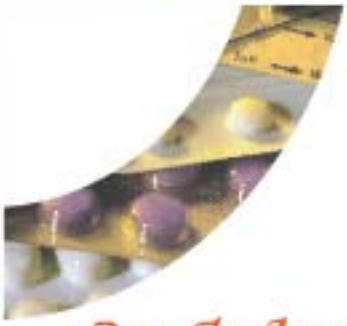
2012 Joint Conference of Drug Safety Research Centres ▪ 2012 藥物安全研究中心聯合會議



Pre - Conference Meeting

A Systematic Approach to Improving Drug Safety and Effective Use

Organisers

Centre for Food and Drug Safety
Faculty of Medicine
The Chinese University of Hong Kong

Prince of Wales Hospital Poison Treatment Centre
Hong Kong

Department of Pharmacovigilance
The University Paris-Est Créteil
Henri Mondor University Hospital (AP-HP), France

Department of Clinical Pharmacology
Institute of Clinical Medicine
University of Helsinki, Finland

School of Pharmacy
The Chinese University of Hong Kong

Department of Ophthalmology and Visual Sciences
The Chinese University of Hong Kong

Department of Health
The Government of the Hong Kong SAR

Medication Safety Committee
Hospital Authority, Hong Kong

20 November 2012

Lecture Hall, 3/F, Hong Kong Eye Hospital
147K Argyle Street, Kowloon, Hong Kong

PROGRAMME BOOK

Organisers and Organising Committee

Organisers

Centre for Food and Drug Safety
Faculty of Medicine
The Chinese University of Hong Kong

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Department of Health
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Medication Safety Committee
Hospital Authority, Hong Kong

Organising Committee

Prof. Thomas Y.K. Chan (Chairman)

Dr. Jones C.M. Chan
Prof. Vincent H.L. Lee
Dr. Joseph Lui
Ms. Linda Woo
Prof. Kalle Hoppu
Prof. Hervé Le Louet
Prof. Brian Tomlinson
Dr. Raymond S.M. Wong (Secretary)

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CME/CNE/CPE Accreditations

CME		
Institution	**Points**	**Category**
The Hong Kong College of Anaesthesiologists	3.92	Non-anaes
Hong Kong College of Community Medicine	Pending	
College of Dental Surgeons of Hong Kong	4	Cat. B
Hong Kong College of Emergency Medicine	Pending	
The Hong Kong College of Family Physicians	3	Cat. 5.2
Hong Kong College of Obstetricians and Gynaecologists	Pending	
College of Ophthalmologists of Hong Kong	Pending	
The Hong Kong College of Orthopaedic Surgeons	3	Cat. B
The Hong Kong College of Otorhinolaryngologists	2	Cat. 2.2
Hong Kong College of Paediatricians	4	Cat. E
The Hong Kong College of Pathologists	4	PP
Hong Kong College of Physicians	2	-
The Hong Kong College of Psychiatrists	3	PP/OP
Hong Kong College of Radiologists	3	Cat. B
The College of Surgeons of Hong Kong	Pending	
CNE: 3 points accredited		
CPE: 3 points accredited		

Programme

13:00 – 13:30 Registration

13:30 – 13:35 WELCOME REMARKS

Prof. Thomas Y.K. Chan, JP
Chairman, Organising Committee, and
Director, Centre for Food and Drug Safety, and
Director, Prince of Wales Hospital Poison Treatment Centre

13:35 – 13:45 OPENING ADDRESS

Dr. Cindy Lai, JP
Deputy Director of Health
The Government of the Hong Kong SAR

13:45– 15:45 ENSURING DRUGS ARE SAFE AND EFFECTIVE

Chair Persons:

Prof. Vincent H.L. Lee

Prof. Benjamin Li

13:45 – 14:20 Cost Effectiveness Analysis Method and Models

Prof. Hervé Le Louet

14:20 – 14:55 Pharmacogenomic Tests for Improving Drug Safety and Effectiveness

Prof. Brian Tomlinson

14:55 – 15:30 Challenges and Opportunities of Developing Paediatric Medicines

Prof. Kalle Hoppu

15:30 – 15:45 Questions and Answers

15:45 – 16:00 Tea Break

16:00 – 17:55 Ensuring Drugs are Used Safely and Effectively

Chair Persons:

Prof. Brian Tomlinson

Prof. Richard Y.H. Yu

16:00 – 16:35 Applications of Pharmacoepidemiology in General Practice

Prof. Martin C.S. Wong

16:35 – 17:10 Cost Effectiveness Analysis and Drug Formulary Decision Making

Prof. Vivian W.Y. Lee

17:10– 17:40 Improving Clinical Outcomes in Subjects with Unstable Anticoagulation

Dr. Raymond S.M. Wong

17:40 – 17:55 Questions and Answers

17:55 – 18:00 Closing Remarks and the Way Forward

Prof. Richard Y.H. Yu

Prof. Brian Tomlinson

Cost Effectiveness Analysis Method and Models

Prof. Hervé Le Louet, The University Paris-Est Créteil, France

Acceptance of cost effectiveness analysis (CEA) as part of the treatment and policy-making decision process is now obvious. Over the 3 last decades, CEA methods have gained respectability in the clinical world and, many medical journals routinely publish these analyses. The main models used for economic assessment of healthcare interventions as decision-tree and Markov model and how exploring uncertainty with sensitivity analysis will be described.

We will focus on how Quality-adjusted life year (QALYs) are used in economic assessment for measuring the benefits of healthcare interventions using a single index that combines life-years and health-related quality of life.

Different approaches of CEA in different countries will be highlighted.

Indeed, CEA has an important input among many factors currently used in healthcare decisions and there is an emerging consensus among private and public decision makers. Cost-effectiveness studies are likely to play an expanding role in the area of managed care but the use of cost-effectiveness analysis in managed care is still in its early stages.

Pharmacogenomic Tests for Improving Drug Safety and Effectiveness

Prof. Brian Tomlinson, The Chinese University of Hong Kong, Hong Kong

Adverse drug reactions (ADRs) are a frequent cause of hospital admission and contribute to significant patient morbidity. Both type A augmented ADRs and type B bizarre or idiosyncratic ADRs may have underlying genetic predisposition. There is increasing evidence that severe hypersensitivity reactions may have a genetic basis. This was shown with the hypersensitivity reaction to abacavir which was found to be associated with the *HLA-B*5701* allele.[1,2] A subsequent study demonstrated that screening for the presence of *HLA-B*5701* could avoid abacavir hypersensitivity.[3] Changes in the drug label for abacavir recommending screening for the *HLA-B*5701* allele before using the drug were introduced by the EMEA and FDA in 2008, but the *HLA-B*5701* allele is rare in southern Chinese[4] and it is not cost-effective to perform this test prior to initiating abacavir treatment in the Hong Kong Chinese population. Conversely, the association between severe cutaneous adverse reactions (SCARs) with carbamazepine and other anticonvulsant drugs and *HLA-B*1502* is more common in southern Chinese because of the higher frequency of this allele.[5,6] Screening for this allele before starting carbamazepine can avoid the SCARs[7] and this practice has been adopted in Hong Kong but is not useful in western countries where other markers are associated with the adverse reaction.[8] The SCARs with allopurinol are strongly associated with the *HLA-B*5801* allele in Han Chinese and other populations,[9,10] but it has not been established whether testing for this allele before prescribing the drug would be cost effective. Likewise, the *HLA-B*5701* genotype has been shown to be a major determinant of drug-induced liver injury due to flucloxacillin,[11] but this has a low positive predictive value and may not be cost-effective.

Genetic polymorphisms involved in drug metabolism or drug responses have also been identified and may be useful to determine the appropriate dose of warfarin or whether to use clopidogrel or alternative antiplatelet agents. Severe myopathy associated with high dose simvastatin has been shown by a genomewide association study to have a single strong association with a single-nucleotide polymorphism in the *SLCO1B1* gene which codes for the hepatic uptake transporter OATP1B1 so that genotyping for this variant would be useful if it was necessary to use high dose simvastatin.[12] These limited examples show the potential promise of pharmacogenomic testing to predict and prevent ADRs and improve the effective use of drugs in the future.

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Challenges and Opportunities of Developing Paediatric Medicines

Prof. Kalle Hoppu, The University of Helsinki, Finland

Children have been known as "Therapeutic orphans" since the 1960ies, because most of the new medicines are not developed for them. About half of the medicines prescribed to children are unlicensed or are used off-label. In newborns the number is even higher. Today children do not fully benefit from progress in drug development. New medicines are not being authorised for children, or are authorised after a long delay (1). This often means, that data on correct dosing, safety and efficacy of the medicines in children is lacking or of low quality. Medicines are also not available in age appropriate formulation. All this is a consequence of both the special challenges of paediatric drug development and the small size of the paediatric market for medicines. New innovations are needed in the development of age-appropriate paediatric formulations as the current standard, liquid formulations, are expensive to produce and problematic for use in resource limited settings. Ethical issues of paediatric clinical trials are important, but possible to solve. The need to minimise recruitment of children for clinical trials requires innovative trial designs appropriate for small sample sizes. Determining safety of new medicines in children is particularly challenging. Limiting trial size affects ability to detect adverse events, and detecting possible long term adverse effects on growth and development require long-term studies. The paediatric drug initiatives in the US (1997), the EU (2007) and the WHO (2007) to improve children's health through improving access to better paediatric medicines have provided new opportunities for developing paediatric medicines (2). In US and Europe paediatric labelling is becoming standard part of the development process of any new medicine of potential therapeutic relevance for children. This paediatric development is funded through significant incentives or rewards. Paediatric research networks have been established to perform the clinical trials required for paediatric development. New paediatric formulations and research methods are developed with funding that has become available. For capacity building training programs, like the one of the EU 7th Framework funded Global Research in Paediatrics (GRIP) -project are becoming available. As drug development today is global, many of these opportunities are available worldwide. However, paediatric clinical trials overseas present their own challenges.

References:

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Applications of Pharmacoepidemiology in General Practice

Prof. Martin C.S. Wong, The Chinese University of Hong Kong, Hong Kong

Pharmacoepidemiology is the study of the use of and the effects of drugs in large numbers of people. It applies the principles of epidemiology to the content area of clinical pharmacology, and remains an important tool to capture useful data for clinicians, researchers and policy-makers. This discipline is now becoming more popular to reflect "real life" clinical practice on the pharmacological effects of medications and their utilization. It has been recognized as a specialty which could supplement the interpretation of study findings of prospective trials.

In clinical practice, the contributions and roles of pharmacoepidemiology apply to various areas – including quantization of the incidence of adverse drug effects; discovery of undetected drug effects; analysis of cost-effectiveness of drugs; assessment of medication utilization and compliance profiles; as well as the association between medication use and clinical outcomes.

In this seminar the speaker will discuss a broad range of its applications, with a particular focus on its use in general practice. The future direction of developing and promoting this discipline among general practitioners will also be highlighted.

Cost Effectiveness Analysis and Drug Formulary Decision Making

Prof. Vivian W.Y. Lee, The Chinese University of Hong Kong, Hong Kong

Health care system in Hong Kong is facing increasing challenges like everywhere else in the world to improve healthcare access, ensure quality and maintain balance of healthcare budget and expenditures. The situation is more challenging due to aging population. Citizens in Hong Kong are known for their longevity. Yearly, there are new drugs, devices and services for disease managements. At most circumstances, these health technologies will be more costly than the older treatment options. How could we ensure that these new health technologies will be cost-effective? Healthcare Technology Assessment (HTA) is a form of policy research that examines the short and long term consequences of the application of a healthcare technology.

In this presentation, the following topics will be discussed:

1. The current issues faced by the healthcare system of Hong Kong;
2. Roles of HTA in evaluating cost effectiveness of new healthcare technology and the impact of drug formulary decision making.

Improving Clinical Outcomes in Subjects with Unstable Anticoagulation

Dr. Raymond S.M. Wong, Prince of Wales Hospital, Hong Kong

For many decades, the vitamin K antagonists (VKAs) have been the only oral anticoagulant drugs available for clinical use for the primary and secondary prevention of venous and arterial thromboembolic events. VKAs have been consistently shown to be highly effective in many settings and are now used by millions of patients worldwide. However, VKAs have many limitations. They have narrow therapeutic windows and are highly susceptible to drug-drug interactions. Patients receiving long-term warfarin therapy are sensitive to fluctuating levels of dietary vitamin K. Nutritional supplements and herbal products are also problematic. Unstable anticoagulation is a common problem in patients taking VKAs.

To improve the clinical outcomes in subjects taking VKAs, a high level of time in therapeutic range (TTR) is necessary. An obstacle to the safety and effectiveness of warfarin therapy is the poor quality of dose management in routine clinical practice. Management of VKA therapy should be done in a systematic and coordinated fashion, incorporating patient education, systematic INR testing, tracking, follow-up, and good patient communication of results and dosing decisions. Significant improvements in the outcomes of hemorrhage or thrombosis have been demonstrated in patients when anticoagulant therapy is managed by managed by an anticoagulation management service or an anticoagulation clinic compared with management by their personal physicians (ie, usual care). For patients treated with VKAs who are motivated and can demonstrate competency in self-management strategies, including the self-testing equipment, patient self-management is an alternative to routine medical care and is proven to increase the TTR. Clinical outcomes can also be improved by using validated decision support tools (paper nomograms or computerized dosing programs).

The new oral anticoagulant drugs have the potential to overcome several drawbacks of the VKAs. These drugs can be administered at fixed doses and do not require laboratory monitoring, thus offering a clear advantage over the VKAs. Limited applications, lack of widely available laboratory tests for monitoring and evidence-based reversal strategy are the major limitations of these new agents