Bongani Mawethu Mayosi: A life remembered

Prof. Ntobeko A B Ntusi

Chair and Head, Department of Medicine, University of Cape Town and Groote Schuur Hospital ntobeko.ntusi@uct.ac.za

Prof. Bongani Mawethu Mayosi was born on 28 January 1967 in Umthatha, Eastern Cape. He was the second son of Dr George Sikhumbuzo Mayosi and Mrs Nontle Mayosi. He attended his primary school in Upper Ngculu village, Ngqamakhwe, Eastern Cape, and completed high school, matriculating from St John's College, Umthatha, with six distinctions, at the age of 15. His first two degrees were a BMedSci, completed in 1986, and concurrently a MB ChB in 1989, at the University of Natal - both obtained cum laude and at the top of his class. He worked as an intern at Livingstone Hospital in Port Elizabeth before moving to Cape Town to work as a senior house officer and later a medical registrar at Groote Schuur Hospital (GSH). Within 3 years, he had been admitted to the Fellowship of the College of Physicians of South Africa (SA). Immediately after this, he was awarded the prestigious Oxford Nuffield Medical Scholarship, allowing him to read for a DPhil in cardiovascular medicine at the University of Oxford under the supervision of Prof. Hugh Watkins. He returned from Oxford to complete his clinical training in cardiology at GSH. Thereafter, he worked as a consultant in the Cardiac Clinic until his appointment as the 7th Chair and Head of the Department of Medicine at the University of Cape Town (UCT) and GSH in 2006. Following an illustrious tenure, during which time he transformed the Department of Medicine, growing it to be the largest and leading medicine department on the African continent, in 2016 he was appointed as Dean of the Faculty of Health Sciences at UCT, and occupied this position until his untimely demise on Friday 27 July 2018.

His legacy is one of research excellence, academic development, and the transforming effect he had on individual lives, institutions and countries, particularly in Africa. His scholarship focused on noncommunicable diseases, including: (i) the epidemiology and genetics of cardiomyopathy; (ii) heart failure; (iii) pathophysiology, clinical outcomes and genetics of rheumatic heart disease (RHD); (iv) pericardial tuberculosis; (v) HIV-associated cardiovascular disease (CVD); (vi) rare genetic disorders among Africans; and (vii) health systems strengthening in SA and the African continent. During his career, he made seminal contributions to all these seven areas. He was considered the doyen of heart muscle disease on the African continent as he clarified the clinical profile, epidemiology and genetic basis of cardiomyopathies in Africans. He was involved in the discovery of novel genes that cause sudden cardiac death and heart failure in Africans. In cardiovascular genetics, Bongani's discoveries included genes causing dilated, hypertrophic and arrhythmogenic cardiomyopathy, coronary artery disease and hypertension. He established an internationally renowned laboratory at UCT, which at the time of his death was leading unique studies of the genetics of RHD and congenital heart disease in Africa. He has also provided the most complete investigation of the contemporaneous aetiology, clinical profile and optimal approaches to management for heart failure among Africans. He advanced our understanding of the biology of RHD, the role of screening and the employment of a strategy of syndromic treatment of pharyngitis to prevent this disease in children. His research has influenced policy and guidelines on the management of RHD globally, and been adopted by the African Union, the World Heart Federation, the World Health Organization and the World Health Assembly. He was an ardent advocate for

widespread availability of penicillin for the eradication of RHD in the global South. Through his study of pericardial tuberculosis, he clarified the appropriate diagnostic strategy and the role of adjunctive steroids in tuberculous pericarditis. He reviewed the state of healthcare in SA and the continent and made important recommendations on how health systems could be strengthened to improve the health of all Africans – in particular those in underserved areas.

While the contributions he made will influence the outcomes of future generations, I believe that his career will be remembered most for the relationships he built. He made friends everywhere he went. He recognised potential and invested substantially in the development of human capacity as part of the academic project. Bongani used research to advance his dream of 1 000 PhDs. He wanted to undertake research that would answer the prevailing fundamental questions on African cardiovascular health, and to answer these questions definitively. He embarked on building research capacity on the African continent and went into countries with no existing research management infrastructure or ethics committees and helped to establish these *ab initio*.

Bongani's professional achievements and accolades are too many to list and include the Order of Mapungubwe (Silver) and an A-rating by the National Research Foundation. He was a member of the Academy of Science of SA and a former President of the College of Physicians, the Colleges of Medicine of SA, the SA Heart Association and the Pan African Society of Cardiology (PASCAR). He was elected to the US National Academy of Medicine (arguably one of the highest honours in the fields of health and medicine, which recognises individuals who have demonstrated outstanding professional achievement and commitment to service).

As a clinician, Bongani was second to none. He was loved by his patients, who remembered his gentle and impeccable bedside manner. He had a fascination for understanding the mechanisms of physical signs, and encyclopaedic knowledge of clinical medicine. As a researcher, he was a global leader in his field. He published over 400 peer-reviewed papers and book chapters. He has an h-index of 87 and over 90 000 citations. As a teacher, he was legendary. He graduated over 30 Masters and doctoral students for whom he had provided supervision, and who remember him as a caring supervisor who invested substantially in them and created opportunities that have defined their careers. Many of his students have gone on to be leaders in academia, industry and government in this country, on the continent and throughout the world. His brand of leadership was honest, full of integrity and characterised by creativity and innovation. His commitment and passion were evident at all times. He was one of the most inspiring people I will ever know. He believed that there was no problem that could not be solved, and his work ethic was unquestionable. He played the long game, and always reminded me: 'A journey of a thousand miles begins with a few steps.' I remember Bongani as a dear friend, mentor, and confidant. I remember his tireless dedication to advancing a great cause. I remember his life of integrity, humility, outstanding intelligence, and absolute pursuit of knowledge and truth.

The UCT Faculty of Health Sciences and GSH colleagues remember him as a consummate professional and the epitome of hard work, and a leader who was exemplary in every way. He is remembered as a man with immense dignity and an infectious optimism. A visionary who imagined an Africa capable of driving its own agenda and using science to improve the health of its nations. He is remembered for his absolute love of UCT students. His fundamental drive was the transformation of society through investment in future generations of scientists, physicians and leaders. He is remembered for his absolute love of the hospital, the Department of Medicine, the Faculty of Health Sciences, the GSH and UCT, this country and the African continent.

Those who knew him well, and those who hardly knew him, spoke of their absolute love of the man and their sense of his apparent and evident affection for them. He is remembered for his unwavering belief in the potential of others and for his excellence in research, and translation of that research into work with a meaningful impact.

Above all, he is remembered for his absolute love of his family. He was a devoted husband and father and never missed an opportunity to share how much his family meant to him. He spoke often of how grateful he was for the support of his wife, and the love he received from his daughters who he constantly referred to as his 'pride and joy'. He is survived by his wife, Nonhlanhla, and three daughters: Nosipho, Sivuyile and Camagu (and many other 'daughters' raised in his home). He is also survived by his mother, Nontle, eldest brother, Sipho, and 2 sisters, Khuthala and Ncumisa.

He is dearly missed by his family, friends, and colleagues.

Reflections on coping with the loss of a leader, my mentor, my hero

Prof. Mashiko Setshedi

Chair and Head, Division of Medical Gastroenterology, University of Cape Town and Groote Schuur Hospital mashiko.setshedi@uct.ac.za

Since his passing, much has been said about the circumstances of this Shakespeareanesque tragedy; the causes of his depression, speculation about the trigger(s) of his suicide and endless conversations about what should and could have been done to prevent it. These are not trivial concerns. In this tribute, however, I have elected to use this platform as an opportunity to 'go there', and take a honest moment to reflect on Bongani Mayosi's passing, the shock of it all and the devastating aftermath it has left for everyone, especially his family, colleagues and the institution. How have we coped? Have we? What have we learned, if anything?

No ordinary day

Friday 27 July 2018 was no ordinary day. It was the day of the total lunar eclipse, and the planet Mars was reported as being at its closest to Earth. This concurrence, it is reported, occurs only once every 25 000 years! As rare as hens' teeth. On that very morning at 06h45 as I left the Mayosi home, I had no idea of the events that lay ahead, and the chaos that would ensue later that day. Unknown to me, this was the proverbial, eerie calm before the storm. This was the day that Bongani, as he insisted we all call him, would succumb to a dreadful, silent disease that ultimately stole his joie de vivre, his can-do, all-ispossible attitude. It was indeed no ordinary day.

I received the call at 14h30; the panicked voice on the line screamed 'Leave everything you're doing and come home NOW!'. Having manoeuvred my way through the early Friday afternoon traffic I finally arrived and was violently jolted into the reality that he was gone; he was no more. From that moment on I knew that nothing would ever be the same again. Preparing for his burial was something surreal; as we started to make plans, we had no idea of the colossal scale that would be required to accommodate all those wanting to attend the funeral service. We were initially looking for venues that could accommodate a few hundred mourners; however, it became rapidly clear that this would not suffice: something bigger was needed, for thousands. As a result, the burial became one massive production. Everything was moving at lightning speed, and the logistical twists and turns at every corner were sometimes difficult to keep up with. We were never prepared for the scale and resources that would be required to lay him to rest. In the end, the universe

co-operated, and he was given a beautiful send-off. It was only on that Saturday morning of his funeral service that I felt peace for the first time since he had passed.

In contrast, amid the chaos of that week, a parallel narrative of ubuntu unfolded. I had never seen such an outpouring of overwhelming emotion, love, support, and a coming together of a diverse people as I witnessed in that week, and perhaps I never will again. This experience I will cherish forever, it was a powerful lesson and testament to the fact that even when all hope seems lost, goodness still abounds.

'Let death by suicide not define him'

Who was Bongani Mayosi? Who was the man we all loved, respected and admired, whose passing touched each and every one of us in so many ways? Through his loss, we have all been afforded the opportunity to reflect on who we are in return, what our values are, and if these indeed align with what we do and say every day. This is the challenge. His passing was a terrible shock to the system. It brought into question everything I have ever believed in. Nonetheless, his passing has not been in vain. I say this being acutely aware that for his family - his wife, daughters, mother, and siblings - his loss is too painful to even consider the remote possibility that there might be any good to come from it. Therefore, I do not want to be insensitive. What I am attempting to articulate is that since his passing was not in our control, given that it happened nonetheless, is there anything that has been learned? I believe UCT is changing, not magically, not overnight, but certainly. Why? Because at the very least, there is an understanding that things cannot simply continue as before. It is early days yet, but that realisation alone is a triumph. At the request of his family, a review into the circumstances leading to his passing, and of the prevailing institutional culture, was instigated. Similarly, the Faculty of Health Sciences Deanery Review, which ironically Bongani himself commissioned, was galvanised into action after his passing. Both these processes are positive steps for a UCT that is opening to inclusivity, compassion for one another (even in the workplace), and the much-needed transformation that should be the foundation of everything we do.

Quoting from John Donne's poem Death Be Not Proud, 'One short sleep past, we wake eternally. And death shall be no more; Death, thou shalt die, in my view Bongani lives eternally; we carry him in our hearts and minds, always; certainly, I do. I do not allow that he is defined by the manner of his passing, but rather, having known him for 30 years, I choose to remember him as an easy-going, fun-loving, incredibly witty geek, who wore trousers that were a tad too short. I know he is resting, and I am at peace with that.

For bringing light and joy into our lives, and through his passing, helping us to discover our true purpose in this life, Enkosi!

Rest in peace RADEBE, BUNGANE, MASHWABADA, NGELENGELE, MTIMKHULU, NDLEBE-NTLE ZOMBINI.

The Bongani Mayosi legacy

Prof. George A Mensah

Director, Center for Translation Research & Implementation Science, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD, USA George.Mensah@NIH.Gov

My friend, Bongani Mayosi, was a brilliant academic and a visionary clinician-scientist. A loving father, husband, brother and mentor to countless researchers and students around the world. He was often the voice for the voiceless and underserved. His passion for scientific research and fundamental discovery knew no bounds. He will long be remembered for his unwavering commitment to accelerate training and career development for African health scientists. It was such a

pleasure exploring with him because his highly regarded writings and lectures demonstrated an unsurpassed clarity of thought, penetrating logic, originality and scientific rigor.

My fondest memory of Bongani will forever be his contagious smile. With that bright, wide, and unpretentious smile, he signalled how happy he was to see you – always bringing out the best in you and making you smile no matter what you might be dealing with in life. His smile revealed humility, hospitality and a willingness to offer you all the help you needed. A smile from Bongani beckoned, even compelled you to join him in his latest idea for addressing the most challenging clinical and public health burdens – eradicating the neglected chronic diseases of the poor and fighting institutionalised social injustice.

To Bongani, no task seemed too impossible to tackle. He had a real knack for bringing individuals of diverse backgrounds and skills together to form long-lasting teams for solving challenging health problems. He had a gift for forging and nurturing international collaborations for health in countries where such collaborations previously never existed. It is therefore no surprise that several of his research findings are now informing health policy development and providing innovative and promising foundations for new medical treatments for diseases of the heart.

I salute UCT for this celebration of Bongani's life and creation of the Bongani Mayosi Legacy Project. This project has replaced my year-long grief with a fitting memory of inspiration and hope that, individually and collectively, we can work together to lift our communities as we rise. And rise to the occasion we must! We can work together to ensure that his vision comes true in our lifetime – that vision of eradicating neglected diseases of the poor among us and creating a lifetime of health for all. Most importantly, this legacy project reminds us and assures us all that we can follow his footsteps and create meaningful and transformative health impact for all in Africa and worldwide.

Bongani Mayosi, a valued colleague Prof. Patrick J Commerford

Emeritus Professor of Medicine, University of Cape Town Patrick.commerford@uct.ac.za

Bongani Mayosi was arguably one of the brightest and best trainees I have ever had, and one of the smartest academic clinicians I have known. From the very first day he joined the Cardiac Clinic at Groote Schuur, his ability and character were evident. His contribution to service, teaching and research was immense. It was my privilege to know and interact with him as a trainee, valued clinical colleague, co-investigator and latterly as my superior. In all those roles, he excelled, and I value his great contributions in those many diverse aspects. I miss him dearly.

Bongani Mayosi: An ambassador for South Africa and the world Prof. Bernard Gersh

Honorary Professor of Medicine, Department of Medicine, University of Cape Town, and Professor of Medicine at the Mayo Clinic College of Medicine, Rochester, USA Gersh.Bernard@mayo.edu

I remember when he visited the Mayo and stayed with my wife and I many years ago, and recall his enthusiasm as he shared his exciting vision for the future of the Department of Medicine, UCT Medical School and cardiology in Africa. His contributions were immense and although tragically cut short, he had a major impact at UCT and in SA, across the African continent through his involvement in PASCAR and globally through his interest in rheumatic fever. Despite these multiple commitments, he and his team continued to publish high-quality research that continued to enhance the role of UCT as the leading scientific institution in Africa.

Prof. Mayosi's engaging and dynamic personality, when coupled with his many accomplishments, made him a great ambassador for SA around the world.

He is sorely missed as a leader, scientist and as a friend.

Prof. Bongani Mayosi: A man of the heart

Dr Reno Morar

Chief Operating Officer, University of Cape Town reno.morar@uct.ac.za

Assoc. Prof. Maylene Shung King

Convenor of the Oliver Tambo Health Leadership Fellowship, University of Cape Town

maylene.shungking@uct.ac.za

I choose to give this personal tribute, on behalf of our family, including our two sons, to whom our beloved colleague and friend, Bongani Mayosi, was simply 'Uncle Bongani'.

I first met Bongani Mayosi in 1984 in 2nd year MB ChB when I joined their class cohort at the UNB – the University of Natal [Black Section]. My association and subsequent friendship with Bongani span a period of 34 years – starting from our early student years in Alan Taylor Residence in Wentworth, Durban, to our final working together in the Dean team at the UCT Health Science Faculty.

Bongani was, in my opinion, one of the brightest minds ever to come out of UNB Medical School. Bongani Mayosi was immensely talented and achieved international recognition for his scientific endeavours – yet remaining humble and always approaching all of life's pursuits with honesty, integrity and kindness. He poured his academic pursuits into matters of the physical heart. He was deeply committed to social justice and equity and determined to change 'cardiac health' of communities most affected by of poverty and deprivation. Notwithstanding his many scientific achievements, I will never forget his smile that appeared after reading a cellphone message informing him that his research group had discovered that gene! The new gene that is a major cause of sudden death among young people and athletes.

Bongani also nurtured his own spiritual heart, as he was a deeply committed Christian. And he unobtrusively urged and inspired others to incline their hearts toward a relationship with God. It was in fact through the Student Christian Fellowship (SCF) at UNB where I first met Bongani and his wife Nonhlanhla.

Since Bongani's passing away, we have had the immense privilege of attending several commemorative occasions celebrating his welllived life through which I reconnected with so many common friends and colleagues, all of whom were deeply touched by Bongani's life in different ways. This is a testimony to who Bongani was, a nurturer of people and relationships, and a networker like none.

I will never forget his wide, bright and beautiful smile. And I, like so many others, will continue to miss him for a very long time.

Hamba Kahle my friend, Hamba Kahle Bongani.

Bongani Mayosi: A dear friend and collaborator Prof. Peter Schwartz

Chair and Head, Center for Cardiac Arrhythmias of Genetic Origin, Istituto Auxologico Italiano IRCCS, Milan, Italy peter.schwartz@unipv.it Luisella, my wife, and I met Bongani more than 18 years ago. It took a very short time for things to develop, both at professional and – more importantly – at personal level, where he became our very best friend in SA.

Professionally, things were easy because he was so brilliant, so determined, so able to visualise the heart of the problem. He was a great partner, always fair in sharing. There were many joint projects, and it was a privilege to contribute to a major genetic discovery that was entirely due to one of his earlier intuitions, followed with incredible persistence for many years, when he was never discouraged by the initial failures; he knew that he was right and he never gave up, until the final success. But research was his turf and, there, he could and would fight to the end. Tragically, other battles – unrelated to real science – broke his heart.

Personally, he was always a joy to be with. Very rapidly, acquaintance became true friendship. The two of us, with him and Nonhlanhla, began to share many happy moments. At our home, at their home (where we often met Vuyi and Gugu), in restaurants such as our regular visits to Mamma Roma, theatres, or museums, our meetings were not just social outings. The best was to talk about everything. With Bongani there never were 'the areas where you don't go'. We were discussing life, politics, our different cultures and habits; it was both fun and serious. Through him we learnt a lot about SA, past and present, good and bad. There was warmth and depth in our being together. When his painful troubles emerged, he was very open with us and we discussed them at length, without being really helpful.

It is difficult to think of SA without him. It is impossible to think of Nonhlanhla without Bongani, and we hug her with all our love. He was indeed our best friend, and we miss him terribly.

Remembering Bongani Mayosi

Prof. Siamon Gordon

Emeritus Professor of Pathology, University of Oxford siamon.gordon@path.ox.ac.uk

I first met Bongani at the UCT Medical School during one of my annual visits to my *alma mater*. I had been alerted to his outstanding promise as a physician who was hoping to obtain further research training in cardiology in England. After a brief introduction, I invited him to Oxford to undertake a DPhil with Hugh Watkins, who had recently returned from Boston. From the arrival of Bongani, Nonhlanhla and their two lively daughters, we became firm family friends over his years at the John Radcliffe Hospital and Wolfson College. The girls grew up fast, loved ice skating and became firm favourites with my wife, Lyndall, and our daughters Anna, away at Cambridge, and Olivia. Bongani always had a smile and infectious laugh, enlivening everyone in his presence.

Our friendship continued after his return to the Department of Medicine at GSH, both socially and academically. We talked about a collaborative immunological project on RHD, an ongoing concern in SA, but alas never managed to get this off the ground. As he grew in prominence, I valued the people he recommended to me, culminating more recently in research training for Mashiko Setshedi and later for Mankgopo Kgatle, in human immunology and epigenetics, respectively.

Whenever I met Hugh Watkins, we would proudly exchange news of Bongani's achievements. The last time we met Bongani was a few weeks before he died, at a lunch hosted by Mashiko at Llandudno. He and Nonhlanhla regaled us with details of the lobola negotiations between representatives of the Mayosi and Khumalo clans to secure their union as Xhosa and Zulu in a marriage across cultural traditions. The climax came from Nonhlanhla's fervent intervention, 'I want him!'.

We miss him dearly.

Bongani was a rare, gentle physician and human being, a prince among men.

My memories of Bongani Mayosi Prof. Salim Yusuf

Heart and Stroke Foundation/Marion W. Burke Chair in Cardiovascular Disease; Distinguished University Professor of Medicine, McMaster University; Executive Director, Population Health Research Institute, McMaster University; Hamilton Health Sciences yusufs@mcmaster.ca

Some 10 or 12 years back, at a steering committee meeting of the ACTIVE and OASIS trials, Pat Commerford had requested whether I would provide some advice to a young person who he had the highest regard for. It was about the design of a study in tuberculous pericarditis. I said that I would be happy to do so, but that I knew very little about tuberculous pericarditis and needed to get educated. Nevertheless, Pat introduced me to Bongani (and Mpiko Ntsekhe), who promptly arrived within a few weeks for a visit to Hamilton, and they shared with me the results of their registry. Knowing that any study in Africa (that is where I presumed tuberculous pericarditis would be most prevalent) would be unique, I invited Jackie to join the discussions for three reasons - first, that Jackie was incredibly creative in finding solutions to problems that we had not faced before; second, that she would enjoy a challenge; and third because in her heart she was a champion for the less advantaged and for 'lost causes'.

Bongani dazzled us with his smile, his enthusiasm and general good cheer, and radiated a 'can do' attitude. Mpiko was an understudy with many of the same attributes. On subsequent trips to Hamilton, we hiked sections of the Bruce Trail, went boating to our cottage, and we discussed and planned how to change the world for the better, but only in gentle and little steps.

We designed the trial – aptly called 'IMPI' (Investigation and Management of Pericarditis In Africa) by Bongani – as it stood for Zulu warrior. Jackie and I were pleased to be designated warriors, and that too Zulu! I invited Bongani and Mpiko home and they both charmed my wife, Wahida, and her parents with stories about life in SA, his interactions with the ANC, his medical school days, how he and Nonhlanhla got a job at GSH, and demonstration of the clicking language Xhosa. It was a most memorable evening having dinner on the deck in the cool Canadian summer.

IMPI was a major challenge as we had to raise money - creative funding from Cadila as a reward for having done the TIPS study, and simultaneously studying their tuberculosis vaccine along with the question of steroids that we were interested in. Several grants were submitted to many funding bodies, and most were turned down but ultimately the Canadian Institutes of Health Research (CIHR) relented, and we were funded on the third attempt. Now, conducting the IMPI study had its own challenges. We started without visible funding and with a modest amount of internal funds from both the Population Health Research Institute (PHRI) and Cape Town. Bongani and Mpiko travelled across Africa setting up the networks and persuading people to join the trial. Jackie worked with the countries and sites to overcome the regulatory approvals (most countries did not have a process and they were making up the rules as we went along; in some countries there was not a single ethics committee). After about 7 short years, we completed the study with important results - it felt like Moses leading his tribe across desert and sea to discover the promised land.

Bongani came to Hamilton for a month to write the papers, and we were delighted when the paper was accepted by the *New*

England Journal of Medicine – one of the most prestigious journals in the world. We debated whether to have the paper under the group authorship of 'IMPI' or have named authors. We settled for both and every one of the named authors were happy to have an authored paper in the *NEJM*. The presentation at the European Society of Cardiology meeting by Bongani of the main results was very special, especially when Sir Rory Collins from Oxford came up to us and said – what a remarkable achievement! And so it was.

IMPI was a journey into the 'hearts and minds' of Africa and the beginning of bigger and more impactful studies in RHD – starting with the REMEDY registry of 3 300 people (by far the biggest study of RHD at that time, and funded by a modest grant of CAD120 000 from our CANNeCTIN programme, the establishment of the large INVICTUS trial and registry of 20 000 people with RHD (led by Bongani and Stuart Connolly – the name INVICTUS was again coined by Bongani and the study was funded by Bayer on a corporate social responsibility ethos), the RHD Summit in Cairo and plans for the future elimination of RHD in Africa and beyond.

We were naive dreamers, who did make some things happen. I am reminded of the words: 'Most men dream in the dark recesses of the night with their eyes tightly shut. Some dream with their eyes wide open during the day. These are the dangerous men, for they may make their dreams come true.' Bongani was a dangerous dreamer and with him many dreams have and will come true.

On a personal note, Bongani was my brother from Africa. We intuitively understood each other. We shared the same desire to make the world a better place without ever speaking about this. In about 10 - 12 years of friendship, we never disagreed (largely because he was so amicable and accommodating), and we often sought advice from each other. Bongani stayed with us for a few weeks several times. During each visit, he valiantly tried to teach me to click and speak but failed (he had a poor student), and Wahida and I taught him how to set the dining table, clear it and wash dishes (he was a fast learner). He learnt to enjoy mildly spicy food. Our most wonderful visit was when Nonhlanhla and Bongani stayed with us, at their last visit, in Burlington and we spent countless hours talking and talking about everything under the sun. The best conversations were about the family and personal events - the haggling about the number of cows for the dowry when he wed Nonhlanhla, the Mayosi daughters who they were both incredibly proud of, how he looked forward to his two daughters' weddings, politics in Africa, his parents and childhood, medical school days, weekends training with the ANC youth, so many little, precious and important things.

My occasional visits to Cape Town were also memorable – especially the most recent one to the Mayosi home, Nonhlanhla's soup in the back yard near the swimming pool, the lunch at a rooftop hotel in Cape Town, being driven in his fast-sporting Audi, the trip up to the top of Table Mountain and so much else.

I sorely miss my dear friend and brother. But he is still here with me.

Bongani Mayosi: A man with his head and heart in Africa

Prof. Solomon Benatar Emeritus Professor of Medicine, University of Cape Town solomon.benatar@uct.ac.za

Prof. Bongani Mayosi had both his head and his heart in Africa. He pursued a highly productive academic medical career in the spirit of a clinician-scientist, with pride in having been educated in the best traditions of both the science and practice of medicine.

While continuing with his own distinguished career as a clinician and researcher, his ambition was to extend to others the educational benefits he had enjoyed, as well as the opportunities to apply these. His long-term goal was to advance medicine and health throughout Africa by guiding new generations of African scholar-practitioners into addressing, with excellence, the diseases most prevalent in, and afflicting, our continent. He envisioned progress towards achieving greater equity in health and healthcare in SA and Africa, with both optimism and insight into the complexity of the challenges that needed to be overcome to make such progress.

While immersed in the best of Western medicine he also had a deep commitment to being an African, proud of his cultural heritage and language. His ability to interact respectfully with those of different backgrounds and traditions earned him the support and admiration of colleagues across diverse fields of medicine and healthcare locally and abroad.

My collegial interactions with him over two decades spanned his time as a registrar in internal medicine and cardiologist during my tenure as head of department in Medicine, his 10 years as a distinguished leader of the Department of Medicine (two of which overlapped with my final years before formal retirement), and his Deanship of the Faculty of Health Science in my post-retirement capacity as a Senior Scholar. I greatly enjoyed working seamlessly with him on many issues, including a now widely cited article on healthcare in South Africa.^[1]

His suicide, with its relation to disruptive events at UCT and how these were handled, deeply scars our university. I shall long remember him with a combination of affection and respect as an exceptional colleague, and with great sadness at the void he leaves for his loving family, UCT, the UCT/GSH Department of Medicine, and many friends, colleagues and patients.

 Mayosi BM, Benatar SR. Health and health care in South Africa: 20 years after Mandela. New Engl J Med 2014;371(14):1344-1353.

The legacy of Bongani Mayosi

Gonda Perez

Previous Deputy Dean, Faculty of Health Sciences, University of Cape Town

Gonda.perez@uct.ac.za

I first heard of Bongani Mayosi when Ralph Kirsch told me that he had found the perfect person to take over as the Head of Department of Medicine. When I met Bongani, I had to agree with Ralph. He looked very young, but I soon realised what Ralph saw in him. He had a way of listening that made one think that what was being said was of vital importance. This was exactly one of the skills we needed in the Department of Medicine with all its complexities.

When I was looking for a high school for my daughter, it was Bongani's counsel that I sought and followed. He was at pains to point out that the school he chose for his daughters was a school where they could continue to learn isiXhosa. We spoke at length about the importance of everyone being able to speak at least one indigenous South African language.

Bongani had a special way with children. He remembered my daughter's name and asked after her every time we met. He made a fuss of the children who visited us in the office. He beamed when we told him of our children's achievements.

We found a common passion in the transformation of the Health Sciences Faculty, and we had long discussions on people we needed to attract to UCT. I must confess that he managed, on a few occasions, to twist my arm to find funding to attract people who could change our demographics and add to the pool of excellent clinicians and teachers in the faculty. Other heads of department were not too happy that the Department of Medicine seemed to have a greater share of the Clinical Training Grant. When Bongani walked into my office with that charming smile and said 'Now Gonda...' I always knew that I would have to dig deep to somehow try to help him find funding. We often brainstormed ideas of where we could stretch the budget to do the things that would forward transformation in the faculty.

Bongani was always willing to teach, and made time in his busy schedule to do so as often as he could. He seemed to connect with students in ways that many would envy. I knew I could refer challenging students to him. A talk with Bongani helped them to change their attitudes and focus on what they wanted to achieve. Bongani was always insistent on very high clinical standards that students had to uphold, emphasising that students needed to be taught the basics of clinical reasoning.

I clearly remember the times when Bongani visited my home. The last time was when I was persuading him to apply for the position of Dean of the Faculty of Health Sciences. We had had the conversation before – Bongani always replying that he wanted to build the Department of Medicine first. I was thrilled when Bongani agreed to apply for the position of Dean.

Reflections on Bongani Mayosi

Valerie Mizrahi

Director, Institute of Infectious Disease and Molecular Medicine and Professor of Pathology, Division of Medical Microbiology, Department of Pathology, University of Cape Town

valerie.mizrahi@uct.ac.za

I vividly remember the first time I encountered Bongani Mayosi. This was in November 2009 when I was still based at Wits University and had come to UCT to interview for the position as Director of the Institute of Infectious Disease and Molecular Medicine. Naturally, I had heard much about Bongani, but nothing prepared me for the immediate impact this brilliant and extraordinarily charismatic man would have on me. In the polite yet probing style that I would come to experience many times in later years, he posed the most challenging question I faced at that interview. I must have answered reasonably well as I was offered the job. But I will never forget the way his eyes sparkled when I talked about science and my philosophy of using excellent research as the vehicle for developing the next generation of scientists. Judging by his slow nod and electric smile, I knew that I had found a soul-mate - a scientist who shared my passion for research and someone with whom I knew I could work.

The second occasion that stands out was when we met at a Dean's Advisory Committee meeting in 2014. As we were helping ourselves to lunch, I casually asked Bongani how things were going. Brimming with excitement, he told me that his manuscript reporting the results of the IMPI trial had just been accepted for publication in the *New England Journal of Medicine*.^[1] He then proceeded to explain the study to me. I felt like a student being taught by a maestro of clinical research! It's hard to know what excited him more: the work itself, or the fact that it was done in Africa, by Africans, but now I understand that these attributes were inseparable to him.

After he became Dean, we worked together on various projects. Foremost among these was establishment of a PET-CT facility that was led subsequently by Ntobeko Ntusi. The facility was launched in November 2019, and I am certain that Bongani would have been proud to see this one of his dreams realised. Since his death, I have spent much time reflecting on the 'Bonganiism' that resonates most deeply with me: 'Lift as we rise'. I cannot think of a better principle by which to live my life.

 Mayosi BM, Ntsekhe M, Bosch J, et al. Prednisolone and Mycobacterium indicus pranii in tuberculous pericarditis. N Engl J Med 2014;371(12):1121-1130.

Lift as you rise: The remarkable legacy of Prof. Bongani Mayosi Jimmy Volmink

Dean, Faculty of Health Sciences, Stellenbosch University jvolmink@sun.ac.za

Friendship with Bongani Mayosi is one of the greatest blessings I have enjoyed in life. Over more than two decades we enjoyed countless happy moments together, sharing many ideas and opinions on a range of subjects. We engaged in political debates, discussed issues affecting academic medicine, brainstormed ideas for research capacity building, planned and executed research projects together, and, importantly, talked about our families and enjoyed good laughs together.

One of my abiding memories is of the few eventful years we enjoyed playing squash together - usually about once a week. In the beginning our skills level were quite evenly balanced, which meant that luck more or less decided who won on any particular day. However, at some point Bongani, for some reason, started falling behind on the score board. Always the problem solver, he decided (without consultation) to come up with a plan to deal with the situation. As I would soon find out, his strategy was to round up some of his young and fit registrars and turn them loose on me, the logic evidently being that if these young warriors could first soften me up a bit he could have a go, perhaps with a better outcome (for him). My valiant efforts to deal with this attack unfortunately proved to be both short-lived, ineffective and painful. And my humiliation was made complete when, a few weeks later, I ended up in hospital with a prolapsed lumbar disc! Following recovery from this unfortunate incident, and after some good laughs at the silliness of it all, Bongani and I decided that it was in my best interest to engage in more age-appropriate activities in future.

How do we remember Bongani? For some it was his brilliant mind and extensive contributions as a researcher that were the most important. We could spend the rest of the evening talking about his many achievements as a world-class researcher. For example, his work on the diagnosis and treatment of tuberculous pericarditis, which culminated in a landmark paper published in the NEJM. We could also discuss his sterling contributions to addressing rheumatic heart disease and his role in establishing a Global Rheumatic Heart Disease Registry. Another research area we could focus on is the genetics of cardiomyopathy and his role in the discovery of the CDH2 gene responsible for sudden death in young people and athletes. Perhaps for others it is his leadership in academic medicine that is at the core of his legacy. And so we can talk about his accomplishments as Head of the UCT Department of Medicine, as President of the SA Colleges of Medicine and the College of Physicians of SA, as President of PASCAR, and so forth. However, what stands out above everything else when I think about my friend, Bongani Mayosi, is his commitment to developing people. This is a theme that emerges in many, if not all, the tributes I have read about him, and in the conversations I have had with

In a tribute I co-wrote with some colleagues who knew him well,

we said the following: 'Perhaps one of Bongani's most remarkable legacies is his dedication to mentoring junior clinician scientists and building research capacity in Africa'. Bongani had a truly remarkable ability to lift people up, which made him an outstanding mentor. He possessed a generosity of spirit rarely encountered in the academy. And it is that generosity, that selflessness that made such a difference to me and to so many around the country, the continent and the world.

An issue of the Harvard Review, a few years ago, carried a banner on its cover which said: 'No one makes it without a mentor!'. Mentors fulfil many roles in our lives. They help us define our goals and aspirations. They provide guidance and advice. They challenge our thinking. They help us clarify our thoughts and moderate our ambitions. They serve as role models of leadership, of ethical behaviour and of excellence. There are many more things I can add. However, for me the most important thing mentors do is captured by the words of Katherine Schrubbe in an article on mentorship: 'Mentors are people who can see more in you than you see in yourself ... Effective mentors are so unshakably convinced that we have greatness in us, and their vision of what is possible is so clear and powerful, that they wind up convincing us too.' You see, mentors give us hope. They can make us feel that despite the odds we may face, we can be successful! Instead of becoming dispirited, we press on and try even harder. For many, Bongani Mayosi was that sort of mentor. The best way we can honour Bongani is by following his outstanding example of mentoring excellence. Research, mainly from the Global North, shows that half of junior university staff are unable to identify a mentor. It also shows that women and individuals from ethnically under-represented groups tend to experience significant difficulty with finding suitable mentors. I have no doubt there is a huge unfulfilled need for mentorship at our institutions in SA.

Bongani Mayosi also worked at the systemic level to lift up those interested in conducting medical and health research. One of his great legacies is the huge contribution he made to making the system of research better and stronger for everyone in SA and beyond. The Academy of Science of SA (ASSAf) Consensus Study Panel led by Prof. Mayosi produced a report titled 'Report on revitalising clinical research in South Africa. The report documented a number of shortcomings in the health and clinical research system and made a number of key recommendations. As a member of the 13-person ASSAf panel I can attest to the fact that Bongani Mayosi ably chaired the panel. But even more impressive was the energy he put into engaging with stakeholders to ensure these recommendations were implemented. The roleplayers included government departments, the SA Medical Research Council, the National Research Foundation, the private sector, etc. Bongani would talk to anyone who would listen if they could exert any influence on policy, and simply would not take 'no' for an answer. As a result of his efforts, either alone or in partnership with others, virtually each one of these recommendations have been adopted.

Strengthening the pipeline of researchers through increasing the number of PhDs was an issue over which Bongani Mayosi was greatly energised. He played a leading role in the establishment of the National Health Scholars Programme (with which his name is now associated) which aims to offer 1 000 PhD scholarships over a 10-year period. The number of PhD graduates in this programme has increased from 122 to 315 – an average annual growth rate of 6.5%. Black doctoral graduates constitute the bulk of this increase. However, it is noteworthy that the number of SA graduates is growing at a lower rate than graduates from the rest of Africa. In closing, Bongani was a great man whose legacy will live on. He lived for a cause bigger than himself. He represented the best there is in leadership. 'Leadership is not about position, authority or hierarchy – it is about choice. It is about the decision to make a meaningful difference in the world and the lives of others.'

We are all better off for having known him. Matshona Dhliwayo once wrote: 'Bless the world with your mind, heal the world with your heart, lift the world with your soul; elevate the world with your life.' That is exactly what Bongani Mayosi did, and that is how we will always remember him.

Bongani Mayosi: A man with profound impact

Denver Hendricks

Professor of Biochemistry and Head, Department of Integrative Biomedical Science, Faculty of Health Sciences, University of Cape Town denver.hendricks@uct.ac.za

Bongani Mayosi had a profound impact on the world around him, and many feel that the best way to honour his memory is to continue the important work that he started. Bongani had a wonderful combination of values and characteristics (often spoken about) and wide interests allowing him to contribute significantly to four large intersecting domains of interest. His research teams and collaborators made significant advances in clinical research, he made enormous contributions to the teaching and training of health professionals in SA and Africa, he provided outstanding health service primarily at GSH and he also contributed to policy on an array of issues. Much has been written and said of those achievements elsewhere, including this issue of the SAMJ. However, my intention here is to focus on his passionate interest in fostering and driving transformation in the health sector in his home institutions at UCT and GSH (while not diminishing his contributions in transformation more broadly in SA and the rest of Africa).

It has been my experience that when the issue of transformation is raised and discussed in the Faculty of Health Sciences at UCT and elsewhere, there is often a parallel conversation which emerges around standards of excellence and how transformation will degrade these standards. Concerns are often also raised about how difficult it is to find enough black students who can be trained, the impact of the large clinical workload in the public sector, leaving less time to provide good training and the lack of funds for transformation. These reasons presumably explain the very poor representation of black academics and clinicians at associate professor and professor level in the UCT Faculty of Health Sciences. However, during the years that Bongani was the Head of Medicine, he quietly implemented his transformation plan. His approach was to make direct contact with promising, bright students at undergraduate level. He never excluded bright white students - however, he focused on identifying promising black students both at UCT and elsewhere. He followed their progress at undergraduate level, opened conversations with them, and discussed the options of registering for an MMed in medicine. He maintained contact with students during their internship and community service training, and encouraged students to register for their MMed in medicine. He discussed opportunities for funding, potential research projects, and explored options to obtain further training internationally. He ensured that the institutional climate in his department facilitated the training and professional development of his young black clinicians and other individuals who worked with him, and together they reached for excellence. In short, he mentored them – he took a personal interest in their progress to facilitate their success!

Currently the Department of Medicine is at the forefront of clinical departments in the UCT Faculty of Health Sciences, with a significant number of African black clinicians at associate professor and professor level, all considered as outstanding, with strong leadership qualities. We need to encourage the heads of departments of the Faculties of Health Sciences across SA to become personally engaged in transformation, to mentor promising black students, and to change the institutional culture within their departments to one that is much more supportive of young black trainees in their midst.

Bongani Mayosi and my destiny

Prof. Gasnat Shaboodien

Director, Cardiogenetics Laboratory, Cape Heart Institute, Faculty of Health Sciences, University of Cape Town gasnat.shaboodien@uct.ac.za

I am a scientist, and it is said that many of us do not believe in God or destiny. *I believe*. I believe my meeting Bongani Mayosi was preordained. I believe that meeting him and being guided by him for over 16 years was my destiny. He changed the trajectory of my life. Where would I be if I had never met him? I've never given that much thought, as I can't imagine it.

I still remember, so very clearly, the day we met. It was mid-2002 and I was looking for a project for my PhD. Someone mentioned that I should speak to a guy called Dr Bongani Mayosi who had just come back from Oxford. We arranged to meet and in walked Bongani. Not what I was expecting - someone tall, buttoned-up and serious: instead, I got, short, funny, thoughtful and visionary Bongani. I remember his infectious giggle, his ability to reduce mountains into molehills, his manner of directly looking at you and making you feel that you were the only one that could solve that problem. That he had been waiting for you. After 1 hour in his company, I had agreed to do a PhD with him and felt ready to 'divide and conquer'. It took one question from a concerned colleague to bring me crashing back down to earth. How had I agreed to do a PhD on a project that had no funding, no cohort and minimal infrastructure in place? That was the Bongani effect, and my life for the next 16 years.

As a researcher, he was admired for his insight, and his outof-the box way of thinking. He built the Cardiovascular Genetics unit from the ground up; took it from a small, insignificant cubicle to a thriving unit. Under his leadership, we made groundbreaking discoveries and large contributions to the field of the genetics of cardiomyopathy, but we are not done yet. We continue to run this unit in his honour; every disease-causing mutation we find, every family we help cements the legacy that Bongani left behind.

As an individual, he had the unique ability to drill down to the core of the problem, articulate it and provide a solution. He was compassionate, honourable, and his word was his bond. People loved him and I guess what made him so special was that he genuinely cared about people. From the lowest in rank to the highest, it didn't matter to Bongani, everyone was treated the same.

I still miss him. His teachings live on in all of us lucky enough to have been in the orbit of this incredible human being. I will forever be grateful that I followed my gut when I embarked on that crazy journey with one Bongani Mayosi.

Prof. Bongani Mayosi: A man with profound impact on my life

Prof. Mark Engel

Director, AFROStrep Research Group, Department of Medicine, University of Cape Town

mark.engel@uct.ac.za

Prof. Bongani Mayosi's departure was indeed a great loss to many of us, but I am comforted by James' reminder in scripture that each day is known to our Creator.

Bongani was a rare breed, an upright person who was able to easily sum up a situation and take control, always firm, but still friendly, with his infectious smile. Seeing this seemingly insignificant man at work was a real treat. I marvelled at his strong leadership, quick at finding solutions while maintaining his vision, regardless of circumstances; and yet, he remained humble, never considering himself more highly than others. In fact, I remember being astounded in the early days, when he would ask me (!), 'What do you think?'

The profound impact of Bongani on my life and career is staggering. At the time of his passing, I found myself trying to hold onto every word, smile, wisdom titbit or thought that flashed through my mind at each passing moment. In many ways – without doubt, Bongani shaped and made me. Most noteworthy was his belief in my talents and abilities, which he brought together in a tailor-made fashion in terms of my career trajectory, like he had done for so many of his mentees. The choice of research focus was spot-on, as he instilled within me a humble confidence to see me through my doctoral studies and beyond. 'Believe in people, trust in them and they will rise to your expectation' still echoes in my mind, as I find myself now in a position of influencing others.

I also best remember Bongani as a 'yes' person, ready to entertain ideas without ridicule, after which he would provide guidance in shaping the core messages one wanted to convey. Always fully supportive, reminding us to 'only strike when you are assured of being successful', Bongani provided much kindling to the flames of success of many aspects of our research. Certainly, the personal experiences and encounters are beyond the finite limitation of words. Indeed, I feel privileged to have known him so closely, even guilty in fact, that I had a lion's share at times (like when we went to the Yemeni Heart Association conference).

So, do I still feel the loss? Profoundly so, often wondering what Bongani would have done

under some of the circumstances I face. But my belief in God tempers that loss with the absolute assurance that Bongani had accomplished the blueprint for his time on Earth. Thus, I dig deep to accept that the time had come for this faithful servant.

Bongani the mentor, a thousand Bonganis for the African Nobel laureate in our lifetime

Prof. Liesl Zuhlke

Acting Deputy Dean: research, Faculty of Health Sciences, University of Cape Town, and Director of the Children's Heart Disease Research Unit, Department of Paeditrics and Child Health, University of Cape Town liesl.zuhlke@uct.ac.za

A mentor is defined as a person who is an experienced and trusted advisor, a guide, a confidante, a counsellor. The mentee is someone who has been advised and helped by a more experienced person over time. And the academic mentoring relationship can be defined as the development of a mutually satisfying, voluntary, one-on-one relationship between a student and an alumnus, where the focus is on the student's career development. To call Bongani just a mentor using these definitions and to describe being mentored by him in these mere terms would be to trivialise one of the most formative relationships in my life and the lives of many.

Bongani was all these things, but infinitesimally more. He changed my life with a simple 'but'. I applied for a research job in the Department of Medicine as a paediatrician with no research experience whatsoever. Needless to say, I did not get the job. However, he called me at my home that evening to tell me the not unexpected news, but also to offer a 'but I have another idea'. A few months later I left the Department of Paediatrics to work for him, just a month short of 10 years ago.

His infectious enthusiasm permeated every interaction we had, and this resulted in far more than just advice or help. What he did was to permanently alter the trajectory of my life, and therefore that of my family. He infused into all his mentees his passion, but urged us to find our own. He created a space for us for introspection and reflection, and urged us to grapple with what our goals were and, more importantly, to find solutions to achieve them, be they scientific or otherwise. He challenged us deeply: about our research questions, how we would serve our communities, what our scientific contribution would be and how we would leave our legacy –what would be *our* footprints in the sand. He taught us academic thoroughness, integrity, clarity of thought and meticulous and constant attention to detail. However, none of this was done without his special brand of 'Bonganisms': 'reach for the stars', 'the journey of 1 000 miles begins with a few steps' and 'success is programmatic'.

In research, we often encounter difficult situations: when Mark Engel and I would go to him for advice and direction, he would remind us to 'share the love'. These Bonganisms were not just about science, they were life lessons, and have become ingrained in us, part of our everyday language, and so he intrinsically altered the fabric of our lives.

He believed resolutely that one could change the world, one act of service at a time, and so we became the members of the orchestra and he our conductor and composer-in-chief, playing that metamorphic symphony.

Some of us were profoundly privileged to be his direct students, when he supervised our Masters or PhD theses. This followed a particular path: first the one-pager and then after that regular science meetings. I always went to the office feeling nervous and worried how the latest draft or thoughts would be received, and yet I left invigorated, energised and renewed. He would listen to the outline or plans unbelievably intently, taking down notes in his diary or Blackberry, and then would come the questions, reflecting on areas you never contemplated, posing challenges you often did not think you could achieve, but in so doing constructing and shaping the direction of the science. He encouraged us to pursue a subject to every depth necessary, to read widely outside our interest and to broaden our academic and scientific outlook. He taught us critical thinking, he stretched us yet allowed us to challenge him and to challenge assumptions. He was ruthlessly honest and did not hold back with the track changes or multiple revisions. But in so doing, he made us better than we ever thought we could be, and, most importantly, he made us believe it. Yet he was not effusive in his praise, nor superficial in his encouragement. It was a momentous day when I received back a scientific paper, with a white square notelet paperclipped to the corner and the impeccably neat handwriting saying,

'Liesl, I have nothing more to add, B.'

We were, I was, unbelievably blessed to be one of his students. But he was also a mentor to many many more, not just his immediate students.

I was privileged to travel with him on several occasions. During these times, I watched him find a moment to interact with colleagues from across the globe, over and over. So many have spoken of that breakfast meeting at PASCAR, a cup of coffee in the ESC fellows lounge, that glass of red wine at Magica Roma, that changed their lives. He would use that time to pose those questions, encourage aspirations and then later, check to see if there had been progress. He never forgot and made sure we didn't either. This special brand of Mayosi mentoring transcended the traditional boundaries of departments and disciplines; it was open to students, researchers, colleagues and staff. It has resulted in a cohort of people in South Africa, Africa and across the world who have been deeply touched, and this spirit will continue to live in their science, their service and their students.

Maya Angelou in her poem 'When great trees fall' said: 'Great souls die and our reality, bound to them, takes leave of us. Our souls, dependent upon their nurture, now shrink wizened. Our minds, formed and informed by their radiance, fall away.' But

'When great souls die, after a period peace blooms, slowly and always irregularly [...]

Our senses, restored, never to be the same, whisper to us.

They existed, they existed.

We can be. Be and be better. For they existed.'

Bongani, you have made an immeasurable and indelible impact upon my life, not just my career. I will honour your lessons and your guidance. It is one of the greatest blessings of my life to have known you and to have loved you.

Establishing the Bongani Mayosi Summer School of Academic Mentorship – an idea to honour Bongani Mayosi's legacy of mentorship and capacity building in Africa

Prof. Lehana Thabane

Professor/Interim Chair, Department of Health Research Methods, Evidence, and Impact, McMaster University; Director, Biostatistics Unit, St Joseph's Healthcare; Hamilton Senior Scientist, Population Health Research Institute, Hamilton Health Sciences thabanl@mcmaster.ca

'Congratulations, Godsent for this milestone. I will pay the publication cost by credit card – will you please send me the invoice?', wrote Bongani on 7 November 2017. Bongani was responding to Godsent Isiguzo's email in which he was letting his PhD co-supervisors (Bongani and myself) know that his first PhD thesis paper had been accepted for publication.^[1,2] This was typical of the man – not only did he offer intellectual support to his mentees, but also provided tangible resources, including his credit cards, to help them.

Bongani had a vision of building a cadre of mentors in Africa whose primary responsibility would be to nurture the next generation of health researchers on the continent (Fig. 1). This was one of the many exciting things that he and I would discuss on our regular Skype or phone calls, and it was to be one of the topics for discussion over dinner during my next trip to Cape Town in February 2019. While that conversation did not take place because of his premature death in July of 2018, it is perhaps fitting that as we celebrate his life, his birthday and his legacies, we consider renewing our commitment to advancing mentorship of junior scientists in Africa and around the world. Bongani understood the power of mentorship to transform the academy – by building confidence,

ßß

We need to dream big for Africa to succeed on the world stage. Cultivating a culture of mentorship to nurture the next generation is an imperative.³⁰

Fig. 1. Bongani's thoughts on mentorship.



Fig. 2. Potential roles of a mentor along a career development path (adapted from^[3]).

hope, support and courage among the future leaders of the academy. The commitment to mentorship and building capacity was central to the manner in which he approached assembling collaborators around Africa for the IMPI program (he fondly referred to the team as the 'IMPI warriors'). He was willing to share, educate, connect, guide, listen, protect, support and coach – all of the qualities we expect to see in a true mentor (Fig. 2).

An idea

As we remember, reflect, commemorate, celebrate and think of different ways to honour Bongani, I think of establishing the Bongani Mayosi Summer School of Academic Mentorship, a bastion in which we cultivate and nurture evidence-based academic mentorship in health. This, I believe, would be a fitting honour, while making his dream of creating a culture of mentorship come true. Additionally, this would provide a great environment for the mentees and mentors to exchange ideas, share best practices in mentorship, and build camaraderie in the

academy. And finally, this would not only be a necessary step to take SA's transformation project to the next phase, but also an extraordinary gesture by all of us to honour Bongani!

- Isiguzo GC, Zunza M, Chirehwa M, Mayosi BM, Thabane L. Quality of abstracts of pilot trials in heart failure: A protocol for a systematic survey Contemp Clin Trials Comm 2017;8:258-263 (protocol manuscript).
 Isiguzo GC, Zunza M, Chirehwa M, Mayosi BM, Thabane L.
- Isiguzo GC, Zunza M, Chirehwa M, Mayosi BM, Thabane L. Quality of pilot trial abstracts in heart failure is suboptimal: a systematic survey Pilot Feasibility Studies 2018;4:107 (results manuscript).
- Odueyungbo A, Thabane L. Mentoring in biostatistics: Some suggestions for reform. J Multidisciplin Healthcare 2012;5:265-272.

Prof. Bongani Mayosi: An exemplary mentor Dr Sarah Kraus

Postdoctoral fellow, Department of Medicine, University of Cape Town and University of Oxford

sarah.kraus@uct.ac.za

The definition of mentorship is elusive, but in essence it is a process of informal

transmission of knowledge, social capital and psychosocial support perceived by the mentee as relevant to work, career or professional development.^[1] While I have been fortunate to have had a number of extraordinary people guide me through my career, Prof. Bongani Mayosi's mentorship of me has been the most formative, both personally and professionally. On reflection of what he taught me, not only during his life, but also through the tragedy of his death, I have found myself revisiting the fundamental philosophy of mentorship. There were two key mentoring techniques he bestowed on me - sowing and catalysing. He planted an idea and then plunged me into change, provoking a different way of thinking and altering my professional identity.

In his inaugural lecture entitled 'The future of medicine', Prof. Mayosi spoke about the four challenges identified by Fanon,^[2] and stated that, 'to produce, to invent, to build and to work are relevant to the project of securing a bright future for medicine in Africa.' This is the ethos he bestowed on me, to not only practise medicine but to produce, invent and build as a clinician scientist and researcher. In the wake of his death, I learnt a fundamental lesson about leadership. Success as a leader can, in some respects, be measured by what is left behind. We, his mentees, are what he left behind. 'Lift as you rise' embodies the idea that individual success comes with the responsibility of empowering others - it requires careful compromise and studious investment in other people. That is what he taught me.

 Fanon F. The Wretched of the Earth. London: MacGibbon & Kee, 1965.

Prof. Bongani Mayosi: A teacher of endless inspiration

Dr Dimakatso Gumede

Scientist, Council for Scientific and Industrial Research

dimakatso.gumede@alumni.uct.ac.za

I met Prof. Bongani Mayosi at the Sports Institute of SA when I attended his talk on sudden cardiac death among young athletes. I was in the process of completing my Masters degree and contemplating doing a PhD. His presentation about genetic cardiomyopathies inspired me to pursue a PhD degree with him.

Bozeman B, Feeney MK. Toward a useful theory of mentoring: A conceptual analysis and critique. Admin Soci 2007;39(6):719-739.

I always looked forward to my meetings with Prof. Mayosi as he had a contagious passion for problem solving: no challenge was too great to solve. He also had a keen interest in the career plans of his students, advising and guiding. One particular moment that stands out was a car ride back to campus with him when he asked me about my career plans. I had just started my PhD and was enthusiastic about the new technology I was learning. He then asked if I had thought of contacting the pioneer of this technology, which I had not. He said to me, 'Dimakatso, always work with the best.' This lesson among others has taught me to be bold in my career and to have the courage to pursue what I have set out to accomplish. Not only did he teach these lessons but he also outstandingly embodied them. What a privilege to have known such a leader! I am incredibly grateful for his mentorship and support during my PhD career.

Bongani Mayosi and his contributions towards rheumatic heart disease Prof. Liesl Zuhlke

Acting Deputy Dean: Research, Faculty of Health Sciences, University of Cape Town, and Director of the Children's Heart Disease Research Unit, Department of Paeditrics and Child Health, University of Cape Town liesl.zuhlke@uct.ac.za

RHD remains a scourge of the medical world, a disease entirely preventable by simple and inexpensive methods, yet rife in areas of disproportionate inequality, injustice and insufficient access to healthcare. It affects children, young adults and women in their childbearing years, and has direct effects on mortality, with a vastly decreased life span and morbidity, with years of life affected by disability and complications.

Bongani was exposed to RHD on a daily basis during his clinical training, but it was an auspicious moment while in Oxford that refocused his attention on the clinical and scientific questions related to RHD. The first investigator on a systematic review was on leave and owing to his interest in the subject, Bongani took over a Cochrane review on the effect of penicillin on the primary and secondary prevention of acute rheumatic fever (ARF) occurrences and recurrences. This now seminal article provided for the first time robust meta-analyses evidence of the intrinsic role of penicillin.^[1] Grappling with the primary prevention puzzle remained a focus of Mayosi's work in this regard, and he continued to direct significant work in the area of primary prevention.

However, the next major event in the RHD world was, as per Bongani's visionary leadership, far broader. The burden of disease estimates of ARF, RHD and streptococcal diseases had demonstrated the immense problem on the African continent,^[2] and thus under his leadership and within the auspices of PASCAR, Bongani convened a meeting at the Drakensberg in KwaZulu-Natal, which defined the ASAP program for the elimination of ARF/RHD in African countries in our lifetimes.^[3,4] The ASAP program encapsulated the key elements of Awareness, Surveillance, Advocacy and Prevention, and brought together key stakeholders from medicine, policy, politics as well as key collaborators from across the world. This seismic event in the world of RHD was critical for many reasons: it was the first multi-country approach to the complexity of the problem of RHD, it used a grassroots, bottoms-up approach that did not rely on funding but rather on commitment and local efforts and it brought together human capital to focus on the problem of RHD. Everyone involved in the Drakensberg meeting has gone on to be involved in many of Bongani's subsequent projects, RHD or otherwise, to conduct and lead research consortia of their own and develop and grow capacity in their respective fields. In

hindsight, it was a think-tank of committed RHD champions, led by the greatest champion and advocate for RHD of them all.

Soon after this meeting, a landmark study on screening for asymptomatic RHD published by a team from Mozambique and Cambodia was published in the NEJM.^[5] This brought RHD to the attention of the medical community, and a new era was introduced, with demonstration sites exploring asymptomatic RHD, screening programmes reporting huge numbers of subclinical disease and validated methods of using portable echocardiography being published.^[6]

However, again Bongani Mayosi's vision for this disease stretched beyond a finite research question, this time beyond asymptomatic disease to clinical conundrums. Together with colleagues from New Delhi and Canada, he reinvigorated a protocol examining the evidencebased interventions and demographic characteristics of people living with symptomatic disease in Africa, India and Yemen, and the Global Rheumatic Heart Disease Registry (REMEDY) was established, with 3 343 patients enrolled and stark findings of significant morbidity and mortality demonstrated.^[7-9] Throughout the final meetings to discuss results and implications, Bongani focused on the most critical stakeholder, the patient, and the need for a more political mandate based on the major findings. This then led to several key policy statements: the Addis Ababa communiqué (adopted by the African Union),^[10] The Cairo accord,^[11] the Mosi-O-Tunya call to action, and then most recently the historic World Health Organization resolution adopted by the 71st World Health Assembly in Geneva against ARF and RHD,^[12-14] and finally, a political mandate dictated by and underpinned by rigorous science and evidence. Bongani was critical to all these statements and events, and the final resolution was passed just months before his death.

Alongside policy and activist involvement was a continued exploration of key scientific questions. The REMEDY study led to the RHDGen study, which focuses on the genetic origins of RHD, and this has now grown even further to the INVICTUS study, which focuses on the use of novel oral anticoagulants in preventing stroke in patients with RHD and atrial fibrillation, the largest randomised controlled trial in RHD to date. In addition, the exploration of streptococcal disease has continued from the first days to include molecular phenotyping, vaccine information discovery, cost-effectiveness analyses and an Africa-wide registry.^[15] He was part of the Global Burden of Disease group, and the AHA/ACC guidelines on ARF/RHD, which redefined the Jones criteria.^[16,17]

But perhaps Bongani's most enduring legacy in this field will be the people that worked alongside him during his RHD journey. His inspiration and commitment to the field was telling in the huge outpouring of grief from the RHD community, demonstrated at several ensuing international meetings.^[18] His resolute belief in those he inspired in the field led to multiple projects in Namibia, Zambia, Sudan and Yemen, to name only a few. His visits to those countries will be discussed for years and the effect of his input and clear scientific eye, together with a listening and encouraging spirit, will not be forgotten for their personal and academic impact. His students, mentees and colleagues will continue to reflect his impact in this field, and his patients speak of him with much fondness and sincere appreciation.

Bongani Mayosi put RHD back onto the world and public health agenda, with significant scientific contributions in every aspect of the disease continuum, by inspiring and galvanizing policy and political mandates and by developing and growing a generation of RHD researchers and activists. Although we were not to have eliminated ARF/RHD in his lifetime, his life and his efforts will be noted as intrinsic to the elimination of this disease in the future. The elimination of RHD is indeed a reality because of the life and work of Prof. Bongani Mayosi.

- 1. Manyemba J, Mayosi BM. Intramuscular penicillin is more effective than oral penicillin in secondary prevention of rheumatic fever - a systematic review. S Afr Med J 2003;93(3):212-218.
- Carapetis JR, Steer AC, Mulholland EK, Weber M. The global burden of group A streptococcal dis 2. Lancet Infect Dis 2005;5(11):685-694.
- 3. 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 Part 2):246 4. Mayosi BM. A proposal for the eradication of rheumatic fever in our lifetime. S Afr Med J 2006;96(3
- Part 2):229-230. Marijon E, Ou P, Celermajer DS, et al. Prevalence of rheumatic heart disease detected by echocardiographic screening. N Engl J Med. 2007;357(5):470-476.
- 6. Mayosi BM. The four pillars of rheumatic heart disease control. S Afr Med J 2010;100(8):506 Karthikeyan G, Zuhlke L, Engel M, et al. Rationale and design of a Global Rheumatic Heart Disease
- Registry: The REMEDY study. Am Heart J 2012;163(4):535. 8. 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(18):1115-1122a.
- 9. Zuhlke L, Karthikeyan G, Engel ME, et al. Clinical outcomes in 3343 children and adults with rheumatic heart disease from 14 low and middle income countries: 2-year follow-up of the Global Rheumatic Heart Disease Registry (the REMEDY study). Circulation 2016;134(19).
- 10. Watkins D, Zuhlke L, Engel M, et al. Seven key actions to eradicate rheumatic heart disease in Africa: nique. Cardiovasc J Afr 2016;27:1-5. the Addis Ababa con
- 11. Yacoub M, Mayosi B, ElGuindy A, Carpentier A, Yusuf S. Eliminating acute rheumatic fever and rheumatic heart disease. Lancet 2017;390(10091):212-213.
- 12. Sliwa K, White A, Milan P, Olga Mocumbi A, Zilla P, Wood D. Momentum builds for a global response to rheumatic heart disease. Eur Heart J 2018;39(48):4229-4232. 13. Zilla P, Bolman RM, Yacoub MH, et al. The Cape Town declaration on access to cardiac surgery in the
- developing world. Asian Cardiovasc Thorac Ann 2018;26(7):535-539.14. Zilla P, Bolman RM, Yacoub MH, et al. The Cape Town Declaration on access to cardiac surgery in the
- developing world. J Thorac Cardiovasc Surg 2018;156(6):2206-2209.15. Barth DD, Engel ME, Whitelaw A, et al. Rationale and design of the African group A streptococcal
- infection registry: The AFROStrep study. BMJ Open 2016;6(2):e010248. 16. Watkins DA, Johnson CO, Colquhoun SM, et al. Global, regional, and national burden of rhe
- heart disease, 1990-2015. N Engl J Med 2017;377(8):713-722.
- 17. Gewitz MH, Baltimore RS, Tani LY, et al. Revision of the Jones criteria for the diagnosis of acute rheumatic fever in the era of Doppler echocardiography: A scientific statement from the American Heart Association. Circulation 2015;131(20):1806-1818.
- 18 Ntsekhe M Cor erford P, Brink P, Yusuf S. Bongani Mayosi, a hero remembered. Cardiovasc J Afr 2018;29(4):206.

A brief summary of Prof. Mayosi's major contributions to pericardial disease research and practice

Prof. Mpiko Ntsekhe

Mauerberger Professor of Cardiology, Department of Medicine, University of Cape Town and Groote Schuur Hospital mpiko.ntsekhe@uct.ac.za

During his first year as a physician trainee, Prof. Mayosi admitted a patient with tuberculous pericarditis - a condition for which the 1-year rate of death, constrictive pericarditis and recurrent tamponade is approximately 30 - 40%. Having looked after many similar patients during his time as an intern and medical officer at Frere Hospital in the Eastern Cape, he thought nothing of doing what he had always done: start the patient on antituberculous therapy and high-dose adjuvant oral corticosteroids. So he was quite taken aback when on the post-intake ward round the next day, his consultant crossed out the prescription for steroids on the drugs chart and enquired about the evidence for their use in the condition. Stunned by the fact that anyone would question what he assumed was accepted practice, and upset at his inability to provide a convincing answer, he made it his mission to do the work that would provide the evidence to shape policy and practice to the benefit of patients with the disease and the many communities at risk. Over the next two-and-a-half decades, Prof. Mayosi would make major contributions to the field. Below, I highlight five of these contributions which fundamentally shifted the field.

First, through a series of state of the art reviews, $^{\left[1-3\right] }$ Mayosi and colleagues updated the state of knowledge on the burden of disease, its clinical manifestations, the diagnostic approach and yield of available tests and optimal management strategies, and they summarised what was known about tuberculous pericarditis-related outcomes and complications in the mid-2000s. This exercise was significant because for the first time it brought to national and global attention a disease which had for too long been neglected and relegated to being one that occurs among the rural poor. Furthermore, the reviews identified and highlighted the major knowledge gaps that needed to be addressed if the burden of disease was to be reduced and outcomes improved. Second, between 2003 and 2006, Mayosi assembled and led a team of investigators under the umbrella name IMPI to conduct the necessary research to improve on what was then the status quo. Over the next 5 years, the IMPI investigators conducted a prospective registry across multiple sites in SA, Cameroon, Nigeria, Sierra Leone and Mozambique, which generated new information that: (i) provided a more contemporaneous description of the clinical phenotypes, management and natural history in the HIV era;[4-7] (ii) investigated the immunopathogenesis and phenotype of the immune response to pericardial tuberculosis and outlined the impact of HIV on important immune response pathways;^[8,9] and (iii) investigated the optimal approaches to the confirmation of the diagnosis in the HIV era.^[10,11]

Besides the important scientific questions that were addressed, one of the main non-scientific outcomes of the registry was that it was able to highlight the lack of standardised approaches to the care of patients with the condition, and demonstrated how this contributed to the high morbidity and mortality. Data generated from the registry were used as an advocacy tool to persuade practitioners and other stakeholders to ensure that patients received the optimal possible care, including a more aggressive use of diagnostic and therapeutic pericardiocentesis (as opposed to empiric treatment), and more referrals for antiretroviral therapy in those who were HIV-infected.

On the basis of the new information generated by the registry and on the back of the research infrastructure and networks that were established across the continent, Mayosi and the IMPI investigators designed, conducted and completed a large randomised controlled study which found that immunotherapy, in the form of adjuvant corticosteroids and Mybacterium indicus pranii, did not have any significant effect on the combined outcome of death, constrictive pericarditis and recurrent tamponade requiring pericardiocentesis.^[12] The results of this study have been adopted by major bodies which provide guidance on heart disease,^[13,14] and have been incorporated into a significant number of national guidelines in tuberculosis endemic countries.

The fourth area of pericardial tuberculosis research in which Mayosi made important contributions was progress on understanding the mechanisms and pathogenesis of constrictive pericarditis with a view to developing targeted treatment to prevent the development of this debilitating complication.[15-17] Post-tuberculous constrictive pericarditis contributes to the heart failure burden in many parts of the world where tuberculosis is endemic and tuberculous pericarditis is common.^[18] However, the definitive treatment for constrictive pericarditis (surgical pericardiectomy) is not available throughout most of these areas (e.g. sub-Saharan Africa), and in the few places where it is available the procedure carries with it a high perioperative mortality,^[19] making strategies to prevent constriction even more important.

The fifth and final major area of contribution was a series of studies that demonstrated that whereas the traditional understanding of pericardial tuberculosis was that it is a paucibacillary condition, (i) in a significant proportion of patients it may actually be multibacillary;^[20] (ii) the mycobacterium load correlates closely with outcomes such as mortality;[20] and (iii) the latter observation may be because antituberculous drugs penetrate poorly into the pericardium, as evidenced by drug levels that are well below the required minimum inhibitory concentration.^[21] These findings may have major implications for the doses and duration of future antituberculous drug regimens for tuberculous pericarditis, considering that most of the recommendations related to both drug dose and duration to date have been extrapolated from pulmonary tuberculosis.

- Mayosi BM, Burgess LJ, Doubell AF. Tuberculous pericarditis. Circulation 2005;112(23):3608-3616. https://doi.org/10.1161/CIRCULATIONAHA.105.543066
- Syed FF, Mayosi BM. A modern approach to tuberculous pericarditis. Prog Cardiovasc Dis 2007;50(3):218-236.
- Ntsekhe M, Wiysonge C, Volmink JA, Commerford PJ, Mayosi BM. Adjuvant corticosteroids for tuberculous pericarditis: Promising, but not proven. QJM 2003;96(8):593-599.
 Mayosi BM, Wiysonge CS, Ntsekhe M, et al. Clinical characteristics and initial management of patients
- Mayosi BM, Wiysonge CS, Ntschhe 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(6):2.
- Wiysonge CS, Ntsekhe M, Gumedze F, et al. Contemporary use of adjunctive corticosteroids in tuberculous pericarditis. Int J Cardiol 2008;24(2):388-390. https://doi.org/10.1016/j.ijcard.2006.12.060
 Marci MD, Wirson CO, Nachku V, et al. (Set Vision vision vision vision vision).
- Mayosi BM, Wiysonge CS, Ntsekhe M, et al. Mortality in patients treated for tuberculous pericarditis in sub-Saharan Africa. S Afr Med J 2008;98(1):36-40.
 Ntsekhe M, Wiysonge CS, Gumedze F, et al. HIV infection is associated with a lower incidence of
- constriction in presumed tuberculous pericarditis: A prospective observational study. PLoS One 2008;4(3):6. https://doi.org/10.1371/journal.pone.0002253
- Matthews K, Wilkinson KA, Kalsdorf B, et al. Predominance of interleukin-22 over interleukin-17 at the site of disease in human tuberculosis. Tuberculosis 2011;91(6):587-593. https://doi.org/10.1016%2Fj. tube.2011.06.009
- Matthews K, Ntsekhe M, Syed F, et al. HIV-1 infection alters CD4+ memory T-cell phenotype at the site of disease in extrapulmonary tuberculosis. Eur J Immunol 2012;42(1):147-157. https://doi. org/10.1002%2Feji.201141927
- Theron G, Peter J, Calligaro G, et al. Determinants of PCR performance (Xpert MTB/RIF), including bacterial load and inhibition, for TB diagnosis using specimens from different body compartments. Sci Rep 2014;11(4):5658. https://doi.org/10.1038/srep05658
 Pandie S, Peter JG, Kerbelker ZS, et al. The diagnostic accuracy of pericardial and urinary
- Pandie S, Peter JG, Kerbelker ZS, et al. The diagnostic accuracy of pericardial and urinary lipoarabinomannan (LAM) assays in patients with suspected tuberculous pericarditis. Sci Rep 2016;6:32924.
- Mayosi BM, Ntsekhe M, Bosch J, et al. Prednisolone and Mycobacterium indicus pranii in tuberculous pericarditis. N Engl J Med 2014;371(12):1121-1130. https://doi.org/10.1056/NEJMoa1407380
- Adler Y, Charron P, Imazio M, et al. 2015 ESC Guidelines for the diagnosis and management of pericardial diseases: The Task Force for the Diagnosis and Management of Pericardial Disease of the European Society of Cardiology Force (ESC) Endorsed by: The European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J 2015;36(42):2921-2964. https://doi.org/10.1093/eurheartj/ ehv318
- Wiysonge CS, Ntsekhe M, Thabane L, et al. Interventions for treating tuberculous pericarditis. Cochrane Database Syst Rev 2017;9(9):CD000526. https://doi.org/10.1002/14651858.CD000526.pub2
 Matthews K, Deffur A, Ntsekhe M, et al. A compartmentalized profibrotic immune response
- Dis matures R, Stellar A, Neskie M, et al. A compatibility of HV-1 Infection. Am J Respir Crit Care Med 2015;192(12):1518-1521. https://doi.org/10.1164%2Frccm.201504-0683LE
- Ntsekhe M, Matthews K, Wolske J, et al. Scientific letter: Ac-SDKP (N-acetyl-seryl-aspartyl-lysylproline) and galectin-3 levels in tuberculous pericardial effusion: Implications for pathogenesis and prevention of pericardial constriction. Heart 2012;98(17):1326-1328. https://doi.org/10.1136/ heartjnl-2012-302196
- Mnguni AT, Engel ME, Borkum MS, Mayosi BM. The effects of angiotensin converting enzyme inhibitors (ACE-I) on human N-acetyl-seryl-aspartyl-lysyl-proline (Ac-SDKP) levels: A systematic review and meta-analysis. PLoS ONE 2015;10(12):e0143338. https://doi.org/10.1371/journal. pone.0143338
- Mayosi BM. Contemporary trends in the epidemiology and management of cardiomyopathy and pericarditis in sub-Saharan Africa. Heart 2007;93(10):1176-1183. https://doi.org/10.1136/hrt.2007.127746
 Mutyaba AK, Balkaran S, Cloete R, et al. Constrictive pericarditis requiring pericardiectomy at Groote
- Schuur Hospital, Cape Town, South Africa: Causes and perioperative outcomes in the HIV era (1990-2012). J Thorac Cardiovasc Surg 2014;148(6):3058-3065. https://doi.org/10.1016/j.jtcvs.2014.07.065
 Pasipanodya JG, Mubanga M, Ntsekhe M, et al. Tuberculous pericarditis is multibacillary and bacterial
- Pasipanodya JG, Mubanga M, Ntsekhe M, et al. Tuberculous pericarditis is multibacillary and bacterial burden drives high mortality. EBioMedicine 2015;2(11):1634-1639. https://doi.org/10.1016%2Fj. ebiom.2015.09.034
- Shenje J, Ifeoma Adimora-Nweke F, Ross IL, et al. Poor penetration of antibiotics into pericardium in pericardial tuberculosis. EBioMedicine 2015;2(11):1640-1649. https://doi.org/10.1016%2Fj. ebiom.2015.09.025

Bongani Mayosi's contributions to improved understanding of cardiomyopathy and heart failure

Prof. Ntobeko A B Ntusi

Chair and Head, Department of Medicine, University of Cape Town and Groote Schuur Hospital

ntobeko.ntusi@uct.ac.za

Following his clinical training as a physician at Groote Schuur Hospital and admission into the Fellowship of the College of Physicians of SA, Bongani Mayosi was immediately awarded the prestigious Oxford Nuffield Medical Scholarship to read for a DPhil in cardiovascular medicine at the University of Oxford under the supervision of Prof. Hugh Watkins. When it became clear that his original idea of a study on the genetics of cardiomyopathy would not be feasible, his doctoral project mutated to focus on heritability and genome-wide linkage analysis of electrocardiographic (ECG) and echocardiographic left ventricular hypertrophy (LVH) in families with hypertension. In this seminal study, he described that stronger genetic signals for LVH were found on ECG compared with echocardiographic measurements, and that the genetic determinants of each of these appeared to be distinct.^[1,2] In addition, he found that chromosomes 10, 12 and 17 were likely to harbour genetic loci that exert a major influence on ECG LVH in hypertension.

During his time in the Watkins lab and following his return to Cape Town, Bongani was involved in a number of important publications on cardiomyopathy and LVH emanating from the Watkins lab. These included the role of mutations in cardiac and skeletal actin gene mutations,^[3] mitochondrial mutations,^[4] interleukin genes,^[5] 11β-hydroxysteroid dehydrogenase type l gene,^[6] fatty acid translocase gene^[7] and several sarcomeric mutations in the pathophysiology and disease spectrum of cardiomyopathy.

On his return to Cape Town, Bongani penned numerous highimpact reviews in the leading cardiology journals of the time on heart failure and cardiomyopathy in Africa. In these reviews, he focused on disease epidemiology, natural history and outcomes and emphasised the dearth of data from sub-Saharan Africa, and always ended each article with a call to action. $^{\scriptscriptstyle [6-13]}$ In addition to the prominence he placed on the contention that heart failure in Africans was both a 'preventable and treatable disease', he regularly proposed a three-stage approach to solving Africa's cardiomyopathy and heart failure dilemma: (i) the first stage - characterised by a preliminary definition of the problem (by addressing lack of data on incidence, prevalence, aetiology, treatment and outcome of heart failure, and geographical variation by region and country in Africa); (ii) the second stage - delineated by a larger registry and comprehensive plan (focusing on diagnosing heart failure and better understanding its existence, severity and type and current management); and (iii) the third stage - which would include randomised clinical trials to assess optimal therapies and studies aimed at population prevention.^[8,9,12-15] In the next 20 years, he would follow this exact template in his scholarship, practice and advocacy on heart failure and cardiomyopathy.

Bongani was firmly committed to the goal of reducing global and sub-Saharan African premature deaths from CVD and stroke by 25% by 2025.^[16] On genomic research in Africa, which he applied to the study of idiopathic cradiomyopathies, he felt strongly that platforms like the Human Heredity and Health in Africa (H3Africa) were important to ensure that African researchers have a fair chance to develop the capacity for genomic research and investigate diseases that they believe are pertinent to Africa, that data would be interpreted in the context where they were collected, and that a new gold standard for collaborative genomic research in Africa, and possibly for broader collaborative health research, would be established.^[17]

Below, I briefly summarise 5 of his major contributions and achievements to improve understanding of different kinds of heart failure in Africa.

Dilated cardiomyopathy

In his early reviews on cardiomyopathy, Bongani extensively described the epidemiology, natural history and outcomes of dilated cardiomyopathy (DCM) in Africans.^[9,12-13] He also reviewed the state of understanding of the genetic basis of DCM in Africans.^[9,10,18] He also provided an authoritative review of the contributions of South Africans to the subject of DCM.^[11] He, together with collaborators, described a common mitochondrial DNA polymorphism (T16189C) that was found to be a genetic risk factor for DCM in a SA cohort, with a population-attributable risk of 6%.^[4] In separate studies, his group reported that mutation screening in SA patients with idiopathic and familial DCM identified a family with early-onset DCM caused by a known mutation in the troponin T gene (Arg141Trp),^[19] but failed to show mutations analysis of the phospholamban gene in 315 South Africans with DCM, peripartum cardiomyopathy (PPCM),

hypertrophic cardiomyopathy (HCM) and arrhythmogenic right ventricular cardiomyopathy (ARVC).^[20]

In a series of clinical studies, he clarified the clinical profile of DCM and its clinical genetics in the SA population. ECG T-wave inversion was significantly more frequent in familial DCM than in idiopathic DCM, whereas idiopathic DCM patients had a higher prevalence of pathological Q waves than familial cases. On echocardiography, cardiac chambers were significantly more dilated with poorer systolic function in idiopathic DCM than familial DCM. A mortality rate of 40% after a median follow-up of 5 years was, however, similar in both groups. The presence of New York Heart Association (NYHA) functional class III and IV symptoms was an independent predictor of mortality, while heart transplantation was an independent predictor of survival in both groups. Digoxin use without serum monitoring was a significant predictor of mortality in idiopathic DCM.^[21] In another study, of 109 unrelated patients with DCM, 27% had familial disease, mean age of onset of cardiomyopathy was significantly younger in familial DCM than that for non-familial cases, and male predominance was noted. Seven percent of familial DC cases had at least one relative diagnosed with PPCM. Pedigree analysis of the 29 familial DCM families was consistent with autosomal dominant inheritance in 72.4%, autosomal recessive inheritance in 17.2% and X-linked recessive inheritance in 10.4%.^[22] He reported on familial clustering of PPCM and DCM in SA families.^[20] He also reported that pregnancy-associated heart failure due to hypertensive heart failure of pregnancy and idiopathic PPCM has important differences in time of onset, clinical features, ECG and echocardiographic findings, natural history and outcomes,^[23] and argued that the presence of hypertension in pregnancy-associated heart failure should not fit the case definition of idiopathic PPCM.[18]

Hypertrophic cardiomyopathy

In a similar approach he had taken to the study of DCM, Bongani started by comprehensively reviewing the African literature and publications on HCM.^[9,10,12,13] He established an important partnership with Hanlie Mollman-Smook, Valerie Corfield and Paul Brink, who made important contributions on the genetics and clinical profile of mixed race and white South Africans with HCM on the basis of founder effects.^[24,25]

In the first study of HCM in black South Africans, genomic DNA was screened for mutations in 15 genes that cause HCM, i.e. cardiac myosin binding protein C (MYBPC3), cardiac β-myosin heavy chain (MYH7), cardiac troponin T2 (TNNT2), cardiac troponin I (TNNI3), regulatory light chain of myosin (MYL2), essential light chain of myosin (MYL3), tropomyosin 1 (TPM1), phospholamban (PLN), α-actin (ACTC1), cysteine and glycine-rich protein 3 (CSRP3), AMP-activated protein kinase (PRKAG2), a-galactosidase (GLA), four-and-a-half LIM domains 1 (FHL1), lamin A/C (LMNA) and lysosome-associated membrane protein 2 (LAMP2). Forty-three consecutive patients, mean age 39 years, 58% male, 30% black African, were prospectively enrolled. The SA founder mutations that cause HCM were not found in the 42 probands. Twenty-nine percent of index cases tested for mutations in 15 genes had disease-causing mutations in MYH7 (60%) and MYBPC3 (40%). No disease-causing mutation was found in the other 13 genes screened. The annual mortality rate was 2.9% per annum and overall survival was 74% at 10 years, which was similar to the general SA population. Cox's proportional hazards regression showed that survival was predicted by NYHA functional class at last visit, but not by the presence of a disease-causing mutation.^[26] The identification of known mutations in <30% of African patients with HCM, using a gene panel with a yield of 60% - 70% in European, British and North American populations, would form the basis of a later study: the African Cardiomyopathy and Myocarditis Registry Program (IMHOTEP), with an aim of unravelling novel genetic underpinnings of heart muscle disease in Africans.^[27]

Arrhythmogenic cardiomyopathy

In a SA family with ARVC, genetic linkage and haplotype analysis provided linkage to the ARVC type 6 locus on chromosome 10p12p14, but potential candidate genes in that region that were screened were all negative.^[28] In the first publication on ARVC clinical characteristics, survival, and genetics in SA, genomic DNA was screened for mutations in plakophylin-2 (PKP2) gene. Clinical presentation was similar to that reported in other studies. The annual mortality rate was 2.82%, the 5-year cumulative mortality rate 10%, and mean age at death was 37 years. Overall survival was similar to the general South African population. Independent risk factors for death were syncope and sustained ventricular tachycardia. Seven PKP2 gene mutations were found in 25% of unrelated participants, five being novel. The novel C1162T mutation occurred in four white South Africans sharing a common haplotype, suggesting a founder effect. Compound heterozygotes exhibited a severe phenotype signifying an allele dose effect.^[29,30] In a landmark study, the work for which had taken over 20 years, Bongani and collaborators were the first to report of cadherin2 (CDH2) as a causative mutation for ARVC.^[31] In patients with an extremely rare autosomal dominant condition characterised by hereditary fibrosing poikiloderma with tendon contractures, myopathy, and pulmonary fibrosis (POIKTMP), Bongani and colleagues identified four variants in the trypsin-like cysteine/serine peptidase domain of FAM111B gene.[32]

HIV-associated cardiovascular disease

Through a series of comprehensive reviews, Bongani described the clinical phenotypes of HIV-associated CVD affecting the entire axis of the cardiovascular system.^[33-35] Between 2002 and 2007, his group compared the prevalence of myocarditis and cardiotropic viral genomes in HIV-associated cardiomyopathy cases with HIVuninfected idiopathic DCM patients (i.e. negative controls for immunodeficiency) and heart transplant recipients (i.e. positive controls for immunodeficiency) at GSH, Cape Town, South Africa. Myocarditis was present in 44% of HIV-associated cardiomyopathy cases, 36% of heart transplant recipients and 25% of participants with idiopathic DCM. While myocarditis was acute in 50% of HIV- and heart transplant-associated myocarditis, it was chronic in all those with idiopathic DCM. Cardiotropic viral infection was present in all HIV-associated cardiomyopathy and idiopathic DCM cases, and in 90% of heart transplant recipients. Multiple viruses were identified in the majority of cases, with HIV-associated cardiomyopathy, heart transplant recipients and idiopathic DCM patients having an average of 2.5, 2.2 and 1.1 viruses per individual, respectively.^[36] They also described a lower body mass index associated with HIVassociated cardiomyopathy.^[37] The role of aptemers in ameriolation of pathophysiological mechanisms of HIV was also described with collaborators.[38,39]

Heart failure

In his early publications on the epidemiology of heart failure in Africans, Bongani noted that there were three major trends evident. First, the vast majority of heart failure cases in sub-Saharan Africa were due to three main non-ischaemic causes, with hypertensive heart disease, RHD and cardiomyopathy accounting for over 75% of cases in most series. Second, ischaemic heart disease remained an uncommon cause of heart failure, with no apparent increase in its contribution to the cases of heart failure. Hence, he felt strongly that non-ischaemic heart disease should be the priority for research and clinical intervention in Africa. Third, the contribution of cor pulmonale and pericarditis to ~20% of cases of heart failure reflected the continuing impact of pericardial tuberculosis CVD in Africa. Cor pulmonale was mainly related to post-tuberculosis lung damage, and pericarditis is overwhelmingly due to tuberculous involvement.^[8,9,12,13,40-42]

Over three decades, he systematically implemented his plan of taking a three-stage approach to the study of heart failure. Having undertaken reviews of the epidemiology, clinical profile, natural history and outcomes of heart failure in hospitalised Africans,^[8,9,13,40,43] he went about designing pan-African registries of heart failure as well as collaborative African-led randomised clinical trials of heart failure. These included important studies such as THESUS-HF,^[44] BA-HEF,^[45] IMPI^[46] and RELY-AF,^[47] which have completely transformed the landscape of CVD and collaboration on the African continent.

Important as his contributions have been to improving our understanding of cardiomyopathy and heart failure in Africans, undoubtedly his enduring legacy will be his mentoring, his unwaving belief in the capacity of Africans to undertake cardiovascular scholarship, and his transformative role in creating an enabling environment for cardiovascular research on the African continent.

- Mayosi BM, Keaveney B, Kardos A, Davies CH, Watkins H. Electrocardiographic measures of left ventricular hypertrophy show greater heritability than echocardiographic left ventricular mass: A family study. Eur Heart J 2002;23:1963-1971.
- Mayosi BM, Avery PJ, Farrall M, Keaveney B, Watkins H. Genome-wide linkage analysis of electrocardiographic and echocardiographic left ventricular hypertrophy in families with hypertension. Eur Heart J 2008;29(4):525-530. https://doi.org/10.1093/eurhearti/ehn028
- Mayosi BM, Khogali SS, Zhang B, Watkins H. Cardiac and skeletal actin gene mutations are not a common cause of dilated cardiomyopathy. J Med Genet 1999;36:797-798.
- Khogali SS, Mayosi BM, Beattie JM, McKenna WJ, Watkins H, Poulton J. A common mitochondrial DNA variant associated with susceptibility to dilated cardiomyopathy in two different populations. Lancet 2001;357(9264):1265-1267.
- Vickers MA, Green FR, Terry C, et al. Genotype at a promoter polymorphism of the interleukin-6 gene is associated with baseline levels of plasma C-reactive protein. Cardiovasc Res 2002;53(4):1029-1034. https://doi.org/10.1016/s0008-6363(0)100534-x
- Rahman TJ, Mayosi BM, Hall D, et al. Common variation in the 11β- hydroxysteroid dehydrogenase type 1 gene is associated with left ventricular mass. Circ Cardiovasc Genet 2011;4:152-162.
- 7. Hall D, Mayosi BM, Rahman TJ, Avery PJ, Watkins HC, Keavney B. Common variation in the CD36 (fatty acid translocase) gene is associated with left ventricular mass. J Hypertens 2011;29(4):690-695.
- Damasceno A, Cotter G, Dzudie A, Sliwa K, Mayosi BM. Heart failure in sub-Saharan Africa. J Am Coll Cardiol 2007;50(17):1688-1693.
- Mayosi BM. Contemporary trends in the epidemiology and management of cardiomyopathy and pericarditis in sub-Saharan Africa. Heart 2007;93:1176-1183. https://doi.org/10.1136/hrt.2007.127746
- Mayosi BM, Somers K. Cardiomyopathy in Africa: Heredity versus environment. Cardiovasc J Afr 2007;18:175-179.
 Watkins DA, Mayosi BM. The contribution of South Africans to the subject of dilated cardiomyopathy –
- With reference to cardiovascular collagenosis with parietal endocardial thrombosis. A clinicopathologic study of forty cases. Cardiovasc J Afr 2009;20(1):11-16.
 Gersh BJ, Sliwa K, Mayosi BM, Yusuf S. The epidemic of cardiovascular disease in the developing world:
- Gersh BJ, Sliwa A, Mayosi BM, rusurb. Ine epidemic of cardiovascular disease in the developing world: Global implications. Eur Heart J 2010;31:642-648. https://doi.org/10.1093/eurheartj/ehq030
 Sliwa K, Mayosi BM. Recent advances in the epidemiology, pathogenesis and prognosis of acute
- heart failure and cardinomy pathy in Africa. Heart 2013;99(18):1317-1322. https://doi.org/10.1136/ heartjnl-2013-303592
- Mayosi BM, Flisher AJ, Lalloo UG, Sitas F, Tollman SM, Bradshaw D. The burden of noncommunicable diseases in South Africa. Lancet 2009;374(9693):934-947. https://doi.org/10.1016/ S0140-6736(09)61087-4
- Kwan GF, Mayosi BM, Mocumbi AO, et al. Endemic cardiovascular diseases of the poorest billion. Circulation 2016;133(24):2561-2575. https://doi.org/10.1161/CIRCULATIONAHA.116.008731
 Sacco RL, Roth GA, Reddy S, et al. The heart of 25 by 25: Achieving the goal of reducing global
- 16. Sacco RL, Roth GA, Reddy S, et al. The heart of 25 by 25: Achieving the goal of reducing global and regional premature deaths from cardiovascular disease and stroke. A modeling study from the American Heart Association and the World Heart Federation. Circulation 2016;133(23):e674-690. https://doi.org/10.1161/CIR.000000000000395
- De Vries J, Tindana P, Littler K, et al. The H3Africa policy framework: Negotiating fairness in genomics. Trends Genetics 2015;31(3):117-119. https://doi.org/10.1016/j.tig.2014.11.004

- Ntusi NBA, Mayosi BM. Aetiology and risk factors of peripartum cardiomyopathy: A systematic review. Int J Cardiol 2009;131(2):168-179. https://doi.org/10.1016/j.ijcard.2008.06.054
- Mayosi BM, Meissenheimer L, Matolweni LO, et al. A cardiac troponin T gene mutation causes earlyonset familial dilated cardiomyopathy in a South African family. Cardiovasc J S Afr 2004;15:237.
 Fish M, Shaboodien G, Kraus S, et al. Mutation analysis of the phospholamban gene in 315
- Fish M, Shaboodien G, Kraus S, et al. Mutation analysis of the phospholamban gene in 315 South Africans with dilated, hypertrophic, peripartum and arrhythmogenic right ventricular cardiomyopathies. Sci Rep 2016;6:22235.
- Ntusi NAB, Badri M, Gumedze F, Wonkam A, Mayosi BM. Clinical characteristics and outcomes of familial and idiopathic dilated cardiomyopathy in Cape Town: a comparative study of 120 cases followed up over 14 years. S Afr Med J 2011;101(6):399-404.
- Ntusi NBA, Wonkam A, Shaboodien G, Badri M, Mayosi BM. Frequency and clinical genetics of familial dilated cardiomyopathy in Cape Town: Implications for the evaluation of patients with unexplained cardiomyopathy. S Afr Med J 2011;101(6):394-398.
- Tibazarwa K, Sliwa K, Wonkam A, Mayosi BM. Peripartum cardiomyopathy and familial dilated cardiomyopathy: A tale of two cases. Cardiovasc J Afr 2013;24(5):e4-7.
- 24. Heradien M, Revera M, van der Merwe L, et al. Abnormal blood pressure response to exercise occurs more frequently in hypertrophic cardiomyopathy patients with the R92W troponin T mutation than in those with myosin mutations. Heart Rhythm 2009;6(11):S18-S24. https://doi.org/10.1016%2Fj. hrthm.2009.07.020
- Moolman-Smook JC, Mayosi BM, Brink PA, Corfield VA. Molecular genetics of cardiomyopathy: Changing times, shifting paragdigms. Cardiovasc J S Afr 2003;14(3):145-155.
 Ntusi NAB, Shaboodien G, Badri M, Gumedze F, Mayosi BM. Clinical features, spectrum of causal
- Ntusi NAB, 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;27:152-158.
- Kraus SM, Shaboodine G, Francis V, et al. Rationale and design of the African Cardiomyopathy and Myocarditis Registry Program: The IMHOTEP study. Int J Cardiol 2021;333:119-126. https://doi. org/10.1016/j.ijcard.2021.02.026
- Matolweni LO, Bardien Sm Rebello G, et al. Arrhythmogenic right ventricular cardiomyopathy type 6 (ARVC6): Support for the locus assignment, narrowing of the critical region and mutation screening of three candidate genes. BMC Medical Genetics 2006;7:29.
- Watkins DA, Hendricks N, Shaboodien G, et al. Clinical features, survival experience, and profile of plakophylin-2 gene mutations in participants of the Arrhythmogenic Right Ventricular Cardiomyopathy Registry of South Africa. Heart Rhythm 2009;6510-517.
- Hendricks N, Watkinds DA, Mayosi BM. Lessons from the first report of the Arrhythmogenic Right Ventricular Cardiomyopathy Registry of South Africa. Cardiovasc J Afr 2010;21(3):129-130. https:// doi.org/10.5830%2FCVJA-2010-037
- Mayosi BM, Fish M, Shaboodien G, et al. Identification of Cadherin 2 (CDH2) Mutations in Arrhythmogenic Right Ventricular Cardiomyopathy. Circ Cardiovasc Genet 2017;10(2):e001605. https://doi.org/10.1161/CIRCGENETICS.116.001605
- Kury S, Mercier S, Shaboodien G, et al. CUGC for hereditary fibrosing poikiloderma with tendon contractures, myopathy, and pulmonary fibrosis (POIKTMP). Eur J Hum Genet 2016;24:779.
- Magula NP, Mayosi BM. Cardiac involvement in HIV-infected people living in Africa: A review. Cardiovasc J S Afr 2003;14(5):231-237.
- Ntsekhe M, Mayosi BM. Cardiac manifestations of HIV: An African perspective. Nat Clin Pract Cardiovasc Med 2009;6(2):120-127. https://doi.org/10.1038/ncpcardio1437
- Bloomfield GS, Alenezi F, Barasa FA, Lumsden R, Mayosi BM, Velazquez EJ. Human immunodeficiency virus and heart failure in low- and middle-income countries. JACC Heart Fail 2015;3(8):579-590.
- Shaboodien G, Maske C, Wainwright H, et al. Prevalence of myocarditis and cardiotropic virus infection in Africans with HIV-associated cardiomyopathy, idiopathic dilated cardiomyopathy and heart transplant recipients: A pilot study. Cardiovasc J Afr 2013;24(6):218-223. https://doi. org/10.5830/CVJA-2013-039
- Lemmer C, Badri M, Visser M, Mayosi BM. A lower body mass index is associated with cardiomyopathy in people with HIV infection: Evidence from a case comparison study. S Afr J Med 2011;101(2):119-121. https://doi.org/10.7196/samj.4348
- London GM, Mayosi BM, Khati M. Isolation and characterization of 20-F-RNA aptamers against whole HIV-1 subtype C envelope pseudovirus. Biochem Biophys Res Comm 2015;456(1):428-433. https://doi.org/10.1016/j.bbrc.2014.11.101
- Lopes de Campos WR, Chirwa N, London GM, et al. HIV-1 Subtype C unproductively infects human cardiomyocytes in vitro and induces apoptosis mitigated by an anti-gp120 aptamer. PLoS ONE 2014;9(10):e110930. https://doi.org/10.1371/journal.pone.0110930
- Ntusi NAB, Mayosi BM. Epidemiology of heart failure in sub-Saharan Africa. Expert Rev Cardiovasc Ther 2009;7(2):169-180. https://doi.org/10.1586/14779072.7.2.169
- Commerford P, Mayosi B. An appropriate research agenda for heart disease in Africa. Lancet 2006;367(9526):1884-1886. https://doi.org/10.1016/S0140-6736(06)68822-3
- Mayosi BM, Burgess LJ, Doubell AF. Tuberculous pericarditis. Circulation 2005;112(23):3608-3616. https://doi.org/10.1161/CIRCULATIONAHA.105.543066
- Szymanski PZ, Badri M, Mayosi BM. Clinical characteristics and causes of heart failure, adherence to treatment guidelines, and mortality of patients with acute heart failure: experience at Groote Schuur Hospital, Cape Town, South Africa. S Afr Med J 2018;108(2):94-98. https://doi.org/10.7196/ samj.2017.v108i2.12519
- 44. Damasceno A, Mayosi BM, Sani M, et al. The causes, treatment, and outcome of acute heart failure in 1 006 Africans from 9 countries. Results of the Sub-Saharan Africa Survey of Heart Failure. Arch Intern Med 2012;172(18):1386-1394. https://doi.org/10.1001/archinternmed.2012.3310
- Sliwa K, Damasceno A, Davison BE, et al. Bi treatment with hydralazine/nitrates vs. placebo in Africans admitted with acute Heart Failure (BA-HEF). Eur J Heart Fail 2016;18(10):1248-1258. https://doi.org/10.1002/ejhf.581