MediCine

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Beyond Eight Years of Age

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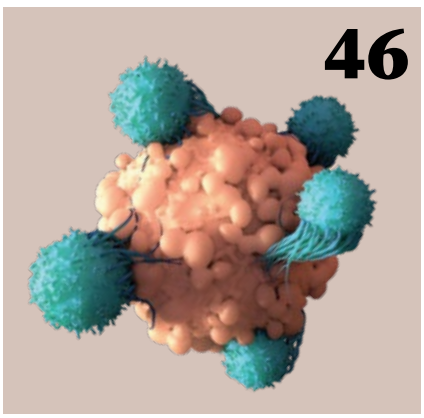

MediCine

MediCine is published quarterly by the communications office of the NUS Yong Loo Lin School of Medicine.

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Dean's Message

Dear Reader,

Recently, the food world was abuzz with news that one of the most celebrated restaurants in the world would shut its doors for good in 2024. In its place, the chef-owner of Noma said he would start a new enterprise thereafter dedicated to food innovation.

Closing a culinary icon at the pinnacle of international fame and starting a food lab in its place would seem an ill-advised and thoroughly illogical move. The new enterprise, the restaurant announced, would pioneer a test kitchen dedicated to the work of food innovation and the development of new flavours.

Conventional wisdom holds that "If it ain't broke, don't fix it." We know, however, that continuous improvement is essential if companies and organisations want to be relevant, meaningful and sustainable. This requires constantly re-examining and even repurposing the work that is being done, perhaps even re-inventing and discarding aspects of it to come up with something far better.

It is very much the case in medical education and biomedical research. Our students are able to benefit from refinements and enhancements to the curriculum, and the ways in which knowledge and skills are taught. As this issue goes to print, about 600 final year Medicine and Nursing students are preparing for their final exams before taking their first steps as healthcare professionals. They will soon be putting years of arduous study into practice in wards and clinics, tracing the paths taken by earlier generations of graduates.

This never-ending search for a better way similarly inspires our academic staff. For example, Professor Theo Kofidis from the Department of Surgery doggedly worked for years to develop a set of new surgical techniques for mitral heart valve surgery. Prof Kofidis who is also Group Chief of Cardiothoracic Surgery at the National University Health System says, these procedures improve on existing techniques that were promulgated nearly 40 years ago and help make mitral valve surgery intuitive, simple and standardised, eliminating variability and render it very easy to repair mitral valves with good outcomes. He has used the techniques on 10 patients thus far, with consistently excellent results.

Another exciting piece of research work: a multi-institution team by Dr Evelyn Law from the Department of Paediatrics has found that excessive screen time during infancy is linked to detrimental outcomes in cognitive functions, which continue to be apparent after eight years of age. The study provides compelling evidence to existing studies that our children's screen time needs to be closely monitored, particularly during early brain development, she says.

The team analysed data from a group of children at 12 months, 18 months and nine years. As the duration of screen time increased, the greater the altered brain activity and more cognitive deficits were measured. Children with executive function deficits often have difficulty controlling impulses or emotions, sustaining attention, following through multi-step instructions, and persisting in a hard task.

> *"Continuous improvement: the quest for a better way is a never-ending one here at NUS Medicine."*

The team is also concerned that families which allow very young children to have hours of unmonitored screen time often face additional challenges. These include stressors such as food or housing insecurity, and parental mood problems. They believe more work needs to be done to understand the reasons behind excessive screen time in young children, and to distinguish the direct association of infant screen use versus family factors that predispose early screen use on executive function impairments.

Continuous improvement: the quest for a better way is a never-ending one here at NUS Medicine.

Yap Seng

Global Ethics Lecture 2023: What is the 'Fair and Equitable' Allocation of Scarce Medical Resources?

Former Obama Health Advisor Dr Ezekiel J. Emanuel speaks at the inaugural Global Ethics Lecture 2023, organised by the Centre For Biomedical Ethics (CBmE) at the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine).

As the healthcare system evolves and more new diseases emerge, the ability to harness resources effectively for greater innovation in the medical sector is paramount. One such challenge to healthcare resource allocation is long COVID, a disease that remains understudied despite its urgency as a medical problem.

This renders the fair allocation of resources ever more important—with crucial ethical considerations among groups with different risk of disease and disadvantages.

Over **200** guests attended the conference

Photo:
Dr Ezekiel J. Emanuel, Vice Provost for Global Initiatives and the Diane v.S. Levy and Robert M. Levy University Professor, Co-Director of the Health Transformation Institute, speaking at the Inaugural Global Ethics Lecture 2023.

Speaking at the inaugural Global Ethics Lecture organised by CBmE at NUS Medicine, Dr Ezekiel J. Emanuel, Vice Provost for Global Initiatives and the Diane v.S. Levy and Robert M. Levy University Professor, Co-Director of the Health Transformation Institute, emphasised that there are fundamental principles in resource allocation.

This is CBmE's first conference, held on 9 January 2023 at the NUS University Cultural Centre. Over 200 guests attended the conference, including senior government leaders as well as leaders from academic and healthcare institutions, healthcare professionals and students.

Titled, "What is the 'Fair and Equitable' Allocation of Scarce Medical Resources?", Dr Emanuel's talk centred on the way countries allocated medical resources such as vaccines during the COVID-19 pandemic. He drew on important ethical values and principles that countries should consider during the resource allocation process, elaborating on the resource situation in the context of malaria and cholera.

Scan here to read the biography of Dr Ezekiel J. Emanuel and the summary report on the Global Ethics Lecture – What is the Fair and Equitable Allocation of Scarce Medical Resources?

From top: Dr Ezekiel J. Emanuel (right), and Professor Julian Savulescu, Director of the Centre for Biomedical Ethics (left), engaging at the Q&A session.

Middle: Participants listening attentively to the talk.

Bottom: Guests engaging in conversation after the lecture.

Innovative Heat Mitigation Strategies to Ensure Safe and Effective Military Training and Operations

The Heat Resilience and Performance Centre (HRPC) was launched at the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine) on 11 January 2023. HRPC is a tripartite collaboration between the Singapore Armed Forces (SAF), NUS, and DSO National Laboratories (DSO) to leverage best-in-class local and global expertise, including thermal physiologists and climate researchers, to address the long-term challenges of maintaining human performance amid rising temperatures in the region and the world.

Minister for Defence, Dr Ng Eng Hen, officiated at the launch and was briefed on various research strategies and ideas that HRPC would be exploring further, together with industry partners, to bolster heat resilience and performance in our soldiers. Dr Ng was also treated to a demonstration of data collection and analysis that used wireless body sensor networks.

"The pool of local experts in the field of heat injury prevention is limited. The HRPC will tap into the best-in-class researchers from both local and overseas... this work of HRPC will be increasingly important for the health of not only our soldiers but the general public as our ambient temperature rises," said Minister for Defence Dr Ng Eng Hen, at the opening ceremony.

MINDEF/SAF/DSO doctors, scientists and engineers have been working with other national experts to deal decisively with and prevent heat injuries for the past decade.

The new Heat Resilience and Performance Centre was launched by Guest-of-Honour, Minister for Defence Dr Ng Eng Hen (second from left).

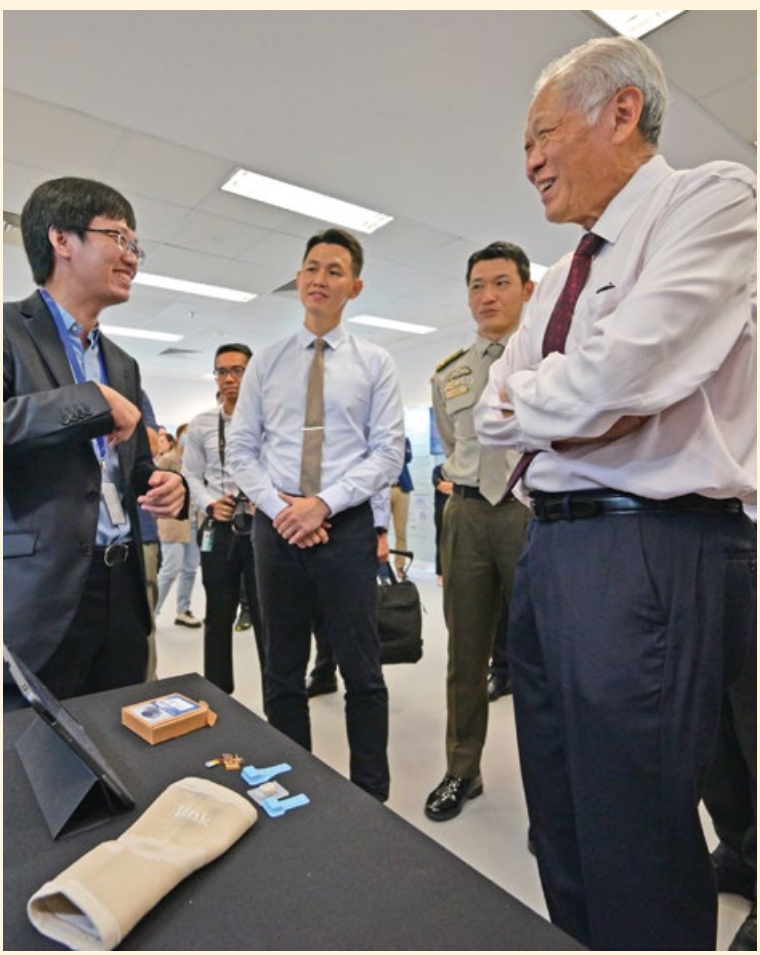
Dr Ng highlighted that collaborating with HRPC is part of the SAF's efforts to understand how to mitigate the impact of heat stress on soldiers so that they are able to continue to train and operate effectively and safely amid rising ambient heat. He highlighted how the tripartite partnership aims to further strengthen linkages between operations, technology and research institutions, tap into local and global expertise, and leverage key technology enablers like deep data science and artificial intelligence to develop innovative heat mitigation strategies.

The HRPC is a dedicated, one-stop research entity that brings together subject matter experts from the local defence ecosystem and NUS Medicine, to drive and conduct heat resilience and performance research together with its partners, for the benefit of the general population. The centre will contribute to and leverage national efforts to support new and existing national initiatives to meet and mitigate similar challenges related to rising global temperatures.

"In addition to heat injuries and performance degradation, excessive heat stress can also compromise decision-making, leading to accidents. Not known to many, heat can be an enabler for physiological adaptations if we know how to use it correctly. HRPC seeks to add value to the expanding narrative of heat health and performance research to provide forward-looking solutions that proactively augment heat resilience in our people amid rising global temperatures," Associate Professor Jason Lee, Director of HRPC, explained.

"In addition to heat injuries and performance degradation, excessive heat stress can also compromise decision-making, leading to accidents. Not known to many, heat can be an enabler for physiological adaptations if we know how to use it correctly. HRPC seeks to add value to the expanding narrative of heat health and performance research to provide forward-looking solutions that proactively augment heat resilience in our people amid rising global temperatures."

Assoc Prof Jason Lee, Director of HRPC



Minister for Defence Dr Ng Eng Hen listening to a presentation on wireless body sensor networks by one of the exhibitors. The wireless body sensor network is able to capture and assess an individual's heat status before he reaches the point of overexertion.

Research foci of HRPC

Discover

Build a robust database through the aggregation and analysis of existing and emerging data that allows the development and continuous refinement of physiological research models.

i. **Data Aggregation:** Physiological data from past and prospective projects will be consolidated for further research to find innovative approaches for active surveillance, continuous monitoring, and data collection.

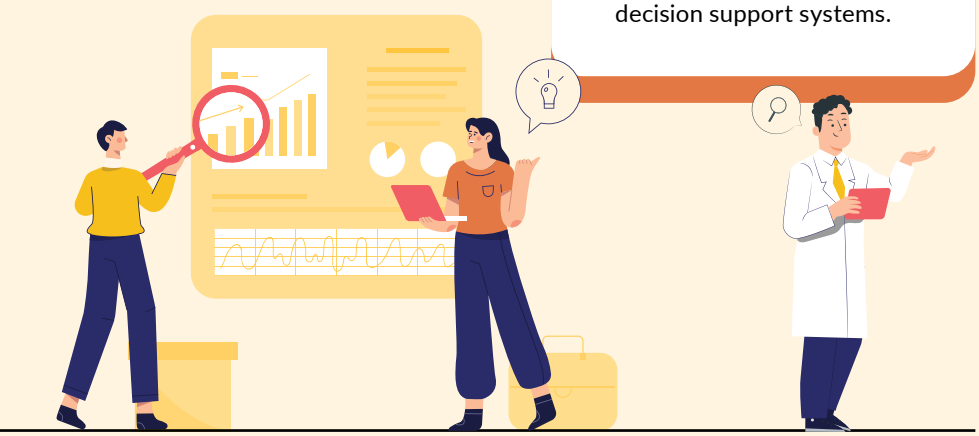
ii. **Data Analysis:** Aggregated data will be analysed to build predictive models to test research hypothesis. Such hypothesis will help to develop new strategies to interpret and transform data into new knowledge and new capabilities.

Detect

Develop the capability to visualise and interpret the heat-health status of individuals in real-time, allowing for the development of personalised training programmes for heat management, active risk management and training optimisation.

i. **Heat Health Visualisation:** New approaches toward physiological sensing will be explored to increase accuracy in predicting and managing the risk of exertional heat injury. Physiological data specific to the causative mechanisms of exertional heat injury will be investigated. Research will also focus on exploring methods to increase the fidelity of physiological sensing by leveraging on the concept of a sensor network to build a more comprehensive heat health map to better analyse the heat health status of an individual.

ii. **Training Personalisation:** Further research will utilise deep data analytics to develop predictive models and algorithms, indices, and decision support systems.



Strengthen

Explore different advanced technologies and approaches to develop more efficient strategies for heat resilience in humans, guided by in-depth understanding of physiology, biology, psychology, as well as the social and behavioural responses to rising heat.

i. **Advanced Material Technologies:** New technologies in advanced materials can potentially be used to enhance body cooling, either actively or passively. Examples include adaptive fabrics which change structures in response to environmental conditions, and super hygroscopic nano fabrics to absorb moisture.

ii. **Role of Gut Microbiome:** Microorganisms in our intestines, or the gut microbiome, may have a significant role in a human's heat health and could be a potential indicator of heat stress. Investigations into this area of study can allow us to predict and improve heat resilience through measuring and manipulating the gut flora.

iii. **Urban Heat Effect of Environments and Urban Infrastructure on Humans:** Understanding the urban heat effect of environments and buildings through the development of virtual models that provide insights on how infrastructure can be used to improve passive heat resilience and promote active cooling.

Medical Students Tread the Boards

BY WONG HUI JIE, PUBLICITY LEAD AND XIA YUELIN, ARTS & CULTURE DIRECTOR, PLAYHOUSE 2022, PHASE II NUS YONG LOO LIN SCHOOL OF MEDICINE STUDENTS

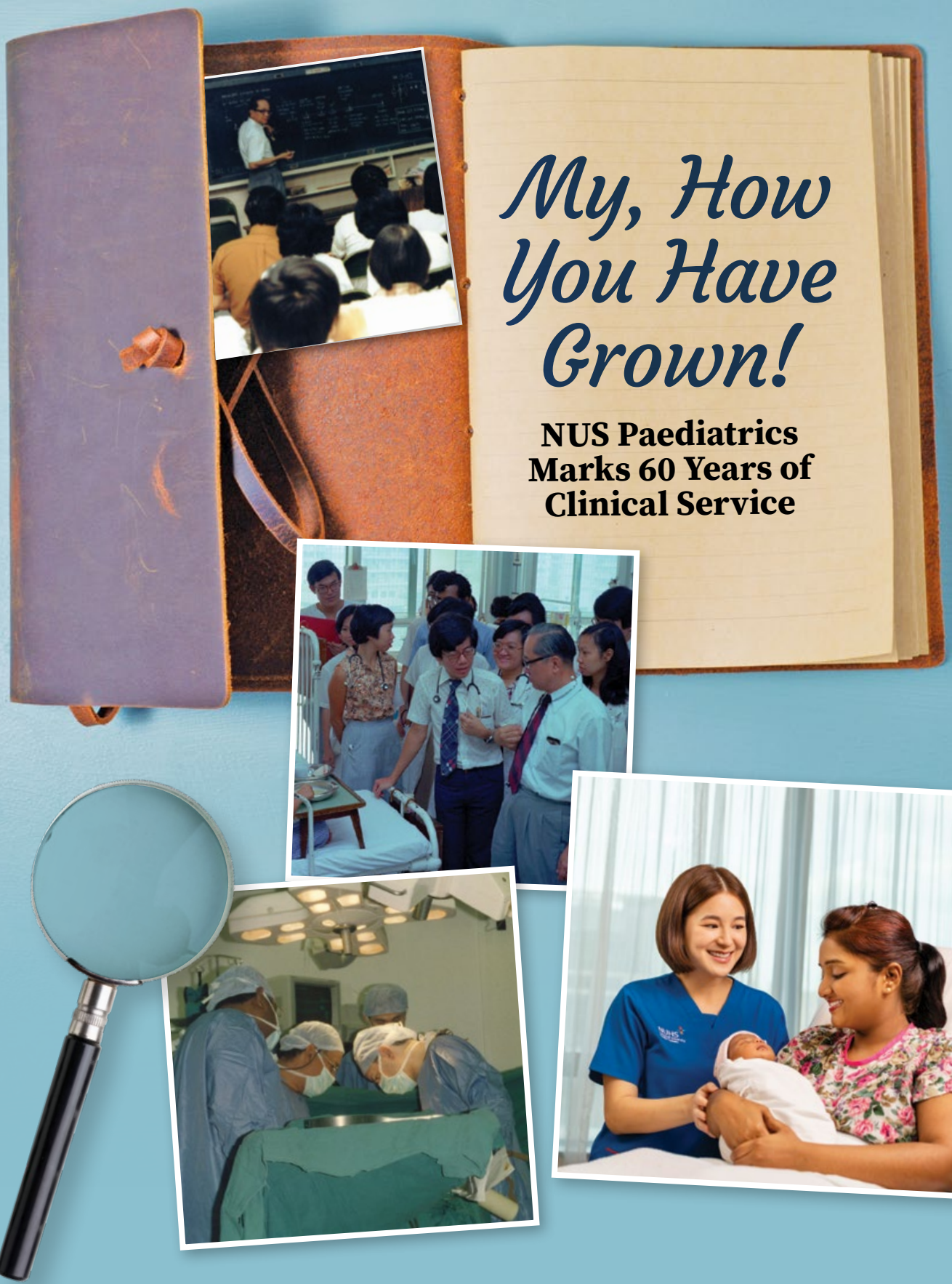
After a pandemic-induced two-year hiatus, Playhouse returned for its premiere in December 2022.

As the longest running theatrical production involving many of our alumni and teachers, including Professor Paul Tambyah, Playhouse took a musical turn. Renaissance, our theme for this year's Playhouse, not only represented the return of Playhouse, but also performances by students from various years.

This year, Playhouse's programme consisted of a comedy, "Helpline", put up by current Phase III and Phase IV NUS Medicine students, as well as the musical, "Lost and Found" performed by Phase I and Phase II students.

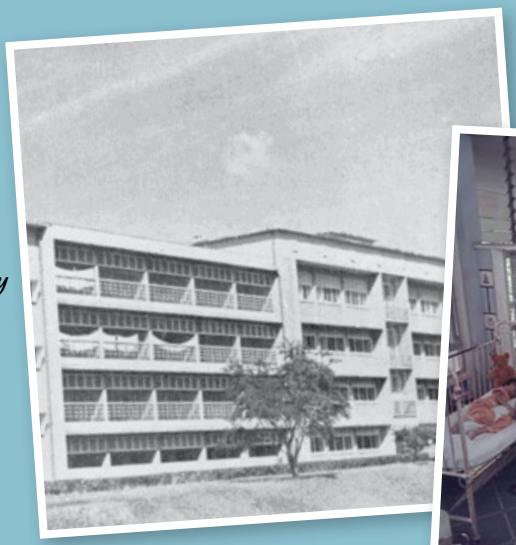
The performances were well-received and we are grateful for the immense support. Playhouse will return in 2023 with a fresh, exciting programme.

Photo:
Cast of *Helpline* and *Lost & Found* with Guests-of-Honour – Professor Chong Yap Seng, Dean of NUS Medicine, and Professor Paul Tambyah.



My, How You Have Grown!

NUS Paediatrics Marks 60 Years of Clinical Service



The Mistri Wing at the SGH. Source: Journal of Singapore Paediatric Society

A typical paediatric ward within the wing. Source: The SGH Museum.

Remembering our roots

Our Beginnings

The history of our paediatric services dates back 60 years to 1962 and the Mistri Wing at the Singapore General Hospital (SGH), where the University of Singapore medical school established the Department of Paediatrics. The four-storey paediatric wing, named after its donor, N.R. Mistri, had eight wards with 280 beds/cots.

Located in the Mistri Wing's west wing, the department was popularly known as Paediatric West and occupied half of the wards, namely Wards 26, 28, 30 and 32. It was led by Emeritus Professor Wong Hock Boon, the Founding Professor of Paediatrics.

In the early days at Mistri Wing, the number of paediatricians was limited. All the doctors were thus trained as general paediatricians. However, as the standard of care improved and expectations from the patients and parents increased, sub-specialties were eventually pioneered in the department.

In 1985, the department moved to the National University Hospital (NUH), which had been newly set up as a teaching hospital to give impetus to medical education in Singapore. Following its move, the department underwent several changes, including a growth in staff strength which allowed the enhancement of paediatric services.

The University Department of Paediatrics led by E/Prof Wong Hock Boon. Source: The SGH Museum.

Our Pioneers

As the only paediatric oncologist back in the day, A/Prof Quah Thuan Chong (foreground, left) was pivotal in the treatment of childhood cancer. He designed the acute lymphoblastic leukaemia (ALL) treatment protocol at NUH, which improved the cure rate of childhood ALL in Singapore from 30% to 62%.

Beneath Prof Low Poh Sim's (centre) gentle demeanour was a powerful trailblazer who has built a firm foundation for paediatric and paediatric neurology services. She has nurtured and mentored countless paediatricians, many of whom are now established leaders in the profession.

Driven by a single-minded passion to enable chronic kidney patients to lead fulfilling lives, Prof Yap Hui Kim (centre) has dedicated her career to the advancement of paediatric nephrology. Together with a paediatric dialysis nurse, she adapted machines and successfully performed peritoneal dialysis and haemodialysis on her first few patients. Source: The SGH Museum.

Prof Quak Seng Hock has played a pivotal role in building up paediatric gastroenterology and hepatology services in Singapore. Under his leadership, major milestones in Singapore and Southeast Asia include pioneering paediatric gastrointestinal endoscopy services, paediatric gastrointestinal motility services and the paediatric liver transplantation programme.

Regarded as the pioneer of paediatric liver transplantation in Singapore, E/Prof Prabhakaran Krishnan (second from left) has had an illustrious career with many firsts in paediatric surgery. He played an instrumental role in establishing the national paediatric kidney and liver transplantation programmes in Singapore, with outcomes comparable to leading centres in the world.

As an astute clinician and researcher, A/Prof Roy Joseph introduced key interventions to the neonatal practice to enable better care for newborns. He pioneered the introduction of transcutaneous screening for severe jaundice in Singapore which greatly improved the care of infants with neonatal jaundice.

The late Prof Tan Kim Leong championed better healthcare for newborns, which took him beyond the hospital and into the community. In the 1980s, he established an intensive care service for newborns that helped reduce neonatal mortality rates from 16 to five per 1,000 live births over the next two decades.

Taking her passion for research in allergy and immunology from bench to bedside led Prof Lee Bee Wah (first from left) to initiate the setup of the first clinical immunology laboratory in Singapore, while also establishing paediatric allergy services at NUH to provide allergy diagnostics for children.

The department's first research scientist, the late A/Prof Nilmani Saha (centre), was known to think out of the box when the odds were against him. Despite the rough and ready conditions that he had to adapt to back in the day, it did not deter him from making an impact and authoring more than 200 research publications.

A New Era: Khoo Teck Puat – National University Children's Medical Institute

The paediatric outpatient service, having been expanded over the years, eventually outgrew its physical location at Clinic A on the ground floor of NUH's main building. In 2019, it relocated to a new outpatient building funded by a generous donation from the Estate of Khoo Teck Puat in 2010.

In recognition of the gift supporting the advancement of paediatric education, research and patient care, the University Children's Medical Institute was renamed the Khoo Teck Puat – National University Children's Medical Institute (KTP-NUCMI).

The KTP-NUCMI outpatient facility welcomed its first outpatients in January 2019.

Our Founding Father

Our story is incomplete without acknowledging the remarkable achievements of Emeritus Professor Wong Hock Boon (1923–2008). Affectionately known as the Father of modern Paediatrics in Singapore, he was an outstanding clinician, researcher and teacher, and a passionate advocate of child health who led the Department of Paediatrics for 26 years until his retirement in 1988.

Known as a "walking encyclopaedia", E/Prof Wong was highly regarded for his unparalleled paediatric knowledge. His published works, including more than 50 volumes of Paediatric Clinical Conference Notes, are testament to his scholarship and even now serve as the go-to sources of information for countless medical students.

E/Prof Wong identified the association between hyperbilirubinaemia, kernicterus and glucose-6-phosphate dehydrogenase (G6PD) deficiency in newborns. Subsequently, he initiated G6PD deficiency screening using cord blood,

In 1962, E/Prof Wong was promoted from Senior Medical Registrar to be the Founding Professor of Paediatrics at the University of Singapore.

E/Prof Wong imparted his knowledge and experience to a whole generation of paediatricians, especially during his daily ward rounds, weekly tutorials and clinical conferences. Source: The SGH Museum.

which has since almost eliminated the incidence of death and permanent disability from severe neonatal jaundice and kernicterus in Singapore. He also discovered three previously unknown hemoglobinopathies, *Hb Singapore, Hb J Singapore and Hb J Meerut*.

As a strong advocate of breastfeeding, he once remarked, "Cow milk is meant for cows and not for human babies." In 1974, he organised the Breastfeeding Mothers' Group and established a breast milk bank in Singapore. His fervent promotion of breastfeeding even earned him the moniker "Mr Breastfeeding".

For his contributions and achievements, E/Prof Wong was accorded the highest honours, including the Most Outstanding Paediatrician in Asia (from the Association of Paediatric Societies of the South East Asian Region); Public Administration Gold Medal; Meritorious Service Medal; Guinness Award for Scientific Achievement; the inaugural National Science and Technology Award; and Emeritus Professorship from the National University of Singapore.

One of the many prestigious awards conferred on E/Prof Wong includes the Meritorious Service Medal by the then President of Singapore, Dr Benjamin Sheares, in 1975. Source: The SGH Museum.

Looking ahead

The paediatric healthcare landscape is ever-evolving. It is imperative that we continually innovate and improve upon our services and programmes to meet the growing health needs of the young.

KTP-NUCMI strives to continue the legacy of advancing child health, and eventually women and maternal wellness, through progressive clinical care, research and education.

Healthy Start to a Healthier Life

Many non-communicable diseases have their origins in early childhood, and the intrauterine and immediate postnatal periods. To enable Singaporeans to live healthier longer, the National University Centre for Women and Children (NUWoC) was instituted. NUWoC integrates the Department of Obstetrics & Gynaecology (O&G) and KTP-NUCMI as a cluster centre.

NUWoC aims to deliver the life-course continuum of care for Singapore's women and children, particularly in the western region. It focuses on the right-siting of appropriate services in the community and builds complementary services based on the National University Health System's (NUHS) strengths and centres of excellence. NUH provides tertiary and complex multidisciplinary care for women and children; Ng Teng Fong General Hospital and Alexandra Hospital provide acute, secondary and step-down care; Jurong Medical Centre provides satellite outpatient services in child development, obstetrics and gynaecology. In addition, a network of children's urgent care clinics provides acute but non-emergency paediatric care.

With the National University Polyclinics (NUP) and NUHS Regional Health System (RHS), NUWoC provides primary care, preventive screening, health promotion, disease prevention and community support for women and children. It will also include services for high-risk pregnancies, medical genetics, fetal therapy, complex neonatal care, fertility preservation, adolescent girls' health and reproductive ageing.

NUWoC's mission is to empower women, children and their families in leading healthier lives. in women and children's health so that every person can achieve their fullest human potential.

A Chance at Life

More than 10 years ago, children with leukaemia who did not respond to chemotherapy had few or no other treatment options and faced imminent death. At the turn of the century, scientists began researching alternative ways to fight cancer. Among them was Professor Dario Campana from St. Jude Children's Research Hospital in the US. He sought to harness the power of the immune system by developing chimeric antigen receptor (CAR)-T cells. Since then, CAR-T cell therapy has revolutionised immunotherapy and the treatment of B-acute lymphoblastic leukaemia (B-ALL), the most common childhood cancer worldwide.

Prof Campana first established the advanced cellular therapy programme in 2011 when he moved to Singapore to join the Department of Paediatrics at the NUS Yong Loo Lin School of Medicine. From multiple early-phase clinical trials involving natural killer cells to the more recently ALaCART and CARTALL clinical trials in 2021, the team is well-recognised as an established cellular therapy unit locally and beyond. Together with the clinical team led by Associate Professor Allen Yeoh, Head and Senior Consultant of the Division of Paediatric Haematology and Oncology, the team has gained considerable clinical experience as the first group to launch paediatric CAR-T cell therapy clinical trials in Singapore and the region.

In recognition of his work as one of the pioneers and world experts in CAR-T cell therapy, Prof Campana was awarded the prestigious Jacob and Louise Gabbay Award in Biotechnology and Medicine in 2019 and the Singapore President's Technology Award in 2020. He continues to lead the team in pushing boundaries for patients with otherwise incurable cancers.

The CAR-T team (clockwise from left): Principal research scientist, Dr Elaine Coustan-Smith, Dr Bernice Oh, Dr Esther Chan from the National University Cancer Institute and A/Prof Allen Yeoh.

Students of the inaugural class of the GDCAH bonding through an activity.

Upskilling for the Future

To meet the changing needs, expectations and demands of child and youth healthcare, the Department of Paediatrics has developed Continuing Education and Training (CET) programmes to support the lifelong learning of practitioners who are keen to reskill and upskill.

Graduate Diploma in Child and Adolescent Health (GDCAH)

With primary care delivery evolving to emphasise family-focused and community-based practices, there is a need to support the CET of physicians practising in primary healthcare who are keen to upskill in the management of child and youth health.

Offered as part of the NUS School of Continuing and Lifelong Education (NUS-SCALE) and supported by Singapore SkillsFuture, the inaugural GDCAH was launched on 6 August 2022. The programme incorporates the three core elements of primary care—comprehensive care, continuity of care and coordination of care.

Early Childhood Development: The Touchpoints Approach

Also offered as part of NUS-SCALE and supported by Singapore SkillsFuture, the Brazelton Touchpoints Individual Level Training course was launched in October 2020 to support the CET of early childhood educators. Taught by an interprofessional team comprising developmental paediatricians, specialist nurses and social workers, this course highlights the key role of inter-professional education and collaboration in supporting early childhood development.

Brazelton Touchpoints is an established evidence-based programme in the US that focuses on building strong family-child relationships before birth through the earliest years, which are vital for children's early learning and healthy development.

Intensive Paediatric Revision Course for Master of Medicine (MMed) in Family Medicine

As a part of the department's efforts to support family practice specialists' professional development, the department has offered an intensive revision course for physicians preparing for MMed (Family Medicine) since 2004. Held over four Saturday afternoons, it prepares physicians for the paediatric component of the clinical examinations. In 2020, the course moved online due to COVID-19, serving the largest cohort of 84 learners since its inception.

KTP-NUCMI is committed to journeying with patients and their families, providing quality, holistic care while pushing the boundaries of medicine for the advancement of child health.

The African proverb, 'It takes a village to raise a child', resonates with us, bringing us together as a community to serve with purpose every day for the past 60 years and hopefully many more.

Scan to access the full 60 Years of Child Health Commemorative book here:

The Art and Science of Medical Sleuthing Goes Digital

Since its inception in 2017, Pathweb, the online pathology teaching resource, has been a go-to for students at NUS Yong Loo Lin School of Medicine (NUS Medicine), and more recently, the international medical community. What began as a labour of love for Associate Professor Nga Min En from the Department of Pathology when she built the resource has become a long-term project. It is one that has also found fans with colleagues and students, and is also shaping the way Pathology is taught and learnt over the years.

From 130 registered users in December 2018 to over 3,000 in December 2022, Pathweb has attracted users from more than 120 countries.

But Pathweb's story harks back to 2013, when a research assistant from the Department of Radiology approached Assoc Prof Nga with an idea to photograph pathology specimens from multiple angles, to create magnifiable, rotatable virtual specimens.

Armed with a full clinical caseload but lacking experience in online content creation, Assoc Prof Nga nevertheless saw value in the proposal. She obtained a grant from NUS Medicine, and in 2014, created the first batch of virtual specimens.

Many hands make light work—the tireless team behind Pathweb

After successive rounds of grants and prototypes with resoundingly positive student

feedback, Assoc Prof Nga and her colleagues decided it was time to scale up the project.

With the technical expertise of Mr Muhammed Aidil, a former staff member in Pathology, and as per his suggestion, the name and its digital avenue, Pathweb, was born in August 2017. Much of the initial website content uploads were managed by Ms Norliana Binti Abdul Aziz, the admin stalwart and the glue that holds Pathweb together.

From a virtual pathology museum housing the fully-annotated virtual pathology pots to a plethora of educational content—mind maps, interactive quizzes and cases, a normal histology atlas and real-life cases, the immense efforts of Assoc Prof Nga and her team have turned Pathweb into an online study tool that has accumulated a large user base across the medical community, both in and out of Singapore today. But that's not all—the team continues to work tirelessly to fine-tune and expand the content to tailor it to students' needs.

For instance, to increase their exposure to different forms of pathology in a single disease, Assoc Prof Nga and her team photographed and digitalised more virtual specimens, from 260 to over 700 today, for students to appreciate a broader range of examples. This also comes with reconditioning degraded physical specimens, a tedious but necessary task, which requires dedicated staff who are able to perform the physically demanding tasks of reconditioning these precious specimens.

To the team's immense delight, students enjoyed the interactive learning that Pathweb offered. "Compared to a single flat image, a 3D impression of the pots is a fantastic reproduction of what you see in person. Being better able to see the angles, textures and depths of the specimen makes the study of pathology more tangible and vivid, helping us appreciate the effects of the conditions in a way we could never do previously," commented Tang Zhichen, a Phase II medical student.

There is no doubt that since Pathweb's inception, benefits to the learning of pathology have been bountiful. But one student took on the challenging task of improving it, conceptualising new features that would benefit the subsequent batches of students.

Dr Darren Chua, now a first year Pathology resident, started working on Pathweb when he was in his second year of medical studies. Reflecting on his learning, he worked on ideas that he believed could value-add to his fellow students.

Veering away from pure rote learning and memorisation, he introduced the idea of Interactive Cases. With real-time self-tests with immediate feedback placed at certain points in an unravelling diagnostic scenario, students simulate the clinical work of a practicing doctor, understanding the relevance of pathology to real patients.

Another feature that Dr Chua helped to start was the Normal Histology section of the website.

"Many students find learning normal histology difficult—it often looks like abstract art to the untrained eye. Pathology, however, deals with abnormal histology, and for students who are less familiar with normal histology in the first place, recognising the abnormalities is very challenging. Hence, with this, students can have a readily accessible reference when looking at abnormal histology in various pathological conditions," said Dr Darren Chua, first year Pathology resident who started working on Pathweb when he was in his second year of medical studies.

Aorta (Low power):
The aorta is the largest artery of the circulatory system. Being an elastic artery, it has a prominent tunica media layer rich in elastic fibres and smooth muscle cells surrounding a large lumen. These features allow the aorta to expand and recoil readily in systole and diastole respectively, maintaining blood pressure and enabling pulsatile blood flow.

Heart

Atrioventricular valve

Blood vessels

In Laptop:
The normal histology of the aorta with full annotations.

On the right:
Normal histology of the Cardiovascular system on Pathweb.

Over
3,000
registered users in December 2022

Pathweb has been accessed by users from over
120
countries

700
virtual specimens have been photographed and digitalised

The pathologist as medical detective

As doctors, pathologists are involved in the care of patients. However, this may not be immediately apparent to undergraduate students.

Through the Pathology in Action section on Pathweb, Assoc Prof Nga shares more about the daily diagnostic work of pathologists, how they handle specimens and work through cases. One might say it is clinical sleuthing. The Interactive Cases also bring out this aspect of working through real life cases and clinching the diagnosis.

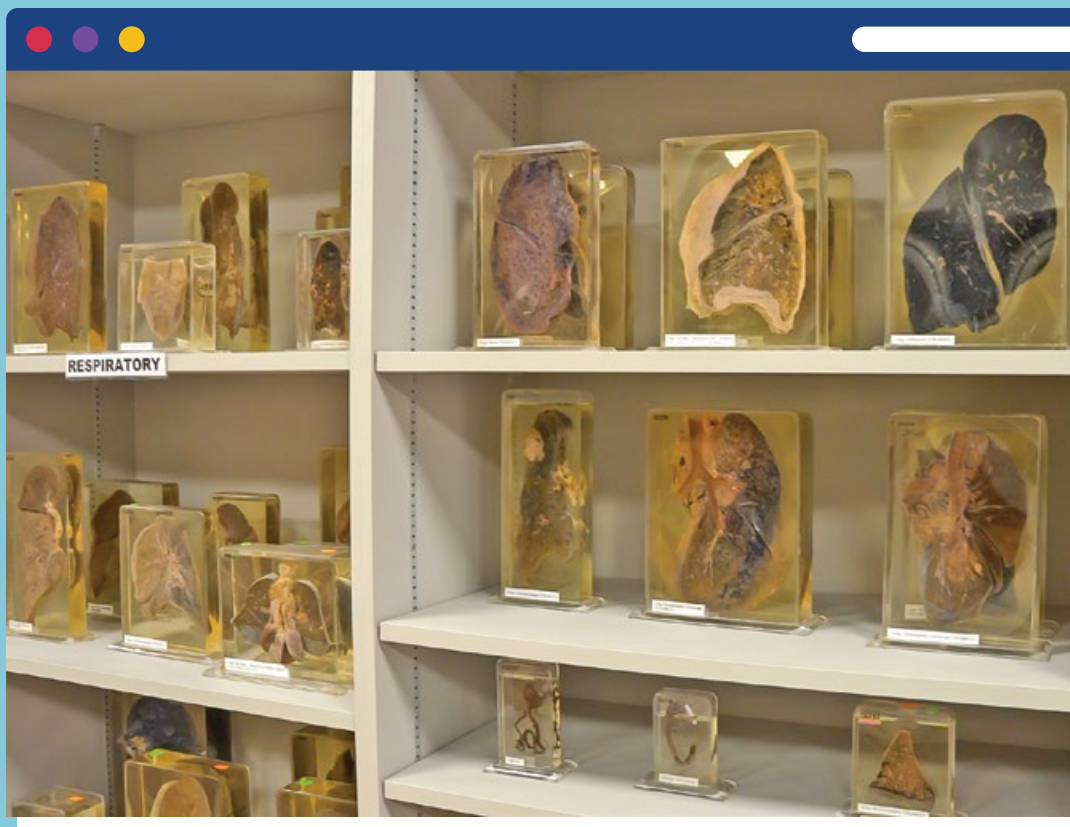
"I enjoy exploring the Interactive Cases on Pathweb a lot. I recall this case about a patient presenting with a neck lump, and the interactive case guided us through taking a thorough history, making possible diagnoses, using pathological investigations and the clinical picture to come up with differentials," said Yau Chun En, a Phase II NUS Medicine student.

"That really helped to bring pathology to life, because I could see how microscopic histological features can mean different prognoses and treatment options for the patients," he added.

"The eye can't see what the mind doesn't know"

Pathweb's popularity is explained by users' appreciation of the online learning tool. Students enjoy the comprehensive and organised content, which is structured to accommodate different learning paces.

"I'm not that much of a fan of didactic teaching, nor do I retain much information taught in such a setting. As I explore Pathweb, I get to pause, take stock of my learning, and continue building on my existing knowledge," said Chun En.



The study of Pathology requires high levels of attention to detail, as pathologists observe minute cells and tissues. This makes it potentially trying for students who have trouble consolidating information on the disease entity in the first place.

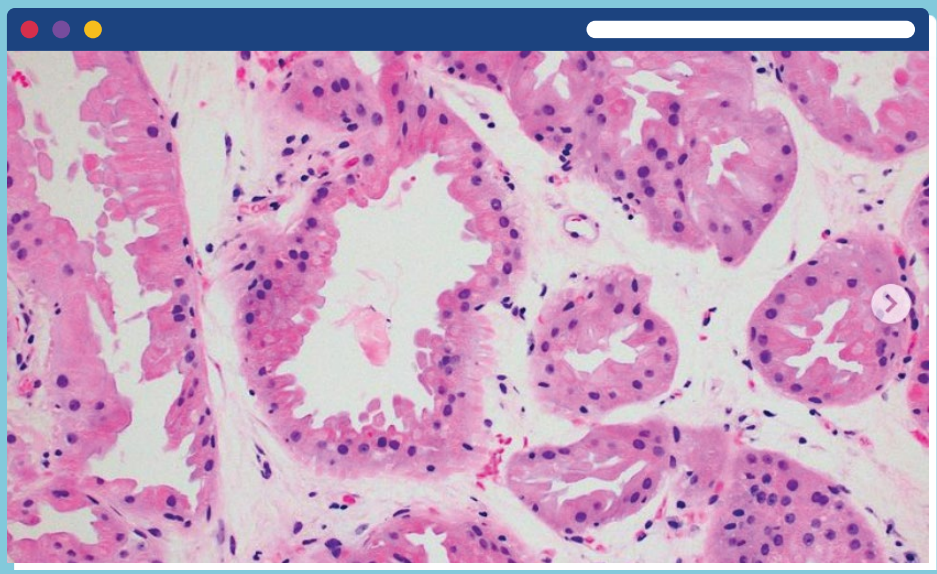
For Chua Yang Jie and Wong Ting Hong, both Phase II students, the annotated specimens highlight and sensitise them to details that may be easily overlooked.

"One of our favourites on the website are the Talking Pots (concise videos on the salient features of pathology specimens preserved in containers of formaldehyde). 'The eye cannot see what the mind doesn't know', so it's very helpful to have a guided voiceover from Assoc Prof Nga as we examine the pot. It has made us much more sensitive to the subtle details which hint at the underlying disease."

While the resources on Pathweb indeed complements in-person lessons, Assoc Prof Nga is careful that it does not become a crutch for students during lessons.

"Students do refer to the pathology virtual specimens in tutorials while I'm going through the specimens. But I don't encourage it, I believe in the fun and mystery of figuring things out from basic principles they have learnt, so I actually instruct students to close Pathweb during my tutorials!" explained Assoc Prof Nga.

Specimens which are digitised and uploaded onto Pathweb.



Microscopic images uploaded onto Pathweb.

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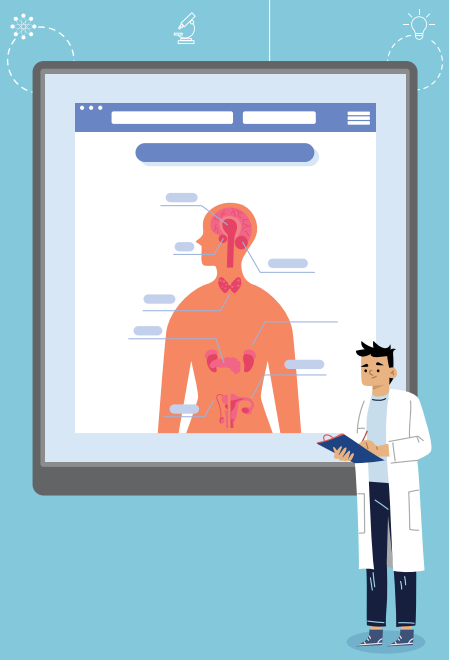
Chua Yang Jie and Wong Ting Hong, Phase II medical students



An international resource, now also on social media

As a free, accessible, and comprehensive learning resource, Pathweb has attracted users from more than 120 countries.

Overseas faculty have shared that Pathweb has been a valuable resource to help them demonstrate real examples of disease to students, especially since not all medical schools have ready access to actual pathology specimens or physical pathology museums.

One overseas faculty that uses Pathweb is Associate Professor Than Than Hwte from the Faculty of Medicine, Universiti Kuala Lumpur, Royal College of Medicine, Perak.

"A huge thank you to the Pathweb team at NUS Medicine Department of Pathology, for allowing my Year 1 and 2 MBBS students and I to use Pathweb as a free resource for learning. It has really helped as a teaching aid, with clear and understandable case-based studies in Pathology," said Assoc Prof Hwte.

"Creating and maintaining specimens can be quite costly, and specimens may not be accessible to every medical school. I'm glad that faculty members and students could access them for their teaching and learning," said Assoc Prof Hwte.

Besides the web portal, Pathweb has its own Instagram, YouTube, and Telegram channels, targeting both undergraduate and postgraduate learners in their pathology training.

Work to improve content is continuous. Tapping into Instagram, Prof Nga invited Dr Wu Bingcheng, Consultant at the Department of Pathology, National University Hospital, to populate the channel, which has over 3,000 followers today.

He employs the use of Instagram stories to post quizzes, teasing out the gaps in knowledge and difficulties that students face in real time. He also answers students' queries on the platform, complementing their self-directed learning.

As an anatomical pathologist, he shares microscopic pictures of real-life cases from his clinical work through posts that are filled with clinical explanations.

Specialising in the head and neck region of pathology, Dr Wu explained the importance of exposing students to real life cases, since a single disease can take many forms in different organs and systems.

"The head and neck regions are anatomically critical as they contain vital structures. Within them lie several organ systems, including the upper digestive and respiratory systems, thus pathology in this area can cause significant repercussions. This explains why knowledge in and across various systems and organs in Pathology is imperative."

Ting Hong agrees. "The exposure it has provided beyond the standard curriculum has helped me develop a sharper eye, and made me think more about pathology than I otherwise would have."

↑ Students in Assoc Prof Hwte's class using Pathweb in their pathology classes.

"Creating and maintaining specimens can be quite costly, and specimens may not be accessible to every medical school. I'm glad that faculty members and students could access them for their teaching and learning."

Assoc Prof Than Than Hwte, Universiti Kuala Lumpur, Royal College of Medicine

Scan to find out more about Pathweb here:

Scan to watch the introductory video on Pathweb here:

Improving CAR-T Cell Therapy for Solid Tumours through Inhibition of Conventional Signalling Pathway

In the context of Chimeric Antigen Receptor-expressing T (CAR-T) cell therapy for cancer, researchers found that the FYN protein, rather than the lymphocyte-specific protein tyrosine kinase (LCK), allows more efficient tumour cell killing through T-cell activation.

CAR-T cell therapy involves re-engineering specific immune cells called T cells to target cancer. The treatment involves the production of CAR-T cells from the patient's own cells, where they are then manipulated to express the CAR gene, grown to very high numbers and then re-infused into the patient. CAR-T cell therapy has not been very effective in treating solid tumours, and is often very costly.

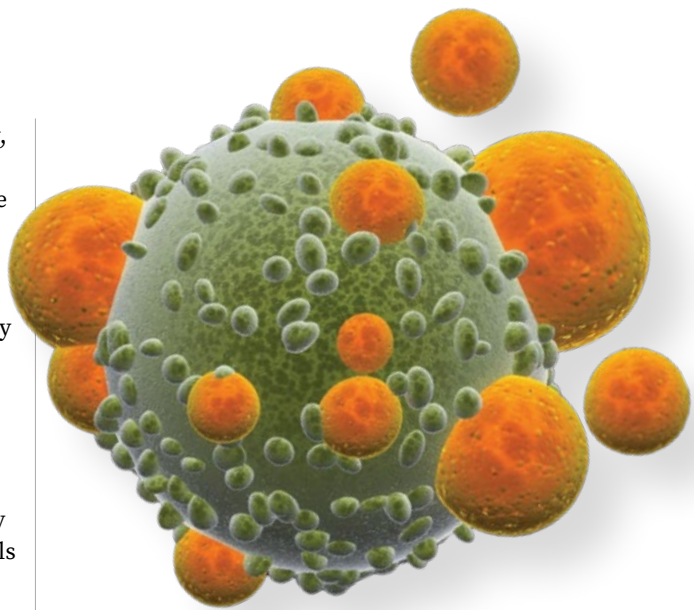
Tackling both issues of efficacy and cost of CAR-T cell therapy, Professor Nicholas Gascoigne, Principal Investigator from the Immunology Translational Research Programme and Professor at the Department of Microbiology and Immunology at the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine), with Dr Ling Wu and team, discovered that in CAR-T cells with CD28, the LCK is dispensable in cell signalling—the process where the cell switches on or off certain cell processes and functions, vital in activating the cell to kill tumour cells. When the LCK is disrupted, another protein, FYN, takes over cell signalling instead.

In the cell signalling pathway, the FYN protein is one of the later switches. However, since the LCK protein is the more dominant switch in T-cell activation, in normal CAR-T cells, LCK signalling is usually the main pathway activated. FYN signalling will take over when LCK signalling is disrupted.

In their study using laboratory tumour models, the CAR-T cells with disrupted LCK showed increased anti-tumour efficacy, as the CAR-T cells were able to persist longer in the body and continue killing tumour cells.

These modified CAR-T cells prevent cells transplanted from the donor from attacking the patient's own cells, allowing for "off-the-shelf" CAR-T cell therapy. This will significantly reduce production costs for CAR-T cells and can make CAR-T cells therapy much more available and accessible to patients.

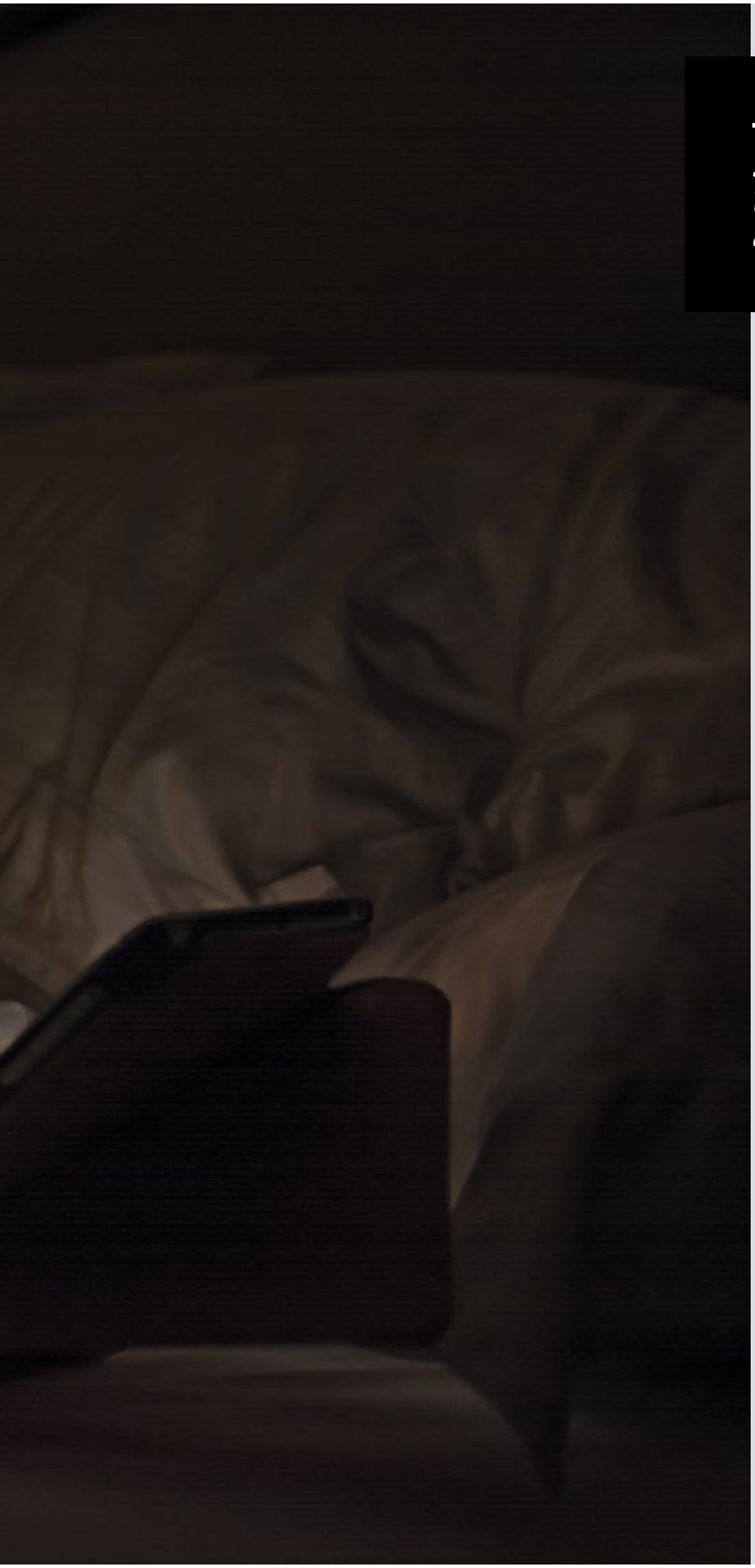
Prof Nicholas Gascoigne said, "The CAR-T field has advanced drastically over the past thirty years and presents an exciting promise of hope in cancer treatment. With this discovery, CD28 CAR-T therapy may now be used to target solid tumours such as breast and ovarian cancers, as well as reduce the cost of CAR-T therapy. This would greatly improve its accessibility to all patients."



↑ In the CAR-T cell, the FYN protein, rather than the lymphocyte-specific protein tyrosine kinase (LCK), is more effective in tumour killing.

Scan to read more about the journal article here:

Infants Exposed to Excessive Screen Time Show Differences in Brain Function Beyond Eight Years of Age



Screen time in infancy is associated with brain waves that suggest brain immaturity and poor self-regulation.

More children are now exposed to mobile digital devices at a young age as an avenue for entertainment and distraction. A longitudinal cohort study in Singapore has confirmed that excessive screen time during infancy is linked to detrimental outcomes in cognitive functions, which continue to be apparent after eight years of age.

The research team looked at data from 506 children who were enrolled in the Growing Up in Singapore towards Healthy Outcomes (GUSTO) cohort study since birth. When the children were 12 months of age, parents were asked to report the average amount of screen time consumed on weekdays and weekends each week. Children were then classified into four groups based on screen time per day—less than one hour, one to two hours, two to four hours and more than four hours. At 18 months of age, brain activity was also collected using electroencephalography (EEG), a highly sensitive tool used to track changes in brain activity over time. Besides undergoing EEG, each child participated in various cognitive ability tests that measured his or her attention span and executive functioning (sometimes referred to as self-regulation skills) at the age of nine years.

The team first examined the association between screen time and EEG brain activity. The EEG readings revealed that infants who were exposed to longer screen time had greater "low-frequency" waves, a state that correlated with lack of cognitive alertness. To find out whether screen time was associated with any adverse findings related to brain function, the research team analysed all the data across three points for the same children—at 12 months, 18 months and nine years. As screen time increased, greater altered brain activity and more executive function deficits were measured. Children with executive function deficits often have difficulty controlling impulses or emotions, sustaining attention, following through multi-step instructions, and persisting in a hard task.

Professor Chong Yap Seng, Dean of Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine) and Chief Clinical Officer, SICS, added, "These findings from the GUSTO study should not be taken lightly because they have an impact on the potential development of future generations and human capital. With these results, we are one step closer towards better understanding how environmental influences can affect the health and development of children. This would allow us to make more informed decisions in improving the health and potential of every Singaporean by giving every child the best start in life."

The brain of a child grows rapidly from the time of birth until early childhood. However, the part of the brain that controls executive functioning, or the prefrontal cortex, has a more protracted development. Executive functions include the ability to sustain attention, process information and regulate emotional states, all of which are essential for learning and school performance. The advantage of this slower growth in the prefrontal cortex is that the imbuing and shaping of executive function skills can happen across the school years until higher education. However, this same area of the brain responsible for executive functioning skills is also highly vulnerable to environmental influences over an extended period of time.

This study points to excessive screen time as one of the environmental influences that may interfere with executive

↑ Lead author, Dr Evelyn Law from NUS Medicine (4th from left), A*STAR's Singapore Institute for Clinical Sciences (SICS)'s Translational Neuroscience Programme, with members of the research team.

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Prof Chong Yap Seng, Dean of NUS Medicine and Chief Clinical Officer, SICS

function development. Prior research suggests that infants have trouble processing information on a two-dimensional screen. When watching a screen, the infant is bombarded with a stream of fast-paced movements, ongoing blinking lights and scene changes, which require ample cognitive resources to make sense of and process. The brain becomes "overwhelmed" and is unable to leave adequate resources for itself to mature in cognitive skills such as executive functions.

Lead author, Dr Evelyn Law from NUS Medicine and SICS's Translational Neuroscience Programme, said, "The study provides compelling evidence to existing studies that our children's screen time needs to be closely monitored, particularly during early brain development." Dr Law is also a Consultant in the Division of Development and Behavioural Paediatrics at the Khoo Teck Puat – National University Children's Medical Institute, National University Hospital.

Researchers are also concerned that families which allow very young children to have hours of screen time often face additional challenges. These include stressors such as food or housing insecurity, and parental mood problems. More work needs to be done to understand reasons behind excessive screen time in young children. Further efforts are necessary to distinguish the direct association of infant screen use versus family factors that predispose early screen use on executive function impairments.

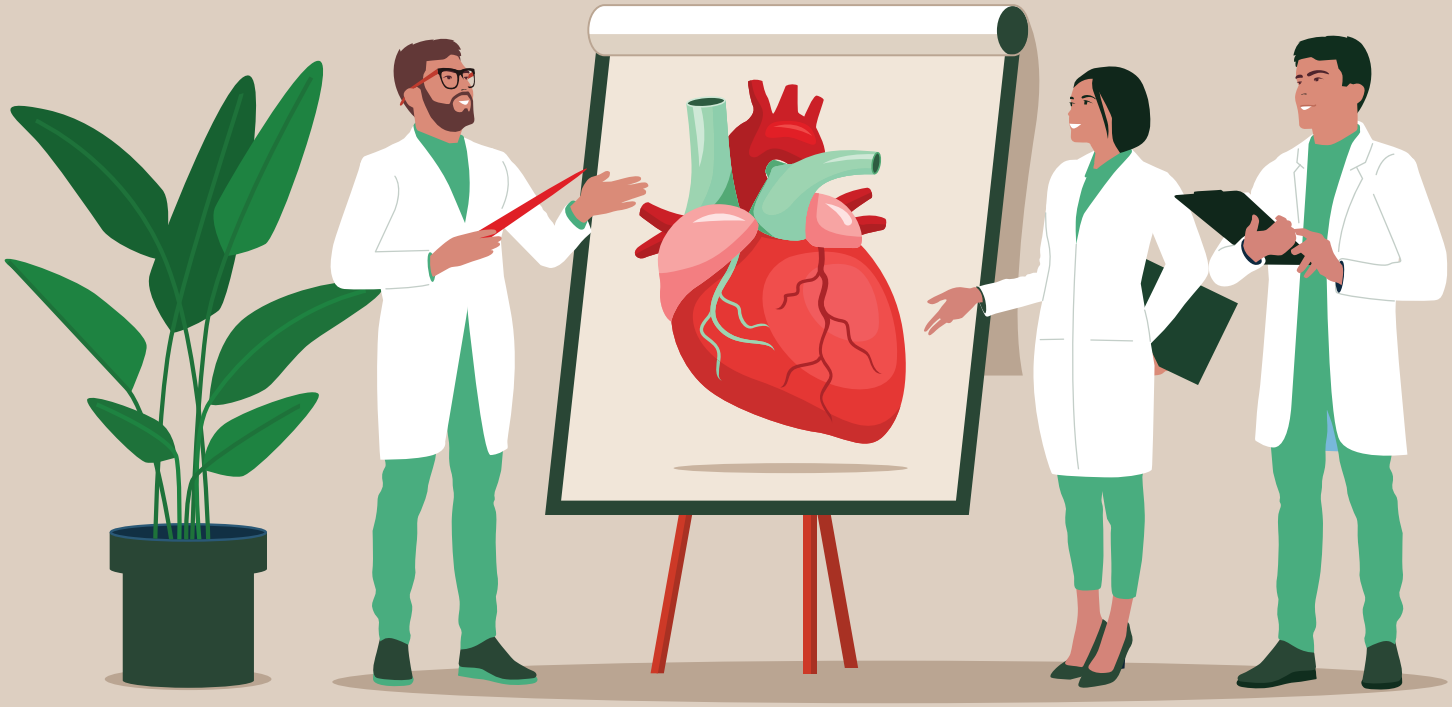
Professor Michael Meaney, Programme Director of the Translational Neuroscience Programme at SICS said, "In a country like Singapore, where parents work long hours and kids are exposed to frequent screen viewing, it's important to study and understand the impact of screen time on children's developing brains."

Dr Evelyn Law with her two daughters.

Scan to read about Dr Law's personal experience on screen time management with her two daughters in a recent Straits Times article:

Scan to read the full paper here:

The study was a collaborative effort comprising researchers from the NUS Medicine, SICS, National Institute of Education, KK Women's and Children's Hospital, McGill University and Harvard Medical School. It was published in JAMA Pediatrics on 31 January 2023.



Mitral Valve Surgery – A Better Way

BY PROFESSOR THEO KOFIDIS, HEAD OF DEPARTMENT OF CARDIAC, THORACIC AND VASCULAR SURGERY, NATIONAL UNIVERSITY HEART CENTRE, SINGAPORE & PROFESSOR, DEPARTMENT OF SURGERY, NUS YONG LOO LIN SCHOOL OF MEDICINE

*The way we perform heart valve surgery (repairs in specific) has been largely defined by Professor Alain Carpentier in 1983 in his seminal paper, "**The French Correction**". He essentially laid down the principles of Mitral Valve Surgery, which surgeons everywhere have followed religiously for 40 years. Small variations were added by other eminent surgeons over the decades, all of which fell within the same framework.*

The Singapore Correction

It occurred to me though, after 27 years in the business, that these techniques, albeit validated, are very inconsistent, not intuitive, allow for too much guesswork, and are also associated with marked surgical outcome variability. The techniques also involve individual neocords, and create

too much tension on the leaflets. They also do not take care of adjacent pathologies, such as clefts, commissural prolapses, annular dilations, etc. These result in variable outcomes, even in the simplest scenarios. It also means that young surgeons cannot reproduce the results, and tend to sacrifice and replace the heart valve.

This prompted me to develop 12 new procedures, which totally depart from the existing principles. The 12 new procedures (which I named The Singapore Correction) help make mitral valve surgery intuitive, simple and standardised, eliminating variability, and render it very easy to repair the valve and produce solid results every time. Also, my techniques use less foreign material for the patient, and are performed faster, while the heart is arrested. They involve, mostly, only one single running stitch.

I have implemented them in about 10 patients thus far, with consistently excellent results. I also recorded videos of these procedures, which the editors of the major Cardiothoracic Surgery journal found very interesting. I have issued professional drawings with the help of a US-based medical artist, and compiled them in two back-to-back papers, Part I and Part II*. We are basically redefining mitral valve repair, hence the title: "Mitral Valve Repair 2.0". The papers were accepted and published in "fast track mode" in the European Journal of Cardio-Thoracic Surgery.

Since there is no way you can patent surgical techniques, the only way for us to take the credit for our intellectual property was to publish extensively and secure the copyright. I have (post publication) presented them at the International Heart Valve Congress in Edinburgh. The responses have been resounding. I was then invited to present them at the turf of one of the world's pioneers, Professor Ottavio Alfieri (who along with Carpentier designed most of the techniques we are using today), at the San Raffaelle Hospital, in Milan, Italy, in February this year. The revered man stood up, shook my hand and congratulated me. I, then, shared with the audience about the work of our department at the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine), and the National University Health System Group.

Hence, many of my techniques are now not only conceptualised, but also verified. Validation occurs when other surgeons have tried them and adopt them, or after follow ups. That's the natural next step. In late February, one of Europe's top surgeons, Professor Francesco Maisano, became the first to implement one of my techniques, 10,000km away in Italy. The patient walked out with an excellent valve repair. No proctorship was necessary, as the techniques that I introduced are very standardised and reproducible.

It is my sincere hope that these 12 procedures will bring value to thousands of surgeons and touch many patients' lives around the world.

From left: Prof Theo Kofidis presenting the 12 surgical techniques to renowned cardiac surgeons, Prof Ottavio Alfieri and Prof Francesco Maisano.

Prof Theo Kofidis performing heart valve repair at the Monzino Heart Institute in Milan, Italy.

"It is my sincere hope that these 12 procedures will bring value to thousands of surgeons and touch many patients' lives around the world."

**Scan to read more about the mitral valve surgery update here:*

Part I

Part II

Who Should We Hold Responsible When AI Goes Wrong?

BY ANANTHARAMAN MURALIDHARAN, RESEARCH FELLOW AT CENTRE FOR BIOMEDICAL ETHICS, NUS YONG LOO LIN SCHOOL OF MEDICINE

Singapore plans to be a global leader in Artificial Intelligence (AI) by 2030[1]. This involves, on the one hand, widespread deployment of AI in a variety of settings, and on the other, widespread trust in these AI solutions. Who do you think should be responsible when AI or algorithms malfunction: The programmer, manufacturer, or user?

Clearly that trust needs to be well-placed, but what does it mean for trust to be well-placed? Certainly, one part of this is these AIs getting things right reliably often. But that alone is not enough.

Consider a mechanic who you want to fix your car. No matter how often he properly fixes cars, if he refuses to take responsibility when he makes a mistake, you wouldn't trust him to fix your car. This is because the ability and willingness to take responsibility is a key component of being trustworthy.

Yet this creates a conundrum: After all, AIs—at least of the kind we're likely to see over the next seven years—are merely highly sophisticated programmes. They can no more take responsibility for mistakes than your computer, or your calculator can.

AI and cognitive technologies

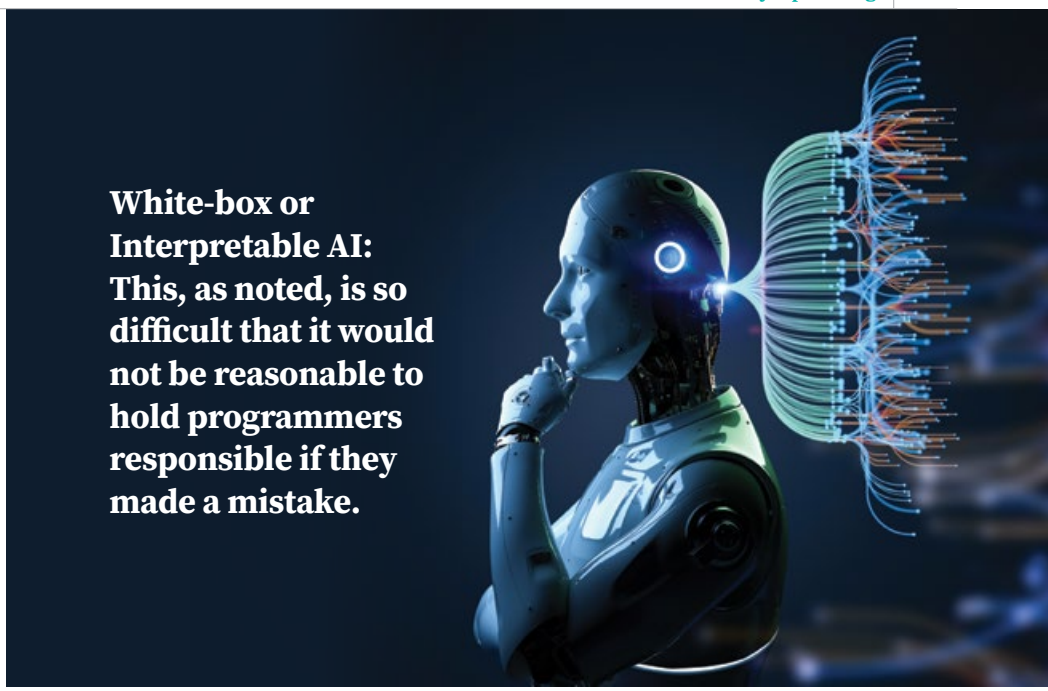
Let us try to look closer at how we interact with calculators and computers, and other technologies that automate some of our thinking. We use computers for a variety of reasons ranging from gaming and connecting with other persons over the Internet to word processing, presentations and performing calculations.

When we use computers in these instances, does that count as trusting computers? Suppose that it does, why do we trust computers in these instances? After all, computers do crash with some regularity.

Plausibly, in most cases except when requiring it to perform calculations, we trust computers because we can immediately verify that the computer is doing what it's supposed to. When we move our mouse, the cursor moves accordingly. When we press a key, the corresponding letter or number appears on our screen. When we click the corresponding button, our player character in the computer game moves accordingly. If it was not working properly, the screen would freeze or something else unexpected would happen immediately.

Even though many complicated operations are happening in the background, we can instantly verify whether the computer is working or not.

What about calculation cases? Consider cases where you use your calculator, or the calculator function on your phone or even the various functions in a spreadsheet. Why do we accept the answer in these cases?



White-box or Interpretable AI: This, as noted, is so difficult that it would not be reasonable to hold programmers responsible if they made a mistake.

One plausible reason why we trust calculators and computers on this score is that we trust the manufacturers and programmers.

Performing various mathematical operations strikes us as obviously being the kind of thing that can be done by a machine that knows only how to blindly manipulate symbols according to an algorithm. It does not require human judgment or knowledge of what those symbols mean.

By contrast, many of the tasks that we want AIs to perform do require judgment. To take just one example, treatment recommendations and medical diagnoses have an element of judgment whereby people bring together information from a variety of sources and put them together in complex ways.

It is no simple matter to explicitly spell out all the factors that could possibly apply in making a given diagnosis. This is likely to be true of many decisions in the areas like freight planning, municipal services, education, and border security. This complexity means that there is very little that manufacturers and programmers can meaningfully do to prevent a given malfunction.

White box, black box or grey box

To illustrate, consider one kind of AI model: white-box or interpretable AI. These types of AIs can be thought of as highly complicated computer programmes. For such an algorithm to get things right, the programmers must anticipate every eventuality and know how to specify which considerations are relevant and to what extent they are so in each situation. This, as noted, is so difficult that it would not be reasonable to hold programmers responsible if they made a mistake.

Consider, instead, black-box AI models: These models involve algorithms that are too complex to understand even for the programmer. This is because the programmer does not explicitly programme the algorithm.

Instead, the algorithm is trained on a large set of cases. The AI, over a large number of cases, is told what the right outputs are for a given set of inputs. The AI comes up with its own decision rule to match inputs to outputs. The hope, with these black-box models, is that it captures the subtleties of our decision making when we exercise judgment. The downside is that we do not know how the AI comes to a decision. Moreover, given how AIs are trained, they inherit all the biases that we have. For instance, consider ChatGPT by OpenAI. Despite the best efforts of programmers, the AI can still generate racist content[2].

There are other models called explainable or grey-box AI that attempt to achieve the best of both worlds. They start with a black-box model as a base and then use another AI to explain the decision of the first AI. With this, we might be able to know why a particular decision was made. However, we would still not be able to predict in advance how the AI will decide. Just because a black-box AI gives weight to certain considerations in one case, it doesn't mean that the AI will give weight to those considerations in a similar case. And since the base AI is still a black-box model we would not be able to know how to train the AI so that it does not malfunction.

User responsibility

All this suggests that manufacturers and programmers cannot be held responsible for AI malfunction (except, perhaps in cases of egregious negligence). However, if not them, then who? One remaining plausible option is the users themselves. In some ways, this makes intuitive sense. After all, without AI, it is these would-be users of AI who ought to take responsibility for their decisions. Technology cannot be a way for people to evade their responsibilities. This, however, has implications for what kinds of AI we deploy and how we deploy them.

After all, without AI, it is these would-be users of AI who ought to take responsibility for their decisions. Technology cannot be a way for people to evade their responsibilities. This, however, has implications for what kinds of AI we deploy and how we deploy them.

First, humans must be kept in-the-loop. Humans must be the final decision-maker in these scenarios. The outputs of AI can never be decisions as such, only recommendations. It would not make sense to hold users responsible for AI malfunction if they could not stop the AI from acting on its wrong decision. Thus, for instance, fully self-driving cars may have to be taken off the table. After all, to be ethically acceptable, drivers must be able to intervene anytime; they should be paying attention to the road. Yet, if they are already paying attention to the road, they might as well be driving the car themselves.

Second, not only should humans be kept in-the-loop, AIs would be useless if people had no way of deciding whether to follow the AI's recommendations. Moreover, being kept in-the-loop would be pointless if people simply rubberstamped the AI's decision. This means that black-box models are also out of the question.

The right kind of AI

Our trust in AI is a matter of trusting the user. AIs after all, do not understand reasons and cannot be said to properly respond to them. Importantly, AIs cannot take responsibility for mistakes.

AIs, to be trustworthy, must be the kind that can aid human users in making sound decisions. As Singapore moves forward in embracing AI, it is important that we do so in a way that is informed by the right understanding of what makes people and technology trustworthy.

This commentary first appeared in CNA on 31 January 2023.

[1] https://www.smartnation.gov.sg/files/publications/national-ai-strategy-summary.pdf.
[2] https://www.thedailybeast.com/openais-impressive-chatgpt-chatbot-is-not-immune-to-racism.

The Petrov Dilemma: Moral Responsibility in the Age of ChatGPT

BY JULIAN SAVULESCU, CHEN SU LAN CENTENNIAL PROFESSOR OF MEDICAL ETHICS, DIRECTOR OF THE CENTRE FOR BIOMEDICAL ETHICS, NUS YONG LOO LIN SCHOOL OF MEDICINE

The way a Soviet officer dealt with potential nuclear armageddon holds an important lesson in how we deal with the myriad challenges thrown up by ChatGPT and others of its kind.

In 1983, Stanislav Petrov "saved the world".

At the height of the Cold War, Lieutenant-Colonel Petrov was the duty officer at a Russian nuclear missile facility when the early warning system flashed red with a heart-stopping alert: The US had launched a missile strike and five Minuteman missiles were streaking towards the Soviet Union.

According to protocol, Lt-Col Petrov should have reported the imminent strike. If he had, Soviet nuclear doctrine called for full nuclear retaliation. But after a nerve-wracking five minutes, he disobeyed orders.

He had his reasons. There was no corroborating evidence from ground-based radar and the missile defence system was new. The number of American missiles was also, to him, suspiciously low for an all-out US first strike.

If he had acted on the information given by the machine, the result would have been catastrophic—an estimated combined death toll of nearly 290 million in the US and Soviet Union and millions more worldwide—from starvation and other spillover effects of nuclear war.

In this instance, faulty new satellite technology set off a false alarm. As a human decision-maker, Lt-Col Petrov's appreciation of the gravity of nuclear war influenced—and enhanced—his judgment. It overrode standing orders and the threat of execution for treason for disobeying them.

In contrast to nuclear missile early-warning systems, ChatGPT does not come laden with doomsday possibilities. At a basic level, it is a piece of machine intelligence that gathers information from billions of human conversations and produces text in response to prompts.

And yet in its own way ChatGPT's abilities and how we deal with it are also potentially world changing, even if not on the scale of nuclear armageddon. The Petrov dilemma is pertinent too as we confront new challenges posed by artificial intelligence (AI).

Consider the world before the arrival of the Internet, smartphones and social media. It was a very different one with none of the benefits and ills that successive waves of technological breakthroughs and innovations have brought to billions of people around the world.

Technology has made possible swift access to information, public health, banking and other services. The flip side is we are struggling with its dark side: fake news, deep fakes, online scams and revenge pornography.

Another iPhone moment

And now we have ChatGPT, the arrival of which has been described as another iPhone moment. As analyst Rowan Curran describes it, the launch of Apple's iPhone in 2007 and the App Store a year later ushered in a period of historic technological change by putting an entire computing experience in our pockets. The ease of use also opened up to everyone vast new opportunities in education, work and play.

ChatGPT appears to put us on the cusp of yet another game-changing moment in our relationship with machines. Our increasing reliance on them has saved lives: averted air disasters, enhanced medical diagnosis and, in time to come, perhaps reduce car accidents.

But like Lt-Col Petrov, we still need to interrogate what the machines tell us. There is still a place for human decision-making when it comes to moral choices in a world of machines.

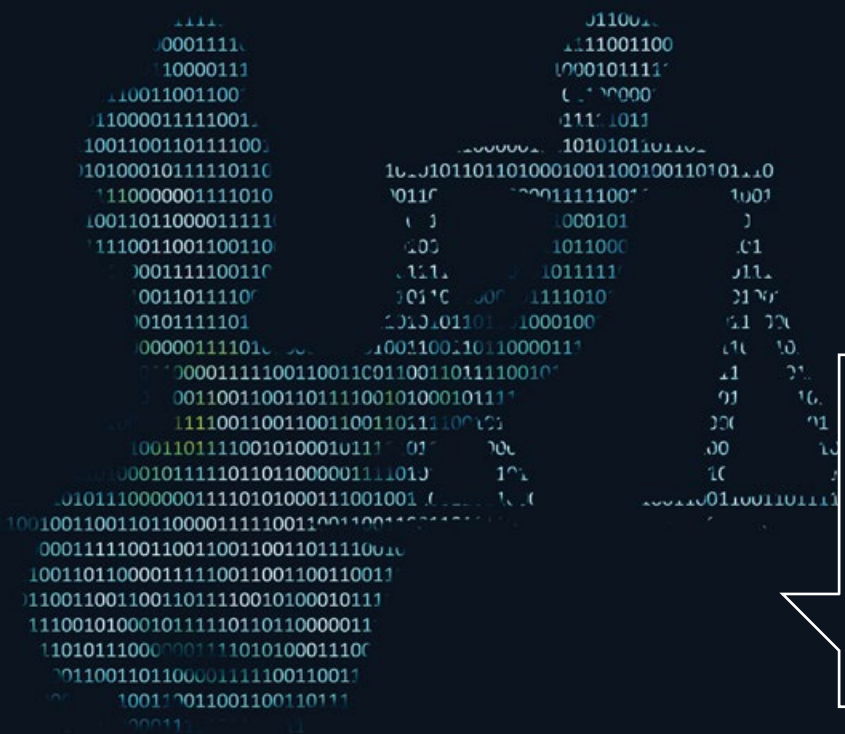
How should we deal with AI?

ChatGPT is posing challenges for educators as well as lawyers and artists on issues from plagiarism to ownership rights. These are important matters and need to be addressed. But in a way they are secondary problems. At the heart of these problems is one about ethics and responsibility—how can ChatGPT and other new technologies be used to enhance society, rather than to endanger or undermine it?

One approach is to view challenges through a set of three guiding principles on technological interaction: Think First, Take Responsibility, Act Ethically.

1. Think first

Lt-Col Petrov did not just accept information he was presented with from an expert system. He actively interrogated it. He asked whether it was consistent with other beliefs he held. When presented with empirical claims about the world by machines, we should ask: are they true? Are they consistent with other beliefs? How confident am I that they are true? Should I gather more information?



ChatGPT is posing challenges for educators as well as lawyers and artists on issues from plagiarism to ownership rights.

In life, trust is necessary as it is not possible to test every claim presented to us. Yet whom and what to trust has become more difficult with the proliferation of dodgy information, a problem that is likely to worsen with ChatGPT and its like.

To counter this, we need to do more to teach the basics of critical thinking to children, equipping them with the skills to question the basis of assertions and think logically and rationally.

Sometimes we are not presented with claims about the way the world is but normative claims: claims about how it should be. That is, claims about ethics, about right and wrong, good and bad.

Our humanity resides in significant part in our capacity to make these ethical decisions. We should ask: what are the ethical reasons to accept this normative claim? To arrive at the best ethical judgment requires that we bring together our ethical theories, principles and concepts to a particular issue, along with the best evidence about the facts. We should aim for maximum consistency across our normative beliefs about the way things should be.

There are many calls for AI to be explainable. What is even more important than explainability is justifiability. Justifiability is being able to provide reasons based on values we hold to perform an action.

2. Take responsibility

We are not responsible for things we can't avoid or foresee. But if an outcome is foreseeable and avoidable, we are responsible for it. And we are equally responsible for outcomes of our omissions when we choose to do nothing. Choosing to accept the information presented to us, or to follow a directive, is a choice for which we are responsible. Stanislav Petrov took responsibility: he chose not to act.

We are not responsible for things we can't avoid or foresee. But if an outcome is foreseeable and avoidable, we are responsible for it.

When presented with an empirical or normative claim by an AI such as ChatGPT, we should ask: do I have good reason to act on this claim? If a piece of technology, like a calculator, is highly reliable, then the answer is yes. But for novel technology, the issue is much murkier.

Blame is a function of the moral responsibility of a person and the degree of harm that results. Praise results from responsibility and benefit. The degree to which someone is responsible also depends on the effort or commitment they exert to bring about a benefit or avoid a harm.

Much of the debate around plagiarism and authorial credit and ChatGPT assumes people will cheat: exert no effort and take credit for value created. One major scientific journal, *Science*, has banned any output from ChatGPT.

But ChatGPT can involve human interaction. It represents data of a certain quality. Co-creativity is possible provided that significant effort is expended in the production, refinement or evaluation of the outputs of AI. If a person "mixes their labour" with ChatGPT, they can be deserving of praise, just as computing power has enhanced our ability to produce new mathematical and scientific research, not undermined its validity or value.

3. Act ethically

What is to act ethically has been debated for thousands of years. But at its heart is a simple answer: add value to the lives of other people. For Lt-Col Petrov, doing nothing was the hardest choice: "All I had to do was to reach for the phone; to raise the direct line to our top commanders—but I couldn't move. I felt like I was sitting on a hot frying pan."

ChatGPT is an extremely powerful technology with enormous potential for human benefit. It can distil human knowledge and wisdom, quickly create factual and normative content, enable communication between speakers of different languages, and ultimately enhance or even surpass human creativity.

As with any powerful technology, there are significant risks. At present, there are numerous mistakes and false claims, but these presumably will be ironed out. Longer term, risks include to threats to privacy; large-scale perpetuation of biases; plagiarism; displacement of human workers and creativity; deception and malicious use.

Acting ethically requires realising the value of technology while ensuring the risks are reasonable. Institutional or structural changes may be necessary, for example, labelling and creation of watermarks to prevent plagiarism.

To be human is to make your own ethical decisions

One ethical question that confronts regulators and industry is: should a driverless car swerve and sacrifice an innocent bystander (pedestrian or cyclist) to save a greater number of lives in the vehicle? I asked ChatGPT whether it is right to kill one to save five. Here is the answer:

"Whether or not it is right to kill one person to save five people is a complex ethical question. Some people may argue that taking one life to save five is the more logical option, and is therefore justified. However, it is also important to consider the ethical principle of respect for autonomy.

"This principle states that all individuals have an inherent right to make autonomous and informed decisions about their lives, including their own death. Taking this into consideration, it may not be morally right to force someone to accept the sacrifice of their life in order to save the lives of five other people. Ultimately, the answer to this question is subjective and depends on one's own ethical and moral beliefs."

But as driverless cars are rolled out, we won't have the luxury of remaining on the fence, or relying on drivers' reflexes to get us out of a decision. We will have to make moral choices and give reasons, and apply them consistently to programming the vehicles. This requires deep—and human—ethical thinking and expertise.

AI is a tool but it is not conscious and it lacks the capacity to make moral decisions.

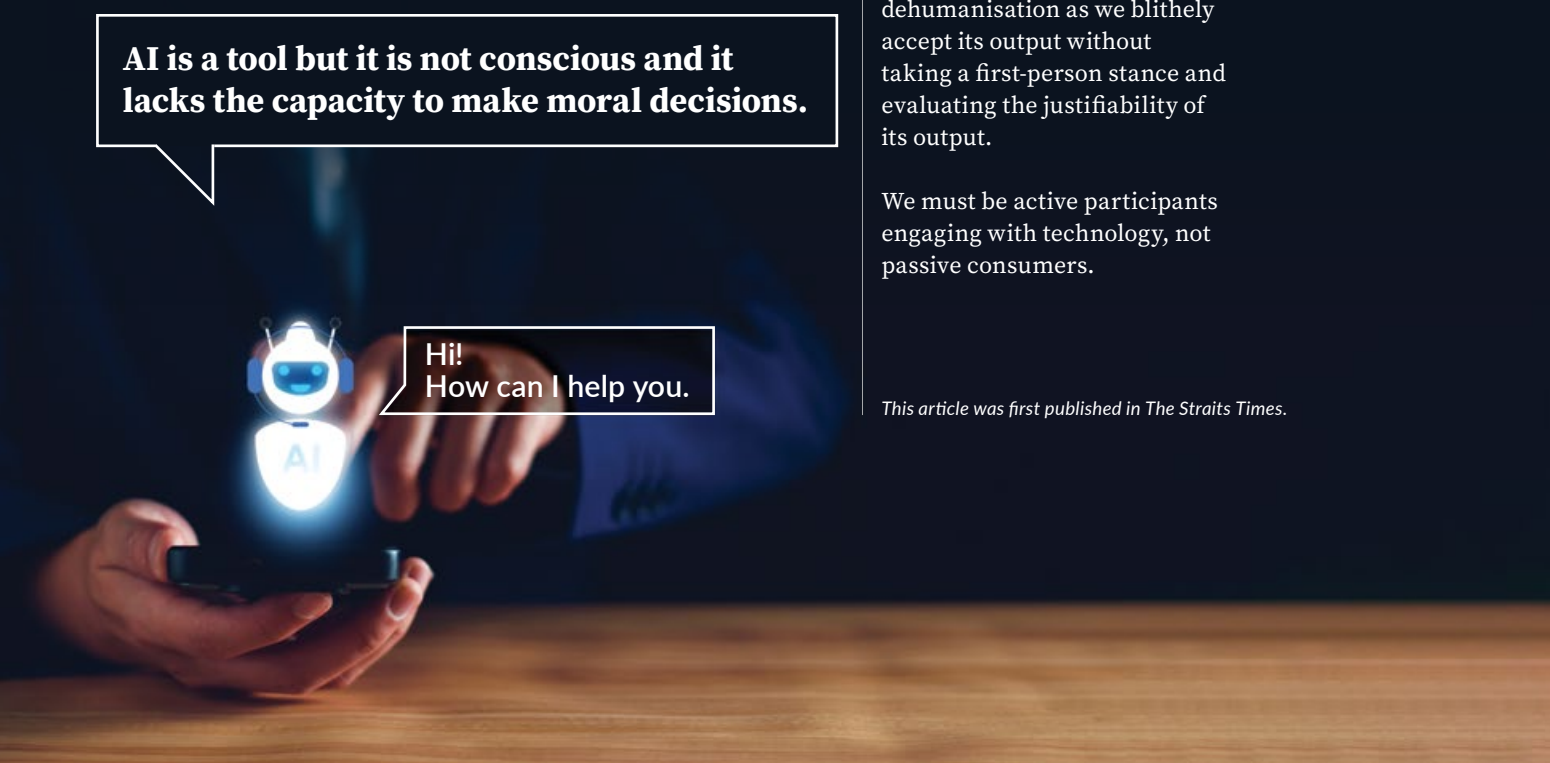
To be human is to make your own ethical decisions. Stanislav Petrov took responsibility in perhaps the grandest way possible. But each of us must take responsibility when we are presented with information and advice: are there good reasons to accept it? What should I do? This doesn't change just because a smart new piece of technology becomes available. The same applies to art. ChatGPT may be able to produce Shakespearean-like sonnets one day but it will be up to us to decide if they are good or bad.

The challenge presented by ChatGPT is not unique—it is a problem raised by the Internet, social media and modern life in general.

With power, comes responsibility. The decision to do nothing accrues responsibility when action is a possibility. We are responsible for the consequences if we choose to do nothing, or simply follow orders. Sometimes we must follow rules, authorities, law or orders: but we should always ask, are they right? AI, such as ChatGPT, can provide us with means to achieve our ends. But it should never dictate to us what our ends should be.

Only humans can make decisions about good and bad, right and wrong. The biggest threat of AI is that it results in dehumanisation as we blithely accept its output without taking a first-person stance and evaluating the justifiability of its output.

We must be active participants engaging with technology, not passive consumers.



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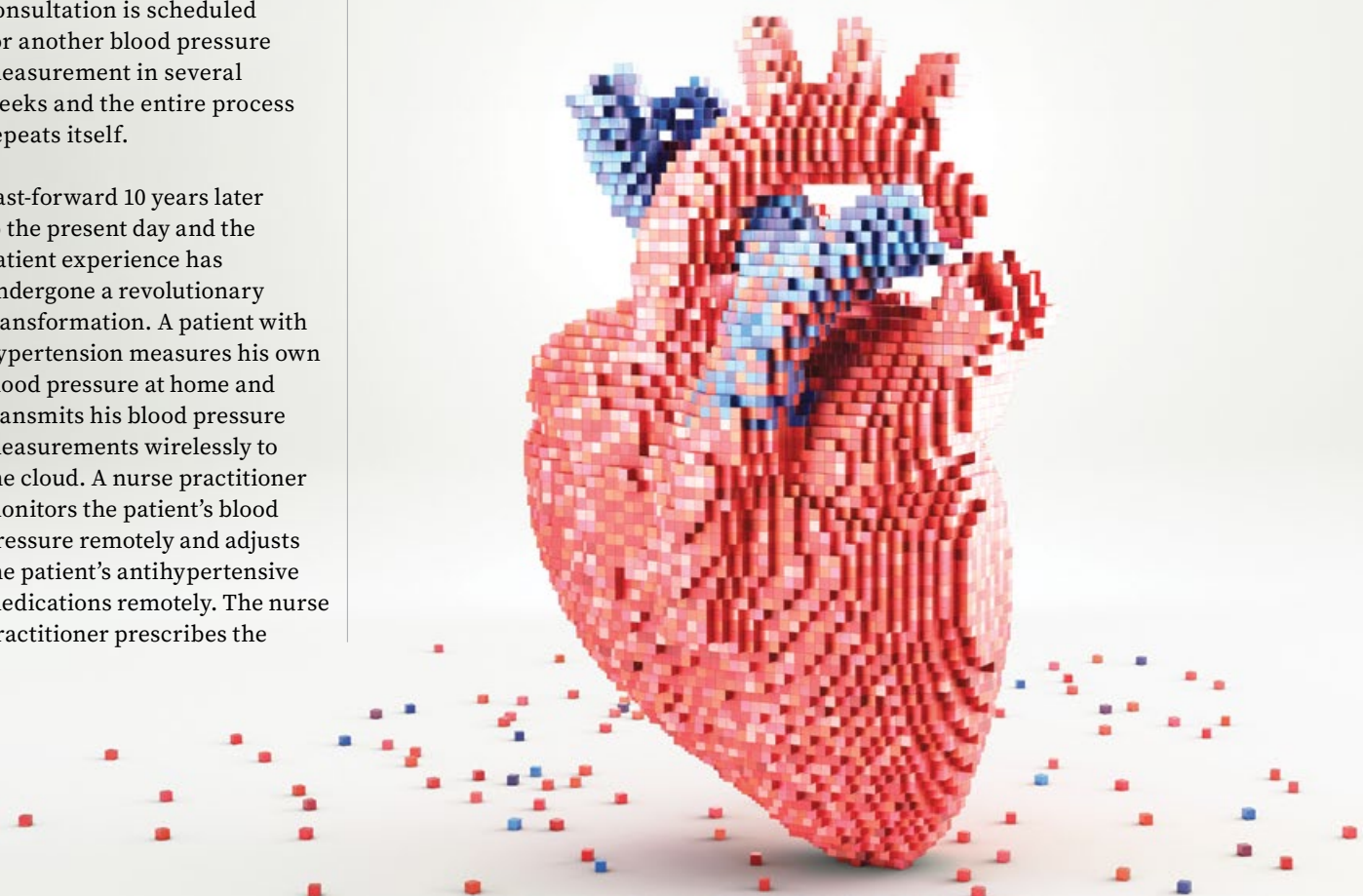
Healthcare Systems 3.0: Perspectives of a Cardiologist and a Patient

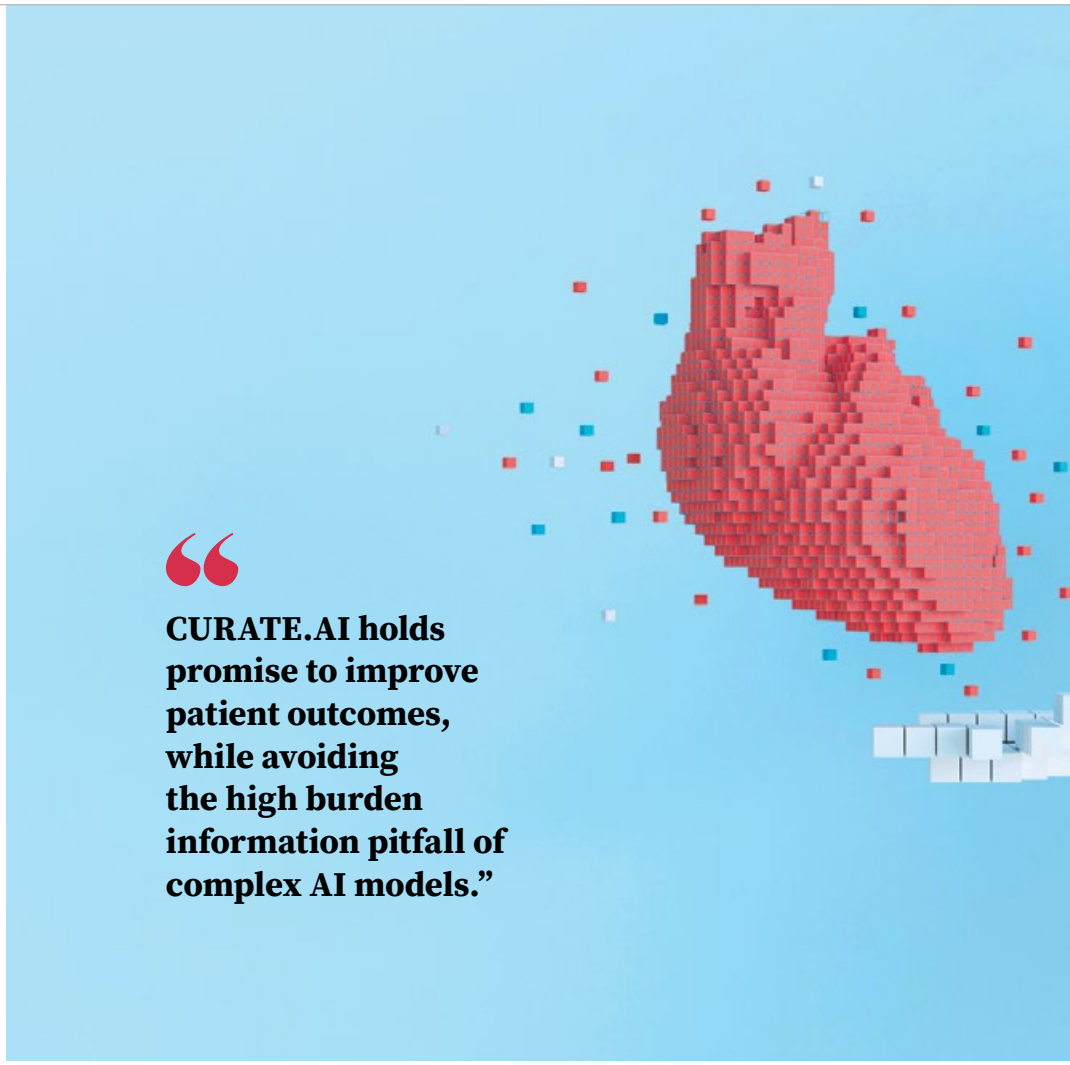
BY ASSOCIATE PROFESSOR MARK CHAN, DEPUTY PROGRAMME DIRECTOR, CARDIOVASCULAR DISEASE TRANSLATIONAL RESEARCH PROGRAMME, NUS YONG LOO LIN SCHOOL OF MEDICINE (NUS MEDICINE) & SENIOR CONSULTANT CARDIOLOGIST, NATIONAL UNIVERSITY HEART CENTRE SINGAPORE (NUHCS), NATIONAL UNIVERSITY HEALTH SYSTEM (NUHS) WITH CONTRIBUTIONS FROM CO-AUTHORS LISTED AT THE END OF THE ARTICLE

I still vividly recall how hypertension, or high blood pressure, was treated 10 years ago. A patient visits a doctor's clinic, often waiting 30 minutes or more to see a doctor for five minutes or less. The doctor measures the patient's blood pressure and then prescribes a first-line antihypertensive medication for lowering blood pressure. The patient then queues up at the pharmacy for another 30 minutes or more before getting the prescribed supply of medication. A repeat consultation is scheduled for another blood pressure measurement in several weeks and the entire process repeats itself.

Fast-forward 10 years later to the present day and the patient experience has undergone a revolutionary transformation. A patient with hypertension measures his own blood pressure at home and transmits his blood pressure measurements wirelessly to the cloud. A nurse practitioner monitors the patient's blood pressure remotely and adjusts the patient's antihypertensive medications remotely. The nurse practitioner prescribes the appropriate antihypertensive medications and these are delivered to patient's home. The patient and nurse practitioner can meet in the cloud virtually at any time. There is a reduced need to commute to the doctor's clinic, to wait to see the doctor or to queue at the pharmacy.

I have intimate knowledge of the experience 10 years ago and now because I was and am that patient with hypertension. Visits to my family physician 10 years back often meant that I had to bring my laptop with me so that I could work on a research grant while waiting for my turn to be seen. Ten years later, with the Primary Technology Enabled Care (PTEC) Hypertension programme[1] led by Professor Gerald Koh at MOH Office for Healthcare Transformation (MOHT), I have only had to make a physical visit to my family physician's clinic when I actually needed a blood test done.





“CURATE.AI holds promise to improve patient outcomes, while avoiding the high burden information pitfall of complex AI models.”

Artificial Intelligence (AI) helps doctors titrate multiple medications for resistant hypertension

When managing patients with resistant hypertension, defined as patients having suboptimal blood pressure control despite being on three or more antihypertensive medications, I am always struck by how much experience counts in managing patients with complex disease. It is really more art than science as I figure out whether to increase the doses of existing medications, swap certain medications or add on a fourth medication. Surely all the AI capabilities at our disposal could distil the collective ‘big data’ experience of thousands of doctors to take the guesswork out of managing polypharmacy?

Professor Dean Ho of the Institute for Digital Medicine (WisDM) at NUS Medicine has developed an alternative ‘small data’ approach to guide doctors in titrating multiple medications simultaneously. Called CURATE-AI, this N-of-1 approach requires only patient-specific data, such as doses (input) and blood pressure responses (phenotypic output), to systematically investigate the patient’s response to a drug and dose range, and dynamically identify personalised doses along the treatment course.[2] Due to its ‘N-of-1’ or patient-specific workflow, CURATE.AI does not require population data to train AI models to subsequently dose individual patients. Instead, it uses only a patient’s own data to prospectively calibrate their unique response to treatment. This patient-specific small dataset is then used to guide only the patient’s own care. This is a critical differentiator of CURATE.AI from traditional AI models and approaches. Therefore, due to its relatively modest resource requirements compared to conventional big data AI as well as prior validation, CURATE.AI holds promise to improve patient outcomes, while avoiding the high burden information pitfall of complex AI models.[3]

The N-of-1 approach is now being tested in a randomised clinical trial here at the National University Heart Centre Singapore, comparing the N-of-1 guided approach against standard care dose titration. Led by Dr Laureen Wang, Consultant at NUHCS’ Department of Cardiology, this pilot trial seeks to determine if the N-of-1 approach achieves better and faster achievement of blood pressure goals compared with standard care dose titration. Interestingly, the N-of-1 approach has already demonstrated impressive results among patients with cancer receiving combination chemotherapy and patients post-transplant receiving combination immunosuppressive therapy. Not only did the N-of-1 approach achieve faster elimination of cancer cells and better transplant graft rates, some of the medication doses could even be lowered, thereby reducing toxicity.[4]

Acute myocardial infarction strikes **11,000** Singaporeans each year. Approximately **5%** year-on-year increase in new heart attacks each year

Raising the human potential of our nurses and pharmacists

The pandemic accelerated the adoption of remote patient management and digital health solutions. It also gave our nurses and pharmacists an opportunity to lead in the care of patients instead of just playing supporting roles. Acute myocardial infarction, commonly known as heart attacks, strikes 11,000 Singaporeans each year. Worse, we are seeing an approximately 5% year-on-year increase in new heart attacks each year.[5] While patients with heart attacks in Singapore receive state-of-the-art care including 24/7 emergency angioplasty procedures to restore blood flow in blocked coronary arteries, post-discharge care is hampered by the limited number of cardiologists available to deliver high-intensity care needed in the first six months after the heart attack. The pandemic greatly exacerbated this problem because of limits placed on in-person visits in the last three years.

Our team therefore decided to conduct the IMproving reModeling in Acute myoCardial Infarction Using Live and Asynchronous Telemedicine (IMMACULATE) trial. In a randomised clinical trial, 301 patients hospitalised for a heart attack at the NUHCS, the National Heart Centre and Tan Tock Seng Hospital were assigned to two different management strategies for six months after discharge: the first group was managed by their cardiologists via regular in-person visits while the second group was managed by nurse practitioners remotely with the assistance of digital health tools for remote patient monitoring.[6] This trial was designed to answer the question of whether nurse clinician-led remote management was as safe as cardiologist-led in-person care. Surprisingly, the group managed remotely by nurse practitioners actually had fewer adverse events and showed far greater patient satisfaction with nurse-led remote care.

The promising results of the IMMACULATE trial has led the Ministry of Health (MOH) to deploy this new model of care across seven hospitals and 15 polyclinics in Singapore in a larger scale pilot. The Acute Myocardial Infarction: Allied Health-Oriented, Patient-Centred Technology-Enabled Care (AMI-HOPE) programme will have pharmacists in the hospitals and polyclinics leading the care of patients with acute myocardial infarction.[7] Pioneered by Associate Professor Doreen Tan 13 years ago at the Khoo Teck Puat Hospital, cardiovascular pharmacists are uniquely suited to managing patients in which medications play a major role in determining health outcomes. Besides possessing an encyclopaedic knowledge of pharmacology and pharmacotherapy—also known as the science of tailoring medications in the management of diseases—pharmacists are also highly trained in smoking cessation counselling, medication reconciliation and adherence coaching.

Over the last two years, our team has trained 36 pharmacists across Singapore to acquire new skills in symptom recognition, cardiac rehabilitation, dietary counselling, health coaching and person-centred communication and other diverse skills required to deliver holistic care to patients with acute myocardial infarction. Many nurses and pharmacists are now legally recognised to prescribe medications independently under the MOH collaborative prescribing practitioner programme. These upskilling opportunities will finally allow clinically-oriented pharmacists to practice at the top of their professional licence. If the AMI-HOPE programme is eventually mainstreamed, it will include plans to train many more pharmacists and nurses to practice both independently and in partnership with doctors.

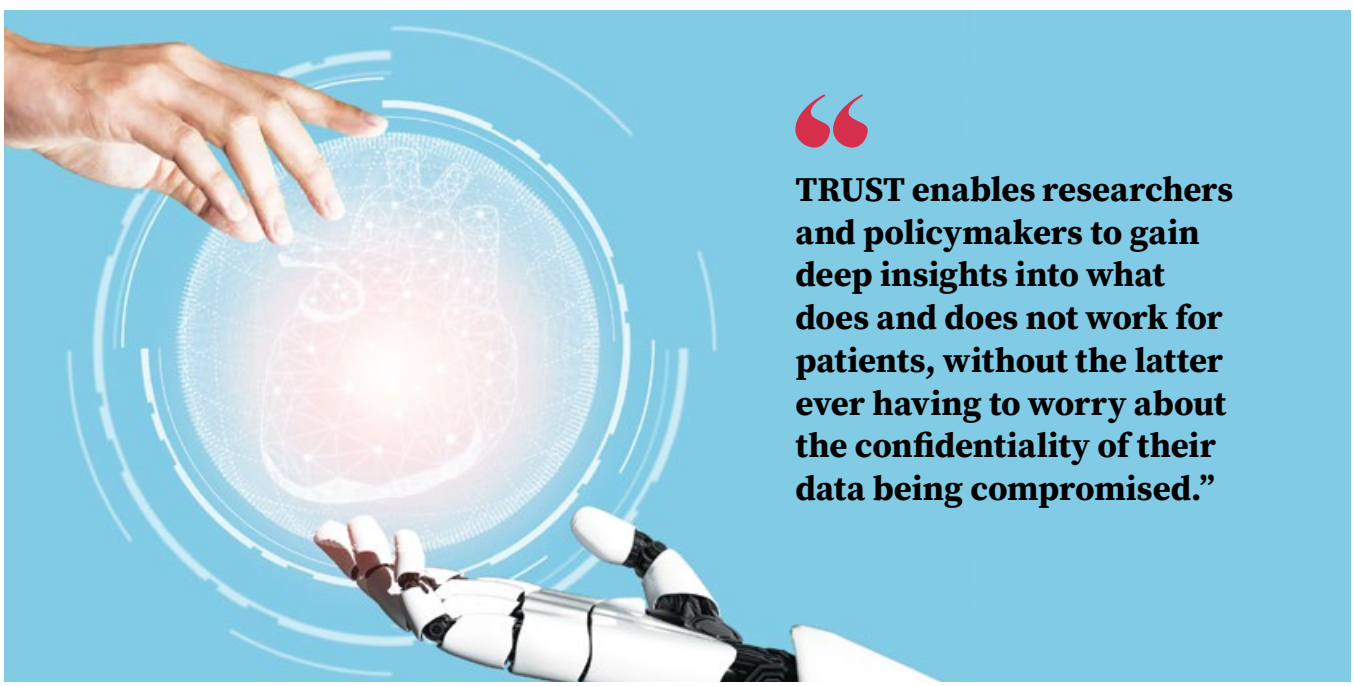
Using TRUST to build a learning healthcare system

In healthcare systems 3.0, data will drive much of the transformative changes. In a highly digitised healthcare system like Singapore, there is a massive opportunity to build a learning healthcare system in which we can harness the collective experience of patients and healthcare providers captured in your and my electronic medical records to deliver new insights in the management of each new patient. An example of how this big data approach can inform healthcare policy is demonstrated in our interrogation of electronic medical record data collected across the patient journey from hospital to specialist outpatient clinic to polyclinic. Anecdotally, cardiologists like myself were seeing patients being admitted for a 2nd or 3rd heart attack two to three years after their 1st attack. Some of these patients admitted to stopping all their medications because they felt well and thought that they no longer needed to rely on their medications to keep them healthy.

Curious to determine if this problem was a rare occurrence or actually more prevalent, we conducted an in-depth review and found that approximately 5% of patients stopped refilling their medications from the 2nd year after their heart attack. More worryingly, the rate of non-refills increased by approximately 5% each year from 3rd, 4th and 5th years after the heart attack. These findings imply that lifelong patient coaching and reminders about medication adherence are critical—once again indicating a fantastic role for our pharmacists in primary care.

Building a true learning healthcare system requires the formation of data rivers. Much of the data in our electronic medical records exist as data lakes with limited interconnectivity to other data lakes. For example, healthcare financial data is kept separately from clinical data but connecting these data lakes is essential to determine the cost-effectiveness of multidimensional care models such as AMI-HOPE. TRUST is a new 'data river' built by MOH to connect these data lakes in a secure manner.[8] Once individual datapoints are connected by a trusted 3rd party, the healthcare data is anonymised before any data analyst can ever see the data. Such a system enables researchers and policymakers to gain deep insights into what does and does not work for patients, without the latter ever having to worry about the confidentiality of their data being compromised.

The digital health systems for remote management in the AMI-HOPE programme (Health Discovery+) were developed by the MOHT and then transferred to Integrated Health Information Systems (IHiS) for deployment at scale. Health Discovery+ is also the system used by PTEC-hypertension and piloted in multiple disease management



"TRUST enables researchers and policymakers to gain deep insights into what does and does not work for patients, without the latter ever having to worry about the confidentiality of their data being compromised."

programmes from stroke to dementia. Despite the clear advantages of a universal remote monitoring system for Singapore, each of the three healthcare clusters in Singapore have embarked on building their own digital health apps. Such efforts are driven by two factors: first, the desire to find lower-cost alternative digital health solutions and, second, to forge a unique identity for each healthcare cluster. Fortunately, technology now allows the healthcare clusters to converge while at the same time retaining their own unique identity.
The best example I know of is Healthhub, the national digital health platform for managing clinic appointments, test results and medications. Data across clusters' apps are integrated into HealthHub such that it remains the common operating system to these three apps even as it allows each cluster's app to retain their own 'skin' or user interface.

The future of healthcare systems is taking shape, slowly

From the Bluetooth-enabled blood pressure device for remote blood pressure monitoring to the most advanced robotic system that allows a cardiologist in one country to perform angioplasty on a patient in another remote country, technology has enabled many of the healthcare innovations I and many other patients have benefitted from. Yet, the 'move fast and break things' mantra upheld by the tech industry has been repeatedly rejected by healthcare systems. While investors in healthcare technology are often in a hurry to see quick returns on their investments, spectacular 'fake it till you make it' scandals in healthcare innovation remind us constantly that human health is complex and does not lend itself to a fail-fast fail-forward approach when human lives are at stake.

A magnificent example of such a spectacular failure in healthcare innovation is the now cautionary tale of THERANOS, the healthcare startup that quickly achieved unicorn status by deploying its EDISON diagnostic machines across America at an unprecedented scale. THERANOS claimed that its EDISON machines could diagnose hundreds of diseases with a single drop of blood. When criminal investigations were finally conducted in THERANOS' laboratories after a whistle-blowing event, not a single EDISON machine could be found that could deliver on THERANOS claims. Instead, investigators found very standard diagnostic machines from other established companies in its laboratories, diagnostic machines often requiring much larger volumes of blood to deliver results.

To make its bold claims, THERANOS staff diluted patients' blood with large volumes of water in order to inject them into the standard machines. Needless to say, this egregious practice led to countless diagnostic inaccuracies and erroneous diagnoses—patients with cancer and heart disease were diagnosed as disease-free but worse, patients who did not have cancer or heart disease were diagnosed as having serious diseases, leading to a cascade of unnecessary tests and surgical procedures.

Interestingly, the EDISON technology touted by THERANOS as game-changing was never published in a scientific journal, a minimum requirement every other innovation that makes it to mainstream clinical practice has to fulfil. Just like every new medication requires extensive testing and validation before it enters mainstream adoption, healthcare systems will not accept high-risk shortcuts. This is understandable given what is at stake in healthcare—mine, yours, and every patient's lives and well-being.

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COVID-19, the Escalation of Diabetes and the Repercussions on Tuberculosis

BY THONG PEI MIN, PHD STUDENT, CHONG HAI TARNG, MASTER STUDENT, ANABEL CHANG, BSC STUDENT AND ASSISTANT PROFESSOR CATHERINE ONG FROM THE INFECTIOUS DISEASES TRANSLATIONAL RESEARCH PROGRAMME

The urgent mobilisation of limited healthcare resources and personnel to combat the pandemic has hindered the management of other communicable and non-communicable diseases.

COVID-19 and its impact on global health

The Coronavirus Disease 2019 (COVID-19) had a devastating impact on global health. The urgent mobilisation of limited healthcare resources and personnel to combat the pandemic has hindered the management of other communicable and non-communicable diseases[1]. Tuberculosis (TB) among many others has seen a rise in cases. Due to difficulties in accessing TB services, an 18% decline in notifications of newly-diagnosed TB disease was observed between 2019 and 2020, with an increase in TB deaths the following year[2,3]. This is further exacerbated by the fact that both TB and COVID-19 are airborne infectious diseases which primarily affects the lungs, making differential diagnosis a challenge. The pandemic also disrupted the control of chronic diseases such as diabetes (DM), a leading cause of deaths in adults[4]. The disruptions to global health brought about by the pandemic raises the need to re-evaluate healthcare strategies to better deal with COVID-19 comorbidities.

COVID-19 and Diabetes

DM is an established risk factor for COVID-19 mortality[5]. It was first reported in China that DM patients had a higher COVID-19 mortality rate compared to non-diabetic individuals, with similar phenomenon observed in the US and England[6,7,8]. As DM patients are relatively immunocompromised, their risk and severity of COVID-19 infection[9] is increased. The reasons DM drives more severe COVID-19 infections remains unclear. Some possible mechanisms include increased oxidative stress and inflammatory cytokines production[10].

While DM could increase one's risk for COVID-19 infection, COVID-19 patients are also at risk of developing diabetes. Compared to non-COVID-19 patients, the relative risk of developing DM after COVID-19 was 1.62 times higher[11]. The situation was worse in younger patients, with the risk of developing DM doubled compared to those without COVID-19 or with other respiratory infections[12]. In a separate study comprising 453 hospitalised COVID-19 patients in China, the reported prevalence of newly-diagnosed DM was 20.8%[13]. These studies show that COVID-19 is a risk factor for new-onset DM.

The mechanisms of COVID-19-induced DM are not well understood. Some proposed mechanisms include (1) direct pancreatic beta cell damage by SARS-CoV2 leading to impaired insulin secretion, (2) indirect pancreatic beta cell damage via autoimmune response against beta cells, (3) overproduction of cytokines leading to insulin resistance, (4) enhanced glucose synthesis due to increased secretion of glucogenic factors by SARS-CoV2-infected hepatocytes, (5) steroid-induced DM for those treated for severe COVID-19, and (6) adoption of sedentary lifestyle due to stay-at-home orders[14,15]. Studying the mechanisms underlying COVID-19-induced DM is crucial as the global incidence of DM is expected to increase drastically.

COVID-19 and the effects on tuberculosis

TB is a leading infectious killer, with approximately 10 million new and relapsed TB diseases globally in 2019. The emergence of the COVID-19 pandemic resulted in a reallocation of healthcare resources and staff to support COVID-19 operations, potentially disrupting the provision of health services, including services for TB care and management. We conducted a study that involved 43 TB centres from 19 countries and reported a substantial decline in the number of newly diagnosed TB infection, TB disease, drug-resistant TB and TB deaths in 2020 compared to 2019[16]. Since TB and COVID-19 share similar clinical manifestations due to the nature by which both are primarily respiratory infections, differential diagnosis is challenging, which may explain missed TB diagnoses and decreased TB notifications during this period. This is further exacerbated by the lockdown measures in many countries, which hinder patients from seeking care and treatment. The consequence is an increase in contact time between infected individuals and family members, thereby resulting in TB transmission within the family. Accordingly, a modelling study of high TB burden countries (India, Kenya and Ukraine) predicted that a three-month suspension of TB services could result in an additional 1.2 million TB cases in the next five years[17]. This could lead to increased TB deaths and incidence, which has already been reported by the World Health Organization in their Global Tuberculosis Report 2022[18].

In addition, coinfection of TB/COVID-19 was associated with higher risk of mortality[19]. This may due to (1) ineffective mounting of immune response to SARS-CoV-2 antigen, (2) reduction in Mycobacterium tuberculosis (M.tb)-specific CD4+ T cell response in COVID-19 patients, or (3) uncontrolled production of inflammatory cytokines in the lungs in response to both SARS-CoV-2 and M.tb, leading to extensive lung injury[20,21].

18% decline in notifications of newly-diagnosed TB disease was observed between 2019 and 2020

The relative risk of developing DM after COVID-19 was **1.62 TIMES** higher

Approximately **10 MILLION** new and relapsed TB diseases globally in 2019

Since TB and COVID-19 share similar clinical manifestations due to the nature by which both are primarily respiratory infections, differential diagnosis is challenging, which may explain missed TB diagnoses and decreased TB notifications during this period. This is further exacerbated by the lockdown measures in many countries, which hinder patients from seeking care and treatment.

Additionally, there is an increased risk of TB reactivation among COVID-19 patients. A study showed that infection of a virus from the same genus as SARS-CoV-2 reactivated dormant TB infections, providing evidence of SARS-CoV2-induced TB reactivation[22]. Overall, coinfection of TB/COVID-19 is associated with higher mortality and increased risk of TB reactivation resulting in increased TB burden globally.

Diabetes worsens tuberculosis

DM is a risk factor for TB; three-quarters of DM burden is found in low- and middle-income countries where TB is prevalent (Figure 1A). The presence of DM is associated with more severe TB manifestations (Figure 1B) and delayed sputum sterilisation, translating to a longer period of infectiousness within the community[23,24]. Findings from animal studies and humans suggest that innate and adaptive immune responses were impaired in DM host, leading to delayed mycobacteria clearance from the lungs. Consequentially, TB-DM patients would experience higher levels of inflammation and slower resolution[25]. This aligns with the human data showing higher systemic matrix metalloproteinases (MMPs), angiogenic factors and pro-inflammatory cytokines in TB-DM patients compared to TB patients[26,27,28]. However, the underlying mechanism remains to be elucidated and would be imperative in managing TB-DM.

The management of TB-DM patients is challenging due to increased risk of drug-drug interactions, higher pill burden and longer treatment duration. Several studies have shown that TB-DM patients have lower plasma TB drug concentration than TB patients, suggesting that vascular integrity and drug delivery may be compromised[29,30]. This is backed up by a study done in TB zebrafish, where treatment with anti-angiogenic agent showed reduced vascular leakiness and mycobacterial burden, with further suppression of mycobacterial growth when in combination with rifampicin[31]. Anti-angiogenic agent could thus potentially be used as adjuvants in TB treatment. Another potential adjunctive therapy is doxycycline, a broad-spectrum MMP inhibitor[32]. Doxycycline works by improving TB drug delivery and/or retention by reducing vascular leakage[33]. Taken together, these studies suggest that there is a need to refine existing TB treatment regimen to improve treatment outcomes of TB-DM patient.

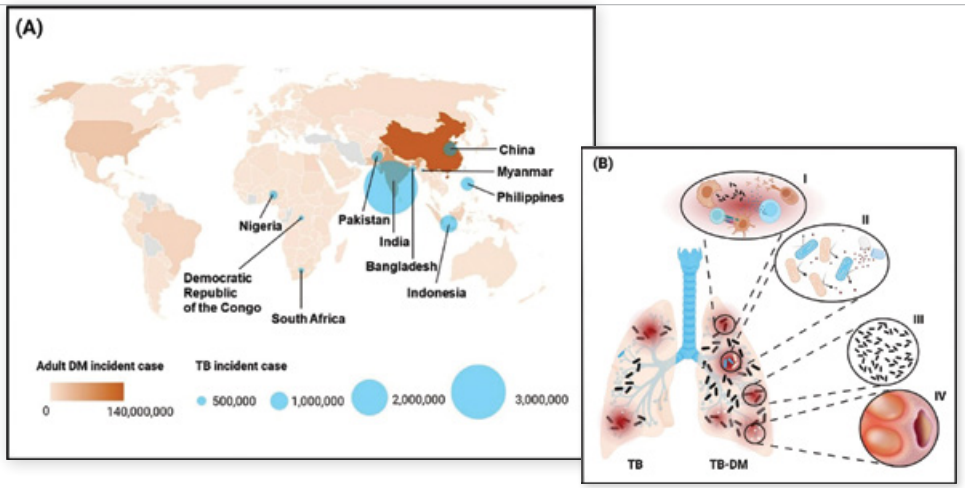

Figure 1: The global incidence of tuberculosis (TB) and diabetes (DM) is set to rise and can disrupt TB control. (A) Estimated incidence of TB and DM co-occurrence. Top ten countries with the highest TB incidence in 2021 are labelled. High incidence of TB and DM are expected in South Asia and China. (B) Compared to TB patients without DM, patients with TB and DM exhibit a worsened clinical phenotype. This include (I) Delayed Mycobacterium tuberculosis (M.tb) clearance and altered immune response, (II) Higher prevalence of drug and multi-drug resistant M.tb, (III) Higher mycobacterial burden due to poor glycaemic control and (IV) More severe lung cavitary and parenchymal lesion. Figure created with BioRender.com.

Conclusion

The increasing incidence of COVID-19 induced DM, and heightened risk of TB reactivation in COVID-19 patients has threatened global TB control. Coinfection of DM and TB are often associated with more severe disease and poorer treatment outcomes. Although the underlying mechanisms remain to be elucidated, optimal glucose control could potentially lower the risk of developing TB disease in DM patients and improving TB treatment outcomes. A modelling study evaluating the impact of DM on 13 high TB burden countries suggests that halting the rise in DM incidence would prevent six million TB cases and 1.1 million TB deaths in these countries in the next 20 years[34]. Measures to prevent TB-DM should therefore be taken at a national level, especially in countries with high TB and DM burdens. Some approaches include bidirectional screening for early detection of DM and/or TB diseases and increased government funding in TB research.

Halting the rise in DM incidence would prevent

6 MILLION

TB cases and

1.1 MILLION

TB deaths in high TB burden countries in the next 20 years

Scan to read the full article here:

This is an abbreviated version of the original article that was first published in the International Journal of Infectious Diseases.

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Communicating with Persons with Disabilities

BY KOH YING YING, PHASE V NUS YONG LOO LIN SCHOOL OF MEDICINE STUDENT, DR VIVIEN LEE, LECTURER AND ADJUNCT ASSOCIATE PROFESSOR VICTOR LOH, EDUCATION DIRECTOR, DIVISION OF FAMILY MEDICINE, NUS YONG LOO LIN SCHOOL OF MEDICINE

"You know, as a deaf individual, it has been especially difficult working with doctors and my nursing colleagues, both as an equal and as a patient myself," Clydia, a nurse with bilateral hearing loss, was sharing about her experience in Nursing school.

During a panel discussion, she described to medical students some of the more common gaps experienced by persons within the deaf community, in the course of their encounters with healthcare workers. Reflecting on her journey towards becoming a nurse, the discussion turned to how facilitated training opportunities and early exposure to persons with disabilities (PWDs) could smoothen some of the bumps.

PWDs in Singapore comprise 13.3% of people who are 50 years old and above[1]. Every healthcare practitioner will encounter such persons in the course of their work. As medical students, we have experienced moments of awkwardness when dealing with PWDs, such as when looking for the right words with which to ask to examine patients with amputated limbs, or when we were uncertain about whether to raise our voices when talking with patients who had difficulty hearing.

Our journey began in 2020. We called ourselves *Team Comm-petent*. We were a crew of seven medical students and two disability advocates, both with bilateral hearing loss. Our goal was to improve awareness of disabilities and help doctors-to-be learn how to communicate with PWDs effectively and sensitively.

We decided to work on a learning activity that would give voice to PWDs. We sought the input of 20 individuals with various disabilities—visual, mobility, and hearing—and also conducted a literature review that would form the basis of our project. It would be a student elective workshop that would run during the recess weeks and students would be invited to sign up on a purely voluntary basis. The team recruited 31 interested clinical year students to participate in two pilot runs.

The lesson plan that we co-designed with PWDs would start with a workshop on key "Dos and Don'ts" when communicating with a PWD, followed by role playing of medical consultations, with PWDs as patient-educators. We modelled this after the standardised patient encounters we experienced as medical students, except that we added the element of PWD patient-educators. These PWD educators would enact a scripted clinical presentation to highlight some conundrums that PWDs

13.3%
of PWDs in Singapore are 50 years old and above

face when engaging with the healthcare system. These included explaining an x-ray result to a patient with visual impairment and communicating with a patient who is hard of hearing and accompanied by a sign language interpreter. Student interviewers would receive feedback from peers and from PWD educators, who often highlighted insightful points on the students' communication skills and sensitivity. More importantly, we set aside time for PWD educators to share their lived experiences with the students.

Through pre- and post-event questionnaires, we noted substantial improvement in students' self-reported empathy and confidence in communicating with PWDs after the workshop.

In addition to positive feedback from both participants and faculty, we received endorsement from NUS Medicine's Medical Education Grand Innovation Challenge, 2021 (MEGIC) when we garnered the Special Mention Award. Our elective had now passed the proof-of-concept stage and was ready for incursion into the main medical curriculum.

The proposal to bring the workshop into the curriculum was welcomed by faculty and staff from the Department of Family Medicine. Since the beginning of academic year 2022/23, the workshop has become a regular fixture within the Phase III Family Medicine posting as the "Communications with Persons with Disabilities" workshop.

Initial response has been positive, with heartfelt student reflections.

As Team-Comm-petent and doctors-to-be, we are optimistic that this initiative is a small step towards more equitable and inclusive healthcare. We hope it will continue to be a part of our school's curriculum.

Acknowledgments

The authors would like to thank Clydia Tan and Caitlin O'Hara for their inputs on this article. They would also like to thank Team Comm-petent (Clydia Tan, Kimberly Quek, Caitlin O'Hara, Chia Eik Chao, Ng Cheng-Ann Winston, See Sin Yee, Cassandra Chan Xian Ci, Ng Zi Hui Celeste), our mentors Dr Ann Toh and Dr Victor Loh, the team at the Department of Family Medicine and the NUS Centre for Healthcare Simulation, and most importantly the patient educators from the disability community for making this initiative possible.

> **"We should see persons with disabilities for their ability instead of their disability."**
>
> *Workshop participants*

A patient educator and Dr Ang Lai Lai (Family Medicine, NUS Medicine) guiding students during the role-play session.

The student organising team comprising Phase IV and Phase V NUS Medicine students, an NUS Nursing alumnus and Yale-NUS College student, who worked on the initiative throughout the COVID-9 pandemic. (From top left to right: Koh Ying Ying, Clydia Tan, Ng Zi Hui Celeste, Caitlin O'Hara, Chia Eik Chao, Cassandra Chan Xian Ci, See Sin Yee, Ng Cheng-Ann Winston, Kimberly Quek)

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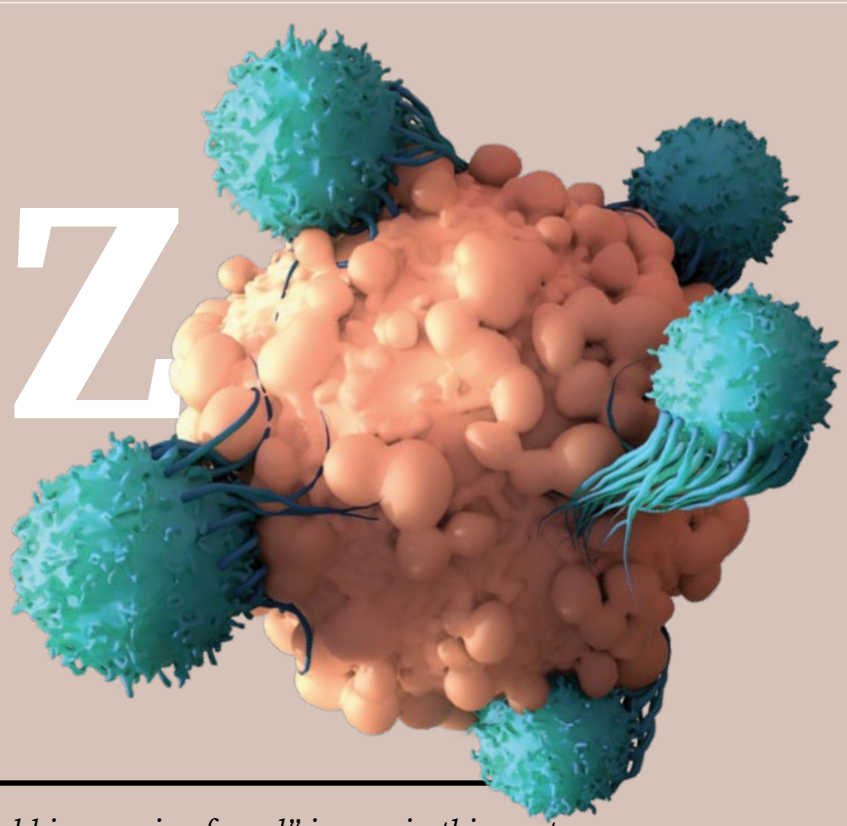
The A to Z of T cells



BY PROFESSOR NICHOLAS R.J. GASCOIGNE, IMMUNOLOGY TRANSLATIONAL RESEARCH PROGRAMME, AND DEPARTMENT OF MICROBIOLOGY AND IMMUNOLOGY, NUS YONG LOO LIN SCHOOL OF MEDICINE

A similar kind of feeling to Blake's "World in a grain of sand" is seen in this quote from George Orwell: "Retaining one's childhood love of such things as trees, fishes, butterflies and....toads, one makes a peaceful and decent future a little more probable[1]."(Elsewhere in the essay, he makes the point that "the toad, unlike the skylark and the primrose, has never had much of a boost from poets", but I digress).

I am still in Awe of Nature, and indeed, I'm still the kid who loves toads and butterflies, but I've spent my career trying to understand the immune system, which one might think is slightly less romantic. (It also doesn't get much of a boost from poets). But consider how much the layperson has been exposed to the importance of the immune system in the last three tumultuous years; I'm pretty sure that everyone knows that a functioning immune system is important to protect you from infectious viruses. Most people now know what an antibody does and may even know about T and B cells too.

My interest, since a lucky break in getting a summer internship at a top T cell immunology lab, has been in T cells and how they recognise foreign material to make an immune response. What is most amazing about the T cell's way of seeing the world is that it is stimulated by something that is just a tiny bit different from what it is used to—the self. The toad sees the movement of potential prey or predator because the photo-receptors in the creature's eyes are saturated when nothing changes, so only the change registers. In a similar way, the T cell generally just sees self. That is enough stimulation to keep the individual cell alive, but not to do much. When the self-protein is slightly changed, perhaps by as little as a single amino acid, a few of the T cells will become activated by this difference, and the immune response will commence. Because the T cells see self-proteins, it is important to select them so that they don't respond too strongly and give us autoimmunity. The T cells learn to tell the difference during their development in the organ that gives them their name, the thymus.

The protein that the T cells see is called the MHC (major histocompatibility complex), the human version of which is called HLA (human leucocyte antigen). Each HLA molecule carries a short fragment of protein (a "peptide") in a special groove at one end of the protein. These peptides are made from worn out self-proteins that have been broken down, mostly for recycling. The T cell has a protein—the T cell receptor or TCR—on its cell surface, that can bind specifically to the HLA

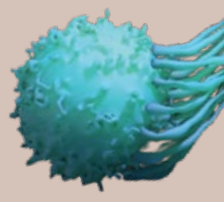
protein in such a position that it sees the peptide as well as the HLA protein. Each developing T cell in the thymus expresses a different TCR since the genes for the recognition part of the TCR come in lots of small modules that can be rearranged in billions of different ways, yet still produce a functional TCR.

The TCR of each individual cell will be exposed to the self-HLA-peptides that are expressed by the cells in the thymus. If the TCR binds too strongly to one of these HLA-peptides, the developing T cell will be over-stimulated and will die in a blaze of glory known as apoptosis or programmed cell death. If the TCR is unable to bind to any HLA-peptide it will not get any stimulus and will die "by neglect". These two fates account for the vast majority of the cells made by the thymus, but those who bind self HLA-peptide just enough to get a little stimulation, turn on genes for survival and maturation. This Goldilocks approach means that the mature T cells that leave the thymus to go on to populate the blood, lymph nodes and spleen see self-MHC-peptide just enough to give stimulation that allows their survival.

The cells can circulate through the body like this until they die or until they are lucky enough to encounter a cell that has a peptide from something different, perhaps a virus. When a virus infects a cell, it causes the cell to make viral proteins and some of these are broken down, by the same processes as the self-proteins, into peptides. Some of those peptides are incorporated into the HLA proteins, so now a TCR has the opportunity to recognise and bind to a non-self-peptide in the self-HLA. Some small number of TCRs will be able to "see" that new foreign peptide on the HLA protein, and they will get a stronger stimulus than the one from self HLA-peptide that helped keep them alive.

For a virus infection, there are the killer T cells, which literally kill the infected cells by squirting poisonous proteins into them, and specialized helper T cells, called TH1 cells, that make pro-inflammatory molecules ("cytokines") that inhibit the virus' transmission and also activate B cells to make antibodies against the virus.

Now these cells turn their economies onto a war footing, they change their metabolism to a high intensity, high energy-use mode. They start proliferating, each cell dividing into millions of new cells over a period of a few days. They change from being small cells that are rather "quiet" in the sense of not really doing much, into large cells that can secrete molecules to either kill or incapacitate virus infected cells or help other cells to do so. These are "effector" T cells. They come in different forms, and the precise type of effector T cell depends on the type of infection. For a virus infection, there are the killer T cells, which literally kill the infected cells by squirting poisonous proteins into them, and specialised helper T cells, called TH1 cells, that make pro-inflammatory molecules ("cytokines") that inhibit the virus' transmission and also activate B cells to make antibodies against the virus.



Recently, my lab decided to find out how much time a T cell needs to see the foreign antigen in order to be stimulated, and how this changes with the strength of the interaction between the TCR and the antigen. We used a set of peptides developed from one original strong peptide and which give gradually reduced strength of T cell activation, and used T cells that all have the identical TCR. We found that the strong-binding peptide needed much less time to activate the cells to proliferate than the weaker binders, and that this was correlated with the activation of one of the molecules that turns on the metabolic changes mentioned above. We were surprised that this was not the case for the secretion of the pro-inflammatory cytokines—those didn't need a longer time of exposure to the weaker antigens for them to be secreted.

Slight differences in how we recognise things make all the difference to how we respond. Both the T cell and the toad need to see something different to what they are used to before they can identify it as friend or foe, prey or target.

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Trailblazer for Advanced Practice Nurses

It is often said that Nursing is a noble profession. Associate Professor Zhou Wentao, a certified Advanced Practice Nurse (APN), aspires to go beyond and develop those who have responded to the call of Nursing. But what exactly is an APN?

According to the Singapore Nursing Board, an APN is a Registered Nurse who has acquired the expert knowledge, complex decision-making skills and clinical competencies for extended practice. They are trained in the diagnosis and management of common medical conditions, including chronic illnesses.

Assoc Prof Zhou, known for her contributions to APN and clinical training, began her journey in Nursing in 1997.

Driven by a perpetual hunger for a deeper understanding of clinical decision processes, coupled with a desire to holistically understand patients' needs, her path led her through an advanced diploma in neuroscience and then to the Master of Nursing programme at Alice Lee Centre for Nursing Studies (NUS Nursing), National University of Singapore Yong Loo Lin School of Medicine.

She has been leading the Master of Nursing programme since 2015, aiming to develop students in advanced clinical knowledge and skills in advanced nursing practice, clinical medicine, social sciences and public health.

Upon completion, graduates can apply for an APN provisional licence with the Singapore Nursing Board to continue a 12-month integrated APN internship and be certified as an APN—what Assoc Prof Zhou had gone through.

"After I became an APN, the expanded clinical practice allowed me to add value to patients' care by filling up multiple clinical gaps. But there were still gaps that I realised were beyond my capability, which is why I started to do research and ended up doing a PhD—to explore how APNs can improve transition care," said Assoc Prof Zhou. "It has made me a conscious learner and sharp observer."

Assoc Prof Zhou regularly teams up with Dr Brigitte Woo, a Research Fellow at NUS Nursing.

With the support of the Chief Nursing Officer (CNO) Office, Ministry of Health (MOH), Singapore, they have conducted nationwide studies to explore the practice patterns, level of acceptance and impact of APNs in Singapore. These studies were eventually published in top nursing journals.

In 2020, Assoc Prof Zhou and Dr Woo won the Equal Opportunities and Career

30%
of the registered nurses in the workforce are interested in becoming APNs

Development (EOCD) Seed Grant to embark on, "Understanding the gender gap in advanced practice nursing: an exploratory study". Elucidated in this study was that men in nursing enjoy opportunistic advantages in entering the APN workforce but are not interested in the role and not staying long enough in the Nursing profession to become APNs.

Assoc Prof Zhou and Dr Woo continue to collaborate with the CNO office and nursing leaders to professionally develop and strengthen the APN workforce through evidence-based inquiry.

As the Programme Director of the Master of Nursing programme at NUS Nursing, Assoc Prof Zhou works with healthcare leaders and other APNs to ensure that the APN-preparatory education remains relevant and cutting-edge. She works with MOH's APN development committee to review APN-related policies, practice models and clinical outcomes. In recent years, she played a critical role in the implementation of the National Collaborative Prescribing programme.

In June 2022, Assoc Prof Zhou attended the American Association of Nurse Practitioners Conference—the first ambassador to be chosen from Southeast Asia. As an ambassador, she is able to build global connections to facilitate international collaborations, thereby elevating APN practice and research in Singapore.

Assoc Prof Zhou hopes to inspire people to join nursing and stresses the need to engage and train nurses based on their interests. She says the nursing workforce is the backbone of the healthcare system but a shortage of nurses is a global crisis—Singapore included—worsened by the COVID-19 pandemic.

"After I became an APN, the expanded clinical practice allowed me to add value to patients' care by filling up multiple clinical gaps. But there were still gaps that I realised were beyond my capability, which is why I started to do research and ended up doing a PhD—to explore how APNs can improve transition care."

Assoc Prof Zhou, NUS Nursing

Findings from her nationwide study (Woo et al., 2020) reported that only 30% of the registered nurses in the workforce are interested in becoming APNs but a large proportion of them are young (less than 35 years old) and inexperienced. This proportion of nurses do not get selected as they have yet to meet the minimum entry requirements for the APN-preparatory education at the Master of Nursing programme in NUS Nursing.

Assoc Prof Zhou said these young nurses who are lacking in years of clinical experience should not be overlooked. Efforts should be made to keep them engaged within the workforce while they build clinical experience in respective health institutions.

"Instead of waiting for others to fix existing problems, I do my part in building a better healthcare ecosystem." This is a work ethos Assoc Prof Zhou goes by and this is truly evident in all that she has done for advancing Nursing in Singapore.

She's a Diver-doctor in NDU

BY KOH ENG BENG, PHOTOS BY KENNETH LIN & COURTESY OF CPT (DR) CHIEW WENQI

She is the first Singaporean woman to undergo the gruelling United States Navy (USN) Diving Medical Officer Course (DMOC). Meet CPT (Dr) Chiew Wenqi, the formation medical officer of the Naval Diving Unit (NDU). Here's five things you need to know about her.

1. She is fascinated with special forces

Since young, Captain (CPT) (Dr) Chiew had always been interested in the military—especially the elite special forces who conduct exciting operations such as parachuting out of planes and diving into the sea.

So it's not surprising that she chose a military career with the Singapore Armed Forces (SAF).

2. She is a doctor

A recipient of the SAF Medicine Scholarship, CPT (Dr) Chiew obtained her medical degree from Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine).

Now as the formation medical officer in NDU, the 27-year-old treats illnesses and injuries associated with diving. An example is decompression sickness, which occurs when a diver swims to the surface too quickly.

3. She is sporty and fit

Back in her school days in Raffles Institution (RI), she was part of the soccer and taekwondo teams. She was also a recreational scuba diver.

For the record, CPT (Dr) Chiew scored 97 points for her latest Individual Physical Proficiency Test (IPPT)—60 push-ups, 60 sit-ups, and 11min 30s for 2.4km run.

4. First SG woman to attend the USN DMOC

The highlight of her military career so far? Attending the USN DMOC in Florida from July to October 2022.

Photo:
CPT (Dr) Chiew goes through dive training to better understand the challenges that naval divers go through.

The Republic of Singapore Navy (RSN) sends one or two medical officers to attend the DMOC annually. CPT (Dr) Chiew was the first woman from the RSN to do so.

The physically demanding course, including a five-week preparatory phase, stretched over three-and-a-half months.

Trainees were put through daily physical exercises that consisted of runs of up to 10km, as well as pool training such as water treading and breath holding.

For one particular training, CPT (Dr) Chiew had to tread water for two minutes, while carrying scuba tanks that weighed about 40kg more than twice her body weight!

"It was very physically challenging," said CPT (Dr) Chiew, who is 1.63m tall and weighs 50kg.

She also learnt to use the closed circuit rebreathing systems used by the US Navy SEAL and Explosive Ordnance Disposal teams. These are similar to the ones used by divers in NDU.

The various dive training, she said, allowed her to better understand the physical and mental challenges that divers go through underwater.

"When they have injuries or when they present with symptoms, I can understand their dive profile better and what they have done. So this helps me to make a better diagnosis and treatment for them."

During the DMOC, she also received hands-on practice in using the hyperbaric chamber as well as extensive training in diving medicine.

The hyperbaric chamber pressurises the air to mimic the underwater environment, and is used in the treatment of diving injuries.

5. She wants to inspire more women to join the Navy

CPT (Dr) Chiew said women who want to join the military need to have a certain level of physical fitness and resilience in order to get through the challenging training in the SAF.

When asked what advice she would offer them, she said: "If you are keen to join the NDU or Navy as a medical officer, take a leap of faith. This career choice will be an extraordinary and exciting one!"

If you are keen to join the NDU or Navy as a medical officer, take a leap of faith. This career choice will be an extraordinary and exciting one!"

This article was published originally in PIONEER (defencepioneer.sg).

CPT (Dr) Chiew checking on a patient in a hyperbaric chamber, which simulates the pressure of varying depths below sea level, in Sembawang Camp.

Is There Really A Good Way to Deliver Bad News?

BY DR NOREEN CHAN, HEAD AND SENIOR CONSULTANT, DIVISION OF PALLIATIVE MEDICINE, NATIONAL UNIVERSITY CANCER INSTITUTE, SINGAPORE

In healthcare, doctors and other healthcare professionals sometimes need to convey bad news to patients and families. It has been so for hundreds of years, for as long as the healing professions have existed. But it may surprise you to know that formal communication skills training for healthcare workers is a much more recent development.

I certainly was not taught how to communicate as an undergraduate nor as a junior doctor (which was a long time ago, many more years than I care to admit). Somehow we were expected to learn on the job, a case of communication skills being "caught" rather than taught.

I am embarrassed to recall the many mistakes I made along the way, but each stumble or blunder was also an important lesson, as was every observed encounter between a senior colleague and patient/family.

Two incidents come to mind: when I was a house officer in surgery, one of the patients in the ward was a man who had come in with abdominal pain and after a series of tests, had been diagnosed with advanced colon cancer.

During the morning ward round, it transpired that the patient had not yet been told the news, because the test results had only been available the previous evening. The medical officer and I looked at each other and our long list of patients, wondering who would volunteer

for the task, when the registrar said, "I'll talk to him, you carry on with the round and I will catch up." As we dashed off with a sense of relief, I glanced back and I saw him pulling a chair up to the patient's bedside and drawing the curtains. It occurred to me that what he was going to say to that man would change his life forever.

The second incident is from my time as a medical officer posted to the Emergency Department. One day a man was brought in. He had collapsed at the hawker centre, and despite our efforts did not survive. When his wife—now widow—arrived, I was asked to bring her to the "Quiet Room" to view the body. I knew the senior doctor in charge of our shift had spoken to her, so it was puzzling when she started peppering me with questions and comments like "How can it be? He's still warm! Look he is moving, I can see his chest moving"

I ended up using my stethoscope to let her hear her own heartbeat, then I placed the bell on the patient's chest so that she could hear that it was totally silent. She went quiet and I thought, aha! she finally gets it. So I was completely unprepared when she suddenly started wailing and crying, beating her fists on her dead husband's body and shaking the trolley rails. I had never witnessed acute grief like that before, and I was literally stunned. Fortunately, a kindly nurse came by and rescued me, and as I beat a hasty retreat, I once again glanced back and saw her put her arms around the shoulders of the grieving widow.

So it is not just about telling the news, it is about dealing with the aftermath of "dropping the bomb".

These days, communications workshops and courses are common, and we have established tips and approaches that are widely taught. One of the best known is the **SPIKES** Protocol[1].

This is how the mnemonic SPIKES can be interpreted:

Set-Up	Find a quiet private space, preferably somewhere everyone can be seated.
Perception	What does the patient/family already know or suspect?
Invitation	What does the patient/family want to know? Should we be detailed and blunt, or go "bit by bit"?
Knowledge	Deliver the information in bite-sized pieces, checking understanding along the way. This is sometimes known as "Tell-Ask-Tell".
Empathy	Respond to emotions and provide support.
Strategy and Summary	Sum-up what has been said, including any plans and "next steps".

"It is not just about telling the news, it is about dealing with the aftermath of 'dropping the bomb'."

The elegance of the approach is its simplicity; it is easy to understand and the principles can be widely applied. But of course, theory is one thing, application and practice something else altogether.

For example, how to deliver the information simply and effectively. A good strategy is "the warning shot", a short statement that warns listeners to brace themselves for what is coming, for example, "I'm afraid the result is serious". Then the news should follow, ideally using simple straightforward language, which is harder than you think. Doctors do have a tendency to want to deliver a lot of information, perhaps because they want to ensure full understanding, or because they want to lead up gradually to the main facts. But this may result in the patient and family's attention being scattered and the conversation losing focus, such that the main messages are not properly understood.

Next, the topic of Empathy, which is the capacity to understand or feel what another person is experiencing from within their frame of reference; in other words, being able to walk in their shoes. Empathy is crucial in building rapport and trust, and I have even heard a hostage negotiator use the term "tactical empathy". Many communications courses teach "micro-skills" which help to convey empathy, some verbal e.g. naming emotions, phrases like "tell me more", and some non-verbal i.e. using body language like nodding, leaning forward etc. These skills are important, but empathy is not just going through the motions, it is making a meaningful connection with the person(s) you are speaking to.

I think there is no one right way, there are better ways and worse ways. But ultimately, it has to be patient- and family-centred. Conveying bad news is like giving bitter medicine; it is done with a purpose and with best intentions, but has to be 'dosed' correctly for the best effect."

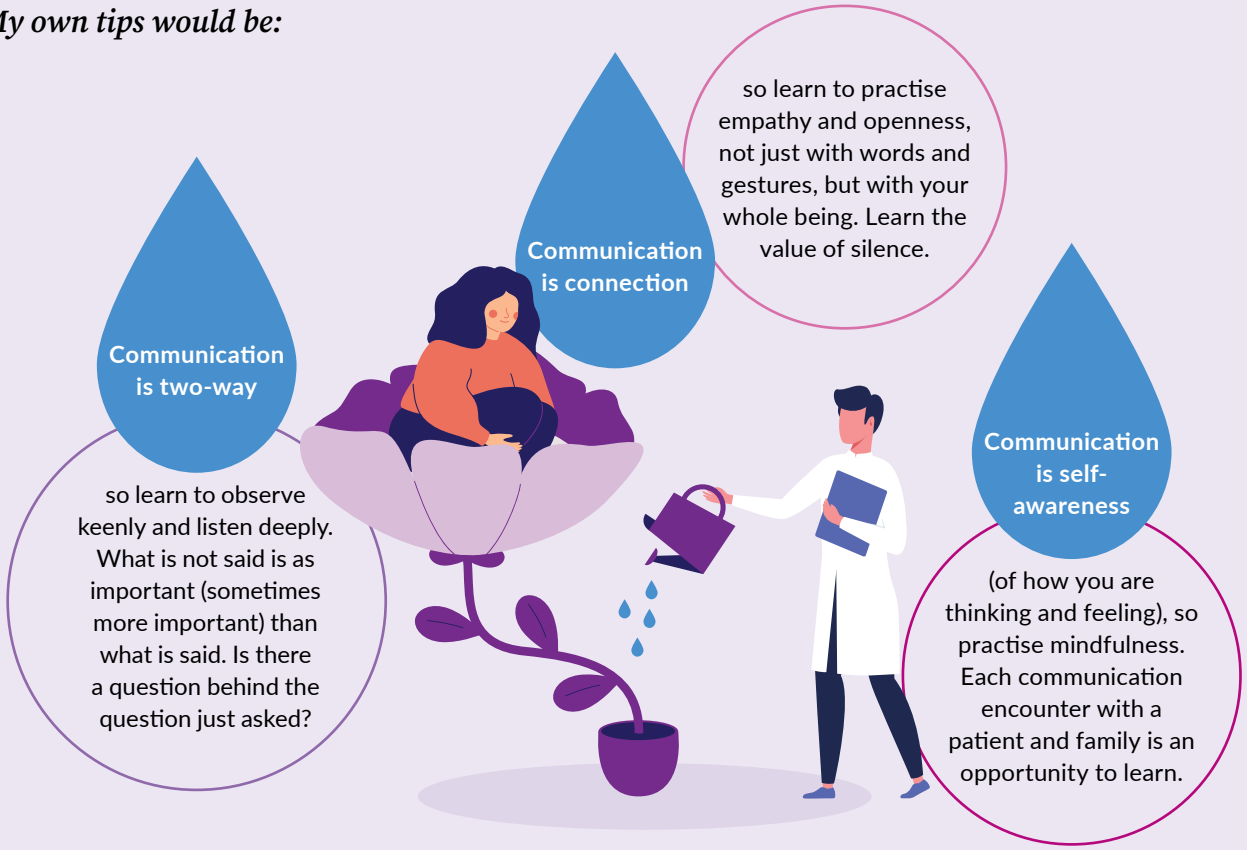
Many doctors find it stressful to convey bad news because of the emotions involved, and of course emotional situations are uncomfortable. It is natural to avoid what is awkward and uncomfortable: therefore many of us may respond to the other party's emotional cues by .... not responding to them! We use avoidance, deflection, distraction, downplaying or any number of strategies to get the conversation over and done with. Most of the time, we are not even aware we are doing it. But the danger with not acknowledging the emotional response, is that people may feel they have not been fully heard.

Finally, it must be emphasised that communication is two-way. It is a common mistake that we are so preoccupied with getting our message across, we forget to "tune into" the other party's message(s), and then wonder why we are not on the same wavelength. We need to listen actively, not just to what is said, but also to what is unsaid and "below the surface". I have learnt not to take questions and statements at face value, and will often ask to clarify e.g. "what do you mean?", "why did you say that?" etc.

So, is there a right way to deliver bad news? I think there is no one right way, there are better ways and worse ways. But ultimately, it has to be patient- and family-centred. Conveying bad news is like giving bitter medicine; it is done with a purpose and with best intentions, but has to be "dosed" correctly for the best effect.

The good news is that communication skills can be learnt and improved upon.

My own tips would be:

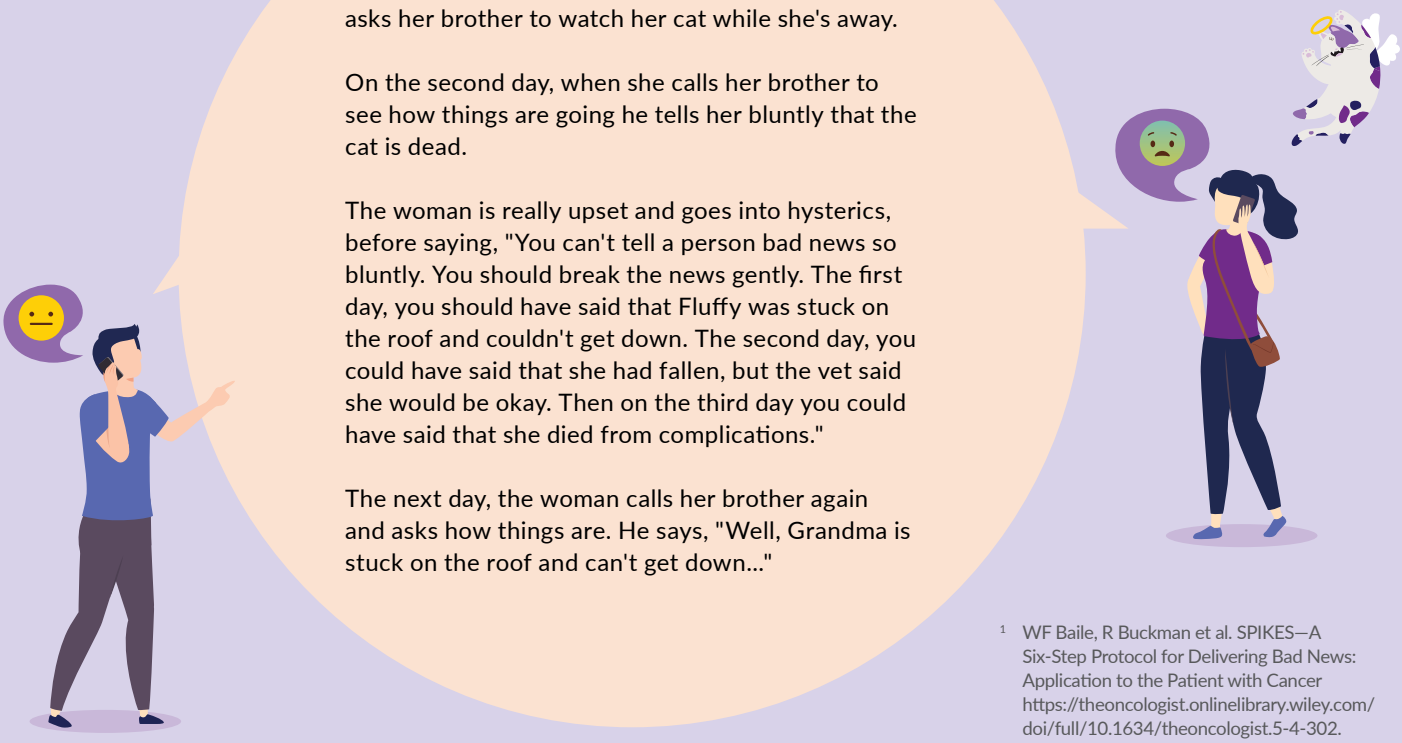


A woman decides to take a well-earned vacation and asks her brother to watch her cat while she's away.

On the second day, when she calls her brother to see how things are going he tells her bluntly that the cat is dead.

The woman is really upset and goes into hysterics, before saying, "You can't tell a person bad news so bluntly. You should break the news gently. The first day, you should have said that Fluffy was stuck on the roof and couldn't get down. The second day, you could have said that she had fallen, but the vet said she would be okay. Then on the third day you could have said that she died from complications."

The next day, the woman calls her brother again and asks how things are. He says, "Well, Grandma is stuck on the roof and can't get down..."



[1] WF Baile, R Buckman et al. SPIKES—A Six-Step Protocol for Delivering Bad News: Application to the Patient with Cancer https://theoncologist.onlinelibrary.wiley.com/doi/full/10.1634/theoncologist.5-4-302.

Artist Behind the Art:
Med Student Goes Viral with His Dystopian Cityscapes

BY NG KAI FROM WONDERWALL.SG

Phase I NUS Yong Loo Lin School of Medicine student Chen Yiming's detailed black-and-white illustrations put concepts like climate change, inequality and class to paper.

"Present Participle", "Babel", "Burrow", and more. Remember these words, because they just might be the title of an exhibition of artworks at a gallery near you one day. But even more memorable are undoubtedly the illustrations themselves. And the mind and hand behind them belong to unassuming Chen Yiming.

The 19-year-old is a med student at the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine) and a part-time artist (he prefers "hobbyist"), and has chalked up more than a 100k followers on Instagram, thanks to his engaging drawing-related content. He's even had juniors from school crediting his style as inspo for their final project.

The works are decidedly mesmerising: one's imagination runs wild just scrutinising the towering skyscrapers, dystopian-looking environments, complex architectural structures, and microscopic details galore.

The stark black-and-white contrast, the focus on buildings, and foreboding imagery all conspire to stir discussions about topics like "inequality", "class", and "climate".

"The easiest way to get people to think about something is to disturb them, hit them in a way that they don't it see coming. When we're comfortable, we don't really like to think outside the box," says Yiming.

"So I want to draw communities in a way that makes people go like, 'Oh, damn that's a bit sad', and then they start to think, 'Oh, that's interesting, maybe this is our future' and stuff like that. That's the way I like to communicate—it makes people have a more genuine and deeper reaction to [the artwork]."

It's clear that Yiming has reflected deeply about the ideas behind his works, detailing his thoughts on them. He shares that the process differs for each piece.

"I'll try to find a complement. So if I have a meaning that I want to express, then I'll find a way to do it aesthetically. And if I have an aesthetic that I want to hit, then I'll find some way I can make that meaningful," he says.

We speak to Yiming about his first encounter with art, the confluence of the worlds of art and medicine, and the pressures of going viral.

Yiming at his first exhibition, *"What Now?"* presented at *notgallery*. Photograph by Daren Tan @ darensnaps

Top: *"Burrow"* by Yiming

Bottom: *"Babel"* by Yiming

Photographs by Yiming @ yimingmade

Q: Do you remember your very first encounter with art?
A: My parents are engineers. Before computerisation, there was a lot of drafting paper around because they would do a lot of drafting. And as a kid, you're just naturally curious. So I picked up pens and just started doodling with them.

I also liked watching "Cars" a lot. It was my favourite animated movie. So I drew a lot of Cars, to the point where there were entire files of just Cars drawings.

Then, it was Minecraft, and then there was a lot of Lego. I was a huge Lego fan back then—maybe it shows in my love for buildings!

Q: How did you develop your style?
A: I tried out this style at the very beginning in Sec 2 because there was this artist I really liked online—Sam Gillett. He does a lot of building drawings. I was like, "Ooh, that's quite cool. I should try this." I remember the very first thing I drew was this cabin and a bunch of trees. And then slowly, it just develped into this. He followed me back [on Instagram] very recently. Super fanboy moment!

Q: Just curious: how come you picked medicine over, say, architecture?
A: Oh, actually, funny story. My parents didn't want me to do medicine. I was very shocked because you hear all the time that that's what every Asian parent wants their kids to do—learn guitar, play tennis, play basketball and pursue medicine!

In Sec 4 and JC1, I was quite lost as to what I wanted to do. There were a few career paths that I considered: mainly, to teach, to do architecture, and also be a doctor. And among these three, medicine gave me the biggest challenge because I was quite a science student last time.

I was never really very good at talking or being interpersonal. So I thought, you know what, being a doctor kind of forces you to apply that science in a way where you have to talk to different people and hold a lot of sometimes very difficult conversations. And being a doctor was something that I could constantly see being meaningful in some way, and being very constructive to other people's lives.

The impact for something like architecture or teaching is a bit more indirect or delayed. For me, I need that direct impact to stay motivated, which is why, in the end, I chose medicine.

Q: How has art helped you become a better student of medicine?
A: Drawing has made me quite a detail-oriented person, which I guess does help, because a lot of learning in medicine comes from self-learning. Sometimes when I draw, I have to think of very small details, like all the textures of the buildings. So I guess that has somehow maybe trained me a little bit to always ask: "Is there something else going on here? Let me go and find out and Google a bit about this."

Q: Do you have a favourite piece?
A: I always come back to "Burrow". I didn't expect to love it that much. I wanted to make a very grim image. I think I was feeling a bit edgy at that point because it started with, I want to do something about climate again. I don't know why, but I just keep going back to climate-related works.

And I think a lot of climate stuff was happening in the news also. It began as a very black piece also, because a bunch of my previous works are bright like "Babel". I didn't really use the blacks a lot, so I was like, okay, this is a good learning opportunity.

I wanted to express the meaning that right now humanity is stuck in this downward spiral of fossil fuels. And now, arguably, maybe we can still get out of it. But I wanted to depict a world where there is literally no way that we can get out of.

And then I thought about how I was going to express it aesthetically. So the idea of digging deeper underground and forcing everyone to live underground because the surface level was too hot. And then the story kind of built itself from there.

Q: You're working on something called "Vital Signs", and the process behind it is different from "Burrow" and "Babel". Walk us through it!

A: I was very interested in the Shibuya crossing and the streets of Tokyo where there are advertisements everywhere. I wanted to include Singapore and a lot of Southeast Asian countries, but do it in like, a San Francisco style.

The work is called "Vital Signs", because I became very interested in different sign boards that we use in Singapore, from historical to more modern ones.

There's always some element of inequality and class in my work. So, from bottom to top, it's like a kind of class difference. At the bottom are the wet markets, the hawker centres, the streets that I grew up in, a lot of those small neighbourhood shophouses, HDBs. And slowly we get up to the malls, the older malls, the newer malls, and finally the CBD.

I wanted to show how different the signages are at these different levels of SES (socioeconomic status).

Congrats man—you've gone viral with reels racking up over a million views! With more than 100k pairs of eyes scrutinising your works, are there any added pressure?

A: I think having that amount of attention is, I guess, some pressure—pressure in a good way because I think it keeps me disciplined in creating content. Content creation is quite a good start for student artists, like, very young artists who don't really know where to start. A lot of good has come out of people from Singapore noticing what I do just because I put it on Instagram. Honestly, I should have started earlier. A good piece of advice for maybe my juniors from the Art Elective Programme (AEP), who want to pursue art as a side hustle, is to really just get on social media. I have no words for how transformative this has been.

There's a very good quote from this random YouTuber: "When you have one follower create like you have one million, and when you have one million, create as if you have one."

Scan to hear from Yiming on how he balances his demanding schedule as a medical student with his artistic pursuits here:

This article was first published on Wonderwall.sg

Photo: Yiming's workspace, where he sketches and creates, in his room in Sheares Hall, NUS. Photograph by Yiming @yimingmade.

Unlocking Singapore's HealthTech Potential: DTX HealthSG Leadership Masterclass

Singapore's healthcare industry is rapidly transforming, with the increasing adoption of digital technologies and the emergence of HealthTech startups offering innovative solutions.

THE BANYAN TREE

This column is dedicated to the pursuit of continuous learning and development and takes its name from the banyan tree. It has roots that grow deep, anchoring it firmly in the soil. The tree spreads its shade wide and far and provides space for reflection and discussion. We invite you to come and take a seat under its shade.

In this context, the DTX HealthSG Leadership Masterclass aims to provide insights and strategies for corporate solution providers, SMEs, entrepreneurs, clinical leaders, managers, and executives seeking to advance healthcare system goals and implement business decisions geared toward sustainable growth and innovation.

Scheduled to take place on 11-12 May 2023 at the NUSS Kent Ridge Guild House, the two-day workshop is designed to offer a practical understanding of the critical uses of technology in advancing healthcare system goals. Mr Maurice Tan, Programme Director, NUS Yong Loo Lin School of Medicine and Senior Consultant at MOH Office for Healthcare Transformation (MOHT), together with Prof Robert Morris, Chief Technology Strategist at MOHT; Prof Chia Kee Seng, Founding Dean of NUS Saw Swee Hock School of Public Health; and Mr Lim Cher Wee, Chief Operating Officer at MOHT will comprise the expert panel of speakers.

Participants will gain an understanding of the challenges and opportunities presented by Singapore's digital health transformation and the evolving HealthTech landscape. They will also acquire strategies for sustainable growth and innovation in the healthcare industry, and learn about the critical healthcare opportunities that can be addressed through innovative products and solutions.

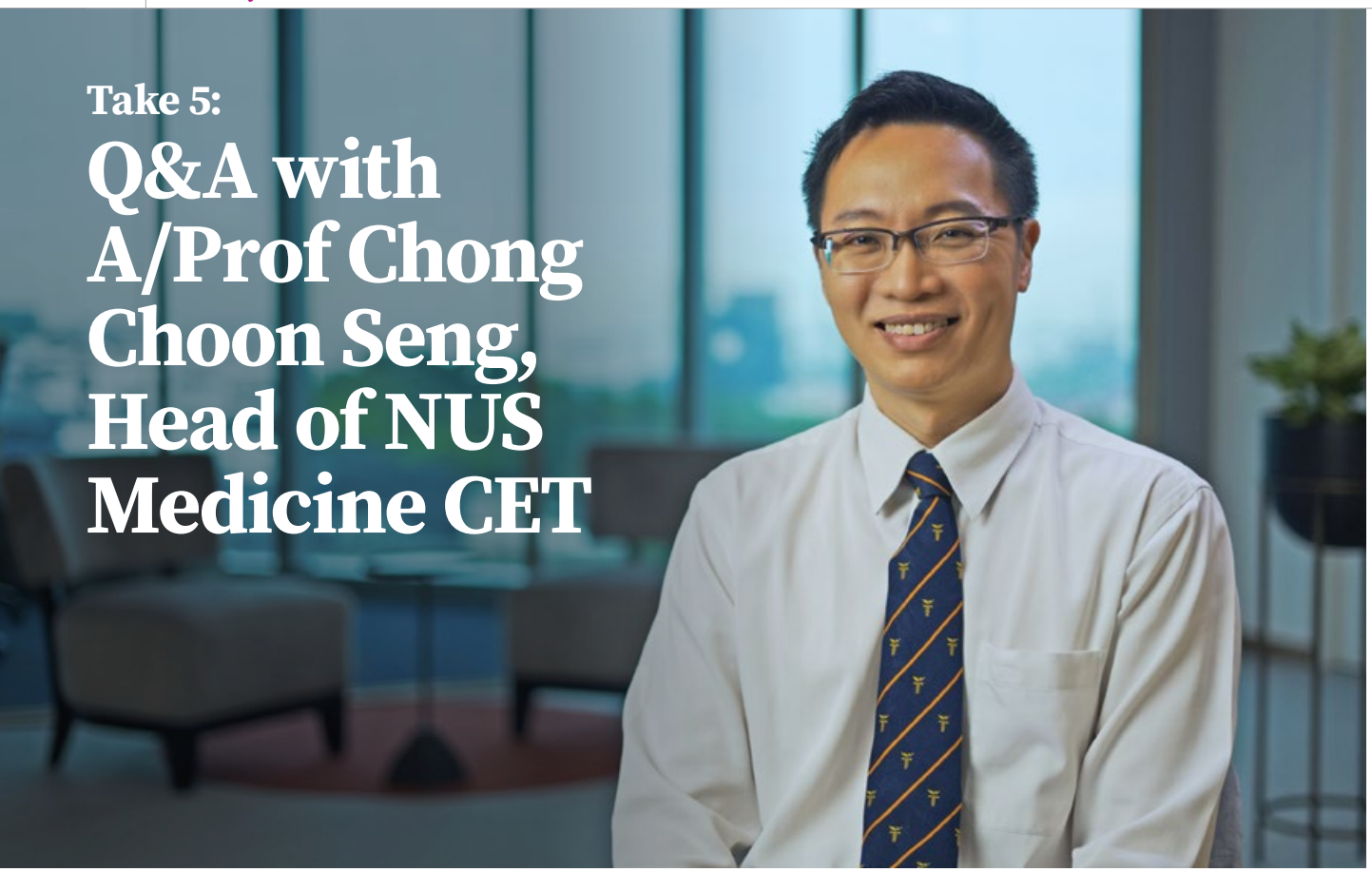
Programme highlights include Mapping the Future of Singapore's Health Ecosystem, Navigating the HealthTech Solution Landscape, Case Studies of Singapore's Digital Health Projects, HealthTech Innovation Showcase, Networking Luncheon and of course, Happy Hour.

The DTX HealthSG Leadership Masterclass is organised by the NUS Medicine Continuing Education and Training (NUS Medicine CET) as part of its Executive Education programme.

This event is an excellent opportunity for healthcare and business leaders who want to future-proof their teams and strategies in a rapidly changing healthcare landscape. Participants will connect with like-minded professionals, gain valuable insights and practical knowledge, and have the chance to develop strategies that can help them achieve their goals. They will be able to identify a point of entry for their business in healthcare, leverage the growth of the healthcare sector, develop a healthcare engagement strategy for their business, understand digital solutions for guiding their team competently, assess digital solutions to see if they align with company objectives, and more.

Please visit the NUS Medicine CET website for registration and programme details. #DTXHealthSG #DigitalTransformation #DigitalHealth

Scan the QR code to learn more about the course:



Take 5:

Q&A with A/Prof Chong Choon Seng, Head of NUS Medicine CET

Q: In its Skills Demand for the Future Economy Report, SkillsFuture Singapore (SSG) identified the Care Economy as an economic growth pillar. What's your take?
A: My view is that the Care Economy refers to the larger ecosystem of healthcare provisions and needs that go beyond hospital, inpatient, and even outpatient care. It encompasses providing social services, support services, as well as education on population needs.

Q: What are the impending challenges facing the Care Economy?
A: Globally, we are facing a healthcare professional manpower shortage. Also, we are facing a lot of different challenges, notably an ageing population. We also see a growth in different kinds of healthcare matters like precision medicine and digital medicine. All these require the training and the preparation of our current and future professionals to meet evolving needs.

Q: So, what can the community in the Care Economy do about it?
A: As healthcare providers, we are the core of this economy, and we also help to coordinate care at a larger scale to the general population. Healthcare in 20 to 30 years' time may be vastly different from how we look at it today. So it is important for us to embrace a culture of change. We need to be agile, understand what today's needs are and embrace change. For it is through this process of lifelong learning that we can aim to shape and mould not just our current healthcare practices, but also a practice that is relevant to the needs of our future generation.

“We need to be agile, understand what today's needs are and embrace change. For it is through this process of lifelong learning that we can aim to shape and mould not just our current healthcare practices, but also a practice that is relevant to the needs of our future generation.”

Scan the QR code to view an excerpt of the interview with A/Prof Chong Choon Seng:

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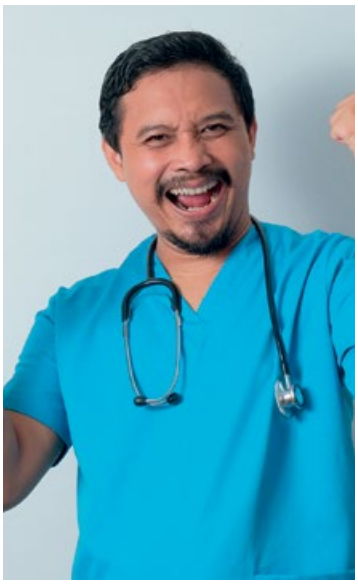

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For more information, visit our website **medicine.nus.edu.sg/continuing-education/**

Contact us: **medicine.cet@nus.edu.sg**

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