European Federation of Statisticians in the Pharmaceutical Industry
Representing Statistical Associations in Europe

EFSPI Newsletter May 2019

In this newsletter:

EFSPI Statistics Leaders Annual Meeting

The 10th annual EFSPI Statistics Leaders meeting is taking place on the 3rd and 4th July in Germany, hosted by Boehringer Ingelheim. Agenda items include reflecting on previous meetings and key lessons learned, assessing and improving critical leadership skills for statisticians in the pharmaceutical industry, applying 'Agile' methods, how to make statisticians bold and entrepreneurial, and a range of hot topics for debate such as data science.

The materials and minutes of the meeting will be available after the meeting on the EFSPI website.

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Regulatory

Adjusting for Covariates in Randomized Clinical Trials for Drugs and Biologics with Continuous Outcomes

The Regulatory Committee is collating comments on the draft FDA guidance: **Adjusting for Covariates in Randomized Clinical Trials for Drugs and Biologics with Continuous Outcomes.** *The guidance will, when finalized, represent the current thinking of the FDA on adjusting for covariates in randomized clinical trials in drug development programs, with a focus on recommendations for*

*adjusting for covariates when endpoints are continuous. Please contact **Kerry Gordon** (kerry.gordon@iqvia.com) and/or **Florian Voss** (florian.voss@boehringer-ingelheim.com) if you wish to comment **no later than 7 Jun 2019.***

Webinar: Adaptive design: updated draft FDA guidance and its implications
Date: 4th July 2019
Time: 14:00 - 15:30 UK time

In September 2018 the FDA published a guidance on adaptive design for clinical trials of drugs and biologics, updating (not finalizing) its initial draft from February 2010. The main focus of the webinar will be to provide an overview of its main contents, which will be presented by Jürgen Hummel (PPD). In addition, Kaspar Rufibach (Roche) will introduce an open-source statistical software for adaptive designs, RPACT (an R package available on CRAN that enables the design and analysis of confirmatory adaptive clinical trials). Kit Roes will also comment on the guidance from a European Regulatory perspective, which will be followed by a brief panel discussion. Click here for more information and to register.

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Scientific

Upcoming event: ***"Precision medicine in drug development"***

On **Tuesday June 4**, the joint meeting with the BBS will take place at Actelion in Allschwill (near Basel). The purpose is to bring together experts from the pharmaceutical industry, academia and the European regulatory bodies to present the current state of the art and discuss the challenges and opportunities ahead. The full agenda is available and more information can be found on the flyer (https://www.efspi.org/Documents/Events/Events%202019/PMJUNE19/BBS_EFSPI_Prec_Med_201_Flyer_2%20(002)Final.pdf) and the registration is open (https://www.efspi.org/Core/Events/eventdetails.aspx?iKey=PMJUNE19)

In addition, the Scientific Committee is planning a 1-day meeting on the topic "**Reproducibility in Clinical Research**". The meeting, to be held in November at BMS (Belgium) intends to bring together speakers form industry, academia and regulatory agencies, who will address questions relating to the topic, and the role statistics (and statisticians) have in ensuring clinical research is conducted and reported in a reproducible manner. The exact date, draft agenda and list of speakers will be distributed shortly; below is a list of proposed topics.

- The regulatory requirement for two independent pivotal studies in marketing applications is intended to ensure reproducibility of results. How good is this criterion, and in what circumstances can we deviate from it? What would be the 'optimal' type-1 error rate?
- What alternative statistical methods are there to hypothesis tests, and how much better are these methods in ensuring reproducibility? Are Bayesian methods the answer?
- What statistical methods are there to ensure reproducibility when extrapolating results from a (planned or unplanned) sub-group analysis?
- How can we ensure reproducibility of phase II results when going into phase III?
- How can real world evidence increase the reproducibility of clinical studies?

- How can we increase 'translational reproducibility', that is, the chance of predicting the outcome of a trial in humans based on animal data? What more can statisticians contribute to the validation of biomarkers?
- What requirements should journal editors make to ensure reproducibility of published data analyses?
- In general, what can statisticians contribute to resolving the reproducibility crisis?

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Country News

BBS (Switzerland)

BBS Spring Seminar: Synthetic controls – what do we need and how far can we go? A very successful 1-day seminar took place on the 10th May 2019 with approximately 250 participants attending. Thanks to Roche for hosting the meeting. Sessions included: an overview of the use of synthetic controls, case study examples, views from regulatory, HTA and academia, and a panel discussion. Click here to access the slides.

PSI (UK)

2019 PSI CONFERENCE: 2 - 5 June, London
Data Driven Decision Making in Medical Research
The scientific programme is available to view online. To view all the latest information on the Conference, please visit the PSI website.

To close this year's PSI conference, we will be holding a joint "Regulatory & HTA Town Hall "plenary session, which will take place on the Wednesday afternoon at the 2019 PSI Conference in London. The session will be led by an experienced panel of experts, including panellists from different regulatory, health technology/payer agencies and a pharmaceutical company. The session will discuss regulatory and HTA hot topics and issues as well as offering the opportunity to compare and contrast the needs of health authorities and payers.

The session will be chaired by Anja Schiel (Chair of EMA biostatistics working party) and the panellists will be:

- Ralf Bender (IQWiG)
- Rose Lovett (NICE)
- Kit Roes (UMC Utrecht)
- James Matcham (Astrazeneca)

To submit a question please click here. Questions can be submitted anonymously.

FEATURED VIDEO: PSI One Day Meeting: New Emerging Topics Around Estimands and the ICH Addendum

The draft ICH E9 addendum on estimands and sensitivity analysis was released back in July 2017 and (more than 1000) comments were received. All stakeholders are gaining the necessary experience and familiarity with estimands along with the associated challenges and methodologies. The language and thinking behind causal inference are well suited to this area. The PSI Scientific Committee put together this one-day meeting to share and discuss new emerging topics around estimands and the ICH addendum.

EFFECTIVE STATISTICIAN

2 new episodes every biostatistician should know about!

50 shades of pre-specification

Prespecified=good and post-hoc=bad. This is how we as statistician see it usually and I did too. However, over the past years I realized more and more, that it's not that easy. How many details do you need to have to call an analysis pre-specified? Should we label a request to analyse a certain subgroup by regulators as well as a fishing expedition to find a significant subgroup both in the same way: post-hoc? In this episode, we dive into this topic and identify different dimension to be considered to understand better the different shades pre-specified analyses. Listen to this episode to avoid oversimplification and confusion in discussions in the future.

Subgroup identification using SIDES and it's practical challenges

Subgroup identification using SIDES and it's practical challenges. One of the most common questions I got asked during my nearly 2 decades of being a statistician sounds similar to this: "Which patients have the best response to treatment?". I'm sure, we all face this situation sooner or later and not surprisingly lots of research has happened in the last years on this area. In today's episode, we will help you to understand one of the best approaches I have come across to solve this problem in a rigorous yet sophisticated way: the SIDES approach. Both Andy Nicholls and I have applied this approach in the past and we'll use an example, which he presented during a PSI webinar. Listen to this episode to learn step by step how to apply the SIDES method.

You can listen to the podcast on the homepage but also on your "podcast" app on your iPhone. If you own an android, you may use an app like Stitcher. Just search for "the effective statistician" in your app. Finally, you can also find it on Spotify.

Enjoy listening! Thanks **Alexander Schacht** for your tremendous leadership on the Effective Statistician series.

Toxicology Special Interest Group Free Webinars

The PSI Special Interest Group "Toxicology" have a series of regular FREE webinars dealing with statistical topics faced in toxicology and related fields. The presentations will run for an hour, with approximately 45 min presentation and a Q&A session in the remaining time.

The webinars planned for 2019 are:

- Tuesday 18th June 2019 – Pig-a Assay
- Tuesday 17th September 2019 – TBC

- Tuesday 10th December 2019 - TBC

All take place at 14:00 UK time. Full details will be released closer to each webinar, or contact Gareth Thomas (gareth.thomas@envigo.com) to be kept up to date on all ToxSIG activities.

Adaptive Designs

24 June 2019, Bath University
Presenters: Chris Jennison & Jonathan Bartlett (University of Bath), Munya Dimairo (University of Sheffield), Beatrice Panico (MHRA), TBC

Adaptive designs are clinical trials that allow for prospectively planned modifications to one or more aspects of the design based on accumulating data from subjects in the trial and can provide a number of advantages over non-adaptive designs. During this meeting we will hear about adaptive sample allocation for phase II/III designs, a new CONSORT extension reporting guideline for adaptive designs, regulatory aspects and case studies. Click here to register.

Introduction to Bayesian Statistics

25th - 26th June 2019, UCB Pharma, Slough, UK
Presenters: Ros Walley, Foteini Strimenopoulou & Phyllis Smetana

The course will focus on the practical implementation of the background and practicalities of Bayesian design, analysis and reporting and will not go into deep statistical methodology or software coding. Examples and practical exercises are used throughout to aid understanding and interaction. References will be to give the attendee links to the statistical formulae and other reading. Click here to register.

Applications open for the 2019/2020 Introduction to Industry Training (ITIT) Course

Next course starts October 2019: The 2019/2020 course will include 3 sessions in continental Europe and 3 sessions in the UK. The course will aim to describe the drug development process, including sessions on drug discovery, toxicology, data management & role of the CRO, clinical trials, health technology assessment and marketing. For further information and to download the application form, please click here. Deadline to enrol is 30th June 2019.

PSI One day Scientific meeting: The analysis and reporting of PROs in Clinical Trials

17th July 2019, Roche, Welwyn Garden City

Patient reported outcomes have become increasingly important in the development, approval and reimbursement of our products. The PSI Scientific Committee have put together this one day meeting to provide statisticians with introductions to PROs, how to include them in clinical trials, considerations about missing data, appropriate statistical methods to analyse and interpret the data and the perspective of an IQWiG assessor. Presenters will give their insight into discussions with colleagues, working groups and

regulators and there will be plenty of opportunity to ask any questions you may have about PROs in your development program. Click here to register.

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Other events

Seminar: Best Practices for Applying Design of Experiments with Quality by Design

On June 13th, Marcello Fidaleo, Associate Professor of Innovation in Biological, Agro-Food and Forest Systems at the University of Tuscia and Teaching Fellow at North Carolina State University, and Massimo Martucci, Senior Systems Engineer for JMP, will co-present the seminar *Best Practices for Applying Design of Experiments with Quality by Design*. This event will be presented in English. You can attend for free:

- In Milan, by registering on http://bit.ly/QbDMilan
- Online, by registering on http://bit.ly/QbDstream

Group Sequential and Adaptive Clinical Trial Designs

The German Region of the International Biometric Society (IBS) is holding a summer school on Group sequential and adaptive clinical trial designs, 17-19 October 2019 in PfalzAkademie, Lambrecht, Germany. This summer school provides an introduction to group sequential and adaptive designs, and also covers advanced topics. The theory will be illustrated with case studies from the pharmaceutical industry. Each module of this course includes a computer practical. We will use the R software package rpact (R Package for Adaptive Clinical Trials, https://www.rpact.com/), a validated, comprehensive and freely available package for the design, simulation and analysis of group sequential and adaptive trials. More information can be found on the EFSPI website. Please register through this link.

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Job Opportunities

There is an opportunity for a Senior Biostatistician. For information on how to submit recruitment adverts, please visit the EFSPI website: Job postings. If you are currently seeking to hire a statistician and wish to post a job advert, EFSPI are offering one free advert for every 3 adverts posted on the website.

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The World of Statistics

The World of Statistics is comprised of 2, 360 organisations across the globe. Participating organizations in The World of Statistics include national and international professional statistical societies, colleges and universities, primary and secondary schools, businesses, government statistical agencies, and research institutes. You can view the current participant and country lists involved in the World of Statistics by going to The World of Statistics website http://www.worldofstatistics.org/.

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Chrissie Fletcher
EFSPI Communications Officer