Food and Health Bureau
The Government of the Hong Kong Special Administrative Region

Health Research Symposium 2019

Genomics and Big Data in Health and Disease

12 June 2019 (Wednesday)

Programme Book

Health and Medical Research Fund

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Message from the Secretary for Food and Health

I wish you all a warm welcome to the Health Research Symposium 2019.

The central theme of this year's Symposium is *"Genomics and Big Data in Health and Disease"*. Genomics and big data are inter-related and cover nearly all aspects of medical and health research including communicable and non-communicable diseases. Research on genomics and use of health big data fully support the Government's stated priority areas in advancing health and medical research in the coming years. Following the announcement in the Chief Executive's 2017 Policy Address, the Steering Committee on Genomic Medicine was set up to recommend strategies for developing genomic medicine to harness the potential of new technology for better public health policies and clinical outcomes.

The Government has allocated about $1.2 billion to implement the Hong Kong Genome Project, under which about 40 000 to 50 000 whole genome sequencing would be performed to establish a genome database of local population, as well as talent pool and testing infrastructure. All these showcase the Government's strong commitment to promoting clinical application and innovative research on genomic medicine for the benefit of patients and their families. The Hospital Authority has also established a Big Data Analytics Platform (Platform) to facilitate healthcare-related research and innovation. The pilot stage of the Platform was launched in December 2018, under which six research projects from different local universities are ongoing. We expect to formally launch the Platform by the end of this year.

Through the Health and Medical Research Fund (HMRF), funding opportunities are provided for investigator-initiated projects, commissioned programmes and research fellowships. Higher priority for funding will be given to proposals addressing thematic priorities, including application of big data analytics to examine clinical information for better management of non-communicable diseases and applied research in genetics and genomics for personalised medicine, in particular target therapies for cancers.

Under the central theme, the Symposium focuses on how genomics, combined with improvements in data analytics, can lead to improved diagnosis, treatment and prevention of disease and bring about the era of personalised medicine. Many of the research topics presented today address these key issues and explore interventions with potential to improve the health outcomes of the community.

This Symposium is a good platform to disseminate research findings, recognise excellent research and health promotion projects funded by the HMRF, facilitate academic exchange and further collaborative healthcare research. Together, these researches have expanded the local scientific evidence, built capacity in terms of research expertise and infrastructure and generated important findings for clinical practices. The Government will continue to strive to apply the findings from locally generated research to improve health policy and practice for the benefits of everyone in Hong Kong.

I would like to express my gratitude to the renowned overseas speakers and our many local experts for participating in the Symposium and sharing their knowledge and experiences with us. I wish the Symposium a great success and you all a most stimulating and rewarding occasion.

Prof. Sophia Siu Chee CHAN, *JP*
Secretary for Food and Health
The Government of the Hong Kong Special Administrative Region

Message from the Permanent Secretary for Food and Health (Health)

It is my great pleasure to welcome our distinguished speakers and all participants to the Health Research Symposium 2019.

The Government is committed to building a healthy society for all. The results obtained from the Government's continuing investment in visionary health and medical research play an important role in informing our health policies.

In the past two years, the Health and Medical Research Fund (HMRF) has attracted a large number of investigator-initiated research and health promotion proposals from local universities and medical experts on a wide range of topics including management of major non-communicable diseases, modification of lifestyle risk factors (i.e. smoking, alcohol drinking, unhealthy diet, physical inactivity), mental health, injury prevention, primary care, control of emerging and re-emerging infectious diseases, palliative and end-of-life care, and Chinese medicine. The HMRF has supported an annual average of 195 investigator-initiated proposals, worth $215 million in the past two years.

Apart from investigator-initiated research and health promotion projects, the HMRF has commissioned a range of research programmes to address health issues of local relevance. A notable example is the study on cost-benefit analysis of the 9-valent human papillomavirus (HPV) vaccine. The research has provided solid evidence to support the Government's decision, as announced in the 2018 Policy Address, that starting from the 2019/20 school year, free HPV vaccination will be introduced to school girls of particular age groups as a public health strategy for prevention of cervical cancer. Other commissioned programmes address important health issues such as projection of manpower need of healthcare professionals in Hong Kong, assessing the risk of breast cancer for local Chinese women, and evaluation of the Government's pilot colorectal cancer screening programme.

The Symposium this year will again showcase the rich knowledge generated from the funded research projects. In addition, the recipients of the first batch of HMRF Research Fellowships awarded in 2015/16 will share their experience of training and how they have applied their new skills in the public healthcare setting. We look forward to nurturing more young talents to tackle future challenges in health care.

With the Government's unfailing support under the HMRF and on other fronts, I very much hope our research community will continue to excel and contribute to the well-being of our society.

I wish all participants an insightful experience at this Symposium that would enlighten you in the pursuit of research excellence in the years ahead.

Ms Elizabeth TSE, *JP*
Permanent Secretary for Food and Health (Health)
The Government of the Hong Kong Special Administrative Region

Organising Committee of the Health Research Symposium 2019

Chairperson

Dr CHUI Tak-yi, JP
Under Secretary for Food and Health
The Government of the Hong Kong Special Administrative Region

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Department of Medicine and Therapeutics
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The University of Hong Kong

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The Hong Kong Polytechnic University

Prof YUEN Kwok-yung, GBS, SBS, JP
Henry Fok Professor in Infectious Diseases
Chair of Infectious Diseases
Department of Microbiology
The University of Hong Kong

Excellent Research Awards

Principal Applicant	Project Title (Project No.)
Prof CHIEN Wai-tong The Chinese University of Hong Kong	An Evaluation of the Effectiveness of Adherence Therapy for Patients with Schizophrenia: A Randomized Controlled Trial (10111671) [Administering Institution: The Hong Kong Polytechnic University]
Prof Richard CHOY Kwong-wai The Chinese University of Hong Kong	Clinical Application of an Established Target-enrichment Massively Parallel Sequencing Method for Genetic Screening and Diagnosis of Hereditary Hearing Loss Patients with Normal array CGH Result (01120256)
Prof JIN Dong-yan The University of Hong Kong	Roles of Epstein-Barr virus-encoded miR-BART microRNAs in viral persistence and transformation of epithelial cells (12110962)
Prof Stephen TSUI Kwok-wing The Chinese University of Hong Kong	Whole Exome Sequencing to Dissect the Genetic Factors behind Developmental Delay and Learning Difficulties (01120596)
Prof Eliza WONG Lai-yi The Chinese University of Hong Kong	Validation and valuation of the preference-based health index using EQ-5D-5L in the Hong Kong population (11120491)
Prof Vincent WONG Wai-sun The Chinese University of Hong Kong	Dietary determinants of endotoxemia and nonalcoholic fatty liver disease - A population study (11120621)

Excellent Health Promotion Project Awards

Principal Applicant	Project Title (Project No.)
Dr Derek CHEUNG Yee-tak The University of Hong Kong	Promotion and brief intervention of smoking cessation at the smoking hotspots (06130205)
Dr TANG Hoi-yin Kwai Chung Hospital	A training workshop for foreign domestic workers caring for elderly with dementia at home (28140014)

The Most Promising Young Researcher Awards

Principal Applicant	Project Title (Project No.)
Dr Jasper CHAN Fuk-woo The University of Hong Kong	Epidemiology, seroprevalence, and clinical manifestations of immunodeficiency due to autoantibody against interferon gamma in Hong Kong (13121342)
Dr Alexander LAU Yuk-lun The Chinese University of Hong Kong	Neutralizing antibodies to interferon-beta therapy in Chinese patients with relapsing and remitting multiple sclerosis: a pilot study (01120486)

HEALTH RESEARCH SYMPOSIUM 2019

Genomics and Big Data in Health and Disease

12 June 2019 (Wednesday)

Time	Programme		
08:30 – 09:00	Registration		
09:00 – 09:10	**Opening Ceremony** Welcome Remarks by **Prof Sophia CHAN Siu-Chee**, *JP*, Secretary for Food and Health		
09:10 – 10:20	**Keynote Lectures** *Moderator: Prof Francis CHAN Ka-leung, JP, Research Council* ***K1 - Towards Precision Medicine*** **Prof Euan ASHLEY** Professor of Medicine, Genetics & Data Science and, by courtesy, of Pathology, Stanford University ***K2 - Genomic Study on Molecular Pathways of Cancer Development and its Relevance to Cancer Precision Medicine*** **Prof LEUNG Suet-yi** Associate Dean (Research), Y W Kan Professor in Natural Sciences, Chair of Gastrointestinal Cancer Genetics and Genomics, Hereditary Gastrointestinal Cancer Genetic Diagnosis Laboratory, Department of Pathology, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Queen Mary Hospital **Panel Discussion**		
10:20 – 10:50	Tea Break / Poster Session	**Sharing Session on Research Fellowship Scheme** **F1** – *The Causal Role of Adiponectin and Triglycerides in Ischemic Heart Diseases Using a Separate Sample Mendelian Randomization Analysis from Publicly Available Data* **Dr Ryan AU Yeung Shiu-lun** School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong	
10:50 – 12:25	**Parallel Session 1 – Health and Health Services** *Moderator: Prof Diana LEE Tze-fan, JP, Research Council* **S1** – *Promoting Alcohol-related Attitudinal and Behavioural Change amongst Adolescents through Internet Intervention: A Cluster Randomised Controlled Trial* **Dr Patrick IP** The University of Hong Kong **S2** – *Promoting Mental Well-being of Pregnant Women with Mindfulness-based Childbirth and Parenting (MBCP): A Randomized Controlled Trial in Hong Kong* **Prof Samuel WONG Yeung-shan** The Chinese University of Hong Kong **S3** – *The Health Effects of Traffic-related Air Pollution in Hong Kong School Children* **Prof LAO Xiang-qian** The Chinese University of Hong Kong **S4** – *Improving Running Biomechanics Prevents Injury in Novice Runners* **Dr Roy CHEUNG Tsz-hei** The Hong Kong Polytechnic University **Panel Discussion**	**Parallel Session 2 – Health and Health Services** *Moderator: Prof Timothy KWOK Chi-yui, Research Council* **S5** – *A Randomised Controlled Trial on Perioperative Elderly Patients Undergoing Colorectal Cancer Surgery with Enhanced Geriatric Input* **Prof Tony MAK Wing-chung** The Chinese University of Hong Kong **S6** – *Cost and Cost-effectiveness Analysis of Renal Replacement Therapy Modalities for Patients with End-stage Renal Disease in Hong Kong: Comparison between Peritoneal Dialysis and Haemodialysis* **Prof Cindy LAM Lo-kuen**, *MH, JP* The University of Hong Kong **S7** – *A Randomised Controlled Trial Evaluating Efficacy of a Psychological Intervention Based on Commonsense Model in Improving Mental Health and Self-care among Type-2 Diabetes Mellitus Patients* **Prof Phoenix MO Kit-han** The Chinese University of Hong Kong **S8** – *Relationship between Chronic Inflammation and Vitamin D Level to Prevalent and Incident Frailty in Older Adults* **Dr Jenny LEE Shun-wah** The Chinese University of Hong Kong **Panel Discussion**	**Parallel Session 3 – Advanced Medical Research** *Moderator: Prof YIP Shea-ping, Research Council* **S9** – *Detection of Methylated Septin 9 DNA in Blood for Diagnosis, Prognosis and Surveillance of Patients with Colorectal Cancer* **Prof LEUNG Wai-keung** The University of Hong Kong **S10** – *A Randomised Controlled Trial of Bilateral Movement-based Computer Games Training to Improve Motor Function of Upper Limb and Quality of Life in Sub-acute Stroke Patients* **Ms Stefanie LAM So-ling** Shatin Hospital **S11** – *Identifying the Genetic Causes Underlying Prenatally-diagnosed Structural Congenital Anomalies (SCAs) by Whole-exome Sequencing (WES)* **Dr Brian CHUNG Hon-yin** The University of Hong Kong **S12** – *Cone Rescue in Retinitis Pigmentosa by the Treatment of Lycium barbarum* **Dr Henry CHAN Ho-lung** The Hong Kong Polytechnic University **Panel Discussion**

Venue : Hong Kong Academy of Medicine Jockey Club Building, 99 Wong Chuk Hang Road, Aberdeen, Hong Kong

Run Run Shaw Hall (1/F) | **Lim Por Yen Lecture Theatre (G/F)** | **Pao Yue Kong Auditorium (G/F)** | **Function Room 1,2 (2/F)**

HEALTH RESEARCH SYMPOSIUM 2019

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Time	Programme	
12:25 – 13:40	Lunch Break / Poster Session	
13:40 – 15:15	**Parallel Session 4 – Health Promotion** *Moderator: Prof Martin WONG Chi-sang, Grant Review Board* **S13** – *A Multi-centre Peer Support Program for Type 2 Diabetes Patients in Hong Kong* **Dr Risa OZAKI** Prince of Wales Hospital **S14** – *Promoting Smoking Cessation for Female Smokers in Hong Kong through Training Female Youth Smoking Cessation and Reduction Ambassadors* **Dr William LI Ho-cheung** The University of Hong Kong **S15** – *Development of Multimedia Interventions to Promote Breast Cancer Prevention among South Asian Women in Hong Kong* **Prof Winnie SO Kwok-wei** The Chinese University of Hong Kong **S16** – *Baby Boomers at the Gate: Creating a Path to Healthy and Productive Aging using Information and Communication Technology (ICT)* **Prof Doris YU Sau-fung** The Chinese University of Hong Kong **Panel Discussion**	**Parallel Session 5 – Infectious Diseases** *Moderator: Prof Joseph Sriyal Malik PEIRIS, SBS, Research Council* **S17** – *Treatment of Severe Influenza A Infection with Celecoxib: A Double Blind Randomised Controlled Trial* **Prof Ivan HUNG Fan-ngai** The University of Hong Kong **S18** – *Impact of Antiviral Therapy on Treatment Options and Outcome in Hepatitis B Virus Related Hepatocellular Carcinoma* **Prof Grace WONG Lai-hung** The Chinese University of Hong Kong **S19** – *Real-time Estimation of the Severity of Influenza Viruses* **Prof Benjamin COWLING** The University of Hong Kong **S20** – *Potential Cost-effectiveness of Herpes Zoster Vaccination for Older Adults in Hong Kong* **Prof Joyce YOU Hoi-sze** The Chinese University of Hong Kong **Panel Discussion**
15:15 – 15:45	Coffee Break / Poster Session	**Sharing Session on Research Fellowship Scheme** **F2** – *Photoacoustic Molecular Imaging of Osteoarthritic Pain – A Proof-of-concept Study* **Dr WEN Chunyi** Department of Biomedical Engineering, The Hong Kong Polytechnic University
15:45 – 17:05	**Keynote Lectures** *Moderator: Prof LEUNG Suet-yi, Research Council* ***K3 - Observational Data for Biomedical Discovery*** **Dr Nicholas TATONETTI** Herbert Irving Assistant Professor of Biomedical Informatics, Departments of Biomedical Informatics, Systems Biology, and Medicine, Columbia University ***K4 - Data Analytics & Applications in Hong Kong Hospital Authority: Past, Present & Future*** **Ms Eva TSUI Lai-hing** Chief Manager, Statistics & Workforce Planning Department, Hospital Authority **Dr Anderson TSANG Chun-on** Clinical Assistant Professor, Division of Neurosurgery, The University of Hong Kong **Panel Discussion**	
17:05 – 17:30	**Closing Ceremony** · Presentation of awards · Closing Remarks by **Dr CHUI Tak-yi**, *JP*, Under Secretary for Food and Health	

Venue : Hong Kong Academy of Medicine Jockey Club Building, 99 Wong Chuk Hang Road, Aberdeen, Hong Kong

Run Run Shaw Hall (1/F) **Lim Por Yen Lecture Theatre (G/F)** **Pao Yue Kong Auditorium (G/F)** **Function Room 1,2 (2/F)**

K1 - Towards Precision Medicine

Prof Euan ASHLEY, *BSc, MB ChB, FRCP, DPhil, FAHA, FACC, FESC*
Professor of Medicine, Genetics & Data Science and, by courtesy, of Pathology,
Stanford University, United States

Born in Scotland, Prof Ashley graduated with first class Honors in Physiology and Medicine from the University of Glasgow. He completed medical residency and a PhD in molecular physiology at the University of Oxford before moving to Stanford University where he trained in cardiology and advanced heart failure, joining the faculty in 2006. His group is focused on precision medicine. In 2010, he led the team that carried out the first clinical interpretation of a human genome. The paper published in the Lancet was the focus of over 300 news stories, became one of the most cited articles in clinical medicine that year, and was featured in the Genome Exhibition at the Smithsonian in DC. The team extended the approach in 2011 to a family of four and now routinely applies genome sequencing to the diagnosis of patients at Stanford hospital where Prof Ashley directs the Clinical Genome Service and the Center for Inherited Cardiovascular Disease. In 2014, Prof Ashley became co-chair of the steering committee of the NIH Undiagnosed Diseases Network. In 2013, Prof Ashley was recognized by the White House Office of Science and Technology Policy for his contributions to Personalized Medicine. He is recipient of the National Innovation Award from the American Heart Association as well as an NIH Director's New Innovator Award. He works with many Silicon Valley companies and investors. He is Principal Investigator of the MyHeart Counts cardiovascular health study, launched in collaboration with Apple in 2015. In 2016, he was part of the winning team of the $75m One Brave Idea competition funded by Google, the AHA and Astra Zeneca. Father to three young Americans, in his "spare" time, he tries to understand American football, plays the saxophone in a jazz quartet, and conducts research on the health benefits of single malt Scotch whisky.

The goal of the session is to introduce the concept of precision medicine and highlight some of the critical contributions made by clinical genomics to its origination and evolution. The session will briefly recap rapid advancements in genomic technology and illustrate the utility of genomics for clinical medicine using specific patient examples. Some of the essential algorithmic approaches to the interpretation of human genomes will be discussed. Areas where current short read technologies perform well are discussed, as well as areas where new approaches are required. In the context of precision and accuracy in genomics, newer technologies such as long read sequencing and new algorithms for improving test performance in complex areas of the genome will be introduced. The use of gold standards in genomics and the limitations of the human reference genome will be discussed. Finally, the session will highlight the near-term future of clinical genomics. Throughout the talk, illustrative patient examples are used including those from the Undiagnosed Diseases Network.

At the end of this session, participants should:
1. Understand what is meant by precision medicine and be able to provide examples;
2. Understand the opportunity and challenge represented by our ability to sequence whole human genomes at scale for clinical medicine;
3. Understand areas of need in the development of clinical genomics;
4. Understand the power and limitations of the human reference genome;
5. Understand the current state of the art in the application of clinical genomics to rare disease; and
6. Understand how genomics will move from rare disease to affect every patient in the healthcare system.

K2 - Genomic Study on Molecular Pathways of Cancer Development and its Relevance to Cancer Precision Medicine

Prof LEUNG Suet-yi, *MBBS, MD, FHKAM (Pathology), FHKCPath, FRCPath (UK), FRCPA*
Associate Dean (Research), Y W Kan Professor in Natural Sciences,
Chair of Gastrointestinal Cancer Genetics and Genomics,
Hereditary Gastrointestinal Cancer Genetic Diagnosis Laboratory,
Department of Pathology, Li Ka Shing Faculty of Medicine,
The University of Hong Kong,
Queen Mary Hospital, Hong Kong

Professor Suet-yi Leung is the Associate Dean (Research), Li Ka Shing Faculty of Medicine at The University of Hong Kong. She is also the YW Kan Endowed Professor in Natural Sciences and Chair in Gastrointestinal Cancer Genetics and Genomics in the Department of Pathology. Her research interests are focused on the molecular genetics, epigenetics and genomics of gastric and colorectal cancers, and their applications in molecular classification and genetic diagnosis to facilitate cancer prevention and treatment. Using genomic technologies, including next generation sequencing, her group has identified many novel gastric cancer driver genes, including ARID1A, RHOA and RNF43, and defined the genomic and epigenomic landscapes of various molecular subtypes of gastric cancer. Her team also established and systematically characterized a large repertoire of organoids from patient gastric normal and cancer tissues, encompassing comprehensive molecular subtypes, thus provides a valuable resource for understanding both cancer biology and anti-cancer drugs that may facilitate the development of precision cancer therapy. Her team has first described the heritable germline methylation of the MSH2 gene promoter as a cause of Lynch Syndrome, and subsequently identified EPCAM deletion as the cause of MSH2 methylation, the latter has become a standard genetic diagnosis test for Lynch Syndrome. Her team also uncovered the critical role of BRAF and RNF43 in the serrated neoplasia pathway, provided critical molecular data to support the pathogenic role of RNF43 germline mutation in Serrated Polyposis Syndrome families. The long term goal of her laboratory is to identify novel genes that are important for the causation of gastric and colorectal cancer, and to explore the use of some of these genes as markers for early detection, prognostication or drug targets.

Genomic studies of cancer have revealed the molecular diversity and organ-specific differences in pathways of cancer development with therapeutic implications. Using gastrointestinal cancers as model, gastric and colorectal cancers shared some common oncogenic pathways yet with marked divergent differential incidence of oncogenic pathway alterations. Some of these molecular alterations are emerging as biomarkers for prognostication, guiding patient treatment as well as prediction of genetic predisposition for focused preventive screening. Emerging technologies including next generation sequencing can facilitate the discovery of novel genes or pathways that contribute to development of inherited or sporadic gastrointestinal cancers. Coupled with development of new generation organoid cancer cell models, it enables direct culture of patients' cancer cells for drug sensitivity testing, and correlation with genomic changes to identify genomic determinant of drug response. Overall, coupling genomics and organoid-based drug screening, linking back to patient pathology and therapeutic response will empower the development of precision cancer therapy.

K3 – Observational Data for Biomedical Discovery

Dr Nicholas TATONETTI, *PhD*
Herbert Irving Assistant Professor of Biomedical Informatics,
Departments of Biomedical Informatics, Systems Biology, and Medicine,
Columbia University, United States

Dr Nicholas Tatonetti is assistant professor of biomedical informatics in the Departments of Biomedical Informatics, Systems Biology, and Medicine and is Director of Clinical Informatics at the Institute for Genomic Medicine at Columbia University. He received his PhD from Stanford University where he focused on the development of novel statistical and computational methods for observational data mining. He applied these methods to drug safety surveillance and the discovery of dangerous drug-drug interactions. His lab at Columbia is focused on expanding upon his previous work in detecting, explaining, and validating drug effects and drug interactions from large-scale observational data. Widely published in both clinical and bioinformatics, Dr Tatonetti is passionate about the integration of hospital data (stored in the electronic health records) and high-dimensional biological data (captured using next-generation sequencing, high-throughput screening, and other "omics" technologies). Dr Tatonetti has been featured by the New York Times, Genome Web, and Science Careers. His work has been picked up by the mainstream and scientific media and generated thousands of news articles.

Observation is the starting point of discovery. Based on observations, scientists form hypotheses that are then tested and evaluated. In the information-age, trillions of observations are being made and recorded every day – from online social interactions to the emergency room visit. With so much data readily available, generating hypotheses using a single scientist's mind is no longer sufficient. Instead, we must turn to computational algorithms to "mine" for new hypotheses and relationships for us. Data mining is an emerging field dedicated to training algorithms to recognize patterns in enormous sets of data to automatically identify new hypotheses.

In this talk, I will discuss how we use data mining algorithms to identify unexpected effects of drugs used singly and in combination with other drugs. Drug-drug interactions (DDIs) are an important and understudied public health concern. DDIs are difficult and expensive to study because of the complex combinatorial nature to their investigation. I have developed new methods for mining clinical data and then discovered and validated two previously unknown novel drug-drug interactions. In the first, published in 2011, I found that paroxetine (selective serotonin reuptake inhibitor) and pravastatin (HMG-CoA reductase inhibitor) together cause hyperglycemia. In the second, published in 2016, I found that ceftriaxone (cephalosporin antibiotic) and lansoprazole (proton-pump inhibitor) are associated with prolonged QT syndrome (LQTS). In both cases, I used a combination of data mining and laboratory experiments to discover and validate the new DDI. First, I mined the FDA's Adverse Event Reporting Systems for signs of drug-drug interactions using supervised machine learning methods. These algorithms were trained to recognize safety signals using single-drug effect and then used to identify when pairs of drugs mimic these effects. I then used electronic health records to corroborate the putative DDIs. In each case, using commonly collected data during clinical practice. For paroxetine and pravastatin we looked at blood glucose values before and after drug combination exposure and, for ceftriaxone and lansoprazole, we used the electrocardiograms recorded post drug combination therapy. I then validated the findings prospectively using model systems (a diabetic mouse model for diabetes and a single cell electrophysiology experiment for LQTS). These studies are the first to use big patient data to discovery a drug interaction and then use prospective experiments to validate the findings.

Using integrative informatics methods, we are able to discover drug-drug interactions that no one considered possible before. In many cases these experiments can be executed in high-throughput and by robotic systems, with the ultimate goal of automating the scientific method.

K4 - Data Analytics & Applications in Hong Kong Hospital Authority: Past, Present & Future

Ms Eva TSUI Lai-hing
BSoc.Sc., MSoc.Sc.(Applied Statistics)
Chief Manager, Statistics & Workforce Planning Department,
Hospital Authority, Hong Kong

Dr Anderson TSANG Chun-on
MBBS(Hons), FRCS(Edin)
Clinical Assistant Professor, Division of Neurosurgery,
The University of Hong Kong

Ms Eva Tsui was graduated from the University of Hong Kong, obtaining bachelor and master degrees with a major in Economics and Applied Statistics respectively. In 1994 she joined the Hospital Authority (HA) head office as a statistician, and since 2008 she has been the Chief Manager overseeing the Statistics Department with over 40 professional statistical staff. Her Department's mission is to translate HA's massive volume of administrative and clinical data into official statistics, useful information and actionable insights, supporting HA in informed decision making in wide-ranging aspects. She contributed to the development of a number of predictive models, analytic and projection tools which are applied corporate-wide. Recently she has been advancing the Department's technical expertise into big data analytics, tapping HA's unstructured data and in collaboration with academia.

Dr Anderson Tsang (MBBS, FRCS) obtained his medical degree in The University of Hong Kong, and completed his specialty training in Neurosurgery at Queen Mary Hospital, Hong Kong. With the support of the HMRF research fellowship scheme, he finished a clinical and research fellowship in endovascular stroke treatment in Toronto Western Hospital, University of Toronto. He is currently clinical assistant professor of Neurosurgery at the University of Hong Kong, with a research focus on endovascular intervention and cross-specialty translational research in cerebrovascular diseases.

Since inception in 1990 the Hong Kong Hospital Authority (HA) has implemented public healthcare IT systems, by phases and by modules incrementally, to collect patient-based administrative and clinical data across almost all aspects of hospital healthcare services. It is a sharing to illustrate how data analytics and statistical modelling skills have been applied to transform this huge volume of real-world data into useful information, and then into actionable insights, to inform clinical service planning and developments in HA, aiming for impacts on the healthcare system and population health.

The first illustrative case dated back to more than 10 years ago when HA intended to launch a community-based Hospital Admission Risk Reduction Program for the Elderly (HARRPE). It portrays a cycle commencing from needs assessment to data-driven tools, implementation and followed by evaluation. In view of the high caseload of elderly patients having unplanned readmission to medical wards within 28 days of hospital discharge, a risk prediction tool was developed to estimate the likelihood for individual elderly patients through a logistics regression model building and validation using over one million of episodes respectively. This Model relies on 14 predictor variables which have a standardized data definition across all HA hospitals and a sustainable data quality over time. The Community Health Call service was piloted in two hospital clusters, involving trained nurses to proactively make telephone calls to high risk elders (with predicted score higher than a predefined cut-off) and their carers within 48 hours after hospital discharge. This pilot intervention was evaluated to be effective in reducing A&E attendances, emergency medical admissions and acute bed days by around 20%, therefore leading to the set-up of one centralized Community Health Call Centre for overall HA in 2009. This risk prediction tool was also automated as a daily screening tool to identify high risk elders for the Centre. To an extent this a-decade-ago project had met the 5-V criteria of a big data application. While this Model is subject to regular review on its predictive performance, continuous data exploratory work is going on to identify additional predictor variables or explore new applications. The 15th predictor variable candidate is "polypharmacy" i.e. number of regular drug items taken. After a complex process to devise an operational rule to quantify this measure from huge volume of drug dispensing transactions, despite it is strongly associated with elderly unplanned readmission, it was ultimately discarded due to its marginal contribution towards overall predictive performance, after striking a balance between gain and investment regarding "small" versus "big" in application.

The second illustrative case is the first HA-HKU big data collaborative project which commenced in end 2017. In the current phase it is a research study aiming to develop a rapid automated tool to predict the likelihood of large vessel occlusion (LVO) based on HA's retrospective data of plain CT images and clinical information. The topic was chosen as LVO is the most severe form of acute ischemic stroke with a very high mortality rate as compared to other types of stroke, but it is highly treatable and the earlier the better. After a collaborative input towards the study design, a version-1 algorithm using the deep learning convolutional neural network model has been developed by HKU research teams, with predictive performance comparable to other validated instruments'. With additional data and expertise input from a panel of HA radiologists on image labelling, now it is being enhanced into version-2 algorithm. Next is to run the enhanced algorithm among a historical full-year cohort of ischemic stroke patients in the HA Data Collaboration Lab. To complement, HA's statistical team has developed text analytics algorithms based on regular expression and XGBoost models to automate extraction of stroke symptoms and GCS scores from free text discharge summary and transform them into structured data for HKU's algorithm to generate the predictive score for individual subjects. With an ultimate aim of translating this research findings and risk prediction algorithm into clinical practice at HA service locations, HKU is planning the next phase of translational research in collaboration with HA and its clinicians, also incorporating evaluation on the structure, process and outcome of the pilot implementation.

S1 - Promoting Alcohol-related Attitudinal and Behavioural Change amongst Adolescents through Internet Intervention: A Cluster Randomised Controlled Trial

Patrick IP[1], LAM Tai-hing[2], HO Sai-yin[2], Wilfred WONG Hing-sang[1], Frederick HO Ka-wing[1], Rosa WONG Sze-man[1], Keith TUNG Tsz-suen[1], CHOW Chun-bong[1]
[1]*Department of Paediatrics and Adolescent Medicine, The University of Hong Kong, Hong Kong*
[2]*School of Public Health, The University of Hong Kong, Hong Kong*

Background and Objectives: Underage drinking is an important public health problem, but previous prevention/intervention yielded mixed results. This study aimed to compare the effectiveness of an Internet intervention against conventional health education.

Design: This is a cluster randomised controlled trial with parallel group design. Participating schools were randomised to the Internet intervention or the conventional health education group (control) with 1:1 allocation ratio.

Participants: Local secondary schools (excluding schools targeting international students and students with special needs) were eligible. Secondary 1–3 students of the participating schools were invited. Students who could not comprehend basic Chinese were excluded.

Interventions: The Internet intervention was a web-based quiz game competition, in which participating students would answer 1,000 alcohol-related multiple-choice quiz questions. They were also incentivised to refer the game in their social circle. Conventional health education group received a promotional package on equivalent alcohol-related knowledge.

Main Outcome Measures: Presence and number of units of alcohol drinking in the past 30 days were self-reported before intervention (baseline), as well as one month, and three months after the intervention completion.

Results: 30 schools were recruited using stratified random sampling, in which 15 (4,294 students) were randomised to the Internet intervention arm and 15 (3,498 students) to the conventional health education arm (control). No between-group differences were identified at baseline. Overall retention rate for students was 86.0%. One month after the completion of intervention, students randomised to the Internet group were less likely to drink (risk ratio [RR] 0.79, 95% confidence interval 0.68–0.92, P=0.003) and drank less alcohol (β -0.06, -0.11 to -0.01, P=0.02). These remained statistically significant three months after the completion of intervention (RR 0.86, 0.74–0.999, P=0.048; β -0.06, -0.11 to -0.01, P=0.02).

Conclusions: This Internet intervention has reduced the risk of underage drinking by 21% post-intervention compared with the conventional health education.

Trial Registration: ClinicalTrials.gov NCT02450344

Project Number: 12132761

S2 - Promoting Mental Well-being of Pregnant Women with Mindfulness-based Childbirth and Parenting (MBCP): A Randomized Controlled Trial in Hong Kong

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Introduction and Project Objectives: A mother's mental health during pregnancy can influence the pregnancy outcome, her child's health and development, and the father/partner's mental health. This randomized controlled trial aimed to evaluate the effectiveness of the Mindfulness-based Childbirth and Parenting (MBCP) program in Chinese pregnant women in Hong Kong as compared to an active control group.

Methods: This trial had two study arms: MBCP versus Antenatal Childbirth Education and Support. A total of 183 pregnant women and their significant others (n=175) were included. The interventions in both conditions consisted of 9 weekly sessions and a half-day retreat delivered prenatally and a reunion session held after childbirth. Outcomes were measured at baseline (T1), at the last prenatal session (T2), 6-8 weeks postpartum (T3), and six months after childbirth (T4). The primary trial outcome was the Mental Component Score (MCS) of the 12-item Short Form Survey (SF-12) at T4.

Results: Compared to the control group, ANCOVA results demonstrated significant beneficial effects in the MBCP group in MCS scores (mean difference and its 95% Confidence Interval: 3.2 (0.1, 6.3), p=0.045) at six months postpartum. Before adjusting to a more stringent significance level, the results favoured the MBCP group on Center for Epidemiologic Studies Depression Scale (CESD) scores (p = 0.018), State-Trait Anxiety Inventory State (STAI-S) scores (-4.5 (-7.4, -1.7), p = 0.002), Five Facet Mindfulness Questionnaire (FFMQ) total scores (5.2 (1.6, 8.8), p=0.005) at T4, Prenatal Pregnancy Anxiety (PPA) scores (-1.4 (-2.6, -0.1), p=0.030), and Multidimensional Assessment of Interoceptive Awareness (MAIA) scores (0.2 (0.1, 0.3), p=0.03) before childbirth at T2, and Edinburgh Postnatal Depression Scale (EPDS) scores at T3 (-1.5 (-2.9, -0.1), p = 0.034). With an adjusted significance level at 0.005 for secondary outcomes, beneficial effects of MBCP were still seen on STAI-S and FFMQ scores. Linear mixed models showed similar results, as did per protocol analysis of those who attended 4 or more sessions in both groups. No significant beneficial effects were seen in clinical outcomes related to childbirth. Subgroup analyses showed that those women at risk for clinical depression at baseline benefited more from MBCP in the long term. No fetal death or severe adverse events were reported by the participants.

Conclusions: MBCP has a positive effect on the mental well-being of Chinese pregnant women during pregnancy that is maintained six months after childbirth.

Project Number: 11120111

S3 - The Health Effects of Traffic-related Air Pollution in Hong Kong School Children

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Introduction and Project Objectives: Traffic exhaust is a principal source of ambient air pollution in urban areas. There are increasing concerns in recent years about the adverse health effects of traffic-related air pollution, especially in schoolchildren. However, there is little information on this topic in Hong Kong. We therefore conducted a cross-sectional study to investigate the impact of all traffic exhaust on air pollution in the school environment and its health effects on the students.

Methods: This was a cross-sectional study design. We selected the primary schools based on their nearby roads and traffic densities. We conducted air quality assessments at the school environment and on-roads surrounding the schools. We also recruited 2,319 primary students (aged between 7 and 14 years old) and each of them received a health survey including spirometry testing and anthropometric measurements. Their parents/guardians were also required to complete a self-administered questionnaire that collected information about respiratory symptoms/diseases. The major health outcomes in the present study were lung function parameters, rhinitis and respiratory diseases. The lung function parameters included the forced vital capacity (FVC), forced expiratory volume in the first second (FEV1), peak expiratory flow (PEF), and maximum mid-expiratory flow (MMEF). Mix linear regression and logistic regression analyses were used to assess the relationships between health outcomes and the school environment air pollution as well as the traffic counts.

Results: The correlations between on-road air pollutions/traffic counts and the air pollution at school environment were weak with correlation coefficients ranged from 0.14 to 0.53. Generally higher levels of air pollution/traffic count were associated with lower lung function parameters. Among the four lung function parameters, MMEF was the most sensitive. Lower level of MMEF was associated with higher PM2.5 (β for an interquartile-range [IQR]: 61.8, 95% confidence interval [CI]: 32.3-92.7), Black Carbon (BC) (β for an IQR: 53.7, 95% CI: 11.5-106.1), and total traffic count (β for an IQR: 26.3, 95% CI: 11.8-60.1). Total traffic count was also associated with rhinitis (OR for an IQR: 1.48; 95% CI: 1.03-2.16). There were no significant associations observed for diesel vehicles and health outcomes in this study.

Conclusions: Higher level of air pollution at school environment was associated with poorer respiratory health in primary school children. Our study also suggests that total traffic surrounding school was associated with poorer respiratory health (i.e. lower MMEF and higher prevalence of rhinitis) in the students.

Project Number: 11121031

S4 - Improving Running Biomechanics Prevents Injury in Novice Runners

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Introduction and Project Objectives: Running is one of the most popular sports worldwide. However, up to 79% of runners incur a single injury in a given year. Compared to experienced runners, beginners are even more vulnerable. Among different biomechanical risk factors, high level of vertical loading rate has been identified as a key marker to be associated with a wide range of injuries in runners. Previous studies have utilized gait retraining to successfully lower impact loading in runners but it remains unknown whether such a change in the running biomechanics prevents prospective injury. Hence, this randomized controlled trial sought to examine the biomechanical and clinical effect of gait retraining in a group of novice runners.

Methods: 320 novice (experience < 2 years) runners were recruited from local running clubs and they underwent a baseline running biomechanics assessment on an instrumented treadmill at 8 km/h and 12 km/h using their usual footwear. We measured vertical average and instantaneous loading rate (VALR and VILR) from the force plate data. All participants were then randomized to either gait retraining or control group. In the gait retraining group, participants received a 2-week gait retraining and they were provided real-time biofeedback of the step-by-step vertical ground reaction force profile. In the control group, participants received treadmill running exercise but we did not receive any feedback on their running biomechanics. The training time was identical between the two groups. Participants were reassessed after the training, and their injury profiles were monthly tracked using an online surveillance platform for 12 months.

Results: Runners in the gait retraining group exhibited a significant reduction in the VALR and VILR following gait retraining ($p<0.001$, Cohen's $d>0.99$), while VALR and VILR were either similar or slightly increased in the control group ($p=0.001$-0.461, Cohen's $d=0.03$-0.14). 16% runners in the gait retraining group and 38% runners in the control group reported injury at the one-year follow-up. The hazard ratio between gait retraining and control groups was 0.38, indicating a 62% lower injury risk in the runners undergone gait retraining, when compared with controls.

Conclusions: A 2-week gait retraining program using real-time biofeedback is effective in lowering vertical loading rates in novice runners. More importantly, by only controlling this biomechanical parameter, the injury risk can be 62% lower in this high-risk group of runners.

Project Number: 12131621

S5 - A Randomised Controlled Trial on Perioperative Elderly Patients Undergoing Colorectal Cancer Surgery with Enhanced Geriatric Input

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Introduction: Colorectal cancer is the second commonest cancer in Hong Kong, affecting a significant number of elderly patients. Major colorectal cancer surgery on elderly patients is associated with higher morbidity, mortality, readmission and longer length of stay. The comprehensive geriatric assessment has been shown to improve clinical management of elderly patients. Orthogeriatric care postoperatively has also been shown to improve outcomes following hip fracture surgery and reduce length of stay.

Project Objectives: To investigate the effectiveness of Enhanced Geriatric input in perioperative management of elderly patients undergoing elective colorectal surgery.

Methods: Seventy-four patients undergoing elective colorectal cancer resection aged 70 years or over were randomly allocated to one of two groups 1) conventional surgical care (SC) or 2) surgical care with enhanced geriatric input (SCG) in a single centre colorectal unit. Patients had comprehensive geriatric assessment preoperatively in addition to a routine preoperative assessment. Patient were jointly managed with a Geriatric team preoperatively with implementation of early discharge planning by the cologeriatric multidisciplinary team. Outcome measures include: Primary outcome will be the postoperative length of stay. Secondary outcomes are 30-day morbidity and mortality, destination of discharge.

Results: During the period between May 2015 to April 2017, 74 patients were recruited for the study. Male patients were more predominant in the SC group ($p<0.05$) but mean age, BMI and ASA grade were similar. Preoperative cognitive assessment found mean mental state score (MMSE) to be lower in the SC group but delirium and confusion scores were similar. Following surgery, the mean time to ambulation and time to flatus were significantly quicker in the SCG group. The SCG group also had a significantly lower 30-day morbidity with less paralytic ileus. Postoperative cognitive functions were similar in both groups. Length of stay was significantly lower in the SCG group compared to SC (7.1days vs 14.0 days; $p<0.0001$), with the majority of patients discharging to home than to rehabilitation care.

Conclusions: The enhanced combined cologeriatric perioperative care on elderly patients undergoing elective colorectal resection reduced hospital stay. Patients had earlier ambulation, passage of flatus and consumption of diet post operatively compared to the standard care group with lower complications. There was no improvement in their general fitness or mental status with enhanced cologeriatric perioperative care.

Project Number: 12130701

S6 - Cost and Cost-effectiveness Analysis of Renal Replacement Therapy Modalities for Patients with End-stage Renal Disease in Hong Kong: Comparison between Peritoneal Dialysis and Haemodialysis

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Introduction: Renal replacement therapy (RRT) by peritoneal dialysis (PD) or haemodialysis (HD) is a life-sustaining treatment for patients with end-stage renal disease (ESRD). According to the Hospital Authority "Peritoneal Dialysis First" policy PD is the first-line maintenance RRT for ESRD patients, but haemodialysis (HD) is preferred in many developed countries. HD can be done in the hospital or at home.

Objectives: 1) To estimate the local annual costs of care of ESRD in the first and second (proxy of subsequent) years of PD, hospital-based haemodialysis (HHD) and nocturnal home HD (NHD), 2) To compare the lifetime cost-effectiveness of PD, HHD and NHD.

Methods: A cost analysis was performed on 402 ESRD patients who were on maintenance PD (n=189), HHD (n=170) and NHD (n=43) from the healthcare provider and societal perspectives. Empirical data on healthcare utilization rates were extracted from their medical records and converted to cost based on unit costs published in the 2017 Government Gazette. We carried out a questionnaire survey on patients / caregivers' out-of-pocket costs and time spent on transportation and dialysis. Data on utility scores of ESRD patients, and annual probabilities of health state transitions, modality switching, renal transplantation, and mortality were identified from published data. Lifetime cost-effectiveness analyses (CEA) by Markov modelling were performed based on empirical annual costs and published outcome data to estimate lifetime costs, quality-adjusted life-years (QALYs) and cost-effectiveness of PD, HHD and NHD.

Results: HHD had the highest annual costs from both healthcare provider / societal perspectives in the initial year (HHD=USD$51,289 / $57,968; PD=USD$15,188 / $24,255; NHD=USD$28,636 / $31,031; P<0.001) and second year (HHD=USD$46,272 / $52,951; PD=USD$10,358/$19,426; NHD=USD$11,157 / $13,552; P<0.001). Lifetime CEA showed that HHD (lifetime cost USD$148,083; 7.14 QALYs) was dominated by PD (USD$78,920; 7.32 QALYs). From the healthcare provider perspective, NHD had the highest effectiveness (13.68 QALYs), but at a higher lifetime cost (USD$155,318) than PD. The incremental cost-effectiveness ratio (ICER) was USD$12,020 per QALY gained for NHD over PD. From the societal perspective, the ICER was USD$10,357 per QALY gained for NHD over PD. Both ICERs fell within generally acceptable CE thresholds. Sensitivity analysis showed that all model parameters had minimal impact on ICER values.

Conclusions: PD was cost-saving relative to HHD as the first-line RRT and NHD was a cost-effective alternative to PD. The findings support the "Peritoneal Dialysis First" policy as maintenance RRT for ESRD patients in Hong Kong. NHD can be recommended as the first-line maintenance RRT for patients whose conditions are suitable.

Project Number: 13142451

S7 - A Randomised Controlled Trial Evaluating Efficacy of a Psychological Intervention Based on Commonsense Model in Improving Mental Health and Self-care among Type-2 Diabetes Mellitus Patients

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Introduction and Project Objectives: Individuals with type-2 Diabetes Mellitus (T2DM) are more likely to develop depression and other mental health problems than the general population. Poor mental health is significantly associated with poor adherence to self-care activities and DM complications among T2DM patients. The Commonsense Model (CSM) posits that how patients view their illness, a concept known as illness representations, plays an important role in their coping and disease outcomes. This study examined whether an intervention based on the CSM would result in better mental health and adherence to self-care activities among T2DM patients.

Methods: A prospective parallel group two-arm randomised controlled trial (RCT) was conducted. A total of 455 T2DM patients were recruited from an outpatient DM clinic and were randomised to intervention or control group. Participants in the intervention group attended five weekly group sessions delivered by a psychologist while those in the control group received five education booklets about DM. They were evaluated at baseline, one month and six months after the intervention. Measures on depression, anxiety, negative affect, diabetes-related distress, coping, self-care, self-care self-efficacy, IR towards T2DM were collected using self-reported survey, while blood glucose level was assessed from medical record.

Results: Results from the 2 x 3 linear mixed model analysis using modified intention to treat showed that participants in the intervention group produced statistically significant improvement in level of self-care ($p<.001$), self-care self-efficacy ($p<.001$), and use of adaptive coping ($p=.010$) compared to the control group over time. Subgroup analyses on gender and DM complications further indicated significant improvement in illness representations of personal control ($p=.035$), treatment control ($p=.004$) and cyclical timeline ($p=.025$) in among male participants in the intervention group; and significant improvement in illness representations of personal control ($p<.009$) and emotional representation ($p<.013$) among participants without any complication in the intervention group, indicating that the intervention produced better improvements among male participants and participants without any complications. Results of the process evaluation indicated that participants reported positive feedbacks to the intervention, perceived improvement in various domains, and wished to participate in similar program in the future.

Discussion: The study showed that intervention based on CSM was effective in improving self-care and coping among DM patients. The intervention also demonstrated high level of feasibility and acceptability. Findings provided important insights on integrating illness representations in improving health-related outcomes for patients with T2DM.

Project Number: 12130751

S8 - Relationship between Chronic Inflammation and Vitamin D Level to Prevalent and Incident Frailty in Older Adults

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Objective: To study the relationship between chronic inflammation as represented by C Reactive Protein (CRP) and vitamin D level in prevalent and incident frailty in older adults in Hong Kong

Method: Archived serum samples from a cohort of 4,000 men and women of age >65 years were analysed for high sensitivity CRP (hsCRP) and 25-OHD. Participant characteristics including demographics, diseases, use of vitamin D supplements, seasons of sample collection were used as covariates. Items in the Fried's phenotype for frailty were recorded at baseline and after 4 years. Logistic regressions and path analysis were used to examine the relationship between hsCRP, 25 ODH with baseline (prevalent) and 4 year (incident) frailty status.

Results: At baseline, significant association with pre/frailty and frailty was found at 25-OHD <40 nmol/L in women (OR 2.4; 95% CI 1.3, 4.6) and <45 nmol/L in men (OR 2.7; 95% CI 1.4, 5.0). After full adjustment, CRP was associated with a small but significant risk for frailty only in women, while vitamin D was protected in both genders. Men with 25-OHD <45 nmol/L were 2.53 time more likely to be frail (95% CI 1.29, 4.95). At 4 years, there was no significant trend found between 25-OHD, CRP and incident frailty. However, very high CRP (>10 mg/L) was associated with 4.8 fold increase in incident frailty (95% CI 1.85, 12.44) in men.

Conclusions: Vitamin D cut-offs associated with frailty were different from that in osteoporosis, and were different between the genders. Low vitamin D level was associated with frailty, irrespective of CRP levels. Both vitamin D and CRP levels cannot predict incident frailty after 4 years.

Project Number: 12133811

S9 - Detection of Methylated Septin 9 DNA in Blood for Diagnosis, Prognosis and Surveillance of Patients with Colorectal Cancer

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Background: With the increasing incidence and mortality of colorectal cancer (CRC), early and accurate diagnosis is of paramount priority to combat this cancer. Epigenetic alterations such as DNA methylation are innovative biomarkers for CRC, due to their stability, frequency, and accessibility in bodily fluids. In particular, detection of methylated septin 9 (mSPET9) DNA in blood was recently approved by the Food and Drug Administration of the United States for the screening of CRC.

Aim: To evaluate the role of detecting methylated SEPT9 in blood for diagnosis, prognosis and surveillance of patients with CRC.

Method: Blood samples were prospectively collected from patients scheduled for colonoscopy in our hospital or newly diagnosed to have CRC. For cancer patients, blood was taken immediately before and serially after resection of the primary tumor. Blood samples were processed for the determination of mSEPT9 and carcinoembryonic antigen (CEA) in a blinded manner. mSEPT9 DNA was determined by a commercially available assay (Epi proColon 2.0, Epigenomics, Germany).

Results: A total of 282 patients (117 CRC, 45 with advanced colorectal adenoma, 50 with non-advanced adenoma and 70 normal control) were included. The overall sensitivity of using mSEPT9 methylation status for diagnosing CRC was significantly higher than using elevated CEA levels (73.2% vs 48.2%; p value < 0.001). The sensitivities of both tests increased with more advanced tumor staging (mSEPT9: P = 0.004 and CEA: P = 0.04). Combined mSEPT9 and CEA had higher accuracy than single CEA or mSEPT9 (P = 0.009 and 0.532 separately). An increase in the methylation level of mSEPT9 detected in the post-operative samples was associated with a higher mortality rate (15.2% vs 1.8%; P = 0.024) and the presence of metastasis (27.3% vs 7.0%; P = 0.013).

Conclusions: mSEPT9 was more sensitive than CEA for diagnosing CRC, and combined mSEPT9 and CEA was even more sensitive for CRC. After curative resection, detection of increased mSEPT9 methylation level may indicate adverse outcomes.

Project Number: 01121026

S10 - A Randomised Controlled Trial of Bilateral Movement-based Computer Games Training to Improve Motor Function of Upper Limb and Quality of Life in Sub-acute Stroke Patients

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Introduction: Sensorimotor impairment, which could significantly affect the motor function of upper limbs and quality of life, is common in stroke survivors. Application of bilateral movement training in a virtual reality-based environment could provide a platform for engaging and motivating the patients, as well as facilitating the effects of self-assisted and highly repetitive task-oriented training.

Objectives: To investigate whether bilateral movement-based computer training (BMCT) would be superior to the conventional training in improving the motor control and functional use of paretic upper limb in sub-acute stroke patients.

Methodology: A stratified, single-blinded, randomised controlled trial (RCT) was conducted in Geriatric Day Hospital of Shatin Hospital. Patients with sub-acute stroke were randomly assigned to one of the two groups for 30 minutes of upper limbs training: (1) BMCT and (2) video-directed conventional training (VDCT). Both groups also received standard conventional physiotherapy training program for 16 intervention sessions over 8-week period. The motor control and function of paretic upper limb were evaluated by Fugl-Meyer Assessment of Upper Extremity (FMA-UE), Action Research Arm Test (ARAT) and Grip Strength (GS). Health-related quality of life was measured by the Hong Kong version of the Short-Form Health Survey (SF-36). All the outcomes were recorded at baseline, after 8 intervention sessions (A_1) and 16 intervention sessions (A_2), and 4 weeks after the end of the whole intervention period (A_{FU}).

Results: Of the 93 patients participating in the study, 47 (50.5%) were allocated to the BMCT group. The average age of the patients in BMCT and VDCT groups were 65.1±10.2 and 66.0±9.0 years old, respectively. Both groups demonstrated statistically significant increases in mean scores of FMA-UE, ARAT and GS (affected hand) from baseline to A_1, A_2, and A_{FU}. The mean changes from baselines in FMA-UE, ARAT and GS (affected hand) scores were statistically significantly greater in the BMCT group than the VDCT group at all visits (all p-values < 0.05). No significant difference between the groups was identified in the mean changes of SF-36 scores from baseline at any time point.

Conclusions: The results of this RCT demonstrated that application of BMCT is effective in improving the motor control and function of paretic upper limb in sub-acute stroke patients. BMCT is regarded as a useful complement to conventional therapy in stroke rehabilitation. Implementation of this technology at home or in day care centres could motivate patients to exercise as well as to maintain or even improve their physical health after being discharged from rehabilitation.

Project Number: 02133096

S11 - Identifying the Genetic Causes Underlying Prenatally-diagnosed Structural Congenital Anomalies (SCAs) by Whole-exome Sequencing (WES)

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Introduction: Whole-exome sequencing (WES) has become an invaluable tool for genetic diagnosis in Paediatrics. However, it had not been widely adopted in the prenatal setting at the time of this study. We evaluated the use of WES in prenatal genetic diagnosis in fetuses with structural congenital anomalies (SCAs) detected on prenatal ultrasound.

Methods: Thirty-three families with fetal SCAs on prenatal ultrasonography and normal chromosomal microarray results were recruited. Genomic DNA was extracted from various fetal samples including amniotic fluid, chorionic villi, and placental tissue. Parental DNA was extracted from peripheral blood when available. We used WES to sequence the coding regions of parental-fetal trios and to identify the causal variants based on the ultrasonographic features of the fetus.

Results: Pathogenic mutations were identified in three families (n=3/33, 9.1%), including mutations in *DNAH11*, *RAF1* and *CHD7*, which were associated with primary ciliary dyskinesia, Noonan syndrome, and CHARGE syndrome, respectively. In addition, variants of unknown significance (VUSs) were detected in six families (18.2%), in which genetic changes only partly explained prenatal features.

Conclusions and Discussion: WES identified pathogenic mutations in 9.1% of fetuses with SCAs and normal chromosomal microarray results. Our diagnostic yield is comparable to the PAGE (Prenatal exome sequencing analysis in fetal structural anomalies detected by ultrasonography) study (Lord et al. Lancet 2019). WES facilitates genetic diagnosis of SCAs, which in turn enables more accurate prediction of prognosis and recurrence in subsequent pregnancies. However, the Joint Position Statement from the International Society for Prenatal Diagnosis, the Society for Maternal Fetal Medicine and the Perinatal Quality Foundation does not support its routine use as a diagnostic test due to insufficient validation data and knowledge about its benefits and pitfalls. Currently it is ideally done in the setting of a research protocol. Databases for fetal genotype-phenotype correlations and standardized guidelines for variant interpretation in prenatal diagnosis need to be established to facilitate the routine use of WES in prenatal diagnosis.

Project Number: 02131816

S12 - Cone Rescue in Retinitis Pigmentosa by the Treatment of Lycium Barbarum

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Introduction: *Lycium barbarum* L. (also known as "Goji berry"), a traditional Chinese herbal medicine, has been a common herb in the traditional Chinese pharmacopoeia for centuries. Its antioxidative effect has been widely shown to provide neuroprotection to the eye, and it would, therefore, be interesting to determine if *Lycium barbarum* help delay vision deterioration in patients with retinitis pigmentosa.

Project Objectives: Cone rescue is a potential method for delaying deterioration of visual function in Retinitis pigmentosa (RP). This study aimed to investigate the treatment effect of *Lycium barbarum* L. (LB) supplement on retinal functions and structure in RP patients after a 12-month intervention trial.

Methods: It was a randomized controlled trial with a double-masked design. RP subjects were recruited and received a detailed eye examination including ETDRS (90% and 10% contrast) Visual Acuity (VA), Humphrey Field Analysis (HFA) (Central 30-2 and 10-2 full threshold), Full-field flash Electroretinogram (ffERG) and macular structural evaluation by Optical Coherence Tomography (SD-OCT) before the intervention. The RP subjects who were fitted for the inclusion criteria were randomly allocated into either LB (treatment) or placebo (control) groups. Each subject would have a 12-month supply of packs of granules (LB or placebo) and have follow up eye examination in every 6 months. Counting the packs of granules had conducted to counter-check the compliance.

Results: A total of 42 RP subjects (23 in treatment group and 19 in control group) completed the 12- month intervention. The compliance rates for treatment and control groups were 89% and 85% respectively. There were no deteriorations of either 90% or 10% contrast VA in the LB group compared with the control group (p=0.001). A thinning of macular layer was observed in the placebo group, which was not observed in the LB group (p=0.008). However, no significant differences were found in the sensitivity of visual field or in any parameters of ffERG between the two groups. No significant adverse effects were reported in the treatment group.

Conclusions: The treatment of *Lycium barbarum* supplement provides a neuroprotective effect on the retina and may help delay or minimize the deterioration of visual function and retinal structure in RP patients.

Project Number: 01121876

S13 - A Multi-centre Peer Support Program for Patients with Type 2 Diabetes in Hong Kong

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Introduction: Despite good access to clinical care and medications for the treatment of diabetes in Hong Kong, there remains a huge care gap whereby more than 90% of patients with Type 2 diabetes fail to attain treatment targets. This is attributable to suboptimal self-management support to these patients who are faced with a complex disease which requires cognitive-psychological-behavioural skills to further optimize treatment targets.

Implementation: In 2015, we implemented a Multicentre Peer Support Programme co-ordinated by diabetes nurse educators from 7 Hospital Authority Diabetes Centres and social workers from Community Rehabilitation Network. Diabetes patients known to the Diabetes Centres to have exemplary metabolic control with good communication skills and positive attitude towards their disease were invited to participate in the programme as Peer Supporters. Selected Peer Supporters were provided with two half-day training workshops to equip them with skills to support their peers. Peers with suboptimal glycaemic control with evidence of emotional distress were identified and consented to participate in the Programme. The Multicentre Peer Support Programme was run for one year during which 5 peers were allocated to 1 peer supporter matched by age, gender and insulin use. Peer supporters were asked to contact peers at least 12 times during the 12-month intervention period using any medium of communication. The purpose for the contacts was to share their experiences, seek clarification and provide mutual support.

Outcomes: We enrolled 357 Peers and 92 Peer Supporters between Jul 2015 and Apr 2016 from 7 HA Diabetes Centres. Among the Peers recruited, the mean age was 61 years with mean disease duration of 16 years. With the exception of LDL-C, risk factor control was fair with 70% exhibiting uncontrolled hypertension. After participating in the programme, there were significant reductions in HbA1c (mean -0.76%) and total cholesterol and LDL-C (mean -0.11 mmol/L for both parameters). The proportion of patients with HbA1c <7% and LDL-C <2.6 mmol/), rose from 6.7% to 23.6% and 69.3% to 77.2% respectively. Patients with higher HbA1c ≥8.0% and ≥5 phone calls with peer supporters had greater reductions in HbA1c, diastolic BP and LDL-C.

Discussion: In this Multicentre 12-month Peer Support Programme across 7 Diabetes Centres, we demonstrated the feasibility and acceptability of using a telephone-based peer support programme to improve risk factors. This suggests that patients with suboptimal metabolic control habouring emotional distress unresolved by conventional patient-doctor-nurse consultation could benefit from a Peer Support Programme to optimize their metabolic and psychological well-being.

Project Number: 07140235

S14 - Promoting Smoking Cessation for Female Smokers in Hong Kong through Training Female Youth Smoking Cessation and Reduction Ambassadors

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Introduction and Project Objectives: There has been a growing concern over an increased number of female smokers worldwide. Given the fact that female smokers are less willing than male smokers to seek help from smoking cessation services, this project aimed to bridge the gap in existing literature by describing how their utilization of smoking cessation services could be enhanced through training up female youth to deliver a brief intervention using the AWARD (Ask, Warn, Advise, Refer and Do-it-again) model.

Methods/Implementation: A coalition with Hong Kong Girl Guides Association was formed. In the first phase of the project, five thousand leaflets on woman smoking cessation were distributed. In the second phase, we trained up 160 Girl Guides who were aged 13-25 years from the Association as well as from other sources to serve as smoking cessation and reduction ambassadors (SCRAs). In the third phase, 50 out of 160 SCRAs delivered a brief intervention based on the AWARD model to at least 2 female smokers in their social circles. To evaluate the effectiveness of the brief intervention, a one-group pre-test and repeated post-test, within subjects design was used. Data collection was conducted at baseline, and 1, 3 and 6 months.

Results/Outcomes: In all, 106 female smokers received the brief intervention. At 6-month follow-up, the self-reported abstinence was 12.2%; the biochemically verified prevalence of quitting was 5.7%. Approximately 7% of participants were motivated to use smoking cessation services between baseline and 6 months.

Discussion and Conclusions: To our knowledge, this was the first project to develop a community-based network to promote smoking cessation for female smokers in Hong Kong by training SCRAs. The results of the present study provide support for the effectiveness and feasibility of using this strategy in promoting smoking cessation for female smokers in Hong Kong. However, a more proactive approach is recommended to enhance the use of smoking cessation services by female smokers. Notably, to overcome the barrier of self-initiation, future practice could consider passing on information about smokers (mainly contact details) to smoking cessation providers could then call the smokers to arrange for more comprehensive interventions. There is some evidence that such a method is effective in enhancing smokers' utilization of cessation services. Additionally, the possibility of using mobile technology to deliver text messages about cessation to support female smokers should also be explored in future research and practice.

Project Number: 07140235

S15 - Development of Multimedia Interventions to Promote Breast Cancer Prevention among South Asian Women in Hong Kong

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Introduction and Project Objectives: Breast cancer is the most common cancer in the female population. Early detection of the disease allows more treatment options and leads to improved survival rates. However, the findings of our research study reported that the uptake rate of breast cancer screening among South Asian women was much lower than that of the Chinese population in Hong Kong. Health literacy, language, access to information on health and cancer preventive services, and cultural issues were the identified barriers to screening. Thus, develop culturally sensitive and linguistically appropriate multimedia health promotion interventions for these minority women is essential to increase their awareness of breast health. The aim of the project was to develop a multimedia intervention to promote breast health among South Asian women and to evaluate its outcomes, using the **R**each-**E**ffectiveness-**A**doption-**I**mplementation-**M**aintenance (RE-AIM) framework.

Methods/Implementation: The project was composed of three phases. The preparation phase involved identifying the themes and format for the intervention. The production phase was to develop a multimedia design. The implementation dealt with delivering the intervention to community partners.

Results/Outcomes: A culturally sensitive multimedia intervention had been developed and 54 community partners engaged in the project. A total of 1,067 South Asian women via conduction of 52 health talks and 3,237 health booklets were distributed. The majority were satisfied with the intervention (96%), and agreed that it was effective in increasing their knowledge of cancer (95%) and screening (93.8%), and how to access such services (93.7%). All the partners agreed to continue their support for the intervention in the future. All outcome indicators far exceeded expectations with range from 13.7% to 671.4% increase.

Conclusions and Discussion: The findings supported the intervention was effective to promote breast health among South Asian women in Hong Kong. By using the multimedia approach, information related to cancer and accessible preventive measures for breast cancer was disseminated more effectively to South Asian women, who are generally underserved and of lower literacy levels. Successful engagement of community partners also enhance the future sustainability of the project.

Project Number: 28140304

S16 - Baby Boomer at the Gate: Creating a Path to Healthy and Productive Aging Using Information and Communication Technology (ICT)

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Introduction and Project Objectives: Aging of the baby boomers sets the 'silver tsunami' to hit the health and social care service in the next decades. Preparing this age cohort for healthy, engaging and productive aging is a highly prioritized public health agenda. Unlike their predecessors, the higher computer literacy and health consciousness of this cohort urges for a unique internet-based health promotion strategy. This project aimed to develop and launch an information and communication (ICT) platform titled "Path to Vitality and Vibrancy (PathVV)" to serve this purpose.

Method/Implementation: This was a collaborative project between a tertiary institution and a non-government organization. Underpinned by the Rown and Kahn's Model of Successful Aging, the PathVV emphasis on not only disease and disability prevention, but also functional optimization and active social engagement. Fifteen health themes were developed by a multi-disciplinary working group accordingly, with the content based on the up-to- date scientific evidence. For each theme, a road map guided the users from self-initiated health assessment, problem recognition, risk factor modification, to problem management. The users could register for the chatroom of each health theme, on which they could have continuous dialogues with a registered nurse and other users on the related health topics. Regular face-to-face activities were scheduled based on the hot topic discussed on the chatroom, and the active users were also offered with opportunities to serve as a volunteer for the elderly service.

Results/Outcomes: The PathVV has formally launched since Oct 2016. A total of 16,679 participants have visited the educative content and the number of hits for the 15 topics ranged from 1,712 to 4,453. Of which, 815 have registered for the interactive chat rooms, and sixteen face-to-face workshops were organized for health empowerment. The users had significant improvement in knowledge towards aging ($p < 0.001$), and mental health ($p = 0.006$) after the 6-month participation. A high level of satisfaction was reported. Focus group interview indicated that the PathVV was a unique and comprehensive health promotion strategy to empower self-directed health monitoring and promotion. The chatroom was regarded as a highly important alternative to supplement the heavily loaded health service for health education.

Conclusions: This project has built a substantial community capacity to support the effective transition of baby boomers to old age. It sets the foundation for building a more innovative volunteer training programme to prepare the baby boomers with more advanced health skills in supporting the socially deprived older adults in Hong Kong.

Project Number: 07140105

S17 - Treatment of Severe Influenza A Infection with Celecoxib: A Double Blind Randomized Controlled Trial

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Background: Influenza A(H3N2) caused excessive hospitalizations and deaths. We assessed the efficacy and safety of celecoxib and oseltamivir combination for treatment of severe influenza requiring hospitalization.

Materials/Methods: We conducted a prospective double-blind randomised controlled trial among adult patients hospitalized between December 2014 and March 2017, for virologically-confirmed influenza A(H3N2) infection. Patients were randomly assigned to either a combination of oseltamivir 75mg twice daily and celecoxib 200mg daily for 5 days, or oseltamivir 75mg twice daily and placebo capsule for 5 days as control (1:1). The primary end-point was 28-day mortality. The secondary end-point was serial changes in post-treatment nasopharyngeal aspirate viral load, National Early Warning Score (NEWS), cytokine IL-6 and IL-10, and the length of hospitalization (NCT02108366).

Results: Between December 2014 and March 2017, we enrolled 120 influenza A(H3N2) patients. Of these, 60 (50%) were randomly assigned to the celecoxib-oseltamivir group. There was no difference in baseline findings between the two groups. Adverse events were uncommon. Twenty-three patients succumbed during the 28-day follow-up. The celecoxib-oseltamivir group had significantly lower 28-day mortality ($p=0.037$) than the control. Despite no difference in the serial viral titre, the serial IL-6 and IL-10 were significantly lower in the celecoxib-oseltamivir group than the control-group from day 1 to 5 post-treatment ($p<0.05$) and the serial NEWS from day 1 to 3 ($p<0.01$) post-treatment.

Conclusions: The combination of celecoxib-oseltamivir reduced mortality, serial NEWS and cytokine in hospitalized influenza A(H3N2) patients without increased adverse effects.

Project Number: RRG-18

S18 - Impact of Antiviral Therapy on Treatment Options and Outcome in Hepatitis B Virus Related Hepatocellular Carcinoma

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Introduction and Project Objectives: Tenofovir disoproxil fumarate (TDF) is a potent antiviral agent. We first aimed to investigate the effectiveness of TDF therapy in chronic hepatitis B (CHB) patients with cirrhosis. Furthermore, we evaluated the risk of hepatocellular carcinoma (HCC) after hepatitis B surface antigen (HBsAg) seroclearance and the impact of gender on HCC.

Methods: In the first study, we studied 808 TDF-treated and 291 untreated CHB cirrhotic patients from 3 centres (Hong Kong, Korea, US). TDF cohort included consecutive patients from three tertiary centres who received TDF 300mg/day for ≥12 months. Control cohort included historical untreated patients. In the second study, all chronic hepatitis B patients under medical care in Hospital Authority, Hong Kong who had cleared HBsAg between January 2000 and August 2016 were identified.

Results: In the first study, at 5-years follow-up, there were 72 decompensating events, 113 HCCs and 41 deaths from both groups combined. 5-year cumulative probabilities in TDF-treated vs. control cohorts were: 8% vs. 22% for decompensation (P=0.002), 10% vs. 15% for HCC (P=0.05) and 1% vs. 12% for death (P<0.001). On multivariate Cox regression, TDF treatment was independently associated with reduced risks of decompensation (hazard ratio [HR] 0.41, P=0.046), HCC (HR 0.43, P=0.001) and death (HR 0.12, P<0.001). In the second study, a total of 4,568 patients with HBsAg seroclearance were identified; 793 (17.4%) were treated by nucleos(t)ide analogues and 60 (1.3%) had received interferon treatment. At a median (interquartile range) follow-up of 3.4 (1.5-5.0)years, 54 patients developed HCC; cumulative incidences of HCC at 1, 3 and 5 years were 0.9%, 1.3% and 1.5%, respectively. Age above 50 years (adjusted hazard ratio 4.31, 95% confidence interval 1.72-10.84; p=0.002) and male gender (2.47, 1.24-4.91; p=0.01) were two independent risk factors of HCC. Female patients aged ≤50 years (n=545) had zero risk of HCC within 5 years of follow-up. Male patients aged ≤50 years (n=769), female patients aged >50 years (n=1,149) and male patients aged >50 years (n=2,105) had a 5-year cumulative incidence of HCC 0.7%, 1.0% and 2.5%, respectively. Similar findings were observed in patients with spontaneous and antiviral treatment-induced HBsAg seroclearance.

Conclusions: Among patients with cirrhosis, TDF treatment reduces risks of hepatic decompensation and HCC by more than 2-fold and death by almost 90% at 5 years. Female patients aged 50 years or below have zero risk of HCC after HBsAg seroclearance, whereas female patients aged above 50 years and all male patients are still at risk of HCC.

Project Number: CU-16-A10

S19 - Real-time Estimation of the Severity of Influenza Viruses

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Introduction and Project Objectives: Timely and reliable estimates of the seriousness of infection (severity) are essential for public health decision-making during an on-going influenza epidemic. However, methods for real-time estimation of severity remain limited, and many of the early estimates of the seriousness of influenza A(H1N1)pdm09 and A(H7N9) virus infections were problematic and misrepresented the seriousness of these infections. The objectives of our proposal study are to identify which approaches can more accurately reflect the severity of emerging and re-emerging infections.

Methods: We compared approaches for real-time estimation of the hospital-fatality-risk of influenza A(H1N1)pdm09 in 2009 in Hong Kong and influenza A(H7N9) in 2013 in China, allowing for right-censoring of final outcomes in patients. We evaluated a new approach for estimation of symptomatic case-fatality-risk of influenza A(H1N1)pdm09 in 2009 and 2011, and influenza A(H3N2) in 2010 in Hong Kong, based on extrapolation of local influenza-like illness surveillance and laboratory detection data.

Results: For the real-time estimation of HFR, models accounting for censoring and allowing for time-varying severity generated reliable estimates earlier than models without these adjustments. The risk of influenza A(H1N1)pdm09 mortality in hospitalized cases increased with age. Had serologic data been available, with 300 samples collected per week and tested in real time, we would have been able to obtain reliable estimates of the symptomatic case-fatality-risk of influenza A(H3N2) virus one week before the epidemic peak.

Conclusions: We identified approaches that can provide more reliable estimates of severity taking into account critical factors such as censoring of data regarding final disease outcomes of the patients. These results improve our understanding of the severity of influenza virus infections and provide a practical approach to reliably estimate the severity of emerging and re-emerging infections. Valid estimates of severity from the recommended methods in this report will inform public health decisions on appropriate control strategies.

Project Number: 14131432

S20 - Potential Cost-effectiveness of Herpes Zoster Vaccination for Older Adults in Hong Kong

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Introduction and Project Objectives: Herpes zoster (HZ) imposes an increasing burden in the aging population of Hong Kong. Adjuvanted HZ subunit vaccine (HZ/su) is recommended by the Centers for Disease Control and Prevention for adults aged 50 years and older. This project aimed to examine the potential cost-effectiveness of HZ vaccination for older adults in Hong Kong.

Methods: The present study was a health economic analysis conducted from the societal perspective of Hong Kong. A life-long Markov model was designed to simulate outcomes of four alternatives: Vaccination at model entry (age 50 years); deferring vaccination to 60 years; deferring vaccination to 70 years; and no vaccination. Outcome measures included direct cost, indirect cost, HZ and post-herpetic neuralgia incidences, quality-adjusted life years (QALYs) loss, and incremental cost per QALY saved (ICER). Model clinical inputs were derived from the medical literature. HZ treatment costs were collected from case records of local HZ patients. One-way and probabilistic sensitivity analyses, and scenario analysis were performed.

Results: In base-case analysis, no vaccination showed the highest QALY loss at lowest cost (0.00492 QALY loss; HKD601), followed by deferring to 70 years (0.00368 QALY loss; HKD1117), deferring to 60 years (0.00291 QALY loss; HKD1444) and vaccination at 50 years (0.00250 QALY loss; HKD1936). Deferring vaccination to age 60 years saved most QALYs at ICER lower than willingness-to-pay (WTP) threshold. Sensitivity and scenario analyses found the cost-effective acceptance of each vaccination strategy sensitive to WTP threshold, vaccine-related and HZ-related factors. In probabilistic sensitivity analysis, the probability to be accepted was highest for deferring vaccination to age 60 years (47.8%), followed by vaccination at 50 years (38.9%), deferring vaccination to age 70 years (13.3%) and no vaccination (0%), at WTP=3× gross domestic product per capita of Hong Kong.

Conclusions: For healthy adults aged 50 years old, all vaccination strategies examined in the present model seems to save QALYs at higher cost in Hong Kong. Deferring vaccination to age 60 years is the most likely option to be accepted as cost-effective. The findings provided important information that zoster vaccination saved QALYs at higher cost. Future research on affordability, budget impact and feasibility of implementing HZ/su in public vaccination programme for older adults are highly warranted.

Project Number: 15140432

F1 - The Causal Role of Adiponectin and Triglycerides in Ischemic Heart Diseases Using a Separate Sample Mendelian Randomization Analysis from Publicly Available Data

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(i) Training Programme

Details of Training Activities: The training programme primarily focused on learning a new technique in Mendelian randomization studies using summary statistics from genome wide association studies. The programme consisted of multiple components. First, I was in an academic attachment to Professor Debbie A Lawlor at the Bristol Medical School: Population Health Sciences. I was supervised by Prof Lawlor via weekly in person meetings and regular email exchanges. I also conducted collaborative projects with other Integrative Epidemiology Unit (IEU) members at the University of Bristol, principally with Dr J Bowden and Dr MC Borges. Second, I attended a short course in Mendelian randomization where I learnt how to implement cutting edge methods in Mendelian randomization which are more robust to violation of assumptions in Mendelian randomization. Lastly, I took the opportunity to attend several seminars from different groups/ institutions such as emulation of randomized controlled trials from Mendelian randomization by Dr Brian Ferrence, and evaluation of environmental impact on mental health using twin status by Dr Claire Haworth.

Benefits of Training: The training has significantly refined my skills in conducting Mendelian randomization, in particular the part on 2 sample Mendelian randomization and the relevant statistical approaches. The training opportunity has also fostered potential long term collaborations between the University of Hong Kong (HKU) and the University of Bristol, and has important implications for my research career using Mendelian randomization. I also focused on how short course was being conducted by the Bristol group, which I eventually adopted some of the approaches back in my own HKU course.

Learning Experience: The learning experience, which included the academic attachment, the short course, and the seminars I attended, was very rewarding. Regular discussion with Prof Lawlor and other IEU members also enriched my thoughts in how causes of diseases should be identified, such as via triangulation of evidence.

Applicability to the Research Project: The training was directly applicable to my research project, particularly on 2 sample Mendelian randomization (formerly known as separate sample Mendelian randomization). These included substantial improvements in the choice of genetic instruments, and the sensitivity analyses needed to conduct such study.

(ii) Research Project

Introduction and Project Objectives: Adiponectin and triglycerides are related to ischemic heart disease (IHD) although results are not always consistent across different study designs. Verifying their role in IHD may help identify new targets of interventions to improve population health. The project objectives were to verify the causal role of adiponectin and triglycerides in IHD using Mendelian randomization.

Methods: We extracted strong, independent genetic instruments (p value <5x10-8), i.e. single nucleotide polymorphisms (SNPs), from ADIPOGen Consortium for adiponectin (n=39,883); and Global Lipids Genetics Consortium (GLGC) for triglycerides (n=188,577), which were then applied to CARDIoGRAMplusC4D 1000 Genomes-based genome wide association studies (GWAS) (IHD cases: 60,801; controls: 123,504). We obtained the causal estimate of adiponectin, triglycerides on IHD risk using inverse variance weighting (IVW). Sensitivity analyses included MR-Egger, weighed median, and exclusion of pleiotropic instruments.

Results: Using 21 SNPs for adiponectin, adiponectin was inversely associated with IHD in IVW (Odds ratio (OR) 0.82 per log transformed adiponectin unit increase, 95% confidence interval (CI) 0.71 to 0.94). However, the results were not robust to sensitivity analyses. On the contrary, using 102 SNPs for triglycerides, triglycerides was positively associated with IHD in IVW (OR: 1.26 per SD increase, 95% CI 1.16 to 1.38), with directionally consistent estimates from sensitivity analyses.

Conclusions: Triglycerides likely causes IHD although the relation of adiponectin and IHD is likely non-causal, reflecting confounding in previous studies. This study implies medications which raise adiponectin unlikely decrease IHD risk. Efforts should be redirected to other more promising targets of intervention, such as triglycerides, with rigorous evaluation from properly designed randomized controlled trials.

Research Fellowship Number: 01150037

F2 - Photoacoustic Molecular Imaging of Osteoarthritic Pain – A Proof-of-concept Study

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(i) Training Programme
Kennedy Institute of Rheumatology (KIR), University of Oxford, is a world leading basic and translational inflammatory science center. KIR is known for the discovery of tumor necrosis factor (TNF)-alpha neutralizing antibody, which leads to a paradigm shift in the treatment of rheumatoid arthritis. Under the auspices of Health and Medical Research Fund Research Fellowship Scheme, Dr Wen received the training in KIR for OA pain behavioral analysis in rodents and established a research platform in Hong Kong. Prof Tonia Vincent, the director of OA pathogenesis research center funded by Arthritis Research UK, provided the training opportunity as the mentor of Dr Wen.

(ii) Research Project
Purpose: Osteoarthritis (OA) is a prevalent debilitating chronic painful condition. Nerve growth factor (NGF) levels are elevated in synovial fluid and associated with arthritic pain in OA patients. NGF is an emerging therapeutic target for OA pain. In this study, we aim to develop a novel theranostic approach targeting NGF using a functionalized gold nanorod for photoacoustic (PA) imaging and management of OA pain.

Methods: Destabilization of medial meniscus (DMM) surgery was performed to induce post-traumatic OA in one knee of the balb/c mouse with the sham operation on the contralateral knee as the control. Gold nanorod conjugated with NGF antibody (NGF-Ab-AuNR) was synthesized and injected via the tail vein at 1-month and 4-month post-surgery. Photoacoustic (PA) imaging was taken to delineate the distribution of the nanoparticles in vivo. DMM knees were then exposed to near infrared (NIR) therapy for 10 minutes under photothermal camera. Von Frey and rotarod tests were performed to assess the locomotive ability and balance of the animals respectively. Knee joints were harvested 24 hours after gold nanorod injection and processed for the histological and immunohistochemical analysis.

Results: PA imaging revealed the accumulation of NGF-Ab-AuNR in the inflamed synovial tissue of DMM knee compared to the contralateral one. ICP-MS biodistibution analysis confirmed the nanoparticles accumulated in the injured knee joint as well as the spleen and liver. Both PA and ICP-MS data showed the accumulation of nanoparticles reached its peak after 6 hours of injection and started to decrease afterwards and cleared out of body at 7 days post injection. All animals showed hindered locomotive ability represented by a lower withdrawal threshold in von Frey test and shorter time on rod in rotarod test after DMM surgery. The locomotive deficits caused by DMM surgery could be rescued by NIR treatment at the early stage of OA but not at later stage of disease. Histological examination identified the nanoparticles leaked from the newly formed blood vessels in the inflamed synovial tissues, and co-localized with TRAPV1-positive peripheral nerve endings around vasculature.

Conclusions: Integration of the cutting-edge nanotechnology and PA imaging modality provides a novel OA pain imaging and management approach. The safety of god nanoparticles as well as NGF neutralizing antibody (Pfizer) has been proved in humans, which will shorten the translation of our research findings into clinical practice.

Research Fellowship Number: 01150087

HHS-1

Helping In-patients to Quit Smoking by Understanding their Risk Perception, Behavior, and Attitudes Related to Smoking

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Introduction and Project Objectives: Patients admitted to hospitals represent an excellent teachable moment for smoking cessation, as they are required to abstain from tobacco use during hospitalisation. Nevertheless, smoking behaviours of hospitalised patients, and factors that lead to smoking abstinence thereafter, remain relatively underexplored, particularly in a Hong Kong Chinese context. This study aimed at understanding the risk perceptions, behaviour, attitudes and experiences related to smoking hospitalized Chinese smokers, and exploring factors leading to their abstaining from cigarette use after being hospitalised.

Methods: In the first phase of the study, a phenomenological research design was used to develop understanding about the needs and concerns of 30 Chinese inpatients who were current smokers, including their behaviour, attitudes, risk perceptions and experiences related to smoking and smoking cessation. In the second phase, a retrospective cross-sectional study was conducted in three outpatient clinics in different regions in Hong Kong. A total of 382 Chinese patients were recruited. They were asked to complete a structured questionnaire which assessed their smoking behaviors before, during and after hospitalization.

Results: In the first phase of the study, four themes were generated: 1) associations between perception of illness and smoking; 2) perceived support from healthcare professionals to quit smoking; 3) impact of hospitalization on behaviour, attitudes, and experiences; and 4) perceived barriers to quitting smoking. For the second phase of the study, the results indicated 23.6% of smokers smoked secretly during their hospital stay, and about 76.1% of smokers resumed smoking after discharge. Multivariate logistic regression analysis found that number of days of hospitalisation admission in the preceding year (OR 1.02; 95% CI 1.01 to 1.27; p=0.036), patients' perceived correlation between smoking and their illness (OR 1.08; 95% CI 1.01 to 1.17; p=0.032), withdrawal symptoms experienced during hospitalisation (OR 0.75; 95% CI 0.58 to 0.97; p=0.027) and smoking cessation support from healthcare professionals (OR 1.18; 95% CI 1.07 to 1.36; p=0.014) were significant predictors of smoking abstinence after discharge.

Conclusion: To our knowledge, this is the first study to investigate the smoking behaviours of hospitalized patients in a Chinese context. The results indicated the importance of developing an intervention that helps to demystify misconceptions about smoking. Most importantly, an innovative and appropriate intervention is essential to help smoking patients achieve more successful smoking abstinence and less relapse.

Project No.: 13143141

HHS-2

A Randomized Controlled Trial Evaluating Efficacy of an Intervention which Enhances Social Support And Positive Affect through Online Social Networking in Smoking Cessations

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Introduction and Project Objectives: Online smoking cessation is effective. Peer support, positive affect, and immediate situational cue to action are new directions for smoking cessation; delivery of combinations of such interventions through online social networking has not been evaluated by randomized controlled trials (RCT). A 2-arm RCT was conducted evaluating the relative efficacy in smoking cessation. The control group (n=203) was sent weekly online messages based on the Health Belief Model to create cognitive changes. The multi-domain intervention group (n=205) included three additional novel and theory-based components: i) a peer support group, ii) positive psychology intervention (Three Good Things), and iii) immediate online interactions among peer group members to resist situational temptations.

Methods: The 2-arm non-blinded RCT design was used. The 2-month activities were conducted via WeChat. Participants included adult (>=18 years) current smokers who can communicate in Chinese. Exclusion criteria applied. Evaluation was conducted through phone interviews at baseline, 3 months and 6 months post-intervention. The primary outcome was self-reported 7-day point prevalence (pp) quit rate. At Month 6, self-reported quitting was validated by positive results of either exhale carbon monoxide test or saliva cotinine test. Secondary outcomes included reduction of cigarette consumption and other psychosocial variables.

Results: At Month 6, the self-reported quit rates were 29.0% and 27.3% in the intervention and active control groups, respectively (RR = 1.06; 95% CI: 0.74-1.53); the validated quit rates among all participants were 18.6% and 12.7% respectively. The average number of cigarettes consumed by the non-quitters decreased from 9.1 to 6.1, and 10.6 to 6.4 in the two groups (p.05). Conclusions: Both groups resulted in similarly large self-reported and validated quit rates. Non-significant between-group differences may be explained by the same active messaging component in the two groups, and that the intervention group showed very poor compliance to the three novel active components.

Conclusion: The effective active control group can be recruited and intervened at low cost and is sustainable, and may not require additional interactive social networking components; implementation of such components needs to consider compliance.

Project No.: 12130491

HHS-3

The effects of an activity-based lifestyle intervention on moderate sleep complaints among older adults: A sequential mixed method stu

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Introduction and Project Objectives: Sleep complaint is a highly prevalent problem affecting over 80% of the older population, and is strongly associated with imparied function, morbidity and even mortality. Research evidence identified a 'Expectation-Evidence paradox' on the sleep-promoting effect of exercise-based lifestyle intervention. This study was to investigate further on the effects and mediating process of a 16-week moderate-intensity endurance exercise on sleep quality and pattern among older adults with moderate sleep complaint, and to explore the users' overall perception on the exercise intervention.

Methods: This was a sequential quantitative-qualitative mixed method study. A RCT with waiting-list attention-controlled intervention randomized 227 older adutls (mean age = 74.6, SD =7.5) with moderate sleep complaint to receive either the 16-week moderate-intensity stepping exercise training or health education. Outcome evaluation included sleep quality as measured by the Pittsburg Sleep Quality Index (PSQI)and sleep pattern as measured by the waist actiwatch. Mood status and exercise capacity (estimated VO2max) were also measured by the Profile of Mood State and the Rockport Fitness Test respecitivty for examining the mediating mechanism. Thirty participants with different sleep-related responses to exercise were interviewed for perceived treatment effect and acceptability.

Results: Compared to the controls, generalized estimating equation indicated that the exercise training had significantly improved the sleep quality and VO2max at 16 weeks, with beta = -0.88 (95% CI = -1.72, -0.04, p = 0.04) and beta = 1.97 (95% CI = 1.22 - 2.72, p =<0.001), respectively. Even though there was significant improvement in the objective sleep parameters including total sleep time (p=0.002), sleep efficiency (p=0.001) and sleep latency (p=0.002) over time, no significant group*time intervention effect on objective sleep parameters was detected. Path analysis did not suggest the hypothesized mediating model. However, by using inductive thematic analysis for the qualitative findings, the participants did report the improvement in sleep latency, total sleeping time, wake after sleep onset and daytime sleepiness are relating to hypothesized mediators including reduced obsessive thoughts, improved temper, peaceful and relaxing mind, and increased daytime physical activity.

Conclusion: In view of the significant role of perceptual aspect of sleep pattern in predicting health and health service utilization outcomes among older adults, the moderate-intensity stepping exercise merits territory-wide application for managing moderate-sleep complaint. According to the narrative findings, the mood-enhancing and physical functioning mediating mechanisms deserve further investigation.

Project No.: 12131441

HHS-4

A case-control-family study of REM sleep behavior disorder: searching for familial aggregation and neurodegenerative biomarkers

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Introduction and Project Objectives: Idiopathic rapid eye movement (REM) sleep behavior disorder (iRBD) is a precursor of alpha-synucleinopathy, such as Parkinson's disease and dementia with Lewy body. In this case-control-family study, we aimed to determine the familial aggregation of iRBD, and the presence of neurodegenerative diseases and related early biomarkers in the first-degree relatives of patients with iRBD.

Methods: A total of 404 and 387 first-degree relatives aged over 40 years were recruited from 102 iRBD and 89 non-RBD control families respectively for evaluation of RBD features, neurodegenerative biomarkers, and diagnoses of Parkinson's disease and dementia. Among them, 204 and 208 first-degree relatives of patients with iRBD and controls underwent face-to-face clinical assessment respectively, while 97 and 75 first-degree relatives of patients and controls underwent further video-polysomnographic assessment, respectively.

Results: Compared with the first-degree relatives of controls, first-degree relatives of patients had higher rates of probable RBD (14.9% vs. 4.9%, OR = 3.42, 95% CI = 2.00-5.85), video-polysomnography-confirmed RBD (8.4% vs. 1.4%, OR = 6.23, 95% CI = 1.81 – 21.74), and RBD features, including chin tonic electromyography activity level (1.5 ± 7.5% vs. 0.3 ± 1.0%, p = 0.01) and behavioral events during rapid eye movement sleep (11.3% vs. 1.9%, OR = 6.54, 95% CI = 2.21-19.23). First-degree relatives of patients had higher rates of clinician-diagnosed Parkinson's disease (3.1% vs. 0.5%, OR = 6.09, 95% CI = 1.38-26.95) and dementia (6.9% vs. 2.6%, OR = 3.16, 95% CI = 1.38-7.29). Moreover, first-degree relatives of patients had more constipation (8.3% vs. 2.4%, OR = 2.76, 95% CI = 1.01-9.00) and impaired motor function (mean Unified Parkinson's Disease Rating Scale part III score = 1.9 ± 3.2 vs. 0.9 ± 2.3, p = 0.001). Overall, unaffected first-degree relatives (without RBD) of patients demonstrated a higher likelihood ratio of prodromal Parkinson's disease (median [P25th-P75th]: 0.27 [0.10-1.29] vs. 0.22 [0.10-0.61], p = 0.02) than unaffected first-degree relatives of controls.

Conclusion: There is a familial aggregation of RBD from increased electromyographic activity, rapid eye movement sleep behavioral events, to full-blown disorder. First-degree relatives of patients with iRBD carry a higher risk of alpha-synucleinopathy in terms of neurodegenerative diseases and prodromal markers. The findings suggested the genetic contribution of iRBD and prodromal markers of alpha-synucleinopathy in iRBD families.

Project No.: 12131501

HHS-5
Serum 25-hydroxyvitamin D and the risk of stroke in Hong Kong Chinese

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Introduction and Project Objectives: Low vitamin D levels have been associated with various cardiovascular diseases; however, whether it is associated with stroke remains inconclusive. We aimed to evaluate the association between serum 25-hydroxyvitamin D and risk of stroke.

Methods: We conducted a cohort study consisting of 3,458 participants from the Hong Kong Osteoporosis Study aged ≥45 at baseline, examined between 1995 and 2010 and followed up using electronic medical records. Ischaemic and haemorrhagic stroke were defined using the ICD-9 code.

Results: In multivariable Cox-proportional hazard regression, quintiles 1 and 4 were significantly associated with increased risk of stroke when compared to the highest quintile (Quintile 1: HR, 1.78; 95 % CI, 1.16-2.74 and quintile 4: HR, 1.61; 95 % CI, 1.07-2.43). A similar association was observed in both men and women. In subgroup analysis, the association was specifically observed for ischaemic stroke, but not haemorrhagic stroke. Using a penalized regression spline, the association between vitamin D and risk of stroke was in a reverse J-shape, with the lowest risk of stroke being observed at 25(OH)D levels between 70 and 80 nmol/l.

Conclusion: In conclusion, a low vitamin D level is associated with increased risk of ischaemic stroke; however, whether high vitamin D level is also associated with increased risk of stroke requires further study.

Project No.: 12132451

HHS-6
Effectiveness of perceptual learning in reading rehabilitation for patients with diabetic macular oedema – Randomized controlled trial

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Introduction and Project Objectives: Our recent study showed that patients with diabetic macular oedema (DMO), after receiving laser photocoagulation, achieved good outcomes in distance acuity. However, some patients, particularly those developing parafoveal scotoma, still had difficulty in reading. The inability to read or reading very slowly can lead to the potential loss of a job, as well as the enjoyment of reading for leisure. This project is aimed at exploring the effectiveness of perceptual learning on reading performance of patients with DMO.

Methods: 55 Type II diabete patients who had complaint of reading difficulties after macular laser photocoagulation or micropulse laser for DMO were randomly assigned to one of the three groups: 1) placebo-control (control); 2) temporal processing speed training (TTT); and 3) combined temporal processing and spatial visual span training (combined). For the two intervention groups, participants received six weekly training session. Participants in the control group received six sessions of leisure reading activities. Temporal and spatial characteristics of visual span measures, reading performance, fixation stability and patient-reported outcome measures were assessed at baseline (Pre-test), immediately after training (Post-1), and 12 weeks after the cessation of training (Post-2).

Results: Results from the generalized estimating equation or mixed-model analysis showed significant improvement in temporal visual processing speed in both training groups (p 0.05).

Conclusion: Perceptual learning significantly improved participants' temporal processing speed and spatial characteristics of the visual span – two factors affecting the reading performance in visually-impaired patients. However, the training effect of the perceptual learning could not be transferred to the untrained reading tasks. The lack of transfer effect might limit our clinical application as patients might not find direct benefits on enhancing their compromised reading abilities due to vision loss. Further studies on improving the training paradigm will be needed to improve its clinical application.

Project No.: 12131601

HHS-7
Evaluating a technology-augmented self-monitoring model for glycemic and blood pressure control and medication adherence in type 2 diabetes and hypertension patients: a randomized controlled trial

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Introduction and Project Objectives: Patients with type 2 diabetes and hypertension are required to self-manage their conditions. Although digital health interventions are emerging as promising tools to improve patient self-care, their clinical effectiveness in managing diabetes and hypertension remains unclear. This study aimed to assess whether the use of a digital health intervention could improve glycemic and blood pressure control and other health-related outcomes compared with usual care.

Methods: A 24-week randomized controlled trial was conducted. Eligible participants were adult patients with comorbid type 2 diabetes and hypertension. Patients were randomly assigned to intervention or control groups. Patients allocated to the intervention group received a tablet-based self-monitoring system to support their self-care, while patients allocated to the control group performed self-monitoring using conventional devices. Primary outcomes included HbA1c, systolic blood pressure (SBP), and diastolic blood pressure (DBP). Secondary outcomes included

medication adherence, general adherence to treatment, adherence to disease-specific activities, diabetes knowledge, hypertension knowledge, and self-efficacy for coping with chronic disease. The outcomes were assessed at baseline, 8, 12, 16, and 24 weeks.

Results: A total of 299 participants were enrolled and randomized (Intervention = 151, Control = 148). Both groups yielded significant decreases in HbA1c after 12 (Intervention: 0.29%; Control: 0.34%) and 24 weeks (Intervention: 0.44%; Control: 0.35%). No significant differences in SBP and DBP were observed for both groups at most of the follow-ups. Significant improvements in adherence to disease-specific activities, diabetes knowledge, and hypertension knowledge were observed after 24 weeks for both groups. Medication adherence in the intervention group and self-efficacy for coping with chronic disease in the control group were significantly improved.

Conclusion: Both technology-augmented and conventional self-care yielded similar benefits. Strategies that can continuously motivate patients to adhere to self-care activities should be studied.

Project No.: 12133231

HHS-8
Development and Validation of a New Aphasia Screening Test for the Cantonese-speaking Population

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Introduction and Project Objectives: A routine aphasia screening test which is short and easy to administer is not available in Cantonse speaking population. The aim of this study was to develop and validate a Cantonese Aphasia Screening Test (CAST).

Methods: The present study was conducted in three phases. Phase I was to determine the overall test structure through literature reviews, expert consultation and pilot study on translated FAST. Phase II was to construct test items under the four aspects of language. Phase III was the validation process in which items were tested on i)160 normal subjects, ii) 157 stroke patients with aphasia and iii) 50 stroke patients without aphasia. All subjects were also tested on the MMSE and MoCA. Obtained scores were compared with the score of CAST.

Results: Good internal consistency with alpha coefficient values larger than 0.90 was obtained in all tests. Inter- and intra-rater as well as test-retest reliability are highly satisfactory, value of coefficients 0.997, 0.999 and 0.890 respectively. Experts were satisfied with the general content of the test items to reflex the language ability of patients with potential aphasia. Close relationship between the CAST and MMSE and MoCA were found in the current study. The construct strength was found to be high, the correlation from 0.848 to 0.96.

Conclusion: An item bank for further development into a new language screening tool (CAST) which encompasses important language domains was developed and validated for patients with stroke. CAST will be simple, sensitive and predictive of aphasia in patients with stroke.

Project No.: 12133761

HHS-9
Age at Menarche and Cardiovascular Risk Factors – a Mendelian Randomization Analysis

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Introduction and Project Objectives: Observational studies show earlier age at menarche is associated with higher cardiovascular disease risk. However, childhood obesity or childhood socioeconomic position may confound the association. A Mendelian randomization design may help ascertain the causal role of age at menarche and cardiovascular disease. We hypothesized that earlier age at menarche is associated with higher blood pressure; poorer lipids and glycemic profile; and higher body mass index and waist hip ratio, which are risk factors of cardiovascular disease.

Methods: We conducted a Mendelian randomization study in a large Southern Chinese cohort, the Guangzhou Biobank Cohort Study (n=12,279). Stepwise regression with cross validation was used to generate a genetic allele score based on genetic predictors of age at menarche identified from genome wide association studies. We obtained the Mendelian randomization estimate using 2 stage least squares regression. To rule out the possibility of underpowered analyses, we included height as a positive control outcome.

Results: We derived a genetic allele score from 5 single nucleotide polymorphisms (rs17268785, rs1859345, rs2090409, rs4452860 and rs4946651). There was little evidence for weak instrument bias based on the allele score F statistics (19.9). Older age at menarche was associated with lower glucose (-0.39 mmol/L per year older menarche, 95% confidence interval (CI) -0.78 to -0.001) but not with other outcomes except height (control outcome).

Conclusion: Our study did not provide strong evidence for associations between age at menarche and cardiovascular risk factors except glucose, which needs to be verified in larger studies. Health care workers may need to monitor more intensively on the glycemic traits of adolescents with earlier age at menarche and provide relevant interventions to reduce their likelihood of developing diabetes in later life.

Project No.: 12132281

HHS-10
Tai Chi Exercise is More Effective than Brisk Walking in Reducing Cardiovascular Disease Risk Factors: A randomized Controlled Trial

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Introduction and Project Objectives: Physical inactivity is a major modifiable lifestyle risk factor associated with cardiovascular disease.

Tai Chi and walking are safe and popular forms of physical activity. The project objective is to evaluate the effects of Tai Chi versus brisk walking on reducing cardiovascular disease risk factors.

Methods: This was a three-arm parallel randomized controlled trial. 246 adults with hypertension and at least two but not more than three modifiable cardiovascular disease risk factors (diabetes, dyslipidemia, overweight, physical inactivity and smoking) were randomly assigned to either Tai Chi, brisk walking, or control groups (n = 82/group). The Tai Chi and brisk walking groups engaged in moderate-intensity physical activity 150 min/week for 3 months; daily home-based practice was encouraged for another 6 months. The primary outcome was blood pressure. Secondary outcomes were fasting blood sugar, glycated hemoglobin, total cholesterol, triglycerides, high- and low-density lipoprotein, body mass index, waist circumference, aerobic endurance, perceived stress, quality of life and exercise self-efficacy. Data were collected at baseline, post-intervention at 3 months and follow-up assessments at 6 and 9 months. Generalized estimating equation models were used to compare the changes in outcomes over time between groups.

Results: The mean age of participants was 64.4 (SD=9.8), age ranged from 30 to 91, with 45.5% men. At baseline, the participants had an average blood pressure = 141/81 and average body mass index = 26; 58% were were diabetics, 61% presented with dyslipidemia and 11% were smokers. No significant difference was noted between groups at baseline. The Tai Chi group significantly lowered blood pressure (systolic -13.33 mmHg; diastolic -6.45 mmHg), fasting blood sugar (-0.72 mmol/L), glycated hemoglobin (-0.39%) and perceived stress (-3.22 score) and improved perceived mental health (+4.05 score) and exercise self-efficacy (+12.79 score) at 9 months, compared to the control group. In the Tai Chi group, significantly greater reductions in blood pressure (systolic -12.46 mmHg; diastolic -3.20 mmHg), fasting blood sugar (-1.27 mmol/L), glycated hemoglobin (-0.56%), lower perceived stress (−2.32 score), and improved perceived mental health (+3.54 score) and exercise self-efficacy (+12.83 score) were observed, compared to the brisk walking group. No significant changes in the other cardiovascular disease risk indicators were observed over time between groups.

Conclusion: Tai Chi is more effective than brisk walking in reducing several cardiovascular disease risk factors and improving psychosocial well-being, and can be recommended as a viable exercise for building a healthy life free of cardiovascular disease.

Project No.: 12130041

HHS-11
Extended evaluation of stakeholder satisfaction of chronic disease management and family medicine training programmes of the Hospital Authority

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Introduction and Project Objectives: To evaluate stakeholders' experience and satisfaction with specific areas of service provided by the Hospital Authority (HA) initiated Resources Allocation Exercise (RAE) Programmes since 2009, including 5 Chronic Disease Management (CDM) programmes: Multi-disciplinary Risk Assessment and Management Programme for Diabetes (RAMP-DM) and Hypertension (RAMP-HT), Nurse and Allied Health Clinics for Wound Care Programme (NAHC-WC) and Continence Care (NAHC-CC), and Patient Empowerment Programme (PEP), as well as the Family Medicine Training (FMT) Programme.

Methods: Patients aged 18 or above who joined the above programmes and their service providers, and FMT participants, were recruited from all 7 clusters of HA for two rounds of cross-sectional questionnaire survey conducted from 2012 to 2017. Modified Chinese version of Consumer Assessment of Healthcare Providers and Systems (CAHPS) Clinician and Group Survey Adult 12-Month Survey 2.0 was adopted as the patient satisfaction questionnaire. Chinese version of Patient Enablement Instrument (PEI) was chosen for measuring patient enablement in PEP. Modified version of Provider Satisfaction Survey developed by The Care Continuum Alliance was adopted as the provider satisfaction questionnaire. Modified version of Physician Worklife Survey (PWS) was used as FMT survey.

Results: 4,815 patients and 540 providers from 5 CDM programmes, and 636 participants from FMT programme were recruited. Results were similar in both rounds of survey. For CDM programmes, about 70-85% of the respondents gave a rating of the programme service, healthcare workers performance and clinic condition an 8 or above on a scale of 10. According to the PEI results, there was about 30% increase of patients who were clinically meaningfully enabled among those who attended more than 70% of the PEP programme, and a 4% decrease among those who defaulted their PEP follow up. There was a significant difference in the mean of PEI score change between completers (+2.72) and defaulters (+0.50). Patients with poorer self-rated overall health expressed lower satisfaction level in all CDM programmes. There was a high satisfaction level among service providers, ranged from 88-100%, in all CDM programmes. There were about 80% of the respondents who were satisfied with the training provided in the GOPC setting in the past 12 months in FMT.

Conclusion: Respondents in this study showed a high satisfaction level towards the CDM programmes. More patients were clinically enabled if they completed the PEP. Majority of the respondents in FMT were satisfied with the training provided. Promote person-centred care to patients with different health needs could improve satisfaction level. Recommend regular Patient Satisfaction Survey (PSS) to monitor the on-going changes.

Project No.: EPC-CUHK

HHS-12
A multi-center prospective study on the evaluation of maternal and obstetric factors leading to the hepatitis B immunization failure in Hong Kong

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Introduction and Project Objectives: To evaluate the maternal and obstetric factors leading to immunoprophylaxis failure (IF) and determine the optimal viral load threshold to predict IF

Methods: A prospective multicenter study was conducted from January 2014 to December 2016 at 5 hospitals in Hong Kong. Women with a positive hepatitis B surface antigen (HBsAg status) were recruited. Women receiving antiviral treatment during pregnancy were excluded. Maternal hepatitis B e antigen (HBeAg) was tested once on recruitment and the hepatitis B virus (HBV) DNA was quantified before and at 28–30 weeks. The duration of rupture of membranes, labour and mode of delivery were recorded. All newborns received standard HBV vaccination and immunoglobulin. HBsAg of infants was examined at 9–12 months. IF of infants (either infant in case of twin pregnancy) was defined as HBsAg positive status at 9–12 months of age.

Results: 641 women and 654 infants (13 pairs of twins) were included for final analysis. All infants completed the whole course of HBV vaccination on schedule. 352 women had HBV quantification 7.2log10IU/mL. The risks of IF with HBV DNA level of 8.2log10IU/mL were 0%, 8.6% and 3.1%, respectively. Positive HBeAg and HBV DNA >7.2log10IU/mL at 28–30 weeks were significant predictors of IF (4.5% [95% CI, 1.83%–9.08%] vs 0% [95% CI, 0%–0.76%], and 5.8% [95% CI, 2.36%–11.56%] vs 0% [95% CI, 0%–0.71%], respectively; P 0.05). Subgroup analysis in viral load > 7log10IU/mL and 8log10IU/mL also did not find a significant association between duration of rupture of membranes and labour with IF.

Conclusion: Viral load of 7.2log10IU/mL at 28–30 weeks of gestation could be the optimal HBV DNA cutoff to predict IF. Viral load quantification could be performed before 22 weeks of gestation to predict IF. Obstetric factors would not affect the risk of HBV vertical transmission following standard HBV vaccination.

Project No.: 11121661

HHS-13
Improving elderly healthcare voucher scheme to incentivise primary care in Hong Kong: How has health service utilisation changed?

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Introduction and Project Objectives: To assess changes over time in awareness and attitudes towards Voucher Scheme amongst elderly persons and service providers, and its long term impact on the primary care system.

Methods: A mix of qualitative and quantitative analysis and data sources were used to permit triangulation in the synthesis of results to draw conclusions for the objectives of the study. It included (i) key informant interview with policymaker, (ii) repeated cross-sectional survey among elderly persons, (iii) longitudinal follow-up survey of elderly persons, (iv) linked administrative data analysis of Hospital Authority and Department of Health data, (v) focus group discussions among service providers, and (vi) public opinion survey of the general public.

Results: Overall, findings from surveys and focus group discussion showed that the current Voucher Scheme was more acceptable to elderly persons and services providers than at the time of initial launch as a pilot in 2009, reflected by the increased awareness and more positive attitudes towards the design of the voucher except for the subsidy amount. The usage has been increased to over 90% in 2016. Regarding its impact, 61.5% of elderly persons from cross-sectional survey thought that the voucher encouraged them to use primary care services in the private sector, in particular for one-off (episodic) curative services (90.3%) rather than for preventive services (40.3%) or for chronic disease management (12.2%). However, this has not been associated with a reduction in the service utilization in the public sector in the linked data analysis. The percentage of dual utilization of both public and private sector as their usual source of care increased to 61.9% in 2016 (up from 48.4% in 2010). The Voucher Scheme did not have a substitution effect of private services on public services utilization, and has led to more service utilization overall as well as an increase in price.

Conclusion: To ensure its financial sustainability and the long term development in view of the ageing population, there should be a re-design of the Voucher Scheme to meet the policy objectives of encouraging preventive services, enable chronic diseases management and facilitate continuity of care. Enhancements which should be considered are: (i) designated vouchers for preventive care especially for the soon-to-be-old group for early detection and treatment, and (ii) designated voucher for chronic diseases management. The effectiveness of vouchers will rely on engaging fully with providers as well as targeting specific populations and simple administrative processes for effective implementation.

Project No.: 12130651

HHS-14
Birth Ball for Pregnant Women in Labour - A Multi-Centre Randomised Controlled Trial

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Introduction and Project Objectives: To examine the level of pain relief, satisfaction with pain control, sense of control in labour and satisfaction with childbirth experience, by comparing birth ball use with those without.

Methods: This is a prospective multi-centre randomised placebo-controlled trial. Participants were randomised based on parity (nulliparous and multiparous) and type of labour onset (spontaneous and induced). Women in the intervention group were actively offered and taught how to use a birth ball; those in the control group receive the usual midwifery care.

Results: We recruited 521 Chinese women with an uncomplicated singleton pregnancy at gestational age of 37 to 42 weeks. The majority(513, 98.5%) completed the study with 8 women withdrew. There were 250 participants in the intervention and 263 in the control group. There was no difference of subjective pain score comparing two groups on various occasions during the labour process. In subgroup analysis, there was pain reduction 15 to 30 min after analgesia in the nulliparous spontaneous intervention group when compared to control (Visual Analog Scale (VAS) 2.43 and 4.17, p=0.01), but not in other occasions during labour. The intervention group was more satisfied with using birth ball as pain control method (3.9/5 and 3.29/5, p=0.04). No difference was found between the intervention and control groups in the satisfaction of overall pain relief, sense of control in labour and satisfaction with childbirth experience.

A separate analysis was done comparing those using (n=182) and not using birth ball (n=331). It was noted a statistical significance in pain reduction when comparing the two groups in first assessment (VAS 3.87 and 5.21, p=0.000), 15 to 30 min after analgesia (VAS 4.01 and 5.95, p=0.000), 2 to 4 hours after first assessment (VAS 5.35 and 6.80, p=0.000) with and without uterine contraction and 4 to 8 hours after first assessment during uterine contraction (VAS 6.5 and 7.55, p=0.001). No difference in other primary outcomes, except the use birth ball group had a higher score in the Chinese version Postpartum Bonding Questionnaire S3 infant-focused anxiety about care (3.81 and 3.08, p=0.01).

Conclusion: Birth ball would be an alternative method for pain relieve during labour. However, the pain reduction effect was only significant comparing those using or not using birth ball, and no difference between intervention and control group. Birth ball had no effect on the sense of control in labour, reduction in assisted delivery and the satisfaction with childbirth experience

Project No.: 12131001

HHS-15
Validation of a New Definition of Lupus Low Disease Activity State (LLDAS): Clinical and Management Implications

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Introduction and Project Objectives: Systemic lupus erythematosus (SLE) is a chronic heterogeneous disease with considerable burden from disease activity and damage. This project is part of a multi-national, multi-ethnic study to evaluate the validity and application of a recently developed disease activity status clinical measurement too – the Lupus Low Disease Activity State (LLDAS).

Methods: A consensus definition of LLDAS was generated using Delphi and nominal group techniques. Preliminary studies using expert opinions, retrospective and prospective data analysis have shown LLDAS to be a valid tool to evaluate lupus disease activity status.

Results: Initial studies showed attainment of LLDAS was associated with a lower risk of lupus disease flare, probably lower accrual organ damage and poorer quality of life. Subsequent studies showed failure to attain LLDAS was associated with lower national social wealth status where the patient resided and was managed, but not her/his ethnicity. Short duration of disease and higher incidence of major organ involvement by lupus at the outset were also associated with a lower attainment of LLDAS. However, data accumulated so far does not allow a more definitive assessment of the relationship between LLDAS attainment and cumulative disease damage and mortality.

Conclusion: The establishment of the APLC has greatly enhanced the scope of lupus research in the Asia Pacific region. Studies on the clinical applications of LLDAS have so far been very encouraging and its evaluation has been extended to research groups in Europe and the North America. In the long term, it is hoped that the LLDAS will become a useful clinical measurement tool to evaluate quality of care, identify management gaps and as a target for the evaluation of drug treatments.

Project No.: 12132961

HHS-16
Meta-analysis of SLE GWAS followed by replication on X chromosome in cross-ethnic populations

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Introduction and Project Objectives: Systemic lupus erythematous (SLE) is a complex autoimmune disease with female predominance, particularly affecting those of childbearing age. We performed analysis of three genome-wide genotyping datasets of populations of both Chinese and European origin.To make the best use of existing GWAS data on X chromosome that would help us to a better understanding of the female preference of this disease without incurring new cost on the GWAS stage.

Methods: This study involved 5695 cases and 10,357 controls in the discovery stage. The lead signal on chromosome X was followed by replication in three additional Asian cohorts, with 2300 cases and 4244 controls in total. Conditional analysis of the known associated loci on chromosome X was also performed to further explore independent signals.

Results: Single-nucleotide polymorphism rs13440883 in GPR173 was found to be significantly associated with SLE (Pmeta=7.53×10-9, ORmeta= 1.16), whereas conditional analysis provided evidence of a potential independent signal in the L1CAM-IRAK1-MECP2 region in Asian populations (rs5987175 [LCA10]).

Conclusion: New X-linked susceptibility loci were identified and confirmed on SLE. Understanding the X-linked susceptibility genes of this complex disease would help elucidate the disease mechanisms. In the long run, the ever increasing awareness of genetic impact on different clinical manifestations of SLE, will move us closer to using

genetics to predict disease risks and disease outcomes, and guiding clinical treatment according to patient's genetic makeup.

Project No.: 12133701

HHS-17

Is It Safe to Use Estrogenic Chinese Herbal Medicines in Breast Cancer Patients? - a Preclinical Evaluation

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Introduction and Project Objectives: Botanicals including Chinese herbal medicines (CHMs) contain estrogenic compounds, which are believed to have beneficial effects for women's health. Nonetheless, the stimulating activity of estrogenic CHMs in breast cancer patients or survivors has been regarded as a paradoxical perception over the decades. The present study aimed to systematically investigate the potential effects of estrogenic CHMs on breast cancer using both preclinical cell-based and tumor-bearing mouse models. Eleven CHMs, which have been previously reported to possess estrogenic effects, were selected in this study.

Methods: The selected estrogenic CHMs were evaluated in four homogeneous breast cancer cell lines with different molecular subtypes for their proliferative responses. The effects of Angelica sinensis (AS) and Cistanche deserticola (CD), both showed potent in vitro stimulatory activities, were also examined on the growth of human breast xenografts and mouse syngeneic tumors in mice. Further verification of the stimulatory activities of AS and CD were performed using primary breast cancer cells isolated from breast cancer patients.

Results: Our results showed that a few tested estrogenic CHMs (including AS and CD) stimulated the proliferation of breast cancer cells in different extents. The stimulatory activities of AS could be observed in short-term oral administration (e.g. 13-20 days) in syngeneic tumor-bearing mice, there was however no significant stimulatory activity of CD observed in human xenografts- or syngeneic tumor-bearing mice, suggesting the oral bioavailable AS or CD might not stimulate breast tumor growth in mice. Furthermore, treatments of AS or CD in cyclophosphamide-treated tumor-bearing mice did not significantly affect the tumor growth or tumor microenvironments. However, AS and CD were shown to enhance the proliferation of primary breast cancer cells, with potential correlation to the expressions of ER in the primary breast cancer cells.

Conclusion: Taking together, the estrogenic herbs AS and CD are not that stimulatory in breast cancer as demonstrated by both cell-based or tumor-bearing mouse models, though these herbs should still be used with caution particularly in ER-positive breast cancer patients. Findings from this study have certainly provided valuable information for breast cancer patients or survivors, Chinese medicine practitioners and clinicians on the safety use of tested estrogenic Chinese herbs in breast cancer, which may affect future clinical practice.

Project No.: 12130471

HHS-18

Lycium barbarum polysaccharides attenuate hepatic oxidative stress, inflammation, fibrosis and apoptosis through NFkappa-B and NLRP3/6 pathways in a non-alcoholic fatty liver disease mouse model

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Introduction and Project Objectives: We aimed to investigate whether LBP could alleviate the hepatic injury in a non-alcoholic steatohepatitis (NASH) methionine-choline deficient (MCD) mouse model.

Methods: NASH was induced in C57BL/6N mice by feeding with MCD diet for 6 weeks. During the experiments, 1 mg/kg LBP was intragastrically fed on a daily basis with or without MCD diet lasting from the 4th to 6th week. Control and vehicle-control (LBP + PBS) were fed with a regular animal chow.

Results: LBP significantly ameliorated NASH-induced injuries, including the increase of serum ALT and AST levels, hepatic oxidative stress, fibrosis, inflammation, and apoptosis. The hepatoprotective effects of LBP were accompanied by the attenuation of thioredoxin interacting protein, nod-like receptor protein 3/6 (NLRP3/6) and reduced NF-κB (nuclear factor-kappa B) activity. Vehicle LBP fed mice showed no adverse effect on the liver.

Conclusion: In conclusion, the suppression of the NLRP3/6 inflammasome pathway and NF-κB activation may partly contribute to the reduction of the hepatic injury during the progression of NASH by therapeutic LBP treatment.

Project No.: 12133881

HHS-19

A Study to Reduce the Toxicity of Xanthii Fructus

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Introduction and Project Objectives: In traditional Chinese medicine (TCM), Xanthii Fructus (XF) is commonly prescribed to treat chronic bronchitis, nasal diseases, headache, urticarial, chronic rhinitis, allergic rhinitis, lumbago and other ailments. However, XF has acute toxicity. To reduce the toxicity, XF is usually processed by stir-baking.

Methods: We used both cell and animal models to compare the toxicities of non-stir-baked XF and stir-baked XF (SBXF) with different stir-baking protocols, and suggested the underlying mechanism of action of how stir-baking can reduce XF toxicity.

Results: Our study clearly showed that water-soluble glycoside carboxyatractyloside (CATR) was reduced progressively while glycoside atractyloside (ATR) was increased progressively as the stir-baking time increased. Since CATR is to known to be more toxic than ATR, we suggest that the non-stir-baked XF is more toxic than SBXF because the former has a higher level of CATR than the latter. However, we found that stir-baking XF for 40 min that resulted in a highly elevated level of ATR had severe toxicity in liver when compared to XF stir-baked for 20 min. Therefore, the stir-baking time is also a critical factor to reduce toxicity. ATR in SBFX can trigger Ca2+ release from mitochondria, causes deregulated Ca2+ matrix in the cells, which leads to matrix swelling and release of apoptotic proteins that cause cell death. Our data clearly showed that ATR triggered internal Ca2+ release and reduced cell viability.

Conclusion: Our study suggest stir-baking reduces XF toxicity because of the decarboxylation of CATR to ATR which is less toxic. Our study has a great implication. We demonstrate a proper stir-baking process that is critical to reduce XF toxicity, and identify CATR and ATR as toxicity markers for XF which will be useful for monitoring the stir-baking process for XF and assessing the toxicity of XF that are available in the market.

Project No.: 12133831

HHS-20
Cardiocrinum Seeds Contain Novel Antitussive Phytochemicals

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Introduction and Project Objectives: Cough is a world-wide concern and the discovery of new, safe and effective antitussive agents is important. Natural products from the traditional Chinese medicines are promising antitussive drugs for further development. Seeds of Cardiocrinum giganteum var. yunnanense (Leichtlin ex Elwes) Stearn (Liliaceae), also known as Doulingzi, have been used as a folk substitute for conventional antitussive herb "Madouling" (Aristolochia species) to treat chronic bronchitis and pertussis. The active antitussive phytochemicals in C. giganteum seeds are not known. The work aims at isolating the active phytochemicals in C. giganteum seeds and confirming their antitussive effects.

Methods: Petroleum ether, ethyl acetate, butanol and water were used to separate the methanol extract into different fractions. Active chemicals were isolated from and identified their structures. Antitussive effects were evaluated with the cough frequency of guinea pigs exposed to citric acid. Electrical stimulation of the superior laryngeal nerve in guinea pigs was performed to differentiate the acting site of potential antitussives.

Results: It was shown, among all the fractions, the n-butanol fraction had the strongest effect to inhibit coughs induced by inhalation of citric acid in guinea pigs. Two racemic biflavonoids (CGY-1 and CGY-2) were isolated from the n-butanol fraction. CGY-1 was identified as (S)-2"R,3"R- and (R)-2"S,3"S-dihydro-3"-hydroxyamentoflavone-7-methyl ether, which are new compounds and firstly isolated from C. giganteum seeds. Racemic CGY-2 was identified as (S)-2"R,3"R- and (R)-2"S,3"S-dihydro-3"-hydroxyamentoflavone. Both CGY-1 and CGY-2 could significantly inhibit coughs induced by inhalation of citric acid. Further, they acted on the peripheral reflex pathway to inhibit cough after electrical stimulation of the superior laryngeal nerve in guinea pigs.

Conclusion: These chemicals from C. giganteum seeds showed good antitussive effects. The data provide scientific evidence to support the traditional use of C. giganteum seeds as an antitussive herbal medicine.

Project No.: 12130851

HHS-21
A Novel Treatment of Intermittent Claudication in Patients with Peripheral Arterial Disease Using a Herbal Formula with Proven Efficacy

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Introduction and Project Objectives: Effective medical therapy for the treatment of intermittent claudication (IC) in patients with peripheral arterial disease (PAD) is limited. Danshen and Gegen (DG) are traditional Chinese medicines with vasodilatory and anti-inflammatory properties which may be a novel treatment in PAD. We conducted a prospective-randomized, double-blind, placebo-controlled trial (RCT) to evaluate the efficacy and safety of DG in symptomatic PAD patients and animal models to evaluate the vasodilatory and angiogenic response to DG.

Methods: We used isolated rat femoral artery to investigate in-vitro vasorelaxant activity and DG mechanisms-of-action. In-vivo functional recovery and in-vitro muscle perfusion and capillary density were assessed in a rat ischemic-limb model. 95 PAD patients with IC were randomly allocated to treatment group (n=48) with oral DG capsules (1.5 g bid) or placebo group (n=47) for 24 weeks. Primary outcome was change in maximal walking distances (MWD) on standardized graded-treadmill testing. Secondary outcomes included pain-free walking distances (PFWD) and functional status measured by Walking Impairment Questionnaire (WIQ) and Euro-QOL 5D.

Results: DG was associated with significant positive vasodilatory and angiogenic response in animal studies. The proportion of patients who achieved ≥50% improvement in walking distances was significantly higher in DG (43.2%) vs. control group (22.0%, P=0.044). Patients with moderate-to-severe IC (baseline MWD)

Conclusion: DG may be an effective treatment for PAD patients with severe claudication compared to placebo. However, long-term research in larger population is needed to better establish its safety and efficacy. (ClinicalTrials.org. ID NCT 02380784)

Project No.: 11120771

HHS-22

Investigation of the effects of Gastrodiae Rhizoma – containing herbal formula (DCXF) in traumatic brain injury rat model

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Introduction and Project Objectives: The aim of this study was to investigate the effects of Gastrodiae Rhizoma – containing herbal formula (DCXF) in traumatic brain injury (TBI) rat model.

Methods: TBI was induced by the electromagnetic controlled cortical impact (CCI) device. DCXF were intragastrically administered daily for one week to the rats before CCI-TBI, and then DCXF treatments were continued post-TBI until the end of the experiments. After the TBI surgery, the animals were subjected to BBB integrity by Evans blue dye and brain water content assessments on day 3, Morris Water Maze test for cognitive assessment, spatial learning and memory were examined for 11 days, the motor coordination and maximal motor performance were tested using an acceleration rotarod motor test and the assessment of gait function was measured by CatWalk quantitative gait analysis test on day 3, 7 and 11, and histology and immunohistochemistry assessments of Nissl, GFAP, Iba-1, nestin in hippocampus nad cortex on day 11. The In vitro anti-inflammatory effects of DCXF were study by LPS-induced gene and protein expression of NO, PGE2, iNOS and COX-2. The NF-κB pathway was also measured by the expressions and phosphorylations of p65 and IκBα pathway.

Results: We demonstrated that herbal formula DCXF could protect the neuronal cell against oxidative insult and alleviate the injuries coming from TBI in rats. Treatment with DCXF significantly improved the learning ability and memory retention in Morris water maze test, and remarkably enhanced motor performances in acceleration rotarod motor test and catwalk quantitative gait analysis test after TBI. Moreover, DCXF treatment was able to reduce blood brain barrier permeability, brain edema, microglia and astrocyte activation, improve the proliferation of neural stem cells and decrease neurons loss in the brain with TBI. Besides, our in vitro studies also indicated that treatment with DCXF significantly suppressed the productions of NO and PGE2 through inhibitions of iNOS and COX-2 expressions in LPS-stimulated RAW 264.7 cells. DCXF significantly decreased IκBα phosphorylation, inhibited p65 expression and reduced p-p65 level. These results suggested the anti-inflammatory effect of DCXF was associated with the reduction of inflammatory mediators through inhibition of NF-κB pathway.

Conclusion: In conclusion, herbal formula DCXF is a potent neuroprotective agent and can impose healing effects in vivo.

Project No.: 12134111

HHS-23

Clinical Assessment of a Topical Application Containing Radix Rubiae for Plaque-Type Psoriasis - A Randomized, Double-blind, Vehicle-Controlled and Left-Right Comparison Pilot Study.

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Introduction: Psoriasis is a common chronic inflammatory skin disease for which currently there is no known cure. Our previous in vitro and in vivo studies have identified a Chinese herbal medicine named Radix Rubiae (茜草根) to have promising anti-psoriatic action.

Objectives: This study aimed to evaluate the clinical efficacy and safety of a topical preparation containing Radix Rubiae extract in patients with chronic plaque type psoriasis.

Methods:
Design: This is a 12-week, left-right intra-patient comparison, vehicle-controlled, randomized, assessor-blinded pilot clinical trial.
Setting: The study was conducted at The Chinese University of Hong Kong Chinese Medicine Specialty Clinic cum Clinical Teaching and Research Centre between February 2015 and April 2017.
Participants: Sixty patients with chronic plaque type psoriasis were enrolled.
Intervention: The patients were instructed to apply the Radix Rubiae-containing topical formulation to one side of the psoriatic lesion and the vehicle preparation to the opposite side of the lesion twice a day for a consecutive 12 weeks.
Outcome measures: The primary outcome assessment was performed using the scores of scaling, erythema, induration, and clearing percentage of target plaques by 2 blinded assessors after 6 and 12 weeks of intervention. Secondary outcomes included physician global assessment, quality of life (SF36) and impact of psoriasis questionnaire.

Results: The scores of induration and scaling showed statistically significant improvement in the active treatment side when compared with the vehicle controlled side after 12 weeks of intervention. The quality of life measure by SF36 remained no change after the treatment. The impact of psoriasis questionnaire showed much improvement after 12 weeks of treatment. Twenty-six (43.3%) participants dropped out during the study, of them 15 were due to some mild or severe adverse effects.

Conclusion: The study suggests the topical application of Radix Rubiae extract had some promising treatment effect for psoriasis; however, the active treatment involved certain degree of adverse effects. Further research is needed to reduce the possible adverse effects via optimizing the formulation making.

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Project No.: 11121011

HHS-24
Chinese Medicine Yuanhu Zhitong Prescription Alleviates Tau Pathogenesis and Ameliorates Memory in the Alzheimer's disease Models

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Introduction:
Background: Alzheimer's disease (AD) is a neurodegenerative disease characterized by the progressive memory dysfunction and the appearance of neurofibrillary tangles. We have identified a novel function of traditional Chinese medicine formula Yuanhu-Zhitong prescription (YZT) in treating AD mice models.

Objectives:
(1) To validate the neuroprotective effects of Yuanhu-Zhitong prescription (YZT, 元胡止痛散 in Chinese) in Alzheimer's disease (AD) mice models;
(2) To discover the molecular mechanisms of YZT and its multifunctional compounds using gene expression microarray and bioinformatics tools.

Methods: Liquid chromatography/quadrupole time-of-flight (LC-ESI-Q/TOF) was performed to quantify the chemical markers of YZT. Two-months old P301S Tau mice and six months old 3XTg-AD mice received two doses of YZT or vehicle in food admixture until 4- and 18- months old, respectively. Rotarod and Morris water maze test were used to assess motor function and memory, respectively. The differential extraction by ultracentrifugation followed by western blotting and immunohistochemistry were used to assess insoluble Tau deposition in the brain. The microarray experiments and Connectivity Maps (Clue) analysis was performed to reveal the up and down-regulated genes in the YZT, RC and RAD-treated SH-SY5Y cells expressing P301L Tau.

Results: From the LC-ESI-Q/TOF chromatograms of aqueous extracts of YZT, protopine, tetradydropalmatine and dehydrocorydaline are the most abundant compounds, followed by other isoquinoline alkaloids and imperatorin. Treatment with YZT significantly ameliorated the motor dysfunction and insoluble tau load learning deficits in P301S-Tau mice compared with vehicle control treatment. In 3XTg-AD mice, YZT treatment significantly ameliorated memory dysfunction and reduced insoluble phospho Tau species. According to microarray/CMaps, one of the mechanisms of action of YZT could be predicted as NF-kB inhibitor and participating in autophagy process. Finally, based on the differentially expressed genes from three hub genes, SQSTM1, TXNRD1, and HMOX1, YZT could be predicted to involve in NRF2-mediated Oxidative Stress Response. Similar analysis was performed and suggested that RC may be involved in Ubiquitination Proteasome pathway.

Conclusion: YZT decreases the phosphorylated, misfolded and total insoluble Tau as demonstrated in in vitro and in vivo studies, and YZT also enhances memory in 3XTg-AD mice. YZT could be a promising candidate for the treatment of AD in the future.

Project No.: 12132061

HHS-25
Impact of the Chinese herbal medicines on the combination therapy with clopidogrel and aspirin: pharmacokinetics and pharmacodynamics outcomes and related mechanisms in rats

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Introduction and Project Objectives: Dual antiplatelet therapy (DAPT) with aspirin (ASA) and clopidogrel (CLP) has been consistently shown clinical effectiveness in patients with coronary artery disease. According to the literature, four traditional Chinese medicine (TCM) herbs effective for prevention cardiovascular diseases, namely Radix Salviae miltiorrhizae (Danshen), Radix Puerariae lobatae (Gegen), Radix Angelicae Sinensis (Danggui), and Rhizoma Chuanxiong (Chuanxiong), are of high potential to be co-administered during DAPT. The current study is proposed aiming to preliminarily evaluate the impact of these four commonly used Chinese medicinal herbs on the pharmacokinetics and pharmacodynamics of the combination therapy with clopidogrel and aspirin and its relevant outcomes and mechanisms.

Methods: In order to mimic the standard dosing regimen for DAPT in human, various Sprague-Dawley rats treatment groups were received a bolus oral dose of DAPT on day 1 followed by DAPT for consecutive 13 days in absence and presence of orally co-administered four TCM herbs (Danshen, Gegen, Danggui and Chuanxiong) at their low and high doses. On day 14, serial blood samples were collected after dosing to obtain the plasma concentrations of ASA, CLP and their corresponding metabolites by LC/MS/MS. At the end of last blood sampling point of each rat, about 4.5 ml of whole blood were collected to estimate the prothrombin time from each treatment groups. After all the blood sampling, the rats were sacrificed followed by collecting their livers for evaluations of enzyme activities and expressions in the related liver microsome preparations and stomach tissues for evaluations of their potential ulcer index.

Results: The results demonstrated that co-administration of Gegen and Danggui significantly altered the pharmacokinetics of ASA and CLP in DAPT with increased systemic exposure of ASA and CLP respectively. Although minimal impact on aspirin esterase activity for all co-administered herbs, significant inhibition on rCyp2c11 and carboxylesterase activities were observed for DAPT with Danshen, Gegen and Danggui co-treatment. In addition, a trend of decrease in PT of DAPT in presence of Gegen, Danggui and Chuanxiong was noticed. Nevertheless, all the treatments did not cause detectable

changes in COX and P2Y12 mRNA and protein expressions.

Conclusion: In conclusion, it was demonstrated that co-administration of Gegen and Danggui could lead to altered pharmacokinetics of DAPT with significant inhibition on rCyp2c11 and carboxylesterase activities. Although Gegen, Danggui and Chuanxiong might potentially offset the anticoagulant activity of DAPT, the overall pharmacodynamics outcome was not considered to be harmful due to lack of risk in bleeding, which warrant further verification for its clinical impact.

Project No.: 12131521

HHS-26
A Study of Efficacy on the Combination Use of Anti-osteoporosis Drug with Topical Chinese Herbal Paste on Facilitation of Fracture Healing

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Introduction: Patients with fracture occupy a lot of hospital beds and demand a lot of special services. Pharmaceutical agents advocated for fracture healing are controversial. Co-treatment using pharmacological medication and Traditional Chinese Medicine might be a beneficial intervention to enhance fracture healing.

Objectives: To study the efficacy of strontium ranelate (SrR) and a Chinese herbal formula containing Carthami Flos, Dipsaci Radix and Rhei Rhizoma (named CDR) on the facilitation of fracture healing, and find out if any synergistic effect exists.

Methods: This project was conducted in two parts: In vitro and in vivo. Part 1, bone-marrow mesenchymal stem cells (BMSC) isolated from rats, UMR106 and RAW264.7 cells were used. The BMSC and UMR106 were used to study the cytotoxic effect and find out the optimal concentrations of the CDR via MTT assays, as well as the bone formation properties of CDR and SrR via BrdU and alkaline phosphatase (ALP) assays. Raw264.7 was used to study the anti-osteoclastogenic and anti-inflammatory properties of CDR and SrR via TRAP and Griess assay, respectively. Part 2, Rats with artificially produced tibial fracture were treated with different regimens consisting of either oral SrR or topical CDR (supplemented with 2% borneol), or their combination. Micro-computed tomography and biomechanical tests were utilized to measure the differences in the physical and biomechanical properties of the calluses. Histomorphometry and measurement of serum biomarkers were checked to analyze the underlying mechanisms.

Results: The in vitro results showed that SrR and CDR were non-cytotoxic and increased the proliferation of BMSC at low concentrations. The combination of CDR and SrR also showed an additive effect on the promotion of ALP activities of BMSC. SrR and CDR alone reduced osteoclast formation and the effective concentration of SrR could be reduced in the presence of CDR. The in vivo results illustrated an additive effect of CDR on SrR on the load bearing strength, the size and the bone density of the callus of the fractured tibia.

Conclusion: This integrative approach by combining oral SrR and topical CDR was effective on promoting fracture healing probably through the additive effects on osteogenesis promotion as well as osteoclastogenesis suppression.

Project No.: 12130581

HHS-27
Tetramethylpyrazine as a Novel HIF Activator for Promoting Angiogenesis and Osteogenesis During Skeletal Regeneration

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Introduction and Project Objectives: In clinic, impaired bone repair or regeneration including fracture non-union, large bone defects, and osteoporosis are difficult skeletal disorders that cause tremendous pain and cost to the patients and society. The pathology of osteoporosis and impaired bone repair is characterized by less capacity of bone formation associated with decreased vascularity. As current therapies remain to be unsatisfied, novel therapeutic agents for patients with impaired bone repair have significant clinical demand. Hypoxia inducible factor-1 alpha (HIF-1a) has been identified as a key transcription factor that involves in the coupling of angiogenesis and osteogenesis during skeletal development and regeneration. This study aims to discover novel small molecule targeting the HIF-1a pathway to enhance skeletal regeneration.

Methods: Small molecule screening and identification based on osteogenic and angiogenic phenotypes and functional assays were performed. Osteoblast and endothelial cell models, and ovariectomy (OVX)-induced osteoporosis and long bone fracture mouse models were employed to evaluate the pharmacological effects and the underling molecular mechanisms of the candidate molecule.

Results: We identify tetramethylpyrazine (TMP), an active ingredient from Ligusticum Wallichii, upregulates HIF-1a and induces its nuclear translocation in osteoblasts. TMP not only activates HIF-1a downstream targets but also enhances osteogenic marker genes expression. Intriguingly, TMP remarkably upregulates adenomedullin, a downstream target of HIF-1a and a potent stimulator of osteoblast function. Those enhancement effects are attenuated by Cre recombinase mediated deletion of HIF-1a in osteoblasts carrying HIF-1a loxP-flanked allele. TMP treatment rescues bone loss in OVX-induced osteoporosis mouse model. This phenotype is accompanied by enhanced angiogenic responses of TMP. In a mouse long bone fracture model, local delivery of TMP at the fracture site results in significantly increased bony callus volume with improved biomechanical properties of the newly formed bone at the consolidation phase of bone healing.

Conclusion: Our results suggest that TMP may serve as a potent anabolic agent to promote angiogenesis and osteogenesis for patients with osteoporosis or fracture repair.

Project No.: 12131041

HHS-28

Biomedical effects of green tea extracts on experimental age-related macular degeneration

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Introduction and Project Objectives: Age-related macular degeneration (AMD) is a leading cause of irreversible visual impairment and blindness in most developed countries, affecting 50 million elderlies worldwide. It is a progressive neurodegenerative disease affecting the macula and resulting in a significant loss of central vision in advanced stages. Oxidative stress and inflammation are the pathological initiators in AMD pathogenesis. Since green tea extracts (GTE) exhibit anti-oxidative and anti-inflammatory actions, we hypothesized that GTE and its catechin constituents ameliorate sodium iodate-induced retinal degeneration in an experimental AMD model by counteracting oxidative stress.

Methods: Retinal degeneration was induced in adult Sprague-Dawley rats by intravenously injecting single dose of sodium iodate. GTE (Theaphenon-E) or combinations of its catechin constituents, including (-)-epigallocatechin gallate (EGCG), were administered intra-gastrically before injection. Photoreceptor degeneration was monitored by in vivo imaging and histological analyses. In addition, the oxidative status in the retina was also evaluated.

Results: Live imaging analysis using confocal scanning laser ophthalmoscopy and spectral-domain optical coherence tomography showed a progressive increase of degenerating profile across the retinal surface and decrease in thickness of outer nuclear layer (ONL) at Day-14 of post-injection. These lesions were significantly ameliorated by Theaphenon-E and catechin combinations with EGCG. Catechins with exclusion of EGCG did not show obvious protective effect. Histological analyses confirmed that Theaphenon-E and catechins containing EGCG protect the retina by reducing ONL disruption. Retinal protective effects were associated with reduced expression of superoxide dismutase, glutathione peroxidase and caspase-3, and suppression of 8-iso-Prostaglandin F2α generation in the retina.

Conclusion: In summary, GTE and its catechin constituents are potent anti-oxidants that offer neuroprotection to the outer retinal degeneration after sodium iodate insult, which EGCG is the most active constituent.

Project No.: 12130791

HHS-29

Therapeutic Treatment Against Ocular Inflammation by Green Tea Extract and Catechins in Experimental uveitis

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Introduction and Project Objectives: To determine the treatment effects of green tea extract (GTE) and catechins against ocular inflammation in experimental uveitis models.

Methods: Endotoxin-induced uveitis (EIU) rat model and experimental autoimmune uveitis (EAU) mouse model. Ocular inflammation in EIU model was assessed by slit lamp photography, whereas that in EAU model was assessed by confocal scanning laser ophthalmoscopy, optical coherence tomography (OCT), fundus fluorescein angiography (FFA) and electroretinography (ERG). Tissue cells and molecules were investigated by confocal microscope, RTPCR, GCMS, and LCMSMS. After EIU induction, 275 and 550 mg/kg GTE were intragastrically fed into the rats 2, 8, 26, 32 hours after LPS injection. For the EAU model, 137.5 and 275 mg/kg GTE or 96.25 and 192.5 mg/kg EGCG catechins were fed once every two days starting from 5 days prior to EAU induction through day 21 post-immunization. The degree of ocular inflammation, amount of infiltrating cells and ocular histology were evaluated. Expression levels of targeted pro-inflammatory factors were determined in appropriate samples including plasma, humor, ciliary body, and retina tissues. Catechins in tissue cells were quantified for correlations with the molecular effects.

Results: Our results revealed the treatment effects of GTE and catechins on ocular inflammation in two established experimental models and provided new insights into the protective mechanisms of GTE and catechins on uveitis pathogenesis.

Conclusion: Our assessments showed that administration of GTE and catechins alleviated EIU and EAU in morphology and gene expressions, providing evidences for their therapeutic effects in ocular inflammations.

Project No.: 12130811

HHS-30

Comparative Effectiveness Analysis of Lung Cancer Data from Randomized Clinical Trials and Observational Studies

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Introduction and Project Objectives: Elderly lung cancer patients are less likely than younger patients to participate in clinical trials. With sparse and conflicting findings, the optimal chemoradiotherapy and management of elderly patients is unclear. To conduct analyses for clinical trials and observational studies on the relative efficacy of chemoradiotherapy treatment paradigms in locally advanced NSCLC. To develop novel statistical methods for a unified analysis that yields efficient and valid estimation of treatment effect.

Methods: For the analysis of trials and observational data, the primary endpoint was overall survival. Statistical methods for selection bias control with propensity score inverse weighting was used to estimate treatment effects to compare the chemoradiotherapy treatment paradigms. We also used simulation to evaluate the finite sample properties of the new statistical estimators

under various conditions in terms of bias and efficiency. Along with the single-source analysis, the novel statistical method was used as a part of the unified approach to address the comparative effectiveness question of various different chemoradiotherapy treatment paradigms versus sequential chemoradiotherapy.

Results: Propensity score adjusted models for locally advanced NSCLC elderly patients showed significant pairwise comparison differences between consolidation chemoradiotherapy vs. sequential chemoradiotherapy, and induction chemoradiotherapy vs. sequential chemoradiotherapy (p

Conclusion: Adequate adjustments for patient characteristics can reduce bias. Combining trials and observational data can provide useful information on comparative treatment effectiveness.

Project No.: 12133251

HHS-31
The effects of the IKKß-specific inhibitor PS1145 on tumor formation and metastasis in nasopharyngeal carcinoma

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Introduction and Project Objectives: We and others have previously shown that the canonical nuclear factor kappa-B (NF-κB) pathway is essential to nasopharyngeal carcinoma (NPC) tumor development and angiogenesis, suggesting that the NF-κB pathway, including its upstream modulators and downstream effectors, are potential therapeutic targets for NPC. The inhibitor of upstream IKB kinase (IKK), PS1145, is a small molecule which can specifically inhibit the IκB phosphorylation and degradation and the subsequent nuclear translocation of NF-κB. The present study aims to determine the anti-tumor activity and drug resistance mechanism of PS1145 on NPC.

Methods: The anti-tumor and anti-metastasis effects of PS1145 were tested by using a panel of NPC cells lines and the nomal immortalized nasopharyngeal epithelial cell lines included as normal controls. Various in vitro and in vivo cell growth, migration/invasion, apoptosis and cell cycle, tumor formation, and metastasis assays were used to test the effects of PS1145.

Results: PS1145-alone could effectively inhibit both the in vitro and in vivo cell gowth of various NPC cell lines, it was likely due to cell apoptosis. Apparently no adverse effects were observed in the animal study. In addition, the cell mobility was also suppressed in the presence of PS1145. Drug resistance aganist PS1145 seems to be associated with the increased levels of active NF-κB p65 and change of expression levels of of kruppel-like factor 4.

Conclusion: As can be seen, PS1145 appears to be a safe agent for animal experiments and its effects are tumor-specific, and the proteins associated with the drug resistance of PS1145 are implied.

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HHS-32
The use of curcumin to circumvent cisplatin resistance in nasopharyngeal carcinoma

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Introduction and Project Objectives: Nasopharyngeal carcinoma (NPC), also commonly known as the "Canton tumour", is endemic in Southern China including Hong Kong. NPC can acquire resistance to cisplatin during treatment which affects the treatment outcome. At present, there is still no effective method to overcome cisplatin resistance in NPC. The current study aims to examine whether curcumin (diferuloylmethane), a natural polyphenol isolated from the rhizome of Curcuma longa, can be used to circumvent cisplatin resistance in NPC.

Methods: Cisplatin-resistant NPC cell line was developed by chronic treatment of cisplatin. In vitro toxicity assay was used to confirm the resistance level of cisplatin-resistant cell line. Liposomal curcumin was prepared by thin-film evaporation. NPC xenograft was generated in nude mice to examine the therapeutic effects of cisplatin and curcumin.

Results: In vitro toxicity assay indicated that cisplatin and liposomal curcumin could significantly inhibit proliferation of the cisplatin-resistant cells. Combination use of cisplatin and liposomal curcumin significantly enhanced the treatment efficacy. Further, combined treatment of NPC xenograft with liposomal curcumin and cisplatin blocked the progression of NPC xenograft in pre-cliniclal model.

Conclusion: Chronic exposure of NPC cells to cisplatin can induce cisplatin resistance. Combination treatment using curcumin and cisplatin offers better efficacy in comparison to the single agent treatment on cisplatin-resistant NPC.

Project No.: 12133541

HHS-33
Association study of susceptibility genes in Wnt signaling pathway with attempted suicide

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Introduction and Project Objectives: The suicide rate in the Chinese population is estimated to be around 12.7 per 100,000. Moreover, the number of suicide victims in China has been estimated to account for approximately 42% of suicide death all over the world. Although the pathogenesis of suicide attempts (SA) is still not explained clearly, it is generally believed that SA is affected by a combination of genetic variants, environmental factors, psychiatric disorders, clinical and psychological correlates. For genetic variants, most of the previous studies focused on the neurotransmitter system, mainly including the serotonergic, dopaminergic and glutamatergic systems. Our study focused on the Wnt signaling pathway which has

also been shown to be important in neuronal differentiation and development.

Methods: Our team performed a pilot genome-wide association study (GWAS) in Hong Kong Chinese samples constituted of 48 suicide attempters and 48 non-suicide attempters, both with major depressive disorder (MDD).

Results: Association analyses identified 8 candidate loci associated with SA passing the genome-wide suggestive threshold. WNT2B (Wnt family member 2B) is the most significantly associated signal with suicide attempts and withstands the multiple corrections out of the 26 candidate SNPs we tested. WNT2B was reported to function as the stem cell factor for neural or retinal progenitor cells during embryogenesis. Four single nucleotide polymorphisms (SNPs) located in a near physical position in Chr.11 that cover the ICEBERG gene in a linkage disequilibrium block (ICEBERG also is known as Caspase 1 inhibitor Iceberg) also associated with SA. The finding was also confirmed by gene-based analysis of the GWAS genomic data, which listed the ICEBERG gene as the top 1 signal associated with SA (p-value=1.70e-05). We have also performed replication studies for the top signals and tagging SNPs in the ICEBERG gene in an independent larger Hong Kong Sample set. Statistical analyses suggested that these SNPs were also significantly associated with SA. As the ICEBERG protein was involved in a negative feedback loop of inflammatory response system (IRS), the findings of this project suggested that the IRS is involved in the pathogenesis of suicidal behavior in Chinese and that the ICEBERG gene is an important biomarker.

Conclusion: An effective multifactorial risk model consisted of the interaction of the HOMER1 polymorphism and the NEO-C personality dimension was successfully identified and evaluated to have improved performance of explaining the variance of SA. We found 5 SNPs (of WNT2B and ICEBERG genes) that associated with SA in the patients with major depressive disorder we tested.

Project No.: 12131101

HHS-34

The effectiveness of group behavioural activation with mindfulness in the treatment of subthreshold depression in primary care in Hong Kong

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Introduction and Project Objectives: Sub-threshold depression is highly prevalent in primary care settings and is associated with significant reduction in quality of life, increased mortality and healthcare burden. To conduct a randomized controlled trial to assess the effectiveness of group behavioural activation with mindfulness (BAM) for reducing subthreshold depression in primary care in Hong Kong.

Methods: Adult patients aged 18 years or older with subthreshold depression were recruited from 16 public primary care clinics in Hong Kong and were randomly assigned to behavioural activation with mindfulness or care as usual (CAU) group. BAM group was provided with eight 2-hour weekly behavioural activation treatment with mindfulness by trained allied healthcare workers. Patients in the CAU received usual medical care with no additional mental interventions. The primary outcome was depressive symptoms measured by Beck Depression Inventory (BDI)-II at 12 month. The secondary outcomes included incidence of major depressive disorder at 12-month. Quality of life, Activity and Circumstantial Change, functional impairment, health service utilization, satisfaction, and anxiety were assessed at baseline, post-intervention, 5-month and 12-month.

Results: 115 participants were randomly allocated to BAM and 116 participants to CAU group (a total of 231). At 12-month, ANCOVA results demonstrated a statistically significant effect of BAM in reducing depressive symptoms when compared to CAU group (between-group mean difference=-3.85, 95%CI: -6.36 to -1.34; Cohen d=-0.46, 95%CI: -0.76 to -0.16). BAM group had lower incidence of major depressive disorder (10.8% in BAM group vs. 26.8% in CAU group) at 12-month. No significant differences were reported on other secondary outcomes at 12-month between the two groups.

Conclusion: Group behavioural activation with mindfulness appears to be beneficial in decreasing depressive symptoms and reducing the incidence of major depression among people with subthreshold depression in primary care. With proper training and supervision, this intervention can be learned by allied health professionals and can be implemented in local primary care settings.

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HHS-35

The Role of Napping in Reducing Negative Attentional Bias in Depression

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Introduction and Project Objectives: Cognitive theories of depression hypothesized that affective-cognitive processing bias of emotional information, such as human faces, is related to the maintenance of depression. Sleep disturbances were found to maintain depression, and the possible role of sleep in the maintenance of depression through emotional processing bias still requires exploration. To further examine the specific sleep mechanism of the maintenance of depression, we focused on one of the affective-cognitive features in depression: attentional bias towards emotional faces. This study adopted a napping design to examine how sleep is associated with attentional bias towards emotional faces among patients with major depressive disorder (MDD).