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

EFSPI Newsletter September 2018

In this newsletter:

EFSPI Council

In August 2018 EFSPI became a legal entity where it is registered in Denmark. A huge thanks to Mette Krog Josiassen and Julie Mellish for achieving this important milestone. The key advantage of being a legal entity is for EFSPI will be officially recognised as a non-for-profit association which will allow EFSPI to formally participate in multi-stakeholder initiatives.

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Regulatory

A series of **training modules** on the **draft ICH E9(R1)** have been released on the ICH website, click here. Statisticians are highly encouraged to share these materials with cross-functional colleagues involved in the design of clinical trials and to use the materials to increase the awareness of the new estimand framework introduced in the draft E9 addendum.

A number of disease-specific estimand working groups are beginning to emerge. An example includes the estimand working group in oncology led by Evgeny Degtyarev (Novartis) and Kaspar Rufibach (Roche). Approximately 28 members from 20 companies are discussing how time to event endpoints can be embedded in the addendum framework. A full list of these working groups with contact details is being collated and will be shared in subsequent newsletters.

The **3rd EFSPI Regulatory Statistics Workshop** took place on the **24/25th September 2018 in Basel, Switzerland.** A record of more than 270 people registered for this 3rd annual workshop. The agenda included sessions on estimands with a variety of case studies shared, complex data types and designs in confirmatory trials, basket/umbrella trials, use of clinical practice data to support confirmatory trials, and phase I dose escalation trials. The workshop finished with a number of contributed short topics allowing feedback from regulators and the audience. Slides from the workshop will be loaded on the EFSPI website in the next few weeks.

The **FDA** have released **draft guidance on Master Protocols- Efficient Clinical Trial Design Strategies to Expedite Development of Cancer Drugs and Biologics and ", "Adaptive Design for Clinical Trials of Drugs and Biologics".** Further information will follow by the regulatory committee on submitting comments within EFSPI.

The EMA have announced that due to preparations for BREXIT, no MAAs will be published in 2019 under POL-0070 and publication of clinical data for medicinal products. The EMA Technical Anonymisation Group (TAG) continue to develop additional supportive materials providing further information relating to approaches available for anonymising documents.

Reminder: The EMA issued a **draft Questions and answers on Data Monitoring Committees issues** (http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2018/08/WC500252790.pdf). Please contact Christoph Gerlinger (christoph.gerlinger@bayer.com) or Anna Berglind (anna.berglind@astrazeneca.com) if you wish to comment.

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Scientific

Decision making in Clinical Development, December 12

On Wednesday December 12 the scientific meeting on '*Decision making in Clinical Development*' will take place at Servier in Paris. *Taking decisions during the development of a new drug requires combining many and varying pieces of information. Decision-makers need quantitative tools to support informed decisions, with transparent processes that synthesize the whole available information in order to evaluate the success associated to different options.* More information can be found on the flyer, which is available on our website, and the registration is open.

For the first time, we will have a poster session. If you wish to present a poster, please send an abstract to Gaëlle Saint-Hilary (gsainthilary@gmail.com) by October 31st 2018. The notification of acceptance will be provided by November 9th 2018.

2019 Meetings

The Scientific Committee is planning for three 1-day scientific meetings for 2018. The first one day meeting will be on "Recent developments in biomarkers and subgroups in drug development", which will take place in March hosted by AstraZeneca in Göteborg, Sweden. Exact date and more information on the program will follow. In addition, we are starting with planning two additional 1-day events, one before summer, one after. More information will follow.

The fourth EFSPI regulatory statistics workshop will also take place in Basel in fall 2019.

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Special Interest Group (SIG) News

Health Technology Assessment (HTA)

The EFSPI/PSI HTA Special Interest Group recently had a virtual round table discussion with Anja Schiel, Senior Advisor / Statistician at the Norwegian Medicines Agency on the 12th September to share recent experiences of HTA in Norway. Anja, who also is the current chair of the European Biostatistics Working Party shared her perspectives of statistics in HTA where she felt the primary purpose is estimating the uncertainty in the evidence available for HTA decision making. She talked positively of the new estimand framework in the draft E9 addendum which is anticipated to have a positive impact especially if health economists are also involved in defining estimands important for HTA.

On the 18th September 2018 PSI hosted a 1-day meeting on the use of RWE to support comparative analyses in particular for HTA and reimbursement. Methods for indirect comparisons with and without adjustment for patient characteristics and methods for generalising clinical trial data into real life settings were presented. Cross-design approaches combining observational and clinical trial data were described using case studies from the IMI GetReal initiative. In recent years artificial intelligence and machine learning methods are being investigated and applied to real world evidence. A big challenge is understanding how data is being modelled with some analysts ignoring missing data resulting in biased results. A series of break-out sessions were held further discussing aspects raised in the presentations.

Data Transparency

On the 19th and 20th September a data transparency conference was held in London hosted by DIA.

There were sessions on sharing clinical study reports, sharing and using deidentified individual participant data, Global data privacy regulation (GDPR) and transparency requirements, clinical trial disclosure in the EU and USA, the EU Clinical Trials Regulation and Medical Device Regulation, summary protocol and results information in ClinicalTrials.gov and EUDRACT, clinical trial results summaries for patients and the public, public accountability around disclosure and the future of data transparency.

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Country News

APF (Germany)

Registration for the annual fall meeting 23. November 2018 in Berlin on Visualization is now open (http://www.biometrische-gesellschaft.de/fileadmin/AG_Daten/PharamzeutischeForschung/PDFs/Agenda_APF_72_Berlin_Nov_2018__Agenda__Anfahrt__Anmeldung_.pdf).

IBIG (Italy)

An Italian Biostatistics Group (IBIG) Forum will be organized in Padova on 22-23 November including the following topics: Bayesian Statistics in Clinical Trials, Micro-Randomized Trials and Expedited Approval Programs. The forum will take place at the NH Hotel in Padova, Italy. For more details click here.

PSI (UK)

FEATURED VIDEO: PSI Conference 2018: Introduction to machine learning for longitudinal medical data

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In the era of big data, there has been a surge in collected biomedical data, which has provided ample challenges for distributed computing but also posed novel inference questions. Classical machine learning techniques, such as logistic regression, neural networks, support vector machine and Gaussian processes performed very well in non-temporal prediction tasks but typically relied on the independence assumption.

However, many recent applications have longitudinal context in the form of short- and long-term dependencies. Hidden Markov Models proved popular to model longitudinal data but increasingly become less computationally feasible for a large number of hidden states. Recently, advances in parallel computing led to widespread use of deep learning approaches, such as recurrent neural networks and convolutional networks, and attracted attention due to their impressive results on sequence data. Finally, we will look in more detail at a case study from healthcare analytics which infers disease type from multiple irregularly sampled longitudinal observations,
such as blood pressure, heart rate and blood oxygen saturation

Two new exciting episodes of The Effective Statistician podcast, created in association with PSI

In these two episodes, we cover very different topics. You will learn about practical problem solving with multiplicity problems from one of the world-class experts: Alex Dmitrienko. Having worked within a big pharma company, a large CRO and running his own consulting business, you will benefit from both his technical but also practical experience. Please find the episode below:

- **Understand and master multiplicity in practical situations - Interview with Alex Dmitrienko**

Benjamin and Alexander talk about something that many statisticians struggle with - explaining achievements to others. We all have been in situations where awesome achievements weren't appropriately recognised. Listen to the latest episode on how to avoid this frustrating situation for you:

- **How to sell your achievements - actionable advise**

Search for The Effective Statistician in your podcast app and subscribe now!

PSI One Day Meeting - Interactive Workshop about Real World Evidence (RWE): Generalisability of Treatment Comparisons for Decision Making

RWE is an increasingly valuable resource in drug development. One area where this data is being used regularly is in the generalisability of treatment comparisons. This 1-day workshop held on the 18th September hosted by Lilly in Germany focused on:

- New advances in indirect comparisons
- Generalisability approaches for clinical trial data into the real world setting
- Cross-design approaches combining observational and randomized data

A number of case studies from the IMI GetReal project were shared and breakout sessions were held allowing different stakeholders to share their views on the latest thinking and recent advances in methodology being used to support comparative effectiveness assessments. Slides from the meeting will be available to members on the PSI website.

PSI Webinar: Avoiding Pitfalls in Supervised/ Unsupervised Learning Thursday 29th November 2018, 14:00 - 15:30 UK Time

Presenters: Ilya Lipkovich (IQVIA), Alexander Schacht (Lilly) and Andy Nicholls (GSK)

As the availability of big data increases and statisticians assist with predicting outcomes or understanding patterns in an ever-wider variety of scenarios then supervised and unsupervised learning methods become increasing called upon. Such machine learning algorithms offer the opportunity to understand potential predictors or clusters amongst large datasets, but are also subject to the risks of overfitting or over-interpretation. This Webinar seeks to introduce ideas and share experiences in this field.

The talks will introduce several supervised and unsupervised learning methods and cover data-driven subgroup identification in clinical trials, and case studies of implementation clustering algorithms.

Click here for further information and to register.

New Emerging Topics around Estimands and ICH Addendum Tuesday 29th January 2019, IQVIA, Reading, UK

The draft ICH E9 addendum on estimands and sensitivity analysis was released for public consultation at the end of August 2017 and more than 1200 comments were submitted. 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 is well

suited to this area. This one day meeting aims to share and discuss new emerging topics around estimands and the ICH addendum, including:

- Sharing the feedback from the public consultation on the draft ICH E9 addendum
- Exploring the estimand concept within health technology assessments
- Describing how casual inference fits into the area of estimands
- Presenting case studies illustrating the implementation of the estimand framework and the use of causal inference methodology

Click here for further information and to register.

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Job Opportunities

Opportunities exist for **Biostatistician Project Leaders – Early Phases, and Medical Affairs**.

For all current recruitment adverts and more 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, 199 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.

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And finally.....

To add your e-mail address to the EFSPI mailing list, click on "Sign up to our newsletter" on the homepage of the EFSPI website.

To view previous newsletters please see the EFSPI website in the "News" area.

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Chrissie Fletcher
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