

David Lye Chien Boon

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Research Interests:

- SARS-CoV-2
- Antimicrobial resistance
- Dengue
- Clinical trials

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Research Profile: Scopus, Google Scholar

Biography

Professor Lye is Group Director (Research), Communicable Disease Agency; Senior Consultant, Department of Infectious Diseases, National Centre for Infectious Diseases; Professor, Lee Kong Chian School of Medicine and Yong Loo Lin School of Medicine; and Deputy Executive Director, Programme for Research in Epidemic Preparedness and Response (PREPARE), Singapore. He is co-director, Respiratory and Infectious Disease Programme, Lee Kong Chian School of Medicine.

He has published more than 410 peer-reviewed manuscripts in journals such as NEJM, Lancet, JAMA, JAMA Oncology, JAMA Pediatrics, Lancet Respiratory Medicine, Lancet Infectious Diseases, Lancet Microbe, Lancet Global Health, Annals Internal Medicine as well as Science, Nature Biotechnology, Nature Reviews Immunology, Nature Microbiology, Nature Communications, Science Translational Medicine, Journal Clinical Investigation and Journal Experimental Medicine. He was a Clarivate Highly Cited Researcher 2022-2024, and Stanford University Top 2% Scientist 2022-2024.

Professor Lye is President, Society of Infectious Disease (Singapore). He is an advocate for HIV prevention as Vice President, Action for AIDS. Internationally, he is President, Asia Pacific Society of Clinical Microbiology and Infection; ex officio, executive committee, International Society of Antimicrobial Chemotherapy.

Selected Publications

• Beigel JH, Tomashek KM, Dodd LE, Mehta AK, Zingman BS, Kalil AC, Hohmann E, Chu HY, Luetkemeyer A, Kline S, Lopez de Castilla D, Finberg RW, Dierberg K, Tapson V, Hsieh L, Patterson TF, Paredes R, Sweeney DA, Short WR, Touloumi G, Lye DC, Ohmagari N, Oh MD, Ruiz-Palacios GM, Benfield T, Fätkenheuer G, Kortepeter MG, Atmar RL, Creech CB, Lundgren J, Babiker AG, Pett S, Neaton JD, Burgess TH, Bonnett T, Green M, Makowski M, Osinusi A, Nayak S, Lane HC; ACTT-1 Study Group Members. Remdesivir for the Treatment of Covid-19 - Final Report. N Engl J Med. 2020 Nov 5;383(19):1813-1826. doi: 10.1056/NEJMoa2007764. Epub 2020 Oct 8. PMID: 32445440; PMCID: PMC7262788.

https://www.nejm.org/doi/10.1056/NEJMoa2007764?url_ver=Z39.882003&rfr_id=ori:rid:cross ref.org&rfr_dat=cr_pub%20%200pubmed

• Goldman JD, Lye DCB, Hui DS, Marks KM, Bruno R, Montejano R, Spinner CD, Galli M, Ahn MY, Nahass RG, Chen YS, SenGupta D, Hyland RH, Osinusi AO, Cao H, Blair C, Wei X, Gaggar A, Brainard DM, Towner WJ, Muñoz J, Mullane KM, Marty FM, Tashima KT, Diaz G, Subramanian A; GS-US-540-5773 Investigators. Remdesivir for 5 or 10 Days in Patients with Severe Covid-19. N Engl J Med. 2020 Nov 5;383(19):1827-1837. doi: 10.1056/NEJMoa2015301. Epub 2020 May 27. PMID: 32459919; PMCID: PMC7377062.

https://www.nejm.org/doi/10.1056/NEJMoa201530

Tan CW, Chia WN, Young BE, Zhu F, Lim BL, Sia WR, Thein TL, Chen MI, Leo YS, Lye DC, Wang LF. Pan-Sarbecovirus Neutralizing Antibodies in BNT162b2-Immunized SARS-CoV-1 Survivors. N Engl J Med. 2021 Oct 7;385(15):1401-1406. doi: 10.1056/NEJMoa2108453. Epub 2021 Aug 18. PMID: 34407341; PMCID: PMC8422514.

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Young BE, Fong SW, Chan YH, Mak TM, Ang LW, Anderson DE, Lee CY, Amrun SN, Lee B, Goh YS, Su YCF, Wei WE, Kalimuddin S, Chai LYA, Pada S, Tan SY, Sun L, Parthasarathy P, Chen YYC, Barkham T, Lin RTP, Maurer-Stroh S, Leo YS, Wang LF, Renia L, Lee VJ, Smith GJD, Lye DC, Ng LFP. Effects of a major deletion in the SARS-CoV-2 genome on the severity of infection and the inflammatory response: an observational cohort study. Lancet. 2020 Aug 29;396(10251):603-611. doi: 10.1016/S0140-6736(20)31757-8. Epub 2020 Aug 18. PMID: 32822564; PMCID: PMC7434477.

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31757-8/fulltext

• Tong SYC, Lye DC, Yahav D, Sud A, Robinson JO, Nelson J, Archuleta S, Roberts MA, Cass A, Paterson DL, Foo H, Paul M, Guy SD, Tramontana AR, Walls GB, McBride S, Bak N, Ghosh N, Rogers BA, Ralph AP, Davies J, Ferguson PE, Dotel R, McKew GL, Gray TJ, Holmes NE, Smith S, Warner MS, Kalimuddin S, Young BE, Runnegar N, Andresen DN, Anagnostou NA, Johnson SA, Chatfield

MD, Cheng AC, Fowler VG Jr, Howden BP, Meagher N, Price DJ, van Hal SJ, O'Sullivan MVN, Davis JS; Australasian Society for Infectious Diseases Clinical Research Network. Effect of Vancomycin or Daptomycin With vs Without an Antistaphylococcal β-Lactam on Mortality, Bacteremia, Relapse, or Treatment Failure in Patients With MRSA Bacteremia: A Randomized Clinical Trial. JAMA. 2020 Feb 11;323(6):527-537. doi: 10.1001/jama.2020.0103. PMID: 32044943; PMCID: PMC7042887.

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- Young BE, Ong SWX, Kalimuddin S, Low JG, Tan SY, Loh J, Ng OT, Marimuthu K, Ang LW, Mak TM, Lau SK, Anderson DE, Chan KS, Tan TY, Ng TY, Cui L, Said Z, Kurupatham L, Chen MI, Chan M, Vasoo S, Wang LF, Tan BH, Lin RTP, Lee VJM, Leo YS, Lye DC; Singapore 2019 Novel Coronavirus Outbreak Research Team. Epidemiologic Features and Clinical Course of Patients Infected With SARS-CoV-2 in Singapore. JAMA. 2020 Apr 21;323(15):1488-1494. doi: 10.1001/jama.2020.3204. https://jamanetwork.com/journals/jama/fullarticle/2762688
- Hansen J, Baum A, Pascal KE, Russo V, Giordano S, Wloga E, Fulton BO, Yan Y, Koon K, Patel K, Chung KM, Hermann A, Ullman E, Cruz J, Rafique A, Huang T, Fairhurst J, Libertiny C, Malbec M, Lee WY, Welsh R, Farr G, Pennington S, Deshpande D, Cheng J, Watty A, Bouffard P, Babb R, Levenkova N, Chen C, Zhang B, Romero Hernandez A, Saotome K, Zhou Y, Franklin M, Sivapalasingam S, Lye DC, Weston S, Logue J, Haupt R, Frieman M, Chen G, Olson W, Murphy AJ, Stahl N, Yancopoulos GD, Kyratsous CA. Studies in humanized mice and convalescent humans yield a SARS-CoV-2 antibody cocktail. Science. 2020 Aug 21;369(6506):1010-1014. doi: 10.1126/science.abd0827. Epub 2020 Jun 15. PMID: 32540901; PMCID: PMC7299284. https://www.science.org/doi/full/10.1126/science.abd0827?rfr dat=cr pub++0pubmed&url v er=Z39.88-2003&rfr id=ori%3Arid%3Acrossref.org
- Tan CY, Chiew CJ, Pang D, Lee VJ, Ong B, Wang LF, Ren EC, Lye DC, Tan KB. Effectiveness of bivalent mRNA vaccines against medically attended symptomatic SARS-CoV-2 infection and COVID-19-related hospital admission among SARS-CoV-2-naive and previously infected individuals: a retrospective cohort study. Lancet Infect Dis. 2023 Dec;23(12):1343-1348. doi: 10.1016/S1473-3099(23)00373-0. Epub 2023 Aug 2. https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(23)00373-0/fulltext
- Wee LE, Tang N, Pang D, Chiew C, Yung CF, Chong CY, Lee V, Ong B, Lye DC, Tan KB. Effectiveness of Monovalent mRNA Vaccines Against Omicron XBB Infection in Singaporean Children Younger Than 5 Years. JAMA Pediatr. 2023 Dec 1;177(12):1324-1331. doi: 10.1001/jamapediatrics.2023.4505.
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- Tan WC, Tan JYJ, Lim JSJ, Tan RYC, Lee ARYB, Leong FL, Lee SC, Chai LYA, Tan TT, Malek MIBA, Ong B, Lye DC, Chiew CJ, Chng WJ, Lim ST, Bharwani LD, Tan IB, Sundar R, Tan KB. COVID-19 Severity and Waning Immunity After up to 4 mRNA Vaccine Doses in 73 608 Patients With Cancer and

621 475 Matched Controls in Singapore: A Nationwide Cohort Study. JAMA Oncol. 2023 Sep 1;9(9):1221-1229. doi: 10.1001/jamaoncol.2023.2271. PMID: 37440245.

COVID-19 Severity and Waning Immunity After up to 4 mRNA Vaccine Doses in 73 608 Patients With Cancer and 621 475 Matched Controls in Singapore - PMC (nih.gov)

Notable Research/Innovation Awards & Grants from Past 5 Years

Name of Awards & Grants	Year Obtained
NMRC COVID-19 Research Fund A Multicenter, Adaptive, Randomized Blinded Controlled Trial of the Safety and Efficacy of Investigational Therapeutics for the Treatment of COVID-19 in Hospitalized Adults	2020
NMRC Clinical Trial Grant Investigator-Initiated Trials Early oral step-down versus continued intravenous antibiotic therapy for uncomplicated Gram-negative bacteraemia	2021
NMRC Clinician Scientist Individual Research Grant (CS-IRG) Gut microbiome recovery in patients with Gram-negative Bacteraemia receiving early oral stepdown antibiotic therapy versus prolonged/continued intravenous antibiotic therapy	2022
NMRC Clinician Scientist Individual Research Grant (CS-IRG) Quantifying the risk of gut microbiome disruption and disease due to antibiotic therapy by leveraging on the Singapore-led multicentre INVEST trial	2023

Translating Research/Innovation Into Healthcare

- Severe symptoms more likely in those who took Sinovac jab. Published on 14 Apr 2022. https://www.straitstimes.com/singapore/health/severe-covid-19-symptoms-5-times-more-likely-in-those-infected-who-got-sinovac-vaccine-than-pfizer-one-study
- Severe Covid-19 symptoms 5 times more likely in patients who got Sinovac rather than Pfizer jab: Study. Published on 14 Apr 2022.
 https://tnp.straitstimes.com/lifestyle/health/severe-covid-19-symptoms-5-times-more-likely-patients-who-got-sinovac-rather-pfizer
- "Local study: Compared with mRNA vaccines, those who received Sinovac vaccine stand five times higher chances of developing severe symptoms after contracting COVID-19本地研究:施打科兴者染冠病 重症风险高5倍". Published on 14 Apr 2022. *No url

- Clinical trials evolving as they advance treatment. Published on 23 May 2022.
 https://www.straitstimes.com/singapore/spore-sets-sights-on-being-regional-centre-for-clinical-trials-from-diabetes-to-cancer
- Local study shows unvaccinated individuals have the lowest antibody against new virus strain even if they had been infected by BA.1 or BA.2 before 本地研究:未接种即使染过BA.1或BA.2 对新毒株抗体量最. Published on 16 Aug 2022. *No url
- New comparative study by Duke-NUS and NCID provides insight on the rise of Omicron. Published on 10 Oct 2022.
- https://www.asiaresearchnews.com/content/new-comparative-study-duke-nus-and-ncid-provides-insight-rise-omicron
- medicineworldcouncil.com/health-news/new-comparative-study-provides-insight-on-the-rise-of-omicron/
- medicalxpress.com/news/2022-10-insight-omicron.html#lightbox
- "Study on contagious nature of Omicron variant ஓமிக்ரான் தொற்றும் விதம் ஆய்வு".
 Published on 12 oct 2022. *No url
- COVID-19 boosters provide better immunity against SARS-CoV-2 variants in elderly Singaporeans.
 Published on 12 oct 2022.
 medicalxpress.com/news/2022-10-covid-boosters-immunity-sars-cov-variants.html
- "本地研究:更能躲开抗体造成感染**奥密克戎毒株**让接种人群更好与冠病共存 (Omicron strain allows vaccinated populations to better coexist with COVID-19)" Published on 13 Oct 2022.
 *No url
- Contagious nature of Omicron variant helped societies transition to living with Covid-19: Study. Published on 13 Oct 2022.
 straitstimes.com/singapore/contagious-nature-of-omicron-variant-helped-societies-transition-to-living-with-covid-19-study
- "**与其他**变异毒株相比 **奥密克戎更能**躲避免疫反应 (Compared to other mutated variant, Omicron better evade immune response)" Published on 13 Oct 2022. *No url

Health Impacts (CY2022 Publications)

- 1. Virological and serological kinetics of SARS-CoV-2 Delta variant vaccine breakthrough infections: a multicentre cohort study
 - a) Paper was cited as part of the scientific opinion analysis by European Food Safety Authority (ESFA) tasked by European Centre for Disease Prevention and Control (An agency of the European Union). EFSA was asked to review the scientific literature related to animal species susceptible to SARS-CoV-2 infection that play a role in its epidemiology. An assessment of the

current epidemiological situation and of the risk for human and animal health posed by SARS-CoV-2 infection in animal species of concern was also conducted, which should serve to recommend options for reviewing the monitoring strategies for SARS-CoV-2 infection in animal species of concern.

- b) Paper was cited as a working paper under Finnish Institute for Health and Welfare (THL, Finnish: Terveyden ja hyvinvoinnin laitos as part of an analysis to study the maintenance of vaccine protection against corona infection and severe coronavirus disease as well as the protection of people in risk groups aged over 70 and aged 16-69 against corona infection after the second vaccine dose and against the coronavirus disease requiring outpatient treatment in Finland THL is the biggest expert organisation under the ministry and its most important source of consultation regarding scientific knowledge.
- c) Paper was cited by the French Society of Hospital Hygiene (SF2H) on the protection of patients and professionals in the context of COVID-19 where the members of the Scientific Council of the SF2H proposed a set of useful measures for the protection of patients and professionals in health and medico-social establishments. These measures must be adapted to the particulars of the establishments and to the local situation of the epidemic. (Note: source is from Google Scholar)

The SF2H society is composed of professionals working in the field of hygiene promotion in health care, to promote safety and quality of care, epidemiology, prevention and the fight against healthcare associated infections including nosocomial infections; safety and health awareness, evaluation, accreditation and risk management in the field of healthcare associated infections.

Policy citation link (Plum X Metrix):

https://plu.mx/plum/a/policy_citation?doi=10.1016/j.cmi.2021.11.010

- 2. Clinical and virological features of SARS-CoV-2 variants of concern: a retrospective cohort study comparing B.1.1.7 (Alpha), B.1.315 (Beta), and B.1.617.2 (Delta)
 - a) Paper was cited by **World Health Organisation (WHO)** as part of COVID-19 Weekly Epidemiological Update to the public on COVID-19. WHO has based on the papers published to focus on SARS-CoV-2 Variants of Interest and Variants of Concern. Recommendation to prevent the spread of COVID-19 pertaining to the new VOCs were then provided based on that. WHO, in collaboration with national authorities, institutions and researchers, routinely assesses if variants of SARS-CoV-2 alter transmission or disease characteristics, or impact vaccine, therapeutics, diagnostics or public health and social measures (PHSM) applied by national authorities to control disease spread. Systems have been established to detect signals of potential Variants of Concern (VOCs) or Variants of Interest (VOIs) and assess these based on the risk posed to global public health. As these risks evolve, WHO updates the list of global VOIs and VOCs (Table 2) to support setting priorities for surveillance and research, and ultimately guide response strategies.
 - b) Paper was cited in the COVID-19 Science Brief of CDC. COVID-19 Science Briefs provide a summary of the scientific evidence used to inform specific CDC guidance and

recommendations. The Science Briefs reflect the scientific evidence, and CDC's understanding of it, on a specific topic at the time of the Brief's publication. 1) All COVID-19 vaccines currently approved or authorized in the United States 2) Available evidence suggests the currently approved or authorized COVID-19 vaccines are highly effective against hospitalization and death for a variety of strains 3)Limited available data suggest lower vaccine effectiveness against COVID-19 illness and hospitalization among immunocompromised people 4) The risk for SARS-CoV-2 infection in fully vaccinated people cannot be completely eliminated as long as there is continued community transmission of the virus.

Policy citation link (Plum X Metrix):

https://plu.mx/plum/a/policy_citation?doi=10.1093/cid/ciab721

- 3. Monkeypox: disease epidemiology, host immunity and clinical intervention
 - a) Paper was cited by Australia Government as part of Communicable Diseases Network Australia (CDNA) National Guidelines for Public Health Unit.

Policy citation link (Plum X Metrix):

https://plu.mx/plum/a/policy_citation?doi=10.1038/s41577-022-00775-4

- 4. Effectiveness of a Fourth Dose of COVID-19 mRNA Vaccine Against Omicron Variant Among Elderly People in Singapore
 - a) Paper is cited as part of Public Health Scotland COVID-19 Statistical Report, A Management Information release for the public. This report summarises the current COVID-19 data in Scotland, presenting statistics on estimated infection levels from the ONS COVID Infection Survey, which is currently our best understanding of community population prevalence. The report also presents data on wastewater infection levels, reproduction (R) number, reported COVID-19 cases, COVID-19 hospital and ICU admissions and COVID-19 vaccine effectiveness. Published management information are non-official statistics which may be in the process of being transitioned into official statistics.

Public Health Scotland is Scotland's national agency for improving and protecting the health and wellbeing of Scotland's people.

Plum X Metrix Link:

https://plu.mx/plum/a/policy_citation?doi=10.7326/M22-2042

- 5. Association of Homologous and Heterologous Vaccine Boosters With COVID-19 Incidence and Severity in Singapore
 - a) Paper was cited by the Federal office of public health (FOPH) and Federal Commission for Vaccinations (CFV), Switzerland as part of the vaccination recommendation against COVID-19 for Spring/Summer 2023. The analysis concluded by FOPH and the CFV based on the scientific papers that there will not be any recommendations for vaccination against

COVID-19 for spring/summer 2023 given the expected low circulation of the virus and the high level of immunity in the population.

b) The Federal Office of Public Health (FOPH) is part of the Federal Department of Home Affairs. Along with the cantons it is responsible for public health in Switzerland and for developing national health policy.

The CFV acts as an advisory order to the Federal Council, the Federal Department of the Interior (DFI) and the Federal Office for Public Health (FOSP) for all questions related to vaccination. It is independent of industry. The CFV is a commission of the Confederation made up of independent experts who play an important role of mediator between the authorities, the specialized circles and the population with regard to vaccination. Its mandate is to scientifically advise the authorities during the development of recommendations in this area.

Plum X Metrix Link:

https://plu.mx/plum/a/policy_citation?doi=10.1001%2Fjama.2022.1922

Collaborator Role

- 6. Efficacy and safety of two neutralising monoclonal antibody therapies, sotrovimab and BRII-196 plus BRII-198, for adults hospitalised with COVID-19 (TICO): a randomised controlled trial
 - a) Paper is cited as a guideline by **World Health Organisation (WHO)** for Therapeutics and COVID-19. This living guideline from the World Health Organization (WHO) incorporates new evidence to dynamically update recommendations for COVID-19 therapeutics.

Policy citation link (Plum X Metrix):

https://plu.mx/plum/a/policy_citation?doi=10.1016/S1473-3099(21)00751-9