



Driving Impactful Research at Clinical Sciences Building



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Challenges in the Assessment of Medical Devices

Health technology assessment (HTA) has increasingly been used and become important in decision-making during recent years. Although the principle of HTA can be applied to all health technologies, we are confronted with methodological challenges due to specific characteristics of technologies ranging from pharmaceuticals, diagnostic tests to medical devices. The pressing need to use HTA as a policy instrument for sustainable health care systems prompted us to look into methodological adaptations for the assessment of medical devices.

Unlike pharmaceuticals, medical devices -comprising a very heterogeneous collection of technologies, are subjected to less stringent regulatory systems. Devices only need to demonstrate performance and safety to achieve a product certification such as a CE mark for marketing purpose. This inevitably will result in a less extensive body of evidence for devices and pose difficulties in comparing the clinical effectiveness of medical devices. Secondly, the pricing of medical devices is also more dynamic than that of pharmaceuticals

because of the rapid diffusion of new entrants in the market. As a result, the cost-effectiveness findings being dependent on the temporal changes in the costs of devices vary over time. We illustrate how we dealt with these challenges with our recent work that assessed the cost-effectiveness of coronary drug-eluting stents.

The development of stents used in patients with coronary artery disease undergoing percutaneous coronary intervention has evolved. To gain insights into the use of a new line of coronary drug-eluting stents in clinical practice, we analysed a real-world population from a prospectively collected clinical database. We generated clinical data to complement evidence synthesised from (limited) existing literature. Besides, randomised control trials may not provide a realistic representation of the economic consequences of use due to the protocol-driven consumption of resources for implantations and follow-ups which differ from routine clinical practice. However, real-world data may suffer from selection bias given that the allocation of patients to either treatment or control group is not

random. Therefore, we applied propensity score matching to account for confounders and minimise treatment selection bias. To overcome the swinging costs of devices, we performed threshold analysis to determine the cost differential demarcating the price of the device which can change the conclusion in our cost-effectiveness analysis. This information on the economic value is pertinent considering the dynamic nature of device cost.

From our study, we have identified several specific issues that need to be addressed to produce reliable and useful information on the assessment of medical devices to support decision making. We presented our study at the recent Annual Scientific Meeting organised by the Singapore Cardiac Society, Singapore.

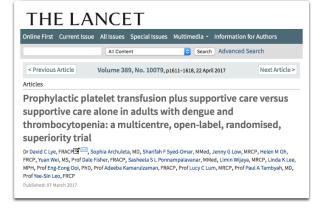
Contributed By: Pharmacy and Therapeutics Office Group Health Informatics National Healthcare Group

Prophylactic Platelet Transfusion Plus Supportive Care Versus Supportive Care Alone in Adults with Dengue and Thrombocytopenia

This multicentre, large randomised trial among the Institute of Infectious Diseases and Epidemiology (IIDE) at Tan Tock Seng Hospital (TTSH), National University Hospital (NUH), Singapore General Hospital (SGH), Changi General Hospital (CGH) and University Malaya Medical Centre (UMMC), Malaysia highlighted the ineffectiveness of prophylactic platelet transfusion compared with supportive treatment alone, in preventing bleeding in adult dengue patients with severe thrombocytopenia.

Dengue is the most common vector-borne infection worldwide. It is often associated with thrombocytopenia, and prophylactic platelet transfusion is widely used despite the dearth of robust evidence. Hence, the aim of the study was to assess the efficacy and safety of prophylactic platelet transfusion in the prevention of bleeding in adults with dengue and thrombocytopenia.

An open-label, randomised, superiority trial was conducted from 2010 to 2014 in five hospitals in Singapore and Malaysia recruiting \ge 21 years old, laboratory-confirmed dengue and thrombocytopenia (\le 20,000 platelets per μ L), without persistent mild bleeding or any severe bleeding. A total of 372 patients were randomly assigned to the transfusion group (n=188) or the control group (n=184).



It was found that clinical bleeding by day 7 or hospital discharge occurred in 40 (21%) patients in the transfusion group and 48 (26%) patients in the control group (risk difference -4·98% [95% confidence interval (CI) -15.08 to 5.34]; relative risk 0.81 [95% CI 0.56 to 1.17]; p=0.16). 13 adverse events occurred in the transfusion group and two occurred in the control group (5.81% [-4.42 to 16.01]; 6.26 [1.43 to 27.34]; p=0.0064). Therefore, in view of the scarcity and potential safety concerns of blood products in resource-limited settings, prophylactic platelet transfusion for patients with uncomplicated dengue is not recommended, since no benefit in reduction of clinical or severe bleeding or improvement in platelet count recovery was shown, and might be associated with adverse events. This clinically significant finding was recently published in Lancet, a prestigious journal.

Contributed By:

Mr Htet Lin Htun, Research Assistant | Associate Professor David Lye, Senior Consultant | Professor Leo Yee Sin, Director

ACRES: An Autism Cognitive Rehabilitation Programme for Executive Functioning Skills

This study aims to develop and evaluate the effectiveness of a computerised cognitive rehabilitation programmes (CRP) that focus on improving each of the executive functions (i.e. planning, mental flexibility and inhibitory control) among children with Autism Spectrum Disorder (ASD). Tasks within the programme will also incorporate tasks that closely mimic daily living demands to help them applying skills learnt to the real-life environment.

Phase 1 of this study is to develop the CRP using a serious game concept. Each task will include instructions, learning trials and difficulty levels automatically adjusted to participants' performance. Autism-friendly strategies will also be incorporated throughout the programme. All levels will

provide immediate feedback regarding accuracy of responses.

In Phase 2, a total of 40 children with ASD aged between 7 to 12 years old will be enrolled. Child participants will be randomised into either the intervention arm or the waitlist-control arm. Both groups will complete a 3-month CRP, with waitlist-control arm receiving the CRP after study completion. Child participants will complete neuropsychological assessment, while parents, teachers and clinicians will complete questionnaires at three time points in the study.

With the development of the proposed CRP, we hope that some individuals with ASD are able to utilise a mobile app at their own convenience in the future. Through this app,

improvements in executive functions can be achieved in a more cost-effective manner and individuals may be able to generalise these skills in real-life setting. As such, manpower and therapy hours needed in the clinic could be reduced.

Contributed by: Ms Goh Tze Jui

Senior Psychologist Department of Child and Adolescent Psychiatry Institute of Mental Health

A/Prof Cai Yiyu

Associate Professor School of Mechanical & Aerospace Engineering Nanyang Technological University

Clinician-Scientist Preparatory Programme (CSPP) Awardees from NSC Share Their Thoughts on Their Respective Research Projects

Assessing the Functional Significance of Candidate Genes Associated with Acne Vulgaris Using Inducible Mutation System in Sebocyte Organoid Models

My project aims to investigate the functional significance of genetic variants associated with acne vulgaris in the local population using in-vitro cellular and organoid models. This will give us better insight into the genetic pathogenesis of this common skin condition, and hopefully allow us to develop targeted therapeutic strategies in the future.

The CSPP equips junior clinicians with early research exposure through formal training and mentorship. I am grateful to have this invaluable platform to further develop my career as a clinician-scientist.



Contributed By:

Dr Kenneth Fong
Seamless Trainee
Dermatology

Pathophysiology of Itch in Atopic Dermatitis: A 3-Dimensional Study of Itch Mediators and Cutaneous Innervation

I am interested in translational research. Itch is the most common symptom and main source of morbidity in dermatology. Despite the high incidence of itch in eczema, the pathophysiology of itch in eczema is still poorly understood. The identification of pathological changes in the cutaneous nervous system and the associated itch receptors can uncover potential targets for effective anti-pruritic treatments. Itch has been an area of interest for me and I have undertaken an eight-month research fellowship under the mentorship of Dr Tey Hong Liang, who subspecialises in pruritus and skin imaging.



Contributed By: Dr Cao Taige Seamless Trainee Dermatology

Through CSPP, I would like to learn, in a systematic manner, research methodology and research ethics, as well as wet bench practices under the mentorship of Dr Tey and Dr Ng Lai Guan from A*STAR. CSPP will be a great primer for my future career as a clinician-scientist in dermatology. I will have the opportunity to work with both the clinician as well as scientist in this project and integrate and correlate the basic science knowledge gained through wet bench work with clinical findings.

Elucidating the Role of Innate Immunity Involving IL-1 Cytokines and Inflammasome Signaling Pathways in the Pathogenesis of Psoriasis

I feel grateful to be a CSPP awardee and delighted to embark on this journey to develop my skills as a clinician-scientist. I seek to investigate the role of innate immunity underlying the pathogenesis of psoriasis, in particular looking at IL-1 cytokines and inflammasome signaling pathways in my research study.

Under this structured training experience and mentoring guidance, I am confident of gaining invaluable skills and insights to take on a leading role in research in future.



Contributed By: **Dr Sophie Cai** Seamless Trainee Dermatology

Congratulations to the following Awardees of the NHG-NTU Clinician-Scientist Fellowship (CSF)!



Dr Melvyn Zhang*Associate Consultant
Addiction Medicine, IMH



Dr Ho Eu ChinConsultant
Otorhinolaryngology, TTSH

The awardees will be pursuing their PhD at the Lee Kong Chian School of Medicine,
Nanyang Technological University, Singapore

For more information, please visit <u>www.research.nhg.com.sg</u> (Research Career Development → Schemes for Doctors)

*NMRC Research Training Fellowship (RTF) Awardee Please click here to find out more about the NMRC RTF

GOOD TO **READ!**

An interesting article on The Living Donor; A Tale of Money, Mania, and Clinical Mastery.

Click here to read!



Data is the lifeblood of any research activity. Hence, it is crucial to have a robust data collection workflow when conducting research. The process of data collection is still largely manual for a significant number of researchers. Research data is first recorded on hardcopy forms and later transcribed into a spreadsheet. This process, while relatively easy to implement, is often plagued by incomplete forms, illegible handwriting and transcription errors. This results in low-quality dataset, the integrity and reliability of which is questionable.

The Research Electronic Data Capture (REDCap) system was selected by NHG to be the Electronic Data Capture (EDC) platform to support researchers by providing an effective solution to the data quality problems faced by them. An EDC system has the ability to ensure quality datasets through the use of real-time data entry validation, audit trails and tools for systematically identifying and resolving

data discrepancies efficiently. REDCap is a software solution and workflow methodology for designing clinical and translational research databases developed by Vanderbilt University in 2014.

REDCap is an easy-to-use web application designed to support electronic data capture for research activities in a systematic and efficient manner. Using a menu-driven interface, researchers can easily create web-based Data Capture Forms with built-in features such as data validation and subsequently export the collected data for analysis, without the need for in-depth technical knowledge or constant IT support. Since its launch on 01 September 2016, REDCap has attracted over 100 users and this number, as well as the number of projects have been climbing steadily. It currently hosts 20 live research projects.

A 5-year Population Health research project is using REDCap and riding on its ability to use tablet devices for offline data collection in the community. This enables the project

to capture higher quality data with better efficiency while using much fewer resources, as compared to the conventional method of collation using printed survey forms.

REDCap training courses are held every quarter and are expected to grow in its popularity among NHG researchers. It is hoped that this tool will contribute to better research outcomes and healthcare for all.

For more information about the NHG REDCap system, please visit: bit.ly/NHGRedcap



Contributed By:
Mr Yeo Kian Wah
NHG REDCap System Administrator
Research & Development Office
National Healthcare Group

Driving Impactful Research at Clinical Sciences Building

Impactful research is the hallmark of a world-class medical school and the Lee Kong Chian School of Medicine (LKCMedicine) is committed to advancing research areas that will improve the quality of life for people in Singapore and beyond. With the opening of the Clinical Sciences Building (CSB) at the Novena Campus, LKCMedicine is integrating not only its students but also its research faculty with the multifaceted clinical environment of HealthCity Novena.

LKCMedicine's Dean Professor James Best said, "The CSB is a symbol of our ambition to bridge the gulf between pre-clinical research or studies with the clinical world... Situated at the heart of the Novena HealthCity, LKCMedicine will act as a catalyst for clinically significant discoveries and innovations in teaching."

The LKCMedicine research laboratories are based on an "open-lab" concept with no walls or partitions separating research groups. This format creates open communication between scientists with varying expertise, promotes synergy in collaborative research and facilitates the establishment of interdisciplinary research units. This collaborative spirit is visible across LKCMedicine's research floors which are linked via a wide open stairwell that ends in an open collaboration space.

Assistant Professor of Molecular Medicine Sanjay Chotirmall, who received the Transition Award awarded by the National Medical Research Council (NMRC) earlier this year, said, "The Collaboration Space in CSB provides a stimulating, high quality and spacious environment for us to do the research aimed at benefiting patients."

Bench space and support rooms are shared, as are core facilities and common shared equipment such as biological safety cabinets, autoclaves, ultracentrifuges, incubators and other bench-top equipment like real-time Polymerase chain reaction (PCRs) and fluorescence plate readers. LKCMedicine's core facilities cover microscopy, flow cytometry, histology and other essential research support services.

Professor of Metabolic Disease Walter Wahli said, "The state-of-the-art laboratories radiate a pleasant and stimulating research atmosphere. Together with access to several technical platforms, they create an enabling environment for leading-edge pre-clinical and patient-oriented research."

The CSB will also be home to the School's upcoming Clinical Research Centre (CRC). The CRC will provide a suite of services, ranging from clinical research space and coordinator support to drugs and biological sample storage, to LKCMedicine researchers, key clinical partners at National Healthcare Group and other collaborating institutions, and industry partners.

In addition to providing space for cutting-edge research, the CSB has proven to be a popular venue for conferences and symposiums, such as the recent Neuroscience and Mental Health Annual Workshop in March 2017 which was attended by many from the healthcare community. Later this year, the CSB will host a number of key conferences including:

- 14 October 2017 Singapore Health & Biomedical Congress' Primary Care Dermatology Symposium
- 8-10 November 2017 FutureHealth 2017 Conference a new signature conference by LKCMedicine, Centre for Healthcare Innovation and NTU Institute for Health Technologies, on healthcare transformation through new technologies and workforce innovations

Contributed By:

Mr Sufian Suderman
Senior Executive
Research Administration & Support Services
Lee Kong Chian School of Medicine
Nanyang Technological University



20-storey Clinical Sciences Building - The latest addition to the LKCMedicine dual campus



The School's open lab concept encourages interdisciplinary research



The Collaboration Space provides a meeting point for researchers

TTSH and Eye on a Journey

I started my journey with National Healthcare Group Eye Institute (NHGEI) as a medical year 4 student doing my posting there. It was this department that sparked my passion for ophthalmology, and I became very interested in this area of research. I met my research mentor Dr Rupesh Agrawal through Dr Augustinus Laude, who was immediately very accepting and encouraging. He entrusted me with really interesting and stimulating projects, and guided me through it step by step. Being very new to the field, it took much guidance and time to get me on my feet. I recall many meetings to develop a new technique together to create a new index measuring choroidal vascularity, termed "Choroidal Vascularity Index (CVI)".

Through Dr Rupesh, I have met many ophthalmologists and researchers that are leaders in their fields, and had the opportunity to collaborate with many of them on different projects. We collaborated with Singapore National Eye Centre

(SNEC) and wrote a paper on the normative index of CVI. This paper was published in Scientific Reports, a Nature research journal. I was also given the opportunity to present our work at Singapore Health and Biomedical Congress (SHBC) 2015. It was a truly exciting and stimulating experience; and I learnt to present our work in an understandable and yet engaging way. I am very humbled to have received the Singapore Young Investigator Award - Gold, and I am deeply grateful for the support I have received.

Additionally, I had the opportunity to represent Tan Tock Seng Hospital (TTSH) at the American Academy of Ophthalmology conference. It was a wonderful experience; presenting our project and receiving many positive responses from international delegates. It was also very inspiring to see TTSH research being recognised at this world-renowned conference. I valued the opportunity to travel with the TTSH ophthalmology team and get to know them

as well. The department has been very warm and welcoming, and I am honored to have made a few friends here.

Since starting my research with TTSH, I have contributed to a number of projects, and I am truly thankful for all the guidance and care I have received so far. Moving forward, I hope to continue working with NHGEI and contribute to this great team.



Ms Tan with Dr Rupesh at SHBC 2015

Contributed By:

Dr Kara-Anne Tan Yong En

Medical Officer

Predicting Responders to Electroconvulsive Therapy Across Schizophrenia and Depression: A Prospective Study

Electroconvulsive therapy (ECT) is used for treating patients with severe mental illness such as depression and schizophrenia who do not respond well to medications. ECT involves applying a strong electrical current to the brain to induce shock and has been demonstrated to be safe and fast-acting (as compared with drugs which may take months to take effect). Some patients show drastic improvements in their symptoms with ECT.

Our multi-disciplinary study team of doctors and scientists will work together

to determine biological signatures that can help doctors identify the type of patients who respond well to ECT.

We will study patient volunteers with schizophrenia and depression before and after ECT, as well as healthy volunteers. We will perform safe, non-invasive brain scans to measure the structure and connections of brain regions responsible for memory and emotions. We will determine the individual's genetic makeup. We will also collect measures related to cognition, memory, sleep and sense of well-being and combine

these data to come up with an ECT response index. This ECT response index will be used to inform doctors on whether the patient is a good candidate for ECT.

Contributed By: **Dr Ho New Fei** Research Fellow Research Division Institute of Mental Health

For more information on NMRC Open Fund - Young Individual Research Grant, please visit <u>www.nmrc.gov.sg</u> (Competitive Research Grants → Open Fund - Young Individual Research Grant)



Hypohidrosis in Individuals with Exertional Heat Injury: A Prospective Open Cohort Study

Find out more on the study conducted on the Soldiers from the Singapore Armed Forces as to determine the prevalence of hypohidrosis in heat injury.

Click here to read!

Experience of a British Research Assistant in Singapore

Initially I was a little nervous about working as a Research Assistant in Singapore. Would there be a huge language barrier? How would I cope with learning the new research governance processes and legislation? Would it be very different?

I was lucky to start working at the National Skin Centre (NSC) shortly after we arrived and immediately noticed the many similarities between the NSC and my previous Dermatology department. Seeing the name of a drug, diagnosis or trial that had been so familiar gave a welcome reassurance that both medicine and research are truly global endeavours.

I do not have to be worried about language barrier either. Apart from my admiration at the ease with which most of my colleagues move fluently between English, and multiple other languages, my lack of skills

haven't been a problem yet. The hilarity of being taught some Singlish words and phrases has proved somewhat entertaining also!

Grasping the local GCP requirements and regulatory procedures required to undertake research in Singapore was one of my first tasks upon starting. The requirement for all research to first gain ethical approval is a fundamental part of research governance in the UK and Singapore. In Singapore these ethical committees are known as Independent Review Boards (IRB's), whilst in the UK they are Research Ethics Committees (REC's). Their remits are the same and both countries have sophisticated online systems to facilitate the transfer of information between all parties. The consent process, another extremely important factor in ensuring ethical

research, is similarly rigorous in both countries.

Having worked at the NSC for 14 months now, I know that the experiences and learning opportunities gained from working in Singapore have far outweighed any concerns. I am grateful that I have the opportunity to pursue my career in Dermatological research in Singapore.

Contributed By:



Ms Kate Hannah Thornberry Research Assistant Research Department National Skin Centre

A Geriatric Psychiatrist's Journey in Research

Following my graduation from the Master of Clinical Investigation (National University of Singapore, NUS) in 2015, I found myself fascinated by the opportunities for innovation and changing practices through research.

With the support of A/Prof Daniel Fung (Chairman of Medical Board of Institute of Mental Health) and A/Prof Chiam Peak Chiang (my Head of Department), I received the National Medical Research Council (NMRC) Research Training Fellowship in 2016 to pursue a PhD at the NUS Saw Swee Hock School of Public

Health (SSHSPH) of NUS. This has been an eye-opening experience for me, being able to have close interactions with and receive intensive training by many respectable researchers at SSHSPH.

In 2017, I was also fortunate to receive the NMRC Health Services Research-New Investigator Grant to expand my previous work on improving emotional support for dementia caregivers. As a geriatric psychiatrist by training, I have keen interest in the area of dementia and mental health of older persons.

I hope to integrate my clinical experience with research methodology, and contribute to the holistic care of older persons.

Contributed By:



Dr Liew Tau Ming
Consultant
Geriatric Psychiatry
Institute of Mental Health

From Social Worker to Researcher

I started working at Tan Tock Seng Hospital (TTSH) as a Medical Social Worker in 1991. Social work is an imprecise science. Most would call it an art and a science. A person is not like a body part. We could study an anatomy, know the location of the organs, how they work and through investigations, find out what is wrong with the body. However, when you see a person, there is no scientific equipment to tell you what is happening inside their minds and how they are feeling. You need to gain trust, ask the appropriate questions and even "confront" inconsistencies in their stories. The patients themselves may not know what the issues are but through the process of facilitation, they discover about themselves. A lot of it is instinctive but it is an instinct which is schooled through years of experiencing people and learning from them. No two humans are alike and the challenge of working with patients keeps my passion alive. It may sound strange and "unscientific" but to keep doing this work, you must "love" your patients. It keeps you interested, excited and makes you give your best.

As a clinician, it was difficult to find a purpose for doing a PhD. I do not want just a paper qualification but it must be meaningful. I have been teaching at the National University of Singapore (NUS) since 2007 and I realise that there is a chasm between social work academia and social work practice. I thought that doing a PhD in social work would bridge this gap and elevate the social work profession. It

would also make me more complete as a social worker and I will not be only a clinician and educator but also a researcher. The PhD process has been an arduous one but it has also been extremely rewarding as I discover the science of social research.

Contributed By:



Ms Ho Lai Peng Principal Medical Social Worker Department of Care & Counselling Tan Tock Seng Hospital

Research Training Events

Date	Training Programme	Course Provider
Monthly	Good Clinical Practice (Online)	NHG RDO
Monthly	(PCR100) Study Start-Up: Budgeting, Case Report Form Design and Database Design	
Monthly	(PCR200) Study Conduct I: Subject Recruitment and Informed Consent	
Monthly	(PCR300) Study Conduct II : Documentation, Safety Reporting and Investigational Products	
Monthly	(PCR400) Monitoring, Audits and Inspections	
16 -18 Aug 2017	Biostatistics	
12 Sep 2017	Manuscript Writing and Poster Presentation	
27 Sep 2017	Questionnaire Design	
5 Oct 2017	Evidence-Based Medicine Core Skills for Protocol Development	
11 Sep 2017	Clinical Trials: Things You Need To Know	TTSH CRIO
23 Oct 2017	Health-Related Quality-of-Life Beginners	I I SH CKIU

^{*}Dates are subject to changes without prior notice.

For registration and full details on courses by:

- \sim NHG Research & Development Office (RDO), please visit <u>www.research.nhg.com.sg</u> (Training & Education \rightarrow Register for Courses and Other Events)
- ~ TTSH CRIO, please contact Ms Siti Aisha Binte Jaffar (Siti_Aisha_JAFFAR@ttsh.com.sg)

Qualité (Issue 27, Jul 2017)

Education to facilitate high standards of research conduct

- For human biomedical research type of studies, what expected serious adverse events must be reported according to the Human BiomedicalResearch Act (HBRA) subsidiary legislation? Read <a href="https://example.com/here-reported-according-rep
- Do you know that the Principal Investigator Self-Assessment (PISA) Programme was revised as part of NHG's monitoring framework? Read <u>here</u> to find out more.

Click on each of the points above to find out more