European Federation of Statisticians in the Pharmaceutical Industry

Representing Statistical Associations in Europe

EFSPI Newsletter June 2022

In this newsletter

Welcome

A warm welcome to the June newsletter from EFSPI!

What a month!

I'm almost tempted to call it "the Swedish month"! Why?

Because the isolation over the last several months has left many of us almost crying for in-person re-connection. This month we finally made it and many of us met in person at the PSI 2022 conference in Gothenburg/Sweden. Enjoy the 'hot of the press impressions' from this great event, read about our ESIG of the month (Real World Data ESIG) and get familiar with our Swedish Society for Medical Statistics (FMS) which is our EFSPI local association of the month!

Enjoy the reading and please help us to spread the word! Follow our official EFSPI LinkedIn page, engage with us by reacting to our posts, commenting or sharing the information with your networks.

Let me also know if you have anything you would like to contribute to our newsletters that may be of interest to our EFSPI community. This monthly newsletter is to provide you a summary of what is happening and to give a heads up about those topics that might become relevant for us in near future.

Stay healthy, stay safe wherever you are!

Justine Rochon, EFSPI President and Editor of EFSPI Newsletters

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EFSPI Council news

EFSPI Statistics Leaders Meeting

The countdown is on: Only a few more days until our 13th EFSPI Statistics Leaders meeting taking place on the 6th and 7th July in Basel, Switzerland hosted by Novartis and Roche. Thirty-six leaders are currently planning to attend the meeting this year, with the majority attending in person. The meeting will include: An interactive team building session, a keynote speaker on what the future might look like and what opportunities that lie ahead, two breakout sessions (on how EFSPI can advance its networking and collaborations with other groups, including two guests to share their experiences, and how to develop NextGen Statisticians, including three guests who will share their career journeys), a panel session on how statisticians can maximise their input and meet the demands of modern development, including three invited speakers and their perspectives of working with statisticians, and finally a walking tour and break times to socialise with each other.

A summary of the meeting and all the meeting materials will be made available to everyone after the meeting via the EFSPI Statistics Leaders Meetings website.

Chrissie Fletcher, Lead for the EFSPI Statistics Leaders Meetings on behalf of the organising committee: Emmanuel Zuber (Novartis), Hans Ulrich Burger (Roche), Tina Christiansen (Novo Nordisk), Justine Rochon (Boehringer Ingelheim) and Chrissie Fletcher (GSK)

7th EFSPI Regulatory Statistics Workshop

7th EFSPI Regulatory Statistics Workshop
14th – 15th September 2022
Face-to-face meeting in Basel, Switzerland

Dates and times (CET):
Tuesday, 14th September 2022, 9-17 (+ 2h wine tasting)
Wednesday, 15th September 2022, 9-18

Please block your calendars and check out the announcement on the EFSPI website here.

FENStatS Accreditation

The Federation of European Statistical Societies (FENStatS) launched a standard for professional accreditation of statisticians. The accreditation is voluntary and is intended as a measure to enhance the quality and importance of statistics in a world in need of facts and high-level statistical literacy. The accreditation requires 1) At least an MSc in statistics or equivalent, 2) At least five years of work experience, 3) Professional development during this time, 4) Communication skills, 5) Compliance with ethical standards, 6) Member of a FENStatS member organisation. Please visit the following website for more details: https://www.fenstats.eu/accreditation.

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ESIG of the month

The Real World Data (RWD) Special Interest Group is our ESIG of the month!

Created in March 2021, the RWD ESIG aims to increase collaboration and enhance awareness of strategies and methodologies applied in the utilisation of Real World Data (RWD) in the pharmaceutical industry.

The objectives include facilitating the sharing of case studies and experiences in this area and identifying emerging news and trends. The ESIG will collate and review publications, articles, presentations, training; organise/participate in workshops related to RWD; discuss and comment on guidelines; and aim to develop or highlight best practices.

ESIG Activity Highlights

In March we held a PSI RWD SIG Webinar: Real-World Evidence Submission - a Case Study in Lung Transplantation. The FDA Real-World Evidence (RWE) Framework was published in December 2018, shedding some light on how Real-World Data (RWD) can be used to support regulatory decision making. In July 2021, tacrolimus was approved for Lung transplantation based solely on RWE. The sponsor, FDA biostatistical reviewer and RWD vendor shared their respective experiences with statisticians in the pharmaceutical community – if you missed it, see the video-on-demand.

On June 14th, we held a well-attended session at the PSI 2022 conference:

- We started with a broad "Introduction to RWD Types and Use Cases". In the early phase emphasis is towards characterising the current treatment, disease burden and unmet need. In the phase 2/3 setting, RWD can help inform our study designs as well as complement clinical data for safety and efficacy purposes. RWD can also support regulatory decision making and facilitate benefit-risk assessments and support post-marketing requirements. Further, it helps with HTA decision making and informing prescribers and patients and even facilitate regulatory label changes. Presented by Elizabeth Merrall (Janssen) and Alexander Schacht (Veramed), this was a lively "ping-pong" presentation interweaving these opportunities across the drug lifecycle with specific examples from a variety of geographies and data sources.
- We then focused in on an important methodological topic, "Leveraging Real-World Data for Time-to-Event Endpoints"
    - Deepak Parashar (Warwick University) walked us through the ambiguity in defining therapy initiation or baseline when comparing clinical trial data with RWD. He reviewed current methods to address this challenge and made recommendations to mitigate the uncertainty. This built on work that the ESIG presented as a poster at EU ISPOR 2021: ISPOR - Leveraging Real-World Data for Time-to-Event Endpoints in Clinical Trials.
    - Barbara Torlinska (University of Birmingham) further illustrated the topic through a current CPRD-HES linked study she is conducting and highlighted the practical issues needing consideration when emulating a target trial, such as treatment switching, event availability, and timing discrepancies between the employed data sources.
- We rounded off with a panel Q&A including plenty of audience interaction

Coming soon…

- We conducted a paper-based survey during the PSI conference – thanks to those who completed it! – analysis is in progress and we will share the results soon.
- We will be launching the "Let's Talk Re@l" corner. Watch out for discussions on RWD topics and event highlights!

In summary

RWD is a fast-moving area these days, with evolving utilisation for multiple purposes and by multiple stakeholders. Our ESIG brings together statisticians working across the lifecycle of drug development and commercialisation, from industry and academia, with an interest in use of RWD.

New members are welcome! If you're interested in finding out more, please contact Josie Wolfram and Anny Stari for further information.

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Other ESIG news

Health Technology Assessment (HTA) ESIG keeping busy with EU-HTA

In 2021, the regulation on EU-HTA was passed. Among other things, the regulation mandates a joint EU-level assessment of all new medicines in parallel with the EMA regulatory review, based on a dossier submitted by the manufacturer. The idea of having a joint assessment covering the needs of all 27 EU member states and tied to EMA timelines, is a completely new paradigm that will have major implications for how companies set up and align HTA and regulatory and statistical work. And, with implementation to start gradually in 2025, it's only a few years away!

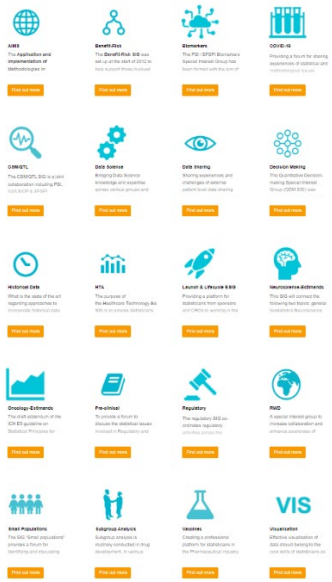
This means that the Health Technology Assessment (HTA) ESIG has been having a busy 2022 so far, reviewing and commenting on the methodological guidelines that are being released for public consultation. Our focus is to ensure that the unique scientific and operational expertise of pharmaceutical statisticians is brought to the table in a timely manner. We are constantly on the lookout for more people willing to help us with this endeavour. To find out how you can become involved, have a look at our webpage or contact Emma Crawford.

If you are in Basel/Switzerland on 14–15th of September for the EFSPI Workshop on Regulatory Statistics 2022, make sure to stop by the poster session on the 14th where the HTA ESIG will be ready to get you up to speed on what to expect from EU-HTA and discuss how we best make our voices heard as a professional association.

Regulatory ESIG & Draft ICH E11 Guidance

The ICH published draft guidance on Pediatric Extrapolation (ICH E11A), and it is now out on public consultation. The Regulatory ESIG is collating comments for that, so please send your comments to Rima Izem and Florian Voss following this template format **by 8th July, 2022.**

General



Our European Special Interest Groups (ESIGs), sponsored by EFSPI and PSI, are playing a key role and foster connections across disciplines, industry, academia and countries/regions.

The PSI 2022 Conference offered a great possibility to hear more from the ESIGs and to finally meet in person. Besides the already mentioned RWD and HTA ESIGs, we had active contributions from the AIMS ESIG, the Data Science ESIG, the Data Sharing ESIG, the Launch & Lifecycle ESIG, and the Biomarkers ESIG.

Do you want to contribute to our ESIGs? For the names and contact details of our ESIG leads, please see our ESIG Lead Contact Page.

Do you want to become our ESIG of the month? Then please contact Emmanuel Pham (EFSPI SIG liaison) or Adam Crisp (PSI Board SIG liaison lead) to be featured in one of our next newsletters.

Picture: Leads of the Biomarkers ESIG Nicole Krämer and Guillaume Desachy together with Adam Crisp, PSI Board SIG liaison lead, at the PSI 2022 Conference in Gothenburg/Sweden.

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Local Association of the month

The Swedish Society for Medical Statistics (Föreningen för Medicinsk Statistik, FMS) was formed in 1987 and is one of four subsections in the Swedish Statistical Society (Svenska Statistikfrämjandet).

FMS organises statisticians within the medical area, i.e. in the pharmaceutical industry as well as in other medical research, public or private, and in biostatistical research and education.

The main objective of FMS is to stimulate the development and promote the use of new and established statistical methods within the medical sector as well as within the areas of pharmaceutical industry and public health.

Every year the FMS arranges a combined spring meeting/annual meeting and an autumn meeting. Every other year, FMS co-organises meetings with the Danish association (DSBS). FMS has also organised meetings and workshops together with the Finnish association (SSL). In addition to organising meetings, FMS distributes information on scientific meetings, courses, EFSPI etc. FMS also promotes discussions on applications or statistical issues through articles in Qvintensen, a quarterly magazine published by the Swedish Statistical Society. The association awards scholarships and a prize for the best student essay is announced each year. FMS currently has over 300 individual members. Companies and institutions that want to support FMS can become partners. The FMS board consists of statisticians from both the Swedish universities and the industry.

More information can be found here.

On June 15th, the Swedish Society for Medical Statistics (FMS) hosted one of the sessions at the PSI conference in Gothenburg/Sweden. The main theme was observational studies.

The first speaker was **Ingeborg Waernbaum**, Professor at Department of Statistics at Uppsala University. Topic: Selection bias and multiple inclusion criteria in observational studies.

Spurious associations between an exposure and outcome not describing the causal estimand of interest can be the result of selection of the study population. Recently, sensitivity parameters and bounds have been proposed for selection bias, along the lines of sensitivity analysis previously proposed for bias due to unmeasured confounding. As a motivating example, bounds were derived for causal estimands in a study of perinatal risk factors for childhood onset type 1 diabetes mellitus where selection of the study population was made by multiple inclusion criteria. It is usually challenging to give plausible input values for the sensitivity parameters for selection bias under multiple selection and to provide further guidance for practitioners. The researchers Stina Zetterström and Ingeborg Waernbaum at the Department of Statistics at Uppsala University have developed a data learner in R (MultiSelBounds) where both the sensitivity parameters and the assumption free bounds are implemented. https://github.com/stizet/Selection-bias-bound

Next speaker was **Robert Szulkin** PhD, SDS Life Science. Topic: Travel vaccines strongly reduce mortality in cancer patients – a real effect or residual confounding?

Swedish studies by Ji et al, using real-world data have shown that administration of an oral cholera vaccine reduces mortality with approximately 50% among patients with prostate cancer (Nature communications 2018), colorectal cancer (Gastroenterology 2018) and breast cancer (Oncology 2020). Can oral vaccine prevent several forms of cancer to progress so effectively? Or are these findings a result of unmeasured confounding? This is always a concern in non-randomised studies.

To further investigate the effectiveness of cholera vaccine in prostate cancer patients, a population-based cohort of men from Stockholm was used, with more detailed cancer data, regarding diagnosis and treatments (including information about other vaccines) than in the studies by Ji et al. Thus, some of the residual confounding could be eliminated. Furthermore, a marginal structural Cox model with time-varying adjustment for confounding was used, to estimate the average treatment effect (ATE). Finally, several sensitivity analyses were performed, using other types of vaccines (Hepatitis A, hepatitis B, typhoid fever vaccine, rabies, Japanese encephalitis vaccine, yellow fever).

The results showed a reduced mortality risk for all the investigated travel medications, not only cholera vaccine. However, it was assessed to be unlikely that all travel vaccines prevent cancer from progressing. Since patients in better health were more likely to travel and take a vaccine than patients with poor health, it was concluded that there is a strong confounding effect that was not possible to adjust for in register studies. Hence, the previously found protective effect of cholera vaccines was probably due to residual confounding, not due to a true vaccine effect.

https://www.sciencedirect.com/science/article/pii/S0264410X22006119

Anna Stoltenberg PhLic, Swedish Orphan Biovitrum was the last speaker. Topic: Statistical approaches and considerations when using an external control arm for a rare disease project

In clinical research, randomised clinical trials (RCT) are considered the golden standard for evaluating the efficacy and safety of new treatments. However, there are situations where a RCT is not an option e.g.: when standard of care or other satisfactory treatments are not available or approved, when it is unethical to give placebo or no-treatment, for rare diseases with few patients available leading, for serious conditions with a high unmet medical need. In a rare disease patient population, with high mortality and no approved treatment, a Phase 2 single-arm trial (SAT) has been performed with promising efficacy data. To help assess the magnitude of the effect and support regulatory approval, an understanding of the historical response rate has been requested. No information has been found in literature regarding the expected outcome and therefore, an external control arm (ECA), using data collected from a similar patient population external to the study by retrospectively reviewing medical charts, was planned to be generated. Known confounding factors influencing the disease outcome needs to be well characterized and adjusted for in the statistical analysis to be able to reduce any bias in the comparison between the arms. Simulation of outcomes using different assumptions and designs were used to help optimise the approach and understand the probability of success. The approaches used were reviewed and the important considerations were highlighted.

Anna Torrång and José Sanchez on behalf of the FMS

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Other Country news

SFdS (France)

The 9th Statistics and Biopharmacy (SnB) Conference organised by the Statistics and Biopharmacy group of the SFdS (French Society of Statistics) will be held in Paris September 19th–21st, 2022. It is a unique event, usually organised every four years, integrating multiple perspectives on innovative applied statistical research for the drug development and an excellent opportunity to meet colleagues from academia, regulatory agencies, and pharmaceutical companies. More information on the SnB 2022 program can be found here.

APF (Germany)

The German region (APF) is planning their yearly meeting ("Herbstworkshop") on Friday, November 25th in Berlin (hosted by Cytel). Suggestions for topics and volunteers for presentations are highly welcomed and can be send to Frank Langer. One day before, on November 24th, there will be a senior face-to-face meeting for our Academia-meets-Industry initiative (Organisers in 2022 are: Jan Beyersmann (Ulm University), Cornelia Kunz (Boehringer Ingelheim), Kathrin Stucke-Straub (THU Ulm)). This meeting is an opportunity to network in particular across academia and industry regarding statistical-methodological topics and partnerships.

PSI (UK)

MEETINGS, WEBINARS AND COURSES:

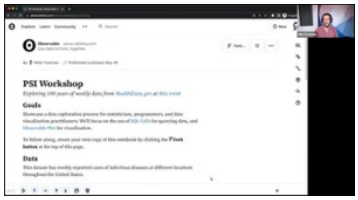
4th July 2022: PSI Training Course: Hybrid Frequentist / Bayesian Power and Bayesian Power in Planning Clinical Trials (TRNG278)

June 13–15th 2022, 427 delegates attended the PSI conference in Gothenburg/Sweden. The conference gave us the first F2F opportunity to come together since 2019. Across 36 sessions and with presentations from almost 100 statisticians there was wide ranging discussion of the application of statistics, new developments and other hot topics impacting on the work of statisticians and other quantitative scientists. A number of themes could be seen across the sessions with a lot of focus on estimands, HTA requirements (specifically EunetHTA21), use of different data types beyond the standard RCT (e.g. external, RWD, synthetic), master protocols and the expanded use of R within industry. Recorded sessions from the conference on these and other topics will be available to PSI members on the PSI Video on Demand platform soon.

The next PSI conference will take place in London June 12–14th, 2023. Make a note in your diaries now!

ON-DEMAND WEBINARS AND PODCASTS:

PSI VisSIG Webinar: Collaborative & Exploratory Data Analysis



Want to quickly explore your data in the browser? Looking to create, collaborate and share interactive visualizations with others? In this session, you will learn how to load data from a SQL database, view and interact with data in JavaScript, create visualizations using a variety of tools including Observable Plot/D3, configure & customize your visualizations through Inputs and much more! → *Watch here!*

PSI VisSIG Wonderful Wednesday 27: Impact of Responder Definition

Lorenz Uhlmann is showing the results of the monthly challenge. It is all about a responder analysis on HiSCR where response is defined by three components. How to display the impact of changes in the definition on the result. All visualisations are available on the Wonderful Wednesday blog. → *Watch here!*

The Effective Statistician Podcast

→ *Listen here!*

Biomarkers – essentials to get you started

In this interview with Guillaume Desachy and Nicole Krämer, we discuss what biomarkers are and why it is essential.

Chats with Jenn: Embracing Vulnerability and Leading With Courage

This is a fun chat with Jenn Fenwick where we talk about navigating fear, opening ourselves up to vulnerability and making courageous decisions…oh and Beyonce gets a mention too!

Extrapolation to paediatrics

An interview with Andrew Thomson. Paediatric research always comes with challenges and understanding paediatric submission is very important. There's always a lack of treatment in this area. In this episode, you'll understand what you can do to get evidence through extrapolation for the children population.

Listen to these episodes and share them with your friends and colleagues who might learn from it.

Ciao and be an effective statistician!

Alexander Schacht

NON-PSI EVENTS:

43rd annual conference of the International Society of Clinical Biostatistics

Date: 21st–25th August, 2022
Location: Newcastle upon Tyne, UK

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Job opportunities

Nowadays, job opportunities for statisticians and data scientists are excellent!

For information on how to submit recruitment adverts, please visit the Job postings on our EFSPI website. 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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And finally…

To add your email address to the EFSPI mailing list, click on "Sign up to our newsletter" on our landing page. To view all newsletters please see the "News" area on the EFSPI website.

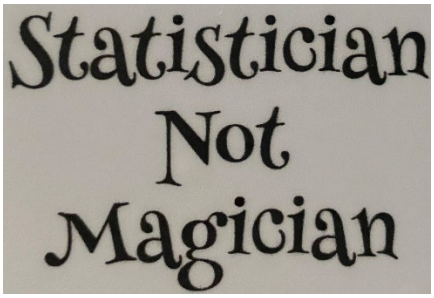
We value your feedback, so let us know what you think! What should we keep, start or even stop doing when creating the EFSPI newsletters?

We would also like to learn from you how we can further improve our EFSPI communication and branding.

Send your feedback to Justine Rochon and Randi Grøn.

In addition, you are cordially invited to join our (closed) EFSPI group by requesting access to the EFSPI LinkedIn Group in order to exchange even more within our EFSPI community.

And finally, I want to wish you a great summer break with the following sticker I discovered when visiting the Royal Statistical Society (RSS) stand at the PSI 2022 Conference 😊:



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