Good health and well-being

SDG 3: Ensure healthy lives and promote well-being for all at all ages

Image by World Bank, Flickr.
Biomarker discovery offers hope for new TB vaccine development

A team of scientists from UCT, Oxford University and the London School of Hygiene and Tropical Medicine have made a discovery that reveals how we can improve development of more effective vaccines against TB.

TB is the biggest killer of humans due to bacterial infection. In 2014, 9.6 million people were diagnosed with TB, and 1.5 million died. The only available vaccine against TB, BCG, is given to infants to prevent severe forms of the disease, but protection against lung disease is very variable – particularly in countries where TB is most common, such as South Africa.

The research team studied young children who had previously participated in a large clinical trial of a new TB vaccine conducted in Worcester, in the Western Cape. They investigated the immune response to BCG, given at birth, to determine the characteristics of this response that are associated with protective immunity against TB. “We looked at a number of factors that could be used as immune correlates, to try and find biomarkers that will help us develop a better vaccine,” said Professor Helen McShane of Oxford University, who led the study. The team carried out tests for 22 immune-response characteristics, and found that elevated activation of CD4 T cells was linked to higher TB disease risk. Higher levels of T cells, that responded to the BCG vaccine by producing IFN, the immune messenger molecule, were linked to reduced risk of TB.

Antibodies to the Ag85A protein made by the TB bacterium were also identified as a possible immune correlate. Higher levels of antibodies targeted against Ag85A were associated with lower TB risk. However, the team cautions that other environmental and disease factors could also cause Ag85A antibody levels to rise, and so there may not be a direct link between these antibodies and TB risk.

TB is an international killer

Professor McShane said: “These are useful results, which ideally would now be confirmed in further trials. They show that antigen-specific T cells are important in protection against TB, but that activated T cells increase the risk.”

Associate Professor Tom Scriba, from the South African Tuberculosis Vaccine Initiative (SATVI) at UCT, said: “TB is still a major international killer, and rates of TB disease in some areas of South Africa are among the highest in the world. These findings provide important clues about the type of immunity TB vaccines should elicit, and bring us closer to our vision – a world without TB.”
Good health and well-being

Low-cost urine test reduces HIV-associated TB death rate

A UCT-led clinical study on a urine test able to diagnose TB in severely ill HIV patients has led to a call for its immediate use in public health programmes, because it has the potential to save lives.

In a randomised controlled trial of the LAM urine test in 2,600 patients in South Africa, Zimbabwe, Zambia and Tanzania, the study evaluated the usefulness of using the simple diagnostic test (similar to a urine pregnancy test) to guide treatment in severely ill HIV-infected patients with suspected TB. The test – which can be conducted by a minimally trained healthcare worker, at the bedside – results in a diagnosis in around 25 minutes, simply from putting a few drops of urine on a low-cost test strip.

“Using a randomised controlled trial design, the study found that compared to existing tests and approaches used to guide treatment, the LAM test reduced the TB death rate in hospitals by almost 20%. Significantly, these were results obtained using a rapid, simple-to-use, low-cost bedside test,” comments Professor Keertan Dheda, the study’s lead investigator. Read more.

Image by Alere Inc via Discovery Medicine.

Inflammatory proteins offer insights into how TB spreads in the lungs

Two scientists at UCT have found proteins in the body that help the bacteria that cause TB to spread.

“Our research looked at one component of the immune system, and found that there were proteins in the body that promote lung inflammation – which helps the bacteria that cause TB to spread throughout the lung,” report Hlumani Ndlouvu, senior postdoctoral fellow in TB Immunopathogenesis, and Mohlopheni Marakalala, senior lecturer and group leader in the Division of Immunology.

“Now that we have identified the proteins associated with disease progression, the next step is to find the drugs that will inhibit these proteins, and limit lung inflammation.” Read more.

Image by Michael Hammond.

The research paper T cell activation is an Immune Correlate of Risk in BCG vaccine infants was published in Nature Communications. (Download media statement.) By SATVI. Image by Yale Rosen, Flickr.

Dr Helen Fletcher, from the London School of Hygiene and Tropical Medicine, said: “For the first time, we have some evidence of how BCG might work – and also, what could block it from working. Although there is still much work to do, these findings may bring us a step closer to developing a more effective vaccine for TB.”

The team is continuing its work to develop a new and improved TB vaccine, with the aim of protecting more people from the disease.
For the first time, more than half of the world’s population lives in urban settings. Many African countries are experiencing rapid, unplanned urbanisation, resulting in a significant proportion of urban dwellers living in informal settlements. A simplistic notion of urbanisation envisages people moving into denser areas with better access to healthcare and improved socioeconomic determinants of health, such as education and employment opportunities. However, the urban poor, who mostly live in such environments, are often exposed to worse conditions than in rural areas. This is exacerbated by the relative deprivation and spatial and environmental discrimination that accompany vulnerability. To improve inhabitants’ and communities’ health and well-being in a changing urban environment, it is important to understand the key factors and determinants that contribute to a healthy city, writes Tolu Oni.

The health and well-being of people living in cities and towns is intricately linked to the natural, built and institutional elements of the urban environment. In a changing urban environment, we need to consider all dimensions of urbanisation and urban living, as well as key social determinants of health. These include access to housing, health services, transport, food security, potable water, physical and environmental safety, social welfare, community resilience and psychosocial support structures.

Urban health and urban health equity

Physical, mental and social health outcomes are linked, and can influence the very determinants of health through positive or negative feedback. For example, poor housing conditions are associated with an increased risk of infectious and chronic respiratory conditions. Urban health and urban health equity have been globally recognised as crucial issues for the global south. Furthermore, we need to understand
the impact on, and consequences of, the urbanisation process on the multidimensional determinants of health in order to intervene effectively.

The UN sustainable development goal (SDG) 3 aims to ensure healthy lives and promote well-being for all at all ages. While this is the only explicit health goal, almost all of the other goals relate or contribute to health. This includes the targets of fostering healthier cities (SDG 11) and preventing disease through safe water and sanitation (SDG 6). This recognises that the health sector is but one player in health and human development; action that involves a number of sectors and takes into account the needs of the whole of society is therefore a key strategy to addressing societal challenges that will improve health and well-being.

South Africa is the most urbanised country in sub-Saharan Africa, with 62% of the population living in urban areas. Urban areas are characterised by significant spatial inequities, in which wealthy urban populations have better access to health services on average, and are associated with better health indicators overall; while in the poorer, more informal areas we see the co-existence of chronic communicable and non-communicable diseases, and the paradox of a high prevalence of obesity in communities that are most food insecure.

Nine health goals

The National Development Plan 2030 identifies nine health goals for South Africa, including raising life expectancy to 70 years, reducing maternal, infant and child mortality, and significantly reducing non-communicable diseases (NCD), injuries and violence. Addressing the social determinants of health and disease is identified as a key priority required to achieve these goals.

These goals and priorities were taken into account in the development of the South African Department of Health Strategic Plan 2014 to 2019: one of the key strategic goals is to prevent and reduce the burden of disease and to promote health. Although many of these factors lie outside the expertise and reach of the health sector, it is clear that they interrelate to health and well-being, and signal the need to build health into all policies when addressing societal challenges to improve health and well-being.

Despite the pressing need for this approach, urban health and urban health equity have not yet emerged as major research and policy priorities in South Africa. This represents a major gap, given South Africa’s high and complex burden of disease, and high levels of health inequity. In response to this gap, I established the Research Initiative for Cities Health and Equity (RICHE), an interdisciplinary collaboration of UCT researchers from public health; anthropology; civil engineering; architecture, planning and geomatics; human biology; psychiatry and mental health; medicine; pathology; and paediatrics.

The aims of RICHE include generating African perspectives on urban health and urban health equity, and identifying potential areas of research collaboration across disciplines, and opportunities for joint supervision of interdisciplinary postgraduate students.

Intersectoral collaboration

A workshop to tackle the urban health research agenda in August 2015 was attended by 40 RICHE members with extensive global and local urban health experience, resulting in the publication of a paper on urban health research priorities in Africa. Another notable achievement was the organising of a Health in All Policies workshop to bring together researchers and senior representatives from the Western Cape provincial government departments of Health, Human Settlements, Environmental Affairs and Development Planning, Transport and Public Works, and the Department of the Premier.

The purpose of this workshop was to identify joint priority areas across these sectors that impact on health, and potential opportunities for intersectoral collaboration to co-develop a research agenda, as well as to inform the application of a health lens across non-health sectors in the development of policy. This workshop resulted in the development of research between RICHE and the departments of Human Settlements and Health.

For academia to contribute significantly to achieving the health-related SDGs, there is a need to re-think our approach to conducting research with a focus of collaboration across disciplinary lines, closing the gap between science and policymakers, with a focus on co-production of knowledge, and the training of a new hybrid of students. This change may be slow and sometimes painful, but the potential to contribute meaningfully to improving population health equitably will make it worthwhile in the long run.

Dr Tolullah Oni is a senior lecturer in the division of Public Health Medicine.
Thought leader

Mental health and the SDGs: building sustainable human capability

Mental health was invisible in the millennium development goals (MDGs). While several researchers have argued that almost all of the MDGs were affected by mental health, and that it would be difficult to attain many of them without addressing mental health, there was no explicit mention of the term. Searching for ‘mental’ in the MDGs yields words such as ‘developmental’ and ‘environmental’, but no ‘mental health’!

This was a missed opportunity, because there is now substantial evidence from low- and middle-income countries (LMIC) that women and men who live in poverty and adversity have increased risk for a range of mental health conditions, including depression, anxiety disorders, trauma and schizophrenia.

Conversely, people who live with mental health problems are at greater risk of drifting into or remaining in poverty; because their condition excludes them from income-generating activities, they are frequently stigmatised and subjected to human rights abuses, and they spend more on healthcare than people who do not have mental health problems. So the relationship between poverty and mental illness is cyclical, including ‘social causation’ and ‘social drift’ pathways.

Encouragingly, there is emerging evidence for how this cycle can be broken. In 2011 we published a systematic review in the *Lancet*, which assessed the evidence for the impact of poverty-alleviation interventions on mental health, and the impact of mental-health interventions on poverty in LMIC. We found that the evidence for the former (such as cash transfers and loans) was mixed, and quite thin. But the evidence for the latter, while still nascent, was quite compelling.
Evidence-based mental-health interventions, such as psychological therapies, psychotropic medications and psychosocial rehabilitation programmes in community settings not only led to clinical and functioning improvements, but also improved the economic circumstances of the individuals concerned. In some cases, the benefits extended to their households.

‘No health without mental health’

This evidence has emerged as part of a growing field of global mental-health research, led by innovators such as Vikram Patel from India, Ricardo Araya from Chile, and Martin Prince and Graham Thornicroft from the UK. Among other things, this field has improved the cultural relevance of mental-health assessment instruments, developed innovative psychological therapies in low-resource primary-care settings, and improved our understanding of the links between mental health and other physical health conditions, under the slogan ‘no health without mental health’.

Armed with this new evidence, a group of global mental-health advocates (including 65 national and international organisations) led by the Centre for Global Mental Health responded to the call for contributions to the new SDGs. Under the banner of ‘FundamentalSDG’, this group campaigned tirelessly to have mental health included in the SDGs, presenting arguments that included human rights, healthcare and economic outcomes. Despite initial setbacks, the campaign was eventually successful, and important commitments to mental health were made.

Specific mental health targets

Among them, the SDGs state that mental health must be included in universal health coverage, and that “…we are committed to the prevention and treatment of non-communicable diseases, including behavioural, developmental, and neurological disorders, which constitute a major challenge for sustainable development”. In addition, mental health was included in SDG 3 (the health goal), with three specific targets:

- Strengthen the prevention and treatment of substance abuse, including narcotic drug abuse and harmful use of alcohol (target 3.5); and
- Achieve universal health coverage, including financial risk protection, access to quality essential healthcare services, and access to safe, effective, quality and affordable essential medicines and vaccines for all (target 3.8).

In addition, there has been a commitment to track suicide rates for all countries.

New set of challenges

This is a major victory for the field, and for the millions of marginalised people who live with mental-health problems, particularly vulnerable populations who live in circumstances of poverty. But of course, these new commitments bring a new set of challenges.

Firstly, there are new national and international policy challenges, to invest in and scale up evidence-based mental-health care, and to address the social determinants of mental health: poverty, violence (particularly gender-based violence), inequality and environmental destruction.

Secondly, there are exciting new research challenges: to understand more about the mechanisms of poverty and mental illness cycles in LMIC; specifically, where and when targeted population-based interventions can be delivered that address the mechanisms of poverty and mental illness.

This requires a change of thinking: joining the dots, to integrate mental-health outcomes into the evaluation of violence reduction and poverty-alleviation interventions, and to evaluate the economic and violence-reduction impacts of mental-health interventions.

We are currently engaged in some of these new challenges through research that we conduct from UCT, including the Programme for Improving Mental healthcare (PRIME), the Africa Focus on Intervention Research for Mental health (AFFIRM) and Emerging mental health systems in low and middle-income countries (EMERALD).

Professor Crick Lund is director of the Alan J Flisher Centre for Public Mental Health, Department of Psychiatry and Mental Health. Image by Halden Krog.
Cancer care meets big data: SA’s latest treatment breakthrough

Two South African chemists have made a breakthrough in cancer research that paves the way for early diagnosis and specialised treatment based on each cancer’s unique genetic expression pattern.

Early diagnosis is critical for cancer survival; and the discovery made by Dr Kevin Naidoo, DST/NRF SARChl Chair in Scientific Computing in the Department of Chemistry at UCT and Dr Jahan Shah Ashkan, also of the department, could therefore have a major impact on the prognosis for cancer patients.

The study, published in the latest issue of Scientific Reports, focused on six common cancer types – breast, colon, lung, kidney, ovarian and brain – and found that each of these has a unique genetic expression pattern that can be used for accurate early diagnosis; and more specifically, for specialised treatment.

Naidoo and Ashkan used statistical classification algorithms on large volumes of tumour gene-expression data. By analysing these vast quantities of data, they found that the GT-expression pattern – or the way in which complex carbohydrates are built – can be used to classify different cancer types early on. Moreover, the expression patterns are specific enough that variations can be identified within each cancer type, which can then guide the treatment route.

"The most immediate application of our finding is that we can detect the specific subtypes of a cancer type; and we have shown this for breast cancer," says Naidoo. "For example, we found distinct patterns for aggressive types of breast cancer, such as what’s commonly termed ‘triple-negative’ breast cancer.”

This application is crucial. Just as early diagnosis has a strong influence on the patient’s prognosis, so too does the choice of treatment. While older cancer treatments typically killed cancer cells, newer, targeted therapies – which may form part of the treatment regimen, rather than being used in isolation – prevent the proliferation of the cells.

Naidoo and Ashkan’s discovery underlines the importance of using computational big data analytics in biomedical sciences and the developing field of personalised medicine.

“We hope that the field of computational data analytics in biomedicine is able to integrate fully into clinical research in South Africa, as is the world trend,” says Naidoo. “We hope that our research results inspire this structural change in clinical research in South Africa, and that it will lead to the growth and development of ‘precision medicine’ that is being shown worldwide to result in improved patient care and greater survival times in cancer.”

Naidoo is now leading a multi-laboratory collaboration, which will include scientists in pathology and human genetics at the UCT medical campus and the Centre for Proteomics and Genomics Research, to analyse the blood samples of South African patients. The aim is to develop a low-cost gene-expression tool for breast cancer – the most common cancer affecting South African women – which can form the basis of a routinely-used early-diagnostic process.

Story adapted from article by Marelise van der Merwe, Daily Maverick. Image of cancer cells by the National Cancer Institute, Wikimedia Commons.
10 years on, SA children continue to experience high levels of violence

A look back at the past ten annual issues of the *South African Child Gauge* has revealed both the progress made for South African children, and the obstacles they still face.

In November 2016, UCT’s Children’s Institute will release the 11th issue of the *South African Child Gauge*: the only publication to provide an annual snapshot on the situation of South Africa’s children.

The Children’s Institute has outlined massive challenges facing children today. For example, levels of violence against children are excessive: South Africa’s child homicide rate is more than double the global average, and most forms of violence are perpetrated by someone known to the child. At the same time, the institute says it is clear that an array of progressive laws and policies have translated into significant gains for children:

**Gains for children in South Africa today**

- Child poverty dropped from 74% in 2003 to 54% in 2013, driven primarily by the expansion of the Child Support Grant, which now reaches just under 12 million children.

- Children’s access to formal housing has increased to 75%, with access to basic sanitation at 72%.

- Deaths of children under five years old have fallen, following the roll-out of the Prevention of Mother to Child Transmission programme.

- Access to early childhood development programmes increased from 55% in 2002 to 91% in 2013, and access to basic education is nearly universal, at 98%.

**Challenges facing children today**

- Poor-quality schooling acts as a poverty trap, starting in the foundation phase and culminating in high levels of high-school drop-out.

- Just over one million learners started grade 1 in 2003, yet only 49% made it to matric in 2014; and only 8% qualified for a university exemption.

- According to the Children’s Institute’s Children Count project, children remain disproportionately affected by child poverty. Over half of children live in households with a per capita monthly income of less than R671.

- One in five children live in overcrowded households, one in three are without water on site, and one in four are without basic sanitation.

- Nearly half of child homicides take place in the context of child abuse and neglect; and of these, 75% of victims are children under the age of five – where most violence is inflicted at home by a person known to the child.

“Although the South African constitution provides children with the right to be free from maltreatment, abuse and neglect, children continue to experience high levels of violence across multiple settings,” said Shanaaz Matthews, director of the Children’s Institute.

“Experiences of violence have long-lasting negative effects on the health, social and psychological well-being of a child. It is therefore imperative that we find innovative ways to protect children from violence, and to build children’s resilience so they are able to recover from negative experiences. In addition, it is vital that projects such as the Child Gauge continue to monitor the status of children, identifying critical gaps and opportunities to strengthen policy and programmes.”

UCT Children’s Institute media release. Image by DLR German Aerospace Center, Flickr.
How neurosurgeons can now look at your brain – through your eyes

For many years, scientists have been trying to find a way to measure the pressure in a patient’s brain without having to drill a hole in the person’s skull. Although this remains the most reliable way to measure pressure in the brain, it is invasive, expensive, and comes with the risk of infection and bleeding.

Assessing pressure inside the brain is an important part of diagnosing certain neurosurgical conditions. These include brain tumours, cranial deformities, traumatic brain injury, and infection.

Several years ago, ultrasound imaging technology – which uses an ultrasound probe, over the eye – was introduced as a non-invasive method to identify this pressure, using static imaging. Although it allows neurosurgeons to assess most cases of pressure inside the brain, static ultrasound imaging does not pick up all cases.

Our study has advanced the current static imaging method. Our technique involves analysing a short video clip of the back of the eye to mark pressure in the brain. It is a faster and potentially more accurate process than the existing technique.

There are limited statistics about children with neurosurgical disorders in Africa, but the number of children with hydrocephalus is thought to be quite high. Hydrocephalus is the result of a build-up of fluid pressure, which compresses the brain and causes the skull to enlarge. Untreated, it can result in death. A reliable technique to estimate the pressure on the brain, therefore, needs to be very accurate.
Using sound waves to see the brain

The eye is directly linked to the brain by the optic nerve, which sits at the back of the eyeball. It delivers the visual information collected by the retina to the brain. The optic nerve sheath is a balloon-shaped structure. As pressure in the brain builds up, fluid from the brain is forced along this sheath. It dilates the sheath in the same way that a balloon is inflated.

The optic pathway therefore allows us to extract important information from the brain using non-invasive imaging techniques. Recent advances in ultrasound imaging technology have made it a very appealing tool for assessing raised pressure inside the skull. The use of ultrasound in neurosurgery is most appealing, because it is radiation-free, portable, widely available and relatively cheap.

The way the technique works is that the ultrasound probe is placed over the closed eye, allowing us to see the deeper optic structures as they connect with the brain. The currently used technique requires a snapshot to be taken of the optic nerve sheath. The width of the sheath is then compared to other clinical and imaging markers, to infer whether or not there is increased pressure in the brain.

How the new technique works

Our study employed several differences from the existing static imaging technique. Aside from measuring the changes in the diameter of the sheath as an indication of increased pressure, we have developed a dynamic technique that analyses the way the sheath moves as a result of the person’s pulse. This motion is then compared with intracranial pressure, and demonstrates a remarkable consistency.

As an initial study, we performed the ultrasound measurement on a large cohort of children. Previous studies using the ultrasound technique on children have not compared it to directly measured pressure in the brain. Diagnosing neurological disease in children is notoriously difficult, because the symptoms are often quite subtle. We also identified certain shortcomings in the current ‘static imaging’ technique, which resulted in limited accuracy – a limitation described in many other studies.

In a resource-challenged environment such as South Africa, where the average child with a neurological condition is referred to the appropriate centre much later than they should be, an accurate tool that allows early diagnosis would make a substantial difference.

The static technique takes two to three minutes to collect all the images that are needed; our technique could significantly decrease the time required to record the information, to around 30 seconds. It is also the first study of its kind to be conducted on such a large group of patients, with significant results.

The use of non-invasive techniques to measure the pressure inside the brain in order to diagnose certain neurological conditions has attracted much attention recently. These techniques include measurement of blood flow to the brain, and the pressure in the ear. But many of these studies have been limited, because of inconsistent accuracy.

Making the technique more accessible

Our goal is to refine the accuracy and improve the simplicity of our technique. If we are successful, we hope that assessing the pressure inside the skull using this modified technique may be performed at primary healthcare level. This would speed up the diagnosis of raised pressure in the brain associated with certain neurological disorders.

In a resource-challenged environment, such as South Africa, where the average child with a neurological condition is referred to the appropriate centre much later than they should be, an accurate tool that allows early diagnosis would make a substantial difference.

From a neurosurgical perspective, diagnosing increased pressure in the brain earlier would be a useful marker of underlying neurological disease. This simplified yet effective technique has the potential to change the way we diagnose certain neurological conditions. But more importantly, perhaps, this could be done at the level of primary healthcare facilities, such as day hospitals and clinics.

This study is a collaboration between UCT’s Division of Neurosurgery and a leading Norwegian research institute. It has received a provisional patent. By Dr Llewellyn Padayachy, paediatric neurosurgeon, Department of Surgery, Faculty of Health Sciences. This article first appeared in The Conversation. Image by Michael Hammond.

Listen to Dr Llewellyn Padayachy describe his research on the US public radio daily programme The Academic Minute.
Biomedical engineer and winner of a 2016 Claude Leon Merit Award for early-career researchers, Dr Sudesh Sivarasu, draws inspiration from nature to design his patented medical devices. He spoke to Helen Swingler about his work.

What attracted you to biomedical engineering?

As a child in Vellore, India, I was fascinated by steam engines. My father was a train driver, so I got plenty of opportunity to see how they operate. After a terrible road accident, I missed a wonderful opportunity to do business studies in the UK. But this was a blessing in disguise. I did a postgrad degree in biomedical engineering. It was during my postgrad studies that I began to appreciate human anatomy and its design; the body is the most amazing, complex, interconnected and efficient machine. It led to further reading and understanding.

Your academic career began in India and was cemented in South Africa?

Yes. I studied electronics and instrumentation engineering – the equivalent of mechatronics – at the Vellore Institute of Technology (VIT). Both electrical and mechanical engineering design skills are essential to medical device design. After completing my PhD, I was at a crossroads: a lucrative corporate career or a career in academic research? At 26, I chose academia. As a young academic at VIT, I designed their undergrad and postgrad programmes in biomedical engineering. These are some of the most popular biomedical programmes in India. But I wanted to explore scenarios in global health. So, after a brief tenure at VIT, I got a lecturership in the Department of Human Biology at UCT in 2011. Here, I’ve had a wonderful opportunity to set up clinician discussion platforms and explore the possibility of establishing an appropriate model for medical device innovation.

How does the Claude Leon Merit Award support your research?

It will be used for clinical trials and potential commercialisation of UCT-patented technology that underpins the novel Laxmeter device. This was recently granted patents in the US, UK and South Africa. The device helps measure laxity [or looseness] in all four major knee joint ligaments at various levels of flexion and at full extension. Ligamentous laxity is characterised by loose ligaments, which causes joint hypermobility and joint instability. Sports injuries often compromise ligamentous laxity. The capacity to measure multi-ligamentous laxity makes the Laxmeter unique.

Is this kind of recognition important to an early career academic?

It is essential. Nothing motivates you better than recognition for your hard work.

Tell me about the Frugal Biodesign Process you conceptualised.

It’s a unique approach to medical device design and it is suited specifically to developing countries. I’ve incorporated this process into my medical device design course. Thus far, we’ve invented several medical devices and some are in clinical trials.

What floats your boat as a researcher?

Trusting that the work that I do will make a difference in someone’s life. I want to serve humanity through my work.

By Helen Swingler. Image by Michael Hammond.