

A NEWSLETTER FOR THE RESEARCH COMMUNITY IN SINGAPORE

# catalyst

ACCELERATING RESEARCH



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Adding years of healthy life



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of LKCMedicine  
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Dear Readers,

TTSH's Department of Rehabilitation Medicine celebrates its 40th anniversary this year! This edition of Catalyst showcases Rehabilitation Medicine's research, in particular, Stroke Rehabilitation. Our other feature article is the interview with Dr Leong Khai Pang who heads research at TTSH. He shares with us on the current state of collaborative research there & why it is crucial for clinicians to collaborate.

While Singapore's third medical school, Lee Kong Chian School of Medicine (LKCMedicine) is busy getting ready to open its doors to the first batch of students this year, the school is also building up its research capabilities. Professor Lionel Lee, Vice-Dean (Administration), LKCMedicine, shares on the school's research strategy and the team of eminent clinician scientists and scientists that the school has appointed to spearhead research there. Being the primary healthcare partner, NHG is excited to collaborate closely with LKCMedicine in research too so as to bring about better care, delivery and outcomes for our patients.

I would like to take the opportunity to inform our Readers on the call for abstracts for the Singapore Health & Biomedical Congress (SHBC) 2013. The competition aims to recognise excellence in research and advancements in medical science through research. You can find more information on the competition at [www.shbc.com.sg](http://www.shbc.com.sg).

I'm confident that you will find the articles in this edition of Catalyst enjoyable and informative.

Till next time!

Yours Sincerely

*Farah*



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**Dr Leong Khai Pang**  
Asst Chairman Medical Board (Research)  
Director Clinical Research Unit  
Senior Consultant, Department of Rheumatology, Allergy and Immunology  
Tan Tock Seng Hospital

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# EVALUATION OF THE MOCA: NAMS STUDY AIMS TO IMPROVE DETECTION OF COGNITIVE IMPAIRMENT AMONG PATIENTS



## Dr Victoria Manning

Senior Research Manager  
National Addictions Management Service (NAMS)  
Institute of Mental Health

## Adjunct Assistant Professor

Program in Neuroscience & Behavioral Disorders  
and Health Services & Systems Research  
Duke-NUS Graduate Medical School

It is now well-established that many alcohol- or drug-dependent individuals experience mild to moderate deficits in cognitive functioning, particularly executive functioning. This is due to the long-term neurotoxic effect of substances on the brain. Executive functioning refers to the higher-order cognitive functions of primarily the prefrontal lobe that control and regulate behaviour.

These functions are necessary for goal-oriented behaviour including the ability to make decisions, weigh up information, organise, prioritise, plan, initiate and inhibit actions and to adapt our behaviour to changing situations. Impaired cognitive functioning can compromise the extent to which one engages in and profits from treatment. The international literature suggests they can strongly influence treatment outcome but yet, routine screening for cognitive impairment rarely takes place in addiction settings.

The dominant psychological interventions for the treatment of addictive disorders (e.g. Cognitive Behaviour Therapy or Relapse Prevention) place heavy demands on

cognitive processing, requiring the individual to draw on a complex system of attention, memory, problem-solving and abstraction, and to exercise selective and sustained attention. Patients who experience difficulties in those areas may not be able to process instructions from the therapist, or remember and apply what they have learnt during the therapy sessions in real-life situations.

With knowledge of patients' cognitive strengths and weaknesses, we can modify the way in which we deliver such interventions to maximise their effectiveness. This allows for realistic goals and expectations with regards to the recovery process. At the same time, increasing clinicians' awareness of cognitive deficits has been shown to enhance therapeutic rapport. However, the relative sparing of impairment in general intelligence and language skills often hinder their detection from patient-clinician interactions alone, and therefore formal neuropsychological assessment is required.

Neuropsychological assessment, generally undertaken by psychologists, is particularly labour-intensive and requires specific training in both administration and interpretation. In comparison, screening tools can be administered by a broad range of clinician's in general medical and psychiatric settings. Currently, the most widely used screening tool for cognitive impairment is the Mini-Mental State Examination (MMSE) due to its brevity and ease of administration. However, this has limited utility with substance misusers (unless severely impaired) because

it lacks items assessing executive functioning.

The Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005) is a brief screening instrument developed to detect mild cognitive impairment across a variety of populations, and contains items assessing several executive functioning domains. Research shows that it is sufficiently sensitive to detect cognitive deficits among western substance misusers. However, it is necessary to validate its use on the local population both with patients and healthy controls where English is often a second language.

The study conducted at the National Addictions Management Service (NAMS) department compares performance on the MMSE with performance on the MoCA, using the Neuropsychological Assessment Battery as the 'gold-standard' to identify true cases of cognitive impairment. The study aims to recruit 100 alcohol- or drug-dependent inpatients and 200 healthy controls to establish normative data for the test in Singapore.

The recruitment of patients commenced in August 2012 and we are currently seeking demographically-matched controls. Patients' feedback concerning their experiences of completing the MoCA is positive so far. If the results of the study provide evidence that MoCA is superior to the MMSE, we hope it will be adopted in routine clinical practice, so that we can tailor treatment more effectively to individual patient needs.

Funded by the Lee Foundation, the study team includes Principal Investigator, Dr Victoria Manning and researchers, Brenda Gomez and Eleni Koukouna, who conduct neuropsychological assessment and research interviews.

*If you are interested in participating in our study as a control subject, please contact the research team on [yang\\_yi@imh.com.sg](mailto:yang_yi@imh.com.sg) or [brenda\\_gomez@imh.com.sg](mailto:brenda_gomez@imh.com.sg) or call 6389 2292.*

*\*\*Please note, we are particularly in need of males in the 30-50 year age bracket and educated up to diploma level.*



Principal Investigator (Dr Victoria Manning) and researcher (Eleni Koukouna) conducting neuropsychological assessments.



# DEVELOPMENT OF LKCMEDICINE RESEARCH

## Professor Lionel Lee

Vice Dean (Administration)

Lee Kong Chian School of Medicine

Solving the puzzle of complex diseases, from diabetes to mental health, requires a holistic understanding of the interplay between factors such as genetics, diet and lifestyle, environment, behaviour and social structures.

The ecosystem in which the healthcare of the individual and community will be effected will require a truly systems approach to predict, prevent, monitor, intervene and care. This is precisely the challenge of translational medicine research which will be the mainstay of the research strategy of Singapore's newest medical school, the Lee Kong Chian School of Medicine (LKCMedicine).

But we cannot do this alone. We will have to draw on the strengths of our parent universities, Imperial College London (Imperial) and Nanyang Technological University (NTU), as well as the expertise of our primary healthcare partner, the National Healthcare Group (NHG), and other hospital partners.

In crafting LKCMedicine's research strategy, we seek to leverage Imperial and NTU's proven track records in science, engineering and technology, while remaining ahead of the curve in anticipating Singapore's healthcare needs, today and tomorrow. LKCMedicine is focussing on these research themes: Metabolic Disease, Infectious Disease, Neuroscience and Mental Health, as well as Dermatology and Skin Biology, underpinned by two cross-cutting themes in Bioengineering including Structural Biology and Health Services Outcome Research.

We have appointed an eminent group of clinician scientists and scientists in the area of metabolic medicine. Professor Bernhard Boehm, a clinician scientist, leads the interdisciplinary area of research in Regulation of Cellular and Systemic Energy Metabolism in health and disease.

Professor Walter Wahli, one of the discoverers of the medically relevant Peroxisome Proliferator-Activated Receptors,

investigates molecular mechanisms and molecules, emanating from the interplay between food, nutrients and microbiota; Professor Sven Pettersson, a clinician scientist, studies the host-microbe interactions and the gut microbiome; Professor Per Olof Berggren, a renowned experimental endocrinologist, leads a research group focussing on pancreatic islet cell biology; Professor Michael Ferenczi heads the laboratory investigating the biophysics and biochemistry of muscle fibres.



Together the research areas of these metabolic disease experts span basic biology to clinical research and they form our starting group of Principal Investigators to lead our metabolic research thrust.

Effective translational neuroscience research requires continuous interactions of fundamental neuroscientists and clinical neuroscientists. We have catalysed the development of translational neuroscience research at the medical school through the activities of Visiting Professors Christer Halldin and Balazs Gulyas. Professor Halldin is Professor of Medicinal Radiochemistry and Director of the Positron Emission Tomography Centre, Karolinska Institutet.

Professor Gulyas is Professor of Neuroscience at Karolinska Institutet

and an expert in molecular translational neuroimaging. Collaborative pre-clinical projects utilising state-of-the-art radioligands manufactured at Singapore RadioPharmaceuticals and with applications to Parkinson's disease and traumatic brain injury have been initiated with the National Neuroscience Institute and DSO National Laboratories.

The plan for infectious disease research will include areas in drug-resistant bacterial infections bacteriology including pulmonary tuberculosis, inflammation and immunology, with provision of access to field sites that will be of importance in training clinicians in the future. As part of Singapore's strategy to broaden the biomedical sciences sector, translational skin research has been singled out as a new strategic research thrust for the Singapore Biomedical Sciences Initiative. At LKCMedicine, we have identified dermatology and skin biology research as one of the priority areas in which to develop a thematic research programme.

One of our newly appointed faculty, Professor David Becker, will conduct research on tissue injury and repair, wound healing and scar formation. To assist the school in formulating a strategic approach to develop excellence in this field, we have in March 2013, invited Professor Alan Irvine, Professor of Human Genetics and Head of the Division of Molecular Medicine, College of Life Sciences at the University of Dundee, and Professor Irwin Mclean, Professor of Dermatology at Trinity College Dublin and Consultant Dermatologist at Our Lady's Children's Hospital and St. James's Hospital Dublin, Ireland to Singapore to study opportunities in the local research ecosystem for further development of dermatology research.

To develop an integrated approach to dermatology research in Singapore, we will be forming a tripartite partnership with the National Skin Centre and Institute of Medical Biology, A\*STAR. We have also attracted two heavyweight faculty to our school. Professor Phil Ingham FRS, is a world-renowned expert in the field of developmental genetics whose work in intercellular signalling pathways has provided fundamental insights into human

development and cancer, paving the way for novel drug discovery.

Professor Daniela Rhodes, FRS, who holds a joint appointment with us and NTU's School of Biological Sciences, is internationally recognised for her ground-breaking research in chromosome biology.

With more faculty joining the school in the

coming months, we will continue to shape the form and texture of our research programmes to spearhead medical innovations that will improve healthcare and patient outcomes.

This will foster an optimal environment for the growth of clinical research in our partner hospitals. As an added boost, LKCMedicine is working with NHG to offer Clinician-Scientist Fellowships, worth about \$1 million per year, which will allow NHG clinicians to

pursue their Doctor of Philosophy (PhD) at NTU, including embarking on attachments at overseas institutions especially Imperial College London.

For more information, please visit: <http://www.lkcmmedicine.ntu.edu.sg/Pages/index.aspx>.

## BRAIN-COMPUTER INTERFACE BASED TRAINING: AN ALTERNATIVE TREATMENT FOR ATTENTION DEFICIT BRINGING SCI FI TECHNOLOGY TO A MENTAL HEALTH FACILITY NEAR YOU

**Ms Lee Xin Yi**

Research Assistant  
Child Psychiatry  
Institute of Mental Health

For fans of the classic Sci-Fi movie Star Wars, the idea of Jedi mind tricks has been seen like a farfetched fantasy. Unlike 2-D scene of the movie, children are now able to move a character across the computer screen by using the sheer force of their concentration. This help to improve their attention levels.

The use of brain activity via an external device as a tool for controlling movement was first developed for helping stroke patients to relearn the use of their paralysed limbs by Dr Guan Cuntai of Institute of Infocomm Research (I2R). This innovative process is known as Brain-Computer Interface (BCI) training. The use has been extended to the area of mental health: Would it aid in the treatment of Attention Deficit Hyperactivity Disorder (ADHD)?

Led by Principal Investigator, Dr Lim Choon Guan of the Department of Child and Adolescent Psychiatry, the BCI technology was adapted as a novel alternative treatment for ADHD in children.

A study which recruited a total of 20 medication-naïve ADHD children was recently completed, with the collaborative effort of our industry partners including Dr Guan's team at I2R as well as the Duke-NUS Graduate Medical School. All 20 children, diagnosed with either inattentive or combined subtypes of ADHD, underwent 24 sessions of BCI training over a span of 8 weeks, followed by 3-monthly revision sessions.

The game-based BCI training involves

the child wearing a headband of two dry electroencephalography (EEG) electrodes that detects the electrical activity in the pre-frontal cortex of the brain (see picture A). Cortical activities related to concentration (beta waves) and inattentiveness (theta waves) are transmitted to the computer through Bluetooth technology and a patented Brain Score is produced.

This Brain Score monitors the concentration level of the child and the game proceeds at a proportional speed according to how focused the child is. The training is intensified over the weeks, with added tasks such as picking fruits along the path, in order to increase the amount of concentration required. In this



Picture of team re-enacting the BCI treatment in progress

way, the child is being trained to be able to stay focused for a prolonged period of time. Additionally, there is an academic component tagged on at the end of every alternate session. This extends the effects of the training session to academic work.

Parents rated significant improvements in both inattentive and hyperactive/impulsivity symptoms of their child. This promising result is the first step in finding an effective alternative treatment to ADHD, where the standard practice is medication or psychosocial treatment. It paves the way for a novel form of treatment which produces no

side-effects and little reliance on medication in the long term.

As the small pilot trial yielded significantly optimistic results, a larger randomised controlled trial (RCT) is in the works, and aims to recruit a total of 160 children over 2 years. The RCT is the gold standard in clinical research and will eliminate any rater biasness.

In our initial trial, the study team is aware of the limitation that parents are not blinded to the effects of the training and the improvement might have been over-reported. In addition to the more rigorous study design, a small sample from this group would also



Picture A: Child wearing a headband of two dry EEG electrodes

undergo functional magnetic resonance imaging (fMRI) scanning to determine any structural changes in the brain after treatment, adding to the validity of the trial.

This foray into the use of BCI technology in the clinical field is but a budding one. To date, the research conducted studied in patients with stroke and ADHD children is only a toe-dip into the vast potential of BCI in many applications. We have definitely witness the rewarding effects of BCI have had on our ADHD participants and expect greater feats from this novel and innovative treatment as an alternative.

# KEYS TO A SUCCESSFUL AND REWARDING RESEARCH CAREER

**Dr Colin Tan**

Senior Consultant

Department of Ophthalmology

Tan Tock Seng Hospital



Research is an exciting and enriching endeavour, bringing with it opportunities to explore new frontiers in medical and scientific knowledge, and the privilege of meeting and working with exceptional clinicians and scientists. In this short piece, I will explore some of the keys which I believe will be essential to anyone embarking on a career in research.

## Good Mentors

It has been said that every generation stands on the shoulders of the preceding one. This has been a fundamental tenet of scientific discovery for centuries and also gels nicely with the Hippocratic Oath taken by doctors to teach and train their juniors.

Throughout the years, I have been honoured to have been mentored by some inspiring and exceptional people from various hospitals in Singapore, as well as from world-class institutions overseas. What makes a good mentor? Is a "good" mentor naturally good, or can he be trained? This is a subject close to my heart, as I have had the immense privilege of mentoring some truly capable junior doctors, even as I continue to learn from my own mentors. I am inclined to feel that a good mentor must have certain innate qualities, although these can be further augmented with appropriate training.

However, there are some qualities that cannot really be taught or trained. A mentor must want what is best for his mentee, and not just "use" the mentee to further his own goals. This is personified by one of my closest mentors who, having guided me and pointed me in the right direction, said, "Now it's up to you. Take the ball and run with it." A good mentor will be cognizant of current trends and identify niche areas, then open doors and gently nudge the fledgling researcher in the right direction. A true mentor will take great pride in his mentees' achievements, and not fear being overshadowed by them.

## Collaborations and Teamwork

No man is an island. This is true in almost any facet of life, and it is certainly true in research.

Over the years, I have had the privilege of collaborating with clinicians and researchers from within National Healthcare Group, A\*STAR, Singapore Eye Research Institute, the National University of Singapore, Nanyang Technological University, Singapore Polytechnic and from overseas, the Doheny Eye Institute, University of Southern California and the Medical Center Ophthalmology Associates, (San Antonio, Texas).

**Some of the most inspiring mentors still retain, after all these years, their enthusiasm, their curiosity and their humility in acknowledging that there is much more to learn.**

I have also worked with industry partners, who share a common vision of doing what is best for our patients. From each of these interactions, I truly feel that all parties have gained and benefited from each other. Each group contributes different talents, experiences and skills, and it is the synergism of all the expertise that allows great goals to be achieved.

A crucial element of any successful research study is the formation a good research team. Individual talent alone, while of course important, is not enough. A collection of capable individuals does not constitute a team; it would serve no purpose to group them together if they are unable to work with one another. A team is greater than the sum of its parts, and utilises the various talents and capabilities of all team members.

A good team must have chemistry, work well together, and share credits with each other. With teamwork, the team is able to achieve more than any one person could have done on his own. A research team with a proven track record should be encouraged

to continue working together by all means possible, and to keep striving together for new heights. For budding researchers, it is essential to find a team that you can work comfortably with. Once you have identified a good team, take a long term view and continue working with that team.

## Humility and Curiosity

A common trait that I have observed in many exceptional people is their humility and their innate curiosity. Nobody knows everything, few ever come close. Some of the most inspiring mentors still retain, after all these years, their enthusiasm, their curiosity and their humility in acknowledging that there is much more to learn. It is through this desire to keep improving, keep learning more and doing things better that great research is born.

There are, of course, many more elements that are required for success in research. However, I believe that the areas discussed above will serve any researcher well throughout his career. Above all, a researcher must love what he does.

Steve Jobs said, "Your work is going to fill a large part of your life, and the only way to be truly satisfied is to do what you believe is great work. And the only way to do great work is to love what you do." This advice would serve all of us well, in all our endeavours.

*Dr Colin Tan is a Mid-level investigator under the NHG Clinician-Scientist Career Scheme (CSCS). His paper "Diurnal Variation of Choroidal Thickness in Normal, Healthy Subjects Measured by Spectral Domain Optical Coherence Tomography" published in Investigative Ophthalmology & Visual Science (a journal by the Association for Research in Vision and Ophthalmology) was one of most read articles of the year (Nov 2011 through Oct 2012).*

*For more information on CSCS Program, visit [www.research.nhg.com.sg](http://www.research.nhg.com.sg) (Grants and Programmes > NHG Intramural Support > NHG Grant Programmes).*

# CREATING A NEW PARTNERSHIP

## Assistant Professor Lim Wei Yen

Saw Swee Hock School of Public Health  
National University of Singapore  
Visiting Research Fellow  
Institute of Mental Health

I am a public health physician and have been with the Saw Swee Hock School of Public Health (SSHSPH) since 2011. My interest is in epidemiology, and at the School, I currently oversee 2 studies. The first is a cohort study of about 25,000 individuals that aims to evaluate risk factors for common chronic diseases, including genetic risk factors.

Recruitment for the cohort closed in 2010 and a revisit of the cohort to update exposure information is underway. The second is a group of studies aimed at evaluating the health of Singaporeans through representative serial cross-sectional surveys.

The first survey has just been completed, and a second one is planned for the end of this year. We also plan to focus on the health of elderly persons, and a study is planned to start end of this year.

My interest in mental health was sparked in 2005, when I was at the Ministry of Health. Then, I worked with a committee of experts (which included A/Prof Chong Siow Ann, Vice Chairman, Medical Board (Research) of Institute of Mental Health) who developed



Asst Professor Lim Wei Yen

the first National Mental Health Policy and Blueprint.

I began to understand the importance of mental health in contributing to the overall wellbeing of a person. I also realized that research into overall mental health status and how mental wellbeing can be enhanced are essential.

In the next two years, I hope to develop an area of focus in mental health epidemiology research, especially in the intersection of mental health and physical health. I would also like to explore how IMH's Research Division (IMH RD) and SSHSPH might work together in research collaborations.

Some areas that I have been exploring include measuring mental wellness and illness in the cohort studies that I oversee. The IMH RD, with its vast experience in



Asst Professor Lim Wei Yen having a discussion with the team members from Institute of Mental Health

performing such measurements, would be an invaluable partner and this partnership could include training our co-ordinators and interviewers in performing these kinds of measurements.

Furthermore, the collaboration may also take the form of new mental health research proposals developed and led by IMH RD investigators, using data collected from our cohort studies.

SSHSPH could also advise IMH RD in areas of its expertise, which could include measurements of physical health, mental health service research, health economics, and mental health promotion.

I look forward to being able to help develop a long-lasting and fruitful partnership between these two institutions!

## FREE SUBSCRIPTION

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## DEPRESSIVE SYMPTOMS IN SINGAPOREAN PRIMARY CARE PATIENTS: DO THEY DIFFER BASED ON AGE, GENDER OR ETHNICITY?

This project was awarded the Allied Health Award (Bronze) at the Singapore Health and Biomedical Congress (SHBC) 2012.

Depression has become the leading contributor of disease burden in middle and high income countries worldwide and has an estimated prevalence of 6.3% locally in 2010. However, although 20% of patients in primary care settings have been found to present clinically significant depressive symptoms (Zung et. al, 1993), little has been done to characterise their depression profiles in the Singaporean context. Hence, this study sought to examine the depression symptom profiles based on the demographic characteristics of 400 patients seen at a local primary care clinic.

Participants completed a series of questionnaires that included two locally validated self-report screening questionnaires (the Patient Health Questionnaire and the Quick Inventory of Depressive Symptomatology - Self Report) as well as demographic data form. Table 1 provides a summary of the sample demographics.

Age Group	n (%)
Younger Adult (21-35 years)	215 (53.8)
Older Adult (36-50 years)	185 (46.2)
Gender	n (%)
Male	139 (34.8)
Female	261 (65.3)
Ethnicity	n (%)
Chinese	208 (52.0)
Malay	91 (22.8)
Indian	62 (15.5)
Others	39 (9.7)

Table 1: Sample demographics

Overall, it was found that younger adults (aged 21-35) presented with more impairment across depressive symptom domains than older adults (aged 36-50), such as anhedonia, appetite disturbance, difficulty falling asleep, feeling sad, feeling



Dr Sharon Cohan Sung and the research team at Child Guidance Clinic (CGC).  
From left: Dr Chin Chee Hon, Ms Tan Yan Lin, Ms Xie Yuhuan, Ms Jade Jung,  
Dr Sharon Cohan Sung, Ms Clare Kwan, Ms Nikki Lim & A/Prof Daniel Fung

bad about oneself and having trouble concentrating. Besides age differences, ethnic differences in depression symptoms were also found. Malay participants reported increased fatigue/loss of energy and having more trouble concentrating than their counterparts of other ethnic origins. Among the few ethnic groups, Chinese participants scored lowest in feelings of fatigue while participants from other minority ethnic groups ("Others") reported least problems with concentration.

Taken together, the study suggests that younger adults may be at a higher risk for depressive symptoms as compared to older adults. The higher level of symptom endorsement by younger people may reflect a greater willingness to disclose depressive symptoms relative to older adults although such a conjecture may warrant further investigation. This study also presents a potentially simple and cost-effective means to screen primary care patients who may be at risk of developing depression, a possible treatment gap.

### Profile Feature on Awardee

After working in the United States for 9 years, Dr Sharon Sung joined Institute of Mental Health (IMH) in 2010 and is currently a Senior Clinical Psychologist with the Mood and Anxiety Clinic in Child Guidance Clinic, Department of Child and Adolescent Psychiatry. She is also an Assistant

Professor at the Duke-NUS Graduate Medical School.

Apart from clinical practice and teaching, Dr Sung is actively involved in research to improve identification, assessment and treatment of mood and anxiety disorders and further knowledge on emotion regulation and dysregulation. She believes that the best research observations occur in clinical practice and she adopts an empirically based treatment approach in her field of work.

Her current clinical research projects involve a broad spectrum of issues, including among others, the following studies: a) developing a virtual-reality exposure therapy for children with selective mutism, b) examining patterns of mood and anxiety disorders in parents of clinically-referred youth, c) evaluating patients with panic disorder in the emergency ward (pilot) and, d) developing a mobile application for cognitive behaviour therapy (CBT) that patients can use to perform self-guided treatment.

Dr Sung is pleased to have the research team's work recognised by SHBC and feels that the award is an acknowledgement of their hard work and dedication. In the near future, she hopes to earn a national level grant to expand her work in these areas and contribute to growing the research culture in mental health issues.



# NURSING RESEARCH IN SINGAPORE ON THE WORLD STAGE



## Dr He Hong Gu

Assistant Professor

Alice Lee Centre for Nursing Studies

Yong Loo Lin School of Medicine

National University of Singapore

A nurse researcher in Singapore has just been inducted to the **International Nurse Researcher Hall of Fame** in 2013, the first time in the history of nursing profession in Singapore. She is Professor Sally Wai-chi Chan, Professor of the Alice Lee Centre for Nursing Studies (ALCNS), Yong Loo Lin School of Medicine, National University of Singapore.

The International Nurse Researcher Hall of Fame is created by the Honor Society of Nursing, Sigma Theta Tau (STTI) in 2010. This Hall of Fame eternally honours esteemed nurse researchers from around the world who are committed to building the knowledge base in nursing. STTI members who have achieved long-term, broad national and international recognition for their work, and whose research has impacted the profession and the people it serves would be considered for induction to this Hall of Fame.

Being a pioneer in nursing research related to mental health nursing in Hong Kong and Singapore, Professor Chan has acquired a total of 57 research grants since 1992. She has more than 300 publications in international nursing and healthcare journals, book and book chapters, keynote speeches, and conference presentations. Her main research focus lies in mental health and psychosocial nursing. She has spent the past twenty years conducting research on the following themes: community mental health, perinatal mental health, old age mental health and nursing education.

Her research studies are designed in partnership with clients and families wherever appropriate. The majority of her research studies involve interdisciplinary and inter-institutional collaborations. Examples of her past and present national and international research partners are from Singapore, Hong Kong, People's Republic of China, Taiwan, Thailand, Australia, the United Kingdom, Finland, Slovakia, Czech Republic, Italy and Portugal.

Apart from being an active researcher, Professor Chan also promotes research through teaching and supervising postgraduate nursing students at both masters and doctoral levels. She has successfully supervised 27 postgraduate students. Through her leadership in the ALCNS, Professor Chan mentors junior faculty members and develops their research capability through joint studies and consultation.

To facilitate the use of research findings, Professor Chan contributes actively in publishing nursing research findings. She has been serving on the editorial and advisory boards of many renowned health and nursing journals. Currently, she is the Editor-in-Chief of the *Journal of Nursing Interventions*, an international nursing journal. She also leads the publishing work of the *Singapore Nursing Journal*, the only local nursing journal. Given the prominent background in health and nursing research, Professor Chan has been appointed as research grant reviewers for many national/government research grants in Hong Kong, Australia and Singapore.

Professor Chan is keen to promote evidence-based healthcare practice through her participation in consultation groups and nurses associations. She is a member of the Primary Care Consultation group for Revision of ICD-10 Mental and Behavioural Disorders, World Health Organization which will significantly impact diagnosis and care of mentally ill persons in primary care settings globally.

She has been appointed to the Expert Group on Mental Health Services by the Hong Kong Food and Health Bureau of the Hong Kong Government to formulate the blueprint to reform mental health services. She is the Convenor of the East Asian Forum of Nursing Scholars, a federation of seven Asian countries to promote doctoral nursing programmes in the region; Co-Chair, Nurses Professional Discipline Forum, International Psychogeriatric Association; and Advisor of the Singapore National University Hospital

Centre for Evidence-based Nursing.

Unlike medical research, nursing research in Singapore has yet been given the necessary support in terms of substantive research grant and award for full-time research work. For example, in the United States of America, there is a national funding for nursing research managed by the National Institute of Nursing Research.

Professor Chan hope nursing research in Singapore continues to grow and obtain substantive support in terms of research grants. For example, in the United States of America, there is a national funding for nursing research managed by the National Institute of Nursing Research. Professor Chan would like to see similar nursing research support in Singapore. She is taking her own time and efforts in generating resources for nurses to conduct research. She is currently the President of Singapore Upsilon Eta Chapter of STTI. This Singapore Chapter is offering seed research grant for local nurses, and facilitation for collaborative studies through its international network.

In the contemporary healthcare system, nursing is a complex and demanding practice. To meet healthcare demands, nurses need to develop a wide range of competencies such as disease prevention, health promotion, care co-ordination, evidence-based practice, quality care and patient safety. Professor Chan points out that nursing research is to discover knowledge for improving nursing and healthcare practice. The outcome of nursing research must aim to produce positive impacts on the patients, their families and the community.

Professor Chan has gone through the path from a frontline clinical nurse to a renowned nurse researcher and sailed through sea of challenges. She regarded the biggest hurdle for nursing research is that some nurses today still do not see the need to conduct research. She hopes that there are more nurses with a positive view on research, and more support for nursing research.

## TRANSFORMING NURSING AND HEALTHCARE THROUGH RESEARCH: PERSPECTIVES OF A YOUNG NURSE RESEARCHER FROM TAN TOCK SENG HOSPITAL (TTSH) ON HER RESEARCH JOURNEY



### Ms Isabel Ng Hui Leng

Nurse Researcher  
Nursing Service  
Tan Tock Seng Hospital

I embarked on the health research career track on a sponsorship by MOH-NHG Nursing Development Scholarship (MNDS) in 2008, to pursue my Masters in Epidemiology at London School of Hygiene & Tropical Medicine (LSHTM).

The knowledge and skills learnt enabled me to design, develop and implement epidemiological studies that are relevant to nursing practice. The research scope that I undertake is intentionally broad to be in line with the development of nursing research in Tan Tock Seng Hospital.

Currently, I am focusing on nursing practices where there is lack of clear evidence or where new evidence indicates that we have to review our practices. These include addressing issues that have a tremendous impact on nursing work.

Nursing research is a continuous process as Nursing Science evolves with new findings. We have seen some success stories through nursing collaboration efforts such as, uncovering the scientific basis of the traditional methods of treating superficial phlebitis with glycerin magnesium sulphate (GMS).

In the last 2 years, we were interested in developing alternative bedside methods to check feeding tube placement when the pH test fails. This was important because our nurses would have to arrange tube-feeding patients for an X-ray if the pH test was negative (i.e. falls outside of safe pH range for feeding). The X-rays are costly when performed many times and are also time-consuming.

Hence, it was a Eureka moment for our team when we were almost certain, with the immense support from the Medical department, that the new bedside algorithm

can help nurses assess the likelihood of wrong tube placement before deciding the need for X-ray.

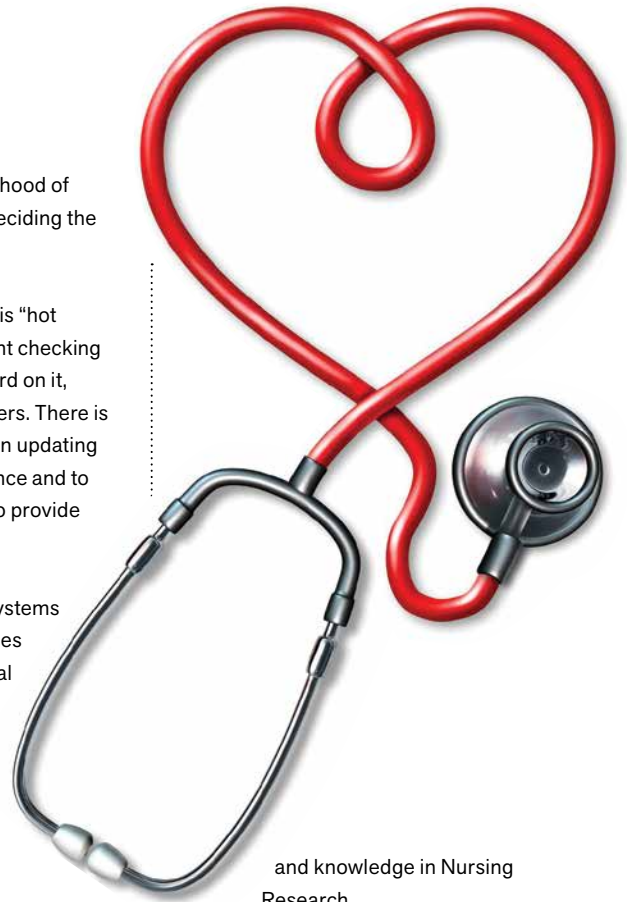
Few ideas have spun off from this "hot potato" to improve the placement checking methods and we are working hard on it, together with our medical partners. There is still great room for us catch up on updating our practices to the latest evidence and to continually discover new ways to provide better care for our patients.

At present, we are developing systems to strengthen our front-line nurses and doctors' responses to clinical deterioration. We hope to collaborate more with our partners in Medical and Allied Health departments and beyond TTSH on research efforts to improve delivery of healthcare as a whole.

Many have asked what Nursing Research is and the role of a Nurse Researcher. The thrust of nursing research is to generate new knowledge that will continually build on our scientific foundation in our clinical practice.

The Nurse Researcher collaborates with clinical nurses to answer a specific clinical enquiry using a systematic and scientific approach. He/she digs into available research literature, ponders deeply, thinks creatively and critically to design and develop research questions that can lead to breakthroughs.

To perform the role well, the Nurse Researcher would be at least Masters-prepared in a research-related program available locally or overseas. Most of the time, the Nurse Researcher is expected to pursue higher education at the Doctor of Philosophy (PhD) level to deepen expertise



and knowledge in Nursing Research.

Besides undertaking research work, the Nurse Researcher provides leadership, promotes, aspires and guides nurses in conducting good research and evidence-based practice.

He/she serves as an important resource on methodology issues and the conduct of research; garners and promotes resources available for research (e.g. linking up with statistician, journals and library resources, data analysis software etc.)

The research nurse also mentor nurses who are progressing on the research career track. What keeps me going is to witness how the nurses improve their nursing care delivery to patients and deepen their scientific understanding of what they do for patients through the research efforts. This builds up our nursing professionalism as we work alongside with our healthcare partners.

# AWARD SPURS NURSE RESEARCHER TO CONDUCT NURSING JOURNAL CLUB TO FACILITATE THE TRANSLATION OF RESEARCH EVIDENCE INTO CLINICAL PRACTICE

## Mr Zhou Zhenyu

Advance Practice Nurse  
Institute of Mental Health

In the previous issue of the Catalyst, the nursing research journey at Institute of Mental Health (IMH) was highlighted. Advanced Practice Nurse (APN) Mr Zhou Zhenyu was the first nurse awardee to be presented the Singapore Nursing Award (Gold) at the 1st Singapore Health and Biomedical Congress (SHBC). Three years after this win, an interview was conducted with APN Mr Zhou Zhenyu to understand how the award had propelled him in his research endeavours.

### How did you feel about winning the Singapore Nursing Award (Gold) in the year 2010?

I was really fortunate as I received full support from my team members and the camaraderie shared among the team allowed for work to be done within a short period of time. More importantly, the nursing senior management at IMH had given me valuable advice that aided the presentation of my research paper. I would like to take this opportunity to show my appreciation for their guidance.

### In what way/s has the award influenced your research endeavors?

The award had definitely added to the experience of my research journey. It serves as both recognition for my past work and a reminder, to motivate me to embark on new projects. When faced with obstacles in my research projects, I would often look at the photograph of the award ceremony; it has been a source of encouragement and been an effective morale booster so far.

### What are your current research interests?

Currently, I am chairing the IMH Nursing Journal Club with the support from nursing senior management and IMH APN team. The Nursing Journal Club serves as a platform to promote evidence-based practice among IMH nurses. 30 nurses meet every 2 months to appraise research



APN Mr Zhou Zhenyu (2nd from left) conducting Nursing Journal Club to fellow nurses.

articles and discuss about the applicability of the research evidence into clinical practice. We coach and mentor the nurses to understand that research evidence is important but not all research findings can be translated into clinical practice. For well-researched evidence deemed useful for translation into clinical practice, the nurses work on strategies to adopt them.

We also seek to continuously improve the Nursing Journal Club. Together with other APNs and members of nursing senior management, we are reviewing

the structure and delivery model of our sessions. With the support of Dr Xie Huiting and APN Xu Changqing, I am in the midst of preparing a curriculum that will link the theory of research with the practical application of research evidence.

Our team hopes that the Nursing Journal Club serves both as a platform to promote evidence-based practice (EBP) and an incubator to groom future research and EBP talent pool. Eventually, I am confident that we can effectively translate empirical evidence into clinical practice.



## WORLD HEALTH SUMMIT REGIONAL MEETING - SINGAPORE IMPROVING MENTAL HEALTH OF THE POPULATION – AN ASIAN PERSPECTIVE

Mental illnesses not only affect individuals, but also families, societies, and economies. These disorders which have an early onset and chronic course interfere with the ability of children and adults to function in families at school and work and in society at large.

Untreated mental illness is associated with school failure, teenage pregnancy, spousal violence, unemployment, substance abuse, suicide, and poorer quality of life. Thus, there is a pressing need to for innovative approaches and solutions that will have a positive impact on individuals burdened by the illness, families, caregivers, and populations as a whole.

This symposium, held in conjunction with the World Health Summit's Regional Meeting in Singapore at the Institute of Mental Health focused on local and International approaches aimed at improving the mental health of the population. Over 150 participants from government agencies, voluntary welfare organisations (VWOs), primary care doctors and healthcare professionals from the various hospitals attended the event.

World renowned speakers, Professor Parminder Raina from McMaster University in Canada and Professor Anthony Jorm from University of Melbourne shared their research findings and experience in the area of caregivers' burden over a life course and the importance of mental health literacy respectively. We also had Associate Professor Chong Siow Ann, Vice Chairman Medical Board (Research) at IMH who highlighted key findings of the



*From left to right : Professor Anthony Francis Jorm (University of Melbourne, Australia), Professor Parminder Raina (McMaster University, Canada), Associate Professor Chong Siow Ann (Institute of Mental Health, Singapore), Dr Alan Ong (Ministry of Health, Singapore) and Associate Professor Chua Hong Choon (CEO Institute of Mental Health, Singapore)*

Singapore Mental Health and the relevance for and translation to policies and service development. Dr Alan Ong, Deputy Director for Community Mental Health at the Ministry of Health, ended the morning session. He gave a policy perspective of the National Mental Health Blueprint and the Community Mental Health Master Plan which is currently being implemented.

Two of the National Mental Health Blueprint programmes which are into their 5th year of operations, Response, Early Interventions and Assessment Community mental Health (REACH) and the Aged Psychiatry Community Assessment and Treatment Service (APCATS), were discussed in two separate breakout sessions during the Symposium.

A third breakout session was conducted by Dr

Hristina Petkova, a Health Economist from Kings' College in London, on the topic of Economic Evaluation in Healthcare.

The Symposium created opportunities for participants to discuss their challenges and share solutions. The importance of the role of research in mental health cannot be over emphasized.

From the conduct of epidemiological studies that provide us the vital data on prevalence and risk factors of mental illness, understanding people's perception of mental illness, delivery of evidence based treatments, understanding challenges faced by caregivers as patients are managed in community settings, to policy initiatives to overcome these barriers and gaps in mental health care research has an all-encompassing role in improving population mental health.

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# ADVANCING REHABILITATION MEDICINE THROUGH RESEARCH



## Dr Kong Keng He

Head of Services  
Senior Consultant  
Rehabilitation Physician and Medical Acupuncturist  
Rehabilitation Medicine  
Tan Tock Seng Hospital

Dr Kong was also the Chairperson of the 2nd Singapore Rehabilitation Conference, held in conjunction with RehabTech Asia 2013 in Singapore on 27 and 28 February 2013.

Research is one of the key strengths of Rehabilitation Medicine. Research activities over the years can be categorised as follows:

- a. Research addressing questions of functional outcome (including quality of life) after rehabilitation in patients with stroke, traumatic brain injury, spinal cord injury and limb amputation;
- b. Drug trials – i) evaluating a Traditional Chinese Medicine drug, Neuroaid in stroke, ii) Botulinum toxin in the treatment of spasticity after stroke and neurogenic bladder in spinal cord injury; and
- c. Research in rehabilitation and assistive technology. These include novel technology like Brain-Computer-Interface, where stroke patients are trained to use electroencephalographic (EEG) activity to help move paralysed limbs, development of assistive and robotic devices to facilitate training of the upper limb and gait, and evaluating the role of interactive computer gaming in rehabilitation. The department is also actively exploring research in tele-rehabilitation.

## Our ongoing projects are:

- "Efficacy of computer gaming in facilitating upper limb recovery in stroke rehabilitation: a pilot randomised

controlled study" – funded by Ministry Of Health (MOH) Health Services Research Competitive Research Grant (HSR CRG);

- "Cognitive stroke movement therapy systems through integration of wearable haptic interfaces" – funded by Agency for Science, Technology and Research (A\*Star) Science & Engineering Research Council Grant;
- "Unified platform for accelerated functional return of grasping, wrist and forearm control in stroke patients with EMG actuated upper extremity orthosis" – funded by National Medical Research Council (NMRC);
- "Advanced rehabilitation therapy for stroke based on Brain-Computer-Interface" – funded by A\*STAR; and
- Prototype development of assistive leg device for partial-paralysis patients" – funded by NMRC.

## Are you aware of any research collaborations in Singapore and/or other countries in this area?

A key project is the "Cognitive stroke movement therapy system through integration of wearable haptic interfaces" which is a jointly funded by A\*STAR and National Office for Research and Technology (NKTH) in Hungary.

## Could you briefly describe your research?

In the Ministry Of Health (MOH) Health Services Research Competitive Research Grant (HSR CRG) funded project "Efficacy of computer gaming in facilitating upper limb recovery in stroke rehabilitation: a pilot randomised controlled study" that I'm involved in, we are looking at the role of interactive computer gaming in facilitating upper limb recovery after stroke.

We recognise that upper limb weakness is a

common complication of stroke and affects patients' ability to perform self-care activities independently.

The conventional treatment is intensive upper limb exercises performed under the guidance of an occupational therapist. However, intensive exercises may not always be feasible because of manpower constraints. Furthermore, it can be monotonous because of its routine and repetitive nature. Exercises using commercially available computer gaming devices may be a novel and enjoyable alternative to conventional therapy.

The aim of this study is to evaluate the efficacy of upper limb exercises using a commercially available computer gaming device (Nintendo Wii) in stroke patients. 105 patients with stroke will be assigned to one of three groups of upper limb exercises: (1) computer gaming, (2) conventional therapy and (3) self-guided exercises.

These exercises will be performed 4 times a week for a total of 3 weeks. Patients will be evaluated for strength and function of the affected upper limb before and after intervention.

Results of this study will help us to understand the role of computer gaming as a therapeutic option for treating upper limb weakness after stroke. The study should be completed by July 2013.

## What are the health outcomes and/or impact on patients and/or the community?

Rehabilitation is a labour and manpower-intensive process. Key to good rehabilitation outcomes are motivation and high intensity repetitive task-specific therapeutic exercises but unfortunately, this may not always be possible. Technology has the ability to address these shortcomings and the potential to change the way rehabilitation is conducted and delivered in the future.

# KNOWING OUR HEALTHCARE LEADERS

## DR LEONG KHAI PANG

ASST CHAIRMAN MEDICAL BOARD (RESEARCH)  
DIRECTOR, CLINICAL RESEARCH UNIT  
SENIOR CONSULTANT  
DEPARTMENT OF RHEUMATOLOGY, ALLERGY AND IMMUNOLOGY  
TAN TOCK SENG HOSPITAL



### What are your thoughts on the current state of collaborative research in your institution?

Let's agree on some definitions. I guess you are thinking of 'research activity involving more than one institution' when you talk about 'collaborative research'.

People in Tan Tock Seng Hospital do work with doctors and scientists in other institutions, such as National University of Singapore (NUS), Nanyang Technological University (NTU), Agency for Science Technology and Research (A\*STAR), and the polytechnics. Increasingly, through Standards, Productivity and Innovation Board (SPRING), we are also working with Small Medium Enterprise (SME)'s.

There are pockets of intense collaborative research activity, but I think, overall, this can be scaled up and managed better.

### Is there a simple analogy that you would use to describe the "As Is" and "To Be" state of your research in your institution?

How about shopping in Hongqiao in Beijing versus in Neiman Marcus on Fifth

Avenue? Hongqiao is rather a messy place with many stall keepers plying their wares without central control. Some may have high-quality goods but many do not. It is hard for the customer to navigate the place. The customer is never sure of the quality of the purchased clothes.

On the other hand, Neiman Marcus has consistently high standards. The customer experiences smooth and assured service. Everything is designed to ensure that the customer is satisfied accomplishes what she sets out to achieve.

This analogy breaks down when we consider the costs. Certainly we do not want research to become prohibitively expensive. Therefore, conducting research in TTSH ought to be like shopping in Neiman Marcus at Hongqiao prices.

### What do you think are the qualities of your institution that allows it to catalyze collaborative research?

We in TTSH realised long ago that we have to collaborate with external researchers not by choice, but by necessity. TTSH is

deficient in laboratory equipment, funding, protected time and dedicated research staff. The only way to access these is to work with people who possess them. TTSH brings ideas, clinical orientation and patient material to the table; collaborators supply laboratory expertise, students, and access to expensive technology. It's a perfect match.

### Could you share an example of a piece of collaborative research that you are involved in and how it has benefited the various stakeholders?

My job is more concerned with research administration than actual research. In fact, my research activity has slowed markedly in the seven years that I've been involved in administration. As an example, I have been working with my colleague Dr Koh Ee Tzun on a large study on rheumatoid arthritis.

We collaborate with a biostatistician, a pharmacoeconomist, a few NTU faculty members and a doctor (SingHealth). The project is large enough to accommodate all and the collaborators can get to work on aspects of the study that interest them.



### On a lighter note, what do you like most about your job?

I am learning a lot about managing people, a skill that cannot be acquired in medical school or in the wards and clinics.

I learn how to interview potential employees, how to temper expectations, how to manage my superiors, how to talk with the finance people, how to make value judgments, how to deal with difficult staff, and how to terminate people (figuratively). OK, I have not been an excellent student and I still do many things far from well but I get better day by day. I also get to meet many people external to TTSH and NHG, which is always a pleasure.

### How do you handle the tight demands of your schedule and yet find time for your family?

Do not ask me how I do it because I do this poorly. I try to spend as much time as I can with my wife. As is now said, it is not work-life balance, implying a 50:50 share, but work-life harmony, in which we apportion

time to each that we feel most comfortable with.

### What do you like to do in your spare time? Do you have any hobbies?

There's very little spare time. Whenever I can, I try to catch a Naruse movie or read the latest Nesbø thriller. I try to keep up with advances in chess theory but I have no time for competitive games anymore.

### Does your personality and love for your hobbies help in making decisions in your research work?

Yes, our personality, including our quirks, addictions and obsessions, permeates all our decisions in life. I would say that every decision I have made is affected by my personality!

Let me give an example of the resolution of a research question offered by reading. I was trying to understand why lupus patients use alternative medicine, Traditional Chinese medicine (TCM), in this case. Is it because they are feel helpless, or paradoxically, because they have exercised their personal choice

after reasoned thought? The literature contains papers supporting both reasons for alternative medicine usage. Steven Pinker's Words and Rules explains how humans convert verbs to the past tense. Conversion is easy for regular verbs like hike (past tense is hiked), walk (walked) and talk (talked).

It is more difficult to convert irregular verbs such as eat (ate), lie (lay) and run (ran). Pinker proposed that when we need to change a verb to the past tense, in our mind, we scan through the list of irregular verbs we have learnt. If there is a match, we use the irregular past tense.

If it is none, we add a -ed to the back of the word. There are two processes in play. In my paper, I proposed that patients who have the Chinese orientation will use TCM in a casual way (such as consuming herbal drinks and tonics) while those who are distressed tend to pay for TCM physician service and receive acupuncture and other intensive therapy.

## NHG RESEARCH TRAINING CALENDAR FOR JULY-AUGUST 2013

Date	Time	Training Programme	Course Category	Course Module	Venue
Ongoing	00:00-23:59	Proper Conduct of Research Online - Basic I & III	Proper Conduct of Research	PC101 & 103	<a href="http://www.elearning.nhg.edu.sg">http://www.elearning.nhg.edu.sg</a>
		Proper Conduct of Research – Basic II ^		PC102	
4 July 2013	08:45 – 17:00	Research Governance and Monitoring, Audits and Inspections Workshop	Research Ethics	RE101C	NHG College (Jackson Square) Block B, Synergy 3
18 July 2013	08:45 – 12:30	Safety Monitoring and Safety Reporting Workshop		RE105C	TBC
1 August 2013	08:30 – 17:30	Investigational Product Management and Essential Documents and Proper Documentation in a Clinical Trial Workshop		RE103C & RE104C	National University Hospital, Kent Ridge Wing, Level 2, Advanced Surgery Training Centre (ASTC), STLab

For registration and full details, please visit [www.research.nhg.com.sg](http://www.research.nhg.com.sg) (Training & Education -> Register for a Course).

There will strictly be no reservations of course seats. All participants must register online.

\*Dates are subjected to changes without prior notice.

^For more information, refer to [www.research.nhg.com.sg](http://www.research.nhg.com.sg) (Training & Education -> Course Categories -> Proper Conduct of Research Courses).

# QUALITÉ

THE PROGRAM WITH A MISSION TO ENSURE AND ENFORCE THE RESPONSIBLE CONDUCT OF RESEARCH MEETING HIGH ETHICAL STANDARDS.



## OVERVIEW OF RESEARCH QUALITY MANAGEMENT (RQM)

The Research Quality Assurance (RQA) division was first established under the auspices of the Research & Development Office (RDO). The division worked closely with the Domain Specific Review Board (DSRB) to ensure that research activities across the cluster were carried out in compliance with applicable regulations and guidelines. This initiative was guided by the mission to promote a research culture that adhered to the highest ethical standards within NHG.

In 2011, the Office of Human Research Protection Program (OHRPP) was instituted, and the RQA division was re-designated as the "Research Quality Management" (RQM) unit, the name it still goes by today. RQM's functions are grounded in two broad-reaching and closely intertwined initiatives – Quality Assurance (QA) and Quality Improvement (QI). This article describes the RQM initiatives that have been implemented within its research ambit, with the noble aim of bettering research standards across the NHG community.

## QUALITY ASSURANCE (QA) INITIATIVES

Central to the QA initiatives is the conduct of random study reviews of ongoing research studies reviewed and approved by the DSRB. Studies selected for study reviews have their documents and research activities evaluated against institutional and regulatory standards. These standards encompass the Singapore Guideline for Good Clinical Practice (SGGCP), Proper Conduct of Research (PCR) standard operating procedures (SOPs), DSRB SOPs, and applicable legislative requirements for research such as the Medicines (Clinical Trials) Regulations and the Medicines Act.

During the study review, the RQM reviewer corroborates the study staff interviews with documentation in the current study records. Any deficiency in the conduct of the study, suggestions for improvements and/or best practices for study management are then shared with the Principal Investigator and his/her study team. Through this iterative

process, a broad understanding of ground practices and the identification of knowledge gaps are achieved. The RQM team evaluates such study, review data on a regular basis and formulates QA and QI initiatives that seek to address pertinent concerns regarding study conduct. One such initiative was a five-month series of roadshows conducted at nine different institutions in 2012, providing researchers with tips on accelerating their DSRB application process.

Aside from randomly selected study reviews, RQM also conducts "for-cause" study reviews, the purpose of which is to ascertain one or more specific aspects of the study conduct. Such study reviews are typically triggered by requests from DSRB, Research Ethics Committee (REC), Institutional Representatives or complaints from subjects.

The formulation of new research policies and renewal of existing guidelines constitutes an improvement cycle, which forms the second pillar of QA. These include the update of existing PCR SOPs, development of new PCR SOPs, work instructions, guidance documents and templates, and informing the research community on new developments and best practices.

Lastly, RQM also maintains and supports the preparatory activities for the Association for the Accreditation of Human Research Protection Programs (AAHRPP) accreditation.

## QUALITY IMPROVEMENT (QI) INITIATIVES

The second core function of RQM is to develop and implement quality improvement initiatives. The QI initiatives focus on ensuring that the cluster research policies, systems, strategies and resources are relevant, updated and harmonised. The QI team seeks to evaluate quality concerns and provide recommendations for the research community.

Current QI initiatives are classified into two domains – one to address the needs of site staff and another devoted to optimising the DSRB's operational efficiency. The former relies on QA activities to generate study review findings, from which measures are identified in an attempt to reduce future similar occurrences of major and critical findings. The latter explores various means to reduce DSRB review timelines, assist the DSRB secretariat in improving their triaging processes, and identify other areas where the quality of DSRB review may be improved.

## CONCLUSION

RQM, through its quality assurance and continuous improvement initiatives, work in synergy with the other OHRPP divisions (DSRB, Researchers Training and Support, Responsible Conduct of Research and Collaboration and Partnership) to achieve human research subject protection. This feeds into its aim of promoting and facilitating ethical conduct of human subject research in NHG and partner institutions.



Team from NHG RQM

## GCP FAQ:

# WHAT ARE THE CLINICAL TRIAL-RELATED SUBMISSIONS THAT PIS NEED TO MAKE TO DSRB AND HSA RESPECTIVELY?

Clinical trials fulfilling the regulatory definition in the Medicines Act are subject to both ethics committee approval (by DSRB) and regulatory approval (by Health Sciences Authority (HSA)) before they can be initiated. However, investigators and research staff are often confused by the different submission requirements for each governing authority, which can include:

- The type of applications that need to be made;
- The documents that need to be submitted; and
- The submission timelines for the different applications.

The tables below seek to provide some clarification with regard to the above issues, and provide a comparison of the clinical trial submission requirements for both authorities.

### (A) Before Initiating the Clinical Trial

The following essential documents need to be submitted to the respective authorities to support the review of the initial application.

Document	Submission to DSRB?	Submission to HSA?
Completed online application form	✓	✓
Study protocol	✓	✓
Investigator's brochure (for industry-sponsored trials)	✓	✓
Package insert or approved labeling of study drug (for marketed drugs)	✓	✓
Informed consent form (ICF)	✓	✓
Copy of approved grant application	✓	Not required
Research tools (e.g. questionnaires)	✓	Not required
Written information to be provided to subjects (e.g. subject diaries)	✓	Not required
Subject recruitment materials (e.g. advertisements)	✓	Not required
Principal Investigator's updated CV	✓	✓
Co-investigators' updated CVs	✓	Not required
At least 2 publications to support the research study	✓	Not required
Certification for PI's completion of minimum training requirements	✓	Not required
Listing of overseas trial sites	-	✓
Good Manufacturing Practice (GMP) certificate for the manufacturer (for unregistered drugs)	Not required	✓
Certificate of Analysis for manufacturer (if GMP certificate for unregistered drug is not available)	Not required	✓

NB: It should be noted that the above list is only meant as a guide and is not exhaustive. Additional documents may be required for the initial submission, and document requirements may vary depending on the nature of the study submitted for review.



**(B) During the Clinical Trial**

Various study notifications, reports and updates need to be submitted to DSRB and HSA during the course of the study. These are detailed in the table below.

Type of Submission	Submission to DSRB?	Submission to HSA?
Protocol and/or ICF amendments	Includes change in PI or study team members	Administrative protocol / ICF amendments do not require submission to HSA
Change in principal Investigator	To be submitted as a study amendment	To be submitted via the "Change of Principal Investigator" module on PRISM
Change in study team members	To be submitted as a study amendment	Not required
Addition of trial site	To be submitted as a study amendment	To be submitted via the "Addition of Clinical Trial Site" module on PRISM
Notification of updated investigator's brochure		
Protocol deviation / non-compliance		
Adverse events	Unanticipated problems involving risks to subjects or others (UPIRTSOs) need to be submitted within the stipulated reporting timelines	Serious adverse events (SAEs) fulfilling the regulatory reporting criteria need to be submitted within the stipulated reporting timelines
Study status report	To be submitted annually, as one of the supporting documents for the renewal of study approval	Trial status reports must be submitted at least every 6-monthly following study approval, or more frequently when there is a change in the status of the study (e.g. termination of trial site)
Renewal of study approval	To be submitted at least 4-6 weeks before end of study approval period	The application for the Clinical Trial Certificate (CTC) extension may be submitted up to 3 months before the CTC expiry date

**(C) Upon Completion of the Clinical Trial**

Principal investigators are required to notify both DSRB and HSA when the clinical trial has been completed. However, it should be noted that both authorities administer different definitions for completion of a clinical trial.

The DSRB deems a study completed when all of the following criteria have been fulfilled:

- a. The research is permanently closed to the enrolment of new participants;
- b. All participants have completed all research-related interventions; and
- c. Collection and analysis of individually identifiable data have been completed.

Conversely, the HSA defines clinical trial completion as the time point when the last patient last visit (LPLV) in Singapore has been completed. Based on their respective definitions, the submission requirements following completion of a clinical trial is as follows:

Document	Submission to DSRB?	Submission to HSA?
Study status report	To be submitted within 4-6 weeks of study completion	To be submitted following LPLV
Clinical study report or publication	Not required	To be submitted within 3 months of study completion, unless otherwise agreed by HSA

**References:**

1. Application Form for Clinical Trial Certificate (CTC), Health Sciences Authority. Available at [http://www.hsa.gov.sg/publish/hsaportal/en/health\\_products\\_regulation/clinical\\_trials/guidelines.html](http://www.hsa.gov.sg/publish/hsaportal/en/health_products_regulation/clinical_trials/guidelines.html)

2. Health Sciences Authority (HSA) Clinical Trials Branch – Frequently Asked Questions. [http://www.hsa.gov.sg/publish/hsaportal/en/health\\_products\\_regulation/clinical\\_trials/faqs.html](http://www.hsa.gov.sg/publish/hsaportal/en/health_products_regulation/clinical_trials/faqs.html)

3. Investigator Manual 1st Edition (Aug 2009).

## RESPONSIBLE CONDUCT OF RESEARCH (RCR)

**AUTHORSHIP & PUBLICATIONS****Ms Valerie Wee**

Senior Executive

Research Quality Management

Research &amp; Development Office

National Healthcare Group

This issue features the sixth component of Responsible Conduct of Research (RCR) – Authorship and Publications.

**Authorship**

Within the research community, authorship is the most visible form of academic recognition and credit. As a result, credit for publication features prominently in disputes.

For example, a researcher trying to solidify their intellectual property claims may attempt to deny authorship as well as inventor-ship to individuals who have contributed to a new discovery or invention.

**Publications**

Responsible writing and publications include giving proper credit or acknowledgment to team members who had contributed and avoiding plagiarism. Plagiarism is defined as the practice of taking someone else's work or ideas and passing them off as one's own.

In an era of increasing emphasis on commercialisation, authorship and credit help to define intellectual property rights. This, and other reasons, may explain scientists' desire for the credit of authorship. Therefore, the assignment of authorship is central in the responsible conduct of research.

In the past, researchers might be advised to name their Head of Department or a key opinion leader in their manuscript to increase its credibility so as to enjoy broader circulation. According to RCR, it is responsible and better practice for researchers to plan ahead and agree on the authorship list and rankings before the start of their research.

This will avoid any friction or misunderstandings and promote future collaborative research.

Prior to publication of manuscripts, researchers should:

**1. Appreciate the minimum standards of responsible publications**

All forms of publications should provide:

- i) A full and fair description of the work undertaken;
- ii) An accurate report of the results; and
- iii) An honest and open assessment of the findings.

In assessing completeness of publications, researchers should ask whether they have described:

- 1) What they did (methods);
- 2) What they discovered (results); and
- 3) What they make of their discovery (discussion).

**2. Understand the elements of a responsible publication**

These elements include abstracts, methods, results, discussions, notes, bibliography and acknowledgements.

**3. Appreciate what contributes to responsible authorship**

Contributions: Although there are standards to limit authorship to individuals who play significant roles in the research and to acknowledge those who play lesser roles, varying practices exist. Decisions on who should be authors are best made early to avoid any dispute.

Importance: Authors are usually listed in their order of importance with the designation of first or last author carrying special weight, although practices may vary by discipline. Academic institutions usually will not promote researchers to the rank of tenured faculty until they have been listed as first or last author on one

or more papers. Corresponding authors: Corresponding or primary authors assume responsibility for all aspects of the journals. Corresponding authors should take note of the fact that they are acting on behalf of their colleagues. Any mistake may affect their colleagues and their own careers.

The following practices should be avoided:

- Honorary Authorship – A significant problem in research publication today where researchers are listed because of their position, funding, or where they had served as mentors to the primary author. This practice is widely condemned and in extreme cases, considered a form of research misconduct;
- Salami Publications – The practice of dividing a significant piece of research into a number of small experiments simply to increase the number of publications. This practice distorts the value of the work and wastes valuable time and resources;
- Duplicate Publications - The practice of publishing the same information a second time without acknowledging the first publication. This practice wastes time and resources, and potentially distorts the research record and endangers public health; and
- Premature Public Statements – Research results should be made public only after they have been carefully reviewed and properly prepared for publication.

*For more information regarding the requirements for submitting manuscripts, do refer to the International Committee of Medical Journal Editors (ICMJE) for Uniformed Requirements for Manuscripts Submitted to Biomedical Journals (<http://www.icmje.org>) and the Singapore Medical Journals – Instructions to Authors (<http://www.sma.org.sg/smj/instructions.pdf>).*

## RESEARCH GRANT CALLS AND TALENT DEVELOPMENT PROGRAMS

NATIONAL MEDICAL RESEARCH COUNCIL (NMRC) GRANTS			www.nmrc.gov.sg
Grant Name	Grant Description	Funding Quantum	Application Period
Clinician Scientist – Individual Research Grant (CS-IRG)	The CS-IRG is provided to Clinician Scientists to enable them to carry out medical research on a specifically defined topic. All CS-IRG applications will be evaluated through a two-stage process with an international peer review stage followed by a Local Review Panel.	Maximum of S\$1.5 million per project for 3 years with additional 20% indirect costs.	May – June 2013
Clinician Scientist – Individual Research Grant – New Investigator Grant (CS-IRG-NIG)	The CS-IRG-NIG is a subcategory of the CS-IRG to cater for new clinical investigators. The CS-IRG-NIG is a step for the new investigator to a first independent national level grant.	Maximum of S\$200,000 per project for 2 years with additional 20% indirect costs.	
Cooperative Basic Research Grant (CBRG)	The CBRG is provided to non-clinical researchers to conduct research proposals in basic and translational clinical research. The CBRGs also aims to promote basic biomedical sciences (BMS) research collaborations across institutions in Singapore.	Maximum of S\$1.5 million per project for 3 years with additional 20% indirect costs.	May – June 2013
Cooperative Basic Research Grant - New Investigators Grant (CBRG-NIG)	The CBRG-NIG is a subcategory of the CBRG to cater for new non-clinical investigators. The CBRG-NIG is a step for the new investigator to a first independent national level grant.	Maximum of S\$200,000 per project for 2 years with additional 20% indirect costs.	
NMRC Clinical Trial Grant (CTG)	The CTG aims to support clinicians in carrying out clinical trial studies for the development of novel therapies for healthcare needs. There will be three schemes under the CTG program, namely the (i) Co-Development Scheme which supports clinicians who wish to collaborate with the industry, and the Investigator-Initiated Trials - (ii) Early Phase and (iii) Late Phase Schemes which support clinicians who wish to conduct clinical trial studies on therapies of their own interest. These will help to develop the next generation of clinical investigators, promote translational and clinical research studies, and move promising ideas from bench to bedside.	<p>The Co-Development Scheme: Co-investment of cash or in-kind is required from an industry partner (50% or more of the total project costs). A maximum of S\$5million for 3 years, inclusive of 20% indirect costs, could be provided for expenditure incurred by the lead PI and institutions.</p> <p>PI-Initiated Scheme(Early Phase Trials): Maximum of S\$5million for 3 years inclusive of 20% indirect costs.</p> <p>PI-Initiated Scheme(Late Phase Trials): Maximum of S\$2million for 3 years inclusive of 20% indirect costs.</p>	<p>The Co-Development Scheme: Open all year round.</p> <p>PI-Initiated Schemes: Twice a year in February and estimated July.</p>
Talent Development Award	Award Description	Eligibility Criteria	Application Period
Transition Award (TA)	The TA is provided to assist budding, young clinicians who have just returned from formal research training, to build up their capability in research. It includes funding support for mentored research project with salary and grant funding for up to three years.	Maximum of S\$375,000 per award for 3 years with additional 20% indirect costs.	May – June 2013
Clinician Scientist Award (CSA)	<p>The CSA aims to provide salary &amp; funding support for selected outstanding clinician scientists, who possess a consistent record of excellence in research, to enable them to carry out internationally competitive translational and clinical research.</p> <p>There are 2 categories in CSA to allow flexibility in time commitment. The Investigator (INV) Category is for clinician scientists who have good track records of research work and demonstrated potential to become leaders in their field. The Senior Investigator (SI) Category is for clinician scientists who have demonstrated sustained, high levels of productivity &amp; leadership in translational &amp; clinical research. They are expected to mentor MBBS-PhD students &amp; junior clinician scientists.</p>	<p>Investigator Category: Maximum of 3 years' salary support and grant support of up to S\$675,000 for 3 years with additional 20% indirect costs.</p> <p>Senior Investigator Category: Maximum of 5 years' salary support and grant support of up to S\$1.75 million for 3 years with additional 20% overhead costs.</p>	May – June 2013

All information are accurate as at time of print. Please refer to respective websites for more information.

## RESEARCH GRANT CALLS AND TALENT DEVELOPMENT PROGRAMS

NATIONAL MEDICAL RESEARCH COUNCIL (NMRC) GRANTS			www.nmrc.gov.sg
Talent Development Award	Award Description	Eligibility Criteria	Application Period
Singapore Translational Research (STaR) Investigator Award	The STaR is a prestigious award offered by the MOH to recognise and support internationally renowned and outstanding investigators in translational and clinical research.	Maximum of 5 years' salary support and grant support of up to S\$5 million for 5 years with additional 20% indirect costs.	May – June 2013
NMRC Research Training Fellowship	The NMRC Research Training Fellowship is awarded to outstanding and talented clinicians, health science professionals (e.g., nurses, pharmacists) and biostatisticians for overseas research training or to pursue a graduate degree in research in local institutions.	<p>Local Training Leading to a PhD or Master's Degree: Maximum of 3 years' salary &amp; tuition fee support and conference support of up to \$4,000 per year (extendable to 4 years for PhD degree). Eligibility to apply for a research seed funding upon completion of training, of up to \$30,000 (subject to the approval of a research proposal).</p> <p>Overseas Research Attachment: Maximum of 3 years' salary, tuition fees, maintenance allowance, return air passage, health insurance support (extendable to 4 years for PhD degree). Conference support of up to \$4,000 per year Eligibility to apply for a research seed funding upon completion of training, of up to \$30,000 (subject to the approval of a research proposal).</p>	Open all year round

MINISTRY OF HEALTH (MOH) GRANTS			www.moh.gov.sg
Grant Name	Grant Description	Funding Quantum	Application Period
Health Services Research - Competitive Research Grant	The Health Services Research Competitive Research Grant is a MOH research grant established in 2009. This HSR CRG aims to promote the conduct of HSR and enable the translation of HSR findings into policy and practice.	<p>Large Projects: For larger scale effectiveness trials in multi-center projects (Phase 3 Projects). Maximum of S\$1 million per project for 2 years with additional 20% indirect costs.</p> <p>Small Projects: For pilot and smaller scale projects and/ or those that are exploratory in nature (Phase 1 &amp; 2 Projects). Maximum of S\$200,000 per project for 2 years with additional 20% indirect costs.</p>	May – June 2013
Health Services Research - Competitive Research Grant – New Investigator Grant (HSR-CRG-NIG)	<p>The HSR-CRG is a MOH research grant established in promote the conduct of HSR and enable the translation of HSR findings into policy and practice.</p> <p>The HSR-CRG-NIG is a subcategory of the HSR-CRG to cater for new investigators. The HSR-CRG-NIG is a step for the new investigator to a first independent national level grant.</p>	Maximum of S\$100,000 per project for 2 years with additional 20% indirect costs.	May – June 2013
Communicable Diseases Public Health Research Grant (CD-PHRG)	The CD-PHRG aims to encourage researchers to work on strategic research topics with major public health impact for Singapore, in the area of communicable diseases (prevention and control. It also supports research that is translational in nature to inform public health risk assessment, interventions and policy formulation for communicable diseases control.	Maximum of S\$1 million per project for 3 years inclusive of 20% indirect costs.	May – June 2013

All information are accurate as at time of print. Please refer to respective websites for more information.



## RESEARCH GRANT CALLS AND TALENT DEVELOPMENT PROGRAMS

NATIONAL HEALTHCARE GROUP (NHG) GRANTS AND PROGRAMMES			www.research.nhg.com.sg
Grant Name	Grant Description	Funding Quantum	Application Period
NHG Clinician-Scientist Career Scheme (CSCS)	The CSCS is a 3 year scheme to develop research capabilities of NHG clinicians and enable them to compete successfully for NMRC's Transition Award (TA) or Clinician Scientist Award (CSA). In the long term, the scheme aims to develop these clinicians scientists to be Key Opinion Leaders (KOLs) in NHG who will contribute to excellence in research innovation and improvement in patient care, delivery and outcomes and lead research in the Lee Kong Chian School of Medicine (LKC SoM). The scheme provides both grant funding and protected time funding.	CSCS Junior: Maximum protected time funding of 0.4FTE for up to 3 years, and maximum grant funding of S\$60,000 per year for up to 3 years.  CSCS Mid-Level: Maximum protected time funding of 0.4FTE for up to 3 years, and maximum grant funding of S\$100,000 per year for up to 3 years.	April – May 2013
NHG-NTU Clinician-Scientist Fellowship (CSF)	The NHG-NTU CSF is a collaboration between National Healthcare Group (NHG) and Nanyang Technological University's Lee Kong Chian School of Medicine (NTU/ LKCMedicine). It is supported under the CSCS.  The objective of the fellowship is to nurture and develop Clinician-Scientists through the provision of an integrated pathway, from clinical residency to PhD training, postdoctoral experience and subsequently appointment as a Clinician-Scientist faculty at LKCMedicine and NHG.	Research funding quantum is the same as for CSCS. In addition, successful awardees receive full sponsorship of PhD tuition fees for 4 years through NTU Research Scholarship and full salary support for 3 years.	

All information are accurate as at time of print. Please refer to respective websites for more information.

## RESULTS OF FY2013 NATIONAL HEALTHCARE GROUP INTRAMURAL GRANTS CALLS

The National Healthcare Group is dedicated to developing Clinician-Scientists and Clinician Investigators and had launched the following research grants between July 2012 and December 2012 last year.

1. NHG Thematic Grant (NTG);
2. NTU-NHG Innovation Collaboration Grant (ICG);
3. NHG-KTPH Clinician Leadership in Research (CLR) Programme; and
4. NHG-KTPH Small Innovative Grant (SIG).

The FY2013 results have been released and the following are the successful awardees from the grants. More details on the grants may be found on the NHG Research Website at [www.research.nhg.com.sg](http://www.research.nhg.com.sg).

## FY2013 NHG THEMATIC GRANT

S/N	Project Title	Principal Investigator	Department/ Institution
1	Vaccines and Respiratory Tract Infections in The Elderly - Assessing Epidemiology, Public Health Service Impact and Scientific Exploration of Pathophysiology and Immunology	Dr Yung Chee Fu	Clinical Epidemiology, TTSH
2	Etio-pathogenesis and Novel Drug Therapy of Age Related Macular Degeneration (AMD) and Polypoidal Choroidal Vasculopathy (PCV) - An Asian Perspective	Dr Colin Tan Siang Hui	Ophthalmology, TTSH

## FY2013 NTU-NHG INNOVATION COLLABORATION GRANT (ICG)

S/N	Project Title	NHG Lead-Principal Investigator	NTU Lead-Principal Investigator
1	Improving Spatial Resolution of MR Diffusion Weighted Imaging Through The Development of Super-Resolution Technology for Improved Prostate Cancer Diagnosis	Dr Tan Cher Heng Diagnostic Radiology, TTSH	Assistant Professor Poh Chueh Loo School of Chemical and Biomedical Engineering, NTU
2	Vesico-Urethral Connector	Dr Chia Sing Joo Urology, TTSH	Professor Subbu S. Venkatraman School of Materials Science & Engineering, NTU

## FY2013 NTU-NHG INNOVATION COLLABORATION GRANT (ICG)

S/N	Project Title	NHG Lead-Principal Investigator	NTU Lead-Principal Investigator
3	A Pilot Study Evaluating Caspase-3 Activation as a Novel Marker of Systemic Toxicity in Breast Cancer Patients Receive Chemotherapy	Dr Tan Ern Yu General Surgery, TTSH	Associate Professor Kathy Qian Luo School of Chemical and Biomedical Engineering, NTU
4	Theranostics Biodegradable Nanoparticles for Prostate Cancer Imaging and Therapy	Dr Tan Cher Heng Diagnostic Radiology, TTSH	Assistant Professor Professor Yong Ken Tye School of Electrical and Electronic Engineering, NTU

## FY2013 NHG-KTPH CLINICIAN LEADERSHIP IN RESEARCH (CLR) PROGRAMME

S/N	Project Title	Principal Investigator	Department/ Institution
1	The Utility of Continuous Glucose Monitoring Systems (CGMS) in Diabetes Patients with Chronic Kidney Diseases (CKD)	Dr Ester Yeoh	Medicine, KTPH
2	Pruritus in Primary Localized Cutaneous Amyloidosis	Dr Tey Hong Liang	Medical, NSC
3	The Thyrotoxicosis QoL Study: Validation of Thy-PRO Questionnaires with Correlation to Clinical, Biochemical and Ultrasound Variables	Dr Liew Hui Ling	Endocrinology, TTSH
4	Treatment of Ventilator Associated TracheoBronchitis with Aerosolized Antibiotics and Effect on Ventilator Associated Pneumonia: A Randomized Double Blind Placebo Controlled Pilot Study	Dr Ling Li Min	Infectious Diseases, TTSH
5	Reducing Incidence of Sepsis of Transrectal Ultrasound guided Prostate Biopsy with a Combination of Iodine Enema and Rectal Swab for Targeted Antibiotic Prophylaxis	Dr Liu Zhenbang	Urology, TTSH
6	Efficacy of Decontamination of Nasendoscopes using Cidex OPA® Solution following Nasendoscopy	Dr Phua Chu Qin	Otolaryngology, TTSH

## FY2013 NHG-KTPH SMALL INNOVATIVE GRANT I (SIG I)

S/N	Project Title	Principal Investigator	Department/ Institution
1	Why Do They Start and Why Don't They Quit: A Qualitative Study to Explore Risk and Protective Factors for Tobacco Use in Youth	Adj. Asst Prof Mythily Subramaniam	Research, IMH
2	Elucidating Structural and Functional Connectivity Disturbances Between Resting State Brain Regions in Schizophrenia: A Multimodal Imaging Connectomics Study	A/Prof Sim Kang	General Psychiatry, IMH
3	Cognitive Profiling and Deep Phenotyping in Schizophrenia	Mr Max Lam Zhan Yang	Research, IMH
4	Biomarkers (C-reactive protein) and Major Candidate Genes (GCK, HNF1a and HNF4a) Mutations Screening For Monogenic Diabetes Using Next-Generation Sequencing (NGS) Among Asians with Young-Onset Diabetes	A/Prof Lim Su Chi	Diabetes Centre, KTPH
5	A Pilot Study To Explore The Possibility Of Using Urinary Exosome MicroRNA As Biomarker For Diabetic Nephropathy In Type 2 Diabetes.	Dr Liu Jian-Jun	Clinical Research Unit, KTPH
6	Study Of Pigment Epithelium-Derived Factor (PEDF) and Its Association With Apoprotein-A1 Expression, and Insulin Resistance	A/Prof Tavintharan S	Diabetes Centre, KTPH
7	Development Of Molecular Targeted Therapeutic Strategy For Atopic Dermatitis	Dr Zacharias Aloysius Dwi Pramono	Research, NSC
8	Clinical And Optical Coherence Tomographic Correlations Of Pathologic Myopia In A Multi-Ethnic Asian Population Using Multi-Modal Ophthalmic Imaging	Dr Colin Tan	Ophthalmology, TTSH
9	A Multi-Centre, Prospective, Randomised Controlled Trial Comparing The Use Of The Proximal Femoral Nail - Antirotation (PFNA) And Dynamic Hip Screw (DHS) For Stable Intertrochanteric Fractures Stable Trochanteric Fractures Intramedullary Versus Extramedullary (STRIVE) Study	Dr Ernest Kwek Beng Hee	Orthopaedic Surgery, TTSH
10	Treatment Of Ventilator Associated Tracheobronchitis With Aerosolized Antibiotics And Effect On Ventilator Associated Pneumonia: A Randomized Double Blind Placebo Controlled Study	Dr Ling Li Min	Infectious Diseases, TTSH
11	A Pilot Study Examining The Ratio Of C-Reactive Protein And Serum Albumin For Predicting Short Term Survival In Advanced COPD: A Novel Biochemical Prognostic Method Reflecting Systemic Inflammation And Respiratory Muscle Reserves	Dr Neo Han Yee	Geriatric Medicine, TTSH
12	Finding The Glaucoma Proteomic Profile - Diagnostic Molecular Biomarkers for the Future	Dr Nicola Gan Yi'an	Ophthalmology, TTSH
13	Pro-Inflammatory Immune Profiling And Transcriptome Analysis In Type 2 Diabetes Mellitus: Exploring Racial Differences	Dr Rinkoo Dalan	Endocrinology, TTSH

# MUSCLE AND CARDIAC BIOPHYSICS AT LKCMEDICINE

## Professor Michael Ferenczi

Assistant Dean

Head of Phase 1

Lee Kong Chian School of Medicine

Michael Ferenczi, Professor of Medical Sciences at NTU receives a prestigious Tier 2 grant from the Singapore Ministry of Education for a project entitled "The molecular basis of the stretch response in skeletal and cardiac muscles", starting in June 2013 for 36 months, with a value of S\$695,753<sup>1</sup>.

It is an exciting time to write about my research, and about the new Lee Kong Chian School of Medicine in NTU which is about to open its doors to our first batch of 54 Singapore students in August 2013. A staff of about 60 has been busy over the past two years to put in place the new Singapore medical school for undergraduate students in Asia's university with the fastest growing reputation.

In my role as Assistant Dean and Head of Phase 1, I participate in the development of the curriculum and exciting teaching methods and teaching infrastructure, and in the recruitment of top class teachers and scientists. It is exciting to build, from the ground up, a new institution which will have a major impact on the Singapore landscape – both because of the excellent doctors it will train, and because of the scientific and translational impact of its research, with the purpose of improving the health, and healthcare of Singapore citizens and of the whole of mankind. My research laboratory is also taking shape. Thanks to the Tier 2 grant from Ministry of Education (MOE), I am recruiting three superb young scientists, from Singapore, United Kingdom and United States. Together we shall be applying novel biophysical techniques to explore fundamental aspects of cardiac contraction. Muscles and the heart, are organs specialised in the conversion of chemical energy into mechanical work, just as car engines convert fuel into movement and acceleration.

The heart is a finely tuned engine, with a performance perfected over millions of years of evolution. The heart converts energy with remarkable efficiency and it does this sixty times per minute, for eighty years or more – not many car engines can claim such

longevity! Unfortunately, eventually the heart fails, as a consequence of mutations which alter the protein constituents of the heart, or clogged arteries causing heart attacks resulting in damaged cardiac tissue that does not repair itself very well. The laboratory will be looking at the effect of mutations in key proteins to understand the factors that lead to cardiac remodelling. Indeed, mutations in some genes cause the heart to grow too much, and this leads to disease. However the growth mechanisms are interesting, as it may be possible to take advantage of the growth



potential to repair the heart when damaged by infarcts. It is a privilege to contribute to Singapore life through my research and through the establishment of the new Medical School.

### The Research Project

Work at Imperial College London has demonstrated that during stretch of active muscle the heart muscle stops utilising Adenosine Triphosphate (ATP), the molecule that fuels contraction. When this happens, less inorganic phosphate is released in the heart cells. Recent work has also highlighted the importance of phosphorylation (a chemical modification of proteins) which alters the speed and force of cardiac contraction. In addition, these modifications may play a part in the signal pathways that cause the heart to change shape or enlarge, a process called remodelling. In Singapore, we shall look at the role of phosphate and of protein phosphorylation on the stretch response in the heart to unravel the link between phosphorylation and cardiac performance. We already know that mutations which give rise to sudden cardiac death alter the contractile performance of the heart.

Here again, the mutations may affect cardiac performance by changing the phosphorylation state of the proteins and their response to phosphate. Thus, the project will look in great detail at the molecular factors

affecting heart disease, and may reveal ways to interfere with heart cells to improve their performance or to stimulate their repair.

For further information, please visit our website, or email [m.ferenczi@ntu.edu.sg](mailto:m.ferenczi@ntu.edu.sg)

### Mike Ferenczi's Research

Mike started his scientific career in the laboratory of Andrew Huxley and Bob Simmons at University College London. He studied protein biochemistry under Alan Weeds at the Laboratory of Molecular Biology in Cambridge and enzyme kinetics with David Trentham and Freddie Gutfreund in Bristol. During post-doctoral years at the University of Pennsylvania, Philadelphia, Mike became passionate for the development of new techniques to study cells. There, his mentors were David Trentham, Yale Goldman and Earl Homsher, who guided his passion for optics, instrumentation and new chemical approaches. Back in the UK, working at the National Institute for Medical Research, Mike applied his skills to understanding the molecular mechanisms of muscle contraction using unique biophysical techniques with high temporal resolutions. In particular he worked out the relationship between power output and the kinetics of ATP hydrolysis in skeletal muscle. He also used low-angle x-ray diffraction using x-rays from the UK's Daresbury Laboratory and Europe's ESRF synchrotron in Grenoble, to observe the changes in shape of the contractile proteins during force generation.

In 2001, a Professor of Physiological Sciences at Imperial College London, Mike extended his work to cardiac muscle, and is now interested in exploring how disease processes affect cardiac performance at the molecular level. Joining NTU in 2012, Mike's ambition is to create a laboratory of cardiac biophysics to rival the best institutes in the world. The opportunities to interact with physicists, engineers, chemists in NTU and with other groups in Singapore will lead to unique, new approaches and exciting ideas.

<sup>1</sup> MOE2012-T2-2-105

<sup>2</sup> <http://www.straitstimes.com/breaking-news/singapore/story/nus-and-ntu-move-global-university-rankings-20130305>

<sup>3</sup> <http://www.lkcmecine.ntu.edu.sg/AboutUs/FacultyandStaff/Faculty/Pages/MikeFerenczi.aspx>

## TARGETED THERAPEUTICS FOR SKIN DISEASES

**Dr Zacharias Aloysius Dwi Pramono Sarengat**

Research Scientist  
Research Department  
National Skin Centre



Zacharias Aloysius Dwi Pramono trained as a medical doctor at the Faculty of Medicine, GadjahMada University, Indonesia, then became a faculty member at its Department of Dermatology. He obtained his Ph.D in human genetics at the Graduate School of Medicine, Kobe University, Japan, also receiving a 2-year clinical training in dermatology. One of AON therapy pioneers, his work is cited in Nature Reviews Genetics (Oct 2003 issue) as the first demonstration of AON-mediated splicing modulation of dystrophin transcript in living human cells. He went on to advance the field after relocating to Singapore. Recently, his work was selected for highlight in the A\*STAR Research bulletin (February 2013 issue). He is currently a National Skin Centre research scientist and was awarded the NMRC EDG Grant to conduct a study to identify the role of microRNA in the development of atopic eczema.

In his initial years as a young physician, he started to realize that for so many diseases there were only very limited drug choices. Today, some 20 years later, the bulk of marketed drugs are small-molecule chemicals targeting only 10% of proteins encoded by the human genome. Many of such small molecules promiscuously target several proteins. Consequently, anticipation of efficacy and side effects in clinical trials becomes problematic, making the realization of the therapeutic value of many protein targets difficult. Very few drugs directly influence the underlying biological pathways in disease development. Given the explosion of advanced biology and disease pathophysiology, the slow progress disturbs as much as it intrigues.

A chance to get involved in doing something about it came about in a chanced encounter with a Japanese professor leading a research team in Duchenne muscular dystrophy (DMD), a fatal disease caused by mutation in the dystrophin gene. He enrolled in a PhD program under his supervision. The group used synthetic antisense oligonucleotides (AONs) to interfere with the endogenous splicing process. The non-coding sequences of a gene transcript (aka introns) are removed, with the coding regions (aka exons) joined to form the messenger RNA.

A novel approach then, they tried to modulate the splicing of dystrophin gene transcripts to correct the reading frame, frequently disrupted by deletion mutations in DMD patients. It restores dystrophin protein

production. He still can recall the day when he finally demonstrated the restoration of dystrophin gene proteins in living human cells. As an affirmation, AON is today a progressive research area delivering new therapeutics options used in clinics.

AONs are chemically-modified DNA/RNA-mimicking molecules. They bind in a sequence-complementary manner to the transcripts of the targeted gene. As all proteins are encoded by gene, AONs can be used to potentially target any gene in the genome. Skin, the biggest human organ, and its accessibility to topical administration, is an ideal target for AON therapy. Targeted treatment is still not available for many rare genetic skin disorders attributed to hundreds of genes to prevalent non-genetic conditions such as atopic eczema that inflicts up to 20% of the population. His group is exploring the application of AON therapy for skin diseases. In particular, the awarded NMRC ED Grant aims to identify the role of microRNAs in the development of atopic eczema. Their ultimate goal is to identify biological targets so that we can design novel AONs for the first targeted therapy of atopic eczema.

He is aware the challenges and the long gestation of translating research outcomes to patient's bed-side. For its use in skin diseases, AONs must be delivered efficiently to the skin cells topically. However, he is encouraged by recent progress in the transdermal delivery of oligonucleotides that shows promising efficiency.

## PRESIDENT'S TECHNOLOGY AWARD 2012

**Associate Professor Louis Phee**

Acting Head, Division of Mechatronics and Design  
School of Mechanical & Aerospace Engineering  
College of Engineering  
Nanyang Technological University



Associate Professor Louis Phee's obsession with medical robotics started when he was an undergraduate. He has always been fascinated about combining state-of-the-art engineering technologies with the science of medicine to bring about benefits for both patients and doctors.



Previously, he had played a major role to develop a self-propelling colonoscope and a prostate needling robot; both of which are now used in hospitals.

Professor Phee started to develop a novel flexible robotic system for endoscopy in 2004. This robotic system incorporates innovative engineering technologies to enable clinicians to perform intricate surgical procedures within the gastrointestinal tract without the need for external incisions. Using this system, patients suffer less pain, less trauma as well as spend less time staying in hospitals. They would also not have any visible scars. The system had been successfully used to remove early stage stomach cancers from five patients. Professor Phee co-founded EndoMaster Pte Ltd in 2011 to commercialise the product known as the Master And Slave Transluminal Endoscopic Robot (MASTER). He hopes that MASTER would cause a paradigm shift from 'keyhole' to 'no hole' surgery. Currently, he is working with doctors from Tan Tock Seng Hospital to develop other innovative medical devices.

For his outstanding contributions in using cutting edge robotics technologies to push the frontier of endoscopic surgery for the benefit of both patients and clinicians, Professor Louis Phee was awarded the 2012 President's Technology Award.



# HEALTH PROGRAM EVALUATION – DESIGNING THE STUDY



**Dr Joseph Antonio Molina**  
Principal Research Analyst  
Health Services & Outcomes Research  
National Healthcare Group

**What is an Evaluation Design?**

Design refers to a plan for meeting an objective. While a research design is a blueprint for conducting a study, an evaluation design is the detailed strategy for conducting an assessment of a health program. The designs used in program evaluation are based on epidemiological methods.

**What are the requirements of an evaluation design?**

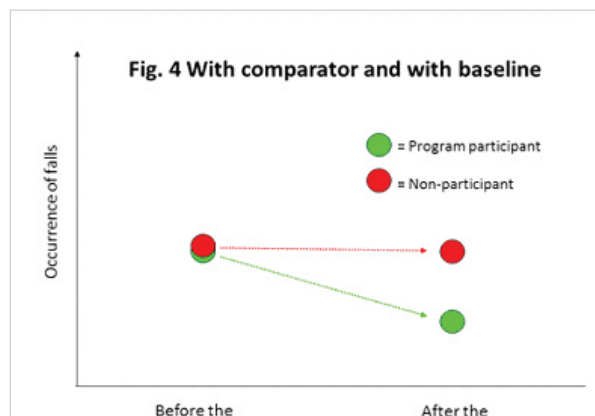
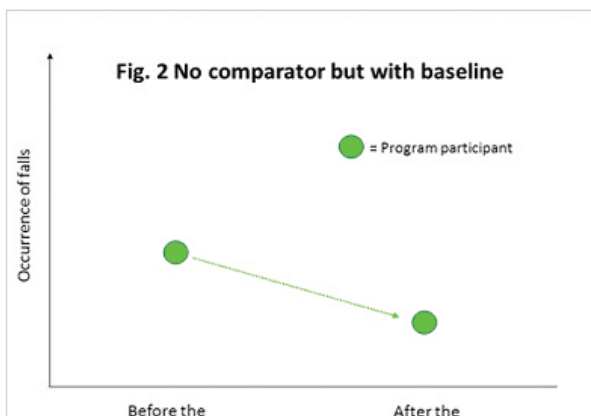
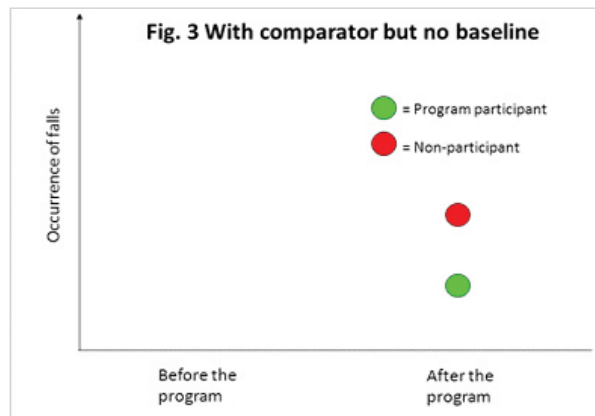
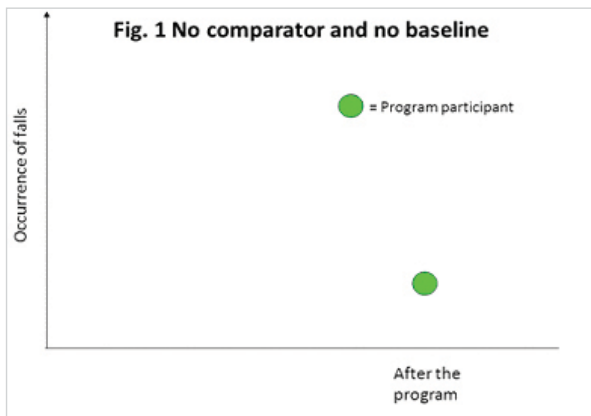
1. Complete and accurate data – While research studies need complete and accurate data, this may be difficult to achieve in real-world research. This is the motivation for using prospective evaluation designs where data are

longitudinally collected from program start (baseline) to program completion (follow-up). It is easier to ensure completeness and accuracy while data is being collected than after the data has already been gathered.

2. Basis for proving that the program is “effective” – As program evaluation aims to measure how well a program is performing, the best way to establish this is by comparing outcomes between:
  - a. A group of program participants versus a group(s) who are not; and
  - b. Baseline and follow-up measurement for both groups

Figures 1 to 4 show hypothetical “evaluation” results from a falls prevention program. When there is no comparator and baseline data, Figure 1 provides the least information to make an assessment of the program outcome.

Although Figures 2 and 3 have additional data with which to compare the occurrence of falls during follow-up among program participants, it is still not enough to make a complete assessment. Figure 4 provides the most complete data for assessing program performance.



**On the issue of comparability of treatment groups:** Similarity in baseline characteristics between participants and non-participants facilitates attribution of program effects. However, there are post-design analytical approaches which can adjust for baseline differences. These include propensity score matching, use of instrumental variables, difference-in-difference analysis and regression-discontinuity design.

# Common evaluation designs:

## 1. Before-after, program-no program design

Comparisons are made within (before-after) as well as between groups (program participants versus non-participants), hence it is possible to attribute effects to the program.

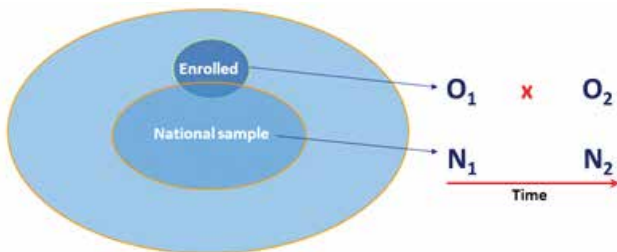
## 2. Chronological series (single group time series)

Multiple serial assessments are done before and after program implementation; trends in the outcome before and after program implementation are compared. Due to the absence of a non-program group, there is no way to discount the effects of adaptation to repeated assessments (testing effect), exposure to interventions from sources other than the program itself, or natural progression of the condition (maturation effect).



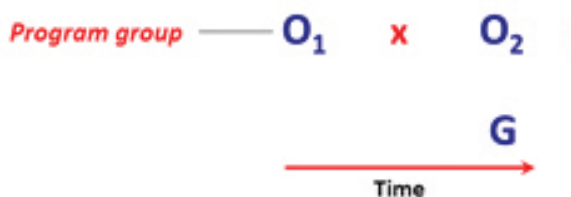
## 3. Before and after studies using national averages as comparison

Similar to design 1, but comparison is with a national sample which may include some program participants.



## 4. Goal-based evaluation model

Targets for the outcome are determined before program implementation. The program is held accountable to prior expectations rather than to relative performance against an actual comparison group. Setting targets for program performance require a strong logic model.



Note: G = Pre-determined program goal/target

## 5. Single group before-after (pre- post-) "design"

No parallel control group; hence results are more suggestive rather than conclusive of program performance. Aside from the limitations of the chronological series design, the single pre-post-design is susceptible to regression to the mean (which implies that at their extreme states, some diseases/conditions may regress to less severe states even in the absence of any intervention).



## 6. Post-test only "design" with non-equivalent groups

No baseline data, hence it is not possible to rule out maturation effects. There is no way to assess comparability of groups at baseline.



## 7. One-group post-test only "design"

The weakest of all "designs," this evaluation is entirely uninformative except to describe the state of participants after enrollment into the program.



Of the above mentioned designs, the last three should be avoided as they are susceptible to many biases. Users of potentially misleading results run the risk of making flawed conclusions about the program.

Evaluation designs can be hybrids of established designs. Ultimately, the program team should aim for a design which can generate accurate and relevant information to aid in decision-making.



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