A NEWSLETTER FOR THE RESEARCH COMMUNITY IN SINGAPORE

catalyst

ACCELERATING **RESEARCH**

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National Healthcare Group
Adding years of healthy life

COVER PAGE The Team from Health Sciences & Outcomes Research (HSOR) Unit, National Healthcare Group

Inside: Exclusive Interview with the Assistant Directors of HSOR

Dear Readers

I hope that you are having a terrific start to the New Year.

Welcome to the first edition of Catalyst for 2013!

We are featuring the NHG's Health Services & Outcomes Research (HSOR) unit. Established in 2005, HSOR was set up with the aim of improving the quality of healthcare in NHG by providing the best available evidence for decision making and translating them into decisions and practice. The multi-disciplinary team consists of more than 20 specialists and researchers from diverse background who work closely with clinical heads and managers on the ground to achieve the unit's aims and NHG's overall vision of "Adding Years of Healthy Life". In this edition of Catalyst, you will be able to read more about their research and staff, including their recent achievements.

Nursing and allied health professional research is a growing interest in NHG. We are pleased to showcase nursing and allied health professionals research at IMH. Some of the projects had also won awards at the Singapore Health & Biomedical Congress 2012 held in September last year.

From 2 November 2012, the NHG Domain Specific Review Board (DSRB) has updated the disease specialties under its Domains A-F. We encourage that you take note of these before submitting your ethics application to NHG DSRB. You can read more on these updates in the "Updates on Local Regulations".

For those who missed out on the HSA's GCP Inspection Findings in 2012 shared at the Combined Clinical Research Professionals - Clinical Research Coordinator Society (CRP-CRCS) Forum held in December 2012, we are pleased to share them with you in this issue. We hope to see you at our future events; do keep a look out for our announcements at our NHG Research website (www.research.nhg.com.sg) or right here in Catalyst.

Till next time!

Yours Sincerely
Farah

CONTENTS

We apologise for the error on page 10 of Catalyst Issue 13. Dr Lim Choon Guan was awarded $200,000 for the NMRC NIG, instead of NMRC EDG.

YOUR NEWSLETTER, YOUR COMMENTS

Do you have... Research articles to share? Research topics that you want covered? Comments /Feedbacks on published contents of this newsletter? Comic strips / Cartoon Illustrations that is science / research-related that can bring smiles to your colleagues?

If you have answered "YES"to any of the above, we invite you to write in and share with us your thoughts, feedback on published articles or cartoon clips (original materials, jpeg format please). And if your contribution is accepted for print, we will send you a token of appreciation with compliments from the Editorial Workgroup!

Do remember to add in your contact details, where applicable for our future communications with you.

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A POINT-OF-CARE-TEST TO DIAGNOSE DENGUE IN YOUR CLINIC?

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Institute of Infectious Disease and Epidemiology (IIDE)
Tan Tock Seng Hospital

Acute febrile illness frequently poses great challenges to doctors in the clinic. Decisions have to be made relying on clinical acumen on how far to investigate, whether to start antibiotics or when to refer for hospital management. Many of these febrile episodes are self-limiting; many are left without an answer of what could have caused the fever.

Dengue, an acute viral febrile illness which frequently incapacitates its victims for many days, continues to be a year-round problem in Singapore. Over 4,000 cases were reported annually for the last three years.

This is likely to be an underestimate of the true number of cases, as many people with dengue fever are not tested and confirmed by laboratory testing.

The non-specific clinical picture during early illness prevents doctors from confidently distinguishing dengue from other acute febrile illnesses. In the absence of early confirmation, patients may not be managed optimally due to uncertainty of the underlying diagnosis.

In a recent survey published last year in the Annals of the Academy of Medicine, Singapore, we found that dengue diagnostic tests were ordered 51-100% of the time by less than half of the surveyed primary care physicians (Lee et al., 2011). Cost, availability and inconvenience are likely causes for failure to test.

We systematically evaluated a commercially available dengue rapid test kit for use as a point-of-care kit handled by the clinic nurse without laboratory interfacing. This was conducted at the Specialist Outpatient Clinic at the Communicable Disease Centre.

A key feature of the kit is that testing used whole blood; typically, serum is used in the laboratory setting which requires both equipment and processing by technicians. This rapid test uses a new approach, detecting both the virus directly by assaying for dengue virus non-structural-1 (NS1) protein, as well as detecting an immune response against dengue virus by detecting dengue-specific IgM and IgG antibodies.

The test can be completed within 20 minutes, reducing the inconvenience of waiting for laboratory testing. The test proved to be robust and easy to use, with no failures of the test controls in any of the strips used. We analysed 247 patients who presented at the clinic, and compared the performance of the combination rapid test kit to a complete diagnostic workup using five different test modalities done at the Environmental Health Institute on the same patients. The performance of the rapid test was excellent, with sensitivities and specificities of >90% using various testing algorithms.

This was the first prospective point-of-care evaluation of a combination test kit for dengue anywhere in the world to our knowledge. We are eager to see its increasing adoption by primary care physicians in Singapore as an additional option in the diagnostic armamentarium and hope that management of dengue and other acute febrile illnesses can thereby be improved.

Reference:

Lee, L.K., Thein, T.L., Kurukularatne, C., Gan, V.C., Lye, D.C., and Leo, Y.S. (2011). Dengue knowledge, attitudes, and practices among primary care physicians in Singapore. Ann. Acad. Med. Singap. 40, 533–538.

NATIONAL ADDICTIONS MANAGEMENT SERVICES (NAMS)

FIRST CLINICAL DRUG TRIAL HOPES TO REDUCE THE OPIATE WITHDRAWAL SYNDROME DURING INPATIENT DETOXIFICATION

Dr Victoria Manning
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Adjunct Assistant Professor
Program in Neuroscience & Behavioral Disorders
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Duke-NUS

At NAMS, approximately half of those seeking treatment for addictions are opiate-dependent patients who wish to achieve abstinence from heroin or other opioids, and the recovery process usually begins with inpatient detoxification.

However, pharmacotherapies usually used during the detoxification process (e.g. opiate substitution therapies) are not available in Singapore, hence given the lack of treatment options, many patients tend to go 'cold turkey', resulting in an intense and unpleasant withdrawal experience. Withdrawal symptoms include intense chills, abdominal and muscle cramps, diarrhoea, aches and pains, vomiting and insomnia, which often occur during the detoxification process.

At present, patients are given only symptomatic medication such as benzodiazepines, which are potentially addictive. As a result, attrition rates are high and many leave the ward prematurely without completing the first week of detoxification, and hence do not benefit from the psychosocial programme where vital skills to maintain abstinence (e.g. relapse prevention strategies) are taught.

As such, these vulnerable patients often relapse frequently and present for treatment again at a later date. These patients are also at heightened risk of physical health complications, blood-borne infections, financial problems, social exclusion as well as crime involvement.

It is therefore essential that we establish an alternative, effective pharmacotherapy for opiate detoxification that will enable patients to undergo and benefit from the full inpatient treatment programme, to optimise their chances of maintaining a drug-free life.

Lofexidine hydrochloride (BritLofex), a second generation alpha-2 adrenergic agonist drug licensed for use in the United Kingdom since 1992, has proven to be effective at accelerating the resolution of withdrawal symptoms.

The mechanism of action is presynaptic binding to alpha-2-adrenergic receptors located on the nerve endings of noradrenergic neurones, thereby reducing the release of noradrenaline which occurs when the inhibitory effect of opiates are removed.

To date, there have been several clinical trials of lofexidine, with only two in Asia thus far. Clinicians at NAMS recognise that being a non-opiate and therefore non-addictive drug, lofexidine has the potential for widespread use in Singapore, if proven to be effective.

This Principal Investigator (PI)-initiated study is funded by the Woodbridge Hospital Endowment Fund, and is NAMS' first clinical trial. It represents a collaborative effort between clinicians, researchers, nurses and pharmacists, and is led by the PI - Consultant Psychiatrist and Research Head, Dr Guo Song. NAMS' inpatient treatment programme lasts for three weeks, with the first week being active detoxification, followed by two weeks of rehabilitation.

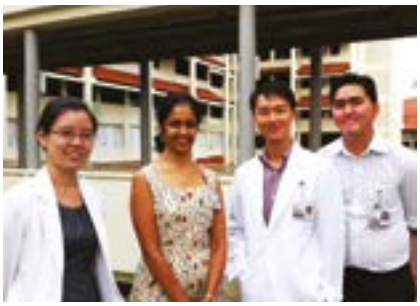
The specific aims of this study are to compare the objective and subjective withdrawal symptoms' severity and treatment completion rates among opiate users undergoing inpatient detoxification at the peak of detoxification (Days 3 and 4) between those on lofexidine and those on the standard treatment (i.e. diazepam).

The medication regime lasts 10 days and it is anticipated that patients randomised to the lofexidine arm will report and exhibit a less severe withdrawal syndrome, hence be more likely to complete inpatient treatment. With a double-blinded, double-dummy randomised control trial design, involving active and placebo lofexidine and diazepam tablets, the study presents several challenges to the study team.

August 2012 marked the trial's official commencement (i.e. when the first patient was recruited) and we aim to recruit a total of 122 patients over an 18-month period.

To find out more about this study, please contact the Principal Investigator, Dr Guo Song, at song_guo@imh.com.sg

PI Dr Guo Song (2nd from left) and the study team



Study pharmacists

Study nursing team

PSORIASIS RESEARCH
AT NATIONAL SKIN CENTRE

Dr Colin Theng
Senior Consultant
National Skin Centre

Psoriasis is a chronic immune-mediated skin disease. It presents with unsightly raised scaly plaques on the skin and causes much physical discomfort such as itching and scaling. In addition, it can cause significant psychosocial impact on the patient.

Psoriasis sufferers often feel embarrassed, and social isolation and depression are common among them. In the last decade or so, there has been tremendous advances in our understanding of the pathogenesis of psoriasis, particularly in the immunopathogenesis of psoriasis.

This has resulted in many new treatments which target specific pathways in the immune system such as TNF-alpha inhibitors and IL-12/23 inhibitors which have now been approved for the treatment of psoriasis. These new treatments have less hepatic and renal toxicity compared to traditional oral treatments like methotrexate and cyclosporine.

Furthermore, they offer a new lease of life for patients who have failed all traditional therapies for psoriasis.

Currently, we are conducting two Phase III trials in psoriasis at the National Skin Centre. These are large multicentre trials conducted in the United States (US), Europe and Asia.

We are one of the few Asian sites selected for participation in the trials. These trials involve the use of drugs that target novel new pathways important in the pathogenesis of psoriasis. Patients who have moderate to severe psoriasis and failed traditional systemic treatments are eligible for the trials.

Many patients with recalcitrant psoriasis have been successfully recruited into the clinical trials and have shown significant improvement in their psoriasis. Prior to participation, patients are thoroughly screened to ensure their safe inclusion into the clinical trials.

Patients also undergo regular monitoring throughout the trial and there is stringent monitoring to ensure the safety of the patients recruited. These trials have given patients access to cutting edge drug therapies and benefited patients with marked improvement in their disease and quality of life.

At present, more of such clinical trials are being explored. Conducting the trials will certainly enrich our knowledge and experience with the use of the latest treatments available for psoriasis, but more importantly, give our patients a new hope to combat this challenging disease.

BRIEF ASSESSMENT OF COGNITION IN SCHIZOPHRENIA: NORMATIVE DATA IN A ENGLISH-SPEAKING CHINESE SAMPLE

Ms Eng Goi Khia
Assistant Research Psychologist
Institute of Mental Health

This project was awarded the Singapore Allied Health Category (Gold) at the Singapore Health and Biomedical Congress 2012

I started working at the Institute of Mental Health (IMH) Research Division in August 2009. My first experience with research began when I served as a student research assistant at the National University of Singapore (NUS). I also had the opportunity to work with A/Prof Simon Collinson, who is also a clinical neuropsychologist, and a collaborator then with the Singapore Translational and Clinical Research Programme in Psychosis (STCRP) at IMH, Research Division. Upon graduation, I was introduced to A/Prof Mythily Subramaniam (Deputy Director, Research Division) at IMH.

The IMH Research Division has always been committed to staff training and I had the opportunity to be trained by original test developers in clinical interviews and neuropsychology tools, and gained exposure to relevant training such as ethics and statistics. I am also privileged to have been able to work with and learn from patients with schizophrenia.

As part of the STCRP, we administered the Brief Assessment of Cognition in Schizophrenia (BACS) to all participants. The BACS consists of a battery of tests that measures cognitive domains consistently reported to be impaired in patients with schizophrenia. In neuropsychology testing, test scores are compared against a normative sample to interpret an individual's performance relative to the "average" performance. However, normative data of neuropsychology tests in Asian samples are limited.

Even though normative data in Western samples are widely available, these are not applicable in the Asian context due to the influences of culture, language and education. Yet, accurate measurements of cognitive performances are important in assessing efficacies of intervention programmes and clinical trials that target to ameliorate cognitive deficits in patients with schizophrenia.

With the support of A/Prof Chong Siow Ann (Principal Investigator (PI) of the STCRP), A/Prof Mythily Subramaniam and collaborators A/Prof Simon Collinson and test developer Prof Richard Keefe, we embarked on a project to use data from STCRP to develop normative data on the BACS in a large sample of healthy English-speaking Chinese subjects, aged between 14 to 55 years.

We developed an algorithm to calculate scores that can be adjusted for any combination of age, gender and education. Our team is excited to share this innovative spinoff with the scientific committee once we have obtained the necessary copyright.

Clinicians and researchers would be able to utilise the algorithm to compute the performance of an individual relative to the normative sample. To date, this is the largest normative study of its kind in Asia, and we hope that our efforts could stimulate neuropsychology research in the region.

We submitted our abstract in the recent Singapore Health and Biomedical Congress (SHBC), and I am honoured that this study has clinched the Gold Award in the Allied Health Category.

The team is very excited and proud of our achievements. We hope that our efforts would encourage research in neuropsychology and translational research. We have submitted our paper to the Archives of Clinical Neuropsychology, and we hope to be able to share our findings in the scientific field.

Lastly, I would like to thank A/Prof Chong Siow Ann, A/Prof Mythily Subramanian, A/Prof Simon Collinson and Ms Janhavi Vaingankar for their support in this research endeavour. On behalf of the team, I thank A/Prof Chong and A/Prof Subramaniam for giving us the honour to collaborate with important figures in this field - A/Prof Simon Collinson and Prof Richard Keefe. I would also like to thank all co-authors and collaborators for their intellectual inputs and expertise.

Last but not least, we would like to acknowledge all funding bodies - the National Medical Research Council and IMH Small Grants for their support in clinical and neuropsychology research.

I am currently involved in the Well-being of the Singapore Elderly (WiSE) Survey and am learning a lot from this study. Moving forward, I would like to further enrich my research experience by enrolling in a graduate programme at the Nanyang Technological University (NTU) to learn about neuroimaging and its applicability in clinical research, as supervised by Dr. Sim Kang (IMH) and A/Prof Annabel Chen (NTU).

I am thankful to IMH Research Division for the opportunities and support that has helped to hone my skills as a young researcher. I look forward to making more scientific contributions in this field.

BRAIN DERIVED NEUROTROPHIC FACTOR (BDNF) MEDIATES THE EFFECTS OF SMOKING IN IMPROVING NEGATIVE SYMPTOMS IN PATIENTS WITH SCHIZOPHRENIA

Ms Milawaty Nurjono
Research Officer
Institute of Mental Health

This project was awarded the Best Poster Award for Basic and Translational Research (Bronze) at the Singapore Health and Biomedical Congress 2012

Schizophrenia is a complex disorder with heterogenous pathophysiology. Currently, available pharmacological agents prescribed by psychiatrists treat only positive symptoms and there is no treatment for negative symptoms and cognitive deficits. Therefore, in the attempt to self-medicate, a substantially high proportion of patients with schizophrenia smoke to alleviate their negative symptoms and cognitive deficits.

However, the mechanism of how smoking helps to improve negative symptoms and cognitive deficits remains unclear. BDNF, a neurotrophin, which has previously been implicated in schizophrenia, was also found to be associated with smoking behaviour.

Therefore, this project aims to examine the association between BDNF and negative symptoms in patients with schizophrenia. As there is currently no treatment for negative symptoms, the findings highlight the potential therapeutic target for negative symptoms.

I have always been fascinated by the complexity of the brain and regarded the brain as the most important organ of the body. With my academic training in the University of Melbourne, I spent the early days of my research career doing laboratory research focused on neurodegenerative disorder at the University of Melbourne and Mental Health Research Institute, Melbourne, Australia.

When I moved to Singapore, I was driven to try something new and thus started my mental health research career at the Institute of Mental Health (IMH) in 2010. Moving from laboratory research to clinical research was not an easy transition but I was fortunate to receive the guidance and support from my mentor, Dr Jimmy Lee, a Clinician-Scientist and Consultant Psychiatrist at IMH.

I worked with Dr Jimmy Lee on various projects to identify potential biomarkers for diagnosis and prognosis of psychosis using lipidomics and transcriptomic analysis. Throughout my 2 years at IMH, I have been greatly inspired. I am most grateful to have been given opportunities to interact closely with patients, learn new skills, present research findings in local and international conferences and also, to authora few publications. I am also privileged to have won the Best Poster Award at this year's Singapore Health and Biomedical Congress.

I am motivated to continue to excel in the field of mental health research and have recently enrolled into the Master of Public Health (MPH) at the National University of Singapore (NUS). Building on my previous experiences, I hope this degree will enable me to bridge the gap between research and implementation of not just treatment but also possibly prevention of illness in Singapore and globally.

The IMH Research Division has provided me with an excellent platform to foster my capabilities, cultivate my passion and realise my aspirations as a junior researcher. I am thankful to A/Prof Chong Siow Ann (Vice Chairman Medical Board, Research), Assistant Prof Mythily Subramaniam (Deputy Director, Research Division) and Dr Jimmy Lee for the opportunities to work with such a great team. Their support and guidance have definitely made my mental health research career a fun and exciting one.

GENETIC VARIATION OF PSYCHOSIS SUSCEPTIBILITY GENE CACNA1C RS1006737 INFLUENCES BRAIN FRONTAL VOLUMES AND WHITE MATTER MICROSTRUCTURES IN SCHIZOPHRENIA

Ms Carissa Nadia Kuswanto
Research Officer
Institute of Mental Health

This project was awarded the SHBC Best Poster Award for Allied Health Category (Silver) at the Singapore Health and Biomedical Congress 2012

Our research project, led by A/Prof Dr Sim Kang, investigates the associations between genetics and brain structures/functions in patients with psychosis.

The study aims to identify genes that can potentially be used as biomarkers to diagnose illness and prognosticate the disease progression. This has significant clinical implication as schizophrenia is a highly heritable chronic disorder with an early age of onset, and impairs normal functioning in the long term.

Also, the social and financial burdens can be significant due to the high cost of treatment and the loss of productivity by the patients and their caregivers.

Recent genetic studies have specified several genes, such as the CACNA1C gene, which can potentially increase the risk of schizophrenia. Our project utilises

varied brain imaging techniques such as magnetic resonance imaging (MRI) and diffusion tensor imaging (DTI) to allow us to investigate the genetic influences on abnormal brain structures and disruptions of white matter connectivity within the brain, which can affect functional impairments commonly observed in patients with psychosis.

We hope that our research findings can contribute to future discoveries on better illness detection and prevention for those who are at risk of psychosis, and optimize the treatment and management for patients with schizophrenia and their caregivers.

My interest in neuropsychology research started during my Honors Bachelor degree at the University of Toronto, with double majors in psychology and human biology. From there, I found the science of the brain to be fascinating – in that a single organ with its great complexity in substructures and functions has allowed humans to think and function, to interact with others, and to adapt to changes in their environment. Under the provision of Dr John Yeomans, a leading scientist on schizophrenia and addiction, I was also "properly" introduced to schizophrenia, and on how an illness can give rise to debilitating symptoms and how for decades researchers have yet to discover the root cause of it!

My first experience with human brain research happened when I was pursuing my Master of Science in Psychological Research at Bangor University. I was involved in an fMRI study with individuals suffering from auditory hallucinations together with Dr David Linden, an expert in social cognition and functional imaging research in schizophrenia.

Having observed the progression of brain imaging research in Singapore, I decided to start my professional career in brain imaging research in schizophrenia with Dr Steven Graham of the National University of Singapore (NUS) in 2009 and with Dr Sim Kang in 2010.

The Institute of Mental Health (IMH) Research Division has provided me with a great platform to learn and live my aspirations as a researcher. I am very blessed to receive guidance and mentorship from Dr Sim Kang, for his wisdom and passion towards research and science have been exemplary to many young researchers like me.

My immense gratitude to A/Prof Chong Siow Ann (Vice Chairman Medical Board, Research), Dr Mythily (Deputy Director, Research Division) and Dr Jimmy Lee for their endless support and guidance. Lastly, I would like to take the opportunity to thank the patients and the IMH staff for their voluntary participation in our projects, and for giving me valuable learning experiences.

CANDID TALK FROM THE TEAM BEHIND PROJECT 'CAMERA'

Dr Augustinus Laude
Consultant
National Healthcare Group Eye Institute

The ageing population and increasing prevalence of diabetes make for a 'perfect storm' of increasing prevalence of diabetic eye disease (DED), with consequential impact on morbidity.

This can translate to increased healthcare costs in caring for these patients. At the same time, hospitals are facing increasing pressure with clinic attendance and bed occupancy such that basic eye examinations for patients with diabetes are increasingly difficult. One solution would be to transfer the care back to the 'community', with the establishment of specialised resources.

This trend is supported by initiatives like a national platform to screen up to 40% of all patients with diabetes in Singapore through the nationwide network of polyclinics. This programme runs entirely by digital retinal fundus photography.

Computer-aided diabetic eye disease assessment: Understanding and exploiting retinal fundus features using online learning through evolutionary programming (CAMERA)

The aim of CAMERA is the creation of computer-aided tools and algorithms that can accurately and repeatedly identify abnormal retinal fundus images with DED. We hypothesise that salient features (eg. haemorrhages, exudates and vascular morphology changes) in retinal fundus images with DED can be exploited in order to better distinguish them from normal eyes.

New biomarkers may also be identified to predict the development or progression of DED. Digital fundal images collected from the community would be used to test novel algorithms and compared with ground truth information from human graders. Importantly, we also set out to explore online learning through evolutionary programming, a technique which is adapted from machine learning (eg. a robot learning to navigate in a new environment), in order to improve the performance of our tool as it 'learns' from past experience. This unique approach permits the addition of new knowledge into the system over time and repeated iterations.

This novel approach to assessing DED, not only brings together an international

collaboration between clinicians and resources from the National Healthcare Group Eye Institute (NHGEI) and the National Healthcare Group Polyclinics (NHGP), biomedical engineers and computer programmers from Ngee Ann Polytechnic (NP), Nanyang Technological University (NTU) and Universiti Teknologi Petronas, Malaysia, but may also lead to a new understanding of the impact of diabetes on retinal fundus features and open up new ways of monitoring DED in the community.

As we anticipate the opening of the Lee Kong Chian School of Medicine, Tan Tock Seng Hospital (TTSH) is poised to collaborate with engineers and technologists to try to address the challenges clinicians face at the frontline of medical care. The scale of the problem is evident and population demographic trends of an ageing population and certain chronic diseases like diabetes mellitus will no doubt hog the centre stage for our urgent attention. We would like to think that human innovations would provide many of the solutions as evidenced by history. Yet, precisely because of the speed of progress, there is an increasing need for greater efficiency if we are to have a chance of surfacing our ideas and potential solutions.

At the heart of it all is effective communication. Clinicians who are intimately aware of the problems at hand and potential solutions, need to be able to communicate these information to folks who can fashion the solutions.

Our project evolved around this ideology. Through the second Joint TTSH-NTU Workshop on Biomedical Engineering in 2010, I shared my work looking at retinal morphology and cognition, which drew interest from a research group from NTU and NP. Although I was still doing my fellowship in Scotland, we were able to communicate through emails and held web conferences using Skype®. By the time I returned to Singapore, we were ready to prepare a grant application and even managed to complete several manuscripts for publication.

Our work gradually evolved to focus on developing computer software algorithms to detect morphological changes in the fundus photograph of the eye with diabetic changes to separate them from normal eyes.

The algorithms developed by CAMERA may have a direct and immediate application to fundus photograph-based eye screening programmes. Computer-assisted image grading could also have a significant impact on the costs of quality assurance, an essential component for systematic screening. Furthermore, computer-assisted grading of DED could potentially help reduce the burden of grading by human graders in these screening programmes.

Dr Augustinus Laude is a Mid-level investigator under the NHG Clinician-Scientist Career Scheme (CSCS).

For more information on CSCS Programme, visit www.research.nhg.com.sg (Grants and Programmes -> NHG Intramural Support -> NHG Grant Programmes)

RESEARCHERS AND THEIR FINISHED WORK

PROTECTING PATIENTS AND HEALTHCARE STAFF FROM INFECTIONS

CLINICAL EPIDEMIOLOGY AND COMPARATIVE EFFECTIVENESS RESEARCH

Dr Angela Chow
Consultant, Department of Clinical Epidemiology
Institute of Infectious Disease & Epidemiology
Tan Tock Seng Hospital

Healthcare-associated infections, due to antimicrobial-resistant bacteria and novel viruses, continue to threaten the health of patients and healthcare staff in acute hospitals.

Surgical masks for protection of healthcare staff against pandemic H1N1 virus

The emergence of the novel swine-origin influenza A (H1N1) virus (pH1N1) in 2009 raised concerns about the risk of infection in healthcare staff who work in close contact with infected patients.

At that time, due to the unanticipated emergence and the rapidity of trans-continental spread of the infection from the Americas, there was no information on infection protection conferred by personal protective equipment such as surgical masks. We undertook a clinical epidemiological study to investigate pH1N1 infections in healthcare staff during the 1st time period (25 April-18 June 2009) when there was no local transmission, the 2nd period (19 June-21 July 2009) when local transmission occurred, and the 3rd period (22 July-31 August 2009) when there was sustained local transmission of pH1N1.

The study revealed that our active healthcare staff sickness absence surveillance and temperature monitoring systems and the universal use of surgical masks in all clinical areas (with N95 respirator use in the emergency department and isolation rooms) were effective in protecting our staff from exposure to pH1N1 in our hospital.

Staff who acquired the infection during the pandemic appeared to have been infected from community or social exposures. Our study findings provided important information that guided infection prevention strategies in the management of the novel infection, as the pandemic unfolded.

Alcohol handrubs are fast and effective for protection of patients against nosocomial infections

Whilst alcohol handrubbing has been widely promoted in our hospital, the effectiveness of handrubbing covering all hand surfaces as per our guidelines (also the U.S. Centers for Disease Control

and Prevention guidelines) compared to handrubbing using the 7-step technique as recommended by the World Health Organisation remained unknown.

We embarked on a 6-week randomised controlled trial on medical and nursing staff in all subsidised general wards during routine inpatient care on weekday mornings which were the busiest times of the week when most patient-care activities were performed. Our comparative effectiveness study on the two alcohol handrubbing protocols and chlorhexidine handwashing found that all three protocols were effective in reducing healthcare staff's hand bacterial load ($P < .01$).

During routine patient care, alcohol handrubbing covering all hand surfaces required less time (median, 26.0 seconds) than alcohol handrubbing using the 7-step technique (median 38.5 seconds; $P = .04$) and chlorhexidine handwashing (median, 75.5 seconds; $P < .001$). Hence, our current alcohol handrubbing protocol was the most time-effective hand hygiene protocol for routine patient-care activities in busy general wards. Our findings provided the scientific evidence and confidence for the continued active promotion of our alcohol handrubbing protocol for day-to-day patient-care activities in our hospital, as well as in other healthcare settings locally and globally. To date, our study remains the only internationally published randomised controlled clinical trial comparing hand hygiene techniques.

From our experience, timely and coordinated clinical epidemiological and comparative effectiveness research can play an important role in improving the scientific understanding of the transmission of emerging infections and guide infection prevention efforts toward both old and new infections.

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USING DECISION MODELS TO SUPPORT PATIENT-CENTERED CARE AND HEALTH SERVICES: A COOPERATIVE EFFORT

Dr Sun Yan
Medical Informatics & Biostatistics Specialist
Health Services & Outcomes Research
National Healthcare Group

The decision-making process in many aspects of the healthcare delivery system is often complicated and intricate, requiring several considerations before arriving at a course of action in patient care. Clinical Decision Models (CDMs) have increasingly been used to assist in the decision-making process aimed at achieving specific clinical outcomes, as well as guide the allocation of healthcare resources and reduce costs.

CDMs integrate evidence from various sources to standardise the care process, reduce variation in decision-making, and achieve faster, cheaper and presumably, better decisions. Methods used to develop CDMs include expert opinions, statistical multivariate models, decision trees and Bayesian networks, etc.

A cooperative effort among researchers, Information Technology (IT) specialists, clinicians and decision-makers, is vital for the success of decision models, particularly as more information on patients' outcomes and their contributing factors continue to expand, resulting in more parameters than the human decision-maker can process effectively.

Our recently completed study on predicting patients' waiting time at the Emergency Department (ED) of Tan Tock Seng Hospital (TTSH) is a good example of a collaborative effort among a multidisciplinary team.

Decision-makers and clinicians in the ED found that long waiting times can affect patient satisfaction and quality of care. However, this problem could not be easily resolved due to the complexity of causes, limited resources and unpredicted surges in demand. Literature reviews suggested that informing patients on their expected waiting time in ED could help make the long waiting more bearable, and deter patients from abandoning the ED before treatment. Our researchers collected retrospective data, and identified factors which affected patients' waiting times at ED with inputs from clinicians and existing literature. A statistical decision model was then developed and validated with a rigorous study design.

The model was assessed by the whole team, and was found to be valid (made accurate predictions of risk), relevant (shown to improve patient-oriented outcomes), easy to use at the point-of-care, and acceptable (with good face validity and transparency of recommendations).

The model was then integrated with the existing electronic health information system, where calculations were performed automatically based on individual patient data to streamline decision-making.

The model was an inexpensive way to improve patients' satisfaction with constrained resources. It could also help clinicians to monitor waiting times, prioritise patients, and minimise the time spent away from frontline patient care.

I am especially thankful to Dr Heng Bee Hoon, Director of HSOR, for her great supervision. She led the way in my career as a health services researcher.

I would also like to thank Dr Tay Seow Yian, Head of Emergency Medicine Department in TTSH, and his excellent team for their passion and open-minds on using new technology in patient care and health services.

I am also deeply appreciative towards the IT specialists from IBM and IHIS for their great contribution in implementing the model. The project's success could only be possible because of everyone's collaborative effort.

About the contributor
Dr Sun received her PhD from the Nanyang Technological University (NTU) in 2002. She joined HSOR in 2005 and has been a health services researcher since.

She was awarded the Healthcare Manpower Development Programme (HMDP) grant to study at The Harvard School of Public Health in 2009. Her current research interests are in clinical decision modelling, microsimulation, statistical modelling, and outcome evaluation using large observational databases.

She is also a Principal Investigator and co-PI of several grants supported by the Ministry of Health and NHG.

REAL WORLD RESEARCH

THE FINAL LEG OF THE JOURNEY TOWARD IMPROVED HEALTH CARE

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

Health research can be classified according to the various stages in the translation continuum, spanning the full spectrum of scientific discovery from basic science (bench) to clinical (bedside) to health services & systems research.

In my work at the Health Services and Outcomes Research (HSOR) department of NHG, I have seen the importance of investing in real-world research. While certain treatments or interventions may lead to favourable outcomes under ideal situations, the same cannot be said of the effects in real world situations. One begins to see that in the real world, a multitude of factors, other than the intended treatment, can determine what happens to the patient.

One such study involved an investigation into the effects of initially admitting critically ill medical patients from the Emergency Department (ED) to the general wards before transferring them to the medical intensive care unit (MICU).

Given that each MICU bed is a precious hospital resource, priority is often given to patients with serious but potentially reversible conditions who may benefit from more intensive observation and treatment than is provided in the general ward. Emergency and critical care physicians understand that each inappropriate admission to the ICU may translate to one less bed for a patient who would otherwise have benefitted from intensive care. In a similar manner, inappropriate admissions of a medical patient to the general wards instead of the MICU may have disastrous consequences.

This was the motivation for a group of ED and MICU consultants from Tan Tock Seng Hospital to embark on the project with the ultimate goal of improving triage decisions. In the study, the magnitude of these indirect admissions, vis-à-vis direct admissions to the MICU from the ED was investigated. Patient outcomes included in-patient and 60-day mortality, MICU and total hospital length of stay (LOS). The study utilised a retrospective cohort design involving patients who were admitted to the MICU within 24 hours of presentation at the ED.

The evidence-based medicine movement has radically changed the way health professionals acquire and assimilate information relevant to patient care. Although observational designs are ranked lower than experimental studies in the hierarchy of evidence, they are nevertheless a rich source of evidence for health services research (HSR).

In the case of the ED-MICU study, indirect admissions hypothesised to be harmful precluded the use of a randomised trial. Additionally, triage decisions and their consequences were best observed under real world situations rather than a stringently controlled environment. After all, the research question posed was a practical one placed in the context of the daily operations in a hospital setting and not with any underlying assumptions and pre-conditions.

HSR or what may be viewed as real-world research draws upon the field of Epidemiology for methods and techniques. Unlike clinical specialties, Epidemiology and HSR do not involve the delivery of care directly to the patient, but rather in the processes in the delivery of care which would have an impact on patient outcomes.

By identifying which treatments, investigations and interventions work best for whom, HSR is ultimately a useful tool for improving outcomes which matter to patients.

NURSING RESEARCH IN IMH

Dr Xie Huiting
Senior Staff Nurse
Nursing Training
Institute of Mental Health

Institute of Mental Health (IMH)'s Department of Nursing Administration started its research journey in 1999 with a group of enthusiastic nursing leaders. This tradition was further enhanced with the introduction of evidence-based practice in 2008.

In 2009, the research culture continued to flourish with the development of five clinical practice guidelines to guide nursing practice in IMH after an intensive workshop with Dr Marita Titler, a guru of evidence-based practice. In 2010, a Memorandum of Understanding (MOU) was agreed upon between the Joanna Briggs Institute (JBI), an internationally-recognised leader in evidence-based practice, and IMH.

The setting up of the JBI-IMH Centre for Evidence-Based Practice in Mental Health Care signified yet another milestone in IMH's journey towards establishing itself as the leading mental health centre globally. IMH aims to advance mental health evidence-based practice and research in the region and translate these to enhance practice, improve patient outcomes, and promote mental health.

In addition, IMH's Department of Nursing Administration sees the importance of developing human capital in research. The existing nursing research and evidence-based practice team is made up of ward-based Staff Nurses, Senior Staff Nurses, and Advanced Practice Nurses who have expressed interest in, and are competent to conduct research and translate evidence into clinical practice.

Steps taken in developing human capital in research have paid off with the return of Dr Xie Huiting in 2012, graduating with a Doctor of Philosophy (PhD) from Case Western Reserve University, a research-renowned university in Ohio, UnitedStates of America. Nurses of various grades have also been performing exceptionally well since the 1st Singapore Health and Biomedical Congress in 2010. In 2010, Advanced Practice Nurse Zhou Zhenyu won the Singapore Nursing Award (Gold).

In the following year, Senior Staff Nurse Li Ziqiang clinched the Best Poster Award (Gold) while Senior Staff Nurse Rajni Parasurum won the Singapore Nursing Award (Gold) for Best Oral Presentation.

Recently, two nurses clinched the Gold and Bronze Awards at the Singapore Health and Biomedical Congress 2012. The following are brief descriptions of their studies:

IMH Nursing Leadership Team with Dr. Prema K (Director of Nursing) (4th from left)

a) Advanced Practice Nurse (Intern) Mao Rui
Singapore Nursing Award (Gold) for Best Oral Presentation

"Clinical Application of the Broset Violent Checklist to Predict Inpatient Violence in a Tertiary Psychiatry Hospital in Singapore: A Preliminary Study"

The team, led by Mao Rui, embarked on a journey to discover the best short-term violence prediction tool by conducting a systematic review. The Broset Violent Checklist (BVC) was utilised to predict inpatient violence in IMH with the aim of establishing the inter-rater reliability (IRR), sensitivity and specificity of BVC.

A two-phased study was conducted on eight Registered Nurses (RNs) and 44 inpatients in two inpatient units in IMH. The IRR among the raters (RNs) from the male and female wards were 0.804 and 0.846 respectively. The sensitivity and specificity of the BVC at the cut-off score of 2 and above were 75% and 100%.

Thus, the BVC is a reliable, sensitive and specific tool in predicting short-term risk of violence among local acute adult psychiatric patients.

b) Nurse Clinician Sharon Tan Chay Huang
Singapore Nursing Award (Bronze) for Best Oral Presentation

"The Effect of Illness Self -Management and Recovery Programme in Reducing Symptoms and Increasing Social Functioning of People with Mental Illness in the Community: A Preliminary Study"

Having learnt about the Illness Self-Management and Recovery (ISMR) programme during her clinical attachment, Sharon decided to embark on a study to examine the effects of the ISMR programme on patients with mental illness living in the community.

50 participants engaged in a randomised controlled trial, where they either participated in 24 sessions of hourly ISMR programme over a year, or received standard care for the same period and duration.

The results showed that the participants in the ISMR programme experienced reduced admissions, better management of their psychiatric symptoms and improved social functioning, compared to those who received standard care.

PLANNING FOR END-OF-LIFE CARE

Ms Anusha Govinda Raj
Senior Research Analyst
Health Services & Outcomes Research
National Healthcare Group

The approach of the silver tsunami brings new challenges for our healthcare. By 2030, 1 in 5 Singaporeans will be over the age of 65. With more elderly residents, longer life expectancies, and increasing complexities of healthcare conditions, healthcare services are set to face increasing demand.

Healthcare utilisation has been shown to increase sharply as one approaches the end of life. Repeated hospitalisations, long hospital stays and deaths in hospital are commonplace at the end of life. This is a consequence of receiving aggressive medical treatment at the hospital till the end. Studies of patient preferences indicate that given a choice, those at the end of life would prefer not to have frequent transfers between their places of care, be it the home or long-term care setting, and the hospital, and also not to pass away in the hospital.

However, most patients do not have documented plans of their preferences for treatment or location of death in the event of being seriously ill. Without this, it is challenging for the medical team and family to decide on a conservative medical management and palliative care for the patient. Studies have shown that palliative care management improves the quality of life of patients. In addition, opting for conservative management also meant fewer hospital transfers and reduced costs.

Amongst the gamut of strategies to prepare the healthcare system for future needs, is the decision to strengthen palliative care services for patients in the last stages of life. The World Health Organisation has defined palliative care as "…an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual." Whereas routine medical treatment is curative in intention, palliative medicine seeks to relief pain and suffering through a multidisciplinary approach addressing physical, emotional, spiritual, and social concerns.

There is a need for palliative care to be strengthened in the nursing homes. There are 61 nursing homes in Singapore with a total capacity of approximately 9,200. About half are voluntary welfare homes and half are privately-run.

Presently, nursing homes do not provide palliative care services due to manpower constraints and the lack of training in palliative medicine and management. Purchasing services from external palliative care providers would also not be a viable option for nursing homes with their limited budget.

In 2009, a pilot project – Project Care for Residents in Elderly homes (CARE), was funded by the Ministry of Health to examine the effectiveness and costs of offering palliative care in nursing homes in Singapore. A palliative care team from Tan Tock Seng Hospital (TTSH) comprising of doctors, nurses, and medical social workers were brought together to offer palliative care in 7 nursing homes within the catchment area of TTSH.

The Project CARE team screened all residents in the nursing homes to identify those with a prognosis of 1 year or less. This determined the eligibility for palliative care. If the resident and/or their family were interested in receiving palliative care, a meeting was organised between the Project CARE team, the resident and his/her family. An advance care planning discussion took place where the Project CARE team document the resident's preferences for treatment type and place of death. Treatment choices included comfort measures in the nursing home, limited additional treatment in the nursing home and/or hospital, or full treatment in the hospital. Residents who chose to receive comfort or limited additional intervention in the nursing home came under the care of the Project CARE team.

Residents who were under the care of the Project CARE team were expected to have fewer hospitalisations and shorter cumulative length of stay. In order to evaluate the effectiveness and costs of Project CARE in reducing hospitalisations, we designed a quasi-experimental study to compare hospitalisations in the last month and 3 months of life in residents under Project CARE with a historical cohort of residents who were deceased prior to the introduction of Project CARE. Results showed that Project CARE residents had lower odds of being hospitalised, fewer hospitalisations, shorter cumulative length of hospital stay, and lower healthcare costs in comparison to the historical cohort of residents in the last month and 3 months of life.

Additionally, families were surveyed 1 to 3 months after the demise of the residents regarding their satisfaction with the care that the resident received in the last week of life. Overall satisfaction levels were higher in families of Project CARE residents, who reported fewer problems in being informed and involved in the residents' medical condition, and felt more satisfied in their ability to manage residents' medication and condition at the time of death.

Project CARE is one example of strengthening palliative care services in our nursing homes. More program such as home palliative and hospice care are also being rolled out in an effort to ease the suffering, ensure quality of life, and preserve dignity for patients nearing the end of their lives.

KNOWING OUR HEALTHCARE LEADERS

ASSISTANT DIRECTORS
HEALTH SERVICES & OUTCOMES RESEARCH
NATIONAL HEALTHCARE GROUP

MR TEOW KIOK LIANG (KL)

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

KL It is certainly fun in collaborative research, where we complement each other's knowledge. In my area of work, my stakeholders have tough and real issues that need to be tackled. They also have extensive domain knowledge. We provide the research capability to help them scale these problems, and at the same time, we learn tremendously from them too!

WS In the last few years, we have been working with clinicians and administrators on research that aided their decisions pertaining to the management of specific diseases and conditions. We can bring this collaboration further by moving upstream to look at health systems and programme design based on the current

MS TAN WOAN SHIN (WS)

knowledge base in literature regarding what works and what doesn't. We are also looking at collaborating more with academic partners to bring more rigour to our research work.

I started working with the operations department of the hospital and developing neater equations that could address patient flow and service variability.

PAL The users provided me with the data and the real-world complexities, and I tried to impose a structure behind the analysis. Now, I am moving towards conducting cost-effective analyses of interventions which require working with clinicians and having a basic understanding of clinical sciences. Our users are pragmatic users of objective and evidence-based findings.

MR PALVANNAN KANNAPIRAN (PAL)

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

KL As-is: bonsai. To-be: garden with thousand flowers.

WS *"To raise new questions, new possibilities, to regard old problems from a new angle, requires creative imagination and marks real advance in science"* - Albert Einstein.

This describes the As-Is and To-Be state, to constantly evolve… research is a process.

PAL *"The mind, once expanded, does not return to original confines."* Internally our department's circumference of analysis is always expanding with time, exposure and interactions. We have to strike a balance between answering the

stakeholder's research questions and raising important research questions.

What do you think are the qualities of your department that allows it to catalyse collaborative research?

KL Diversity among us, sharing culture, trust built over the years, and the many fun things that we do together help make working together fun.

WS The strength of the department is in keeping an open mind regarding techniques. Rather than look for questions that will utilise our individual technical expertise, we seek to provide the evidence to answer questions using the most relevant techniques. Having a multi-disciplinary team is definitely our key strength.

PAL There are analytical professionals from all domains of sciences: life sciences, social science and physical science. The viewpoints and tools of analysis cover an impressive breadth and a test ground for collaboration first. Two mantras shape the department's research approach: clarity of the research question, and the impact on patient's health outcomes.

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

KL This project involved working with Tan Tock Seng Hospital (TTSH), National Healthcare Group Polyclinics (NHGP) and National University Hospital (NUH) pharmacists. The institutions were on the journey of automating the pick-and-pack process, and use of the automation machine.

In order to optimise the machines, a very detailed and complex planning analysis had to take place. By taking a very scientific approach, we expect to have cost savings and greater efficiency in running the processes.

WS The percentage of elderly Singaporeans is estimated to increase from 8.4% in 2005 to 18.7% in 2030. Population ageing has major implications on health and social services, with increased age comes a greater likelihood of having a disability and needing assistance.

The Marine Parade Elderly Needs Survey 2011 was designed to assess a broad range of factors impacting on the needs of the older person. Care needs cannot be defined on age alone but also on the individual's general health and well-being, risk status, social support and socio-economic status.

We worked closely with the Health Promotion Board, Ministry of Health, Agency for Integrated Care, Ministry of Community Development, Ministry of National Development and the Centre for Enabled Living and the Marine Parade grassroots to design the survey tool.

After the project was completed, the results were utilised by the various agencies to design health and social interventions to meet the needs of the Marine Parade residents.

PAL Recently I worked with the infectious disease control department to study if using Polymerase Chain Reaction (PCR) for universal screening would be cost-effective.

Dr Brenda Ang explained the decision context, Dr Heng Bee Hoon raised the key questions, the nurses described patient care, clinicians gave the background of Methicillin-resistant Staphylococcus aureus (MRSA), economists carefully identified cost elements and comparative framework, the hospital's Information Technology (IT) department provided the data, operations department explained the ground issues, vendors described their specifications and the academia was a sounding board.

I put together the decision model to inform what was to be done for improved patient health outcome. Now that is collaboration.

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

KL Contributing a little to society, having good colleagues, using my grey matter somewhat, and getting paid!

WS That I get to learn new things and life doesn't get boring. And of course, working with a bunch of like-minded people makes work enjoyable.

PAL: There is research, consulting and teaching with a hospital focus for public good.

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

KL To be both happy at home and work, things just work out well.

WS Time has to be set aside. Making a commitment to do so will ensure work-life balance.

PAL Work does flow into my personal life. But reading is not a bad hobby and fits into research.

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

KL I practice Chinese calligraphy with a group of friends on Saturdays and I bring my family along. Sad to say, my skills are still so-so.

WS Reading, travelling, cooking for friends and family, and watching movies.

PAL I don't take to travel unless required. With friends I enjoy chats about the tiny red dot and nostalgia and watch movies. On my own, I learn playing the piano and go to the gym. I enjoy watching my daughter draw and hear my son speak Tamil too.

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

KL Maybe it does, but preferably I should not be thinking about work when I am enjoying my hobbies. Retrospectively, they may turn up useful.

WS I like to learn new things (reading, travelling, trying out new recipes) so this is translated in my approach to work as well. I try to read widely across a range of subjects. It helps to keep an open mind about things and approaches to take, since there are many ways to Rome.

PAL Generally, I think I have a multidisciplinary perspective and like to connect the dots. In that regard, health services research is invigorating.

QUALITÉ

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

RESEARCH REQUIRING BOTH ETHICS AND REGULATORY APPROVALS

ETHICS APPROVAL FOR RESEARCH STUDIES

Current institutional policies require Principal Investigators (PIs) to seek ethics approval from the National Healthcare Group (NHG) Domain Specific Review Board (DSRB) prior to conducting research studies. Whilst the interpretation of what constitutes a research study may vary from one source to another, the NHG DSRB Investigator Manual (Chapter 1) specifies the following sources from which the definition of "research" (or equivalent terminology) will be observed:

- The Medicines Act;
- The United States Department of Health and Human Services;
- The United States Food and Drug Administration;
- The Singapore Guideline for Good Clinical Practice; and
- The Bioethics Advisory Committee Guidelines for Institutional Review Boards.

Across these definitions, the scope of DSRB's ethical governance covers research studies fulfilling the following criteria:

- a systematic investigation;
- develop or contribute to generalisable knowledge;
- to be performed on human subjects; and
- involve NHG institutions, or institutions under the purview of NHG DSRB.

These research studies may run the gamut from surveys, retrospective medical record reviews, tissue repository studies and database studies, to complex studies investigating novel drugs, medical devices or surgical techniques. The requirement for ethics approval seeks to protect the rights, safety and well-being of human subjects participating in these research studies.

Regulatory Approval for Research Studies

Concurrently, some clinical research studies require regulatory approval from the Health Sciences Authority (HSA) prior to their initiation, in the form of a Clinical Trial Certificate (CTC). However, in contrast to the all-encompassing scope of DSRB's ethical jurisdiction, the boundaries of regulatory purview only extend to clinical research studies fulfilling specific legislative criteria.

Acquiring sufficient understanding of the applicable regulatory requirements will allow investigators to pre-empt the amount of time and resources that should be dedicated to both the ethics and regulatory submissions processes.

Legislative Definitions

The Medicines Act and the subsidiary Medicines (Clinical Trials) regulations provide the basis for determining whether a clinical research study requires regulatory approval. Most importantly, the research study should fulfill the definition of a "clinical trial" under the Act. This definition is reproduced below:

"Clinical trial" means an investigation or series of investigations consisting of the administration of one or more medicinal products of a particular description by, or under the direction of —

- *a doctor or dentist to one or more of his patients; or*
- *two or more doctors or dentists, each product being administered by or under the direction of one or other of those doctors or dentists to one or more of his patients,*

where (in any such case) there is evidence that medicinal products of that description have effects which may be beneficial to the patient(s) in question and the administration of the product or products is for the purpose of ascertaining whether, or to what extent the product has, or the products have, those or any other effects, whether beneficial or harmful.

The Medicines Act goes on to define a "medicinal product" as a substance which is administered to human beings for a medicinal purpose. The term "medicinal purpose" is further defined in the Act as one or more of the following uses:

a. treating or preventing disease;
b. diagnosing disease or ascertaining the existence, degree or extent of a physiological condition;
c. contraception;
d. inducing anaesthesia;
e. otherwise preventing or interfering with the normal operation of a physiological function, whether permanently or temporarily, and whether by way of terminating, reducing or postponing, or increasing or accelerating, the operation of that function or in any other way.

Determining the Need for Regulatory Approval

The legislative definitions above reveal several pertinent facts about the type of research studies that constitute clinical trials.

Firstly, the study should involve the use of a medicinal product, with the study objective(s) seeking to examine the safety and/or efficacy profile of the said product in human subjects. Instinctively, one may be inclined to apply this description exclusively to investigational new drugs undergoing clinical trials.

While such an application is not incorrect, investigators should pay heed to the fact that the legislative boundaries of clinical trials are not limited to new and unapproved drugs alone. Studies involving registered drugs undergoing testing in human subjects for new indications, as well as those involving marketed drugs

being administered to human subjects for approved indications, are included and will require regulatory approval prior to their conduct.

The second key detail of interest would be the fact that the regulations require the PI of clinical trial to be a doctor or dentist. It is dictated in the Medicines Act that such a person should be registered under the Medical Registration Act or Dental Registration Act respectively (as applicable). While DSRB allows adequately-qualified nursing and allied health staff to be PIs for greater-than-minimal risk studies, caution should be exercised when such studies also fulfill clinical trial regulatory requirements. In such circumstances, it is imperative that an appropriately qualified medical doctor (or dentist) be appointed as the PI of the trial.

Consequently, for greater-than-minimal risk studies that are not clinical trials, DSRB may at their discretion approve the conduct of the study under the purview of a non-clinician PI. Where the PI is unable to determine if his/her study requires regulatory approval, he/she should write in directly to HSA to seek advice and clarification.

References

- Medicines Act and Medicines (Clinical Trials) Regulations
- Health Sciences Authority Website, Frequently Asked Questions on Clinical Trials (http://www.hsa.gov.sg/publish/hsaportal/en/health_products_regulation/clinical_trials/faqs.html#(A))
- NHG DSRB Investigator Manual (Chapter 1, Section 1.4)

NON-COMPLIANCE REPORT: PLACING SUBJECTS' INTERESTS BEFORE RESEARCH PURSUITS

Background

The National Healthcare Group (NHG) Research Quality Management (RQM) team conducts regular and random study reviews on ongoing clinical research studies carried out in NHG and its partner institutions under the oversight of the NHG Domain Specific Review Board (DSRB).

The purpose of these study reviews is to increase awareness among investigators and their study staff on proper research practices and documentation techniques.

A recent study review performed by RQM unearthed a series of critical research-related non-conformities arising from a single study. While most of these breaches were unintentional, many valuable lessons could be gleaned from the study review findings.

Firstly, the Principal Investigator (PI) had failed to secure the investigational medical device supplies prior to study initiation, but had proceeded with subject enrolment for the purpose of reporting some progress in the study to the grant authorities.

The downstream consequence of this was that one of the main protocol-mandated procedures could not be performed and had to be deliberately omitted, resulting in a major protocol deviation. The data collected from the subjects had thus been incomplete, rendering it ineligible for per-protocol analysis.

Secondly, the Informed Consent Form (ICF) had been amended, in the absence of the Domain Specific Review Board's (DSRB's) approval, in an attempt to remove the procedures involving the use of the unavailable medical device. Consent from subjects had been taken using this unapproved ICF. Some subjects were approached for consent just prior to the study procedures being carried out.

On other occasions, informed consent had not been taken from subjects at all, prior to their enrolment in the study and before research-related activities was performed on them. Where consent was taken, the ICF dates written by some subjects had been intentionally amended by the study staff to reflect an erroneous date of consent.

The shortcomings in the informed consent process had been further compounded by the fact that consent for all enrolled subjects was taken by an inadequately trained study administrator.

The study administrator had not undergone any basic training for the role, such as attending the Collaborative Institutional Training Initiative (CITI) or Singapore Guideline for Good Clinical Practice (SGGCP) courses.

Findings & Implications

- The PI had wilfully deviated from the approved study design by recruiting subjects before ensuring that sufficient resources were available to initiate study procedures.

  `This had not only compromised the scientific validity of the study, but had also unnecessarily subjected patients to the risks of the research study, and from which the data collected could not be used for meaningful analysis.

- The questionable manner in which the informed consent process had been carried out surfaced doubts as to whether subjects had been adequately informed before agreeing to participate in the study.

- The study administrator's lack of SGGCP training exemplified the PI's comparable unfamiliarity with these guidelines. Furthermore, placing the scientific pursuits of the study and personal accountabilities above the interests of the subjects portended research misconduct on the part of the PI.

Actions Taken by DSRB

These ethical and procedural infringements were subsequently escalated to the DSRB, which resulted in a warning letter being meted out to the PI to suspend the study with immediate effect. The urgent need for the PI to attend the SGGCP course was resolutely enforced, being imposed as a mandatory requirement for which the PI had to fulfill before approval to the conduct of the study could be reinstated.

These findings were also escalated to the Research Ethics Committee in tandem, who responded by issuing an equally stern warning to the PI.

Useful Tips and Recommendations

- It is the PI's responsibility to commit sufficient time in acquiring manpower and procuring adequate resources for the foreseen duration of the study, prior to initiating any study activities.

- The PI is responsible for ensuring that the study staff members are appropriately qualified and trained on their delegated tasks before study initiation.

- Should any amendments to the study documents and/or procedures be necessary, the PI should ensure that written approval is received from the DSRB (and the regulatory authority, if applicable) before implementing these changes.

- Regular and open communication within the study team is encouraged.

- Protocol deviations and any other pertinent information should be promptly and accurately reported to the DSRB (and the regulatory authority, if applicable) for review.

GCP FREQUENTLY ASKED QUESTIONS

WHAT ARE THE PRINCIPAL INVESTIGATOR'S RESPONSIBILITIES WITH REGARD TO THE MANAGEMENT OF A STUDY TEAM?

The Singapore Guideline for Good Clinical Practice (SGGCP) places much responsibility on the Principal Investigator (PI) to secure sufficient manpower and resources, to ensure that a study can be properly carried out. A crucial element to this end would be having appropriately trained and qualified study staff to assist with the delegated responsibilities.

Section 4.1.1 of the SGGCP states that investigators must be "qualified by education, training and experience to assume responsibility for the proper conduct of the trial". Section 4.2.3 further elaborates that "the investigator should have available an adequate number of qualified staff and adequate facilities for the foreseen duration of the trial to conduct the trial properly and safely".

The PI's Role

Listed below are some pointers that PIs should take into consideration prior to the commencement of a clinical research study:

- As a prerequisite, the PI must bear qualifications that satisfy the ethics committee's requirements (and the regulatory authority's requirements, where applicable) to lead the study. These may include having appropriate medical credentials, as well as completing the Collaborative Institutional Training Initiative (CITI) and Singapore Guideline for Good Clinical Practice (SGGCP) courses;

- When conducting clinical trials, the PI should be thoroughly familiar with the study protocol, and the appropriate use of the investigational product as described in the Investigator's Brochure, product information or any other information sources provided by the sponsor;

- The PI should maintain a list of appropriately qualified persons to whom he/she has delegated significant research-related responsibilities. Additionally, the PI will be required to train the study team on their respective roles in the study, based on the protocol requirements; and

- The PI should ensure that all persons assisting with the research are adequately informed about the protocol, investigational product(s) and their research-related duties.

Change of PI

If it is anticipated that the PI will be going away for an extended period of time or resigning from his/her institution, the research project should be formally transferred to another PI to oversee. The incoming PI will then assume the same responsibilities as the outgoing PI as detailed above.

In the process of ensuring a smooth transition of duties, it should be noted that any change of PI must first be reviewed and approved by the ethics committee (and the regulatory authority, where applicable) prior to implementation. Once approval is received, the new PI's start date and delegated responsibilities should be updated accordingly on the delegation log.

The Study Team

Each study staff plays a similarly crucial role in ensuring that the conduct of the study goes smoothly. Aside from accruing study team members with the necessary qualifications to discharge their study responsibilities, the PI needs to ensure the following:

- For any new additions to the study team after study initiation, the PI is responsible for providing protocol-related training for the new staff member(s). Such training should also be documented;

- The delegation log will need to be updated with the roles, responsibilities and signatures of the new study staff, endorsed by the PI ;

- For current staff exiting the study, the PI should ensure that there is a proper handover of responsibilities from the outgoing staff to another member of the study team; and

- The delegation log should be similarly updated with the end date of the outgoing study staff member.

Paying heed to these details will go a long way in ensuring that PIs are better equipped to manage changes in their study team, which will in turn translate into more efficiently-run research studies.

References

- *Singapore Guideline for Good Clinical Practice (SGGCP)*
- *NHG DSRB SOP 201-E01 Responsibilities of Investigators*
- *Good Clinical Practice: A Question & Answer Reference Guide. May 2011. Chapters 2.13 and 2.14*

RESPONSIBLE CONDUCT OF RESEARCH (RCR)

COLLABORATIVE RESEARCH

This issue features the fifth component of Responsible Conduct of Research (RCR) - Collaborative Research. In general, we recognise collaboration to be intrinsic to the research process and the term "Collaborative Research" should not be foreign to the research realm.

Collaboration here usually refers to researchers who work within the same discipline, either within or across institutions. Multidisciplinary research, on the other hand, is a form of collaborative research that involves researchers working across disciplines, either within or across institutions (academia, private industries or even internationally).

So why is there a need for collaborative research? Well, it is because a single individual is less likely to be able to have the skills, knowledge, and resources to address all research problems, and breakthroughs in research are often more likely to come from collaboration across disciplines. A careful selection of collaborators can also help save considerable time and money.

Collaborative research has been eased considerably with new telecommunication technologies. Web based technologies today allow researchers to input and manipulate data in shared databases easily. Technology also allows people from across the world to communicate, simulating face- to-face meetings.

Responsible collaborative research should include (but not limited to) the following:

Establish agreements for each collaboration

- An agreement should be reached in writing with the partners on the management of the research in a joint research project; and
- The agreement should cover issues such as intellectual property, confidentiality and copy right; sharing of commercial returns (if applicable); responsibility for communicating with ethics and regulatory authorities (if applicable) including submissions for approvals and the reporting to appropriate funding agencies.

Management of conflicts of interest

- A policy for managing conflicts of interests that may potentially arise in collaborative research must be readily available in the respective collaborators' institutions.

Discussing in advance the roles and responsibilities of collaborators

- Goals and aims of the research project should be defined so that all involved will have the same end in mind.
- In the beginning, each individual needs to be clear about their roles and responsibilities in the research project. Setting goals leads to expectations and outcomes. For example, who will take charge (i.e. who will be the Principal Investigator) of the collaboration needs to be defined, and not assumed.
- As multiple laboratories or groups of researchers may be involved, coordinating the effort among the collaborators requires management (and communication). When a research project changes direction, how that will impact each of the collaborators' needs to be addressed as well. Authors may be added or removed. It is also pertinent for researchers to determine when the collaboration is over.

Discussing data and material management in advanced

- The issue of who owns the data is governed by the type and source of funds used to support the research project. Collaborators should adhere to their institutions' policies and/ or guidelines on "material transfer agreements", custody and retention of data.

  All parties should know their institutional and granting-agency policies regarding intellectual property and patent procedures.

Discussing authorship in advance

- The criteria for authorship among collaborators have to be established beforehand, so that everyone involved will know what to expect as different disciplines have varying standards for determining authorship.
- Collaborators need to determine how they will deal with the differing expertise levels of each author. Who will actually write the manuscript and be responsible for the input from collaborators has to be established. Finally, who will be included in acknowledgments should also be addressed.

Comply with multi-institutional agreements

- Researchers involved in a joint research endeavour must be aware of, adhere and comply with their institutional policies and written agreements affecting the project, particularly to those relating to the dissemination of research findings and the management of research data and primary materials across institutions.

Declaration of conflicts of interest

- Researchers must disclose as soon as possible any actual, apparent or perceived conflict of interest to any aspect of the project when establishing research collaboration. For example, if there is a financial conflict of interest (i.e. stocks, stock options or other ownership interests) or intellectual property rights involvement (i.e. patents, copyrights and royalties from such rights), it should be disclosed prior to the start of the research project.

Contributed by Valerie Wee
Senior Executive
Research Quality Management
National Healthcare Group

NHG - DOMAIN SPECIFIC REVIEW BOARDS (DSRB)

With effect from 2 Nov 2012

DOMAIN A	DOMAIN B	DOMAIN C
▪ Ophthalmology ▪ Psychiatry ▪ Neurology / Neurosurgery ▪ Genetics ▪ Geriatric Medicine ▪ Palliative Medicine	▪ Oncology ▪ Hematology ▪ Pathology ▪ Paediatrics ▪ Respiratory Medicine	▪ Cardiovascular Science ▪ Pharmacology ▪ Emergency Medicine ▪ Diagnostic Imaging ▪ Family Medicine *
DOMAIN D	**DOMAIN E**	**DOMAIN F**
▪ Obs/Gynaecology ▪ Anaesthesi ▪ Surgery # ▪ ENT ▪ Dentistry ▪ Sports & Rehab Medicine ▪ Allied Health	▪ Infectious Disease ▪ Gastroenterology ▪ Renal Medicine ▪ Rheumatology / Immunology ▪ Dermatology	**(Population Health)** ▪ Health Services & Outcomes Research ▪ Education Research ▪ Research on Prevention & Health Promotion Programs ▪ Social & Behavioral Research ▪ Epidemiological Research ▪ Community-based Participatory Research

* Non organ / disease specific Family Medicine studies only.

\# Includes General Surgery, Orthopaedic Surgery, Plastic Surgery and Urology

DSRB UPDATES
UPDATED DSRB DOMAIN DISEASE SPECIALTIES

With effect from 2 November 2012, the NHG Domain Specific Review Board (DSRB) has updated the disease specialties grouping to include Palliative Medicine (Domain A), Family Medicine (Domain C) and Population Health Research (Domain F). With this update, it should be noted that Domain C will review non organ/disease-specific Family Medicine studies only. In addition, Surgery (Domain D) will include specialties such as General Surgery, Orthopaedic Surgery, Plastic Surgery and Urology. You can refer to the updated diagram for more details, and some examples of Population Health Research.

Do take note of the updated information when submitting your research applications!

Contributed by Chen Siya
IRB Analyst
Office of Human Research Protection Program
National Healthcare Group

DSRB Analyst
NHG Research & Development Office (RDO)

All research conducted in NHG premises or involving NHG staff currently falls under the purview and ethical oversight of the Domain Specific Review Board (DSRB) of the Office of Human Research Protection Program (OHRPP) at the NHG Research & Development Office.

Right now, DSRB is seeking a dynamic and meticulous Analyst to be part of this highly systematic team to ensure that rights, safety and welfare of participants are protected by creating a culture of research that operates on high ethical standards.

As an Analyst, you provide secretariat support to the DSRB and facilitate the review process of research protocols submitted to DSRB.

This includes screening and processing all applications, preparing and coordinating review meetings, maintaining documentation of minutes of the meetings and follow-up actions including correspondence to Investigators / Sponsors / Regulatory Authorities.

Key responsibilities includes ensuring that submitted research protocols are reviewed efficiently, and are consistent with the regulations, guidelines and policies.

The successful candidate will also be required to interpret and apply ethical principles applicable to human biomedical and population health research, and serve as a resource for DSRB reviewers and researchers in ethics related matters and be involved in cross unit projects and work as assigned by the Supervisor & Head of Department.

Interested candidates may apply for this position by submitting their resume through the NHG website: https://corp.nhg.com.sg/Careers/Pages/Your-Career.aspx

WE ARE HIRING

Requirements:

- Degree, preferably in Science/Life Sciences / Public Health/ Health Sciences / Pharmacy / Medicine / Nursing or similar from an accredited university.
- At least 1-2 years of working experience within clinical research settings (e.g. clinical research associate, study coordinator, or research administrator) is advantageous but not essential.
- Knowledge of SGGCP, applicable regulations and guidelines of clinical research, or ethical principles related to human biomedical research.
- Able to work independently, as well as part of a team.
- Able to work with a high degree of accuracy and attention to detail
- Possess excellent analytical, organizational, communication, and interpersonal skills

GCP INSPECTIONS 2012 - UPDATES FROM HEALTH SCIENCES AUTHORITY (HSA)

The Health Sciences Authority (HSA) and the National Healthcare Group (NHG) hosted the Combined Clinical Research Professionals (CRP) and Clinical Research Coordinators Society (CRCS) Forum at the 2 Bukit Merah Central Auditorium on 7 December 2012. The theme of this forum was 'Good Clinical Practice (GCP) Inspections 2012 – Updates from HSA'. The forum was attended by about 260 clinical research professionals from pharmaceutical companies, Contract Research Organisations (CROs) and healthcare institutions.

Mr Foo Yang Tong (Director, Clinical Trials Branch, Health Products Regulation Group, HSA) shared on the "Common GCP Inspection Findings" noted from GCP Inspections conducted in 2012.

Ms Sumitra Sachidanandan (Compliance Inspector, Clinical Trials Branch, Health Products Regulation Group, HSA) presented on "Alternative Measures on Investigational Product (IP) Management" for Investigator-initiated clinical trials; whilst Ms Yang Yi (Senior Research Officer, National Addictions Management Service, Institute of Mental Health) shared her site's experience in "Investigational Product Repackaging and Relabelling" for a randomized, double-blind, placebo-controlled clinical trial.

The forum noted that 11 GCP Site Inspections were conducted by HSA in 2012; 10 were protocol-specific GCP Inspections and 1 was a systems GCP Inspection on Informed Consent and Investigational Products.

There was a decrease in the incidence of critical and other GCP Inspection Findings, but an increase in major GCP Inspection findings in 2012 in comparison to 2011 (Refer to Figure 1). Informed Consent, IP and Case Review accounted for the top three major GCP Inspection findings, whilst IP, Investigator's Site File and Biological Samples accounted for the top three other GCP Inspection findings in 2012.

Mr Foo shared best practices noted in the conduct of clinical trials on unconscious or mentally incapacitated subjects with regard to documentation of Informed Consent in the subject medical records, significance of capturing the timing of Informed Consent and obtaining consent from the subject for continued participation in the clinical trial if the subject was able to provide consent at a later date.

Mr Foo updated that the template Informed Consent forms for substituted consent by the subject's spouse / parent / guardian / person having charge / legally acceptable representative and consent for continued participation by the subject are available on the HSA website.

Ms Sachidanandan reviewed the alternative measures for IP management for investigator-initiated clinical trials at this forum. She explained that investigator-initiated clinical trials on locally-registered medicinal products whereby the hospital pharmacy is involved in managing the IP will be eligible for alternative measures for IP management. Further information on these alternative measures is available on the HSA website. Some alternative measures include the following:

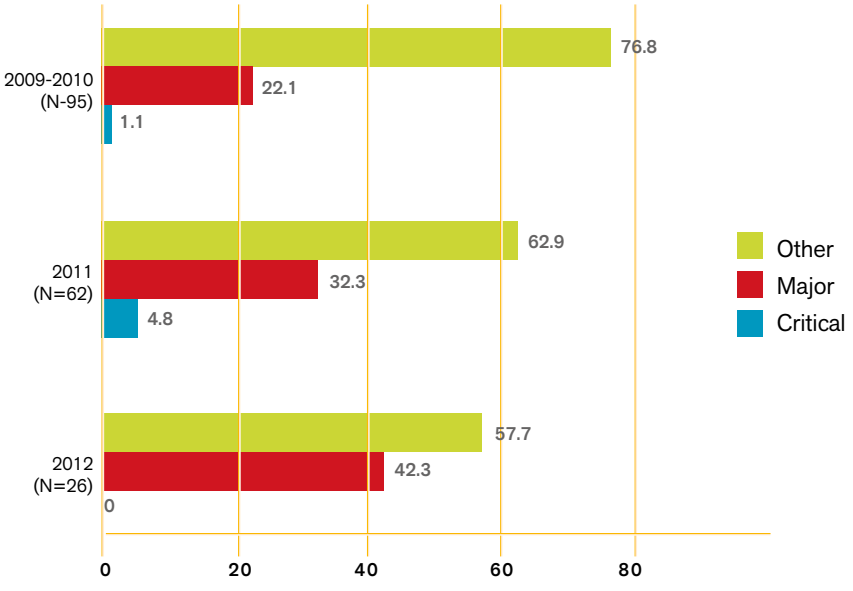
IP Inventory Logs may not be required if the inventory could be managed by the hospital pharmacy system. However, it would be necessary to document the batch number and expiry date of the IP dispensed to the subjects; IP Storage Temperature Records may not be required if the hospital pharmacy has an existing system to monitor the storage temperature of medicinal products;

IP Dispensing and Accountability Logs may not be required if it is not critical to determine the subject compliance prior to dispensing IP for the next study visit or if subject compliance could be captured through alternative documentation like subject medical records or questionnaires; and

IP Destruction Records may not be required if the hospital pharmacy system for disposal of pharmaceutical waste could be utilised. However, it would still be pertinent to document the IP returns.

Ms Yang Yi shared her study team's experience in managing IP for a randomised, double-blind, placebo-controlled investigator-initiated clinical trial involving the use of three medicinal products and their matching placebos. She elaborated on the study team's experience of consulting HSA on Investigational Product management from developing written procedures to conducting a mock session on IP Repackaging and Relabeling prior to subject recruitment.

Please refer to the HSA website at www.hsa.gov.sg for the presentation slides.



NMRC NEW INVESTIGATOR GRANT (NIG) 2011

THE IMMUNOMODULATORY ROLE OF SPHINGOSINE KINASE IN TCELL/NEUTROPHIL INTERACTIONS

Dr Chia Li Ann, Faith
Consultant
Rheumatology, Clinical Immunology & Allergy
Tan Tock Seng Hospital

In the recent years, there has been a move towards targeted immune therapies in chronic inflammatory diseases such as rheumatoid arthritis (RA). The discovery of novel and safe immunomodulators are of considerable importance in the treatment of these conditions.

Sphingosine kinase (SphK) is the enzyme that phosphorylates Sphingosine in Sphingosine-1-phosphate (S1P). Immune cell activities including cytokine production, proliferation, differentiation, motility and survival have been shown to be modulated by the dynamic balance between Sphingosine and S1P.

Influx of inflammatory cells into target tissue is a feature of RA, resulting in destruction and remodeling of the extracelullar matrix. This tissue destruction is mediated by proteases such as MMPs and controlled by many factors including cytokines and direct cell-cell contact.

The therapeutic potential of SphK blockade in a human cell-cell contact system has not been explored. Our project represents a series of studies to dissect the functional role of SphK 1 and 2 in human cells and in the neutrophils isolated from peripheral blood of patients with RA, aiming to find out if SphK1 and 2 blockade can modulate neutrophil function, which component of SphK 1 and 2 is active in regulating inflammation and which signaling pathways underlie these effects.

AWARDS & RECOGNITION

Awards received by Health Sciences & Outcomes Research (HSOR) Unit, NHG

Grant Name	Receipient	Title of Work
Singapore Health & Biomedical Congress 2012	**Ms Anusha Govinda Raj**, Senior Research Analyst *Young Investigator Award – Silver* *(Quality & Health Services Research)*	Effectiveness of a palliative care programme in reducing hospital admissions for nursing home residents
1st Singapore International Public Health Conference & 7th Singapore Public Health & Occupational Medicine Conference	**Ms Tan Woan Shin,** Principal Research Analyst *Young Investigator Best Oral Presentation – Runner-Up*	Results of the liberalisation of Medisave for a population-based diabetes management programme in Singapore
	Mr Pradeep Paul George, Senior Research Analyst *Young Investigator Best Poster Presentation – Runner-Up*	Evaluation of a comprehensive management programme for COPD
	Ms Charis Ng Wei Ling, Research Analyst *Student Best Oral Presentation – Runner-Up*	Association of socioeconomic status and social support with depressive symptoms among the elderly in Singapore

Ms Anusha Govinda Raj receiving the award from NHG Chairman, Mdm Kay Kuok

Ms Charis Ng (Extreme left) & Mr Pradeep Paul George (2nd from left)
Reproduced with kind permission from the 1st Singapore International Public Health Conference 2012

NTU-NHG INNOVATION SEED GRANT 2011
PRECISE VISUALISATION OF FINE NEEDLE ASPIRATION UNDER ULTRASOUND GUIDANCE USING MEMS TECHNIQUE

Prof Zhou Yufeng
Assistant Professor
Division of Engineering Mechanics
School of Mechanical & Aerospace Engineering
College of Engineering
Nanyang Technological University

Adjunct Assistant Professor Vu Kien Fong, Charles
Gastroenterology & Hepatology (GE) Clinic
Head of Department, Senior Consultant
Tan Tock Seng Hospital

Fine-needle biopsy or aspiration is widely used in the diagnosis of cancer, and safer and less traumatic than an open surgical biopsy. With continuous ultrasound imaging, the physician is able to view the biopsy needle or wire as it advances to the location of the lesion in real-time.

However, precise needle placement using ultrasound can be difficult because of the poor visibility of the needle. Device misplacement may result in multiple "stabs", lengthy procedures, other tissue or organ injuries, and incomplete interventions needing repeat procedures.

The resulting injuries are estimated to cost over $1 billion in healthcare expenditure annually, not to mention the potential medico-legal costs. We have successfully added a mini ultrasound element (actuator) on the needle tip (see Figure 1). The mini actuator (<1 mm) manufactured by a microelectromechanical system (MEMS) radiates a low-intensity ultrasound burst with acoustic intensity less than 720 mW/cm2 according to the Food and Drug Administration's regulation.

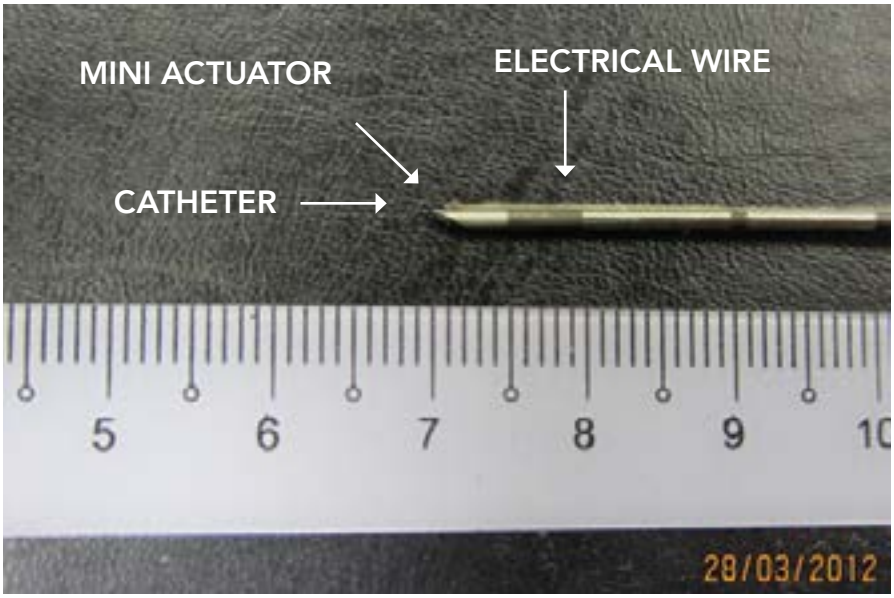


Figure 1. Representative photo of mini actuator attached on the tip of a catheter.

MEMS devices are fabricated using photolithography. Very small devices with low power consumption are possible. Because of the interference with the B-mode ultrasound imaging, there will be bright lines shown on the screen, although sometimes the catheter itself does not appear clearly in the sonography.

A test of the new catheter in a breast phantom with both hyper- and hypo-echoic lesions was carried out in the lab (see Figure 2). After activating the mini actuator, the interference is clear. With the already-known distance between the mini actuator and catheter tip, the precise location of catheter could be determined.

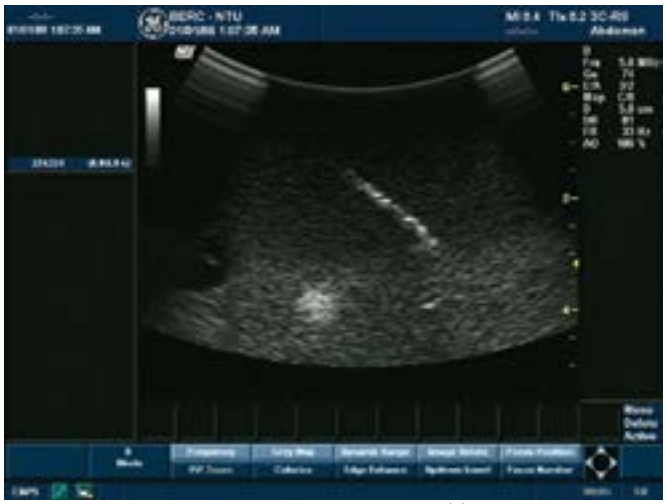


Figure 2 (a)

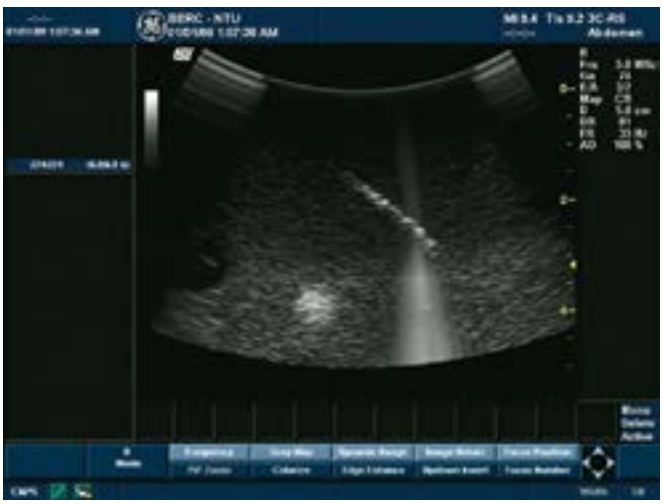


Figure 2 (b)

Figure 2. Comparison of the sonography guided biopsy in a breast phantom with both hyper- and hypo-echoic lesions (a) before the activation of mini actuator, the catheter is displayed on the screen as shown in the white arrow, and (b) after the activation of mini actuator, the interference comes from the tip of the catheter.

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
Clinical Trial Grant ***UPCOMING NEW GRANT***	The new clinical trial grant aims to support innovative and high-impact clinical trials which look into developing novel healthcare therapies. The grant also seeks to foster new directions in translational biomedical research, and further encourage multidisciplinary and multi-institutional collaborations. *Note: More details on the upcoming Clinical Trial grant will be available on the NMRC website once it is launched, estimated to be in February 2013.*	**The Co-Development Scheme:** An industry partner is required for this scheme. NMRC will match a maximum of S$5million for 3 years with the amount put in by the industry partner. **PI-Initiated Scheme (Early Phase Trials):** Maximum of S$5million for 3 years **PI-Initiated Scheme (Late Phase Trials):** Between S$500,000 and S$2 million for 3 years.	**The Co-Development Scheme:** Estimated to be launched in February 2013. Will remain throughout the year **PI-Initiated Schemes:** Estimated to be launched in February 2013.

Talent Development Award	Award Description	Eligibility Criteria	Application Period
NRF-MOH Healthcare Research Scholarship - Master of Clinical Investigation (MCI) Programme	The National University of Singapore - Master of Clinical Investigation (NUS MCI) Programme aims to meet the needs of clinicians in healthcare institutions who desire to incorporate scientifically sound research into their clinical practice. The goal of the programme is to equip clinicians with the basic methodological and practical skills to design and conduct clinical investigations that are relevant to patient care. These include studies aimed at evaluating: new treatments and technologies, diagnostic modalities, mechanisms of human disease, determinants of disease outcomes, and effectiveness of health services. The course also provide the foundation for those who may wish to pursue advanced clinical research training, including that leading to a PhD degree.	The scholarship offered by MOH is open to clinicians who are Singapore Citizens or Permanent Residents. Applicants who meet the eligibility criteria will automatically be considered for the scholarship.	1 January 2013 – 31 March 2013

NATIONAL RESEARCH FOUNDATION (NRF) GRANT — https://rita.nrf.gov.sg

Grant Name	Grant Description	Funding Quantum	Application Period
NRF Proof-of-Concept (POC) 9th Grant Call ***UPCOMING NEW GRANT***	The NRF Proof-of-Concept (POC) grant scheme provides funding for proof-of-concept development to researchers in the institutions of higher learning (IHLs), so as to facilitate the commercialisation of technologies developed in the IHLs. The grant scheme supports projects which are technically proven and commercially viable, as well as developmental cost in building a fully functional prototype.	Maximum of S$250,000 for up to 1 year	3 January 2013 – 1 March 2013

THE NATIONAL KIDNEY FOUNDATION (NKF) GRANT — www.nkfs.org

Grant Name	Grant Description	Funding Quantum	Application Period
Venerable Yen Pei - National Kidney Foundation (NKF) Research Fund	The Venerable Yen Pei-National Kidney Foundation (NKF) Research Fund is started specifically to fund research in kidney diseases. The acceptable areas of research are basic science and clinical research that are of renal or renal related projects. If the research has relevance to NKF activities, the proposals would be considered as well.	Maximum of S$300,000 for up to 3 years.	Opens in January 2013

CAUSALITY - MODELS, REASONING AND INFERENCE

by Judea Pearl

Li Rui Jie
Senior Research Analyst
Health Services & Outcomes Research
National Healthcare Group

"Correlation does not imply causation." This is an often repeated admonition by our statistics or epidemiology professors to caution us that correlation alone is not sufficient for evidence of causation. If correlation does not imply causation, then what does? This is the central theme around the book "Causality: Models, Reasoning and Inference" by Judea Pearl, winner of the Turing Award 2011.

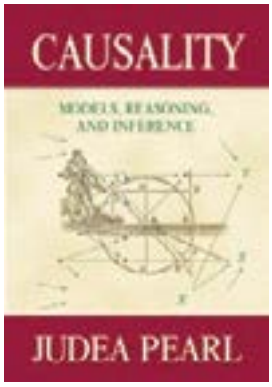
The book starts off by laying down the foundational groundwork for topics like probability, graphs and causal models. Inevitably, there is a good dose of mathematical representations of the concepts and theories presented. However, there are clear expositions of these concepts and theories which make them easy to follow.

The subsequent chapters introduce the various tools to identify and formalise causal inferential problems. These tools include structural equation which is a common recurring theme in the book as it fits the general framework of defining causal inference by Pearl.

Common issues plaguing causal inferences like Simpson's paradox and confounders are also explained. Finally, counterfactuals are presented to complete the model of causal inference that Pearl proposes.

This book is definitely not an easy read but the concepts presented are very understandable and within grasp of someone without much prior knowledge on the topic. With the wide interest in causality across domains, this book provides the reader with a framework to consider such problems.

It is a recommended read for anyone interested in any form of scientific inquiry that aims to determine causal relationships. Readers of the book should also know that Professor Pearl is a regular participant on the Structural Equation Modelling Discussion Network (SEM-NET) mailing list where he readily discusses and clarifies many of the concepts he proposed in this book. The URL for information on the list is http://www2.gsu.edu/~mkteer/semnet.html.



Pearl, J. (2000). Causality: Models, Reasoning and Inference. Cambridge University Press.

NHG RESEARCH TRAINING CALENDAR

for February – March 2013

Date	Time	Training Programme	Venue	No of Seats
Ongoing	00:00 - 23:59	Proper Conduct of Research Online - Basic I & III (PC101 & PC103) Workshop	http://www.elearning.nhg.edu.sg	100
		Proper CConduct of Research – Basic II^ (PC102) Workshop		
20 – 22 Feb 2013	09:00 –18:00	Biostatistics Workshop	PSB Academy, Level 2, E-202	25
22 Feb 2013	09:00-16:30	Proper Conduct of Research - Advanced II (PC302) Workshop	PSB Academy, Level 2, A-202	30
25 Feb 2013	09:00-18:00	Advanced Biostatistics Workshop	PSB Academy, Level 2, E-206	30
11 - 13 Mar 2013	09:00-17:00	Intellectual Property Seminar	NHG College (Jackson Square) Block B, Synergy 3	30

For registration and full details, please visit www.research.nhg.com.sg (Training & Education > Search for a Course)

*Dates are subjected to changes without prior notice

^For more information, refer to www.research.nhg.com.sg (Training & Education -> Proper Conduct of Research Courses)

HEALTH PROGRAMME EVALUATION
THEORY OF CHANGE AND LOGIC MODEL

Mr Pradeep Paul George
Senior Research Analyst
Health Services & Outcomes Research
National Healthcare Group

HAVE A QUESTION REGARDING RESEARCH?
Drop us a note at the researchtraining@nhg.com.sg and we'll have it answered by experts in upcoming editions!

Fundamental to all health programme evaluations is a clear definition of what is effectiveness (or "success"); this would be determined by the aim of the programme and the hypothesised mechanism of expected effect. This requires a theoretical understanding of how the intervention causes change and of the links within the causal chain ("theory of change"). Theories of Change (TOC) and Logic Models (LM) are critical elements in programme design and evaluation. TOC is the "theory" that explains how the interventions achieve the outcome, and LM is a "roadmap" from actions to outcomes.

WHAT IS **THEORY OF CHANGE**?

A TO is the chain of reasoning that explains why you believe your project will make a difference in the problem you want to impact. It draws on research and knowledge of "best practices" to validate each step in a "causal pathway" between the interventions and the final outcomes of the project (Figure 1).

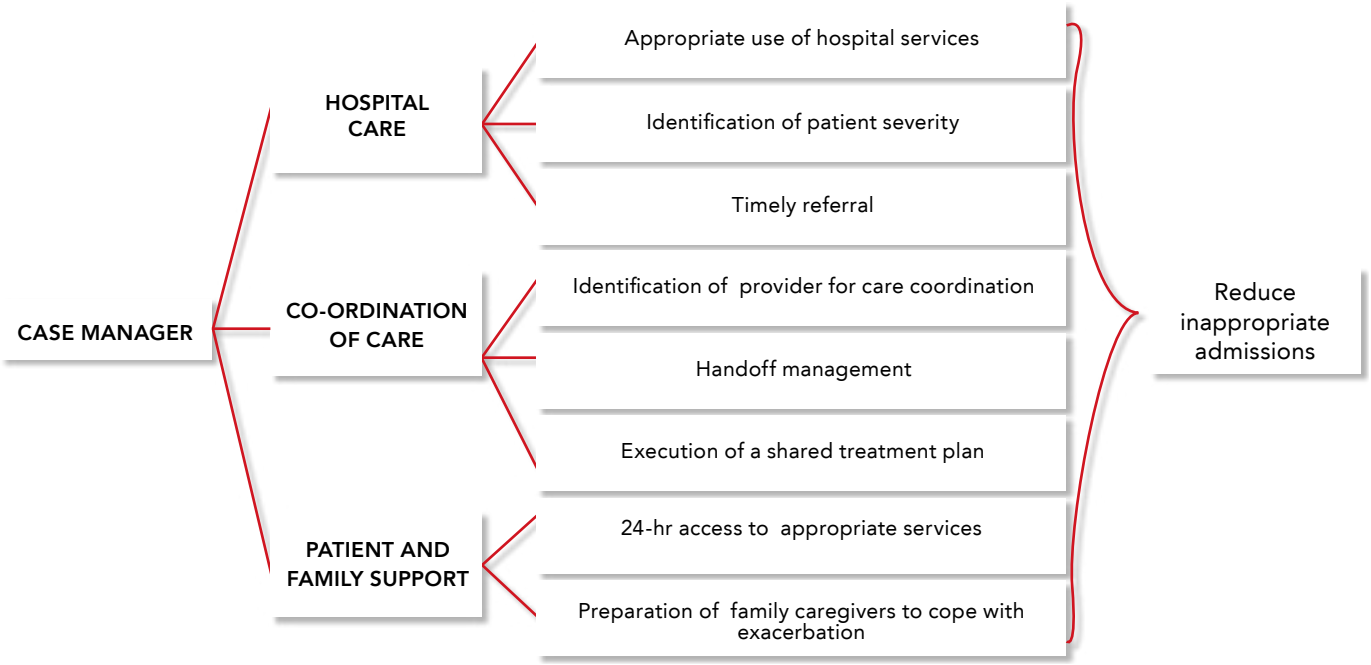


Figure 1 – Theory of change example: Case management to reduce re-admissions

WHAT IS A LOGIC MODEL?

LM is a graphical or textual representation of how a programme should work and links outcomes with processes and the theoretical assumptions of the programme (Figure 2). LM is a successful tool for programme planning, implementation and performance management. Funding decisions are favourable if we can demonstrate how and why they will succeed.

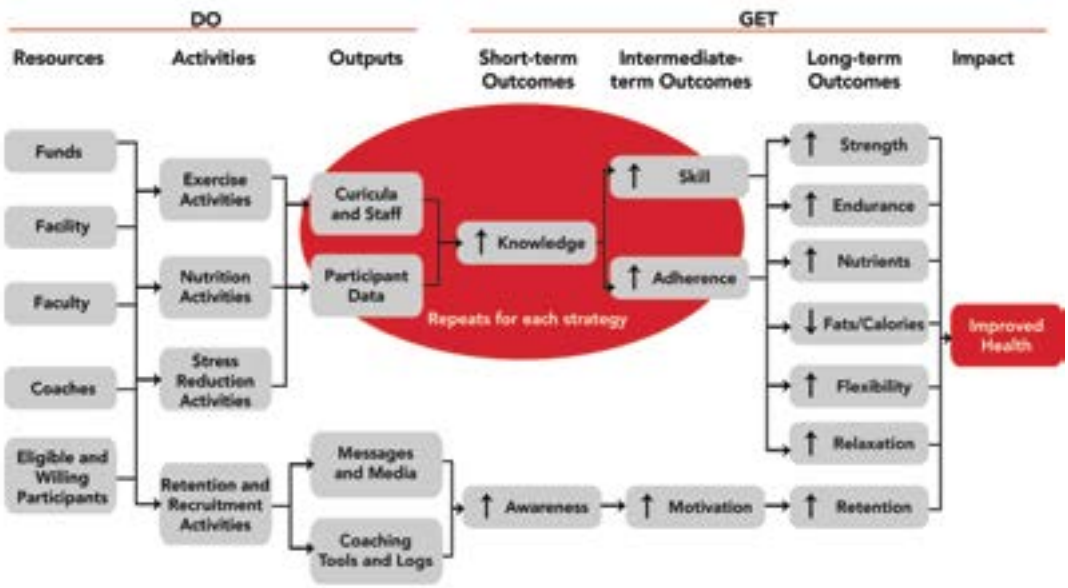


Figure 2 – Logic Model example: Health Improvement programme

THEORY OF CHANGE AND LOGIC MODEL SEQUENCE

TOC is necessary in the design stage while LM is important in the implementation planning stage. Both form a continuous loop that can provide feedback about a programme throughout its lifecycle. Figure 3 demonstrates key points of the design, planning, implementation, and evaluation that the two types of models can support.

Developing a TOC model is time consuming, and LMs used without a clear TOC are often too simplistic. In a LM without a distinct TOC, we would not:

- know which processes are critical to achieve intended outcomes;
- be able to identify processes which lead to a programme failure/success; and
- be able to identify if the programme failure is due to failure in theory or implementation.

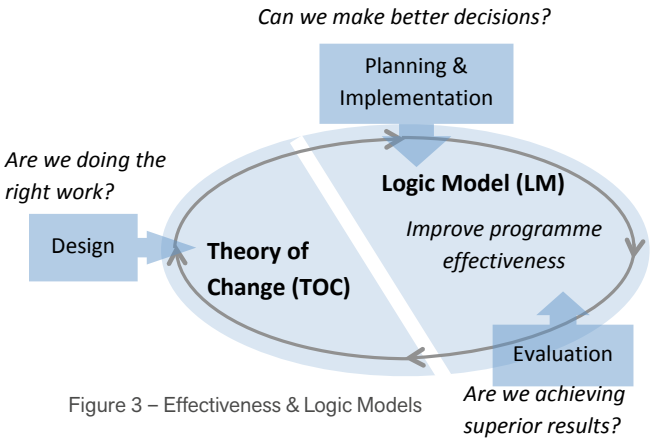


Figure 3 – Effectiveness & Logic Models

DEVELOPING A LOGIC MODEL WITH A THEORY OF CHANGE

- Identify the programme objectives and the intended outcomes;
- List activities that would help achieve the outcomes, document TOC and the assumptions. Review and clarify the links between activities and outcomes;
- Add inputs (resources e.g. manpower) and outputs (quantify services e.g. clinic sessions) for each activity. Note that outcomes are different: they are the ultimate clinical impact;
- Construct a draft model, use arrows to show the connections between inputs and activities, between activities and outputs, and between outputs and each sequence of outcomes. Specify the assumption and TOC in each link; and
- Check that activities are comprehensive, outcomes are significant and understandable, and connections are evidence-based.

Conduct a TOC within a manageable programme scope and stakeholder buy-in. Then summarise TOC alongside the LM in ways that serve the stakeholders' purpose. A logic model that is a summary of an underlying theory is a much more powerful tool than just being a graphical road map.

GUIDE TO PROGRAMME EVALUATION

Successful programmes often have a sound TOC and LM. For example, a programme with a faulty TOC but sound LM indicates a causal logic problem.

		Theory of Change (TOC)	
		Sound	Faulty
Logic Model (LM)	Sound	Programme success	Casual logic problem
	Faulty	Implementation problem	Programme failure

Reference

1. *Mertens, Donna M. Program Evaluation Theory and Practice: A Comprehensive Guide. Program Evaluation Theory and Practice: Guilford Press, 2012. Print.*
2. *Grembowski, David. The Practice of Health Program Evaluation. Thousand Oaks, CA: Sage Publications, 2001. Print.*

Improving the Mental Health of the Population – an Asian Perspective

A mental health symposium held in conjunction with the WORLD HEALTH SUMMIT REGIONAL MEETING – ASIA, SINGAPORE 2013

Mental disorders are among the most common causes of disability. Poor mental health impedes individuals' capacity to realise their potential, work productively, and make a contribution to their community, while positive mental health is linked to a range of beneficial outcomes and is fundamental to coping with adversity. To improve mental health and lessen the burden of disease, mental health services must be provided in ways which are proactive and can effectively impact on relevant factors at both population and individual levels.

This one-day symposium is focused on innovative and multidisciplinary approaches to improving mental health. Participants will learn about the state of mental health and approaches to improve it from leading mental health professionals and researchers. Break-out sessions focusing on specific areas such as child and geriatric mental health and cost of mental health delivery will be discussed in small groups using case-studies. The venue of the workshop – Singapore's only tertiary psychiatric hospital – offers participants an opportunity to see first-hand, tertiary facilities to support mental health recovery.

Symposium

8 April 2013
9.30am – 4.00pm

Institute of Mental Health, Buangkok Green Medical Park, 10 Buangkok View, Singapore 539747

8.30am	**Registration**
9.30am	**Opening Address** *A/Prof Chua Hong Choon* CEO, Institute of Mental Health, Singapore
9.40am	***Conceptual and Empirical Approaches to Understand Physical and Psychological Well-being of the Caregivers of Children with Developmental Disability and Older Adults with Dementia: A Life Course Perspective to Caregiver Health*** Professor Parminder Raina Raymond and Margaret Labarge Chair in Optimal Aging Department of Clinical Epidemiology & Biostatistics Faculty of Health Sciences, McMaster University Hamilton, Ontario Canada
10.10am	**The Singapore Mental Health Study: Translating Research to Policy** *A/Prof Chong Siow Ann* Vice Chairman Medical Board (Research) Senior Consultant Psychiatrist Institute of Mental Health, Singapore
10.40am	**Tea Break**
11.00am	**Mental Health Literacy and Population Mental Health** *Professor Anthony Francis Jorm* Professorial Fellow ORYGEN Research Centre University of Melbourne, Australia
11.30am	**A City-State of Mind - Facing the Challenge of Mental Health in Singapore** *Dr Alan Ong* Deputy Director (Community Mental Health) Community Mental Health Branch Primary and Community Care Division Ministry of Health, Singapore
12.00pm	**Panel Discussion**
12.30pm	**Lunch & Tour of IMH Facilities**
2.00pm	**Breakout Sessions** **Session 1** REACH: An Evidence-based Delivery System that is Cost Effective for Singapore *REACH Team, IMH* **Session 2** Advancing Psychogeriatric Care: A Multidisciplinary Approach *Geriatric Psychiatry, IMH* **Session 3** Economic Evaluation in Healthcare *Dr. Hristina Petkova* *Researcher, Health Economics Centre for the Economics of Mental and Physical Health, Institute of Psychiatry, King's College London*
3.30pm	**End**

Transport to Ritz Carlton Hotel for opening of WORLD HEALTH SUMMIT REGIONAL MEETING – ASIA

Symposium fees:
S$100 (excluding 7% GST) per participant

For registration, please visit
www.imh.com.sg

For more information please contact
symposium@imh.com.sg

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IMH 1928-2013 85 YEARS ADVANCING MENTAL HEALTHCARE

INSTITUTE of MENTAL HEALTH

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