Educational Session Program:

ISPE's Tenth Asian Conference on Pharmacoepidemiology 2017

as at 31 August 2017 (program subject to change)

SUNDAY 29 OCTOBER 2017

PLEASE SEE THE FOLLOWING PAGES FOR A FULL DESCRIPTION OF EACH INDIVIDUAL SESSION

	Introductory/Intermediate session		Advanced session
08:00-08:30	**Designing studies from clinical questions**		**ADVANCED SESSION 1:** **Big data - How to use and not to use them in Pharmacoepidemiology** **Instructors:** Ian Wong, UCL School of Pharmacy, UK, Yola Moride, Faculty of Pharmacy, Université de Montréal and YOLARX Consultants, Canada and Judith Jones, The Degge Group, USA
08:30-08:45	Biobreak and transition to rooms for Track A and B		
08:45-10:15	**TRACK A: PRINCIPLES OF PHARMACOEPI USING LARGE DATABASES**	**TRACK B: NON-DATABASE PHARMACOEPIDEMIOLOGY: LEARNING THROUGH EXAMPLES FROM RESOURCE-LIMITED AND RESOURCE-RICH COUNTRIES**	
	Use of automated databases for Pharmacoepidemiology research **Instructor:** Vincent Lo Re, University of Pennsylvania, USA **Evaluation of drug exposure in Pharmacoepidemiologic databases** **Instructor:** Wei Zhou, Merck Research Laboratories, USA	**Principles of descriptive Pharmacoepidemiological study designs** **Instructor:** Krishna Undela, JSS University, India	
10:15-10:45	**Morning tea**		
10:45-12:30	**Evaluation of clinical outcomes in automated Pharmacoepidemiologic databases** **Instructor:** Vincent Lo Re, University of Pennsylvania, USA **Thought exercise using Pharmacoepidemiologic databases to answer a clinically relevant question** **Instructors:** Vincent Lo Re, University of Pennsylvania, USA, Wei Zhou, Merck Research Laboratories, USA and Sallie Pearson, University of New South Wales, Australia	**Principles of analytic Pharmacoepidemiological study designs** **Instructor:** Geoffrey Liu, University of Toronto, Canada	**ADVANCED SESSION 2:** **Interrupted time series analysis and instrumental variable analysis: You can't fix by adjustment what you bungled by design** **Instructor:** Stephen Soumerai, Harvard Medical School and Harvard Pilgrim Health Care Institute, USA
12:30-13:30	**Lunch**		
13:30-15:15	**Practical skills in protocol writing and statistical analytic programming relevant to pharmacoepidemiology** *Part one* **Lead instructor:** Chih-Ying (Natasha) Pratt, PhD, USA **Small group instructors:** Nicole Pratt, Vin Lo Re, Wei Zhou, Geoff Liu, Krishna Undela		**ADVANCED SESSION 3:** **Patient/citizen generated data in Pharmacoepidemiology Instructor:** Alison Bourke, Center for Advanced Evidence Generation, QuintilesIMS Real-World Insights, UK, Cynthia de Luise, Worldwide Safety and Regulatory, Pfizer, USA and Adrian Levy, Dalhousie University, Canada
15:15-15:45	**Afternoon tea**		
15:45-18:00	**Practical skills in protocol writing and statistical analytic programming relevant to pharmacoepidemiology** *Part two* **Lead instructor:** Nicole Pratt, University of South Australia, Australia **Small group instructors:** Natasha Chen, Vin Lo Re, Wei Zhou, Geoff Liu, Krishna Undela		**ADVANCED SESSION 4:** **Advanced methods in assessing safety and effectiveness of medications and medical devices in Pharmacoepidemiology** **Instructors:** Jesper Hallas, President, International Society for Pharmacoepidemiology; University of Southern Denmark, Denmark, Robert Platt, McGill University, Canada and Soko Setoguchi, Rutgers School of Public Health, USA
18:00-20:00	**Welcome reception**		

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INTRODUCTORY/INTERMEDIATE EDUCATIONAL SESSION TRACK A

TRACK A: PRINCIPLES OF PHARMACOEPI USING LARGE DATABASES	
08:45-09:30	**Use of automated databases for Pharmacoepidemiology research** **Instructor:** Vincent Lo Re, University of Pennsylvania, USA - Overview of strengths, weaknesses of automated databases - Types of databases for pharmacoepidemiologic research ○ Appropriate database selection → Determining database adequacy - Study design choices in automated database studies - Defining study populations in automated databases - Potential biases (i.e., selection bias, confounding bias, misclassification bias) and generalizability issues related to choice of database, study design, and study population definitions

09:30-10:15	**Evaluation of drug exposure in Pharmacoepidemiologic databases**
	Instructor: Wei Zhou, Merck Research Laboratories, USA
	
	- Choosing the right drug exposure variables
	  ○ Methods available to measure drug exposure
	  ○ Limitations of availability of exposure data
	  ○ NDC and ATC coding to assess exposure
	  ○ Estimating exposure duration
	- Options in study design for assessing drug exposure
	  ○ Cohort, case-control
	  ○ New user design
	- Choice of comparators
	- Potential biases related to exposure definitions: misclassification bias, confounding bias, healthy use bias, immortal person time bias

10:45-11:30	**Evaluation of clinical outcomes in automated Pharmacoepidemiologic databases** **Instructor:** Vincent Lo Re, University of Pennsylvania, USA - Translating clinically meaningful outcomes into measurable endpoints within data source - Defining clinical outcomes through algorithms - Steps in validation of clinical outcome - Discussion of outcome validation procedures - Example of outcome validation (hepatic decompensation) - Selection of primary, secondary, and exploratory endpoints - Types of analyses based on outcomes (logistic, time to event, competing risks) - Potential biases related to outcome definitions and follow-up: Misclassification bias, protopathic bias, survivor bias

11:30-12:30	**Thought exercise using Pharmacoepidemiologic databases to answer a clinically relevant question**
	Instructors: Vincent Lo Re, University of Pennsylvania, USA, Wei Zhou, Merck Research Laboratories, USA and Sallie Pearson, University of New South Wales, Australia
	
	You wish to evaluate the risk of acute liver injury assoc. with oral azole antifungals. You have concern that ketoconazole may be especially hepatotoxic.
	- Questions:
	  ○ What study design would you use?
	  ○ How to define the study population?
	  ○ What outcomes should be evaluated?
	  ○ What data source to use to answer the aim?
	  ○ What potential effect modifiers, confounders to collect?
	  ○ What major biases to consider?

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INTRODUCTORY/INTERMEDIATE EDUCATIONAL SESSION TRACK B

TRACK B: NON-DATABASE PHARMACOEPIDEMIOLOGY: LEARNING THROUGH EXAMPLES FROM RESOURCE-LIMITED AND RESOURCE-RICH COUNTRIES	
08:45-09:00	**Instructors:** Geoffrey Liu, University of Toronto, Canada and Krishna Undela, JSS University, India Discussion with Participants Identify the expectations of participants from the session Get to know the basic understanding of participants about Pharmacoepidemiological study designs
09:00-10:15	**Principles of Descriptive Pharmacoepidemiological Study Designs** **Instructor:** Krishna Undela, JSS University, India How to conduct Drug Utilization Review, Spontaneous Reporting, Cohort Event Monitoring, Medication Adherence, Cross-sectional and other descriptive Pharmacoepidemiological studies in non-database settings with multiple real-world examples. Participants will get an idea how to conduct descriptive Pharmacoepidemiological studies in non-database settings.
10:45-11:00	**Principles of Descriptive Pharmacoepidemiological Study Designs** *cont'd*
11:00-12:30	**Principles of Analytic Pharmacoepidemiological Study Designs** **Instructor:** Geoffrey Liu, University of Toronto, Canada How to conduct Cohort, Case-Control and Randomised studies in non-database settings by using primary data with multiple real-world examples Calculation and interpretation of outcome measures (Prevalence, Incidence Proportion and Incidence Rate) and risk measures (Relative Risk, Odds Ratio, Hazard Ratio, Absolute Risk Reduction, Number Needed to Treat and Number Needed to Harm). Participants will be aware of different analytic Pharmacoepidemiological study designs and their outcome and risk measures. Participants will get an idea how to conduct analytic Pharmacoepidemiological studies in non-database settings.

INTRODUCTORY/INTERMEDIATE EDUCATIONAL SESSION

13:30-18:00	**PRACTICAL SKILLS IN PROTOCOL WRITING AND STATISTICAL ANALYTIC PROGRAMMING RELEVANT TO PHARMACOEPIDEMIOLOGY**

Instructors: Chih-Ying (Natasha) Pratt, PhD, USA and Nicole Pratt, University of South Australia, Australia
Small group instructors: Nicole Pratt, Vin Lo Re, Wei Zhou, Geoff Liu, Krishna Undela

Pharmacoepidemiologic studies that involve the use of electronic healthcare data have complex and unique characteristics that must be taken into consideration when planning and conducting these types of studies. This highly interactive course will engage participants in the following topics:

1. Pre-specifying study components of a protocol, including design, analysis, and reporting of the study, along with a science-based rationale for the choices pertaining to these components; and
2. Translating elements of the study protocol into a statistical analytic program.

Educational Objectives:

- To introduce a framework for translating study questions into a clear and detailed protocol supported by a rational thought process that is tailored to available data for pharmacoepidemiologic studies using electronic healthcare data
- To develop skills in health care data manipulation to support the conduct of a statistical analysis
- To translate a pharmacoepidemiologic study protocol into a statistical analytic program.
- To develop skills to document and report pharmacoepidemiologic studies using electronic healthcare data in a transparent and reproducible way

Target Audience:

- People interested in conducting pharmacoepidemiologic studies using electronic healthcare data, in learning about protocol writing, and/or implementing the protocol components into a statistical analytic programming
- An understanding of **basic statistical programming language** is **required** for this course

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ADVANCED SESSION	
08:00-10:15	**ADVANCED SESSION 1:** **Big data - How to use and not to use them in Pharmacoepidemiology** **Instructors:** Ian Wong, UCL School of Pharmacy, UK; Yola Moride, Faculty of Pharmacy, Université de Montréal and YOLARX Consultants, Canada and Judith Jones, The Degge Group, USA The availability of very large datasets on healthcare delivery in medically insured populations has served as a central resource for pharmaco-and medical product epidemiology. These data that map the many components of healthcare management allow assessment of prescribing, utilization, outcomes and costs of medical product use over time, often in thousands of persons, and thus are invaluable for differentiating effects of products from underlying conditions. As with all data sources, there are pitfalls including the fact that some key variables impacting outcomes are not recorded. Thus, future uses of Big Data will need to address these limitations and create opportunities for gathering still more information, such as genetic markers, to further understanding of medical product effects.
10:45-12:30	**ADVANCED SESSION 2:** **Interrupted time series analysis and instrumental variable analysis: You can't fix by adjustment what you bungled by design** **Instructor:** Stephen Soumerai, Harvard Medical School and Harvard Pilgrim Health Care Institute, USA Observational studies using instrumental variables (IV), an increasingly popular method for medical treatment effectiveness have increased from approximately 2 in 1992 to 341 published articles in 2016. IV analyses are statistical analyses, not research designs. In theory, instruments (e.g., distance to the hospital in studies of the outcomes of cardiac cath labs) control for unobserved and observed patient characteristics. But the results may be biased if an unadjusted confounder (e.g. use of a "clot buster") is associated with the IV and the outcome (e.g., death). Unfortunately, most, but not all IV studies, use the weakest research designs, such as cross sections, which rarely protect against bias even with heroic statistical adjustment. This problem generalizes to other methods, such as propensity score adjustment which is more valid in longitudinal or interrupted time series versus cross-sectional designs where control for confounding is more challenging. In this session we will review: 1. A recent systematic review of the validity of the four most common IVs (distance to facility, regional variation, facility variation, and physician variation) in studies of the effects of health care interventions on mortality. Garabedian's 2014 analysis, published in Annals of Internal Medicine, identified major confounders, such as health status, race and SES, in all IV studies (cross-sectional). A major weakness of the IV studies was not to consider potential confounders outside the study data, such as in prior published data. 2. A case study: an IV that assumes that the greater use of advanced life support vs. basic life support ambulances (fewer personnel and equipment) "leads" to increased mortality. Sanghavi's 2015 Annals study implied that withdrawal of reimbursement for advanced ambulances could save hundreds of millions of Medicare dollars. However, we found a statewide study indicating that the advanced ambulance patients were more likely to die from a large number of severe conditions (e.g., respiratory depression, very low blood pressure) occurring at the time they were picked up (~30% to 500% difference in a presumably "random" variable. 3. An analysis comparing cross-sectional adjustment in a study of reported benzodiazepine cessation and hip fracture with controlled interrupted time series designs of drug cessation and hip fracture incidence. Two studies (Wagner, Briesacher) using controlled ITS, to control for history and selection, failed to confirm the results of decades of cross-sectional epidemiological studies of an association between benzodiazepine use and risk of hip fracture. Strong research designs are a more potent weapon than adjustment in efforts to control bias in intervention studies.

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13:30-15:15	**ADVANCED SESSION 3:** **Patient/citizen generated data in Pharmacoepidemiology** **Instructors:** Alison Bourke, Center for Advanced Evidence Generation, QuintilesIMS Real-World Insights, UK, Cynthia de Luise, Worldwide Safety and Regulatory, Pfizer, USA and Adrian Levy, Dalhousie University, Canada Real World Data (RWD) is increasingly utilised for research, and there has been a welcome recent move towards more emphasis on patient centricity. The knowledge that factors outside the formal clinical environment (such as social deprivation, exercise, environment and diet) have a huge impact on healthcare has highlighted the importance of a new stream of evidence – Patient Generated Health Data (PGHD). Looking at people holistically is increasingly important in supplying some of the missing pieces from the pharmacoepidemiology puzzle. In the past few years the creation of Patient or Citizen Generated Health Data has exploded with the ubiquity of mobile technology. Consequently, this health information collected directly from and by people rather than clinicians promises to deliver key insights on many of the drivers important in understanding the journey between states of wellness and disease. However, success with PGHD comes with many new social and technical challenges. This session describes what PGHD is, why it is vital in healthcare research, and how we need to comprehensively address the challenges associated with such massive and multifaceted data sources. Learning objectives: • To understand what Patient/Citizen Generated Data is and how it is created. • To recognise the reasons why Patient/Citizen Generated Data may be valuable in healthcare research and development. • To identify the challenges in accessing and utilising Patient/Citizen Generated Data in real-world healthcare research
15:45-18:00	**ADVANCED SESSION 4:** **Advanced methods in assessing safety and effectiveness of medications and medical devices in Pharmacoepidemiology** **Instructors:** Jesper Hallas, President, International Society for Pharmacoepidemiology; University of Southern Denmark, Denmark, Robert Platt, McGill University, Canada and Soko Setoguchi, Rutgers School of Public Health, USA **Estimating the average postponement of outcome when using preventive medication** Jesper Hallas, President, International Society for Pharmacoepidemiology; University of Southern Denmark, Denmark Using preventive medication, such as statins, have the purpose of postponing the occurrence of an adverse outcome, such as cardiovascular death. The average outcome postponement can be used as a measure for conveying the treatment effect to patients. We have recently developed an approach for calculating the outcome postponement achieved within a trial's duration, based on published trial data. During the presentation, the method will be demonstrated, and results from a recent meta-analysis of outcome postponement will be presented **Targeted learning in Pharmacoepidemiology** Robert Platt, McGill University, Canada Targeted maximum likelihood estimation (TMLE) is a framework for estimation of parameters of scientific interest that can efficiently leverage information in large datasets. In this session, I will describe TMLE, with a focus on defining the target parameter. I will illustrate the process with a study estimating the effect of statins on mortality post-myocardial infarction. **Non-statistical methods to combat cofounding by indication and healthy user bias - data linkage and design-based methods in studying medical devices** Soko Setoguchi, Rutgers School of Public Health, USA When studying comparative effectiveness of medications and medical devices, the biggest threats to the validity include confounding by indication/severity and healthy user/candidate bias. Many commonly used and newer statistical approaches such as multivariate adjustments, propensity score analyses and inverse

	probability weighted methods fail to address these biases in large database studies. This lecture will introduce data linkage and design based methods to address these biases using CER examples for medical devices and medications. Learning objectives: • To recognise potential methodological issues in assessing safety and effectiveness of medications and medical devices in Pharmacoepidemiologic studies. • To become familiar with the strengths and limitations of advanced analytic approaches to overcome the methodological issues in comparative effectiveness research using observational data • To understand limitations of data sources and become aware of potential methods to improve data sources and their limitations