Overview of Epidemiology & Drug Safety SIG

Jonathan Alsop

Numerus Ltd

EFSPI Statistics Leaders Meeting, 11 June 2014

Objective

- ⇨ Update on Epi SIG
- ⇨ Current plans
- ⇨ Seek your support/guidance

Outline

- ⇨ Who we are
- ⇨ What we do
- ⇨ How to contact us

Who we are

- ⇨ We are a small group of Statisticians/Real World Data (RWD) Scientists within Industry & Academia
- ⇨ We have diverse backgrounds & Professional interests
- ⇨ We share a common interest in good Science, Collaboration, Education, and Innovative problem-solving

Sub-committee members

George Quartey (Genentech-Chair, USA)

Maurille Feudjo-Tepie (Amgen, UK)

Volker Hoesel (StatSciConsult, UK)

Jonathan Alsop (Numerus, UK)

Nilani Liyanage (Ipsen Group, France)

Athula Herath (Medimmune, UK)

Joseph Kim (IMS Health, UK)

Jixian Wang (Novartis, Switzerland)

Arlene Gallagher (MHRA, UK)

Alex Thompson (Roche, UK)

Usher Gungabissoon (GSK, UK)

Have 100 affiliates on mailing list.

Mission

- ⇨ To promote the application of Epidemiology & Statistical Safety Methods in Drug Development.
- ⇨ To motivate and encourage PSI members to consider Epidemiology methods as part of their everyday toolkit.
- ⇨ To share information proactively between Epidemiology SIG Members
- ⇨ To contribute presentations, posters, articles and papers to PSI/EFSPI scientific meetings, Pharmaceutical Statistics journal and SPIN.
- ⇨ To provide a forum for discussion and the sharing of experiences: on the use Real World Data in pharmaceutical development.
- ⇨ To form an opinion on any new developments in the area of Statistical Epidemiology methods and to pass on any learning to the wider membership

Communication plan

- ⇨ Emails to mailing list of contacts
- ⇨ Articles in SPIN including write-ups of meetings
- ⇨ Presence at PSI/EFSPI Conference (parallel sessions)
- ⇨ Discussion meetings on specific topics
- ⇨ Use of the SIG area on the PSI website
- ⇨ Summary of activities to the AGM
- ⇨ Publications

Past/recent activities

2008

- SIG Formation: Inaugural Meeting

2009

- Parallel Section PSI Conference
- Comments to EMA on behalf of PSI on new EMA/CHMP draft guideline.
- One Day Workshop on Advanced Data Mining Techniques for Observational Databases

2010

- Paper on Bias Minimization Techniques
- ISCB Conference Presentation on Bias Minimization
- Article in SPIN-IT on Data Mining

2011-2013

- 6 papers on various topics Pharmaceutical statistics Journal
- Handbook on Real World Data for Statisticians (in progress)

2014

- Parallel Session at PSI Annual Conference
- PASS/PAES One day meeting

MAIN PAPER

Pharmaceutical Statistics

(wileyonlinelibrary.com) DOI: 10.1002/pst.528 Published online 30 November 2011 in Wiley Online Library

Opportunities for minimization of confounding in observational research

George Quartey,[a*] Maurille Feudjo-Tepie,[b] Jixian Wang,[c] and Joseph Kim[e]

Observational epidemiological studies are increasingly used in pharmaceutical research to evaluate the safety and effectiveness of medicines. Such studies can complement findings from randomized clinical trials by involving larger and more generalizable patient populations by accruing greater durations of follow-up and by representing what happens more typically in the clinical setting. However, the interpretation of exposure effects in observational studies is almost always complicated by non-random exposure allocation, which can result in confounding and potentially lead to misleading conclusions. Confounding occurs when an extraneous factor, related to both the exposure and the outcome of interest, partly or entirely explains the relationship observed between the study exposure and the outcome. Although randomization can eliminate confounding by distributing all such extraneous factors equally across the levels of a given exposure, methods for dealing with confounding in observational studies include a careful choice of study design and the possible use of advanced analytical methods. The aim of this paper is to introduce some of the approaches that can be used to help minimize the impact of confounding in observational research to the reader working in the pharmaceutical industry . Copyright © 2011 John Wiley & Sons, Ltd.

Keywords: case-crossover; case series; marginal structural model; instrumental variable; propensity score; selection model

MAIN PAPER

Pharmaceutical Statistics

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Why a Bayesian approach to safety analysis in pharmacovigilance is important

David Prieto-Merino,[a*] George Quartey,[b] Jixian Wang,[c] and Joseph Kim[a,d]

Large databases of routinely collected data are a valuable source of information for detecting potential associations between drugs and adverse events (AE). A pharmacovigilance system starts with a scan of these databases for potential signals of drug–AE associations that will subsequently be examined by experts to aid in regulatory decision-making. The signal generation process faces some key challenges: (1) an enormous volume of drug–AE combinations need to be tested (i.e. the problem of multiple testing); (2) the results are not in a format that allows the incorporation of accumulated experience and knowledge for future signal generation; and (3) the signal generation process ignores information captured from other processes in the pharmacovigilance system and does not allow feedback. Bayesian methods have been developed for signal generation in pharmacovigilance, although the full potential of these methods has not been realised. For instance, Bayesian hierarchical models will allow the incorporation of established medical and epidemiological knowledge into the priors for each drug–AE combination. Moreover, the outputs from this analysis can be incorporated into decision-making tools to help in signal validation and posterior actions to be taken by the regulators and companies. We discuss in this paper the apparent advantage of the Bayesian methods used in safety signal generation and the similarities and differences between the two widely used Bayesian methods. We will also propose the use of Bayesian hierarchical models to address the three key challenges and discuss the reasons why Bayesian methodology still have not been fully utilised in pharmacovigilance activities. Copyright © 2011 John Wiley & Sons, Ltd.

Keywords: Bayesian analysis; pharmacovigilance; disproportionality; pharmacoepidemiology; multiplicity

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A semi-parametric approach to analysis of event duration and prevalence

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ABSTRACT

Event duration and prevalence are important features for assessing outcomes of medical treatment. Although semi-parametric approaches have been well developed for analysis of recurrent events, applications to analysis of event duration, in particular the duration of multiple overlapping events, are relatively rare. Various approaches are considered using semi-parametric multiplicative models for cumulative duration and prevalence of events with time-varying coefficients, and a simple algorithm is proposed to fit the models. The relationships between parameters in the semi-parametric multiplicative models for prevalence and cumulative duration, particularly for models with time-varying treatment effects, are examined. The models can be extended to take overlapping intervals of multiple events with varying severity into account, and can be used in the presence of censoring due to informative dropouts and/or a terminal event. The approach can be implemented in standard software such as SAS. The approach was applied to a dataset of recurrent pulmonary exacerbations in patients with cystic fibrosis. Simulation was also conducted to examine the small-sample properties of the approaches.

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MAIN PAPER

Pharmaceutical Statistics

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A review of risk measures in pharmacoepidemiology with tips for statisticians in the pharmaceutical industry

George Quartey,[a*] Jixian Wang,[b] and Joseph Kim[c,d]

Pharmacoepidemiology is the study of the therapeutic effects, risk, and use of drugs in large populations, which applies epidemiological methods and reasoning. As reflected in the recent strengthening of the pharmacovigilance legislation in Europe, greater attention has been placed to epidemiological research in response to an increasing call by the public for further post-marketing studies on the safety and efficacy of drugs. Various measures of risk are used in pharmacoepidemiology to quantify the probability of experiencing an adverse outcome and capture the relative increases in risk between treated and untreated populations: cumulative incidence, incidence rate, absolute risk reduction, relative risk, odds ratio, incidence rate ratio, and time to event outcomes. We review in this paper the commonly used measures of risk in pharmacoepidemiology and provide some practical tips for the industry statistician. Copyright © 2011 John Wiley & Sons, Ltd.

Keywords: effect measures; risk measures; pharmacoepidemiology; relative measures; absolute measures; benefit–risk

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Nonparametric estimation for cumulative duration of adverse events

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Analysis of adverse events (AE) for drug safety assessment presents challenges to statisticians in observational studies as well as in clinical trials since AEs are typically recurrent with varying duration and severity. Routine analyses often concentrate on the number of patients who had at least one occurrence of a specific AE or a group of AEs, or the time to occurrence of the first event. We argue that other information in AE data particularly cumulative duration of events is also important, particularly for benefit-risk assessment. We propose a nonparametric method to estimate the mean cumulative duration (MCD) based on the nonparametric cumulative mean function estimate, together with a robust estimate for the variance of the estimate, as in Lawless and Nadeau (1995). This approach can be easily used to analyze multiple, overlapped and severity weighted AE durations. This method can also be used for estimating the difference between two MCDs. Estimation in the presence of censoring due to informative dropouts and/or a terminal event is also considered. The method can be implemented in standard softwares such as SAS. We illustrate the use of the method with a numerical example. Small sample properties of this approach are examined via simulation.

PAES/PASS One-Day Meeting

Post Authorization Safety and Effectiveness Studies:
Regulatory, Industry Perspective and Challenges.

21 October 2014 *Amgen, Middlesex, UK*

- Recent Changes in EU Legislations
- PASS & PAES Process: Reviewers perspective, organization, reactions to practical challenges such as market penetration issues, etc.
- How industry can organize themselves to face new demands
- Methodological challenges in conducting PASS/PAES effectively
- PAES/PASS data: Opportunities, challenges, and use of CPRD

How to Contact us

- PSI Epidemiology SIG webpage

  www.psiweb.org

- quarteyg@gene.com (Chair)

Areas of support

- What areas should Epi SIG focus upon?
  - ⇨ What would you (or your staff) find of value?

- How can we drive workshop attendance?
  - ⇨ What topics should we address?
  - ⇨ Financial support of speakers (e.g. travel costs)

Areas of support (cont.)

- How can we best link in with other groups, e.g. non-PSI Epi SIGs, ISPE, ISPOR, etc?
- How can we make better use of EFSPI/PSI websites?
- How can we ensure allocation of committee members' time to Epi SIG?

Thank-you for your attention