient along very ragged, bumpy roads" in the remote Eastern Cape Province of South Africa (4).

Professor Mayosi graduated with multiple distinctions from St. John's College in uMthatha. His passion for biomedical research came later, in the middle of his undergraduate training in medicine at the University of KwaZulu-Natal, now the Nelson Mandela School of Medicine. He was the first person in that medical school to graduate with 2 degreesone in medicine (MbChB) with distinction and another in medical sciences (BMedSci) with distinction given for the research he conducted during an extra year. This year of research instilled in him a lifelong passion for accelerating capacity-building for clinical and biomedical research in Africa. His reputation and international recognition for highquality, scientific research have been impeccable. His scientific publications, now numbering >330 in the PubMed database of the U.S. National Library of Medicine, demonstrate an unsurpassed clarity of thought, originality, and scientific rigor. Three areas of scientific interest he actively investigated-acute rheumatic fever and rheumatic heart disease, tuberculous pericarditis, and the genetic etiology of cardiomyopathy-deserve mention.

First, Professor Mayosi has published >3 dozen papers with primary emphasis on acute rheumatic fever and rheumatic heart disease, the prototype of neglected cardiovascular disease of poverty. For example, he and his colleagues documented the persistently high incidence and burden of rheumatic heart disease in Soweto, at a time when the burden of this disease was declining in other regions of the

From the Center for Translation Research and Implementation Science, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland. The views expressed in this article are those of the author and do not necessarily represent the views of the National Heart, Lung, and Blood Institute, the National Institutes of Health, or the U.S. Department of Health and Human Services.

TABLE 1 Selected Clinical Studies and Trials Published by Professor Bongani Mayosi and Collaborators, 2014 to 2018		
Study Name	Study Title	Selected Publication
MANAGE	Dabigatran in patients with myocardial injury after non-cardiac surgery (MANAGE): an international, randomized, placebo- controlled trial	Lancet 2018;391: 2325-34
INTERSTROKE	Practice patterns and outcomes after stroke across countries at different economic levels (INTERSTROKE): an international observational study	Lancet 2018;391: 2019-27
CREOLE	Rationale and design of the comparison of 3 combination therapies in lowering blood pressure in black Africans (CREOLE study): 2 × 3 factorial randomized single-blind multicenter trial	Am Heart J 2018;202: 5-12
THESUS-HF	Symptoms and signs of heart failure at admission and discharge and outcomes in the Sub-Saharan Acute Heart Failure (THESUS-HF) registry	J Card Fail 2017;23: 739-42
PURE	Availability and affordability of blood pressure- lowering medicines and the effect on blood pressure control in high-income, middle-income, and low-income countries: an analysis of the PURE study data	Lancet Public Health 2017;2:e411-9
AFROStrep	Rationale and design of the African group A streptococcal infection registry: the AFROStrep study	BMJ Open 2016;6: e010248
REMEDY	Clinical outcomes in 3343 children and adults with rheumatic heart disease from 14 low- and middle-income countries: two-year follow- up of the Global Rheumatic Heart Disease Registry (the REMEDY Study)	Circulation 2016;134: 1456-66
BA-HEF	Bi treatment with hydralazine/nitrates vs. placebo in Africans admitted with acute HEart Failure (BA-HEF)	Eur J Heart Fail 2016;18: 1248-58
IMPI	Prednisolone and Mycobacterium indicus pranii in tuberculous pericarditis	N Engl J Med. 2014;371: 1121-30
COPPS-2	Colchicine for prevention of post-pericardiotomy syndrome and postoperative atrial fibrillation: the COPPS-2 randomized clinical trial	JAMA 2014;312: 1016-23

world (5). More recently, in the REMEDY (Global Rheumatic Heart Disease Registry), he initiated and directed the first prospective, multinational study of rheumatic heart disease demonstrating a high burden of cardiovascular complications and low uptake of proven-effective interventions in this disease (6). In declarations from Drakensberg (7) and Mosi-o-Tunya (8), he galvanized researchers across Africa to join him in fighting these diseases of poverty and training the future generation of health scientists in Africa. His additional research efforts and results in this area have informed health policy development and provided promising foundations for vaccine development against rheumatic heart disease (9-11).

Second, Professor Mayosi has produced an equally impressive list of publications on the diagnostic evaluation and management of tuberculous pericarditis. For example, he was the architect of the studies on the Investigation of the Management of Pericarditis, named IMPI for the Zulu warriors, the Impi (12). The IMPI studies enrolled 1,400 patients with tuberculous pericarditis from multiple centers in Kenya, Malawi, Mozambique, Nigeria, Sierra Leone, South Africa, Uganda, and Zimbabwe. Findings from these studies have contributed substantively to our understanding of the clinical characteristics, outcome, immunology, diagnosis, and treatment of tuberculous pericarditis (13-15). His team's pursuit of both human and animal research in tuberculous pericarditis, including the description of a unique pro-fibrotic cytokine signature in effusive-constrictive pericarditis in tuberculous pericardial effusion, holds significant promise for new treatment targets in this disease (16,17).

Third, Professor Mayosi also carried out fundamental discovery and basic science research in cardiomyopathies. For example, he and his colleagues explored the spectrum of causal genetic mutations and clinical outcomes of hypertrophic cardiomyopathy (18-20). In 2017, after 20 years of work, Professor Mayosi led the South African team of researchers who, in partnership with collaborators from Italy and Canada, published for the first time several lines of evidence that implicated mutations in the Cadherin 2 (*CDH2*) gene as a likely new genetic cause of arrhythmogenic right ventricular cardiomyopathy (21). This major breakthrough could lead to improved diagnosis and treatment of arrhythmogenic right ventricular cardiomyopathy (21).

In addition to the research conducted in these 3 areas, Professor Mayosi had a gift for forging and nurturing strategic partnerships and scientific collaborations to advance clinical research in countries across the full range of sociodemographic indexes, and especially in sub-Saharan Africa. Several of his research collaborators came from countries and centers where neither formal cardiology practices nor a previous track record of clinical research existed. Several of the multicenter and multinational studies that Professor Mayosi organized or contributed to over the past 4 years are shown in Table 1. They include studies in myocardial injury after noncardiac surgery, differences in the management of stroke across countries at different levels of economic development, comparative effectiveness of strategies for hypertension control, the clinical epidemiology and outcomes of heart failure in Africans, and the prevention of post-pericardiotomy syndrome and post-operative atrial fibrillation.

In all his research activities, he made teaching, research training, and career development of the future generation of researchers a top priority, especially for under-represented black African men and women in South Africa. In his inaugural address as chair of the Department of Medicine at the University of Cape Town, Professor Mayosi called for a national program to train "at least 1,000 clinical PhD scholars who will change the fortunes of clinical medicine in Africa for the next 100 years" (3). He was instrumental in working with the Academy of Science of South Africa, the National Health Research Committee, the Medical Research Council, and the National Department of Health to make this a reality in South Africa (22). The government of South Africa has now launched a PhD training program that is on track to enroll 1,000 new PhD students in the health sciences by 2022 (22).

Above all, Professor Mayosi was a kind and gentle giant. He was engaging, empathetic, and always giving with his characteristic big smile and a wonderful sense of humor. He was also a creative force of unparalleled vision, dedication, energy, optimism, and inspiration for thousands. He will be sorely missed by all of us who had the opportunity to know him and by many more who knew of him. Professor Mayosi left behind his wife, Professor Nonhlanhla Khumalo, 3 daughters, his mother, and his extended family.

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ADDRESS FOR CORRESPONDENCE: Dr. George A. Mensah, Center for Translation Research and Implementation Science (CTRIS), National Heart, Lung, and Blood Institute, National Institutes of Health, One Rockledge Centre, 6705 Rockledge Drive, Suite 6070, Bethesda, Maryland 20892. E-mail: George.Mensah@ nih.gov. Twitter: @NHLBI_Translate, @ProfMensah.

REFERENCES

1. Child K. UCT health dean Bongani Mayosi took his own life, says devastated family. Times Live. Available at: https://www.timeslive.co.za/news/south-africa/2018-07-28-uct-health-dean-bongani-mayosi-took-his-own-life-says-devastated-family/. Accessed July 28, 2018.

2. Republic of South Africa, Department of Arts and Culture. The Order of Mapungubwe. Available at: http://www.dac.gov.za/order-mapungubwe. Accessed July 27, 2018.

3. Mayosi BM. The Future of Medicine: Inaugural Address as Chair, Department of Medicine, Faculty of Health Sciences, University of Cape Town, 2007. Available at: http://www.cehi.uct.ac. za/downloads/uct.ac.za/news/lectures/inaugurals/ inaug_bongani_mayosi.doc. Accessed July 27, 2018.

4. Kirby T. Bongani Mayosi: targeting heart diseases of poverty in Africa. Lancet 2012;380: 1985.

5. Sliwa K, Carrington M, Mayosi BM, Zigiriadis E, Mvungi R, Stewart S. Incidence and characteristics of newly diagnosed rheumatic heart disease in urban African adults: insights from the heart of Soweto study. Eur Heart J 2010;31:719-27.

6. Zuhlke L, Engel ME, Karthikeyan G, et al. Characteristics, complications, and gaps in evidence-based interventions in rheumatic heart disease: the Global Rheumatic Heart Disease Registry (the REMEDY study). Eur Heart J 2015; 36:1115–1122a.

7. Mayosi B, Robertson K, Volmink J, et al. The Drakensberg declaration on the control of rheumatic fever and rheumatic heart disease in Africa. S Afr Med J 2006;96 3 Pt 2:246.

8. Mayosi BM, Gamra H, Dangou JM, Kasonde J. Rheumatic heart disease in Africa: the Mosi-o-Tunya call to action. Lancet Glob Health 2014;2: e438-9.

9. Engel ME, Muhamed B, Whitelaw AC, Musvosvi M, Mayosi BM, Dale JB. Group A streptococcal emm type prevalence among symptomatic children in Cape Town and potential vaccine coverage. Pediatr Infect Dis J 2014;33:208-10.

10. Dale JB, Fischetti VA, Carapetis JR, et al. Group A streptococcal vaccines: paving a path for accelerated development. Vaccine 2013;31 Suppl 2:B216-22.

11. Yacoub M, Mayosi B, ElGuindy A, Carpentier A, Yusuf S. Eliminating acute rheumatic fever and rheumatic heart disease. Lancet 2017;390:212-3.

12. Mayosi BM, Ntsekhe M, Bosch J, et al. Rationale and design of the Investigation of the Management of Pericarditis (IMPI) trial: a 2 x 2 factorial randomized double-blind multicenter trial of adjunctive prednisolone and Mycobacterium w immunotherapy in tuberculous pericarditis. Am Heart J 2013:165:109–15.e103.

13. Mayosi BM, Wiysonge CS, Ntsekhe M, et al. Clinical characteristics and initial management of patients with tuberculous pericarditis in the HIV era: the Investigation of the Management of Pericarditis in Africa (IMPI Africa) registry. BMC Infect Dis 2006;6:2.

14. Imazio M, Mayosi BM, Brucato A, Adler Y. Pericardial effusion triage. Int J Cardiol 2010;145: 403-4.

15. Mayosi BM, Ntsekhe M, Bosch J, et al. Prednisolone and Mycobacterium indicus pranii in

tuberculous pericarditis. N Engl J Med 2014;371: 1121-30.

16. Ntsekhe M, Matthews K, Wolske J, et al. Scientific letter: Ac-SDKP (N-acetyl-seryl-aspartyllysyl-proline) and Galectin-3 levels in tuberculous pericardial effusion: implications for pathogenesis and prevention of pericardial constriction. Heart 2012;98:1326-8.

17. Ntsekhe M, Matthews K, Syed FF, et al. Prevalence, hemodynamics, and cytokine profile of effusive-constrictive pericarditis in patients with tuberculous pericardial effusion. PloS One 2013;8:e77532.

18. Ntusi NA, Shaboodien G, Badri M, Gumedze F, Mayosi BM. Clinical features, spectrum of causal genetic mutations and outcome of hypertrophic cardiomyopathy in South Africans. Cardiovasc J Afr 2016;27:152-8.

19. Mayosi B, Watkins H. The diagnosis of familial hypertrophic cardiomyopathy in children. Eur Heart J 1998;19:1276-8.

20. Moolman-Smook JC, Mayosi B, Brink P, Corfield VA. Identification of a new missense mutation in MyBP-C associated with hypertrophic cardiomyopathy. J Med Genet 1998;35:253-4.

21. Mayosi BM, Fish M, Shaboodien G, et al. Identification of cadherin 2 (CDH2) mutations in arrhythmogenic right ventricular cardiomyopathy. Circ Cardiovasc Genet 2017;10:e001605.

22. University of Cape Town. Go big on PhDs, says Mayosi. May 2, 2012. Available at: https://www. news.uct.ac.za/article/-2012-05-02-go-big-onphds-says-mayosi. Accessed October 11, 2018.