

FALL 2010

# SCRIBE



ISPE NEWSLETTER - VOLUME 14, Number 2

## A NOTE FROM THE EDITOR

Dear ISPE members,

I hope you will enjoy this issue of SCRIBE, which focuses on the 26<sup>th</sup> International Conference on Pharmacoepidemiology and Therapeutic Risk Management that took place in Brighton, England in August as well as the 5<sup>th</sup> Asian Conference on Pharmacoepidemiology that took place in Tainan, Taiwan in October. Both conferences were a huge success due to the growth in ISPE membership, participation, and sponsorship which led to exciting, international forums for advancing our field.

I would also like to take this opportunity to thank Jill Lavigne for her contributions as co-editor of SCRIBE these past two years. It was a lot of fun collaborating with Dr. Lavigne on SCRIBE and a wonderful way of getting involved in the society and networking with other members.

We have a new co-editor and an associate student editor joining SCRIBE this year. Haley Kaplowitz, PhD, a senior director of epidemiology at Allergan, Inc., is now the co-editor and Nadya Belenky, a doctoral epidemiology candidate at the University of North Carolina School of Public Health is the new student editor. Dr. Kaplowitz has more than 20 years experience in pharmacoepidemiology, built and has led the epidemiology function at Allergan for the past 6 years. She's looking forward to being more involved in ISPE. Nadya is currently studying methodology, with an emphasis on infectious diseases. She hopes to become more involved with ISPE and appreciated the opportunity to contribute to SCRIBE.

Please join me in thanking the SCRIBE volunteers this year – we could not have done it without your help! 2010 SCRIBE volunteers: Emily Brouwer, Suzanne Cook, Kourtney Davis, Julia DiBello, Sara Ephross, Michael Irizarry, Jessica Jalbert, Sarah Landis, Christina Mack, Hana Muellerova, Jeanne Pimenta, Susan Roberts, Rachael DiSantostefano, Monika Stender, Robert Suruki, Irini-Alexia Terzakis, and Keele Wurst.

We are looking for volunteers for the spring issue of SCRIBE. If you will be attending the 2011 Mid-Year meeting and are interested in getting involved, please consider contacting one of us to become a SCRIBE volunteer. We also welcome other contributions as well.

Warmest regards,

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# ICPE 2010 ANNUAL MEETING HIGHLIGHTS

## KEYNOTE ADDRESS

*Contributed by Kourtney Davis*

*Presenter: Thomas Lönngren (EMEA, UK)*

The keynote address was given by Dr. Lönngren and titled “The Future of Medicines Regulation: Where Does Pharmacoepidemiology Fit into Risk Management and Comparative Effectiveness Measurement?” The address began by describing changes in the environment that drive medication regulation, ranging from the decline in R&D productivity to unmet public health needs to globalization of manufacturing and research. These changes have led to an increased need for collaboration between governments and payers to address budgetary challenges. The decline in the industry’s application for new chemical entities has resulted in increasingly stringent requirements for data to justify reimbursement in the form of comparative effectiveness studies. The context for the decline was considered, leading to a lively discussion on increased complexity of drug targets.

Dr. Lönngren proceeded to discuss the idea of adjustments to entry bars by offering conditional market designation, especially in the case where unmet patient needs relating to their illness are high. He went on to describe a similar strategy, for lesser degrees of severity, of shifting the entry bar by requiring more information at time of approval. Dr. Lönngren pointed out that with post-marketing surveillance systems in place, approval of medication by regulators would happen more quickly.

The risk-benefit discussion that followed began by questioning whether pharmacoepidemiology



had become too risk averse. Dr. Lönngren emphasized the need for more transparency from regulators on decision-making. He went on to cite a paper by Eichler from *Nature Review Drug Discovery*, and discussed the failures in drug development that result from an intersection of complex biology, less than optimal drug development programs, and an increased level of regulatory requirements. As a point of reference, the (European Medicines Agency) EMA declined 40% of recent years’ applications.

The following consequences of the productivity decline in drug approvals were noted: gaps in the

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## KEYNOTE ADDRESS (continued)

pipeline of antibiotics that respond to resistance, public health gaps that do not match research areas (e.g. infectious disease), and the balance between patented medications versus generics.

Dr. Lönngren met the remaining questions regarding how pharmacoepidemiology should respond and what role scientific development should play with a multi-faceted answer.

Personalized medicine was the first element of the strategy, with a focus on maximization versus optimization. The ability to increase the response rate in the target patient population through the use of biomarkers (e.g. Herceptin) was used as an example of personalized medicine. Second, government responses, in the form of comparative effectiveness research, in the US and Health Technology Assessment (HTA) within the EU, are required. Finally, benefit-risk analyses will require collaboration between regulators and HTA. To avoid duplication and increased cost and time for drug development, it was recommended that post-authorization studies coordinate between risk management planning (RMP) requirements and HTA pricing decisions.

How to improve drug use in accordance with label? The answer is simple: optimize benefit risk. Epidemiology is a critical component in the strategy and design of an RMP (e.g. IMI:Protect and ENCePP). New EU legislation includes collecting suspected adverse drug reaction (ADR) reports in databases and creating comprehensive EU data dictionaries. Studies with clear justification will be legally binding; the Benefit-Risk Management Plan will require key effectiveness studies post-approval and Periodic Safety Update Reports (PSUR). PSUR will include benefits and risks to produce a balanced summary of evidence, while an EMA has a clear legal responsibility for measuring outcomes of risk minimization. In addition, oversight of non-interventional studies will be provided by a new Pharmacovigilance Committee. Overall, there is a need to improve coordination between diagnostics and medicine, divided in regulatory approvals, when a biomarker exits. Dr. Lönngren concluded with the fact that pharmacoepidemiology methods and data are expanding areas and will be critical to optimizing drug development and balancing regulatory and reimbursement decision-making.



## SOCIAL EVENTS

*Contributed by Sarah Landis*

Brighton's historic Metropole Hotel and Corn Exchange provided wonderful venues for our celebratory events! Despite the fickle south coast weather forcing our beachside opening reception indoors on Thursday, everyone got into the spirit by sipping beach-themed cocktails and reuniting with colleagues and friends. The chair of the 2010 Scientific Program Committee, Corrine de Vries, FISPE, and ISPE President Sebastian Schneeweiss, FISPE, provided welcoming remarks and kicked off the 26<sup>th</sup> ICPE.

At Saturday night's evening social, we discovered some hidden dancing talents among our community!! Everyone unleashed their inner "Dancing Queen" and got their groove on with tribute band "ABBA's Angels!" The evening was set in a historic Grade 1 building, The Corn Exchange, which was originally built as the Prince Regent's riding house and stable block in 1805, is situated in the newly renovated Brighton Dome arts complex within the Brighton Pavilion Gardens. It was then one of the largest buildings of its kind in the world, with room to stable up to 60 horses. In more recent years, it has hosted some of the biggest names in entertainment, and was the venue where Swedish pop band ABBA won the Eurovision Song Contest in 1974 with their hit "Waterloo." This spirited, high energy event is sure to be remembered for years to come!



# ISPE PRESIDENTIAL ADDRESS SUMMARY

*Contributed by Monika Stender*

*Presenter: Sebastian Schneeweiss, FISPE*

*(Brigham and Women's Hospital/Harvard Medical School, USA)*

The president of ISPE, Sebastian Schneeweiss, greeted conference participants with an overview of the state of the society and its new developments over the past year. He began his speech with some impressive illustrations on the economics of ISPE: combining the number of members in addition to sponsorship with economic markers such as the Dow Jones index and concluding: "ISPE grows, the markets slows."

He went on to explain the growth of the society with the increased activity in governmental and regulatory requirements, such as post-marketing commitments, risk management plans, an increased interest from governments in safety surveillance as well as the call for comparative effectiveness research. Another contributor to growth was the increased citation of articles published in *Pharmacoepidemiology and Drug Safety* (PDS) – which President Schneeweiss nicknamed "The New England Journal of PE," thanks to the editorial efforts of editors: Brian Strom, FISPE Chief; Sean Hennessy, FISPE Americas; George Hasford, Europe; B.J. Park, FISPE Asia.

ISPE's finances are in a good state due to increased membership, better attendance at meetings, more training programs (now on 8 different topics in addition to the pharmacoepidemiology core), more successful fundraising, including sponsors, exhibitors and the Academic Showcase.

ISPE has undergone a healthy growth spurt and can now be considered a clear leader in the field. Nevertheless, the society needs to nurture and groom talent by activating willing mentors in academia, industry, service providers and in government. The Society

relies on its advocates at the regulatory authorities, especially at the FDA and ENCePP, and it needs a critical yet constructive peer review. ISPE has gone global and because it no longer is a niche discipline, it needs even more advocates for science and education.

Highlights of 2009-2010 include the internationalization of ISPE, mainly through Asia and in particular in Taiwan, Japan, and Korea. Of particular note is the recent 5th ACPE 2010 in Tokyo and the upcoming May 2011 ISPE Symposium in Mexico.

The president finished by making a pledge to encourage members' active involvement in the society – not simply encouraging authorship of the oral and poster presentations at the conferences, but also seeking other opportunities through the special interest groups, committees, or support functions at ISPE!



## EMA SCIENTIFIC DEBATE

*Contributed by Sara Ephross*

***Presenters: Stuart Pocock (London School of Hygiene and Tropical Medicine, UK) and Stan Young, (National Institutes of Statistical Sciences, USA) spoke for the motion, while Sonia Hernandez-Diaz, FISPE (Harvard School of Public Health, USA) and Kenneth J. Rothman, FISPE (RTI Health Solutions, USA) argued against it.***

A lively English Mace style debate, co-sponsored by ISPE and EMA, was a highlight of the 26<sup>th</sup> ICPE. The debate was moderated by Professor Hans-Georg Eichler, Senior Medical Officer of the EMA.

The motion discussed was: *“Results from epidemiology and pharmacoepidemiology studies mislead the public because of a failure to adjust for multiple comparisons. Journals should not publish studies that do not account for multiplicity”.*

Stuart Pocock (London School of Hygiene and Tropical Medicine, UK), spoke first for the motion, stressing the importance of accounting for multiplicity. He compared clinical trials with a single pre-specified primary outcome to epidemiology studies, which often include exploratory data analysis and less formal results reporting. He described several aspects of multiplicity in epidemiology studies, including: disease outcomes, risk factors, population selection (overall, subgroups, study selection in systematic reviews), methods of analysis (choice of confounders, categorization, alternate models) and timing of publication. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines ([Annals of Internal Medicine](#) (2007)) were highlighted. Pocock advised authors to report which analyses were, and were not, planned, concluding that: 1) the full extent of multiplicity is hard to determine; 2) unreported analyses add to multiplicity; 3) formal statistical adjustment is of

limited value; 4) authors need to document clearly all aspects of multiplicity; 5) underpowered studies are particularly susceptible to multiplicity issues; 6) multiplicity requires more cautious interpretation; 7) multiplicity needs to be more carefully assessed in the limitations section; 8) beware of selective reporting in abstracts; and (9) consider multiplicity across studies, publication bias, and citation bias.

Sonia Hernandez-Diaz, FISPE (Harvard School of Public Health, USA) spoke next, against the motion. She considered the motion in three parts: 1) “results from pharmacoepidemiology studies mislead the public.” While acknowledging possible false positive results, she noted that misuse and misinterpretation of correct results from pharmacoepidemiology studies and clinical trials were common, suggesting that authors rigorously review press releases and interviews before their publication, keeping the interpretation clear, careful, and honest. Publication bias in epidemiology studies and clinical trials in terms of review, publication and citation could be improved by encouraging publication or posting of non-significant results. Regarding 2) epidemiology studies are incorrect “because of a failure to adjust for multiple comparisons”, she clarified that incorrect (non-causal or not replicated in clinical trials) results may be due to chance, bias or asking different questions, and that bias (confounding, information bias, selection bias) tends to be a larger issue than

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## EMA SCIENTIFIC DEBATE (continued)

random error. For 3) "journals should not publish studies that do not account for multiplicity," Hernandez-Diaz suggested that this would lead to delays in replication studies and the dissemination of critical public health information. She recommended instead that epidemiology investigators optimize the quality, replication and transparency of studies, citing both a recent IOM report and a statement from the European Medicines Agency. Hernandez-Diaz summarized by reiterating that multiple comparisons are neither necessary nor sufficient to mislead the public, adjusting for multiple comparisons is often infeasible and potentially harmful in epidemiologic research and that high quality, replication and transparency are alternative solutions to establish the validity of results.

Stan Young (National Institutes of Statistical Sciences, USA) was the third speaker, representing the "for the motion" side. He submitted that claims coming from observational studies fail to replicate as the result of bias, multiple testing and multiple modeling, providing examples of nutritional epidemiology studies that were not replicated in clinical trials. Examining many hypotheses leads to a higher possibility of nominally statistically significant results; the extent of hypothesis testing and the differentiation of pre-specified and post-hoc analyses are often not reported in publications, limiting interpretation of results. He recommended several potential approaches to account for multiple comparisons, including multiplicity adjustments, p-value plots versus number of tests, splitting data sets for exploratory and

confirmatory analyses and making datasets and code publicly available.

The final speaker was Kenneth Rothman, FISPE (RTI Health Solutions, USA) representing the "against the motion" side. He discussed the challenge of counting hypotheses, especially multiple correlated hypotheses, and stressed the importance of Type II, as well as Type I, errors. Ignoring Type II error could lead to delays in reporting and replicating results of public health impact. Rothman recommended an alternative approach: 1) report exactly what was done (include all associations examined); and 2) report effect estimates and confidence intervals, limiting reliance on significance testing (because multiplicity adjustment reduces Type I, but increases Type II error).

A vote was held, with a majority voting against the motion as written. However, there was agreement that epidemiology studies should report all associations examined, and that the role of random error should be incorporated into the interpretation of results. Stephen Evans, FISPE, proposed that the motion be amended by replacing "adjust" with "account for and describe," a suggestion that was met with resounding applause.

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For more information  
on ISPE Councils,  
please visit  
[pharmacoepi.org!](http://pharmacoepi.org)

## Student Council

Students of the International Society for Pharmacoepidemiology (SISPE) is an international network for students interested in or studying pharmacoepidemiology. SISPE is organized by student members of the International Society for Pharmacoepidemiology (ISPE).

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Each participating institution has a designated contact person. Please visit [pharmacoepi.org](http://pharmacoepi.org) for the contact information specific to your institution of interest.

### *ACADEMIC COUNCIL UPDATE*

*Contributed by  
Susan Roberts*

During the annual meeting of the Academic Council, members tackled the complex issue of workforce shortages in pharmacoepidemiology, a directive from the 2010 Board Meeting, by examining ISPE's role in addressing the shortage of pharmacoepidemiologists and developing strategic recommendations. Discussion centered around the importance of industry and government funding of academic programs to promote enrollment; the need to raise awareness of the profession beginning at the undergraduate level; the need for role development in doctoral programs to expand employment expectations beyond academia; the importance of internships during training programs; and the unique needs of resource-poor countries in training pharmacoepidemiologists. The Academic Council is developing a plan to address this issue and recommends collaboration with other Councils. Ongoing work of the Academic Council includes an updated list of academic programs currently posted on the ISPE website. Academic programs not currently listed are encouraged to contact the Academic Council.



# SELECTED COUNCIL UPDATES

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## INDUSTRY AND SERVICE PROVIDERS COUNCIL UPDATE

*Contributed by*

*Haley J Kaplowitz*

The Industry and Service Providers Council met at the recent ISPE annual meeting in Brighton, England. The meeting was called to order by co-chairs Wei Dong and Harry Seifert. A number of timely and important topics were discussed, including issues regarding compliance in observational studies and risk management. Doug Watson reviewed the ISPE Statement endorsing the opportunity for registration of observational studies on a public web site (see the “ISPE Statement on the Registration and Public Disclosure of Pharmacoevidence Research Protocols” on [pharmacoepi.org](http://pharmacoepi.org)), such as [clintrials.gov](http://clintrials.gov). It was acknowledged that the registration form for [clintrials.gov](http://clintrials.gov) is not optimal for observational studies, and Council members decided to form a group that would recommend data fields in [clinicaltrials.gov](http://clinicaltrials.gov) appropriate for observational studies. In addition, Nancy Santanello led a discussion of approaches and processes to determine cost metrics for observational studies. It was noted that, while there are metrics to guide costs of clinical trials, no analogous metrics are available for observational studies. It was suggested that a group of industry and service provider representatives meet to discuss the processes for determining such metrics (with legal advice to avoid the appearance of collusion).

Wei Dong briefly updated the group on the BIO Pharmacovigilance and Benefit-Risk Management Working Group and its contribution to the July FDA-sponsored workshop on REMS (<http://bio.org/reg/20100831.pdf>). Contact Andrew Emmett at [aemmett@bio.org](mailto:aemmett@bio.org) for more information regarding this BIO Working Group.

Harry Seifert led a discussion, seeking feedback for the Executive Board, regarding whether ISPE should make its membership available for surveys by outside organizations. The Council consensus was that these should generally not be allowed, unless the Board or Executive Council determined that at least one of the following conditions was met:

- If a scientific survey, that it was scientifically and methodologically valid
- If business-related, that ISPE or its members would directly benefit

Other issues discussed included the CER Curriculum Development, sponsored by the PHRMA Foundation (Nancy Santanello), and the EMA Framework Program (Henry Fitt, of the Government Council), which will fund drug safety research in the EU. There is interest in increasing the number of small and medium enterprises (SMEs) participating in the program. Henry noted that a workshop was held on the 13th of September, 2010, where the planned and ongoing projects were explained and discussed (contact Alejandro Arana at [arana.riskmr@gmail.com](mailto:arana.riskmr@gmail.com) for more information). Finally, Robert Reynolds and Jamie Robinson shared the latest update on the PROTECT project under the EU IMI initiative. For more details please see <http://www.imi-protect.eu/>.

# SUMMARY OF SELECTED COURSES GIVEN AT 26TH ANNUAL INTERNATIONAL CONFERENCE ON PHARMACOEPIDEMOLOGY AND THERAPEUTIC RISK MANAGEMENT

PRESENTATIONS FROM ICPE 2010 ARE POSTED IN  
THE MEMBERS ONLY SECTION OF  
[WWW.PHARMACOEPI.ORG](http://WWW.PHARMACOEPI.ORG)

## MEDICATIONS IN PREGNANCY, WITH A FOCUS ON BIRTH DEFECTS

*Contributed by Michael Irizarry*

*Presenters: Carol Louik (Slone Epidemiology Center at Boston University, USA), Sonia Hernández-Díaz, FISPE, (Harvard School of Public Health, USA)*

*The safety of medications in pregnancy was a well-represented topic in the 2010 ICPE program of platform presentations, poster sessions, courses, and special interest groups. The pre-conference course taught by Carol Louik and Sonia Hernández-Díaz provided an excellent review of the history and state of the field.*

Dr. Louik led by relating the history of thalidomide and describing the challenges of identifying, as well as evaluating, the safety of medications in pregnancy. Thalidomide had been marketed in over 40 countries by 1961, as a “safe” sedative, hypnotic alternative to barbiturates. In the US, the thalidomide NDA was rejected by the (newly-hired) FDA medical officer Frances O. Kelsey, M.D., Ph.D., because of concerns of peripheral neuropathy. Thalidomide was withdrawn from the world market in 1961-1962 after an epidemic of rare limb birth defects was identified, affecting as many as 20-50% of births to those exposed in the 6<sup>th</sup> and 7<sup>th</sup> week of pregnancy (compared to a background rate of 1.5 per 10,000).

Dr. Louik stressed that teratogenicity must be studied for every drug, and unlike most other drugs effects, can only be studied in the post-marketing setting. Animal studies, therapeutic mechanism of action, drug class, and clinical toxicity do not reliably predict human teratogenicity. Clinical trials generally exclude pregnant women and are underpowered for teratogenicity. Teratogenic mechanisms are largely unknown (even for thalidomide). The potential scope of the issue is large. Major birth defects (life-threatening, requiring major surgery or resulting in significant disability) affect 2-3% of live births, although specific defects may only affect 1/1,000 or 1/10,000 live births. At least 50% of women take at least one drug

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# SUMMARY OF SELECTED COURSES

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## MEDICATIONS IN PREGNANCY, WITH A FOCUS ON BIRTH DEFECTS

*(Continued)*

during the first trimester of pregnancy; over 25% take 4 or more drugs during the first trimester of pregnancy (Slone Epidemiology Center Birth Defects Study).

Dr. Hernandez-Diaz reviewed epidemiology design considerations in the post-marketing evaluation of drugs in pregnancy, highlighting the recommendations of Allen Mitchell (NEJM 349:2556-2559). To identify drugs with dramatic fetal risks (e.g., 25% of exposed fetuses, such as thalidomide, isotretinoin), small ad hoc cohorts may have appropriate efficiency and power. To identify drugs with intermediate fetal risks (e.g., 5-20 fold increased risk such as neural tube defects and carbamazepine, valproic acid), databases and case-control surveillance have appropriate efficiency and power. Most study designs will be limited for low relative risks and drugs that have low prevalence of use; in these cases accumulating evidence over time is reflected in the 95% confidence intervals of the relative risk estimates. The design and interpretation of these studies require careful considerations of exposure measurement (compliance, recall, over-the-counter medications, sharing of medications, timing during pregnancy), outcome definition and assessment (major/minor malformations, miscarriages, early terminations, ultrasound screening, detection window after birth), confounding (indication, comorbidities, smoking, etc.), and suitable reference groups. Results must be placed into clinical context, including the implications of false positive results - discontinuation of appropriate treatment in pregnant women with serious illness may have adverse effects on the mother and her baby.

The course concluded with a case exercise based on Bendectin. Bendectin was a combination of doxylamine and pyridoxine used by up to 10-25% of pregnant women in the US in 1980 to treat nausea and vomiting in pregnancy. Case reports and ecological studies raised public concerns about the teratogenicity of Bendectin. There were no significant associations of Bendectin with all-malformations in over 10 cohort studies, and no consistent associations for specific malformations in case-control studies. Nonetheless, Merrell Dow withdrew Bendectin from the market due to the increasing legal liability. Ironically, both ingredients of Bendectin are currently available as over-the-counter preparations.

# SUMMARY OF SELECTED COURSES

*(continued)*



## COMPARATIVE EFFECTIVENESS RESEARCH SUMMARY

*Contributed by Julia Dibello, FISPE*

***Presenters: Eric Johnson (Kaiser Center for Effectiveness and Safety, USA), David Magrid (Kaiser's Institute for Health Research, USA), Sebastian Schneeweiss, FISPE, (Harvard Medical School, USA), Ken Paterson (Scottish Medicines Consortium, UK)***

The first presenter for the course was Eric Johnson from Kaiser's Center for Effectiveness and Safety Research who spoke about pragmatic cohort studies. His talk focused on the need to define the correct comparator group for effectiveness research as well as important design features for these studies. He mentioned the acronym PICO that highlights the important features of study design: population, intervention, cohort, and outcome. Dr. Johnson also mentioned that it is essential for effectiveness studies to be accessible to regulators as well as systematic reviewers so that the results from the study can be used appropriately and synthesized with other available data.

The second presenter was David Magrid from Kaiser's Institute for Health Research. He began by speaking about data sources for comparative effectiveness research and the focus of his talk was the use of claims data supplemented with clinical information. He illustrated the combination with comparative effectiveness study of second-line anti-hypertensive agents in which the use of clinical data on blood pressure allowed confounders to be controlled for. Without the augmentation of claims data, the confounding would have led to a biased analysis.

The third presenter for the course was Sebastian Schneeweiss, Harvard Medical School. Dr. Schneeweiss spoke about methodological challenges in non-randomized comparative effectiveness research. He specifically touched on case-crossover studies as well as methods that aid non-experimental research, such as the use of instrumental variables.

## SUMMARY OF COURSES

*(continued)*

### INTRODUCTION TO THERAPEUTIC RISK MANAGEMENT AND EVALUATION WITH A FOCUS ON SURVEY DESIGN

*Contributed by Jeanne Pimenta*

*Presenters: Elizabeth Andrews, FISPE, (RTI Health Solutions, USA), Stella Blackburn, FISPE, (EMA, UK), Carla van Bennekom (Slone Epidemiology Center, Boston University, USA) and Judith Jones, FISPE, (Degge Group, USA)*

Dr. Elizabeth Andrews began this session with an overview of the ‘why’ and ‘what’ of risk management. Starting from a historical perspective of how risk management has developed over the years, initially as a safety specification to currently comprising an in-depth discussion of the risks and benefits associated with a product, and how risk can be appropriately mitigated while maintaining benefits. Dr. Andrews outlined the seven major mileposts that should be considered in development of a Risk Minimization Program (RMP). The outline provided a useful “checklist” to allow successful development of an RMP. The steps suggested by the “checklist” were: identifying the risk, with special emphasis on high-risk groups, anticipating use, including off-label usage, and using summary risk mitigation tools. In addition, the role of evaluation within the RMP was emphasized and that RMPs should not represent static plans, but should evolve based on new findings.

Dr. Stella Blackburn followed with a regulator’s perspective of how risk management has evolved in Europe. An audit by the EMA revealed that RMPs have been slowly improving over time, though relatively few RMPs submit full study protocols, which would be extremely beneficial to the EMA. However, we learned that new RMP guidelines will be available soon from the EMA that raise the bar for EU-RMPs.

Dr. Andrews then gave a clear and concise overview of methodologic aspects of survey design, encompassing selection of sample frame and sampling methods, helpful hints for designing questionnaires to maximize data accuracy and highlighted some critical pitfalls for RMP surveys, including whether the intervention/survey itself could influence behaviour and modify results.

The last talk of the session was by Carla Van Bennekom on select examples of real RMPs conducted by Slone. It was an insightful journey through the decision-making process of RMP design and delved into the trade-offs of using different approaches to sample and reach participants while maximizing enrollment and minimizing bias.

The final portion of the workshop was an interactive session where the group divided into two and worked through case studies to design patient and physician surveys. The case studies were real examples graciously provided by Judith Jones, complete with a few pitfalls to promote debate! Discussion with colleagues is always a great learning experience and the sessions were helpfully facilitated by the session leaders. At the end, everyone reconvened and presented their work on the case studies to the entire group, moderated by Judith Jones. In summary, the session was an interesting and effective overview of the key considerations of risk management planning.

# SUMMARY OF COURSES

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## COURSE ON ADVANCED TOPICS IN PHARMACOEPIDEMIOLOGY

*Contributed by Hana Müllerova*

***Presenter: Paddy Farrington (Open University, UK), Til Stürmer, FISPE, (University of North Carolina at Chapel Hill, USA), Reed Johnson (RTI Health Solutions, US)***

Dr. Farrington introduced the case series methodology as one of the self-controlled methods available. In his talk titled “The Self-Controlled Case Series Method in Pharmacoepidemiology,” he demonstrated a case series method that requires only cases for data analysis that has been used in epidemiological practice for a long time, often in vaccine pharmacoepidemiology. It offers advantages over the conventional cohort methods controlling for all fixed confounders and allowing explicit modeling of temporal variations in the event rate. However, the case series method is usually limited to studies of uncommon or non-recurrent events or events with independent recurrent events. New advances in statistics and computing power allow, to certain degree, for more complicated situations such as when an occurrence of an event increases mortality or affects subsequent exposure history.

Dr. Stürmer presented a talk titled “Treatment Decisions and Propensity Scores” which dealt with confounding and its management through propensity scores (PS). Confounding is a major source of bias in epidemiologic data. A “pragmatic” approach to detecting confounding is represented by testing the collapsibility of exposure vs. outcome tables split by a potential confounder. In the case of confounding, propensity scores offer an alternative to conventional outcome modeling. The aim of propensity scores is to reduce dimensionality of confounders and quantify a probability that a person is treated given his/her given covariates. The scores can be implemented through stratification by PS, matching, inverse probability of treatment weighting and modeling. Care needs to be taken when selecting variables for constructing PS and covariates not affecting outcomes should not be included. However, all covariates related to the outcome must be included and manual selection of variables is preferable over automated techniques.

Dr. Johnson discussed methods of quantitative benefit-risk analysis and the importance of benefit-risk strategies that are feeding into the comparative effectiveness research. Several strategies can be used to define benefit, mainly based on already known evidence data on benefit and harm rates (incremental net benefits) and patient-stated preferences (‘tradeoff’, maximum acceptable risk). Conjoint analysis was presented as one of the options to define benefit. Various benefit risk measures then can be combined into one model to assess net benefits.

Finally, one of the lectures focused on Medication Errors (ME). Medication errors represent the most common cause of iatrogenic harm. About 1-2% of in-patients are harmed due to medication error. It is challenging, but important, to study both the prevalence and consequence of ME. Several types of ME can be defined, including prescribing errors, dispensing errors, administering errors and monitoring errors. The presentation was focused on prescribing and monitoring errors. Finding a simple, generalizable definition of ME represents an important methodological issue. The lack of consensus on a definition of ME impacts on methods of collecting or measuring ME, often in practice using retrospective chart reviews. Optimally, a system allowing a prospective detection would be appropriate; however, the challenge is to measure the effectiveness of such an approach.



## **INDUCTION OF ISPE FELLOWS (FISPE)**

**During the 26<sup>th</sup> International Conference of Pharmacoepidemiology (ICPE), Sebastian Schneeweiss, FISPE, ISPE President and Miriam Sturkenboom, FISPE, Chair of the Fellowship & Awards Committee inducted new ISPE Fellows and conveyed an Honorary Lifetime Fellow Award to Ronald D. Mann.**

**Corinne S. de Vries, FISPE**

**Stephen JW Evans, FISPE**

**Kiyoshi Kubota, FISPE**

**Susan Ann Oliveria, FISPE**

**Miriam CJM .Sturkenboom, FISPE**

**Douglas J.Watson, FISPE**

**Honorary Lifetime Fellow:**

**Ronald D. Mann, FISPE**

## STUDENT ACTIVITIES AT THE ICPE IN BRIGHTON

*Contributed by Irini-Alexia Terzakis,  
Student Council Chair 2009/10*

Most ISPE members probably know the hard, rewarding, at times confusing but also insight-providing experience that is being a postgraduate student in pharmacoepidemiology. As the co-chairs of the ISPE student council, it was our aim to make the annual meeting in Brighton an event where students get to know each other, exchange ideas, learn from each other and from senior ISPE members and have fun together. Like in previous years, we organised four unique student events for socialising, evaluating our past efforts and setting sail for new endeavours in the future.

The first student event at this year's annual meeting was the preconference student skills workshop. Three students had the rare opportunity to practice their presentations in front of the student audience and receive feedback from Derren Toh, Harvard Medical School, and Brian Strom, FISPE, University of Pennsylvania. The second half was filled with career talks from Sean Hennessy, FISPE, University of Pennsylvania, Robert Reynolds, Pfizer, Ken Rothman, FISPE, RTI, and Stella Blackburn, FISPE, EMA. Our aim was to create a session that was relevant to students, interactive and personal, and we received great feedback from this session from both the students and the senior members who kindly participated. Their help and advice was greatly appreciated. To welcome new members to the Student Council and to catch up with friends and acquaintances from the previous years, we had organised a meet and greet at Revolution Cocktail bar in Brighton. A slice of pizza and a Strawberry Woo Woo go a long way when you are surrounded by so

many interesting people!

The student council meeting was a great success with a turnout of about 30 members and a very dynamic and excited atmosphere. We discussed how we can better use the Internet to stay closely connected during the year and voted on legislation that will allow students outside North America and Europe to become student council co-chairs. We talked about the support and training we need and how we can make it accessible for ISPE students around the world in webinars and pre-conference courses. We also elected the new chair and co-chair for the year 2010/11 – Congratulations to Wendy Camelo Castillo from the University of North Carolina and Vera Valkhoff from the Erasmus Medical Centre, Rotterdam. We are very confident that they will do a fantastic job and enjoy the experience as much as we did.

The student highlight of every ICPE was, as always, the dinner and night out. We enjoyed a lovely meal at Al Duomo, with over 50 people attending. After three courses, most of us were ready for an early night to digest the Italian food and the proverbial brain food provided throughout the day in the conference sessions. But for about 15 of us, the night couldn't have ended without throwing some shapes at Oceana, Brighton's biggest night club. Overall, we have had fantastic feedback about the student activities and are looking forward to the opportunities, the learning, new friends and great experiences the new academic year will bring.

# AN EXCITING AND NOVEL PROGRAM FOR THE 5<sup>TH</sup> ASIAN CONFERENCE ON PHARMACOEPIDEMIOLOGY

*Contributed by Jessica Jalbert*

This year, the Asian Conference on Pharmacoepidemiology (ACPE), a joint meeting with the Japanese Society for Pharmacoepidemiology (JSPE), took place October 25-31, 2010 in Tokyo, Japan. In keeping with the theme of the 5<sup>th</sup> ACPE/16<sup>th</sup> JSPE meeting, "Activities and Co-Operation for Drug Safety in Asia," the program represented a fusion of the educational and scientific of both Asian and Western countries. This year, a novel approach to post-marketing drug strategy was revealed, including a discussion of its conceptual framework.

A unique feature of the ACPE5/JSPE16 was the opportunity to showcase the Asian Pharmacoepidemiology Network (AsPEN), first proposed by Dr. B.J. Park, of South Korea. The purpose of AsPEN is to connect researchers in a variety of countries within the Asia-Pacific region, allowing them to collaborate more easily to answer drug safety questions using national databases. The participating AsPEN countries (Australia, Japan, Korea, Taiwan, and the USA) shared their experiences investigating the relationship between antipsychotic use and diabetes onset during a special two-hour workshop on October 31<sup>st</sup>.

During the conference, emphasis was placed on topics of special interest to Asia. For instance, the program featured a symposium on databases within Asia where speakers from China, Taiwan, Japan and Korea presented on their available pharmacoepidemiologic resources. The oral presentations and posters at ACPE5/JSPE16 also increased exposure to and awareness of databases within Asia, as a sizeable portion of scientific abstracts selected for presentation were from studies conducted in Asian countries using national databases or in-country commercially available databases. Finally, the program included a symposium addressing regulatory issues specific to Asian countries.

Though the primary focus of the conference was drug safety in Asian countries, ACPE5/JSPE16 included important contributions from non-Asian countries as



well. A key aspect of the symposium on therapeutic risk management, and of the conference as a whole, was to foster intellectual exchange with Western countries and the educational sessions featured presentations from renowned pharmacoepidemiologists from around the world.

The student body of represented countries was also very proactive in devising novel and enjoyable ways for students to connect and learn about opportunities within pharmacoepidemiology. Students first met informally during the Welcome Reception. The reception was followed by a student-organized lunch on October 31<sup>st</sup>, in which representatives from academia, government and industry spoke to students about opportunities within pharmacoepidemiology in Asian countries as well as other current topics within the field.

The ACPE5/JSPE16 program showcased the range and wealth of pharmacoepidemiologic activities in Asia. The purpose of the conference was also to encourage further development of pharmacoepidemiology in Asia by facilitating collaboration with Western countries on established and novel pharmacoepidemiologic activities. The energy and novelty of the presentations and workshops at ACPE5/JSPE16 made Tokyo the perfect backdrop in terms of excitement and dynamism. All in all, ACPE5/JSPE16 delivered on its promise to be a distinctively stimulating conference!

**2009 BEST PAPER AWARDS**  
**J PHARMACOEPIDEMIOLOGY AND DRUG SAFETY**  
**(VOLUME 18)**

**Best Paper**

**Traditional versus marginal structural models to estimate the effectiveness of  $\beta$ -blocker use on mortality after myocardial infarction**

Joseph A. C. Delaney, Stella S. Daskalopoulou, Samy Suissa.  
PDS Volume 18, Issue 1, January 2009.

**Contact:**

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Department of Biostatistics  
Collaborative Health Studies Coordinating Center  
University of Washington  
Bldg. 29, Suite 310, 6200 NE 74th Street  
Seattle, WA 98115, USA

**Commended**

**Emergency department visits attributed to selected analgesics, United States, 2004-2005**

Mary Willy, Judith P. Kelly, Parivash Nourjah,  
David W. Kaufman, Daniel S. Budnitz, Judy Staffa

**Contact:**

Mary Willy  
[Mary.willy@fda.hhs.gov](mailto:Mary.willy@fda.hhs.gov)

10903 New Hampshire Ave., Room 2488,  
Silver Spring, MD 20993-0002, USA

**Commended**

**Hemorrhagic stroke associated with antidepressant use in patients with depression: does degree of serotonin reuptake inhibition matter?**

Yan Chen, Jeff J. Guo, Nick C. Patel

**Contact:**

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[Yance@email.uc.edu](mailto:Yance@email.uc.edu)

Division of Pharmacy Practice and Administrative  
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## STUDENT AWARDS

During the 26<sup>th</sup> International Conference of Pharmacoepidemiology (ICPE), the ISPE members were invited to the Annual Meeting of ISPE Members & Awards Ceremony. Corinne S. de Vries, FISPE, Chair of the 2010 Scientific Program Committee, presented the student awards. All student award recipients have demonstrated extraordinary contribution to pharmacoepidemiological research.



### *Edlavitch Award*

*(Best Student Abstract)*

Caitlyn T. Wilke

**Sensitivity of Hazard Estimates to Exposure Definition:  
A Simulation Study**



### *Second Best Abstract*

Sigrid Müller-Schotte

**Risk of Cataract in Patients with Multiple Sclerosis:  
A Population-Based Cohort Study**



### *Third Best Abstract*

Joshua Gagne

**Switching of Antiepileptic Drugs and Seizure-Related Events After Refill  
Adjustment**



### *Best Drug Utilization Abstract*

Krista Huybrechts

**Explained Variation in Antipsychotic Medication Prescribing in Patients  
Admitted to Nursing Homes**

## UPCOMING PROFESSIONAL CONFERENCES THAT MAY BE OF INTEREST TO ISPE MEMBERS

Society	Location	Dates	Abstract Open	Abstract Deadline
National Health Policy Conference	Washington, DC	Feb 7-8, 2011	Not applicable	Not applicable
ISPE Mid-Year	Florence, Italy	Apr 9-11, 2011	Not applicable	Not applicable
ISPOR ( <a href="http://ispor.org">ispor.org</a> )	Baltimore, MD	May 21-25, 2011	Open	Jan 13, 2011
Academy Health ( <a href="http://academyhealth.org">academyhealth.org</a> )	Seattle, WA	Jun 12-14, 2011	Open	Jan 13, 2011
DIA Meeting ( <a href="http://diahome.org">diahome.org</a> )	Chicago, IL	Jun 19-23, 2011	Open	Jan 31, 2011
Society for Epidemiologic Research ( <a href="http://epiresearch.org">epiresearch.org</a> )	Montreal, Canada	Jun 21-24, 2011	Open	Jan 5, 2011
SER Student Disseration Workshop	Montreal, Canada	Jun 21-24, 2011	Application due: Feb 10, 2011	
27 <sup>th</sup> ICPE	Chicago, IL	Aug 14-17, 2011	Open	Feb 16, 2011
ISPOR Latin America Conference	Mexico City, Mexico	Sep 8-10, 2011	Jan 17, 2011	Mar 17, 2011

Please submit additional conference information that you would like to be included in upcoming issues of Scribe to Brian Quilliam at [bquilliam@uri.edu](mailto:bquilliam@uri.edu).

## ISPE SPECIAL INTEREST GROUPS (SIG)

### **Biologics (est. August 2008)**

**Contact(s):**

Joanna Haas, MD, MSc

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Neal Grabowski

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**For more information on  
ISPE Special Interest  
Groups, please visit  
[pharmacoepi.org!](http://pharmacoepi.org)**

### **Comparative Effectiveness Research (est. April 2010)**

**Contact:**

Tobias Gerhard

[tgerhard@ifh.rutgers.edu](mailto:tgerhard@ifh.rutgers.edu)

### **Drug Utilization and Health Services Research (est. April 2006)**

**Contact:**

Morten Anderson

[Morten.anderson@ki.se](mailto:Morten.anderson@ki.se)

### **Database (est. August 2007)**

**Contact:**

Robert LoCasale

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### **Medical Devices (est. August 2010)**

**Contact(s):**

Danica Marinac-Dabic

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Art Sedrakyan

[Ars2013@med.cornell.edu](mailto:Ars2013@med.cornell.edu)

### **Molecular Epidemiology, Biomarkers and Pharmacogenetics (est. 2008)**

**Contact(s):**

Amalia Issa

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Kim Lowe

[klowe@exponent.com](mailto:klowe@exponent.com)

Geoff Liu

[Geoffrev.liu@uhn.on.ca](mailto:Geoffrev.liu@uhn.on.ca)

### **Medications in Pregnancy (est. August 2006)**

**Contact(s):**

Sonia Hernandez-Diaz

[shernan@hsph.harvard.edu](mailto:shernan@hsph.harvard.edu)

Elena Rivero

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## ***MEDICATIONS IN PREGNANCY SPECIAL INTEREST GROUP***

*Contributed by Susan Roberts*

Clinical trials typically exclude pregnant women and as a result, little is known about the safety of marketed, biopharmaceutical products in pregnancy and the risk to the mother and developing fetus. Approaches to assessing medication exposure during pregnancy include pregnancy exposure registries, case-control studies, cohort studies, and studies using administrative databases – all with methodological and operational challenges. However, interest and research activity in this area are high, and this was evident at the 26th Annual ICPE. Attendees had many opportunities to learn about this evolving area of pharmacoepidemiology: a Pre-Conference Educational Session, three sessions of Contributed Papers, a Symposium, a Workshop, and a Poster Walk. The Medications in Pregnancy Special Interest Group's annual meeting was well-attended with many updates from the field and networking opportunities. Expect to see more “growth and development” in the study of medications in pregnancy at the 27th Annual ICPE in Chicago!



**27th International Conference on  
Pharmacoepidemiology  
and Therapeutic Risk  
Management**



**AUGUST 14-17, 2011**  
**HYATT REGENCY CHICAGO**  
**CHICAGO, ILLINOIS**

*Abstract  
Deadline:  
FEBRUARY 16, 2011*

*The online abstract site will be  
operational by mid-December 2010.  
Meeting information will be posted  
at [www.pharmacoepi.org](http://www.pharmacoepi.org)*

Photo courtesy of Chicago Convention and Tourism Bureau

# ISPE 2011 Mid-Year Meeting

## Florence, ITALY

> APRIL 9-11, 2011

Jointly sponsored by



• **ISPE**  
International Society for Pharmacoepidemiology



• **EACPT**  
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• **ISoP**  
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• **SIF**  
Italian Society of Pharmacology



• **SIMG**  
Italian College of General Practitioners



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