



PRESS RELEASE

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Less is more – shortened antibiotic treatment for ventilatorassociated pneumonia in ICU patients just as effective as standard course

26 January 2024 – Less is also better – that is what researchers have found while conducting a tri-nation clinical trial to see if shorter courses of antibiotics are as effective as longer prescriptions of the drug to treat ventilator-associated pneumonia.

The four-year long REducing Antibiotic tReatment Duration for Ventilator-Associated Pneumonia (REGARD-VAP) study involved 460 patients in 39 hospital intensive care units in Nepal, Thailand and Singapore. While personalised short-course treatment duration for patients with ventilator-associated pneumonia (VAP) was just as effective in reducing the duration of pneumonia in comparison to the standard treatment duration, the short-course treatment strategy also successfully reduced antibiotic side effects from 38% to 8%.

VAP is a common lung infection among critically ill patients in hospital intensive care units, who are dependent on ventilators to breathe. It occurs when bacteria invade the lower respiratory tract and thin lung tissues via the breathing tube. The infection leads to longer hospital stays, increased antibiotic use, and the risk of death is as much as 40%. The study's findings serve as a point of reference for antibiotic usage reduction and titration, so that the onset of antibiotic resistance can be prevented.

The study's author and infectious diseases physician Dr Mo Yin from the Infectious Diseases Translational Research Programme at the Yong Loo Lin School of Medicine (NUS Medicine) and Consultant from the Division of Infectious Diseases in the Department of Medicine at National University Hospital (NUH) said, "Antibiotics are the default treatment used for patients with ventilator-associated pneumonia, which is the commonest hospital-acquired infection in the intensive care units. However, antibiotics when used in indiscriminately in large amounts will make antibiotics less effective overtime and increase bacteria's resistance to antibiotics. This clinical study shows that the duration and the strategy of antibiotic treatment can be tailored based on how the patient responds to treatment and is feasible enough to be adopted even in settings with limited resources, coupled with constant evaluation by attending physicians."

The 460 patients with VAP were randomly assigned into two groups – a three-to-five day individualised, short-course antibiotic treatment plan and a longer, standard-of-course treatment plan of a minimum eight days. The main aim was to determine if the individualised short-course strategy is non-inferior to the usual standard-of-care duration, in terms of the increased risk of death or the recurrence of pneumonia happening within 60 days of enrolling into the study. Of the 460 participants, 41% in the individualised short-course group and 44% in the standard-of-care group either died or had pneumonia recurrence.

Participants were reviewed daily to assess if they met the criteria to stop antibiotics; the criteria included a core body temperature of less than or equal to 38.3 degree Celsius for 48 hours and a stable blood pressure. When the criteria were met, all participants in the short-course treatment strategy group were weaned off antibiotics after three to five days of receiving VAP treatment. For patients in the standard care duration group, the antibiotic treatment strategy lasted at least eight days, as determined by their primary physicians. Current standard-of-care antibiotic treatment can last up to two to three weeks, accompanied by higher risks of side effects and unnecessary economic costs.

The REGARD-VAP clinical trial was jointly funded by the Singapore National Medical Research Council and the United Kingdom Medical Research Council. The paper is titled *Reducing antibiotic treatment duration for ventilator-associated pneumonia (REGARD-VAP): a trial protocol for a randomised clinical trial*, and was published in the Lancet Respiratory Medicine on 23 January 2024.

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Interviewee Profiles

37-year-old Kara Lee-Wong Hui was recruited in 2019. She was admitted into the ICU at National University Hospital for 8 days due to meningoencephalitis, resulting in seizures. Meningoencephalitis is a rare and life-threatening condition where the brain tissues and the brain become infected at the same time. She has been returning to the hospital for annual follow-ups and is currently seizure-free for 4 years. As a participant of the REGARD-VAP study, Kara recalled that the process was easy to do and stress-free, which required her to provide samples of her stools and/or urine every month for three months. Kara feels heartened that she is able to add meaning and purpose to her life by doing her bit to advance medical research.

27-year-old Khairul Anwar Bin Silmi was recruited in 2021. He was hospitalised for trauma from a road traffic accident. In his groggy state, he was admitted to the ICU for 35 days and hospitalised for 51 days at National University Hospital. To get back on his feet, he persevered with 12 months of physiotherapy sessions, interspersed with many check-up appointments. He is currently well with no regular follow-ups needed at the hospital.

For media enquiries:

Amanda YAP Assistant Manager, Communications Yong Loo Lin School of Medicine National University of Singapore Email: <u>medajyjy@nus.edu.sg</u>

About 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 16 colleges, faculties and schools across three campuses in Singapore, with more than 40,000 students from 100 countries enriching our vibrant and diverse campus community. We have also established more than 20 NUS Overseas Colleges entrepreneurial hubs around the world.

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, research centres of excellence, corporate labs and more than 30 university-level research institutes 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.

For more information on NUS, please visit <u>nus.edu.sg.</u>

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 interprofessional 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 our doors.

In our pursuit of health for all, our strategic research programmes focus on innovative, cuttingedge 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 one of the leading medical schools in Asia and ranks among the best in the world (Times Higher Education World University Rankings 2024 by subject and the Quacquarelli Symonds (QS) World University Rankings by subject 2023).

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

About the National University Hospital (NUH)

The National University Hospital (NUH) is Singapore's leading university hospital. While the hospital at Kent Ridge first received its patients on 24 June 1985, our legacy started from 1905, the date of the founding of what is today the NUS Yong Loo Lin School of Medicine. NUH is the principal teaching hospital of the medical school.

Our unique identity as a university hospital is a key attraction for healthcare professionals who aspire to do more than practise tertiary medical care. We offer an environment where research and teaching are an integral part of medicine, and continue to shape medicine and transform care for the community we care for.

We are an academic medical centre with over 1,200 beds, serving more than one million patients a year with over 50 medical, surgical and dental specialties. NUH is the only public and not-for-profit hospital in Singapore to provide trusted care for adults, women and children under one roof, including the only paediatric kidney and liver transplant programme in the country.

The NUH is a key member of the National University Health System (NUHS), one of three public healthcare clusters in Singapore.