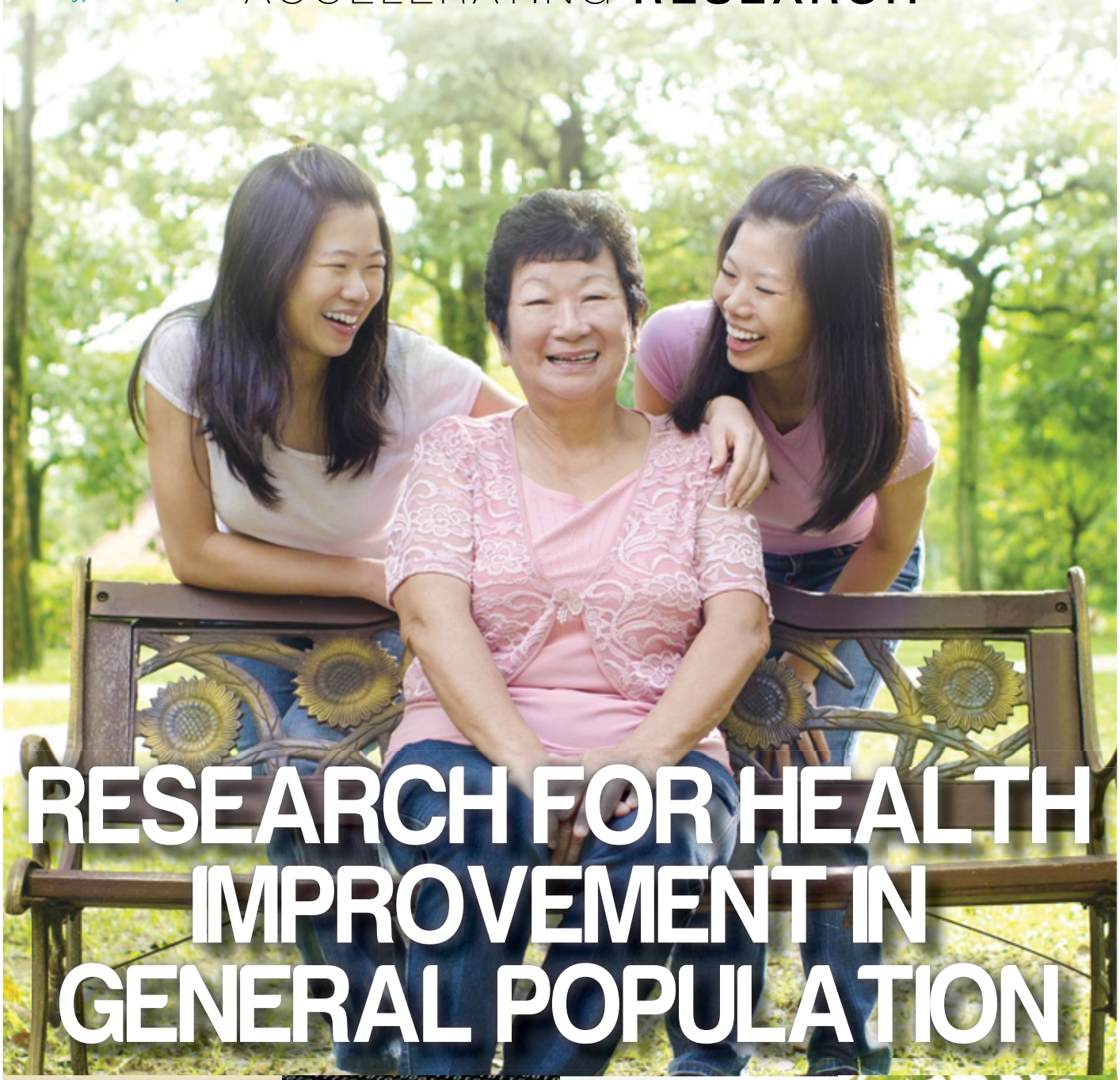
Issue 19 **June - July 2014**
MiCA (P) 128/06/2014

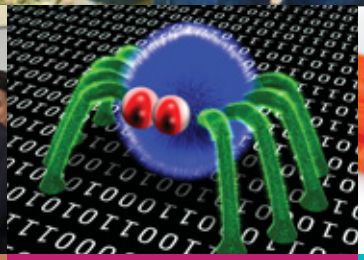
A Newsletter For The Research Community In Singapore

National Healthcare Group
Adding years of healthy life

catalYst
ACCELERATING RESEARCH



RESEARCH FOR HEALTH IMPROVEMENT IN GENERAL POPULATION



contents

Your Newsletter, Your Comments

Please send us your comments and feedback to
researchtraining@nhg.com.sg
(Attn: NHG Research Editorial Workgroup)

Dear Readers,

In this issue of Catalyst, I am pleased to report on the signing of a Memorandum of Understanding (MOU) between Singapore Health Services (SingHealth)'s Centralised Institutional Review Board (CIRB) and the National Healthcare Group (NHG)'s Domain Specific Review Board (DSRB) on 22 May 2014. With the signing of this MOU, researchers doing multi-centre studies in public hospitals will no longer have to undergo multiple ethics board reviews. The mutual recognition of the two IRBs could potentially save time, effort and costs, ultimately benefitting research in Singapore. Along with this report, we have prepared some, Frequently Asked Questions (FAQs), to help researchers understand better this mutual recognition process.

Related to research ethics, NHG together with U.S. PRIM&R (Public Responsibility in Medicine & Research) successfully organised the 3rd Asia Pacific Research Ethics Conference (APREC) 2014 from 26-28 March 2014. The conference featured over 50 local and international speakers and saw over 300 professionals in research ethics. The conference discussed topics in areas of Institutional Review Board / Ethics Review Board, Quality Management & Quality Improvement in Research, Industry & Clinical Research Professionals, and Hot Topics in Research Ethics. My sincere thanks to all who had contributed to the success of this conference, in particularly members of the APREC 2014 Organising Committee, led by Associate Professor Chin Jing Jih (Chairperson, NHG Research Ethics Committee, Divisional Chairman, Integrative & Community Care, Specialist in Geriatric Medicine, and Senior Consultant, Department of Continuing & Community Care, Tan Tock Seng Hospital).

We are also pleased to have the opportunity to co-organise the Biomedical Engineering Forum Programme (BEP) with A*STAR on, "Neurological Disorders and Rehabilitation: The Technological Disorders and Rehabilitation", as well as hosting a visit by delegates from the Medical University of Vienna (MUV), Austrian Institute of Technology (AIT) and NTU to explore collaborative opportunities in areas of bio-imaging. Coverage of these events can be found in this issue of Catalyst!

On the research front, according to a Infocomm Development Authority of Singapore's (IDA) Annual Survey on Infocomm Usage in Households and by Individuals, in 2013, 87% of the households in Singapore have access to internet from home – a steady 20% increase over the past 10 years. We all know that the internet is a double-edged sword – the accessibility of information comes with challenges like Internet Addiction and Cyber-bullying amongst Singapore's youths. In this issue of Catalyst, read about how research at Institute of Mental Health (IMH) can help you and your kids overcome these threats. On the same note of cyberage, "Text Neck" is a rising global epidemic. Find out how exercise-based programmes in Tan Tock Seng Hospital (TTSH) Physiotherapy Department have helped patients with chronic neck pains. Also in this issue, the NHG Health Services and Outcomes Research (HSOR) unit shares on what can be done to reduce your waiting time at the out-patient pharmacies.

2014 also marks the 10th anniversary for NHG Research & Development Office (RDO). Within a decade, RDO has grown from a humble research support office into one of the largest in Singapore providing a diverse research support services to the NHG institutions and beyond. I am pleased to share with you some of our office's key achievements in facilitating and supporting NHG Research in the last decade.

Lastly, please be informed that Catalyst will be moving fully online to bring you greater convenience. So don't forget to fill out the form and send it to us to ensure you continue to receive a copy in your email!

'Till next time!

Yours Sincerely,

Farah Haniff
Editor-in-Chief

National Healthcare Group
Adding years of healthy life

Designed by creativessence design & communications

Mutual Recognition of Ethics Review between NHG DSRB and SingHealth CIRB

Singapore Health Services (SingHealth) and National Healthcare Group (NHG) marked a major milestone in medical research on 22 May 2014 with the signing of a Memorandum of Understanding (MOU) between the SingHealth Centralised Institutional Review Board (CIRB) and the NHG Domain Specific Review Board (DSRB). The MOU facilitates the mutual recognition of multi-site studies approved by the 2 review boards.

Under the current system, multi-centre research sites are required to submit their protocols for review by both CIRB and DSRB, if the research sites fall under the purview of either board. With effect from 01 July 2014, multi-centre studies will only need to submit protocols to one IRB. A cross-cluster research study approved by SingHealth CIRB will be recognised by NHG DSRB, and vice versa. This translates into a more streamlined approval process. One tenth of research currently conducted involves multiple sites across NHG & SingHealth.

Frequently Asked Questions about CIRB-DSRB Mutual Recognition

1. What types of cross-cluster studies are eligible for single IRB reviews?

All new research applications involving both NHG* and SingHealth** sites are eligible to benefit from the DSRB-CIRB mutual recognition arrangement and have their studies reviewed by only 1 IRB.

For the period from 1st July 2014 through 30th September 2014, all cross-cluster research applications will be reviewed by DSRB. Subsequently, research applications will be allocated for review by either IRB. More details on the IRB arrangements will be released in the near future.

Note: Research studies involving only SingHealth or NHG sites will continue to be reviewed by the respective cluster IRBs (i.e. SingHealth CIRB or NHG DSRB).

*including partner institutions under NHG DSRB purview, i.e. National University Hospital, NUS – Yong Loo Lin School of Medicine, NUS – Saw Swee Hock School of Public Health, NUS – Faculty of Dentistry, Alice Lee Centre for Nursing Studies, Khoo Teck Puat Hospital, Jurong Health Services at Alexandra Hospital, Health Sciences Authority, Ang Mo Kio Thye Hua Kwan Hospital, Dover Park Hospice, Agency for Integrated Care, Health Promotion Board

**including partner institutions under SingHealth CIRB purview, i.e. Changi General Hospital, HCA Hospice Care, Singapore Civil Defence Force

2. When can cross-cluster studies be submitted?

Cross-cluster studies can be submitted to DSRB via the NHG online research portal (ROAM) from 15th June 2014 onwards. The applications will only be processed from 1st July onwards.

Note: Full Board studies must be received by NHG DSRB by 1st July 2014 to be considered for review at the July Full Board meeting.

The PI should submit with sufficient lead time for the Department Representative and Institutional Representative to endorse prior to the 1st working day of the month.

Submissions received after the 1st working day would be tabled for the subsequent full board meeting.

3. How does this affect current studies?

All new research applications, approved from 1st July 2014 onwards, are eligible to benefit from the DSRB-CIRB mutual recognition arrangement and have their studies reviewed by only 1 IRB.

Current studies approved before 1st July 2014 will remain under the oversight of the respective IRBs until study closure.

4. Can single cluster studies add on additional sites from a different cluster, and continue to be reviewed by the original IRB?

New single cluster studies approved from 1st July 2014 onwards can add on additional sites from a different cluster, and have these amendments reviewed by the initial approving IRB.

The request should be submitted as a cross-cluster site(s) addition amendment to the initial approving IRB. This is subjected to a review fee of $1,000 (excluding GST).

Single cluster studies approved before 1st July 2014 do not meet the criteria for the DSRB-CIRB mutual recognition arrangement. A new application should be submitted to the respective cluster IRBs (i.e. SingHealth CIRB or NHG DSRB) for the review of the new site(s).

If you have any enquiries, please contact the DSRB Hotline at 6471 3266 (office hours) or CIRB Hotline at 6323 7515 (office hours).

The full list of FAQs is available on the NHG Research Website www.research.nhg.com.sg and on the ROAM Announcements page.

This translates into a more streamlined approval process

Professor Ivy Ng, Group Chief Executive Officer, SingHealth (Left) and Professor Chee Yam Cheng, Group CEO, National Healthcare Group (Right) exchanging the signed MOU

MUV, ATI and NTU Visit to Tan Tock Seng Hospital

A/Prof Lim Tock Han (right) engaging in an informal discussion with Prof Wolfgang Knoll (middle) and Prof Markus Müller (left)

Mr Zheng Wei Xiong
Executive
Research Training and Development Unit
Research & Development Office
National Healthcare Group

On 9 April 2014, the National Healthcare Group hosted a visit for delegates from Medical University of Vienna (MUV), Austrian Institute of Technology (AIT) and Nanyang Technological University (NTU) .The visit was co-ordinated by Research and Development Office (RDO) and included thirteen delegates from the various institutes. Amongst them were Professor Markus Müller (Vice Rector for Research, MUV), Professor Wolfgang Knoll (Managing Director, AIT), Professor Christian Herold (Head, Department of Biomedical Imaging and Image-Guided Therapy and Director, Medical Imaging Cluster, MUV) and Associate Professor Ser Wee (Programme Director, NITHM Medical Imaging and Signal Analysis (MISA) and Director, VALENS, School of Electrical and Electronic Engineering, NTU). The group was welcomed by NHG's Deputy Group CEO (Education & Research), Associate Professor Lim Tock Han.

The key objective of the visit was to explore possible areas of research interests and discuss potential collaborative opportunities in the areas of Medical Imaging, Image Analysis and eHealth. A/Prof Lim gave an introductory presentation on the healthcare landscape in Singapore and the role played by NHG towards improving health and reducing illness in population of Singapore. He also shared on the development of NHG's research capabilities and the initiatives in terms of developing talents and providing support to encourage quality research within NHG institutions.

To provide the delegates with a better understanding of NHG's medical imaging capabilities, the group was guided by Dr Tan Cher Heng (Consultant, Diagnostic Radiology Department) to visit TTSH's Diagnostic Radiology Department. Dr. Tan highlighted the Department's strengths and its current research collaborations. The team were then directed to research presentations by three NHG's Clinician-Scientists, whose research involves significant imaging techniques. Dr Tey Hong Liang (Consultant, National Skin Centre) spoke on "High Definition Optical Coherence Tomography: Clinical Application", following which Dr Augustinus Laude (Deputy Head, Research and Consultant, NHG Eye Institute), and Dr Colin Tan (Consultant, NHG Eye Institute) presented on"Retina Imaging in Sickness and in Health" and "Optical Coherence Tomography Imaging of the Retina and Choroid in Ocular Diseases" respectively. Following each presentation, there were further discussions on the projects and potential scopes for collaborations.

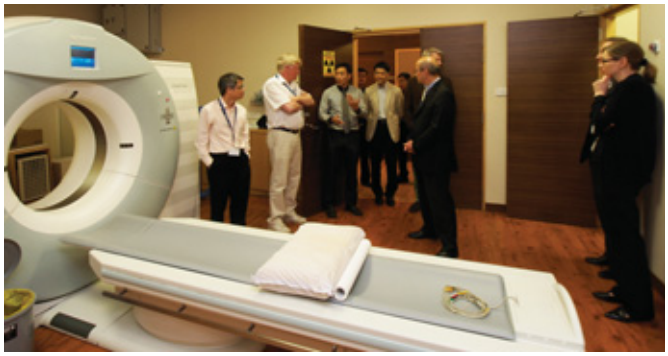
As part of the visit, the delegates were also brought on a tour to the TTSH's Heritage Museum, which was opened on 25 July 2001 to honour the legacy of its founder Mr Tan Tock Seng and to the Health City Novena Master Plan Exhibition, which focuses on NHG's development plan designed to provide facilities to create an integrated community for healthcare, medical education and translational research in a vibrant and sustainable environment.

About MUV, ATI and NTU

MUV and ATI are leading Austrian institutions that actively engage in research, innovation and partnership. MUV was originally founded as a medical faculty under the University of Vienna but has been operating as an independent institution since 2004. It is now the largest medical university in Austria and is also one of the world's largest medical universities.

AIT is Austria's largest non-university research institute that is co-owned by the government of Austria and the Federation of Austrian Industries. Partnering industries and public institutions, AIT is involved in the research and development of innovative technologies, methods and tools targeting at solving problems of the future.

NTU is one of the four public universities in Singapore, with around 33,000 undergraduate and postgraduate students. Highly committed to research and innovation, NTU is currently one of the fastest-rising Asian universities and is ranked among the top 50 universities (QS World University Ranking 2013) around the world.



Delegates from MUV, ATI and NTU visiting the CT scanner suite located in the Diagnostic Radiology Department.

Epigenetics of Addictions

Pilot study to explore the epigenetic mechanisms behind pathological gambling and its links with substance addiction.

Dr Guo Song
Senior Consultant and Head (Research)
National Addictions Management Service
Institute of Mental Health

Dr Guo Song is a senior consultant psychiatrist and the head of research at NAMS, IMH, with a joint position as adjunct assistant professor at Duke-NUS Graduate Medical School. He holds a PhD in Psychopharmacology and has practiced in addictions medicine since 1990, including serving as the director of the National Drug Dependence Treatment Centre, Beijing (2003-2004). He has been conducting research in addictions for over 20 years and published over 30 peer-reviewed papers including a genetic study of nicotine dependence as Principal investigator.

Imagineasentencethat-doesnothavespacesnor-punctuation.

Can you make out the above sentence? Formatting, spacing and punctuation in language allow us to see words, sentences, and interpret information that is there.

Epigenetics, the study of heritable changes in gene expression and phenotype, is a new area of molecular biology that looks at how epigenetic marks "punctuate" the genome. Each cell in our bodies come with epigenetic marks that serve various purposes, such as demarcating start and end points of genes, providing appropriate structure to our chromosomes and also altering the way in which genes are read. In this way, some genes can be "switched" on or off, depending on epigenetic mechanisms such as DNA methylation, histone modifications and chromatin remodeling. Such marks have been shown to be essential throughout an organism's development, and, in cases of disease, to malfunction.

Epigenetic regulation has been shown to be important in many aspects, such as learning and memory. This may account for some of the behavioural and neurological plasticity that explains psychological and physiological cravings for substances long after the absence of the drug of choice, as well as increased tolerance to substances of choice. In particular, prolonged use of substances have been known to alter brain chemistries in profound ways, and our interest in this study is to see how much of these changes are epigenetic in nature. To date, epigenetic misregulation has been implicated in studies of cocaine, nicotine, smoking, heroin, methadone and alcohol, and it is suggested that such misregulation can also occur in other compulsive behaviors such as exercise, sex and gambling.

Our Study

Our pilot study involves a collaboration between NAMS, IMH and the Singapore Institute of Clinical Sciences (SICS), A*STAR, who will be involved in both data and tissue analysis, and involves a sample of 48 male Chinese participants.

In our initial phase, all participants will complete screening and interview questionnaires to determine their eligibility for the study, and subsequently the severity of their disorder. Three groups have been selected for our study, patients who have been assessed to have pathological gambling and alcohol dependence, as well as a third healthy control group.

The study will involve the use of buccal swabs for epithelial (cheek) cells for collection of DNA. Buccal swab samples have been found to be one of the better surrogates for epigenome-wide association study (EWAS), as compared to other human tissue samples such as blood or saliva, and also demonstrate a higher proportion of hypomethylated regions, and are thus the best candidate for our study. DNA extracted from samples will be bisulfite-converted, which causes deamination of unmethylated cytosine to uracil, while preserving methylated cytosine, thus allowing for profiling of cytosine-phosphate-guanine (CpG) islands. These CpG islands will then be matched across difference groups for analysis.

Through this study we aim to investigate epigenetic profiles across gambling and alcohol patients, versus healthy controls. We hypothesise that patterns of DNA methylation across both pathological gambling and alcohol dependent patients will be similar, and these will differ from healthy controls. In addition, we hypothesise that the degree of methylation should also be correlated with the severity of the illness, as assessed by DSM-IV scores.

This is the first pilot study in epigenetics of addictions in our region. We hope to be able to identify certain target genes which relate to the etiology of these addictions, which may ultimately allow us to explore targeted pharmacological intervention in future. We also believe our study will have important contributions to the growing literature on epigenetic treatment of the long-lasting psychological and physiological effects of addictions.

"When the human genome was sequenced, some scientists were saying, "That's the end. We're going to understand every disease. We're going to understand every behavior…And it turns out, we didn't, because the sequence of the DNA isn't enough to explain behavior. It isn't enough to explain diseases." *– Dr. Jean-Pierre Issa, Director, Fels Institute for Cancer Research and Molecular Biology.*

Main Study Team (from Left to Right): Yang Yi, Guo Song, Andrew Ng

RDO Turns 10 - Celebrating a Decade of Achievements!

The National Healthcare Group Research & Development Office (RDO)

"Steering research into impactful health outcomes and sustainable patient care delivery" is the principle that guides the NHG Research & Development Office (RDO) in achieving greater heights in facilitating medical research at our institutions.

The NHG Research & Development Office (RDO) was established in 2004 to achieve the cluster's strategic goal of promoting relevant research through the facilitation and harmonization of research initiatives amongst NHG Institutions.

Currently under the oversight of A/Prof Lim Tock Han, Deputy Group CEO (Education & Research) and Ms Farah Haniff, Director, RDO, NHG RDO comprises of two operating arms – the Office of Human Research Protection Programme (OHRPP) and the Office of Research Support (ORS).

Office of Human Research Protection Program (OHRPP)

The OHRPP ensures the safety and well-being of human research participants. This is achieved through its four units – the Domain Specific Review Board (DSRB), Research Quality Management (RQM), Research Education (RE) and Partnership & Outreach (P & O).

The NHG DSRB is a centralised institutional review board (IRB) comprising of 6 Domains (A to F) based on broad disciplines in biomedical and population health research. This allows NHG to better provide specialised and efficient review of a range of research projects.

A major milestone was achieved on 22 May 2014, when a memorandum of understanding (MOU) was signed between NHG and SingHealth to facilitate the mutual recognition of multi-site studies approved by the ethics review boards of each cluster. With this, multi-centre studies will only need to submit protocols to one IRB, with effect from 01 July 2014. This potentially translates into a more streamlined approval process and time and cost savings.

Through RDO, NHG also received the first testimony of its robust Human Subject Protection Program (HSPP) and the organisation's continuous efforts and commitments towards the protection of human subjects when it received the Full Accreditation by the U.S. Association for the Accreditation of Human Research Protection Programs (AAHRPP) in 2007. It was successfully re-accredited in 2010.

To promote lifelong learning and sharing on critical issues and industry developments, NHG RDO hosted the Asia Pacific platform focusing on Human Subject Protection – the Asia Pacific Research Ethics Conference (APREC) in 2010, 2012 and 2014. The conference brought together more than 800 delegates from ethics committees, research and academic institutions, top national health authorities and the pharmaceutical industry in over 17 countries.

Office of Research Support (ORS)

The ORS focuses on providing a full range of research support services for NHG research including conceptualization and implementation of programs for research manpower and capability development through intramural grant schemes, database and online portal development and maintenance through research informatics and facilitating collaborations and partnerships at institutional, program and project levels.

Capability Development

Some of the key initiatives under Capability Development include development of complete road map for the clinician scientist career scheme. Tailored to each stage of the research journey of NHG clinicians, the various programs under the scheme include – the NHG Clinician Leadership in Research (CLR) Programme, the NHG Clinician Scientist Career Scheme (CSCS) (3 levels – Junior, Mid and Senior), the Clinician Investigator (CI) Scheme, the NHG-NTU Clinician-Scientist Fellowship (CSF).

Collaborations & Partnership

Collaborations and Partnerships have been strengthened through establishment of framework of collaborations and harmonizing of Intellectual property within the cluster institutions.

Various initiatives were introduced to promote research collaborations between NHG and its primary academic partner – NTU/Lee Kong Chian School of Medicine (LKCMedicine) as well as its strategic partners such as A*STAR. These include development of joint grants with NTU – the NTU-NHG Innovation Seed Grant (ISG), the NTU-NHG Innovation Collaboration Grant (ICG), and convergence of research strategies between NHG and LKCMedicine through co-organization of thematic research seminar series with LKCMedicine – the NHG-NTU/LKCMedicine Research Seminar.

Developing Strengths in Focus Areas

NHG's areas of focus are being developed further through joint grants in thematic areas such as the NTU-NHG Ageing Research Grant ($2million in total) and the A*STAR-NTU-NHG Skin Research Grant ($4.75million in total). RDO has served as the administrative body and main secretariat for the thematic grants. These joint grants have further nurtured collaborations between NHG and strategic partners. Efforts are underway to further develop other areas of focus including Population Health/Health Services Research, Metabolic Medicine, Rehabilitative Medicine, Infectious Diseases, Mental Health.

Here's a snapshot of NHG RDO's key milestones over the years:

2004
- NHG RDO was set-up
- Set up of centralised IRB in NHG (later known as DSRB)

2006
- Launched the Research Quality Assurance Unit
- The Clinical Research Coordinator Society (CRCS) was established

2007
- Received AAHRPP Accreditation

2008
- Formation of HRPP & 5th DSRB Domain

2009
- Hosted the Society of Clinical Research Associates, Inc. (SoCRA) Certification Program for Clinical Research Professionals (CCRP) for the 1st time

2010
- Hosted the inaugural APREC, in partnership with Public Responsibility in Medicine and Research (PRIM&R)
- Established the Office of Human Research Protection Programme (OHRPP) & Office of Research Support (ORS)
- Received AAHRPP Re-accreditation

2011
- Launched NHG Research Online Administration & Management (ROAM) portal foronline ethics application and review

2012
- Set up NHG DSRB Domain F – Population Health
- Received Organisational Accreditation by the Singapore Workforce Development Agency (WDA) to provide nationally-accredited courses under the Singapore Workforce Skills Qualifications (WSQ) – Clinical Research Framework
- Established the Collaborations & Partnerships (C&P) Office to facilitate research collaborations & technology transfer
- Launched the Clinician-Scientist Career Scheme (CSCS) for Junior and Mid-levels.

2013
- Developed complete career development pathway for NHG clinician-scientists and clinician investigators
- Organised the NHG Public Forum - Research and You – What You Need to Know about Participating in Research
- Launched Ageing Research Grant (ARG) and Skin Research Grant (SRG)

2014
- Launched the Singapore Guideline for Good Clinical Practice (SGGCP) Online Course – 1st in Singapore
- Launched the CSCS (Senior) and Clinician Investigator (CI) Scheme

RDO would like to thank its past and present staff for contributing to its decade of achievements.

Going forward, RDO is committed to continue facilitating and supporting research that will contribute to NHG's vision of "Adding Years of Healthy Life."

NHG-NTU/LKCMedicine Research Seminars

Mr Zheng Wei Xiong
Executive
Research Training and Development Unit
Research & Development Office
National Healthcare Group

The National Healthcare Group (NHG) and Nanyang Technological University's (NTU) Lee Kong Chian School of Medicine (LKCMedicine) co-organised a research seminar on "Infection and Immunity" on 21 May at the Headquarters LKCMedicine, Novena Campus. This seminar is the third installation of the bimonthly research seminar series. Through these seminars, both NHG and LKCMedicine aim to provide clinicians and scientists with the opportunity to come together to explore and forge collaborations. The introductory session of the seminar series was held on 29 November 2013 and the second seminar on "Vascular and Metabolic Diseases" was held on 5 March 2014.

The constant evolution of pathogens and emergence of new infectious diseases have been of great concern all along. The appearance of new pathogens such as Nipah Virus, Ebolavirus, SARS-CoV and more recently the MERS-CoV and the development of more Multi-Drug Resistant Organisms (MDRO) have brought about an increased attention on research on Infectious Disease, a key research focus area for both NHG and LKCMedicine. The session was opened by Professor Philip Ingham (Toh Kian Chui Distinguished Professor, Vice-Dean Research, LKCMedicine, NTU) and Associate Professor Lim Tock Han (Deputy Group CEO (Education & Research) NHG). A total of 6 speakers presented at this seminar; 3 speakers from NHG and LKCMedicine respectively. The seminar was supported by participants from NHG, NTU and A*STAR.

The three NHG speakers who presented their research were Professor Leo Yee Sin (Director, Institute of Infectious Disease & Epidemiology (IIDE), Clinical Director, Communicable Disease Centre (CDC) and Senior Consultant, Department of Infectious Diseases, TTSH), Dr Ng Oon Tek (Consultant, Institute of Infectious Disease & Epidemiology (IIDE), TTSH) and Dr Ding Ying (Coordinator of Singapore ID Clinical Research Network (SCRN) and Senior Research Fellow, Institute of Infectious Diseases & Epidemiology (IIDE), TTSH).

In addition to an introduction and the research conducted at IIDE, Prof Leo shared on the teams' efforts in the development of test kits for the quick and accurate diagnosis of patients in the early stages of a Dengue infection. She also presented data on how the team's work has contributed in terms of reducing the healthcare burden in identifying and treating dengue.

Dr Ng's presentation was titled "Pathogen genomics: Application to public health, and clinical medicine". He gave insights on how advances in genomics sequencing technology could possibly impact the way clinicians treat infectious disease. The use of high speed sequencing to identify the specific subtype of the pathogens would allow the clinicians to use targeted drugs to more effectively deal with infectious diseases.

Dr Ding Ying shared on how the framework of the Singapore ID Clinical Research Network (SCRN) helps to promote collaborations among local ID clinicians and also assist with the implementation of cross institutional projects. She also shared on the different cross institutional projects currently facilitated by SCRN.

The three speakers from LKCMedicine were Professor Artur Schmidtchen (Professor of Dermatology and Skin Biology, LKCMedicine, NTU), Assistant Professor Yeo Tsin Wen (Assistant Professor of Infectious Disease, LKCMedicine, NTU) and Assistant Professor Luo Dahai (Nanyang Assistant Professor, LKCMedicine, NTU).

In Prof Schmidtchen's presentation titled "Host defence peptides - next-generation anti-infective agents?", he shared his research findings on wound healing, the inflammation process and the roles of the host defence peptides. He also shared on the possibility of future development of using these peptides in treating infection.

Malaria is a prevalent disease within the Southeast Asian region and the two common causative strains that we are familiar with are Plasmodium falciparum and Plasmodium vivax. At this seminar, Asst Prof Yeo provided an insightful update on the epidemiology, diagnosis and management of Plasmodium Knowlesi. This strain of Malaria parasite (despite being a primate strain) is able to infect human naturally via a mosquito vector and is becoming an increasingly prevalent strain causing severe malaria in human in the Southeast Asian region.

The last speaker Asst Prof Luo gave a presentation on the "Molecular Portraits of The Dengue Virus Replication Machinery". He shared on the various components employed by the virus to interact and exploited infected cell's mechanism to its benefit in its replication process.

Participants had the opportunity to engage with the speakers through the Question and Answer Session and during dinner which follows the Seminar.

For more information on this seminar series, please refer to our website, www.research.nhg.com.sg (Training & Education). Read more about IIDE in Catalyst Issue 16 (Page 2).

Introducing a New Resource Guide to Optimise Formulary Management

Mr Lim Boon Peng
Head, Pharmacy & Therapeutics Office
Group Corporate Development
National Healthcare Group

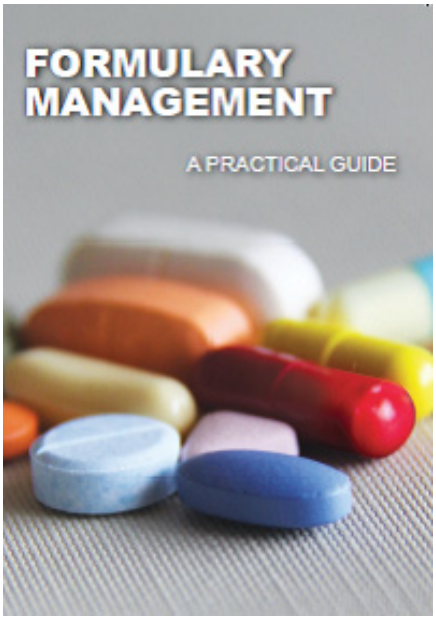
A formulary system is a process which a healthcare institution establishes policies for the use of medications. The most clinically appropriate and cost-effective drugs are then identified to best serve the patients. Effective formulary management in our hospitals and clinics therefore safeguards rational drug use and optimises health outcomes.

The National Healthcare Group (NHG) Pharmacy & Therapeutics (P&T) Office published ***Formulary Management – A Practical Guide*** in April 2014 – to support formulary management in local healthcare institutions and optimise formulary decision-making processes. This guide was produced in tandem with the Formulary Management programme (FY2011 to FY2013), which brought together stakeholders from NHG's Tan Tock Seng Hospital, Institute of Mental Health, National Healthcare Group Polyclinics and National Skin Centre, and the National University Hospital.

The Pharmacy & Therapeutics Committee, or an equivalent body, in each institution reviews and selects drugs for formulary inclusion based on criteria such as safety, efficacy / effectiveness, cost-effectiveness and clinical need. Formulary decisions need to be informed by valid and good quality drug reviews.

This can be facilitated by incorporating the principles of health technology assessment or HTA. HTA involves systematic drug evaluation and the synthesis of all available evidence. It allows the objective identification of effective treatment options that offer value for money. This is especially relevant in today's environment where the high costs of new drugs and burgeoning chronic diseases in our ageing population challenge healthcare affordability and sustainability.

HTA concepts are applied throughout this guide which presents a comprehensive and transparent process for managing an institution's formulary. Recommendations from international HTA agencies and professional pharmacy organisations have been adapted to identify best practices in various aspects of formulary management. These include formulary drug submission, evidence review, appraisal and synthesis, and formulary decision-making.



Cover page of the publication

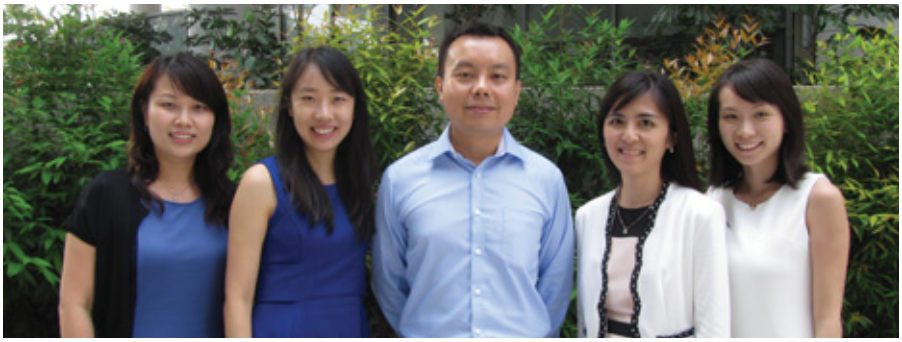
The guide takes users through the steps to carry out a systematic review – from formulating a research question, doing a systematic literature search, performing evidence appraisal with quality assessment tools, evidence synthesis and reporting. It also covers key concepts and analytical tools in pharmacoeconomic evaluation and budget impact analysis.

An additional feature is the framework on continual assessment of the existing formulary or formulary maintenance. It systematically details the process of formulary review, from identifying drugs or drug classes for review, to performing drug class reviews and recommending subsequent actions based on the findings.

Formulary Management – A Practical Guide is now available. NHG P&T Office provides formulary management services and conducts HTA research that aims to provide decision-makers with quality evidence on the safety, efficacy / effectiveness and cost-effectiveness of health technologies using various research methods including systematic review, meta-analysis, network meta-analysis and pharmacoeconomic analysis.

For more information and to obtain a copy of the guide, you can write to us at NHG_P&T@nhg.com.sg.

The Pharmacy & Therapeutics Committee, or an equivalent body, in each institution reviews and selects drugs for formulary inclusion based on criteria such as safety, efficacy / effectiveness, cost-effectiveness and clinical need.



From left: Monica Teng, Zhao Yingjiao, Lim Boon Peng, Khoo Ai Leng, Lin Liang from Pharmacy & Therapeutics Office

BEP MedTech Forum - Bringing Together Clinicians and Engineers in Neurological Disorders and Rehabilitation

Ms Clara Lim
Assistant Manager
Research Training and Development Unit
Research & Development Office
National Healthcare Group

National Healthcare Group (NHG) had the privilege of co-organising the Biomedical Engineering Programme (BEP) MedTech Forum with A*STAR's Healthcare and Lifestyle (H&L) Programme on 28 May 2014, at Tan Tock Seng Hospital, home to the largest and longest-running rehabilitation facility in Singapore.

Themed "Neurological Disorders and Rehabilitation: The Technological Perspective", a stellar line-up of 9 speakers from healthcare, academic and research institutions provided a holistic viewpoint of the topic. They were:

- Dr Guan Cuntai (Department Head, Neural & Biomedical Technology, Institute for Infocomm Research (I2R)) – Topic: Neuro-technologies for clinical applications
- Dr Kong Keng He (Senior Consultant, Department of Rehabilitation Medicine, Tan Tock Seng Hospital (TTSH)) – Topic: Advanced Technology for Rehabilitation
- Dr Bijan Dorri (MedTech Advisor, Agency for Science, Technology and Research (A*STAR)) – Topic: Functional Magnetic Resonance Imaging
- A/Prof Vijay Kumar Sharma (Consultant, Department of Medicine, National University Health System (NUHS)) – Topic: Unmet Clinical Needs in Stroke
- A/Prof Justin Dauwels (Assistant Professor, Division of Control & Instrumentation, School of Electrical & Electronic Engineering, NTU) – Topic: Neural Signal Processing
- Dr Jai Rao Prashanth (Associate Consultant, Neurosurgery Department, National NeuroScience Institute (NNI)) – Topic: Neurosurgery and intensive care for stoke and brain injury
- A/Prof Zhou Juan Helen (Principal Investigator, Neuroscience Research Partnership, A*STAR-Duke NUS GMS) – Topic: Multimodal Brain Connectome Analysis and Neuropsychiatric Disorders
- Dr Chong Mei Sian (Senior Consultant, Department of Geriatric Medicine, Tan Tock Seng Hospital (TTSH)) – Topic: Innovations and Dementia Care
- Dr Alex Gu Yuandong (Technical Director, Miniaturized Medical Devices, Institute of Microelectronics (IME)) – Topic: Sensors and Systems for Neural Applications

A renowned veteran in the field of Epilepsy and the founding editor and editor-in-chief of the medical journals Epilepsy & Behavior and Epilepsy & Behavior Case Reports, keynote speaker Dr Steven Schachter provided insights into new technologies in Epilepsy management and treatment. He urged cross-disciplinary developments amongst clinicians and technologists, to create more effective therapies and new approaches to closing the treatment gap.

While the technical speakers demonstrated the benefits of combining technology with science to improve clinical applications, clinical speakers provided insight into current clinical practices and unmet needs. These sparked interests in areas of potential collaborations such as easing the rehabilitation process through facilitation in patients' residences through robotics (highlighted by Dr Kong Keng He), and predictive modeling, minimally invasive surgical devices and neuro-regeneration (highlighted by Dr Jai Rao Prashanth).

Speakers also discussed the diagnosis, treatment and management of neurological disorders including Epilepsy, Stroke, and Dementia.

The event concluded with a highly interactive panel discussion moderated by Dr Schachter on the topic what engineers expect for clinicians and vice versa. Noteworthy pointers include better communications, understanding clinical needs and feasibility of ideas, commitment, and setting of common goals and research questions.

The audience and speakers commended that the forum for being an excellent platform for facilitating the exchange and understanding of the needs and unmet needs of clinicians and engineers. This helps identify collaborative opportunities to create synergetic excellence to address pressing clinical needs.

Dr Bijan Dorri sharing his work in "Functional Magnetic Resonance Imaging"

*Dr Kong Keng He providing insights on advanced technology for rehabilitation and his collaborative work with A*STAR*

Panel discussion moderated by Dr Steven Schachter

Challenges of CYBERAGE

The development of internet comes with a set of unique challenges to our young population.

Mr Tan Yi Ren
Assistant Psychologist
Child and Adolescent Psychiatry
Institute of Mental Health

Almost every Singapore youth has used the internet; with majority of them having access to it at home and/or at school. Such ease of access has made the internet part of their everyday life by providing avenues for communication, information sharing and entertainment.

However, developments of the internet have also presented a unique set of challenges to our young population. Internet addiction, or the excessive use of internet that significantly interferes with daily life, is one of the major areas of concern among internet users.

Internet addiction

Affected individuals may be preoccupied with online social media, gaming or other forms of online activity, so much so that they will be yearning to use the internet even when offline. Such pathological use of the internet may result in various negative life consequences such as academic failure, relationship breakdown and health deterioration.

Past research studies have shown that internet addiction is associated with various physical and mental health issues. Nevertheless, as these studies are mainly conducted in the Western counterparts, it will be desirable to examine these relationships in the Asian context, specifically in Singapore.

Cyber-bullying

Another challenge to our current cyber environments is the increasing phenomenon of cyber-bullying, which is defined as "an aggressive, intentional act carried out by a group or individual, using electronic forms of contact, repeatedly and over time against a victim who cannot easily defend him or herself."

Examples of cyber-bullying include threatening others using text messages, uploading embarrassing photos of the victim on social media and spreading rumours that are meant to hurt the victim online. Because of the nature of anonymity and accessibility of the internet, cyber-bullies are able to carry out such acts at almost anytime and anywhere. Moreover, its negative impact can be more far-reaching than that of traditional bullying. As these bullying behaviours may result in long term psychological harm on the victims, it is pertinent to explore more about this worrying phenomenon to support the development of potential intervention strategies.

Study on internet addiction and cyber-bullying

This study is part of an international research initiated by the University of Turku, Finland. Some Asian countries including Singapore, Hong Kong and Japan have been invited to be part of their research project.

In Singapore, Dr Ong Say How, Senior Consultant and Chief of the Department of Child and Adolescent Psychiatry, IMH, is leading this study as the Principal Investigator. In collaboration with the Singapore Children's Society and A/Prof Angeline Khoo from the National Institute of Education, Dr Ong and his team are conducting this cross-cultural epidemiological study on 'The Impact of Cyber Environments on Health, Help-seeking and Risk Behaviour among Singaporean and Finland adolescents.' This study is supported by the NHG-KTPH Small Innovative Grant.

The main aims of this study are to investigate the prevalence of internet addiction and cyber-bullying, as well as to examine possible associations with physical and mental wellbeing among Singaporean adolescents. Findings gathered can be used to raise public awareness of the unhealthy cyber usage and may aid in early detection of internet addiction and cyber-bullying among adolescents.

The team is also interested to examine patterns of healthy internet usage and help-seeking behaviours to determine potential protective factors that can be tailored into future intervention strategies. Lastly, as part of the international research, the team will also compare data with other countries to explore cross-cultural similarities and differences.

Data collection started in January 2014 and is still on-going. It involves about 3,000 students aged 13 to 17 years old from secondary schools, junior colleges, polytechnics and the Institute of Technical Education in Singapore. By using a stratified sampling technique, 30 schools will be randomly selected according to their types and geographical areas.

After identifying the schools, the second stage of sampling involves stratifying classes of students based on different academic streams. Such techniques will provide a more representative sample for this study. Students will be asked to complete an online survey anonymously at their respective schools during school hours. This survey contains questions pertaining to internet usage, perceptions of school, substance abuse, traditional bullying, cyber-bullying as well as physical and mental health. The results are expected to be out by late 2015.

As Singapore is one of the top three Asian countries to have a high proportion of its population accessing the internet, it is important to examine the internet-use behaviours and their impact on our young population. We hope that, through this research study, we are able to understand more about these phenomena in order to drive the development of intervention strategies to assist the affected individuals and their families.

Dr Ong Say How
Principal Investigator of the study

Deciphering Molecular Mechanisms and Signaling Pathways by which Microbiome Communities Influence Host Physiology

Prof Sven Pettersson
MD, PhD
Visiting Professor
Lee Kong Chian School of Medicine
Nanyang Technological University

The extended phenotype.

The unique experimental and analytical platform now being developed at Lee Kong Chian School of Medicine (LKCMedicine) and in close collaboration with Singapore Centre on Environmental Life Sciences Engineering (SCELSE), School of Biological Sciences (SBS) and clinical colleagues from the health care sector in Singapore, will aim to decipher the underlying molecular mechanisms and signaling pathways by which the resident microbiota influence host physiology. The focus of our research is on health mediated regulatory functions early in life and those potentially connected to healthy ageing. Our efforts may further the current understanding of the metabolic language of mammalianmicrobial communication that have significant influence on brain development and function. Ultimately, we aim to generate new information that can be used for future design of personalized healthcare guidelines.

Why the microbiota?

Robert Koch and Louis Pasteur established that infectious diseases are caused by microbes but Ilya Mechnikov was the first to recognise that microbes might also have beneficial effects on human health. However, host–microbe interactions are as diverse as the organisms involved but the outcome for the host follows a simple rule: lifelong health or intermittent disease.

The complement of microbiota exceeds at least 10-fold the number of human origin cells and their total gene pool exceeds by at least 100 times the complement of genes present in the human nuclear genome. The diversity and composition of microbiomes, a term used to describe the constituents of the microbiota, encompassing bacterial genes, proteins and metabolites, is highly variable between host species. This is the result of a maternal hand-over of microbes or its metabolites during pregnancy and immediately after birth which will shape the interactions with diet, lifestyle, disease and antibiotic in the newly formed individual throughout life.

The newly formed microbiome will considerably influence host biochemistry, biology and susceptibility to disease throughout life. These influences are transmitted via a vast and poorly understood set of signaling processes and mechanisms that harness metabolites and pathways involving many tissue and organ systems including distal organs such as the brain and Central Nervous System.

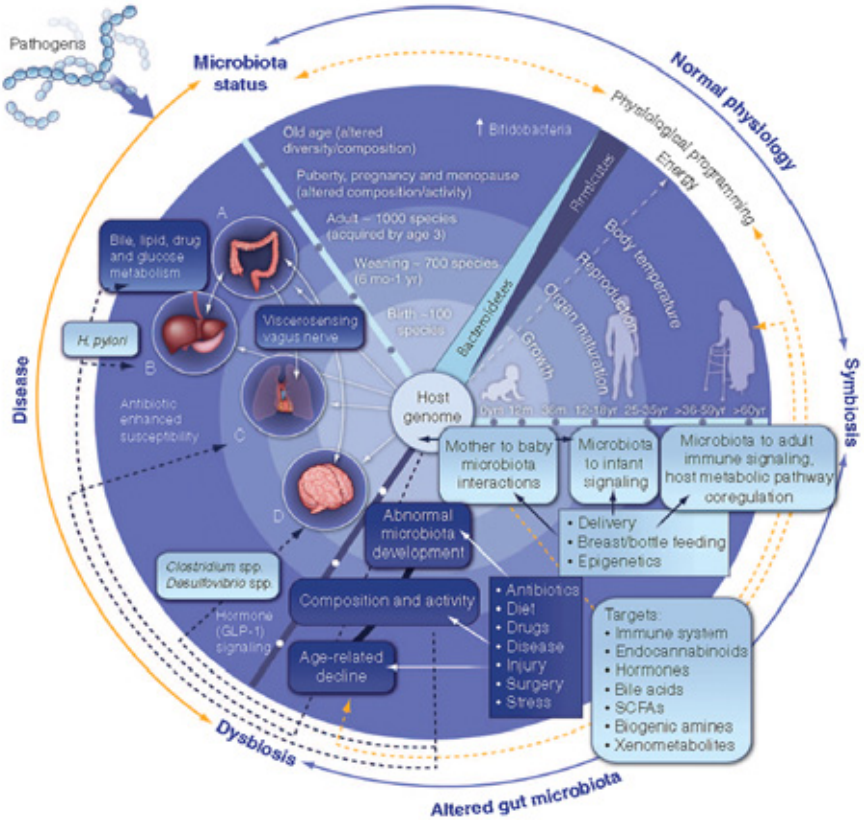


Figure 1 Published in Science ref 3.

The gut microbiome in development and disease. The influence of the gut microbiota on health is continuous from birth to old age. The maternal microbiome influences the intrauterine and postnatal health of the offspring. Early environmental factors, nutritional factors and epigenetic factors have been implicated in the development of a healthy gut and its microbial symbionts. Changes in gut microbial composition in early life can influence risk for developing disease later in life. During suckling, the microbial community develops rapidly; shifts in microbial diversity occur throughout childhood and adult life; and in old age, there is a decrease in the Bacteroidetes and an increase in Firmicutes species. The gut microbiota is important for maintaining normal physiology including, energy production, body temperature regulation, reproduction, immune function liver and brain function.

Disruption of the gut microbiota (dysbiosis) can accelerate a variety of different diseases, including (A) IBS, IBD, and colon cancer, (B) gastric ulcers, nonalcoholic fatty liver disease, and obesity and metabolic syndromes; (C) asthma, atopy, and hypertension; and (D) mood and behavior through hormone signaling (e.g., GLP-1). The gut microbiota is also important for drug metabolism and preventing the establishment of pathogenic microbes.

to be continued on page 10

continued from page 9

The Medical importance of the gut microbiome: the "holobiont" concept

The hologenome theory of evolution proposes that natural selection acts not on the individual organism but rather on the "holobiont", which consists of the organism plus its microbiome. When challenged by malnutrition, excessive dietary intake, low grade inflammation, unhealthy psychological stress, etc, the holobiont can employ strategies and adaptation mechanisms by swapping microbial communities or reshuffling the relative proportions of resident bacteria.

The last decades of reductionistic research, trying to understand the mechanisms responsible for the epidemic development of metabolic diseases has not considered the holobiont perspective and consequently missed the adapation strategies by the microbiome. Furthermore, accumulating evidence suggest the gut microbiome to be implicated in the etiopathogenesis of many of our lifestyle-related diseases including obesity, diabetes atherosclerosis, inflammatory bowel disease and rheumatoid arthritis and to be able to influence drug metabolism, toxicity and dietary calorific bioavailability, When considering these functions of the commensal microbiota communities in sustaining health, we are still in its infancy (Figure 1). Knowing the "right" and functional microbiome is a desired but elusive goal, and may only be achieved through global analytical techniques.

By applying a systems biology approach to deciphering molecular mechanisms underlying life style related disorders and to perform quantitative analysis of the gut microbiome and its activities, we hope to learn more about the interplay within the holobiont and its physiology. The joint experimental Life Science platform currently under way at LKCMedicine, SCELSE and SBS are geared to address these questions.

References

1. Faith JJ, Guruge JL, Charbonneau M, Subramanian S, Seedorf H, Goodman AL, Clemente JC, Knight R, Heath AC, Leibel RL, Rosenbaum M, Gordon JI. The long-term stability of the human gut microbiota. Science 2013, 341
2. Rochellys Diaz Heijtza, Shugui Wangc, Farhana Anuard, Britta Björkholm, Hans Forssberg, & Sven Pettersson. 2011. Normal gut microbiota modulates brain development. and behavior. PNAS, 108: 3047–3052.
3. Nicholson JK, Holmes E, Kinross J, Burcelin R, Gibson G, Jia W, Pettersson S. Host-gut microbiota metabolic interactions. 2012.. Science. 336:1262-7.
4. Selkrig J, Wong P, Zhang X, Pettersson S. 2014 Metabolic tinkering by the gut microbiome: Implications for brain development and function. Gut Microbes. 5 ahead of print

Misconceptions about Insulin Therapy

Ms Carolyn Chan Mei Fong
Advanced Practice Nurse
Jurong Polyclinic

APN Chan graduated as a registered nurse from the School of Nursing in 1994. She obtained the Advanced Diploma in orthopaedic nursing from Nanyang Polytechnic in 1998 and a Bachelor of Science (Nursing Management) from Curtin University of Technology in 2003.

She joined NHG Polyclinics in 2005. In 2008, she graduated from the National University of Singapore with a Masters in Nursing under the Human Manpower Development Programme (HMDP) Scholarship from the Ministry of Health. She served her internship at Jurong polyclinic and registered as an Advanced Practice Nurse in Community Health in 2009.

Study on the perception of patients with Type 2 diabetes on insulin therapy in primary healthcare setting in Singapore.

Type II diabetes is characterised by defects in both insulin secretion and action, which seems to be progressive. Most patients will eventually require insulin therapy to achieve and maintain good glycaemic control.

However, patients who could benefit from insulin therapy do not receive it timely. At National Healthcare Group Polyclinics, approximately 60 per cent of patients with HBA1c ≥9% were not started on insulin. This could be attributable to reluctance of both patients and healthcare professionals to initiate insulin therapy attributed to patients' reluctance to initiate insulin therapy.

There has not been any comprehensive descriptive study done in Singapore to describe the perception of type 2 diabetes patients and beliefs of clinicians towards insulin initiation.

This study was carried out to answer the following questions:

1) What are the perceptions of insulin therapy among insulin-naïve patients with type II diabetes at the primary care setting in Singapore?
2) What is the association between patient characteristics and the resistance to insulin therapy?

And the study revealed that:

- 93 per cent of the subjects reported that they were unlikely to require insulin therapy in the future.
- 67 per cent of the subjects were unwilling to take insulin even if it was recommended.
- The most commonly expressed negative attitudes were failure to manage the disease, being viewed as a sicker person, fear of pain, difficulty in injecting insulin at the right time and amount.
- When compared with subjects who were willing to initiate insulin, unwilling subjects were more likely to be afraid of injection and perceive injection as painful.

The study identified the key misconceptions or barriers regarding insulin therapy. In addition, education programmes will be reviewed to focus on increasing patient's knowledge about the progressive nature of diabetes and addressing the barriers and patients' fear of insulin injections.

Future directions

Currently lifestyle modifications and oral hyperglycaemia drugs can delay but not stop the progression of type II diabetes. Ultimately, some patients will require insulin therapy to maintain good glycaemic control. Accepting the recommendation to start insulin therapy in addition to integrating the demands of insulin injections can be a challenge for patients and clinicians. However, clinicians need to address the negative attitudes identified in this study. I hope to conduct a study to test the appropriate intervention to help patients overcome their barriers to insulin initiation.

Impact of Chronic Urticaria on QoL

Dr Lucinda Tan
Associate Consultant
National Skin Centre
lucindatan@nsc.gov.sg

Study shows that females seem to be more severely affected than males

Chronic urticaria (CU) is defined as wheals, occurring daily or almost daily, persisting for more than six weeks. Epidemiological studies are lacking, but it appears to be a common disease, with prevalence ranging from 0.6 per cent to 1.8 per cent (Zuberbier T, Clin Exp Dermtol 2010).

This chronic skin disease has a major impact on the patient's quality of life (QoL), potentially affecting career, social activities and self-esteem. Published literature shows consistent moderate impact on QoL in various populations, further affirming the depressive effect that chronic urticaria has on QoL (Liu JB, J Eur Acad Dermatol Venereol 2012). This study is the first in Singapore, designed to evaluate the impact of CU on patients' QoL.

Patients were recruited from the dermatological outpatient clinics at National Skin Centre between April and December 2011. All patients older than 21 years of age, with a diagnosis of CU, were eligible to participate in the questionnaire. CU was defined as the presence of urticarial wheals for at least three days per week for six consecutive weeks.

> Chronic skin disease has a major impact on the patient's quality of life (QoL), potentially affecting career, social activities and self-esteem.

Patients who had urticarial vasculitis, other pruritic dermatologic conditions, hepatic or renal insufficiency and connective tissue disorders were excluded from the study. Patients who cannot comprehend English, are pregnant or lactating, or not mentally capable of giving consent were also excluded.

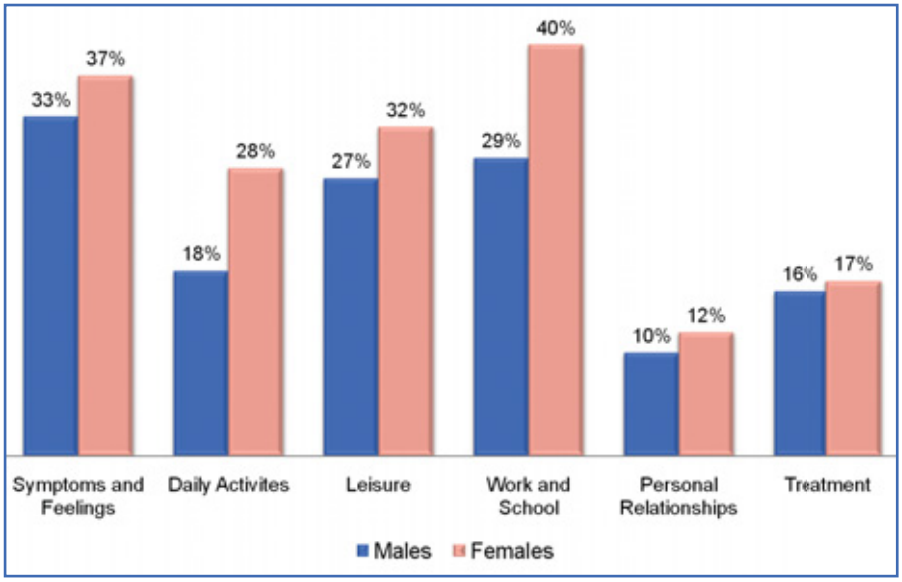
We recruited 54 patients between 17 and 60 years old. Their mean age was 34.6 years. The majority of our patients were professionals (41 per cent) with tertiary education (57 per cent). Most patients have had CU for duration of one to four years (33 per cent). Patients commonly have more than one trigger for CU (46 per cent) and frequently cite changes in temperature (37 per cent), contact with heat (30 per cent) and pressure (30 per cent) as triggers. The most popular antihistamines used include loratadine and cetirizine. Symptomatic relief is achieved in 41 per cent of patients, one hour after ingestion of antihistamines.

In our patient cohort, the mean DLQI score was 7.11, indicating that CU has a moderate impact on their QoL (range from six to 10). Reviewing the impact of CU on the various aspects of QoL, the greatest impact was on symptoms and feelings (35 per cent of subjects affected), followed by leisure (27 per cent) and daily activities (23 per cent). Females tend to more severely affected across all aspects of QoL compared to males, with a significant difference in work and school-associated QoL ($p = 0.038$).

In summary, CU has a moderate impact on QoL with a mean DLQI score of 7.11, with the greatest impact seen in aspects assessing symptoms and feelings. Females fared poorer for all aspects of QoL, with significant differences in the work and school aspect. This is also comparable to previous studies (Maurer M, Allergy 2009 and Maurer M, Br J Dermatol 2009).

Plausible reasons included different life experiences, ways of thinking or different sensitivities to irritation. We might be able to better evaluate gender differences with a questionnaire that is gender neutral, or one with an in depth probe into different gender needs. There is a possible response bias in this study, as the DLQI is self-administered. Patients may not have interpreted the questions correctly when they are asked to answer the questionnaire on their own. Another limitation would be the small sample size.

As physicians, we need to be aware of our patients' exasperation and difficulties coping with the disease. By recognising differences based on gender and disease duration, we can individualise management, counseling and intervention. This would hopefully translate to better patient care and satisfaction.



Females are more severely affected across all aspects of QoL compared to males, with a significant difference in work and school associated QoL.

Discrete Event Simulation to Improve Services at The Pharmacy

Dr Zhu Zhecheng
Operations Research Specialist
Health Services and Outcomes Research
National Healthcare Group

The outpatient pharmacy is usually the last stop of a patient's outpatient visit in a hospital. The generic workflow in pharmacy includes four steps: 1) receive and confirm prescription, 2) pick and pack medications, 3) check and dispense medications, and 4) payment. A smooth experience in pharmacy is crucial to the patient's satisfaction of his/her visit.

There are many initiatives to improve service levels, enhance accessibility and reduce waiting time in the pharmacy. For instance, setting up satellite pharmacies next to specialist outpatient clinics would provide a better service experience and reduce patient travelling time. One-stop billing that combines consultation and pharmacy fees would simplify the payment procedure. Deploying automatic pick and pack machines can accelerate the processing time and reduce error rates. All these initiatives need to be evaluated to ensure their operational efficiency before applying them to actual practice.

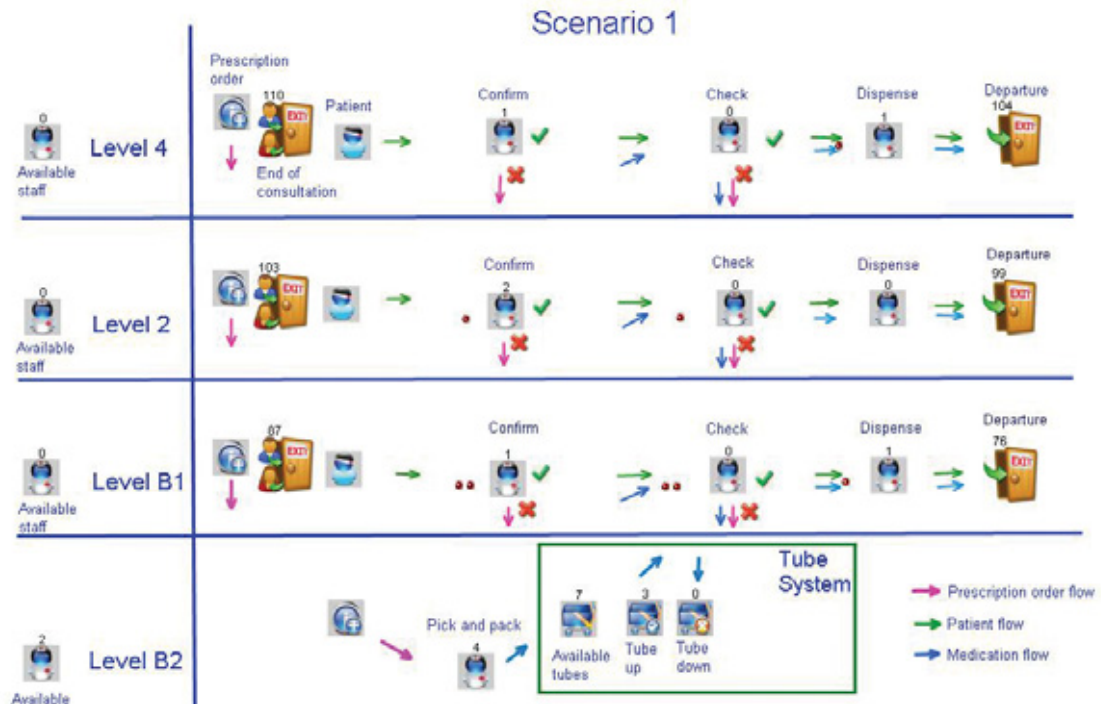
Discrete event simulation (DES) is a simulation technique of constructing a simulation model of a real system mainly for two purposes – the first is to understand the behaviour of the current system, and the second is to test various what-if scenarios. The following case study illustrates how DES can be applied to outpatient pharmacy planning.

The pharmacy department in Tan Tock Seng Hospital planned to set up satellite pharmacies on each level of specialist outpatient clinics to create a better service experience for private patients. A DES analysis was conducted to evaluate different scenarios of satellite pharmacy setup in terms of patient waiting time and manpower configurations. DES models were constructed to simulate different scenarios of satellite pharmacy setups – to pack at centralised pharmacy or satellite pharmacy; to pack upon confirmation or pre-pack before confirmation.

Data was then collected to estimate the model parameters including daily prescription load; timing of receive, confirm, pick and pack, check, dispense, billing; timing of tube system; rework rate, etc. Different manpower configurations were then tested to ensure that the 95th percentile patient waiting time was within 15 minutes.

Sensitivity analysis was conducted on the tube system and rework rate to detect the system bottleneck. Simulation results showed that more manpower would be needed in the satellite pharmacy to maintain the same patient waiting time in the centralised pharmacy. It was not suggested to pack at the centralised pharmacy if the tube system becomes the bottleneck. Pre-packing was suggested to streamline the process if the rework rate was relatively low.

> **Discrete event simulation (DES) is a simulation technique of constructing a simulation model of a real system**



Example of a scenario of satellite pharmacy setup in the simulation model

Research in Outpatient Parenteral Antibiotic Therapy (OPAT) Clinic

Dr Monica Chan
Consultant
Department of Infectious Diseases
Tan Tock Seng Hospital

Outpatient Parenteral Antibiotic Therapy (OPAT) clinic allows stable patients to continue intravenous antibiotic treatment in an outpatient setting rather than in hospital. The practice of administering intravenous antibiotics in the home and alternate care settings was first described in 1974 by Rucker and Harrison in Texas, USA for treatment of chronic lung infections in children with cystic fibrosis. Since then, the practice has expanded worldwide and there is a wealth of evidence which has accumulated supporting its safe use and cost-effectiveness. Tan Tock Seng Hospital was the first hospital in Singapore to offer OPAT in 2001.

OPAT is suitable for a wide range of infectious conditions including cellulitis, urinary tract infections and intra-abdominal abscesses. The patients benefit from avoidance of hospital admission, or reduction in length of hospital stay, improvement in patient satisfaction and earlier return to home and work. In 2013, we treated 326 patients, a saving of 5123 hospital bed days, with a readmission rate of 9.8 per cent, similar to international standards. The median length of treatment in OPAT was 10 days.

We have several ongoing research studies in OPAT. For example:

- Increasing the uptake of OPAT in Emergency Department Treatment & Diagnostic Centre (EDTC): A Clinical Practice Improvement Program (CPIP)
- In overseas practice, skin and soft tissue infection including cellulitis is a common indication for OPAT. Recent studies in UK show good success rate for cellulitis treated in OPAT.
- The use of OPAT in Singapore for treatment of cellulitis is relatively new. Intravenous antibiotics are recommended for patients with moderate cellulitis but otherwise do not require hospitalization.
- This collaboration with Emergency Department (ED) in TTSH looks at ways of using the CPIP methodology to improve the uptake of OPAT for patients presenting with cellulitis to TTSH EDTC.
- Factors identified to improve uptake included streamlining of referrals to OPAT, improve awareness of OPAT through educational talks and improving financial counseling through financial packaging of OPAT related treatment costs.
- We currently have ongoing plans with TTSH ED to improve this service and are grateful to Dr Ooi Chee Kheong and TTSH ED team for this collaboration opportunity.

> The patients benefit from avoidance of hospital admission, or reduction in length of hospital stay, improvement in patient satisfaction and earlier return to home and work

The Effectiveness of a General Group Exercise-based Program for Patients with Neck Pain: A Retrospective Study

Mr Mark Chan
Senior Physiotherapist
Physiotherapy Department
Tan Tock Seng Hospital

Exercise-based programmes have been used in some Singapore hospitals to treat various subacute to chronic neck pain conditions. A study was conducted with an aim to evaluate the effectiveness of a group exercise-based programme conducted in Tan Tock Seng Hospital Physiotherapy department for managing of patients with chronic neck pain.

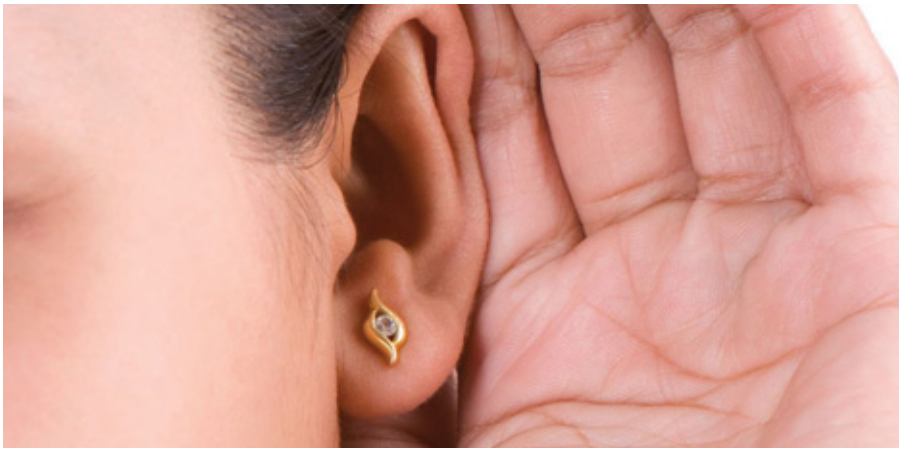
A retrospective study involving 97 subjects was performed. Subjects who were deemed suitable were referred by their physiotherapist to attend the group exercise-based therapy. The therapy was conducted by a supervising physiotherapist, and the exercises performed were part of a standardised neck exercise regime. These exercise sessions were conducted weekly for a total of three to six sessions. The exercises performed in the class are aimed at improving the mobility of the neck and trunk, to strengthen the neck and shoulder musculature, and to retrain correct spinal postures.

The Neck Disability Index, a universally used questionnaire which assesses neck pain and self-reported function was utilized to determine the effectiveness of this exercise-based therapy programme. The questionnaire was administered to the participants before and after the programme. The effectiveness of the program was evaluated by comparing the mean change between Neck Disability Index scores. The results of the study show a minimal mean Neck Disability Index point change of 2.78 (SD = 3.93) between pre- and post-intervention, with a median of 3 sessions attended. However, the participants were found to have low mean Neck Disability Index scores of 12.10 for pre-exercise programme (SD = 6.35) when enlisted into the programme. It was found that patients who were referred into the class have already made improvements in their neck pain and associated function, after having sought direct treatment from their referring physiotherapist. As a result, patients made minimal improvements in the class as they may have already reached a therapeutic recovery plateau.

The results of this study suggest that patients who are more likely to respond to exercise-based intervention should be identified, and referred to the group-based exercise programme as early as possible. Classification systems for neck conditions, and the clinical predictors of a good response to exercise therapy should be further explored. Clinicians need to consider these when referring their patients into the exercise-based programme.

I would like to acknowledge Mr Khalid Anuar and Ms Lee Soak Yee for their contributions to this study.

> As a result, patients made minimal improvements in the class as they may have already reached a therapeutic recovery plateau.



Research on hearing impairment in Singapore

Dr Ho Eu Chin
Consultant
Otorhinolaryngology
(Ear, Nose and Throat) Department
Tan Tock Seng Hospital

Dr Ho Eu Chin wants to help those with hearing impairment and also dispel the stigma attached to it.

As a junior doctor, I had difficulties deciding on a final career pathway until the opportunities arose for me to observe some operations for restoring function of patients with diseased ears. After I became an Ear, Nose & Throat (ENT) trainee, I then found the many sub-specialties fascinating but I kept true to my first love and I finally decided to become an Ear doctor. I was fortunate to have had many opportunities to participate in and later on, led varied research projects that resulted in many publications and conference presentations.

Following my move to Singapore in November 2011, I was able to further pursue my clinical, surgical and research interest in the management of patients with ear diseases. They present with multiple symptoms with the commonest being hearing impairment and balance problems.

While I continue to enjoy operating on patients to improve their hearing, amongst other symptoms; these patients represent the tip of the iceberg of the large population with hearing impairment. Some studies have suggested that 10 per cent of the population have some degree of hearing impairment. Many of them have hearing impairment that is not correctable through surgery or medication.

Denial and ignorance about hearing impairment

I have made many interesting observations of the public's perception towards hearing impairment and the seeking of help to overcome this impairment. Many will deny or ignore their hearing impairment. They frequently seek help rather late and sometimes they come 'dragged in' by concerned family members. Some patients have allowed their 'untreated hearing impairment' to progress to disability and handicap; resulting in underemployment, negative impact on education performance, compromised family and social relationships, occasionally leading to social isolation, and in some cases, accelerated cognitive decline.

Yet, most patients are reluctant to consider the use of hearing aid to regain their hearing. 'People will think I am deaf if they see me wearing hearing aids' is a frequent comment, notwithstanding the irony that people who use hearing aids to regain their hearing are 'no longer deaf'. Negative perceptions about hearing aids abound, with myths and misconceptions.

Research on hearing impairment

I came to realise that there is a need for a robust advocacy by doctors to encourage patients to overcome their hearing impairment. Yet, in order to improve the hearing health of our ageing population, there remain a dearth of good quality data and information about hearing impairment in our Singapore population, and within Asia, in general. Most good quality studies have been performed in Western populations. The results are not always directly transferable due to significant differences in language, culture and health care provision. A lack of good quality data also results in difficulties for policy makers to address this problem.

Any studies to understand impairment and disability in the population are always resource heavy and costly to execute. I am very grateful to NHG for the Clinician Scientist Career Scheme (CSCS) that has allowed me to conduct hearing impairment research in Singapore. There are four main components to my research project. One of them will hopefully lead to the validated translation of Quality of Life Questionnaires into the common languages used in Singapore. Concurrently, I am also working with a team of scientists from Nanyang Technological University (NTU) to develop a novel assistive hearing device.

Dr Ho Eu Chin is an awardee of the FY2013 NHG Clinician Scientist Career Scheme (CSCS). To find out more about NHG CSCS, please visit www.research.nhg.com.sg (Grants & Programmes).

Some studies have suggested that 10 per cent of the population have some degree of hearing impairment.

Applied Epidemiological - Research on Vaccines and Infectious Diseases

Dr Yung Chee Fu
Consultant Clinical Epidemiologist
Tan Tock Seng Hospital

No other medical modality, including antibiotics or surgery, has saved more lives than vaccines. Their impact on the history of human health is only surpassed by the availability of clean water.

We have benefited from its legacy, such as the eradication of smallpox and it is now acknowledged that vaccine health benefits overflow into economic growth and national development; but investment in vaccine research remains critical.

Vaccines play an important and expanding role as we face new and evolving challenges in infectious diseases, such as the threat of pandemics or emerging infectious diseases, resurgence of measles and mumps, as well as the rise of antibiotic resistant organism. Unlike most routine medical interventions, vaccines impact not just the individual, but society as a whole via the phenomenon of herd protection.

This effect on infectious disease transmission and alteration of its epidemiology, together with its tremendous potential on public health, was what attracted me to the field. Also, research in vaccines is never dull as it encompasses a broad range of disciplines including: medicine, disease surveillance, epidemiology, outbreak control, health service planning, health inequality, economics, modelling, immunology, genomics, and even sociology and human psychology.

To be honest, when I was going through medical training at the University of Bristol in the United Kingdom (UK), vaccines, epidemiology and public health were of little interest to me. Like many of my fellow students and colleagues, our focus and interest were on the unwell individual in front of us. There was enough work to be done in this respect, without worrying about the issues that had not yet appeared on our hospital doorstep.

Looking beyond the patient

However increasingly over time, I started to notice the importance of looking beyond the patient in healthcare. Therefore, I made the decision to pursue postgraduate training in a Masters of Public Health at the University of Cambridge, UK. Perhaps the most important moment in my specialist training came from working at the National Epidemiology Unit and Public Health Laboratory of Public Health England (then known as the Health Protection Agency) in Colindale, London.

Learning about infectious disease and vaccine epidemiology under the guidance and mentorship of national as well as global experts, such as Professor Elizabeth Miller, Dr Mary Ramsay and many others, I realised the importance and impact of applied research to directly inform practice, which would enable improvement of not just an individual's health but also the better protection of a whole population. I developed an understanding of how an integrated health infrastructure or system could be greater and more efficient than the sum of its parts.

Following completion of my specialist training, I became a Fellow of the Faculty of Public Health, Royal College of Physicians, UK and continued to pursue my passion in infectious disease epidemiology, vaccines and public health whilst working as a Consultant at the Health Protection Agency, UK.

'Care Transformation' in NHG

Change is in the air for healthcare in Singapore. Previous emphasis on acute hospital care has enabled our hospitals to develop into centres of technical excellence in many areas, regionally as well as internationally. However, the health needs in Singapore are changing, as we face a silver tsunami in the not too distant future.

At NHG, we have embarked on the 'Care Transformation' journey, which will place greater emphasis on populations as well as integrate with primary, social and community care. It is clear that continued reactive focus on acute care in hospitals, or only when someone is unwell, will not be enough to address the rising healthcare burden.

In line with this change and our vision of 'Adding Years of Healthy Life', I have started to develop an applied research programme with a focus on prevention in terms of vaccination and populations, especially for the vulnerable elderly, in a holistic manner regardless of whether or not they have ventured into our hospital. The team is multi-disciplinary and multi-institutional, with partners in hospitals as well as at polyclinics/primary care leveraging on the state-of-the-art laboratory and technical expertise at NPHL, A*STAR institutions (GIS, IMCB, SIgN), and the Respiratory Virus Laboratory at Public Health England, Colindale, UK.

Epidemiology of respiratory infections in the elderly

Our research programme aims to study the epidemiology of respiratory infections in the elderly, as well as the impact of influenza vaccination (ElderFlu). Influenza epidemics can also overwhelm healthcare institutions directly, as large numbers of people present for treatment due to influenza itself, as well as indirectly by predisposing the onset of other diseases such as myocardial infarction, diabetes mellitus, asthma and bacterial pneumonia.

This broad impact of influenza, which stretches beyond the viral illness itself but contributes to other infectious disease burden as well as chronic diseases, makes it a key public health issue affecting most medical specialties, directly or indirectly. Hospitals in Singapore are already facing high bed occupancy rates, and with an ageing population, this pressing public health problem is likely to worsen. The increasing cost of healthcare, especially the cost of hospitalisation, also makes this a major economic issue.

Cutting through the middle of our programme's strategy is a 'highway' with many branches extending into the various levels of research, ranging from patient experience, clinical outcomes, epidemiology and public health, to complex scientific analysis in laboratories. We have adopted this model to improve the productivity of our research programme, with the ultimate aim of speeding up the translation of research findings to improve individual and population health.

I am grateful to my fellow team members for their support, and would like to thank NHG for awarding us the grant to develop this research programme. We look forward to our project findings and outputs being directly applied to generate evidence based clinical and public health policies for NHG as well as Singapore as a whole.

The Gut Microbiome

Dr Barnaby Young
Associate Consultant
Infectious Diseases Department
Tan Tock Seng Hospital

Dr Young is an awardee of the FY2012 NHG Clinician Scientist Career Scheme (CSCS) and this study is funded by the scheme.

Dr Barnaby Young investigates the changes in the gut during and after antibiotic treatment. The gut contains a huge number of bacteria. These bacteria are estimated to contribute 1 to 3 per cent to human body weight, while outnumbering human cells by a factor of 10 to 100. The amount of genetic information is similarly enormous.

Bacterial ecosystems in the gut and other organs are being characterised through large studies such as the Human Microbiome Project. Their role in the development of diseases – including diabetes, cancer and inflammatory bowel disease is beginning to be understood, as is their importance to health, from infant development to obesity.

Not surprisingly, antibiotics can have catastrophic effects on the gut microbiome. Antibiotics select antibiotic resistant bacteria already present within the gut, and increase susceptibility to colonisation by resistant bacteria from the environment. They also trigger genetic recombination between bacteria – through bacteriophages for example – which generate new resistant organisms. The clinical effect of this includes Clostridium difficile diarrhoea, and infections such as pneumonia or urinary tract infections from antibiotic resistant bacteria.

Understanding factors which affect susceptibility to these microbiome shifts is the aim of this study. We hope to identify patients with a 'resilient' microbiome. This is where the gut bacteria are either less disturbed by antibiotics, or recover back to normal quickly. We also want to see if particular changes predispose to colonization with clinically significant antibiotic resistant bacteria.

This study uses 'Next Generation Sequencing' (NGS) to explore the microbiome in great detail. Technically, DNA extraction and sequencing is reasonably straight forward with commercial machines and protocols although there are questions about completeness and accuracy. However application of this technology requires the computational expertise to analyse huge amounts of data – 100s of gigabases from this study are expected. For this, we are fortunate to be collaborating with computational biologist Dr Niranjan Nagarajan at the Genome Institute of Singapore. The study is currently recruiting patients and samples - a process which will continue through much of 2014.

The NHG CSCS award has been a great opportunity for me. Apart from providing the start-up grant for this study, it supports 40 per cent of my time in research. As I had little research experience, this has enabled me to take ownership of a study, and provided the time to develop ideas, and work out how to implement them. I have also been able to get involved in several related studies, which I might not have been able to otherwise. The next step for me to develop as a 'clinician-scientist' is to focus on a particular area – and become an expert in it. Hopefully this will be with a clinical PhD project.

To find out more about the NHG Clinician Scientist Career Scheme (CSCS), please visit www.research.nhg.com.sg (Grants & Programmes).

Ergonomics and Doctors

Dr Augustinus Laude
Consultant
NHG Eye Institute @ Tan Tock Seng Hospital

Dr Lee Lay Tin
Senior Consultant and Head
Occupational Health Service
Tan Tock Seng Hospital

Doctors especially surgeons are susceptible to Musculoskeletal Disorders from working in awkward postures.

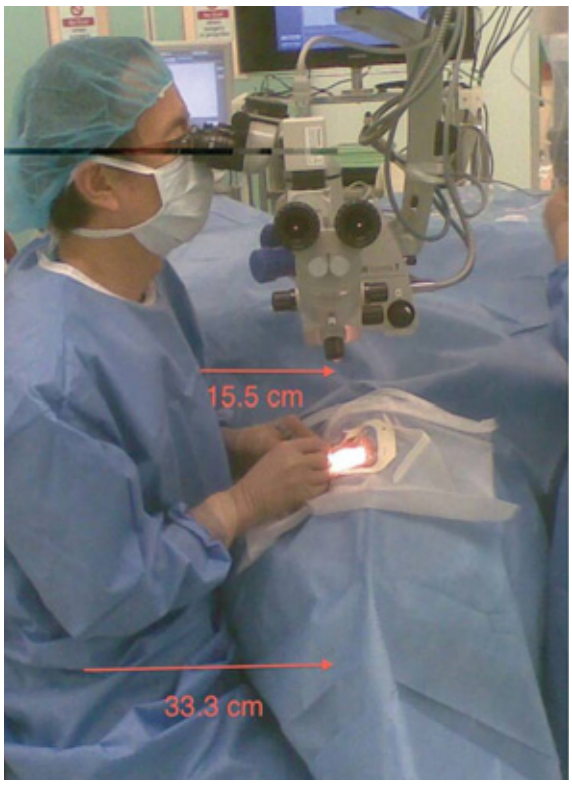


Photo 1: Offset of the eye piece of the microscope.
**Photo courtesy of Dr Fam Han Bor.*

Ergonomics and human factors in design is a relatively new field of study, receiving focused attention of study and investigation within the last century. It involves understanding of interactions among humans and other elements of a system, and applies theory, principles, data, and other methods of design in order to optimise human well-being and overall system performance.

This project is a collaboration between Tan Tock Seng Hospital's (TTSH) Occupational Health Service and Nanyang Technological University (NTU), and serves to improve the comfort level of ophthalmologists from the National Healthcare Group Eye Institute (NHGEI) at TTSH. Through this study, several ergonomic mis-matches were found, perhaps due to the use of clinical equipment manufactured and designed for population with different anthropometry as our local population.

As a doctor, one has to take care of others. This can cause stress and put a strain on the physical state and well-being. Doctors, especially surgeons, are also known to be at a higher risk of developing musculoskeletal disorders (MSDs). Common MSDs experienced by doctors include: back pain, neck pain and shoulder pain. These MSDs may be more common among ophthalmologists due to their unique working conditions . They are often required to work in awkward postures while gripping precision instruments with control to ensure stability. They also sometimes have to remain or maintain a particular static position or make repetitive movements for a significant period of time. These are contributing factors to the development of MSDs. In mild cases, pain and discomfort are experienced; but in severe cases, surgery could be required or even an early retirement.

Aims of study

To study the factors contributing to discomfort experienced by the ophthalmologists during:

- Clinical examination
- Outpatient procedures like laser treatment
- Eye surgeries in operating theatres

To improve the ergonomics of the ophthalmologists' workstations and explore ways to improve comfort level of the ophthalmologists.

Methodology:

- Questionnaires administered to ophthalmologists
- Measurements of the workstations and instrumentation (Photo 1 is one example)
- Anthropometric measurements of the ophthalmologists
- 3-D modeling for analysis

We found that that the most common locations for aches and pains among ophthalmologists were the neck and back, in keeping with the findings reported in other studies. The pain is due to a range of factors, including the prolonged awkward posture; the cumbersomeness of some equipment that causes muscle fatigue; lack of rest periods; and lack of awareness about the importance of ergonomics or ways to relieve using appropriate stretches. The study also found for example, that using a specially designed saddle-shaped stool capable of a forward tilt can significantly help improve the posture and potentially reduce the pain in the neck, shoulder and back. Our anthropometric measurements of 34 ophthalmologists found a wide variation in body measurements. In order to improve the comfort level of the ophthalmologists, modification may need to be performed on the current equipment. These include: modifications to the adjustability to the heights of the table and seating. Other improvements that may be considered include the modification or change of chairs and introduction of new devices specifically designed to improve postures.

The ergonomic problems faced by ophthalmologists have been brought up in the recent years. This collaboration focusing specifically on our population is an important first step towards better understanding of the issues and may in future provide customized solutions to better protect our ophthalmologists. More work and time are required to improve the situation that the ophthalmologists are facing.

References:

1. Chaffin, D. B., Andersson, G., & Martin, B. J., 2006. Occupational biomechanics.
2. Kitzmann, A. S., Fethke, N. B., Baratz, K. H., Zimmerman, M. B., Hackbarth, D. J., Gehrs, K. M., 2012. A Survey Study of Musculoskeletal Disorders Among Eye Care Physicians Compared with Family Medicine Physicians. Ophthalmology, 119(2), 213-220.

Building Vibrant, Sustainable and Resilient "Ecosystems" for Research in Singapore

Dr Chen I-Cheng Mark
Consultant
Department of Clinical Epidemiology
Tan Tock Seng Hospital

Assistant Professor
Saw Swee Hock School of Public Health
National University of Singapore

The research scene in Singapore needs "research ecosystems" with many different "species" playing different roles.

In the natural world, an ecosystem is a "biological community of interacting organisms and their physical environment". However, the term "ecosystem" has also found wider use as a means of describing how human activities and organisations interact in a given social or economic environment. For example, a "business ecosystem" has been defined as the network of organisations – including suppliers, distributors, customers, competitors, government agencies and so on – involved in the delivery of a specific product or service through both competition and cooperation.

Likewise, "research ecosystems" involve the formation of a network where there are key parties from different disciplines fulfilling important roles in answering the research questions – this may involve various types of expertise in the biomedical sector such as clinical and laboratory partners, but also non- biomedical expertise such as colleagues in social sciences and engineering. In such a scenario, the interactions and activities become almost natural and autonomous. There need not be any clear leader giving "top-down" directions within the ecosystem, but each party would have its own "ecological niche". Yet there would also be some parties playing critical roles within that ecosystem, akin to what would be known as "keystone species" in natural ecosystems – these are basically organisms that, in spite of their being a relatively small part of the system in terms of numbers or "biomass", have a disproportionate effect on the health and functioning of that ecosystem.

In the several years that I have been involved in research, I have become increasingly convinced that research endeavors are most productive when it is not just a collection of individual ideas and projects but organised into an ecosystem. I also feel strongly that this is what is needed for long-term success in any particular area of research.

The research scene in Singapore needs "research ecosystems" that are vibrant, with many different "species" playing different roles. Taking the analogy further, we also want these "ecosystems" to be self-sustaining given the environment that they inhabit. And while not all natural "ecosystems" are resilient, we would want our "research ecosystems" to be of the resilient variety, being able to adapt to changing environments to reach a new equilibrium so that the activities continue to thrive in the face of new difficulties and challenges.

As I continue in my research career, and move from focusing just on my own research projects to being involved in networks of research activities, I have been asking myself hard questions about the status of "research ecosystems" in my given area of research. Does the ecosystem even exist in the first place? If it does, what is the health of the ecosystem that is relevant to my area of research? And where am I in that "research ecosystem"? Does the group I work with have an "ecological niche"? May we even be one of the "keystone species" on which the ecosystem's health depends?

I also ask myself, if the "research ecosystem" does not yet exist here, or if the ecosystem is unhealthy and failing, what can I do about it? Should I get out of that area of research? Or should I play the "ecologist" and help build that ecosystem? Increasingly, I believe the onus lies on us to build ecosystems, and I hope that other researchers are coming to the same conclusion, with the recognition that we inhabit the same research environment, and in a sense are "in it together". Yes, one tempting path to take is always to outcompete and dominate the entire environment available to us, but this is also what would make an ecosystem less diverse, less vibrant, less adaptable and more vulnerable in the long run. So the alternative must be that we work to find relevant partners, and build a network that settles into a semi-equilibrium, with each party evolving to settle into its own ecological niche.

My hope is that some of us may also develop into that "keystone species" that makes the ecosystem vibrant, sustainable and resilient, and in doing so play a critical role in delivering the kind of research that improves care for our patients, and improves the health of the nation.

Modelling of the Health Care Delivery System

Dr Meng Fanwen
Operations Research Specialist
Health Services and Outcomes Research
National Healthcare Group

Dr Meng Fanwen traces his journey to becoming an operations researcher.

My journey began when I first obtained my bachelor degree in Mathematics in China, and then moved on to pursue my PhD in Operations Research (OR) at the National University of Singapore (NUS). Subsequently, I worked at NUS and University of Southampton as a research assistant, research fellow, and senior research fellow for many years.

My research interest focuses on a broad range of modelling work, ranging from basic mathematical formulations and their properties to computation and algorithm analysis, to applications in engineering, supply chain management and logistics, and many more. I enjoy challenging myself and am always keen to explore the mysterious world of mathematics to come up with practical applications to solve real-world problems.

My interest in Health Services Research (HSR) started when I was with The Logistics Institute – Asia Pacific, where I was involved in Healthcare Supply Chain, a collaborative project with the NUS Business School, National University Hospital (NUH), and overseas experts from the United States. It was exciting to investigate health services problems using mathematics, statistics, basic and advanced OR models.

From there I went on to join the Health Services and Outcomes Research (HSOR) unit at the National Healthcare Group, and this was where I embarked on my journey as an operations researcher specialising in healthcare.

While working at HSOR, I furthered my knowledge through attending conferences and training, and developed myself through participating in research projects. I witnessed how research plays a critical role in improving patient care, learned the importance of using modelling to prepare for changing healthcare needs, and translational science. In particular, I have used mathematical modelling, computer simulations and quantitative analyses to tackle a range of healthcare problems.

With support from my Director, Dr Heng Bee Hoon and the team, I have been involved in various HSR projects, research grant applications, and publications. Among the projects involved, HSOR projects I collaborated with the Emergency Department (ED) of Tan Tock Seng Hospital in using modelling techniques for nurse shift planning. Clinical management of patients in the ED is complex due to the urgency, dynamic status, and uncertainty of patient's diagnoses. Workloads change greatly by day of week, time of day, and by shift. Thus, balancing workload with nurse staffing can be very complicated. A mixed integer programming was developed to derive an optimal nurse shift plan. To understand patient flow at ED, graph theory was applied to reduce the complexity of visualising patient flows. With the use of a mathematical mode, we were able to propose a solution for the hospital managers to implement at ED to improve manpower management and balance workloads.

Geriatric Care - From Frustration to Passion

Dr Liew Tau Ming
Registrar
Institute of Mental Health

Dr Liew Tau Ming shares how he ventured into geriatric research.

I remember as a medical student, I had a biased view of geriatric care. I told myself – "There is little that doctors can do for the elderly population. There is no cure to their illnesses. Neither can we bring back their youth".

Little did I expect, I was posted as a young medical officer to a department which I was least excited about – Geriatric Medicine! In my initial months there, I remember feeling frustrated that one after another of my patients had this common diagnosis – 'Dementia with BPSD' (Behavioural and Psychological Symptoms of Dementia). It meant, to me, a diagnosis of hopelessness. How wrong I was!

Gradually, I learnt to appreciate that there was more to just curing a patient. The human touch and compassion I provided as a doctor made a huge difference to my elderly patients and their families. And it was heartening to bring joy and quality of life to them when their circumstances suggested to them otherwise. Over time, this interest in geriatric care grew into a consuming passion. I felt most alive when I am seeing elderly patients and their families, and noticing the impact I had in their lives. This passion was fuelled further when I met many great teachers like Dr Lydia Au, Dr Lawrence Tan, Dr Philip Yap, Dr Seng Kok Han, Dr Joshua Kua and Associate Professor Chiam Peak Chiang.

Research - a key to good clinical care

It was in this context that I began to realise that there is more that we can do for the elderly populations. And, the current boundaries of geriatric care can be pushed much further through research. My initial involvement in geriatric research with Dr Philip Yap opened my eyes further to the world of research. I started noticing areas in my clinical practice which can be improved through research, and my limitations in research experience to bring such improvements. This led me to appreciate the need for sound research skills, as a prerequisite to a good clinician. I was most grateful when IMH supported my application for Master of Clinical Investigation, and the Ministry of Health awarded me the scholarship to do this. Associate Professor Chong Siow Ann had also been most helpful to me when I started this research journey in IMH.

The present and the future

With the funding from Master of Clinical Investigation and IMH Centre Grant, I currently have the opportunity to engage in a research very close to my heart – dementia caregiver support. This project is still in its infancy, but I am fortunate to have a great team involving Dr Philip Yap (Geriatrician), Ms Sanni Leong (Medical Social Worker), Ms Hia Soo Boon (Psychologist), Mr Mihir Gandhi (Biostatistician) and Assistant Professor Luo Nan (Health Service Researcher).

While there have been many challenging and exhausting moments so far, it was the grace of God and the encouragement of my wife that kept me persevering. I do not know what the future holds. If given the opportunities, I see fertile research grounds in the area of dementia and geriatric psychiatry. Ultimately, I hope to do what I set off doing – to bring comfort to the elderly people and their families.

Executive/Senior Executive/ Assistant Manager

(Research & Development Office)

Key responsibilities include:

You will be part of the Finance/Grant Management/ Fund Raising team. You will be required to carry out the following as part of the role-

The key role will be to-

- Administer NHG research grants and liaise with our hospitals and national funding bodies on matters relating to grant calls, grant applications and grant awards.
- Prepare claim forms for submission to funding agencies, analyze research expenditure trends and provide expenditure reports.
- Manage financial aspects relating to the department such as account payables, monthly financial reports, yearly budgeting cycle, business planning and models and account related duties.
- Develop brochures to launch and actively promote NHG RDO's fundraising initiatives, initiate fund raising campaigns and plan events to achieve fund raising objectives.
- Engage in research of foundations and other potential donors, establish and maintain relationships with champions and donors to secure donations and sponsorships.
- You may be required to perform other duties assigned by the Supervisor/Head of Department as part of your development.

Requirements

- Degree in, Accountancy, Finance, Business Administration or equivalent
- Meticulous, a good team player and able to work independently
- Conversant with Microsoft Word, Excel, Access and Power Point
- Ability to work effectively with multiple departments within and outside the organization
- Good oral and written communication and presentation skills
- Proven track record of fund raising is certainly an asset

Executive- Project Management

(Research & Development Office)

Key responsibilities include:

The applicant will assist in all aspects of grant, project and account management for Clinician Scientists within NHG.

The key role will be to-

- Act as Account Manager and proactively interact with NHG Clinician Scientists and identify their needs in terms of project progress and budget management.
- Serve as liaison person to initiate kick-off meetings for projects and ensure smooth progress of projects at all stages.
- Work with team members to improve existing and develop new grant administration policies and procedures in accordance with institute's regulations and policies.
- Work with NHG institutions to actively monitor Research Outcomes and prepare Management reports for NHG Research Indicators.
- Provide on the ground support to Clinician Scientists whenever applicable.

Requirements

- A good degree in biomedical sciences
- Experience in grant management or project management is an advantage
- Careful and meticulous with a well-organized approach to work
- A team player with the ability to communicate and work well with people at all levels
- Ability to work independently under tight deadlines
- Positive attitude and a pleasant disposition

National Healthcare Group

Adding years of healthy life

The National Healthcare Group (NHG) is a leading public healthcare provider in Singapore. We manage:

Two Hospitals — Tan Tock Seng Hospital and the Institute of Mental Health/Woodbridge Hospital;

One National Centre — National Skin Centre;

NHGP chain of nine polyclinics in — Ang Mo Kio, Bukit Batok, Choa Chu Kang, Clementi, Hougang, Jurong, Toa Payoh, Woodlands, and Yishun;

One Specialty Institute — NHG Eye Institute;

Five Business Divisions — NHG 1-Health, NHG Diagnostics, NHG Pharmacy, Singapore Footcare Centre, and Primary Care Academy; **and**

Johns Hopkins Singapore International Medical Centre.

Recruitment of (A) DSRB Analyst and (B) Assistant Analyst, Research & Development Office

All research conducted in NHG institutions, involving NHG patients, staff and/ or facilities, currently falls under the purview and ethical oversight of the Domain Specific Review Board (DSRB). You can be part of this highly motivated team to ensure that the rights, safety and welfare of research participants are protected by creating a culture of research that operates on high ethical standards.

DSRB Analyst

Key responsibilities include:

- Ensuring that submitted research protocols are reviewed efficiently and consistent with the regulations, guidelines and policies.
- Screening and processing all applications and correspondence received from investigators.
- Serving as a resource for investigators regarding the adaptation and implementation of DSRB policies, procedures and forms.
- Ensuring that the Review Board's reviewing processes are properly conducted, including documenting minutes of the meetings, follow up actions, etc.
- Communicating and documenting all communications with investigators, sponsors, and regulatory authorities, including the Review Board's determinations.
- Ensuring that meeting minutes are in sufficient details to document Review Boards' deliberations.

The 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 GCP guidelines and applicable regulations and guidelines of clinical research, or ethical principles relating 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, organisational, communication, and interpersonal skills.

Assistant Analyst

Key responsibilities include:

- Ensuring investigators are informed of deadlines for continuing reviews and performing preliminary review of study renewals in consultation with the DSRB Analyst.
- Performing administrative reviews of study amendments, non-compliances, UPIRTSO, and other notifications to ensure completeness of submission and correctness of information.
- Serving as a resource for investigators regarding the adaptation and implementation of DSRB policies, procedures and forms.
- Preparing outcome letters and maintaining accurate records of the ethics reviews in the study folders and databases.
- Providing administrative support for the Review Boards' meetings, including collating RSVPs, arranging meeting logistics, book meeting room, presentation equipment, etc.
- Assisting in organising research ethics seminars and training sessions.

The Requirements

- "A" Level / Diploma of any discipline or equivalent.
- Preferably with experience as an Administrative Support Staff in the Healthcare Industry.
- Proficient in MS Office applications is essential. Preferably with experience using Databases (e.g. MS Access).
- Able to work independently and meticulously.
- Possess strong organisational and time-management skills, and demonstrate strong written and verbal capabilities.
- Ability to handle extremely detailed and highly confidential information with tact and discretion.
- Performs well under pressure, meeting deadlines, and willing to assume responsibilities as directed.

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

RESEARCH SUPPORT / ALLIED HEALTH PERSONNEL

A Pharmacist's Research Journey

Ms Esther Bek
Principal Pharmacist (Clinical)
Bukit Batok Polyclinic
NHG Pharmacy

In my years as an undergraduate in NUS, completion of a final-year project in the final year of studies was a requirement. I knew back then that bench research would not be something I would be interested in, so I chose a clinical project which was done in collaboration with a pharmacist from KK Women's and Children's Hospital. Reading thick case notes for my final-year project gave me my first taste of clinical research.

To obtain a license to practise as a pharmacist in Singapore, a one-year internship (called pre-registration training) is required after graduating with a pharmacy degree. As part of pre-registration training, a research project also has to be submitted. As I did my pre-registration training in Tan Tock Seng Hospital (TTSH), my project was naturally clinically-based and I found myself once again ploughing through case notes.

I received invaluable guidance from various preceptors who were practising pharmacists at TTSH then. Upon completing my pre-registration training, I stayed on at TTSH as an inpatient pharmacist and my job scope included being a preceptor to pre-registration pharmacists.

Mentoring

I moved to NHG Pharmacy in 2007. As a preceptor in NHG Pharmacy, I was in charge of co-coordinating the training of pre-registration pharmacists and ensuring that each of them completed the mandated pre-registration training project. As a result, it was guaranteed that I had at least one research project each year done in collaboration with each batch of pharmacy graduates from NUS. These projects have been submitted as abstracts and posters to the annual Singapore Pharmacy Congress and in more recent years, the Singapore Health and Biomedical Congress (SHBC).

Camaraderie

In a busy polyclinic setting, finding time to carry out research activities is difficult. But this is made easier by having a team of collaborators who are always willing to contribute and share the load in every project. Over the years, I have collaborated with doctors from NHGP, colleagues in NUS, being a project supervisor for final year pharmacy students in NUS, and fellow pharmacists practising in NHG.

Continuous Learning

I did not have any formal training in research besides a few modules completed as a student in NUS and attending ad hoc NHG research training events. As such, my foray into research may be described as rather serendipitous. With each project completed, I learn and strive to improve from past mistakes.

Last year, a project which I collaborated with other pharmacy colleagues titled "Patient Satisfaction with Pharmacist-managed Hypertension, Diabetes and Lipids Clinic and its relation to Medication Adherence and Beliefs About Medication" won Silver in the Singapore Primary Care Research Scientific Competition (Poster Category) at the SHBC.

My latest research project is about the impact of the ConviDose™ Medication Management System on the medication adherence of patients, especially the elderly and those with multi-morbidities.

Communicating Research Findings at Conferences

Dr Xie Huiting
Covering Nurse Educator
Institute of Mental Health

Communication of findings is as important as the research itself.

How do we get to know about the latest developments and medical breakthroughs? It is through communication. Without it, we would find it much harder to keep track of scientific developments, from pioneering treatments to engagement in evidence-based practice. Thus, communication of research findings is just as vital as the science itself.

Two budding nurse researchers, Ms Lubna Shah and Mr Wang Jia communicated their research findings to the scientific community after having their abstracts selected for presentation after peer review.

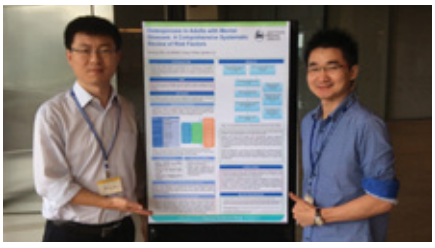
Ms Shah, a staff nurse from the Institute of Mental Health developed her interest in research while pursuing her nursing degree, conducted a pilot study on "Examining the Efficacy of a Virtual Reality-based Stress Management Programme on Stress Related Variables in People with Mood Disorders."

She found that participants in the programme showed improvement in terms of both subjective (eg perceived stress levels) and objective measures of stress (eg skin temperature) as well as knowledge levels on stress and stress management strategies.

In addition, the study also showed promising outcomes in terms of perceived anxiety and depression in study participants. The findings of this study were communicated to the healthcare community at large during the 2nd NUS-NUH International Nursing Conference. She was presented with the First Place Award for Best Oral Presentation for her excellence in communicating the study results orally to conference participants.

Poster presentation is another way of communicating study results. A systematic review titled "Osteoporosis in Adults with Mental Illnesses: A Comprehensive Systematic Review of Risk Factors" by Mr Wang Jia and his colleagues was selected for presentation at the 2th Asia Pacific Evidence-Based Medicine and Nursing Workshop & Conference. The review included 26 articles on people with schizophrenia, bipolar disorders, depression and depression with borderline personality disorder who were found to have increased risk of osteoporosis than healthy individuals as evidenced by their lowered bone mineral density.

Ms Lubna Shah sharing her research findings at the conference.



Mr Wang Jia, on the left and Mr Yuan Peng sharing their systematic review findings at the conference.

HIGHLIGHTS from the Asia Pacific Research Ethics Conference 2014

The Asia Pacific Research Ethics Conference (APREC), a biennial event with its first two runs held in 2010 and 2012, was successfully held at Grand Copthorne Waterfront Hotel from 26-28 March 2014. The pre-conference programme comprised two workshops, while the main conference featured 50 local and international speakers presenting on various topics across 4 scientific tracks. The Domain Specific Review Board (DSRB) 10th Anniversary Dinner was also held on the last day of APREC. Notable highlights from APREC 2014 are featured here.

Ms Qiu Shijia
IRB Analyst
Domain Specific Review Board (DSRB)
Office of Human Research Protection Programme (OHRPP)
Research & Development Office
National Healthcare Group

Pre-conference workshops: Dr Susan Fish (left) and Dr Bruce Gordon (right), from the US Public Responsibility in Medicine and Research (PRIM&R), were the facilitators for the Institutional Review Board (IRB) 250 workshop.

Opening keynote address by Professor Nancy Kass on "International Research Ethics: Rules, Guidelines, and Experiences from the Field".

Exhibition booths put up by the NHG Research and Development Office.

NHG Group CEO Professor Chee Yam Cheng and distinguished guests at the Domain Specific Review Board (DSRB) 10th Anniversary Dinner.

Networking lunch – tables were colour coded to represent the different scientific tracks. This was to facilitate networking among delegates with similar interests within each scientific track.

Dr Jeremy Sugarman speaking at one of the conference breakout sessions, on the topic of "Ethical Issues in the Clinical Translation of Stem Cell Research".

Introducing the secretariat committee from the NHG Research and Development Office who had worked hard to put together APREC 2014!

SoCRA Certification Programme for Clinical Research Professionals

The Society of Clinical Research Associates (SoCRA) is one of the global leaders supporting the professional development of clinical research associates internationally. It establishes and conducts the Certification in Clinical Research Professional (CCRP) for Clinical Research Professionals (CRPs) to develop an internationally accepted level of knowledge, education and experience to support clinical research.

The NHG Research & Development Office's (RDO) Office of Human Research Protection Programme (OHRPP) successfully hosted the 3rd SoCRA CCRP Certification, Preparation and Review Programme in March 2014. A total of 24 candidates from NHG institutions, partner institutions and private organisations enrolled for the CCRP Preparation and Review Programme, and 27 candidates sat for the CCRP examination.

The proctor and lecturer was Ms. Carolyn E. Rugloski, Director of Project Management at Worldwide Clinical Trials (WCT). Ms Rugloski has accrued more than 25 years of clinical research experience in data management, monitoring, training, project management, quality assurance and business development, and is recognised internationally as a Good Clinical Practice (GCP) subject matter expert.

During the preparation programme, Ms Rugloski emphasised important learning points from the US Code of Federal Regulations (CFR), International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) and Safety Reporting guidelines. She also imparted her knowledge on pertinent concepts applicable to clinical research work.

Participants with Ms Rugloski at the SoCRA CCRP Certification, Preparation and Review Programme.

CRCS-CRP Forum

In addition to administering the CCRP programme and examination, Ms Rugloski was also invited to share her experience and insights at the Clinical Research Coordinator Society (CRCS)-Clinical Research Professional (CRP) forum held on the same afternoon. Themed "Research Misconduct – Ensuring Compliance with ICH GCP Standards", the forum attracted more than 180 attendees from various institutions.

As the first speaker, Ms Rugloski captivated the local audience's attention by sharing prominent research misconduct cases that had occurred in the US, explaining the resultant regulatory sanctions that had been imposed by the US Food and Drug Administration (FDA) in response to these significant transgressions. The second speaker Mr Edwin Barbarin shed light on the DMAIC (define, measure, analyse, improve, control) approach to implementing corrective and preventive action plans (CAPAs). While keeping the crowd entertained with his natural humour, Mr Barbarin also provided some insight on the multitude of challenges faced by Quality Assurance (QA) teams in a contract research organisation (CRO) setting, in implementing changes. Concluding on a high note, the forum was well-received by attendees, as evidenced by their generous compliments of both speakers.

Ms Valerie Wee and Ms Lim Boon Hwee
Senior Executives
Research Education Unit
Office of Human Research Protection Programme (OHRPP)
Research & Development Office
National Healthcare Group

Participants with Ms Rugloski at the SoCRA CCRP Certification, Preparation and Review Programme.

Ms Doreen Lim, chairperson of CRCS, delivering the welcome address at the CRCS-CRP forum.

Qualité

The program with a mission to ensure and enforce the responsible conduct of research meeting high ethical standards.

Qualifications and Requirements for Principal Investigators of Clinical Trials

Introduction

The conduct of clinical trials within National Healthcare Group (NHG) and partner institutions is regulated by both the Domain Specific Review Board (DSRB) and the Health Sciences Authority (HSA). The overarching intent of such regulation seeks to protect the rights, safety and well-being of subjects participating in these studies. Each authority administers a separate set of requirements for principal investigators (PIs) of clinical trials, to which researchers must comply should they wish to initiate and oversee the conduct of a clinical trial.

In addition, the DSRB has introduced several changes over the past year, with regard to the qualifications and minimum requirements for PIs of clinical trials. This article provides a summary of the PI requirements that apply.

What qualifications must an individual fulfill to be the PI of a clinical trial?

Based on DSRB's requirements, clinical trials are considered to be "greater than minimal risk" studies. As such, PI requirements for such studies are more stringent than that for minimal risk studies. To qualify as a PI for a more than minimal risk study that does not require a Clinical Trial Certificate (CTC) from HSA, the individual should be:

- A fully-registered or conditionally-registered medical practitioner who is an Associate Consultant and above; or
- A senior staff nurse and above, and where at least one member of the research team is an Associate Consultant and above; or
- An allied health staff who is a senior therapist / pharmacist, and where at least one member of the research team is an Associate Consultant and above.

For clinical trials regulated under the Medicines Act and Medicines (Clinical Trials) Regulations, the study will require a CTC from HSA and the PI must be a locally registered doctor or dentist. In most cases, the medical practitioner must be of rank Associate Consultant and above to oversee the conduct of a clinical trial. To avoid unnecessary delays in the review timelines, individuals submitting applications for regulatory and ethics approvals are strongly encouraged to ensure that both HSA's and DSRB's requirements are fulfilled in proposing the PI for a study.

When does a clinical trial require a Clinical Trial Certificate (CTC) from the Health Sciences Authority (HSA)?

Under the Medicines (Clinical Trials) Regulations, a clinical trial is as an investigation where one or more medicinal products are administered by a doctor or dentist to his patients, to ascertain any beneficial or harmful effects of the product. Please refer to the regulations for the full definition of a clinical trial.

In general, clinical trials seeking to examine the safety and/or efficacy of the following types of medicinal products will require a CTC from HSA:

- Registered and unregistered drugs;
- Radiopharmaceuticals;
- Complementary health products, e.g. health supplements, Chinese proprietary medicines, traditional medicines.

More than minimal risk studies that do not fulfill the legislative definition of a clinical trial will not require a CTC from HSA. However, an approval from DSRB will still be required to initiate conduct of the study.

When in doubt, the principal investigator is advised to write directly to HSA to clarify the need for a CTC. For clinical trials requiring HSA's approval, a study protocol should be submitted for review as part of the application dossier. The DSRB application form is not an acceptable substitution for a formal protocol document.

What are the minimum training requirements for principal investigators of clinical trials?

The Singapore Guideline for Good Clinical Practice (SGGCP) requires that the PI and all study team members be adequately trained before conducting the study. The DSRB further specifies that, with effect from 1st August 2014, PIs of clinical trials will be required to complete both the web-based Collaborative Institutional Training Initiative (CITI) and the SGGCP course, as the minimum research-related training requirements. The PI is required to provide proof of attendance or completion of both trainings to the DSRB, at the point of application for ethics approval.

References

Medicines (Clinical Trials) Regulations
Singapore Guideline for Good Clinical Practice.
NHG DSRB SOP 201-E03 – Minimum Training and Minimum Requirements for Investigators.

Ms Lim Boon Hwee
Senior Executive
Research Education Unit
Office of Human Research Protection Programme (OHRPP)
Research & Development Office
National Healthcare Group

DSRB Announcement: Changes to the Informed Consent Form Requirements for Studies Involving Prospective Collection of Biological Sample(s) and Re-Consenting Subjects for Ongoing Studies

Changes to the Informed Consent Form Requirements for Studies Involving Prospective Collection of Biological Sample(s)

The NHG Domain Specific Review Board (DSRB) recently handled a complaint where a subject had requested the investigator to return the tissue samples which had been collected as part of the research study. The subject had wanted to use the tissue samples for further clinical tests, and mentioned that the Informed Consent Form (ICF) did not state that she could not make such a request. However the investigator did not agree to the return of the tissue samples.

The NHG Research Ethics Committee deliberated over this case and concluded that biological sample(s) collected for research are deemed to be gifted to the study team for the research study. Therefore, the biological sample(s) should not be returned to subjects and subjects should be made aware of this during the consent process. However, subjects should be allowed to request that the investigators discard or destroy the biological sample(s) (e.g. upon withdrawal) if it has not already been anonymised (i.e. the sample can still be traced) and their wishes must be respected.

In order to avoid potential disputes between the subjects and the investigators regarding the return of biological sample(s), the DSRB has revised the ICF requirements for studies involving prospective collection of biological sample(s).

With effect from 01 April 2014, studies that involve the prospective collection of biological materials must include a statement in the ICF to seek consent from subjects that all biological samples collected for the study will be gifted to the institution/sponsor for the purposes as described in the ICF and will not be returned to them, and to inform subjects that they retain their rights to ask the Principal Investigator to discard or destroy any remaining sample(s) if it has not been anonymised.

Re-consenting Subjects for Ongoing Studies that Involve the Prospective Collection of Biological Sample(s)

As this change is being implemented to protect the interest of both the subjects and study teams, investigators of ongoing studies where the subjects will be returning for study visits are also required to make the same changes to the ICF over a one year period.

The Principal Investigator must submit a study amendment to DSRB to update the ICF(s) and re-consent returning subjects BEFORE **01 April 2015**. A tracked change copy and a clean copy of the amended ICF(s) will have to be uploaded for the acknowledgement from DSRB prior to its use.

Please refer to Section 11 "Voluntary Participation" in the updated DSRB Informed Consent Form Template (Document No. 207-001, Version 5, dated 3 Mar 14).

Jean Foo
IRB Analyst
Domain Specific Review Board (DSRB)
Office of Human Research Protection Programme (OHRPP)
Research & Development Office
National Healthcare Group

GCP FAQ: Guidelines on Source Documentation of Subjects' Study Progress

Inadequate documentation of subjects' study involvement and progress in the source documents and/or medical case notes is a common issue noted during study reviews. Documentation is important as it allows reconstruction of study events, which in turn helps to support the evaluation and validation of research findings.

The following are some tips on how you can improve the source documentation practice at your site and ensure that sufficient information is captured to substantiate the integrity of your study data.

Source documents to be used for the study should be pre-determined

Source documents are all documents that contain original records and certified copies of original records of clinical findings, observations, or other activities in a study that is necessary for the reconstruction of the research.

Prior to study initiation, the Principal Investigator (PI) should clearly identify the types of source documents required in the research and ensure that they are accessible by the study team.

Examples of source documents: Hospital records, clinical and office charts, laboratory notes, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, microfilm or magnetic media, x rays, subject files, and records kept at the pharmacy and laboratories.

Develop appropriate templates and/or tools to capture pertinent study information

The study team may also develop and utilise source document templates or stamps for the study, to ensure that all study-related procedures are carried out and appropriately documented.

Study templates developed for the study should also include:

i. A document version control (e.g. version number and/or date)
ii. Page numbering (e.g. page 1 of 2)
iii. Space/line for the person performing the data entry to initial and date to document that he/she was responsible for completing the information.

Examples of templates / tools: Subject eligibility assessment checklist, source document templates to record specific study assessments, stamps to capture information on informed consent process and adverse event reviews.

Ensure study documentation is maintained by an appropriate personnel

Only personnel who has been adequately trained on the protocol (i.e. training recorded in a training log / record form) and delegated by the PI (i.e. delegated tasks specified in the study responsibility / delegation log) should perform study related activities and maintain documentation at site.

Guidance Table on Documentation in Source Documents / Subject Medical Records:
The table on the next page aims to provide guidance on the study documentation required when recording a subject's study involvement and progress in source documents and / or medical case notes.

References

1. Singapore Guideline for Good Clinical Practice (SG GCP)
2. NHG Proper Conduct of Research Standard Operating Procedures (PCR SOP) 501-B05- Documentation available at: https://www.research.nhg.com.sg/wps/wcm/connect/romp/nhgromp/resources/research+sops
3. NHG Proper Conduct of Research Standard Operating Procedures (PCR SOP) 501-C01 - Informed Consent Form and Process available at: https://www.research.nhg.com.sg/wps/wcm/connect/romp/nhgromp/resources/research+sops

Ms Maggie Lee
Senior Executive
Research Quality Management
Office of Human Research Protection Programme (OHRPP)
Research & Development Office
National Healthcare Group

Item	Requirements	Reference
Eligibility Assessment	(1) The eligibility assessment of each subject should be documented and information should include: ▪ Who conducted the eligibility assessment ▪ When the eligibility assessment was completed ▪ Whether the subject met all the eligibility criteria ▪ The diagnostic test(s) (type / date of tests / results) used to assess the subject's eligibility – if any ▪ Diagnostic reports used to assess eligibility should be filed and made available for review – if any. (2) An eligibility criteria checklist may be developed to facilitate the eligibility assessment. The person(s) completing the assessment should initial and date on the checklist.	NHG PCR SOP 501-B05
Informed Consent Process	The study team member who conducted the informed consent discussion should record: ▪ Protocol reference, e.g. protocol title or number ▪ Date the informed consent was obtained ▪ The informed consent process, e.g. any impartial witness and/or translator used, and the reason for these) ▪ Language used to conduct the informed consent process ▪ How the subject was given adequate time to consider participation ▪ That a signed copy of the informed consent form (ICF) was given to the subject.	NHG PCR SOP 501-C01
Study Progress	The following items should be included when documenting the subject's progress in the study.	NHG PCR SOP 501-B05
Study Visits	Each study visit completed by the subject should be recorded in the source documents. Documentation should include: ▪ Date of study visit ▪ Name of study team members who conducted the visit ▪ Procedures completed, e.g. blood draw timings, physical examination, vital sign measurements, investigational products (IP) dispensed to and/or collected from subject (where applicable) ▪ Instructions provided to subjects, e.g. handling of IP, completion of subject dosing diary, etc. ▪ Other relevant information, e.g. reasons for deviations from study schedule or procedures, discrepancies noted in IP accountability, etc.	NHG PCR SOP 501-B05
Serious Adverse Events (SAE), Adverse Events (AE) and Safety Monitoring Assessments	(1) Assessment of subjects for AEs should be performed at every study visit and recorded in source documents. (2) Investigators should review all study-related laboratory / diagnostic test results to assess the clinical significance of any abnormal findings. This review should be documented. (3) SAE and AE documentation should include: ▪ Protocol number or title ▪ Description of AE, e.g. fever, rash ▪ Onset date ▪ Severity, e.g. mild, moderate, severe ▪ Expectedness of event ▪ Relatedness to the study drug and/or study procedures ▪ Action taken, e.g. treatment provided, study drug / procedures interrupted / altered / stopped ▪ Outcome of event ▪ Date or resolution or death	NHG PCR SOP 501-B05
Study Completion / Termination / Withdrawal	At the last study visit, in addition to documenting the activities completed during the visit, the site should also record: ▪ Subject's status / condition ▪ Date of last study visit / end of study participation ▪ If subject was prematurely withdrawn from the study, the reason for withdrawal and need for further follow up (where necessary) should be documented.	NHG PCR SOP 501-B05

Responsible Conduct of Research - Protection of Human Subject

Research involving the use of human subjects has benefited the society by contributing to the medical advancement and development of new drugs and treatment. However, these may imposed unacceptable risks on research subjects. Therefore, all individuals involved in human subject research have the onus to ensure that the rights, safety and the well-being of research subjects are protected by complying with ethical boards' guidance as well as any applicable regulations related to the protection of human subject.

The example below illustrates some RCR concepts.

Case Study

Based on DSRB's requirements, clinical trials are considered to be "greater than minimal risk" studies. As such, PI requirements for such studies are more stringent than that for minimal risk studies. To qualify as a PI for a more than minimal risk study that does not require a Clinical Trial Certificate (CTC) from HSA, the individual should be:

- Dr V has no prior research experience; however, he is interested in carrying out a research on an experimental new drug which has claimed to be effective in lowering the HIV (viral) load in HIV positive individuals thus lowering of their incidence of contracting secondary infections.
- An advertisement for the recruitment of five participants; promising free physical examination, free health care for three months and $1000 compensation was placed at the hospital's communicable disease centre's (CDC) outpatient clinic.
- Upon expressing interest in the research, Dr V will hand the participant an informed consent document and obtain their consent at the clinic's general waiting area immediately. .
- As only five participants will be recruited for the research, Dr V decided that data and safety monitoring for this research would not be required.
- To test the efficacy of the experimental new drug, blood samples will be taken for the entire duration of the research (12 months) from the participants. At each blood taking, 20mls of blood will be taken and an additional of 15mls of blood will be taken and stored for "future research".
- This research was not submitted to the institutional review board (IRB)/institutional ethics board (IEC) for approval as Dr V thought that it was unnecessary.

What should Dr V do prior to conducting the research? (Please select the best answer.)

a. As Dr V is inexperienced in research, he should approach his Head of Department/ a respectable researcher (with track record in research) in his institution and discuss his research proposal and seek guidance on how to carry out his research. After discussion, he should write up a protocol specifying the details of his research (i.e. supporting literature for the new experimental drug, informed consent process, the study team members, inclusion and exclusion criteria, stopping criteria, etc.) and submit his research application to the IRB and local regulatory authority (if applicable) for approval.

b. Dr V should approach the CDC pharmacists as the research involves an experimental new drug. Submission to IRB and local regulatory authority (if applicable) is not necessary as only five participants will be recruited.

c. As Dr V is inexperienced in research, he should approach a pharmaceutical agency to conduct this research on his behalf.

d. Nothing, Dr V is doing everything right.

As there are no safeguards (i.e. the research was not submitted and approved by IRB, there is no data and safety monitoring etc.) in place to protect these participants. Which component or RCR would the above case study be categorized under?

a. Improper conduct of research

b. Protection of Human Subject

c. Mentor & Trainee Relationship

d. Research Misconduct

Useful pointers before starting a research:

- Is the study design scientifically and ethically sound?
- Are processes in place to ensure that subjects are informed of the study and are able to exercise their rights (i.e. subjects may discontinue participation at any time without penalty or loss of benefits to which they are otherwise entitled)?
- Are mechanisms in place to ensure subjects' safety during participation?
- Are safeguards in place to ensure the well-being of the subjects?
- Has the research application received approval from the ethics board and regulatory authority, if applicable?

To find out more about the RCR unit, please visit: https://www.research.nhg.com.sg/wps/wcm/connect/romp/nhgromp/hspp/responsibleconductofresearch/responsibleconductofresearch

To find out more about the RCR components, please visit: https://www.research.nhg.com.sg/wps/wcm/connect/romp/nhgromp/hspp/responsibleconductofresearch/corecomponentsofrcr

References

Shamoo, A.E. and Resnik, D.B (2009). Responsible Conduct of Research 2nd Edition. Oxford University Press.
NHG Investigator's Manual 2nd Edition.

Ms Valerie Wee
Senior Executive
Research Education Unit
Office of Human Research Protection Programme (OHRPP)
Research & Development Office
National Healthcare Group

Correct Answers for Case Studies
1. a 2. b

Research Bundle Deal – Investigator's Manual and Investigator Resource Kit

Obtain your copy of the Investigator's Manual and Investigator Resource Kit at only $18/set!

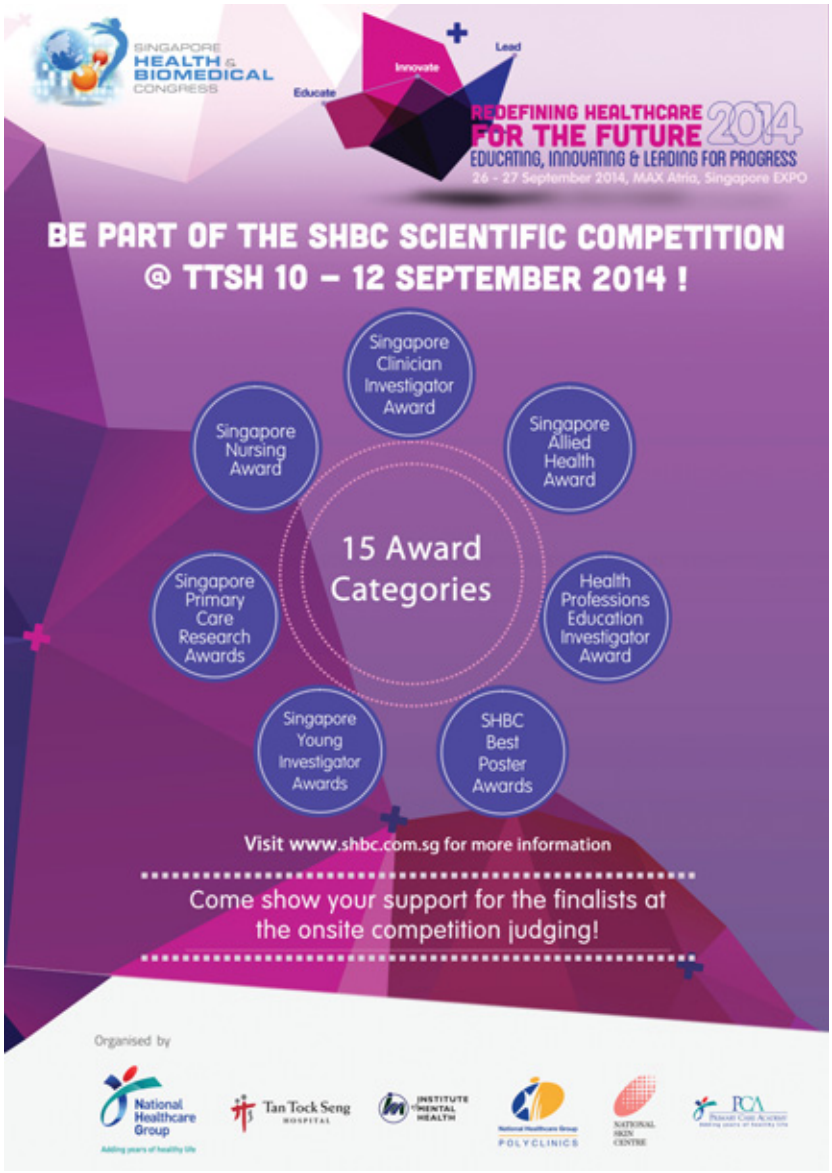
Investigator's Manual

This is a handy reference for obtaining detailed information on the Domain Specific Review Board's (DSRB) application procedures and requirements. Also, keep in touch with the latest updates on research conduct as the manual guides you through the regulations, institutional policies and SOPs governing research, including topics on informed consent, vulnerable subjects, principal investigator responsibilities and audit preparation.

Investigator Resource Kit

Launched during the Asia Pacific Research Ethics Conference (APREC) in March 2014, the Investigator Resource Kit is a comprehensive guide to help new investigators compile their Investigator File for research studies. Highlights of the kit include detailed explanatory notes on the essential documents to be maintained, website resources and Good Documentation Practice guidelines.

Please email researchcoord@nhg.com.sg for any enquiries or purchase requests.



Health Services Research Courses (August – December 2014) By Health Services & Outcomes Research (HSOR), National Healthcare Group

Topic	Tentative Date
Operations Research Appreciation Course (ORAC)	14-15 Aug '14
Systematic Review, Health Technology Assessment and Health Economics	9 Sept '14
Data analysis in HSR - Introduction to medical informatics, predictive modeling and methods of risk adjustment	14 Oct '14
Planning and Evaluating Health Services and Programs	11 Nov '14
Introduction to Qualitative Methods and Mixed Methods Research	TBA
Introduction to Economic Evaluation	TBA

For registration and full details, please email Ms Cheryl Lobo at Cheryl_lobo@nhg.com.sg

Research Grant Calls and Research Manpower Development Programmes

National Medical Research Council (NMRC)

Website: www.nmrc.gov.sg

NMRC Research Grant	Grant Description	Funding Quantum
NMRC Clinical Trial Grant (CTG)	The CTG aims to support clinicians carrying out clinical trials for the development of novel therapies/therapeutics/ medical devices. There are 3 schemes under CTG as below: Co-Development (Co-D): The Co-Development scheme is a public-private partnership (PPP) model which will comprise of a local lead PI and an industry partner collaborating on a clinical trial project. Investigator Initiated Trials -Early Phase (IIT-E): This scheme will support the conduct of investigator-initiated Phase I and II clinical trials. Investigator Initiated Trials -Late Phase (IIT-L): Between S$500,000 and S$2 million for 3 years.	Co-Development (Co-D): An industry partner is required for this scheme, and must contribute at least 50% of total project costs (cash or in-kind). NMRC can support the remaining 50% or less of the project cost in the application, to be capped at maximum S$5million for up to 5 years, inclusive of indirect costs. Investigator Initiated Trials -Early Phase (IIT-E): Maximum of S$5million for 5 years, inclusive of indirect costs. Industrial partnership is optional. Investigator Initiated Trials -Late Phase (IIT-L): Maximum of S$2 million for 5 years, inclusive of indirect costs. Industrial partnership is optional.
	Application Period: Co-Development (Co-D): Open throughout the year **Investigator Initiated Schemes: Next Grant Call in November 2014**	
MOH Industry Alignment Fund Category 1 (MOH IAF Cat 1)	The MOH IAF Category 1 aims to facilitate partnerships between clinicians and industry in pre-clinical and clinical studies to encourage commercially relevant research, foster new directions in translational biomedical research and support multi-disciplinary and multi-institutional collaborations which will bring new perspectives to the field. MOH IAF Category 1 applications can be composed of: (i) Multiple individual projects involving multiple local research partners and multiple industry partners, forming comprehensive, long-term collaborations with a high probability of leading to substantive R&D programs or impactful outcomes. (ii) Individual projects that are of significance to the national Biomedical Sciences (BMS) research agenda and industry relevance.	MOH IAF Category 1 will cover up to 30% of the Total Project Costs, and the remaining 70% of project costs must be contributed (cash or in-kind) by the industry partner. For projects where the industry partner has agreed to contribute more than 70% of costs, MOH IAF Category 1 will cover the remaining project costs. Funding support from MOH IAF Category 1 will be capped at (inclusive of 20% indirect costs): (i) S$500,000 per project for pre-clinical projects; (ii) S$1mil for clinical projects; (iii) In the case of translational projects involving both pre-clinical and clinical elements, a cap of S$1.5mil will apply. The maximum funding duration is 2 years.
	Application Period: Open throughout the year	

NHG Research Training Calendar for August – September 2014

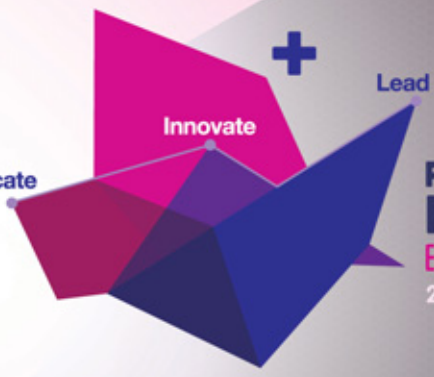
Date	Time	Training Programme	Venue
Ongoing	00:00 – 23:59	Proper Conduct of Research Online – Basic I & III (PC101 & PC103) Workshop	http://www.elearning.nhg.edu.sg
		Proper Conduct of Research – Basic II^ (PC102) Workshop	
14 August 2014	13:00 – 17:30	Informed Consent and Documentation in a Clinical Trial Seminar	NHG College, 3 Fusionopolis Link, Nexus@one-north, Level 3, Skills 1 & 2, Singapore 138543
21 August 2014	13:00 – 18:00	Subject Recruitment & Follow up & Safety Reporting Seminar	To be advised
3 – 4 September 2014	09:00 – 18:00	Singapore Guideline for Good Clinical Practice	To be advised

For registration and full details, please visit www.research.nhg.com.sg (Training & Education → Register 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)

SINGAPORE HEALTH & BIOMEDICAL CONGRESS



REDEFINING HEALTHCARE FOR THE FUTURE 2014
EDUCATING, INNOVATING & LEADING FOR PROGRESS
26 - 27 September 2014, MAX Atria, Singapore EXPO

BIOMEDICAL RESEARCH SYMPOSIUM

held in conjunction with SHBC 2014

26 - 27 September 2014 | Level 1, Opal 103 -104

The symposium aims to showcase collaborative projects between clinicians and technologists/scientists that focus on 5 main areas of research namely:

- Skin
- Metabolic Diseases
- Rehabilitation
- Ageing
- Mental Health

Distinguished speakers in these tracks will be sharing with the audience their exciting research findings and outcomes from their collaborations which are aimed towards the betterment of health and healthcare.

Alongside the symposium, find out more about NHG's efforts in developing clinician scientists and fostering collaborations with our research partners through a series of posters. Look out for the prototype displays of the collaborative projects too!

Visit www.shbc.com.sg for more information.
Interested particpants are required to register via SHBC 2014.

ORGANISED BY

National Healthcare Group
Adding years of healthy life

Tan Tock Seng Hospital

Institute of Mental Health

National Healthcare Group Polyclinics

National Skin Centre

PCA Primary Care Academy
Adding years of healthy life