



PRESS RELEASE

Transforming the future of healthcare through artificial intelligence

NUS Medicine's Institute for Digital Medicine pilots novel N-of-1 (single subject) trial designs to improve patient outcomes with rapid and economical solutions

Singapore, 16 October 2020 — The stuff of science fiction not so long ago, artificial intelligence (AI) is now powering a dynamic new range of customised, single patient trials that are proving to be more effective than traditional, templated clinical treatments.

The trials led by the Institute for Digital Medicine at the NUS Yong Loo Lin School of Medicine (NUS Medicine) and involving teams drawn from backgrounds as diverse as engineering, healthcare economics, behavioural sciences, computing, public health, and public policy, are helping to improve patient outcomes through rapid and economical solutions.

These outcomes are being achieved by the use of AI to integrate ground-breaking advances in medicine and digital technology. The aim – to drive revolutionary trial design protocols and targeted healthcare solutions that deliver faster, and more effective clinical interventions. The Institute (also known as WisDM) has thus far pioneered a way to pinpoint effective drug mixes against COVID-19, and developed digital therapies to address cognitive decline for post-brain radiation therapy and other oncology patients as well as other aging and illness-related challenges.

Digital drug development for COVID-19

Through an interactive digital platform called IDentif.AI (Optimising Infectious Disease Combination Therapy with Artificial Intelligence), which leverages AI to calculate the most effective combination of drugs and doses, the NUS Medicine researchers have found that the most optimal drug combination regimen against COVID-19 comprises remdesivir, lopinavir and ritonavir.

The IDentif.AI platform looked at a pool of 12 drugs that were selected based on their status of being under evaluation in multiple clinical trials. IDentif.AI differs from conventional AI approaches, and does not rely on using pre-existing data to train algorithms and predict treatment regimens. Instead, it designs experiments using different permutations of drugs and doses to crowdsource the live virus to determine the combinations that optimise anti-viral activity. At the heart of IDentif.AI is a powerful, AI-discovered relationship between drugs and doses to efficacy and safety using a quadratic algebraic algorithm. This allows for the optimal combination, which resides among more than 530,000 possible combinations to be identified with only a few hundred experiments within 2 weeks. Through the platform's ability to leverage unforeseen drug interactions within each combination, optimised recommendations of the drugs and corresponding doses were then suggested. Results from the IDentif.AI platform have been observed independently from a team of international

collaborators on another strain of SARS-CoV-2, and two study protocols have been cleared to enable clinical studies should they be needed.

Said Professor Dean Ho, Director of WisDM, “We need rapid and economical solutions, and the IDentif.AI allows for digital drug development for COVID-19. Even as the world continues to race toward a vaccine, leveraging on AI can potentially open up a new pathway to accelerate the search for an accessible and optimised intervention that may help take the strain off healthcare systems.”

Novel trial designs for digital oncology

Through another AI-derived technology platform, CURATE.AI which provides actionable N-of-1 (i.e. single patient) combination therapy for the entire duration of patient care, trials are customised based on individual profiles, to develop drug therapies and interventions that achieve better outcomes for patients. Dynamically adjusting drug doses, CURATE.AI sustains the optimisation of combination therapy as patient responses are recorded.

In a previous pilot clinical study conducted in collaboration with a US-based hospital, a patient with advanced prostate cancer was recommended a 50% reduction in dose of an investigational inhibitor drug for increased efficacy. The patient subsequently resumed an active lifestyle as the lower dose also proved to be more tolerable. Another patient in Singapore with advanced cancer who was prescribed a reduced dose of nab-paclitaxel saw his lung tumour shrink while also maintaining a stoppage in progression of the cancer. This has further allowed for the patient to continue treatment for a much longer duration compared to most patients who are being given this drug. These findings have led to a clinical pilot trial that is currently recruiting patients¹.

Assistant Professor Raghav Sundar from the Department of Medicine and WisDM at NUS Medicine, and Consultant with the Department of Haematology-Oncology at the National University Cancer Institute, Singapore (NCIS) said, “In the current clinical context, the doses of chemotherapy drugs given in combination can be further optimised. Drug dosing in cancer treatments are typically based on the degree of side effects experienced by the patient. With CURATE.AI, each patient’s recommended dose is calibrated using clinical data generated from their individual response to treatment. This may redefine how we care for patients and leverage digital medicine to treat cancers.”

Medicine without the pill

In another expanded study using CURATE.AI, the team leveraged software as therapy to address aging and illness-related challenges in cognitive and physical performance, such as diabetes, cognitive decline and Alzheimer’s disease. Using the subject’s own input data (e.g. training intensity, current performance level) and output data (e.g. degree of improvement), a personalised three-dimension (3D) profile can be constructed to identify how different subjects perform under different intensities.

“Conventional learning approaches involve training on the same intensity or a paced increase in difficulty. However, these training regimes do not often result in the optimal outcome in every subject. In the context of digital therapy, CURATE.AI can create individualised profiles so that training may eventually be customised to improve performance,” said Prof Ho.

Moving forward, the team has received funding and clearance for a clinical study to assess a digital therapeutic addressing cognitive decline in patients who have received radiation

¹ More information can be found at: <https://clinicaltrials.gov/ct2/show/NCT04522284>

therapy to the brain. This study design will pair CURATE.AI with dynamically changing intensities of the software to provide diagnostic information regarding each patient's responses. These responses will in turn be used to personalise treatment. It is envisioned that this study will eventually lead to a therapy that can be remotely deployed in patient's homes.

Digital medicine for good

Beyond clinical diagnosis, the WisDM team aims to leverage AI and digital solutions to build sustainable and cost-neutral methods and treatments that can be deployed by all communities globally. Challenging the status quo early, their work centres on precision testing enabled by N-of-1 trial designs that have proven more effective than standardised clinical trial methods.

"The biggest tragedy that can happen with a one-size-fits-all approach is that we lose against the disease. We believe the future of healthcare lies in AI, and using N-of-1 trial designs allows us more time to innovate, so that we don't miss out on what is truly necessary to bring about better patient outcomes," Prof Ho added.

Delivering research aligned to national priorities

WisDM is one of nine new Translational Research Programmes (TRPs) at NUS Medicine aimed at creating a strong and coherent scientific base to deliver impactful and meaningful research outcomes for the School and Singapore's health system. Besides digital medicine, the other areas are Cancer, Cardiovascular Disease, Healthy Longevity, Human Potential, Immunology, Infectious Diseases, Precision Medicine and Synthetic Biology. These nine key focus areas, which are multi-disciplinary, and health and disease-based will create greater synergies and collaboration between basic scientists and clinician scientists, strengthen programmatic research and deliver research outcomes to address clinically relevant issues and applications that are aligned to national priorities.

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About the National University of Singapore (NUS)

The National University of Singapore (NUS) is Singapore's flagship university, which offers a global approach to education, research and entrepreneurship, with a focus on Asian perspectives and expertise. We have 17 faculties across three campuses in Singapore, as well as 12 NUS Overseas Colleges across the world. Close to 40,000 students from 100 countries enrich our vibrant and diverse campus community.

Our multidisciplinary and real-world approach to education, research and entrepreneurship enables us to work closely with industry, governments and academia to address crucial and complex issues relevant to Asia and the world. Researchers in our faculties, 31 university-level research institutes, research centres of excellence and corporate labs focus on themes that include energy; environmental and urban sustainability; treatment and prevention of diseases; active ageing; advanced materials; risk management and resilience of financial systems; Asian studies; and Smart Nation capabilities such as artificial intelligence, data science, operations research and cybersecurity.

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About the NUS Yong Loo Lin School of Medicine (NUS Medicine)

The NUS Yong Loo Lin School of Medicine is Singapore's first and largest medical school. Our enduring mission centres on nurturing highly competent, values-driven and inspired healthcare professionals to transform the practice of medicine and improve health around the world.

Through a dynamic and future-oriented five-year curriculum that is inter-disciplinary and inter-professional in nature, our students undergo a holistic learning experience that exposes them to multiple facets of healthcare and prepares them to become visionary leaders and compassionate doctors and nurses of tomorrow. Since the School's founding in 1905, more than 12,000 graduates have passed through its doors.

In our pursuit of health for all, our strategic research programmes focus on innovative, cutting-edge biomedical research with collaborators around the world to deliver high impact solutions to benefit human lives.

The School is the oldest institution of higher learning in the National University of Singapore and a founding institutional member of the National University Health System. It is Asia's leading medical school and ranks among the best in the world (Times Higher Education World University Rankings 2019 by subject and the Quacquarelli Symonds (QS) World University Rankings by Subject 2019).

For more information about NUS Medicine, please visit <https://medicine.nus.edu.sg/>